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Highly enantioselective synthesis of chiral imides and derived products via chiral base desymmetrisation

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Abstract—The enantioselective deprotonation of several ring-fused imides with a chiral base, followed by electrophilic quenching, gives a range of chiral products in good yield and in ≥91% ee. The absolute stereochemistry of two of the products was determined by X-ray crystallography. A number of the imide products were subjected to further, highly regioselective, transformations, including enolate substitution, reduction and thionation. © 2002 Published by Elsevier Science Ltd.

1. Introduction

The asymmetric desymmetrisation of various types of prochiral substrate using chiral lithium amide bases is now becoming an accepted method for the synthesis of certain chiral products.[1] Of particular importance in this regard are the enolisation reactions of cyclic ketones,[2] and the rearrangement of epoxides to allylic alcohols,[3] both of which have been carried out with various ring sizes and substitution patterns in the substrate.

Other types of desymmetrisation are less well known, and we have expended a substantial effort in establishing chiral base reactions of a range of alternative types of substrate, e.g. Fig. 1.

These include sulfoxides,[4] phosphine oxides,[5] chromium arene complexes,[6] piperidine diesters[7] and, most recently, some bridged ketones that undergo enantioselective bridgehead substitution.[8]

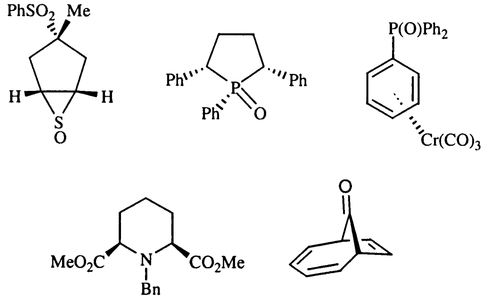


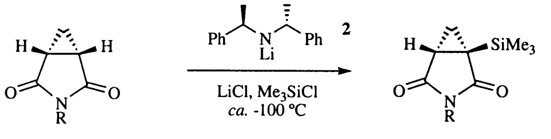
Figure 1.

In an effort to further extend this type of asymmetric deprotonation approach to include more complex substrates, especially those possessing multiple carbonyl functions, we recently described reactions involving a number of imide systems.[9] This chemistry enables highly enantioselective access to a range of imides and derived products such as lactams and lactones, and is described in full below.

2. Results and discussion

2.1. Chiral base reactions of ring fused imides

Preliminary studies focussed on the possible desymmetrisation of cyclopropyl imide systems of general structure **1**. Initial studies were not promising, attempted enolisation reactions using several lithium amide bases, followed by quenching with electrophiles, such as MeI, resulting only in destruction of the starting material. We reasoned that metallation was probably taking place but that the intermediate anion was undergoing undesired side reactions before addition of the electrophile. We therefore turned to the use of in situ quenching conditions, involving addition of a solution of chiral lithium amide base **2** to a mixture of imide **1** and Me_3SiCl at low temperature, Scheme 1.



1a-c

3a R = Ph 80%, 91-95% ee
3b R = Bn 67%, 91% ee
3c R = OBn 66%, 89% ee

Scheme 1.

Keywords: asymmetric synthesis; chiral lithium amide; imides.

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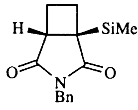
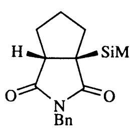
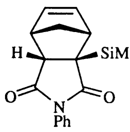
This method gave excellent results, the desired mono-silylated imides **3a–c** being isolated in good yield and with very good levels of enantioselectivity. In some cases small quantities of doubly silylated by-products were also observed. The synthesis of **3a** was repeated a number of times, on various scales, and reproducibly gave ee values in the range indicated. We found that this reaction could be applied to other simple imide systems, giving silylated products **4–6** with excellent selectivity (the chemical yields have not been optimised).[10]



4 37%, 93%ee



5 72%, 91%ee



6 76%, 98%ee

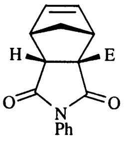
In each case clean *C*-silylation was observed with no sign of the corresponding silylketene hemiaminals and very little, if any, recovered starting material that might have come from their hydrolysis.[11] The chiral *C*-silylated compounds proved to be stable and crystalline and, in the cases of **3a** and **6**, we were able to secure X-ray crystal structures following recrystallisation, Figs. 2 and 3.

The structure determinations allowed us to assign the absolute configurations as shown. These two structures indicate an analogous mode of asymmetric desymmetrisation of the starting imides, and we expect that the other products have undergone the silylation in the same stereochemical sense, although that has not been rigorously proven.

The asymmetric substitution of imides such as **1** was interesting as a possible entry to cyclopropane natural products, and at this point we carried out similar reactions with two related systems **7** and **9**, Scheme 2.

Both the *cis*-diester **7** and the 1,3-diketone **9** gave good to excellent levels of enantioselection under the standard chiral base conditions. In the latter case, HPLC assay of the enantiomeric purity of **10** proved difficult and so we first converted the silylated product into triketone **11**. These reactions were conducted as an aside to the main programme of work, and to date we have no proof of the absolute stereochemistry shown (drawn as analogous to the imide results).

As indicated above, it proved impossible to carry out enolate substitutions of the cyclopropylimide systems **1**, except using an in situ quench. The reactivity of the chiral enolate from the norbornene system proved more controlled, and we were able to carry out direct asymmetric substitution with reactive electrophiles like MeI, allyl bromide and PhSSPh to give products **12–14**.



12 E = Me 36%
13 E = allyl 33%
14 E = SPh 50% (97% ee)

The poor yields in these cases are presumably due to the rather hindered nature of the system, the bulky enolate being rather reluctant to form a quaternary centre.[12] Pleasingly, the reaction with PhSSPh was shown to occur with very high enantioselectivity, indicating that we should, in principle, be able to avoid recourse to the in situ quench procedure without loss of chiral base selectivity.

2.2. Manipulation of chiral ring fused imides

Since efficient direct substitution of the cyclic imides appeared limited to silylation, we were keen to expand the scope of this chemistry by exploring the synthetic repertoire of the silylimide products. It was also important to discover if the initial silylation would enable regiocontrolled imide functional group conversions.

We first examined further enolate chemistry using enantiomerically enriched **3a** and determined that substitution at the remaining activated position was possible, Table 1.

In all of these reactions the presence of LiCl seems to enhance the yields, although we are uncertain of the

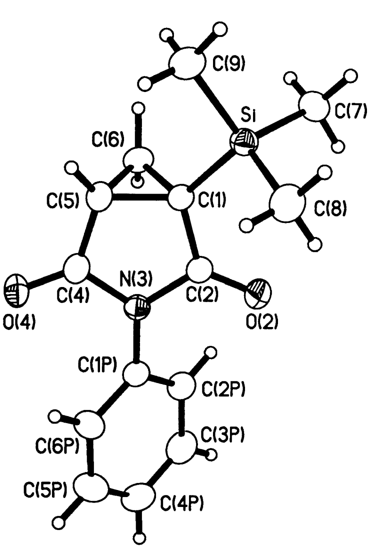


Figure 2. Structure of compound **3a**.

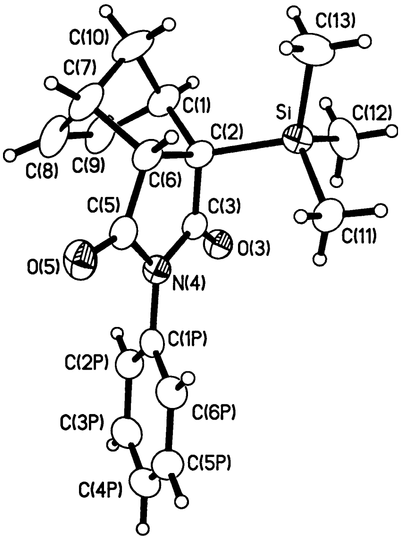
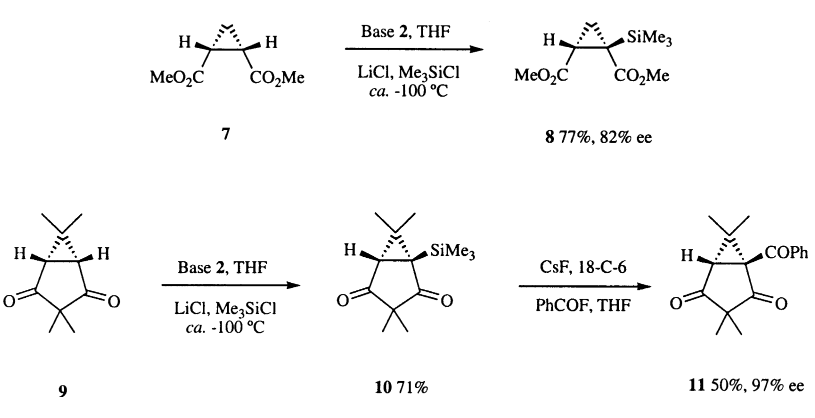


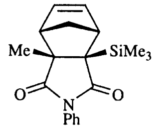
Figure 3. Structure of compound **6**. The H atom bonded to C(9) is wholly obscured by it.



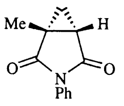
Scheme 2.

mechanism of this effect.[13] It was interesting to note the effectiveness of the enolate substitution chemistry using the silylimide **3a**, compared to the difficulties experienced with the parent compound **1**. Presumably the silicon substituent has a protective effect that enables substitution to compete with destructive side reactions involving self-condensation. Although stereochemical scrambling by some mode of silyl transfer (inter- or intramolecular) appeared unlikely, we checked the ee of compound **15** formed this way, and found the value to be the same as that of the starting imide **3a**. The same is assumed to hold for the other products.

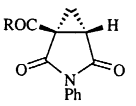
In a similar fashion, we carried out a single alkylation of silylimide **6** (using a racemic sample), using MeI, to give the methylated product **22** in moderate yield (48%). The reluctance of this system to alkylate in high yield dissuaded us from further exploration.



22 (48%)



23(54%)



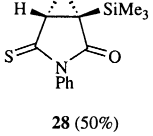
(+)-**24** R = Ph (90%)
25 R = $CH_2CH(CH_3)_2$ (79%)

We considered that the substitution reactions listed in Table 1 could give access to products that represent asymmetric *C*-alkylation of parent imide **1**, provided that the silyl group could be removed. This proved reasonably straightforward, using either CsF or TBAF in THF, and in the cases of **15**, **20** and **21** gave the chiral imides **23–25** in the yields indicated.

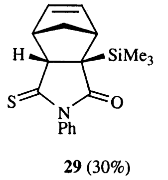
An alternative strategy for accessing such compounds was to effect fluoride-mediated substitution of the silicon group of the chiral silylimides.[14] This idea was briefly explored, and gave access to (−)-**24**, **26** and **27**, starting from **3a**, and sulfide **14**, starting with **6**, Scheme 3.

In order to check that this type of substitution occurred without erosion of enantiomeric purity we required to analyse these compounds by HPLC. Unfortunately, analysis of ketone **24** was thwarted by the extreme insolubility of this compound in solvents suitable for HPLC separation, and the formation of **26** as inseparable diastereomers also made analysis difficult. Fortunately we were able to assay both of the sulfur compounds **27** and **14**, and in both cases the ee was shown to be within 5% of the value for the corresponding silyl compounds (**3a** of 95% ee gave **27** of 91% ee; **6** of 98% ee gave **14** of 93% ee), indicating minimal loss of enantiomeric purity.

We were also interested to see if the silicon substituent present in imides such as **3a** and **6** could exert a useful level of control on the reactions of the imide carbonyl functions. Polonski and co-workers have demonstrated that imide thionation of systems related to **3a** using Lawesson's reagent is highly selective for the C=O group at the least substituted position.[15] We subjected **3a** and **6** to typical thionation conditions and observed the formation of single regioisomeric products, assigned the structures **28** and **29**, albeit in poor yield.

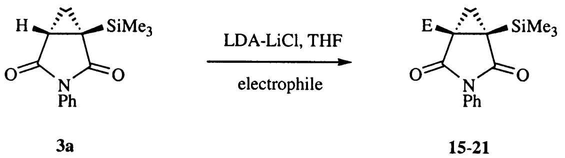


28 (50%)



29 (30%)

Table 1. Substitution of silylimide **3a**

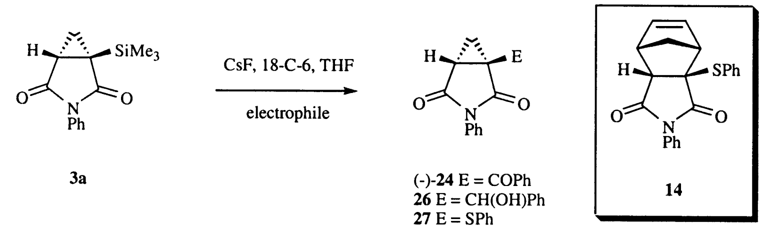


3a

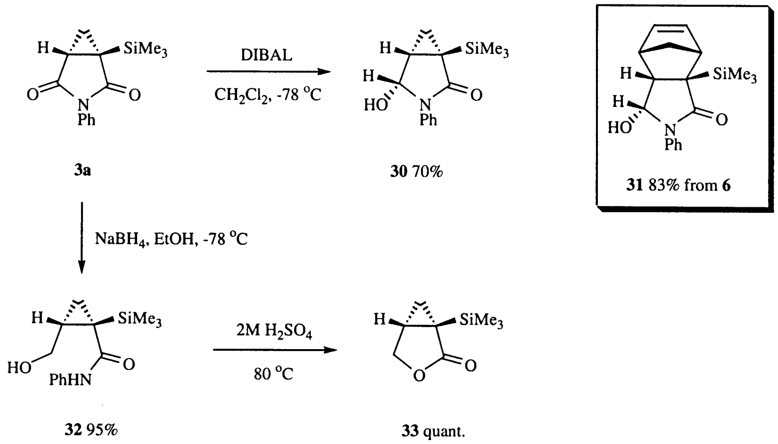
15-21

Electrophile	MeI	AllylBr	BnBr	PhSSPh	PhCHO	PhCOCl	$(CH_3)_2CHCH_2COCl$
Compound (%)	**15** (93)	**16** (73)	**17** (67)	**18** (71)	**19** (61)[a]	**20** (57)	**21** (47)

[a] Formed as a mixture of diastereomers.



Scheme 3.



Scheme 4.

By analogy with the literature precedent we believe that these compounds arise by highly selective reaction of the C=O group distal to the bulky silicon substituent. The assignment is supported by the observation of substantial downfield shifts (ca. 0.5 ppm) in the ^{1}H NMR spectrum for the signal due to the methine adjacent to the newly installed C=S group, compared to the starting imide.

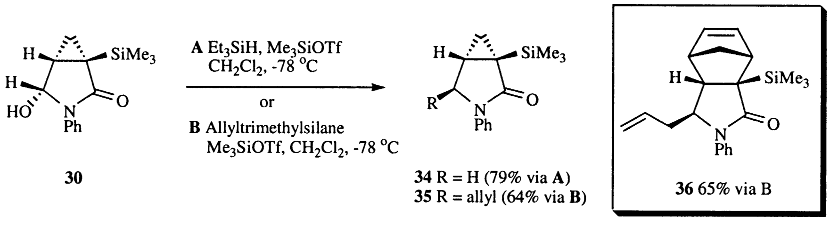
Speckamp and Hiemstra had observed an analogous mode of regioselective reduction on reaction of certain imides with DIBAL.[16] We used these conditions with silylated imides **3a** and **6** and observed high-yielding conversion into the hydroxylactams **30** and **31**, Scheme 4.

In each case we were unable to detect the other possible regioisomeric product. The reduction was also highly stereocontrolled, giving solely **31**, although we did observe a small amount (ca. 4%) of the epimeric hydroxyl product in the case of **30**. Additional experiments showed that the use of $NaBH_4$ resulted in ring opening to give **32**, which could then be transformed by acid treatment into the silyllactone **33**.[17]

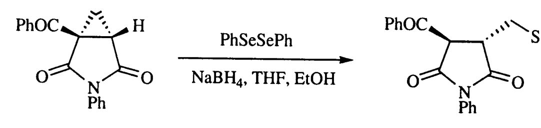
The successful enantioselective synthesis of hydroxylactams, shown in Scheme 4 also suggested an opportunity for reduction or further substitution via *N*-acyliminium chemistry.[18] We found that this type of reaction could be performed by activation of **30** using Me_3SiOTf. Reduction using triethylsilane, and allylation using allyltrimethylsilane, could be effected in high yield to give **34** and **35**, respectively, Scheme 5.

We also carried out the allylation starting with **31**, and obtained the desired product **36**. Both of the allylated products **35** and **36** were obtained as single diastereomers, with the stereochemistry shown being readily assigned from examination of coupling constants in the ^{1}H NMR spectra.

Finally, we were interested in testing the possibility of cyclopropane ring-opening reactions of various fused imides, which might be effected using nucleophilic reagents. The activation to such a process that would be provided by an additional carbonyl substituent prompted us to examine reactions of the ketone system **24**. We found that excellent results were obtained using the reagent



Scheme 5.



(+)-**24**

37 (68%)

Scheme 6.

generated from diphenyldiselenide and sodium borohydride, Scheme 6.[19]

The ring opened product **37** was obtained as a single compound, assigned the *trans* stereochemistry shown. Preliminary experiments to probe a number of alternative methods for cyclopropane ring opening in such systems, for example using cuprate reagents, have proved less fruitful to date.

3. Conclusion

The desymmetrisation of imides, described above, constitutes another addition to the growing list of reactions that can be efficiently carried out using chiral lithium amide bases. The chiral imides formed are rather versatile, and can be converted into diverse types of chiral product, including lactams and lactones. We are actively pursuing additional work in this area, along with applications to target synthesis, and further results will be reported in due course.

4. Experimental

4.1. General details

General experimental details can be found in the accompanying paper. Starting imides **1** were prepared by condensation of the commercially available cyclopropylanhydride with the appropriate amine, according to the method of Beckwith and Boate.[20] The diester **7** was prepared using the method of McCoy,[21] and the diketone **9** by the route described by Krief.[22]

4.2. Typical procedure for chiral base reactions using Me_3SiCl in situ quench

4.2.1. (1*R*,5*S*)-3-Phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0] hexane-2,4-dione 3a. Chiral lithium amide base **2** was prepared from the corresponding chiral amine HCl salt (1.68 g, 6.41 mmol) in THF (20 mL) at −78°C under an atmosphere of nitrogen, by addition of ^{n}BuLi (8.01 mL of a 1.6 M solution in hexanes, 12.8 mmol), followed by warming to room temperature for 15 min. The resulting solution of the chiral base **2** was cooled to −100°C before being added dropwise over 1 h to a stirred solution of the imide **1a** (1.00 g, 5.34 mmol) and chlorotrimethylsilane (6.78 mL, 53.4 mmol) in THF (120 mL) maintaining a temperature of −107±2°C. The solution was then allowed to warm slowly over 4 h to room temperature before quenching with saturated aqueous $NaHCO_3$ (30 mL). Most of the THF was evaporated in vacuo and then the solution extracted with Et_2O (5×100 mL), dried ($MgSO_4$), filtered and the solvent evaporated under reduced pressure to give a crude product. Purification by flash column chromatography on silica gel (10% EtOAc–light petroleum) gave the imide **3a** as a white solid (1.10 g, 80%), mp 104–105°C; $[\alpha]_D^{28}=-88$ (*c* 1.00 in $CHCl_3$); (Found: C, 64.65; H, 6.60; N, 5.24. Requires C, 64.83; H, 6.61; N, 5.40%); ν_{max} ($CHCl_3$)/cm^{-1} 2958, 1768, 1707, 1599, and 1500; δ_H (250 MHz, $CDCl_3$) 0.21 [9H, s, Si(CH_3)$_3$], 1.52 (1H, dd, *J*=7.5, 4.3 Hz, C*H*H), 1.66 (1H, dd, *J*=4.3, 3.3 Hz, CH*H*), 2.43 (1H, dd, *J*=7.5, 3.3 Hz, C*H*) and 7.20–7.47 (5H, m, Ar*H*); δ_C (68 MHz, $CDCl_3$) −2.9 (Si*C*H_3), 20.2 (*C*), 24.0 (*C*H_2), 24.2 (*C*H), 126.3 (Ar*C*H), 128.1 (Ar*C*H), 128.9 (Ar*C*H), 131.8 (Ar*C*), 175.0 (*C*O) and 176.6 (*C*O); *m/z* (EI) 259 (M$^+$, 70%), 244 (100), 216 (4), 150 (10) and 73 (37) (HRMS: found M$^+$, 259.1033. $C_{14}H_{17}NO_2Si$ requires M, 259.1028). The ee was determined as 95% by HPLC (OD column, 1% IPA in hexane), the retention times were 22.8 min (minor) and 25.0 min (major).

4.2.2. (1*R*,5*S*)-3-Benzyl-1-trimethylsilyl-3-azabicyclo[3.1.0] hexane-2,4-dione 3b. This was prepared using the above procedure, starting with **1b** (500 mg, 2.48 mmol). The crude product was purified by flash column chromatography on silica gel (5% EtOAc–light petroleum) to yield imide **3b** as a white solid (455 mg, 67%), mp 59–62°C; $[\alpha]_D^{23}=-62$ (*c* 1.22 in $CHCl_3$); (Found: C, 65.57; H, 7.02; N, 5.26. Requires C, 65.90; H, 7.00; N, 5.12%); ν_{max} ($CHCl_3$)/cm^{-1} 2928, 2855, 1762, 1698 and 1602; δ_H (400 MHz, $CDCl_3$) 0.14 [9H, s, Si(CH_3)$_3$], 1.31–1.35 (2H, m, C*H*H and CH*H*), 2.25 (1H, dd, *J*=7.2, 3.7 Hz, C*H*), 4.45 (1H, d, *J*=14.5 Hz, PhC*H*H), 4.50 (1H, *J*=14.5 Hz, PhCH*H*), 7.21–7.30 (5H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) −3.0 (Si*C*H_3), 19.8 (*C*), 23.8 (*C*H), 24.0 (*C*H_2), 41.5 (*C*H_2), 127.5 (Ar*C*H), 128.1 (Ar*C*H), 128.5 (Ar*C*H), 136.2 (Ar*C*), 175.4 (*C*O) and 177.3 (*C*O); *m/z* (EI) 273 (M$^+$, 74%), 259 (5), 258 (27), 245 (10), 232 (4), 91 (100) and 73 (38) (HRMS: found M$^+$, 273.1195. $C_{15}H_{19}NO_2Si$ requires M, 273.1185). The ee was determined as 91% by HPLC (OD column, 5% IPA in hexane), the retention times were 8.7 min (major) and 9.4 min (minor).

4.2.3. (1*R*,5*S*)-3-Benzyloxy-1-trimethylsilyl-3-azabicyclo [3.1.0]hexane-2,4-dione 3c. This was prepared using the above procedure starting with imide **1c** (540 mg, 2.49 mmol). The crude product was purified by flash column chromatography on silica gel (10% EtOAc–light petroleum) to yield imide **3c** as a white solid (472 mg, 66%), mp 46–48°C; $[\alpha]_D^{23}=-85$ (*c* 1.00 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2958, 2888, 1772, 1716, 1603 and 1497; δ_H (400 MHz, $CDCl_3$) 0.08 [9H, s, Si(CH_3)$_3$], 1.22 (1H, dd, *J*=4.5, 3.5 Hz, C*H*H), 1.29 (1H, dd, *J*=7.4, 4.5 Hz, CH*H*), 2.05 (1H, dd, *J*=7.4, 3.5 Hz, C*H*), 5.02 (2H, s, PhC*H*H + PhCH*H*), 7.33–7.43 (5H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) −3.1 (Si*C*H_3), 16.7 (*C*), 20.1 (*C*H), 24.5 (*C*H_2), 78.2 (*C*H_2), 128.4 (Ar*C*H), 129.3 (Ar*C*H), 130.0 (Ar*C*H), 133.4 (Ar*C*), 170.6 (*C*O) and 172.4 (*C*O); *m/z* (EI) 274 [(M−CH_3)$^+$, 2%], 184 (3), 168 (7), 140 (2), 91 (100), 77 (10) and 73 (8) [HRMS: found (M−CH_3)$^+$, 274.0912. $C_{15}H_{19}NO_3Si-CH_3$ requires (M−*C*H_3), 274.0899]. The ee was determined as 89% by HPLC (OD column, 1% IPA in hexane), the retention times were 29.2 min (major) and 37.7 min (minor).

4.2.4. (1*R*,5*S*)-3-Benzyl-1-trimethylsilyl-3-azabicyclo[3.2.0]heptane-2,4-dione 4. This was prepared using the above procedure starting with *N*-benzyl-3-azabicyclo[3.2.0]heptane-2,4-dione (50 mg, 0.23 mmol). The crude product was purified by flash column chromatography on silica gel (5% EtOAc–light petroleum) to yield imide **4** as a white solid (25 mg, 37%), mp 63–64°C; $[\alpha]_D^{28}=-65$ (c 0.92 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2959, 1756, 1689 and 1600; δ_H (400 MHz, $CDCl_3$) 0.07 [9H, s, Si(CH_3)$_3$], 2.15–2.25 (2H, m, CH_2CSi), 2.42–2.57 (2H, m, CH_2), 3.07 (1H, dd, J=10.1, 3.7 Hz, C*H*), 4.67 (1H, d, J=14.1 Hz, PhC*H*H), 4.71 (1H, J=14.1 Hz, PhCH*H*) and 7.23–7.36 (5H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) −4.6 (SiCH_3), 22.8 (CH_2), 25.5 (CH_2), 39.7 (*C*), 40.8 (*C*H), 42.5 (CH_2), 127.7 (Ar*C*H), 128.3 (Ar*C*H), 128.6 (Ar*C*H), 136.3 (Ar*C*), 180.0 (*C*O) and 182.4 (*C*O); m/z (EI) 287 (M^+, 56%), 272 (10), 160 (5), 91 (100) and 73 (42) (HRMS: found M^+, 287.1337. $C_{16}H_{21}NO_2Si$ requires M, 287.1342). The ee was determined as 93% by HPLC (OJ column, 1% IPA in hexane), the retention times were 16.0 min (major) and 34.9 min (minor).

4.2.5. (1*R*,5*S*)-3-Benzyl-1-trimethylsilyl-3-azabicyclo[3.3.0]octane-2,4-dione 5. This was prepared using the above procedure starting with *N*-benzyl-3-azabicyclo[3.3.0]octane-2,4-dione (0.15 g, 0.65 mmol). The crude product was purified by flash column chromatography (5% EtOAc–light petroleum) to yield imide **5** as a white solid (0.14 g, 72%), mp 71–73°C; $[\alpha]_D^{28}=-60$ (c 1.11 in $CHCl_3$); (Found: C, 67.33; H, 7.85; N, 4.63. Requires C, 67.73; H, 7.69; N, 4.65%); ν_{max} ($CHCl_3$)/cm^{-1} 2956, 2870, 1758, 1687, 1602 and 1449; δ_H (400 MHz, $CDCl_3$) 0.01 [9H, s, Si(CH_3)$_3$], 1.22 (1H, m, C*H*H), 1.58–1.80 (3H, m, CH_2+CH*H*), 2.14 (1H, m, C*H*H), 2.25 (1H, m, CH*H*), 2.91 (1H, m, C*H*), 4.60 (2H, m, PhC*H*H+PhCH*H*), 7.22–7.36 (5H, m, Ar*H*); δ_C (68 MHz, $CDCl_3$) −4.2 (SiCH_3), 25.7 (CH_2), 31.3 (CH_2), 33.1 (CH_2), 42.4 (CH_2), 46.7 (*C*), 48.2 (*C*H), 127.6 (Ar*C*H), 128.4 (Ar*C*H), 128.5 (Ar*C*H), 136.3 (Ar*C*), 180.1 (*C*O) and 182.6 (*C*O); m/z (EI) 301 (M^+, 74%), 273 (28), 91 (88) and 73 (46) (HRMS: found M^+, 301.1489. $C_{17}H_{23}NO_2Si$ requires M, 301.1498). The ee was determined as 91% by HPLC (OD column, 0.25% IPA in hexane), the retention times were 14.4 min (minor) and 16.3 min (major).

4.2.6. (1*R*,2*R*,6*S*,7*S*)-4-Phenyl-2-trimethylsilyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione 6. This was prepared using the above procedure starting with *N*-phenyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione (1.00 g, 4.18 mmol). The crude product was purified by flash column chromatography on silica gel (10% EtOAc–light petroleum) to yield imide **6** as a pale yellow solid (0.99 g, 76%), mp 132–133°C; $[\alpha]_D^{24}=-58$ (c 1.11 in $CHCl_3$); (Found: C, 69.13; H, 6.53; N, 4.39. Requires C, 69.42; H, 6.80; N, 4.50%); ν_{max} ($CHCl_3$)/cm^{-1} 2987, 2956, 2880, 1761, 1694, 1600 and 1500; δ_H (400 MHz, $CDCl_3$) 0.27 [9H, s, Si(CH_3)$_3$], 1.62 (2H, s, CH_2), 3.25 (1H, d, J=4.4 Hz, COC*H*), 3.39 (1H, m, C*H*CSi), 3.51 (1H, m, COCHC*H*), 6.20 (1H, dd, J=5.6, 2.9 Hz, CH═C*H*), 6.41 (1H, dd, J=5.6, 2.9 Hz, C*H*═CH) and 7.10–7.44 (5H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) −2.4 (SiCH_3), 46.4 (*C*H), 47.1 (*C*H), 47.3 (*C*), 49.0 (*C*H), 50.8 (CH_2), 126.6 (Ar*C*H), 128.3 (Ar*C*H), 129.0 (Ar*C*H), 132.1 (Ar*C*), 132.2 (*C*H), 138.5 (*C*H), 177.2 (*C*O) and 180.1 (*C*O); m/z (EI) 311 (M^+, 67%), 245 (63), 105 (3) and 73 (100) (HRMS: found M^+, 311.1349. $C_{18}H_{21}NO_2Si$ requires M, 311.1342). The ee was determined as 98% by HPLC (OD column, 0.25% IPA in hexane), the retention times were 38.8 min (minor) and 41.8 min (major).

4.2.7. (1*R*,2*S*)-1-Trimethylsilyl-1,2-cyclopropanedicarboxylic acid dimethyl ester 8. This was prepared using the above procedure starting with 1,2-cyclopropanedicarboxylic acid dimethyl ester **7**. The crude product was purified by flash column chromatography on silica gel (20% EtOAc–light petroleum) to yield diester **8** as a colourless oil (2.23 g, 77%); $[\alpha]_D^{22}=+59$ (c 1.04 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2953, 2901, 2843 and 1732; δ_H (250 MHz, $CDCl_3$) 0.06 [9H, s, Si(CH_3)$_3$], 1.10 (1H, dd, J=7.2, 4.1 Hz, C*H*H), 1.72 (1H, dd, J=5.1, 4.1 Hz, CH*H*), 1.80 (1H, dd, J=7.2, 5.1 Hz, C*H*), 3.64 (3H, s, CH_3) and 3.66 (3H, s, CH_3); δ_C (100 MHz, $CDCl_3$) −3.2 (SiCH_3), 16.0 (CH_2), 22.4 (*C*H), 25.4 (*C*), 51.9 (CH_3), 52.0 (CH_3), 172.0 (*C*O) and 172.05 (*C*O); m/z (EI) 215 [$(M-CH_3)^+$, 100%], 199 (32), 171 (14), 157 (1) and 89 (13) [HRMS: found $(M-CH_3)^+$, 215.0731. $C_{10}H_{18}O_4Si-CH_3$ requires $(M-CH_3)$, 215.0740]. The ee was determined as 82% by HPLC (OD column, 1% IPA in hexane), the retention times were 9.0 min (minor) and 10.0 min (major).

4.2.8. (1*R*,5*S*)-3,3,6,6-Tetramethyl-1-trimethylsilylbicyclo[3.1.0]hexane-2,4-dione 10. This was prepared using the above procedure starting with 3,3,6,6-tetramethylbicyclo[3.1.0]hexane-2,4-dione **9**. The crude product was purified by flash column chromatography on silica gel (5% EtOAc–light petroleum) to give the required product **10** as a colourless oil (1.02 g, 71%); $[\alpha]_D^{27}=-20$ (c 1.20 in $CHCl_3$); (Found: C, 65.27; H, 9.44. Requires C, 65.50; H, 9.30%); ν_{max} ($CHCl_3$)/cm^{-1} 2958, 2936, 2901, 2874, 1741 and 1704; δ_H (250 MHz, $CDCl_3$) 0.17 [9H, s, Si(CH_3)$_3$], 1.03 (3H, s, CHCCH_3), 1.05 (3H, s, CHCCH_3), 1.12 (3H, s, COCCH_3), 1.30 (3H, s, COCCH_3) and 2.29 (1H, s, C*H*); δ_C (100 MHz, $CDCl_3$) −0.5 (SiCH_3), 15.5 (CH_3), 20.4 (CH_3), 24.5 (CH_3), 25.7 (CH_3), 32.8 (*C*), 40.7 (*C*), 44.4 (*C*H), 55.9 (*C*), 211.6 (*C*O) and 214.2 (*C*O); m/z (EI) 238 (M^+, 28%), 223 (7), 195 (17), 168 (14) and 73 (100) (HRMS: found M^+, 238.1381. $C_{12}H_{22}O_2Si$ requires M, 238.1389).

4.2.9. (1*S*,5*R*)-1-Benzoyl-3,3,6,6-tetramethylbicyclo[3.1.0]hexane-2,4-dione 11. To a solution of flame dried CsF (48 mg, 0.31 mmol) and 18-crown-6 (5 mg, 0.02 mmol) in THF (1 mL) at room temperature, under an atmosphere of nitrogen, was added a mixture of diketone **10** (50 mg, 0.21 mmol) and benzoyl fluoride (0.21 mL, 1.93 mmol) in THF (1 mL). The solution was then stirred overnight before quenching with saturated aqueous NH_4Cl (4 mL) and extracting with CH_2Cl_2 (3×30 mL). The combined extracts were dried ($MgSO_4$), filtered and the solvent evaporated in vacuo to give crude product. This was then purified by flash column chromatography (5% EtOAc–light petroleum) to give the triketone **11** as a white solid (28 mg, 50%), mp 69–70°C; $[\alpha]_D^{23}=+76$ (c 0.76 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2977, 2933, 2873, 1756, 1719, 1667, 1598 and 1582; δ_H (400 MHz, $CDCl_3$) 1.10 (3H, s, CHCCH_3), 1.15 (3H, s, CHCCH_3), 1.23 (3H, s, COCCH_3), 1.33 (3H, s, COCCH_3), 2.97 (1H, s, C*H*), 7.55 (2H, t, J=7.2 Hz, Ar*H*), 7.66 (1H, t, *J*=7.2 Hz, Ar*H*) and 8.01 (2H, d, *J*=7.2 Hz, Ar*H*); δ_C (100 MHz, $CDCl_3$) 15.4 (*C*H_3), 19.3 (*C*H_3), 23.4 (*C*H_3), 24.5 (*C*H_3), 35.2 (*C*), 42.6 (*C*H), 57.1 (*C*), 57.7 (*C*), 128.5 (Ar*C*H), 130.6 (Ar*C*H), 134.1 (Ar*C*H), 136.2 (Ar*C*), 191.3 (Ph*C*O), 205.2 (*C*O) and 208.6 (*C*O); *m*/*z* (EI) 270 (M^+, 2%), 200 (3), 172 (4), 165 (2), 122 (8), 105 (100) and 77 (50) (HRMS: found M^+, 270.1250. $C_{17}H_{18}O_3$ requires M, 270.1256). The ee was determined as 97% by HPLC (OD column, 1% IPA in hexane), the retention times were 9.9 min (major) and 15.1 min (minor).

4.3. Typical procedure for chiral base reactions using external quench

4.3.1. (1*R*,2*S*,6*R*,7*S*)-2-Methyl-4-phenyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione 12. Chiral lithium amide base **2** was prepared from the corresponding chiral amine HCl salt (131 mg, 0.50 mmol) in THF (4 mL) at −78°C under an atmosphere of nitrogen, by addition of ^{n}BuLi (0.63 mL of a 1.6 M solution in hexanes, 1.00 mmol), followed by warming to room temperature for 15 min. The resulting solution of the chiral base **2** was cooled to −78°C before being added dropwise over 15 min to a stirred solution of the starting *meso* imide (100 mg, 0.42 mmol) in THF (8 mL). The mixture was stirred for 1 h before addition of MeI (1.03 mL, 16.7 mmol). The solution was warmed slowly overnight, and then quenched with saturated aqueous $NaHCO_3$ (4 mL). Most of the THF was evaporated in vacuo and the remaining solution extracted with Et_2O (3×50 mL), dried ($MgSO_4$), filtered and the solvent evaporated under reduced pressure. The crude mixture was purified by flash column chromatography on silica gel (10% EtOAc–light petroleum) to yield imide **12** as a white solid (38 mg, 36%), mp 109–112°C, lit.[12] mp 108–110°C; $[\alpha]_D^{23}=-45$ (*c* 1.18 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2974, 2951, 2875, 1773, 1709, 1599 and 1500; δ_H (250 MHz, $CDCl_3$) 1.63 (3H, s, C*H_3*), 1.82 (1H, d, *J*=1.6 Hz, C*H*H), 1.84 (1H, d, *J*=1.6 Hz, CH*H*), 2.99 (1H, d, *J*=4.5 Hz, C*H*CO), 3.03 (1H, m, C*H*CCH$_3$), 3.46 (1H, m, C*H*CHCO), 6.24 (1H, dd, *J*=5.6, 2.6 Hz, CH═C*H*), 6.35 (1H, dd, *J*=5.6, 2.6 Hz, C*H*═CH), 7.14–7.47 (5H, m, Ar*H*); δ_C (68 MHz, $CDCl_3$) 21.4 (*C*H_3), 46.2 (*C*H), 50.2 (*C*H_2), 51.3 (*C*H), 51.4 (*C*), 52.9 (*C*H), 126.6 (Ar*C*H), 128.5 (Ar*C*H), 129.0 (Ar*C*H), 131.8 (Ar*C*), 134.2 (*C*H), 136.7 (*C*H), 176.4 (*C*O) and 180.0 (*C*O); *m*/*z* (EI) 253 (M^+, 100%) and 103 (9) (HRMS: found M^+, 253.1101. $C_{16}H_{15}NO_2$ requires M, 253.1103).

4.3.2. (1*R*,2*S*,6*R*,7*S*)-2-Allyl-4-phenyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione 13. The above typical procedure was followed using starting imide (300 mg, 1.25 mmol) and allyl bromide (3.00 mL, 34.7 mmol), and the resulting crude product was purified by flash column chromatography on silica gel (10% EtOAc–light petroleum) to give **13** as a colourless oil (115 mg, 33%), $[\alpha]_D^{23}=-60$ (*c* 0.83 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2982, 2949, 2877, 1774, 1706, 1641, 1599 and 1500; δ_H (400 MHz, $CDCl_3$) 1.50 (2H, m, C*H*H+CH*H*), 2.40 (1H, dd, *J*=13.7, 7.8 Hz, C*H*HCH═CH$_2$), 3.00 (1H, dd, *J*=13.7, 7.1 Hz, CH*H*CH═CH$_2$), 3.07 (1H, m, C*H*), 3.11 (1H, d, *J*=4.5 Hz, C*H*CO), 3.47 (1H, m, C*H*), 5.17–5.26 (2H, m, CH$_2$CH═C*H$_2$*), 5.77–5.87 (1H, m, CH$_2$C*H*═CH$_2$), 6.26 (1H, dd, *J*=5.7, 2.9 Hz, CH═C*H*), 6.35 (1H, dd, *J*=5.7, 2.9 Hz, C*H*═CH), 7.12 (2H, d, *J*=7.2 Hz, Ar*H*), 7.36 (1H, t, *J*=7.4 Hz, Ar*H*) and 7.43 (2H, t, *J*=7.2 Hz, Ar*H*); δ_C (100 MHz, $CDCl_3$) 39.8 (*C*H_2), 46.2 (*C*H), 49.9 (*C*H), 50.5 (*C*H_2), 50.6 (*C*H), 56.5 (*C*), 119.6 (*C*H_2), 126.6 (Ar*C*H), 128.6 (Ar*C*H), 129.0 (Ar*C*H), 131.9 (Ar*C*), 132.6 (*C*H), 134.9 (*C*H), 136.7 (*C*H), 176.4 (*C*O) and 179.1 (*C*O); *m*/*z* (EI) 279 (M^+, 30%), 238 (9), 213 (100), 77 (7) and 66 (66) (HRMS: found M^+, 279.1252. $C_{18}H_{17}NO_2$ requires M, 279.1259). Some diallylated product was also isolated.

4.3.3. (1*R*,2*R*,6*S*,7*S*)-4-Phenyl-2-thiophenyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione 14. The above typical procedure was followed using starting imide (240 mg, 1.0 mmol) and a solution of diphenyl disulfide (1.09 g, 5.0 mmol) in THF (10 mL), and the resulting crude product was purified by flash column chromatography on silica gel (20% EtOAc–light petroleum) to give **14** as a white solid (175 mg, 50%), mp 130–132°C; $[\alpha]_D^{23}=-45$ (*c* 1.0 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2984, 2950, 2875, 1776, 1705, 1598, 1574 and 1499; δ_H (400 MHz, $CDCl_3$) 1.96 (1H, dt, *J*=9.1, 1.6 Hz, C*H*H), 2.39 (1H, d, *J*=9.1 Hz, CH*H*), 3.29 (1H, m, C*H*CHCO), 3.37 (1H, d, *J*=4.5 Hz, C*H*CO), 3.57 (1H, m, C*H*CSPh), 6.31 (2H, m, C*H*═C*H*), 6.88–7.68 (10H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) 46.7 (*C*H), 50.4 (*C*H), 51.3 (*C*H_2), 53.6 (*C*H), 62.3 (*C*), 126.5 (Ar*C*H), 128.6 (Ar*C*H), 129.0 (Ar*C*H), 129.3 (Ar*C*H), 130.0 (Ar*C*H), 131.6 (Ar*C*), 135.9 (Ar*C*H), 136.2 (*C*H), 136.4 (*C*H), 174.6 (*C*O) and 175.6 (*C*O); *m*/*z* (EI) 347 (M^+, 11%), 134 (100) and 77 (26) (HRMS: found M^+, 347.0989. $C_{21}H_{17}NO_2S$ requires M, 347.0980). The ee was determined as 97% by HPLC (OJ column, 10% IPA in hexane), the retention times were 31.5 min (minor) and 38.7 min (major).

4.4. Typical procedure for substitution on 3a (Table 1)

4.4.1. (1*R*,5*S*)-5-Methyl-3-phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexane-2,4-dione 15. LDA was prepared by addition of ^{n}BuLi (0.58 mL of a 1.6 M solution in hexanes, 0.92 mmol) to a solution of DIPA (128 μL, 0.92 mmol) and LiCl (38 mg, 0.92 mmol) in THF (6 mL) at −78°C and warming to room temperature for 15 min before recooling to −78°C. A solution of the cyclopropane **3a** (200 mg, 0.77 mmol, 91% ee) in THF (2 mL) was added dropwise over 10 min and the solution stirred for 45 min. Methyl iodide (1.92 mL, 30.8 mmol) was then added and the solution warmed overnight to room temperature before quenching with saturated aqueous NH_4Cl (4 mL). The solution was extracted with CH_2Cl_2 (3×30 mL) and the combined extracts dried ($MgSO_4$), filtered and the solvent evaporated under reduced pressure to yield crude product. The resulting crude mixture was purified by flash column chromatography on silica gel (20% EtOAc–light petroleum) to give **15** as a white solid (195 mg, 93%), mp 113–114°C; $[\alpha]_D^{24}=-44$ (*c* 1.12 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2957, 2900, 1766, 1702, 1600 and 1502; δ_H (250 MHz, $CDCl_3$) 0.28 [9H, s, Si(C*H_3*)$_3$], 1.44 (1H, d, *J*=3.9 Hz, C*H*H), 1.60 (3H, s, C*H_3*), 1.73 (1H, d, *J*=3.9 Hz, CH*H*) and 7.21–7.46 (5H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) −1.4 (Si*C*H_3), 12.2 (*C*H_3), 24.2 (*C*), 31.3 (*C*H_2), 31.5 (*C*), 126.3 (Ar*C*H), 128.0 (Ar*C*H), 128.9 (Ar*C*H), 132.1 (Ar*C*), 177.2 (*C*O) and 177.4 (*C*O); *m*/*z* (EI) 273 (M^+, 64%), 258 (77), 184 (4) and 73 (100) (HRMS: found M^+, 273.1180. $C_{15}H_{19}NO_2Si$ requires M, 273.1185).

4.4.2. (1*R*,5*S*)-5-Allyl-3-phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexane-2,4-dione 16. The above typical procedure was followed using **3a** (100 mg, 0.39 mmol, 91% ee) and allyl bromide (1.00 mL, 11.6 mmol) and the resulting crude mixture was purified by flash column chromatography on silica gel (20% EtOAc–light petroleum) to give **16** as a pale yellow oil (84 mg, 73%); $[\alpha]_{\rm D}^{26}=-36$ (*c* 1.29 in $\mathrm{CHCl_3}$); $\nu_{\max}$ ($\mathrm{CHCl_3}$)/cm^{-1} 2957, 1766, 1703, 1643, 1598 and 1501; $\delta_{\rm H}$ (400 MHz, $\mathrm{CDCl_3}$) 0.27 [9H, s, $\mathrm{Si(C}H_3)_3$], 1.43 (1H, d, *J*=4.0 Hz, C*H*HCSi), 1.72 (1H, d, *J*=4.0 Hz, CH*H*CSi), 2.20 (1H, dd, *J*=16.1, 6.0 Hz, $\mathrm{CH_2{=}CHC}H\mathrm{H}$), 3.18 (1H, dd, *J*=16.1, 6.3 Hz, $\mathrm{CH_2{=}CHCH}H$), 5.13 (1H, m, C*H*H=CH), 5.17 (1H, m, CH*H*=CH), 5.91 (1H, m, $\mathrm{CH_2{=}C}H$) and 7.21–7.43 (5H, m, Ar*H*); $\delta_{\rm C}$ (100 MHz, $\mathrm{CDCl_3}$) −1.5 $\mathrm{Si(}C\mathrm{H_3)}$, 23.7 (*C*), 29.6 ($C\mathrm{H_2}$), 30.7 ($C\mathrm{H_2}$), 36.3 (*C*), 117.4 ($C\mathrm{H_2}$), 126.3 (Ar*C*H), 128.0 (Ar*C*H), 128.9 (Ar*C*H), 132.0 (Ar*C*), 134.2 (*C*H), 176.2 (*C*O) and 177.2 (*C*O); *m/z* (EI) 299 (M$^+$, 43%), 285 (18), 284 (79), 271 (8) and 73 (100) (HRMS: found M$^+$, 299.1356. $\mathrm{C_{17}H_{21}NO_2Si}$ requires M, 299.1342).

4.4.3. (1*R*,5*S*)-5-Benzyl-3-phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexane-2,4-dione 17. The above typical procedure was followed using **3a** (100 mg, 0.39 mmol, 91% ee) and benzyl bromide (0.92 mL, 7.71 mmol) and the resulting crude mixture was purified by flash column chromatography on silica gel (7% EtOAc–light petroleum) to give **17** as a colourless oil (87 mg, 67%); $[\alpha]_{\rm D}^{26}=-10$ (*c* 0.46 in $\mathrm{CHCl_3}$); $\nu_{\max}$ ($\mathrm{CHCl_3}$)/cm^{-1} 2958, 2927, 2872, 1766, 1702, 1600 and 1496; $\delta_{\rm H}$ (400 MHz, $\mathrm{CDCl_3}$) 0.17 [9H, s, $\mathrm{Si(C}H_3)_3$], 1.53 (1H, d, *J*=4.0 Hz, C*H*H), 1.78 (1H, d, *J*=4.0 Hz, CH*H*), 2.93 (1H, d, *J*=16.4 Hz, PhC*H*H), 3.73 (1H, d, *J*=16.4 Hz, PhCH*H*) and 7.20–7.44 (10H, m, Ar*H*); $\delta_{\rm C}$ (100 MHz, $\mathrm{CDCl_3}$) −1.6 (Si*C*H$_3$), 24.7 (*C*), 30.4 ($C\mathrm{H_2}$), 32.2 ($C\mathrm{H_2}$), 37.1 (*C*), 126.3 (Ar*C*H), 126.6 (Ar*C*H), 128.0 (Ar*C*H), 128.3 (Ar*C*H), 128.5 (Ar*C*H), 128.9 (Ar*C*H), 132.1 (Ar*C*), 138.4 (Ar*C*), 176.8 (*C*O) and 177.0 (*C*O); *m/z* (EI) 349 (M$^+$, 48%), 335 (14), 334 (53), 321 (66), 276 (10), 248 (73), 91 (37) and 73 (100) (HRMS: found M$^+$, 349.1490. $\mathrm{C_{21}H_{23}NO_2Si}$ requires M, 349.1498).

4.4.4. (1*R*,5*S*)-3-Phenyl-1-thiophenyl-5-trimethylsilyl-3-azabicyclo[3.1.0]hexane-2,4-dione 18. The above typical procedure was followed using **3a** (100 mg, 0.39 mmol, 95% ee) and a solution of diphenyl disulfide (420 mg, 1.93 mmol) in THF (1 mL) and the resulting crude mixture was purified by flash column chromatography on silica gel (5% EtOAc–light petroleum) to give **18** as a white solid (99 mg, 71%), mp 111–113°C; $[\alpha]_{\rm D}^{25}=-78$ (*c* 1.10 in $\mathrm{CHCl_3}$); (Found: C, 65.12; H, 5.84; N, 3.93. Requires C, 65.38; H, 5.77; N, 3.81%); $\nu_{\max}$ ($\mathrm{CHCl_3}$)/cm^{-1} 2957, 1770, 1708, 1600 and 1501; $\delta_{\rm H}$ (250 MHz, $\mathrm{CDCl_3}$) 0.33 [9H, s, $\mathrm{Si(C}H_3)_3$], 1.86 (1H, d, *J*=4.3 Hz, C*H*H), 2.13 (1H, d, *J*=4.3 Hz, CH*H*) and 7.28–7.54 (10H, m, Ar*H*); $\delta_{\rm C}$ (100 MHz, $\mathrm{CDCl_3}$) −1.4 (Si*C*H$_3$), 29.2 (*C*), 32.7 ($C\mathrm{H_2}$), 39.8 (*C*), 126.3 (Ar*C*H), 127.3 (Ar*C*H), 128.3 (Ar*C*H), 128.9 (Ar*C*H), 129.1 (Ar*C*H), 130.0 (Ar*C*H), 131.8 (Ar*C*), 134.5 (Ar*C*), 174.2 (*C*O) and 175.3 (*C*O); *m/z* (EI) 367 (M$^+$, 27%), 352 (7), 77 (5) and 73 (100) (HRMS: found M$^+$, 367.1048. $\mathrm{C_{20}H_{21}NO_2SSi}$ requires M, 367.1062).

4.4.5. (1*R*,5*R*)-5-(1′-Hydroxyphenylmethyl)-3-phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexane-2,4-dione 19. The above typical procedure was followed using **3a** (100 mg, 0.39 mmol, 95% ee) and benzaldehyde (0.20 mL, 1.93 mmol) and stirring at −78°C for 3 h before warming to room temperature over 1 h. This gave a crude mixture which consisted of a 1:1 mixture of diastereomers of adduct **19**, along with a small amount of by-product which appeared to have arisen by addition followed by silyl group transfer to oxygen. Purification by flash column chromatography on silica gel (10% EtOAc–light petroleum) allowed almost complete separation of the diastereomers of **19**, total yield (86 mg, 61%).

Data for less polar diastereomer of **19**: $\nu_{\max}$ ($\mathrm{CHCl_3}$)/cm^{-1} 3605 (OH), 2926, 2854, 1766, 1702, 1601 and 1496; $\delta_{\rm H}$ (250 MHz, $\mathrm{CDCl_3}$) 0.36 [9H, s, $\mathrm{Si(C}H_3)_3$], 1.71 (1H, d, *J*=4.4 Hz, C*H*H), 1.89 (1H, d, *J*=4.4 Hz, CH*H*), 2.85 (1H, d, *J*=8.0 Hz, O*H*), 4.87 (1H, d, *J*=8.0 Hz, C*H*) and 7.21–7.60 (10H, m, Ar*H*); $\delta_{\rm C}$ (100 MHz, $\mathrm{CDCl_3}$) −1.2 (Si*C*H$_3$), 25.3 (*C*), 28.7 ($C\mathrm{H_2}$), 40.9 (*C*), 71.6 (*C*H), 126.4 (Ar*C*H), 127.9 (Ar*C*H), 128.1 (Ar*C*H), 128.3 (Ar*C*H), 128.4 (Ar*C*H), 128.9 (Ar*C*H), 131.7 (Ar*C*), 141.6 (Ar*C*), 175.0 (*C*O) and 176.4 (*C*O); *m/z* (EI) 365 (M$^+$, 1%), 351 (1), 350 (9), 337 (24), 264 (32), 75 (100) and 73 (75) (HRMS: found M$^+$, 365.1450. $\mathrm{C_{21}H_{23}NO_3Si}$ requires M, 365.1447).

Data for more polar diastereomer of **19** $\nu_{\max}$ ($\mathrm{CHCl_3}$)/cm^{-1} 3534 (OH), 2958, 1765, 1699, 1599 and 1495; $\delta_{\rm H}$ (250 MHz, $\mathrm{CDCl_3}$) 0.18 [9H, s, $\mathrm{Si(C}H_3)_3$], 1.85 (1H, d, *J*=4.2 Hz, C*H*H), 2.00 (1H, d, *J*=4.2 Hz, CH*H*), 4.16 (1H, d, *J*=11.2 Hz, O*H*), 4.65 (1H, d, *J*=11.2 Hz, C*H*) and 7.22–7.48 (10H, m, Ar*H*); $\delta_{\rm C}$ (100 MHz, $\mathrm{CDCl_3}$) −1.6 (Si*C*H$_3$), 25.4 (*C*), 29.9 ($C\mathrm{H_2}$), 40.2 (*C*), 73.6 (*C*H), 126.2 (Ar*C*H), 126.4 (Ar*C*H), 128.3 (Ar*C*H), 128.4 (Ar*C*H), 128.7 (Ar*C*H), 129.0 (Ar*C*H), 131.3 (Ar*C*), 141.2 (Ar*C*), 176.5 (*C*O) and 177.3 (*C*O); *m/z* (EI) 365 (M$^+$, 2%), 351 (2), 350 (10), 337 (22), 264 (28), 75 (100) and 73 (71) (HRMS: found M$^+$, 365.1462. $\mathrm{C_{21}H_{23}NO_3Si}$ requires M, 365.1447).

4.4.6. (1*R*,5*R*)-5-Benzoyl-3-phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexane-2,4-dione 20. The above typical procedure was followed using **3a** (100 mg, 0.39 mmol, 95% ee) and benzoyl chloride (0.22 mL, 1.9 mmol) and warming of the reaction mixture overnight to room temperature. Purification of the crude mixture by flash column chromatography (7% EtOAc–light petroleum) gave the imide **20** as a white solid (81 mg, 57%), mp 168–170°C; $[\alpha]_{\rm D}^{25}=-9.6$ (*c* 1.23 in $\mathrm{CHCl_3}$); $\nu_{\max}$ ($\mathrm{CHCl_3}$)/cm^{-1} 2927, 1770, 1708, 1683, 1598, 1500, 1450, 1376 and 1342; $\delta_{\rm H}$ (250 MHz, $\mathrm{CDCl_3}$) 0.14 [9H, s, $\mathrm{Si(C}H_3)_3$], 2.03 (1H, d, *J*=4.3 Hz, C*H*H), 2.33 (1H, d, *J*=4.3 Hz, CH*H*) and 7.30–7.97 (10H, m, Ar*H*); $\delta_{\rm C}$ (68 MHz, $\mathrm{CDCl_3}$), −2.1 (Si*C*H$_3$), 27.7 ($C\mathrm{H_2}$), 29.5 (*C*), 43.1 (*C*), 126.2 (Ar*C*H), 128.4 (Ar*C*H), 128.8 (Ar*C*H), 128.9 (Ar*C*H), 129.1 (Ar*C*H), 131.5 (Ar*C*), 134.2 (Ar*C*H), 135.7 (Ar*C*), 172.7 (*C*O), 175.4 (*C*O) and 190.9 (*C*OPh); *m/z* (EI) 363 (M$^+$, 1%), 349 (26), 348 (100), 105 (35), 77 (35) and 73 (19) (HRMS: found M$^+$, 363.1281. $\mathrm{C_{21}H_{21}NO_3Si}$ requires M, 363.1291).

4.4.7. (1*R*,5*R*)-5-(3′-Methyl-2′-oxobutyl)-3-phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexane-2,4-dione 21. The above typical procedure was followed using **3a** (100 mg, 0.39 mmol) and isovaleryl methyl ester (0.15 mL, 1.2 mmol) and stirring the reaction mixture at −78°C for 1 h before quenching with saturated aqueous NH_4Cl. Purification by flash column chromatography (5% EtOAc–light petroleum) gave imide **21** as a white solid (62 mg, 47%), mp 80–82°C; $[\alpha]_D^{24}=+61$ (*c* 1.02 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2960, 2933, 2901, 2874, 1770, 1707, 1683, 1598, and 1501; δ_H (400 MHz, $CDCl_3$) 0.24 [9H, s, Si(C*H*$_3$)$_3$], 0.97 (3H, d, *J*=6.7 Hz, C*H*$_3$), 1.00 (3H, d, *J*=6.7 Hz, C*H*$_3$), 1.87 (1H, d, *J*=3.9 Hz, C*H*HCSi), 2.24 (1H, m, C*H*), 2.31 (1H, d, *J*=3.9 Hz, CH*H*CSi), 2.56 (1H, dd, *J*=18.2, 6.7 Hz, COC*H*H), 3.14 (1H, dd, *J*=18.2, 6.7 Hz, COCH*H*), 7.24 (2H, d, *J*=7.2 Hz, Ar*H*), 7.37 (1H, t, *J*=7.3 Hz, Ar*H*) and 7.45 (2H, t, *J*=7.3 Hz, Ar*H*); δ_C (100 MHz, $CDCl_3$) −1.4 (SiCH_3), 22.6 (*C*H$_3$), 22.6 (*C*H$_3$), 23.8 (*C*H), 30.1 (*C*H$_2$), 31.2 (*C*), 44.0 (*C*), 51.3 (*C*H$_2$), 126.3 (Ar*C*H), 128.4 (Ar*C*H), 129.0 (Ar*C*H), 131.5 (Ar*C*), 172.8 (*C*O), 175.0 (*C*O) and 200.3 (*C*OCH$_2$); *m*/*z* (EI) 328 [$(M-CH_3)^+$, 100%], 286 (30), 73 (10) and 57 (2) [HRMS: found $(M-CH_3)^+$, 328.1367. $C_{19}H_{25}NO_3Si-CH_3$ requires ($M-CH_3$), 328.1369].

4.4.8. (1*R*,2*R*,6*S*,7*S*)-6-Methyl-4-phenyl-2-trimethylsilyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione 22. LDA was prepared by addition of ^{n}BuLi (0.19 mL of a 1.6 M solution in hexanes, 0.31 mmol) to a solution of DIPA (44 μL, 0.31 mmol) and LiCl (13 mg, 0.31 mmol) in THF (3 mL) at −78°C and warming to room temperature for 15 min before recooling to −78°C. A solution of (±)-**6** (80 mg, 0.26 mmol) in THF (2 mL) was then added dropwise over 10 min and the solution stirred for 1.5 h before the addition of methyl iodide (0.63 mL, 10.3 mmol). The solution was warmed overnight to room temperature before quenching with saturated aqueous NH_4Cl (4 mL). The solution was extracted with CH_2Cl_2 (3×30 mL) and the combined extracts dried ($MgSO_4$), filtered and the solvent evaporated under reduced pressure to yield crude product. This was purified by flash column chromatography (10% EtOAc–light petroleum) to yield the imide **22** as a colourless oil (40 mg, 48%); ν_{max} ($CHCl_3$)/cm^{-1} 2985, 2955, 1759, 1691, 1600 and 1500; δ_H (400 MHz, $CDCl_3$) 0.35 [9H, s, Si(C*H*$_3$)$_3$], 1.66 (1H, dt, *J*=9.1, 1.6 Hz, C*H*H), 1.70 (1H, s, C*H*$_3$), 1.85 (1H, d, *J*=9.1 Hz, CH*H*), 2.99 (1H, m, C*H*CSi), 3.40 (1H, m, C*H*CCH$_3$), 6.26 (1H, dd, *J*=5.5, 2.8 Hz, CH=C*H*), 6.33 (1H, dd, *J*=5.5, 2.8 Hz, C*H*=CH), 7.12 (2H, d, *J*=7.2 Hz, Ar*H*), 7.35 (1H, t, *J*=7.4 Hz, Ar*H*) and 7.42 (2H, t, *J*=7.8 Hz, Ar*H*); δ_C (68 MHz, $CDCl_3$) −0.6 (SiCH_3), 21.4 (*C*H$_3$), 48.8 (*C*H), 49.6 (*C*H$_2$), 50.7 (*C*), 53.7 (*C*H), 54.8 (*C*), 126.7 (Ar*C*H), 128.4 (Ar*C*H), 128.9 (Ar*C*H), 132.2 (Ar*C*), 133.9 (*C*H), 137.6 (*C*H), 180.1 (*C*O) and 180.6 (*C*O); *m*/*z* (EI) 325 (M^+, 82%), 310 (11), 259 (87), 231 (12), 142 (100) and 73 (81) (HRMS: found M^+, 325.1485. $C_{19}H_{23}NO_2Si$ requires M, 325.1498).

4.4.9. (1*R*,5*S*)-1-Methyl-3-phenyl-3-azabicyclo[3.1.0]-hexane-2,4-dione 23. A solution of **15** (50 mg, 0.18 mmol, 91% ee), CsF (42 mg, 0.27 mmol) and 18-crown-6 (5 mg, 0.02 mmol) in THF (2 mL) was stirred overnight before quenching with saturated aqueous NH_4Cl (4 mL). The solution was then extracted with CH_2Cl_2 (2×50 mL), washed with brine (100 mL), dried ($MgSO_4$), filtered and the solvent removed in vacuo. The resulting crude product was then purified by flash column chromatography (20% EtOAc–light petroleum) to yield **23** as a white solid (20 mg, 54%), mp 143–145°C; $[\alpha]_D^{26}=+41$ (*c* 0.37 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2938, 1780, 1715, 1600 and 1500; δ_H (250 MHz, $CDCl_3$) 1.49 (1H, dd, *J*=8.0, 4.7 Hz, C*H*H), 1.59 (3H, s, C*H*$_3$), 1.69 (1H, dd, *J*=4.7, 3.2 Hz, CH*H*), 2.43 (1H, dd, *J*=8.0, 3.2 Hz, C*H*), 7.23 (2H, d, *J*=7.3 Hz, Ar*H*), 7.36 (1H, t, *J*=7.4 Hz, Ar*H*) and 7.44 (2H, t, *J*=7.4 Hz, Ar*H*); δ_C (68 MHz, $CDCl_3$), 12.8 (*C*H$_3$), 26.0 (*C*H), 26.9 (*C*), 26.9 (*C*H$_2$), 126.4 (Ar*C*H), 128.2 (Ar*C*H), 129.0 (Ar*C*H), 131.7 (Ar*C*), 174.1 (*C*O) and 176.2 (*C*O); *m*/*z* (EI) 201 (M^+, 62%), 82 (100) and 77 (7) (HRMS: found M^+, 201.0799. $C_{12}H_{11}NO_2$ requires M, 201.0790).

4.4.10. (1*R*,5*S*)-1-Benzoyl-3-phenyl-3-azabicyclo[3.1.0]-hexane-2,4-dione (+)-24. To a solution of **20** (350 mg, 0.96 mmol, prepared from **3a** of 95% ee) in THF (35 mL) at −78°C was added TBAF (1.16 mL of a 1.0 M solution in THF, 1.16 mmol) dropwise. The reaction mixture was stirred for 1 h at −78°C before quenching with water (15 mL) and allowing to warm to room temperature. The solution was extracted with CH_2Cl_2 (4×50 mL) then the combined fractions dried ($MgSO_4$), filtered and the solvent removed in vacuo to give crude product. This was purified by flash column chromatography (20% EtOAc–light petroleum) to give **24** as a white solid (252 mg, 90%), mp 217–220°C; $[\alpha]_D^{24}=+58$ (*c* 0.88 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2926, 1778, 1722, 1679, 1599 and 1498; δ_H (250 MHz, $CDCl_3$) 2.11 (1H, dd, *J*=4.7, 4.1 Hz, C*H*H), 2.40 (1H, dd, *J*=8.4, 4.7 Hz, CH*H*), 3.15 (1H, dd, *J*=8.4, 4.1 Hz, C*H*) and 7.25–7.98 (10H, m, Ar*H*); δ_C (68 MHz, $CDCl_3$) 26.1 (*C*H$_2$), 27.9 (*C*H), 38.6 (*C*), 126.3 (Ar*C*H), 128.6 (Ar*C*H), 128.7 (Ar*C*H), 129.0 (Ar*C*H), 129.1 (Ar*C*H), 131.1 (Ar*C*), 134.1 (Ar*C*H), 135.6 (Ar*C*), 170.9 (*C*O), 171.7 (*C*O) and 190.4 (Ph*C*O); *m*/*z* (EI) 291 (M^+, 64%), 263 (3), 172 (1), 105 (100) and 91 (3) (HRMS: found M^+, 291.0899. $C_{18}H_{13}NO_3$ requires M, 291.0895).

4.4.11. (1*R*,5*S*)-1-Isovalerylketone-3-phenyl-3-azabicyclo[3.1.0]hexane-2,4-dione 25. To a solution of **21** (40 mg, 0.12 mmol) ($[\alpha]_D^{24}=+61$ (*c* 1.02 in $CHCl_3$)) in THF (2 mL) at −78°C was added TBAF (0.14 mL of a 1.0 M solution in THF, 0.14 mmol) dropwise. The reaction mixture was then stirred for 1 h at −78°C before quenching with water (3 mL) and allowing to warm to room temperature. The solution was extracted with CH_2Cl_2 (3×30 mL), then the combined fractions dried ($MgSO_4$), filtered and the solvent removed in vacuo to give crude product. This was purified by flash column chromatography (10% EtOAc–light petroleum) to give **25** as a colourless oil (25 mg, 79%); $[\alpha]_D^{23}=+171$ (*c* 1.17 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2961, 2874, 1782, 1721, 1598 and 1496; δ_H (400 MHz, $CDCl_3$) 0.97 (3H, d, *J*=6.7 Hz, C*H*$_3$), 1.00 (3H, d, *J*=6.7 Hz, C*H*$_3$), 1.98 (1H, dd, *J*=4.5, 4.2 Hz, C*H*HCSi), 2.23 [1H, m, C*H*(CH$_3$)$_2$], 2.33 (1H, dd, *J*=8.5, 4.2 Hz, CH*H*CSi), 2.84 (1H, dd, *J*=16.7, 6.7 Hz, COC*H*H), 3.02 (1H, dd, *J*=8.5, 4.5 Hz, COC*H*), 3.05 (1H, dd, *J*=16.7, 6.7 Hz, COCH*H*), 7.23 (2H, d, *J*=7.0 Hz, Ar*H*), 7.40 (1H, t, *J*=7.1 Hz, Ar*H*) and 7.47 (2H, t, *J*=7.0 Hz, Ar*H*); δ_C (100 MHz, $CDCl_3$) 22.5 (*C*H$_3$), 24.4 (*C*H), 29.8 (*C*H$_2$), 30.4 (*C*H), 38.7 (*C*), 50.9 (*C*H$_2$), 126.4 (Ar*C*H), 128.7 (Ar*C*H), 129.2 (Ar*C*H), 131.1 (Ar*C*), 171.2 (*C*O), 171.3 (*C*O) and 200.4 (*C*OCH$_2$); *m*/*z* (EI) 271 (M^+, 100%), 257 (12), 256 (81), 243 (24), 230 (3), 229 (28), 228 (20), 186 (12) and 95 (48) (HRMS: found M^+, 271.1203. $C_{16}H_{17}NO_3$ requires M, 271.1209).

4.5. Typical procedure for CsF mediated substitution reactions of 3a

4.5.1. (1*S*,5*R*)-1-Benzoyl-3-phenyl-3-azabicyclo[3.1.0] hexane-2,4-dione (−)-24. To a solution of flame dried CsF (0.12 g, 0.77 mmol) and 18-crown-6 (10 mg, 0.04 mmol) in THF (1 mL) at room temperature, under an atmosphere of nitrogen, was added a mixture of **3a** (0.10 g, 0.39 mmol, 95% ee) and benzoyl fluoride (0.21 mL, 1.93 mmol) in THF (2 mL). The solution was stirred overnight before quenching with saturated aqueous NH_4Cl (4 mL) and extracting with CH_2Cl_2 (3×30 mL). The combined extracts were dried ($MgSO_4$), filtered and the solvent evaporated in vacuo to give crude product. This was purified by flash column chromatography (5% EtOAc–light petroleum) to give **24** as a white solid (49 mg, 44%), mp 217–220°C; $[\alpha]_D^{24}=-62$ (*c* 0.88 in $CHCl_3$) with data as described above.

4.5.2. (1*S*,5*R*)-1-(1′-Hydroxyphenylmethyl)-3-phenyl-3-azabicyclo[3.1.0]hexane-2,4-dione 26. The above typical procedure was followed using **3a** (0.10 g, 0.39 mmol, 95% ee), CsF (0.60 g, 0.39 mmol), 18-crown-6 (10 mg, 0.04 mmol) and benzaldehyde (0.20 mL, 1.93 mmol) and the resulting crude mixture was purified by flash column chromatography (10% EtOAc–light petroleum) to give a white solid as a 1:1 mixture of inseparable diastereomers **26**, total yield (77 mg, 68%); (Found: C, 73.50; H, 5.12; N, 4.76. Requires C, 73.69; H, 5.16; N, 4.78%); ν_{max} ($CHCl_3$)/cm^{-1} 3606 (OH), 2897, 1779, 1714, 1598 and 1496; *m*/*z* (EI) 293 (M^+, 46%), 292 (23), 265 (10), 201 (10), 107 (3) and 77 (44) (HRMS: found M^+, 293.1054. $C_{18}H_{15}NO_3$ requires M, 293.1052). For less polar diastereomer δ_H (400 MHz, $CDCl_3$) 1.62 (1H, dd, *J*=4.7, 3.6 Hz, C*H*H), 1.72 (1H, dd, *J*=8.3, 4.7 Hz, CH*H*), 2.35 (1H, dd, *J*=8.3, 3.6 Hz, C*H*), 3.47 (1H, brs, O*H*), 5.59 (1H, s, C*H*OH) and 7.16–7.45 (5H, m, Ar*H*). For more polar diastereomer δ_H (400 MHz, $CDCl_3$) 1.18 (1H, dd, *J*=8.3, 4.9 Hz, C*H*H), 1.60 (1H, dd, *J*=4.9, 3.6 Hz, CH*H*), 2.52 (1H, dd, *J*=8.3, 3.6 Hz, C*H*), 3.27 (1H, brs, O*H*), 5.59 (1H, s, C*H*OH) and 7.16–7.45 (5H, m, Ar*H*).

4.5.3. (1*R*,5*S*)-3-Phenyl-1-thiophenyl-3-azabicyclo[3.1.0] hexane-2,4-dione 27. The above typical procedure was followed using **3a** (0.10 g, 0.39 mmol, 95% ee), CsF (0.60 g, 0.39 mmol), 18-crown-6 (10 mg, 0.04 mmol) and diphenyl disulfide (0.42 g, 1.93 mmol) and the resulting crude mixture was purified by flash column chromatography (10% EtOAc–light petroleum) to give **27** as a white solid (70 mg, 61%), mp 152–154°C; $[\alpha]_D^{24}=-51$ (*c* 1.00 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2927, 2854, 1778, 1720, 1598, 1499, 1456 and 1375; δ_H (250 MHz, $CDCl_3$) 2.01 (1H, dd, *J*=8.5, 5.1 Hz, C*H*H), 2.11 (1H, dd, *J*=5.1, 4.0 Hz, CH*H*), 2.85 (1H, dd, *J*=8.5, 4.0 Hz, C*H*) and 7.19–7.58 (10H, m, Ar*H*); δ_C (68 MHz, $CDCl_3$) 29.4 (*C*H_2), 29.9 (*C*H), 34.8 (*C*), 126.4 (Ar*C*H), 128.1 (Ar*C*H), 128.5 (Ar*C*H), 129.1 (Ar*C*H), 129.3 (Ar*C*H), 131.4 (Ar*C*H), 133.1 (Ar*C*), 172.0 (*C*O) and 172.9 (*C*O); *m*/*z* (EI) 295 (M^+, 22%), 176 (44), 175 (5) and 147 (40) (HRMS: found M^+, 295.0666. $C_{17}H_{13}NO_2S$ requires M, 295.0667). The ee was determined as 91% by HPLC (OJ column, 15% IPA in hexane), the retention times were 56 min (minor) and 74 min (major).

4.5.4. (1*R*,2*R*,6*S*,7*S*)-4-Phenyl-2-thiophenyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-ene-3,5-dione 14. To a solution of flame dried CsF (73 mg, 0.48 mmol) and 18-crown-6 (8 mg, 0.03 mmol) in THF (1 mL) at room temperature under an atmosphere of nitrogen was added a mixture of **6** (100 mg, 0.32 mmol, 98% ee) and diphenyl disulfide (350 mg, 1.61 mmol) in THF (3 mL). The solution was then stirred overnight before quenching with saturated aqueous NH_4Cl (4 mL) and extracting with CH_2Cl_2 (3×30 mL). The combined extracts were dried ($MgSO_4$), filtered and the solvent evaporated in vacuo to give crude product. This was purified by flash column chromatography (10% EtOAc–light petroleum) to give **14** as a white solid (72 mg, 65%), mp 131–133°C; $[\alpha]_D^{24}=-45$ (*c* 0.85 in $CHCl_3$), other data as previously described. The ee was determined as 93% by HPLC (OJ column, 10% IPA in hexane), the retention times were 73 min (minor) and 83 min (major).

4.5.5. (1*R*,5*R*)-3-Phenyl-1-trimethylsilyl-4-thioxo-3-azabicyclo[3.1.0]hexan-2-one 28. To a solution of **3a** (100 mg, 0.39 mmol, 95% ee) in toluene (5 mL) was added Lawesson's reagent (78 mg, 0.19 mmol). The solution was then heated to reflux for 4 h before being cooled and the toluene removed in vacuo to give crude product. This was purified by flash column chromatography (10% EtOAc–light petroleum) to give pure product **28** as yellow solid (53 mg, 50%), mp 172–173°C; $[\alpha]_D^{27}=+9$ (*c* 1.27 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2956, 2926, 2853, 1742, 1601 and 1498; δ_H (400 MHz, $CDCl_3$) 0.22 [9H, s, Si(C*H*$_3$)$_3$], 1.65–1.70 (2H, m, C*H*H+CH*H*), 3.10 (1H, dd, *J*=7.2, 3.4 Hz, C*H*) and 7.16–7.50 (5H, m, Ar*H*); δ_C (68 MHz, $CDCl_3$) −3.0 (Si*C*H_3), 23.1 (*C*), 27.5 (*C*H_2), 35.4 (*C*H), 127.7 (Ar*C*H), 128.9 (Ar*C*H), 129.1 (Ar*C*H), 133.9 (Ar*C*), 178.4 (*C*O) and 209.6 (*C*S); *m*/*z* (EI) 275 (M^+, 74%), 260 (21), 127 (15) and 73 (100) (HRMS: found M^+, 275.0799. $C_{14}H_{17}NOSSi$ requires M, 275.0800).

4.5.6. (1*R*,2*R*,6*R*,7*S*)-4-Phenyl-2-trimethylsilyl-5-thioxo-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one 29. To a solution of **6** (100 mg, 0.32 mmol, 98% ee) in toluene (5 mL) was added Lawesson's reagent (65 mg, 0.16 mmol). The solution was then heated to reflux for 4 days before cooling and removal of the toluene in vacuo to give crude product. This was purified by flash column chromatography on silica gel (5% EtOAc–light petroleum) to give **29** as a yellow solid (31 mg, 30%); $[\alpha]_D^{24}=-45$ (*c* 0.30 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2957, 2929, 2856, 1731, 1709, 1597 and 1498; δ_H (400 MHz, $CDCl_3$) 0.27 [9H, s, Si(C*H*$_3$)$_3$], 1.60 (1H, dt, *J*=8.9, 1.7 Hz, C*H*H), 1.68 (1H, d, *J*=8.9 Hz, CH*H*), 3.37 (1H, m, C*H*CSi), 3.62 (1H, m, C*H*CHCS), 3.72 (1H, d, *J*=4.5 Hz, C*H*CS), 6.18 (1H, dd, *J*=5.5, 2.9 Hz, CH=C*H*), 6.45 (1H, dd, *J*=5.5, 2.9 Hz, C*H*=CH), 7.04–7.49 (5H, m, Ar*H*); δ_C (100 MHz, $CDCl_3$) −2.4 (Si*C*H_3), 47.3 (*C*H), 49.1 (*C*), 49.7 (*C*H), 50.1 (*C*H_2), 59.8 (*C*H), 127.7 (Ar*C*H), 129.1 (Ar*C*H), 129.3 (Ar*C*H), 132.5 (*C*H), 134.8 (Ar*C*), 139.0 (*C*H), 181.7 (*C*O) and 213.1 (*C*S); *m*/*z* (EI) 327 (M^+, 100%), 73 (79) (HRMS: found M^+, 327.1120. $C_{18}H_{21}NOSSi$ requires M, 327.1113).

4.5.7. (1*R*,4*R*,5*S*)-4-Hydroxy-3-phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexan-2-one 30. To a solution of **3a**

(50 mg, 0.19 mmol, 95% ee) in CH_2Cl_2 (1 mL) at −78°C was added DIBAL (0.38 mL of a 1.0 M solution in CH_2Cl_2, 0.38 mmol). The reaction mixture was then stirred for 10 min before quenching with water (2 mL). The solution was filtered to remove aluminium salts and the filtrate added to CH_2Cl_2 (25 mL). Water was added (25 mL) and the organic layer separated, dried ($MgSO_4$), filtered and the solvent evaporated off in vacuo to give crude product. This was then purified by flash column chromatography (20% EtOAc–light petroleum) to give **30** as a white solid (35 mg, 70 %), mp 121–123°C; $[\alpha]_D^{28}=-146$ (*c* 0.48 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3584, 2957, 1694, 1600 and 1496; δ_H (400 MHz, $CDCl_3$) 0.14 [9H, s, Si(C*H*$_3$)$_3$], 1.02 (1H, dd, *J*=6.9, 4.4 Hz, C*H*H), 1.24 (1H, dd, *J*=4.4, 4.1 Hz, CH*H*), 2.14 (1H, m, C*H*), 2.50 (1H, d, *J*=8.5 Hz, O*H*), 5.85 (1H, dd, *J*=8.5, 5.5 Hz, C*H*OH) and 7.16–7.37 (5H, m, Ar*H*); δ_C (68 MHz, $CDCl_3$) −2.9 (Si*C*H$_3$), 13.3 (*C*H$_2$), 20.0 (*C*), 22.9 (*C*H), 81.5 (*C*H), 123.0 (Ar*C*H), 125.4 (Ar*C*H), 128.9 (Ar*C*H), 136.6 (Ar*C*) and 175.0 (*C*O); *m/z* (EI) 261 (M^+, 100%), 246 (17) and 73 (98) (HRMS: found M^+, 261.1186. $C_{14}H_{19}NO_2Si$ requires M, 261.1185).

4.5.8. (1*R*,2*R*,5*R*,6*S*,7*S*)-5-Hydroxy-4-phenyl-2-trimethylsilyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one 31. To a solution of **6** (100 mg, 0.32 mmol, 98% ee) in CH_2Cl_2 (2 mL) at −78°C was added DIBAL (0.64 mL of a 1.0 M solution in CH_2Cl_2, 0.64 mmol). The reaction mixture was then stirred for 8 min before quenching with water (2 mL). The solution was filtered to remove aluminium salts and the filtrate added to CH_2Cl_2 (25 mL). Water was added (25 mL) and the organic layer separated, dried ($MgSO_4$), filtered and the solvent evaporated off in vacuo to give crude product. This was then purified by flash column chromatography (50% EtOAc–light petroleum) to give **31** as a white solid (83 mg, 83%) mp >230°C; $[\alpha]_D^{22}=+39$ (*c* 0.31 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3594 (OH), 2983, 2955, 2900, 1678, 1599 and 1496; δ_H (400 MHz, $CDCl_3$) 0.19 [9H, s, Si(C*H*$_3$)$_3$], 1.47 (1H, d, *J*=1.6 Hz, C*H*H), 1.48 (1H, d, *J*=1.6 Hz, CH*H*), 2.29 (1H, br d, *J*=6.8 Hz, O*H*), 3.06 (1H, dd, *J*=7.6, 3.8 Hz, C*H*CHOH), 3.20 (1H, m, C*H*CSi), 3.26 (1H, m, C*H*CHCHOH), 5.62 (1H, br t, *J*=6.8 Hz, C*H*OH), 6.25 (1H, dd, *J*=5.6, 2.8 Hz, CH═C*H*), 6.43 (1H, dd, *J*=5.6, 2.8 Hz, C*H*═CH), 7.20 (1H, t, *J*=7.2 Hz, Ar*H*), 7.30 (2H, d, *J*=7.2 Hz, Ar*H*) and 7.36 (2H, t, *J*=7.1 Hz, Ar*H*); δ_C (100 MHz, $CDCl_3$) −2.5 (Si*C*H$_3$), 45.0 (*C*H), 46.6 (*C*H), 48.0 (*C*H), 50.2 (*C*), 50.3 (*C*H$_2$), 82.6 (*C*H), 124.3 (Ar*C*H), 126.1 (Ar*C*H), 129.0 (Ar*C*H), 133.3 (*C*H), 136.6 (Ar*C*), 138.4 (*C*H) and 176.0 (*C*O); *m/z* (EI) 313 (M^+, 73%), 311 (14), 296 (26), 295 (100), 294 (19), 247 (68) and 73 (37) (HRMS: found M^+, 313.1474. $C_{18}H_{23}NO_2Si$ requires M, 313.1498).

4.5.9. (1*R*,2*S*)-2-Hydroxymethyl-1-(*N*-phenylcarboxamido)-1-trimethylsilylcyclopropane 32. To a solution of **3a** (50 mg, 0.19 mmol, 95% ee) in EtOH (10 mL) at −78°C was added $NaBH_4$ (75 mg, 1.9 mmol). The reaction was then stirred at −78°C for 4 h before quenching with water (10 mL) and extracting with $CHCl_3$ (3×30 mL). The combined extracts were dried ($MgSO_4$), filtered and the solvent removed in vacuo to give **32** as a white solid (48 mg, 95%), mp 119–122°C; $[\alpha]_D^{23}=+51$ (*c* 0.95 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 3430 (OH), 2956, 1650, 1597 and 1500; δ_H (400 MHz, $CDCl_3$) 0.12 [9H, s, Si(C*H*$_3$)$_3$], 0.91–0.97 (2H, m, C*H*H+CH*H*), 1.45 (1H, m, C*H*), 3.13 (1H, t, *J*=11.3 Hz, C*H*HOH), 3.85 (1H, br s, O*H*), 2.57 (1H, dd, *J*=11.3, 4.3 Hz, CH*H*OH), 7.10 (1H, t, *J*=7.10 Hz, Ar*H*), 7.31 (2H, t, *J*=7.8 Hz, Ar*H*), 7.49 (2H, d, *J*=8.0 Hz, Ar*H*) and 7.85 (1H, br s, N*H*); δ_C (100 MHz, $CDCl_3$) −3.1 (Si*C*H$_3$), 12.8 (*C*H$_2$), 23.2 (*C*H), 24.8 (*C*), 65.4 (*C*H$_2$), 119.9 (Ar*C*H), 124.3 (Ar*C*H), 129.0 (Ar*C*H), 137.8 (Ar*C*) and 172.5 (*C*O); *m/z* (FAB) 264 [$(M+H)^+$, 55%], 246 (32), 93 (64),77 (30), 73 (100) [HRMS: found $(M+H)^+$, 264.1422. $C_{14}H_4NO_2Si+H$ requires (M+*H*), 264.1420].

4.5.10. (1*R*,5*S*)-1-Trimethylsilyl-3-oxabicyclo[3.1.0]-hexan-2-one 33. A solution of **32** (90 mg, 0.34 mmol, $[\alpha]_D^{23}=+51$ (*c* 0.95 in $CHCl_3$)), in 2 M H_2SO_4 (8 mL) was heated at 80°C for 2 h before cooling and extracting with $CHCl_3$ (3×50 mL). The combined extracts were then dried ($MgSO_4$), filtered and the solvent removed in vacuo to give pure product **33** as a colourless oil (58 mg, quantitative); $[\alpha]_D^{22}=-84$ (*c* 0.96 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2959, 2906, 1755; δ_H (400 MHz, $CDCl_3$) 0.11 [9H, s, Si(C*H*$_3$)$_3$], 0.95 (1H, app. t, *J*=4.3 Hz, C*H*H), 1.14 (1H, dd, *J*=7.0, 4.3 Hz, CH*H*), 2.08 (1H, m, C*H*) and 4.24 (2H, m, C*H*$_2$O); δ_C (100 MHz, $CDCl_3$) −3.1 (Si*C*H$_3$), 15.8 (*C*H$_2$), 16.2 (*C*), 22.6 (*C*H), 68.4 (*C*H$_2$) and 178.8 (*C*O); *m/z* (FAB) 171 [$(M+H)^+$, 35%], 155 (70), 127 (29), 111 (52), 81 (100) and 73 (50) [HRMS: found $(M+H)^+$, 171.0840. $C_8H_{14}O_2Si+H$ requires (M+*H*), 171.0841].

4.5.11. (1*R*,5*S*)-3-Phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexan-2-one 34. To a stirred solution of **30** (50 mg, 0.19 mmol) in CH_2Cl_2 (2 mL) at −78°C was added triethylsilane (61 μL, 0.38 mmol) and trimethylsilyltriflate (70 μL, 0.38 mmol). The reaction mixture was stirred at −78°C for 2 h before allowing to warm to room temperature and stirring overnight. The reaction was then quenched with saturated aqueous $NaHCO_3$ (2 mL) before extracting with CH_2Cl_2 (4×10 mL). The combined extracts were dried ($MgSO_4$), filtered and the solvent removed in vacuo to give crude product. This was purified by flash column chromatography (5% EtOAc–light petroleum) to give pure **34** as a white solid (37 mg, 79%), mp 74–76°C; $[\alpha]_D^{22}=+115$ (*c* 1.02 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2956, 2883, 1681, 1598 and 1492; δ_H (400 MHz, $CDCl_3$) 0.15 [9H, s, Si(C*H*$_3$)$_3$], 0.90 (1H, dd, *J*=4.1, 4.0 Hz, C*H*H), 1.11 (1H, dd, *J*=6.9, 4.1 Hz, CH*H*), 1.87 (1H, m, C*H*), 3.81 (1H, d, *J*=9.9 Hz, C*H*HNPh), 4.02 (1H, dd, *J*=9.9, 5.8 Hz, CH*H*NPh), 7.08 (1H, dt, *J*=7.5, 1.0 Hz, Ar*H*), 7.32 (2H, dt, *J*=7.5, 0.8 Hz, Ar*H*) and 7.56 (2H, dd, *J*=7.8, 0.9 Hz, Ar*H*); δ_C (100 MHz, $CDCl_3$) −2.8 (Si*C*H$_3$), 16.0 (*C*H), 16.3 (*C*H$_2$), 20.4 (*C*), 49.8 (*C*H$_2$), 119.2 (Ar*C*H), 123.7 (Ar*C*H), 128.7 (Ar*C*H), 139.7 (Ar*C*) and 176.8 (*C*O); *m/z* (EI) 245 (M^+, 78%), 230 (100), 156 (39), 145 (20) and 77 (9) (HRMS: found M^+, 245.1263. $C_{14}H_{19}NOSi$ requires M, 245.1236).

4.5.12. (1*R*,4*S*,5*S*)-4-Allyl-3-phenyl-1-trimethylsilyl-3-azabicyclo[3.1.0]hexan-2-one 35. To a stirred solution of **30** (100 mg, 0.38 mmol) in CH_2Cl_2 (3 mL) at −78°C were added trimethylsilyltriflate (0.14 mL, 0.77 mmol) and allyltrimethylsilane (0.12 mL, 0.77 mmol). After stirring at −78°C for 1 h the reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction was then quenched with saturated aqueous $NaHCO_3$ (2 mL), extracted with CH_2Cl_2 (3×10 mL), dried ($MgSO_4$), filtered and the solvent removed in vacuo to give crude product. This was purified by flash column chromatography (2% EtOAc–light petroleum) to give **35** as a white solid (70 mg, 64%), mp 78–81°C; $[\alpha]_D^{22}=+45$ (*c* 0.99 in $CHCl_3$); (Found: C, 71.11; H, 8.15; N, 5.05. Requires C, 71.53; H, 8.12; N, 4.91%); ν_{max} ($CHCl_3$)/cm^{-1} 2956, 2901, 1668, 1559 and 1492; δ_H (250 MHz, $CDCl_3$) 0.14 [9H, s, Si(C*H*$_3$)$_3$], 0.87 (1H, dd, *J*=4.1, 4.1 Hz, C*H*HCSi), 1.07 (1H, dd, *J*=6.9, 4.1 Hz, CH*H*CSi), 1.70 (1H, dd, *J*=6.9, 4.1 Hz, C*H*CHNPh), 2.22–2.43 (2H, m, CH_2=CHC*H*$_2$), 4.29 (1H, dd, *J*=6.5, 3.2 Hz, C*H*CH_2CH=CH_2), 5.05–5.16 (2H, m, CH=C*H*$_2$), 5.76 (1H, m, CH_2=C*H*CH_2), 7.12 (1H, t, *J*=7.3 Hz, Ar*H*), 7.32 (2H, t, *J*=7.4 Hz, Ar*H*) and 7.42 (2H, d, *J*=7.5 Hz, Ar*H*); δ_C (100 MHz, $CDCl_3$) −2.9 (SiCH_3), 15.7 (*C*H_2), 19.9 (*C*), 20.9 (*C*H), 38.0 (*C*H_2), 59.8 (*C*H), 118.9 (*C*H_2), 123.1 (Ar*C*H), 124.8 (Ar*C*H), 128.8 (Ar*C*H), 132.4 (*C*H), 138.1 (Ar*C*) and 176.3 (*C*O); *m/z* (EI) 285 (M^+, 3%), 270 (4), 244 (100), 104 (7), 77 (14) and 73 (97) (HRMS: found M^+, 285.1543. $C_{17}H_{23}NOSi$ requires M, 285.1549).

4.5.13. (1*R*,2*R*,5*S*,6*S*,7*S*)-5-Allyl-4-phenyl-2-trimethylsilyl-4-azatricyclo[5.2.1.0^{2,6}]dec-8-en-3-one 36. To a stirred solution of **31** (50 mg, 0.16 mmol, $[\alpha]_D^{22}=+39$ (*c* 0.31 in $CHCl_3$)), in CH_2Cl_2 (2 mL) at −78°C were added trimethylsilyltriflate (58 μL, 0.32 mmol) and allyltrimethylsilane (50 μL, 0.32 mmol). After stirring at −78°C for 2 h the reaction mixture was allowed to warm to room temperature and stirred overnight before being quenched with saturated aqueous $NaHCO_3$ (2 mL), extracted with CH_2Cl_2 (3×10 mL), dried ($MgSO_4$), filtered and the solvent removed in vacuo to give crude product. This was purified by flash column chromatography (10% EtOAc–light petroleum) to give **36** as a white solid (35 mg, 65%), mp 97–100°C; $[\alpha]_D^{23}=+33$ (*c* 0.61 in $CHCl_3$); ν_{max} ($CHCl_3$)/cm^{-1} 2966, 1695, 1668, 1596 and 1493; δ_H (400 MHz, $CDCl_3$) 0.26 [9H, s, Si(C*H*$_3$)$_3$], 1.43 (1H, dt, *J*=8.5, 1.7 Hz, C*H*H), 1.46 (1H, d, *J*=8.5 Hz, CH*H*), 2.00 (1H, m, CH_2=CHC*H*H), 2.46 (1H, m, CH_2=CHCH*H*), 2.58 (1H, dd, *J*=4.1, 2.4 Hz, C*H*CHNPh), 3.10 (1H, m, C*H*), 3.26 (1H, m, C*H*), 3.65 (1H, ddd, *J*=10.8, 3.4, 2.4 Hz, C*H*NPh), 5.11–5.16 (2H, m, CH=C*H*$_2$), 5.74 (1H, m, C*H*=CH_2), 6.21 (1H, dd, *J*=5.6, 2.9 Hz, C*H*=CH), 6.41 (1H, dd, *J*=5.6, 2.9 Hz, CH=C*H*), 7.16 (1H, t, *J*=7.4 Hz, Ar*H*), 7.23 (2H, d, *J*=7.3 Hz, Ar*H*) and 7.33 (2H, t, *J*=7.4 Hz, Ar*H*); δ_C (100 MHz, $CDCl_3$) −1.7 (SiCH_3), 38.9 (*C*H_2), 44.7 (*C*H), 47.8 (*C*H), 47.9 (*C*H), 49.3 (*C*H_2), 50.2 (*C*), 61.2 (*C*H), 118.1 (*C*H_2), 124.5 (*C*H), 125.5 (*C*H), 128.8 (*C*H), 132.6 (*C*H), 133.8 (*C*H), 137.9 (*C*), 140.7 (*C*H) and 177.0 (*C*O); *m/z* (EI) 337 (M^+, 2%), 296 (35), 271 (10), 230 (100) and 73 (32) (HRMS: found M^+, 337.1874. $C_{21}H_{27}NOSi$ requires M, 337.1861).

4.5.14. (3*S*,4*R*)-4-Benzoyl-3-phenylselenomethyl-1-phenylpyrrolidine-2,5-dione 37. $NaBH_4$ (22 mg, 0.58 mmol) was added to a solution of diphenyl diselenide (90 mg, 0.29 mmol) in EtOH (1.5 mL) and the reaction mixture stirred for 10 min before addition of a solution of **24** (50 mg, 0.19 mmol) in EtOH (3 mL). This was stirred for a further 30 min before quenching with 1 M HCl (5 mL) and adding water (30 mL). The solution was extracted with CH_2Cl_2 (3×30 mL) and the combined extracts dried ($MgSO_4$), filtered and the solvent removed in vacuo. The crude product obtained was purified by flash column chromatography (20% EtOAc–light petroleum) to give **37** as a white solid (59 mg, 68%), mp 127–129°C; $[\alpha]_D^{24}=+13$ (*c* 0.91 in $CHCl_3$); (Found: C, 64.25; H, 4.21; N, 2.92. Requires C, 64.29; H, 4.27; N, 3.12%); ν_{max} ($CHCl_3$)/cm^{-1} 2927, 2855, 1781, 1716, 1684, 1598, 1580 and 1500; δ_H (400 MHz, $CDCl_3$) 3.37 (1H, dd, *J*=13.4, 7.2 Hz, C*H*H), 3.44 (1H, dd, *J*=13.4, 4.6 Hz, CH*H*), 4.08 (1H, dt, *J*=7.2, 4.6 Hz, CH_2C*H*), 4.90 (1H, d, *J*=4.6 Hz, C*H*COPh) and 7.18–7.93 (15H, m, Ar*H*); δ_C (68 MHz, $CDCl_3$) 27.6 (*C*H_2), 44.3 (*C*H), 54.9 (*C*H), 126.3 (Ar*C*H), 126.5 (Ar*C*H), 128.0 (Ar*C*), 128.6 (Ar*C*H), 128.8 (Ar*C*H), 129.1 (Ar*C*H), 129.6 (Ar*C*H), 129.8 (Ar*C*H), 131.5 (Ar*C*), 133.5 (Ar*C*H), 134.2 (Ar*C*H), 133.5 (Ar*C*), 170.9 (*C*O), 176.1 (*C*O) and 192.3 (Ph*C*O); *m/z* (FAB) 450 [$(M+H)^+$, 100%] [HRMS: found $(M+H)^+$, 450.0616. $C_{24}H_{19}NO_3Se$ + H requires (M+*H*), 450.0608].

4.6. X-Ray crystallography

4.6.1. Cyclopropylimide 3a. Crystal data. $C_{14}H_{17}NO_2Si$, M=259.38, orthorhombic, *a*=6.385(2), *b*=12.228(2), *c*=17.906(3) Å, *U*=1398.0(5) Å^3, *T*=150(2) K, space group $P2_12_12_1$ (No. 19), *Z*=4, D_c=1.237 cm^{-3}, μ(Mo Kα) = 0.162 mm^{-1}, 2444 unique reflections corrected for absorption (R_{int} 0.023) and used in all calculations. Final R_1 [2368$F>4\sigma(F)$]=0.0445 and *wR*(all F^2) was 0.0969. The Flack absolute structure parameter refined to 0.1(2). CCDC deposition number 179331.

4.6.2. Tricyclic imide 6. Crystal data. $C_{18}H_{21}NO_2Si$, M=311.45, monoclinic, *a*=6.2395(4), *b*=14.8305(11), *c*=9.4695(11) Å, β=106.490(5)°, *U*=840.22(13) Å^3, *T* = 298(2) K, space group $P2_1$ (No. 4), *Z*=2, D_c=1.231 cm^{-3}, μ(Mo Kα)=0.146 mm^{-1}, 2953 unique reflections measured (R_{int} 0.035) and used in all calculations. Final R_1 [2608$F>4\sigma(F)$]=0.0358 and *wR*(all F^2) was 0.0893. The Flack absolute structure parameter refined to 0.00(14). CCDC deposition number 179330.

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