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Use of temporary tethers in the intramolecular [2+2] photocycloaddition reactions of tetrahydrophthalimide derivatives: a new approach to complex tricyclic lactones

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Abstract—The intramolecular [2+2] photocycloaddition reactions of a series of alkenols tethered to ethanolamine, L-(+)-valinol and *R*-(−)-2-phenylglycinol derived 3,4,5,6-tetrahydrophthalimides via a carbonate or silicon linkage have been examined. These [2+2] photocycloadditions gave the corresponding cyclobutanes in high yield with complete *endo* control in all cases and with diastereoselectivities as high as 8:1 with the chiral tethers. The cleavage of the temporary tethers by either desilylation or hydrolysis provided the *endo* diols. Cleavage of the ethanolamine linkage by reduction/hydrolysis precipitated an acid-catalysed fragmentation/ring expansion sequence to generate complex tricyclic lactones.

1. Introduction

Inter- and intramolecular [2+2] photocycloaddition reactions have long been recognised as important and efficient synthetic transformations for the construction of cyclobutanes and cyclobutenes. As such they have found application as pivotal steps in synthesis of natural products and pharmacologically active compounds.[1] Although simple intermolecular [2+2] cycloadditions (e.g., enone/alkene) can be very efficient, they often suffer from poor stereocontrol as a result of a typically stepwise triplet biradical reaction manifold. In recent years, there has been increasing attention given to the use of temporary silicon tethers as stereocontrol elements for various reactions such as radical cyclisations,[2] [4+2] cycloadditions[3] and hydrosilylation reactions.[4] Fleming et al.,[5] Crimmins and Guise[6] and Penkett et al.[7] have reported the use of silicon tethers in [2+2] photocycloadditions as a regio- and stereocontrolled carbon–carbon bond forming methodology. The use of disposable tethers has also been widely applied to other cycloadditions.[8]

Asymmetric [2+2] photocycloaddition methodology using chiral auxiliaries is far less developed than other areas of asymmetric synthesis, although a number of systems have been studied.[9] For example, Piva and co-workers[10] developed some promising results using chiral hydroxy acids as spacers for controlling asymmetric intramolecular [2+2] photocycloadditions. Around this time we also reported highly diastereoselective [2+2] photocycloadditions of alkenols tethered via a silicon or carbonate linkage to L-(+)-valinol derived tetrahydrophthalimides.[11]

In the last 10 years, highly efficient intermolecular [2+2] imide photocycloadditions have been investigated by us for the synthesis of polycyclic cyclobutanes and cyclobutenes.[12] For example, 3,4,5,6-tetrahydrophthalic anhydride (THPA, **1**) and the corresponding imide (THPI, **2**) underwent efficient intermolecular photocycloaddition with alkenols to give the corresponding cyclobutanes in excellent yields with diastereoselectivities as high as 10:1.[12] The major product in all cases was the *exo* isomer **3**, which, due to the absence of any absolute stereochemical control, was formed as a racemic mixture. We then elected to study the cycloaddition reactions of alkenols linked to THPI derivatives in order to achieve two goals: (a) the selective formation of the *endo* isomer **4** and (b) by the use of chiral linkers to control the absolute stereochemistry during [2+2] cycloaddition to **4**. If the cycloadducts **6** or **7** could be formed selectively from **5** then cleavage of the linker 'X' would lead to synthesis of enantiopure *endo* cycloadducts (Scheme 1). Our key postulate involved the assumption that **5** could adopt a 'double chairlike' conformation whereby the chirality at C* may control the facial selectivity during cycloaddition.

Keywords: Photochemistry; Cycloadditions; Temporary tethers; Acid-catalysed rearrangements.
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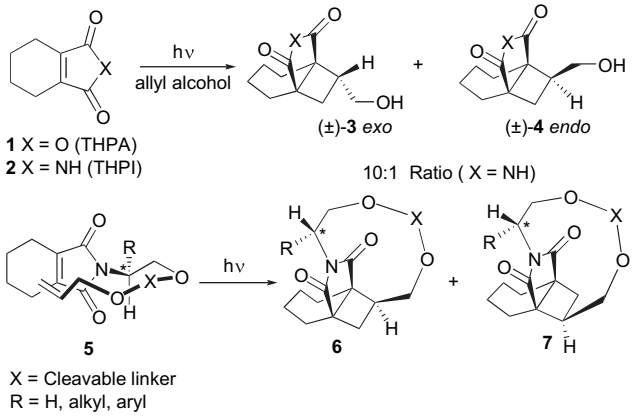
Appropriate tuning of this selectivity could be engineered by choice of R.



Scheme 1.

2. Results and discussion

2.1. Ethanolamine tethers

We firstly elected to study the intramolecular [2+2] photocycloaddition reactions of alkenols linked to THPI derivatives with non-chiral derived tethers in order to ascertain if complete *endo* selectivity could be achieved during cycloaddition. Initially the use of ethanolamine as the simplest linker was investigated. Thus the tetrahydrophthalimide derivative **8** was synthesised in excellent yield (98%) by the reaction of THPA and ethanolamine at reflux in toluene. In order to tether **8** to allyl alcohol, a mixed carbonate linkage was investigated. Reaction of **8** with allyl chloroformate yielded the carbonate **9** in excellent yield (95%). Irradiation of **9** in MeCN for 2 h resulted in formation of the (±)-*endo* cycloadduct **10** in excellent yield (95%). Pleasingly, none of the corresponding *exo* isomer could be detected. Hydrolysis of **10** formed the racemic *endo* diol **11** in good yield (75%) (Scheme 2).[13] Synthesis of the silicon-tethered variant **12** (X=Si^{i}Pr$_2$) was achieved, in overall moderate yield (53%), by treatment of **8** with $Cl_2Si^iPr_2$ followed by an excess of allyl alcohol. A by-product in this reaction is the Si^{i}Pr$_2$-linked bisallyl ether.[3,6,7] Irradiation of **12** in MeCN for 90 min again gave the (±)-*endo* cycloadduct **13** as the sole product in 74% yield. Treatment of **13** with Bu_4NF yielded the racemic diol **11** in good yield (82%) (Scheme 2). The use of a diphenylsilyl linker was also investigated in this series and the silaketal **14** was prepared by treatment of diphenyldichlorosilane in similar fashion.[2,5,6] Irradiation of **14** again yielded the (±)-*endo* cycloadduct **15** as the sole product in excellent yield (91%). Desilylation of **15** under standard conditions yielded the racemic diol **11** in excellent yield (95%) (Scheme 2).

The highly selective *endo* mode of cycloaddition obtained in these three experiments was confirmed by NOE experiments on both the carbonate **10** and diol **11** as illustrated in Figure 1.

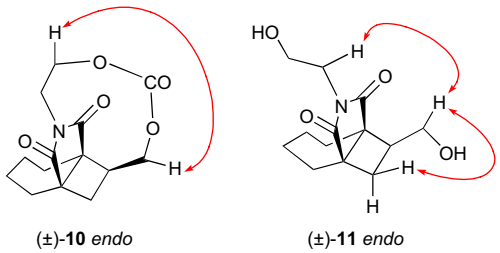
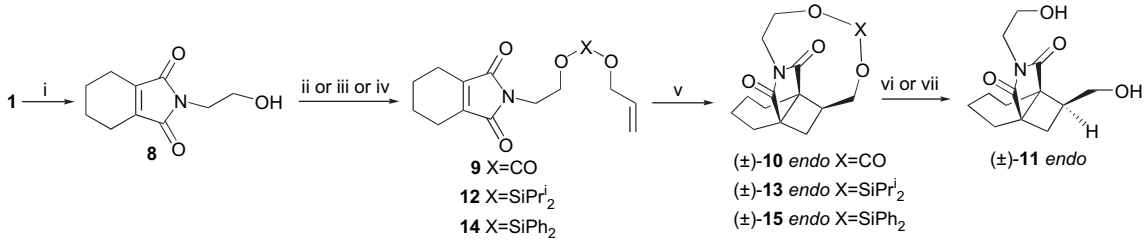


Figure 1. NOE correlations of (±)-**10** and **11** *endo* isomers.

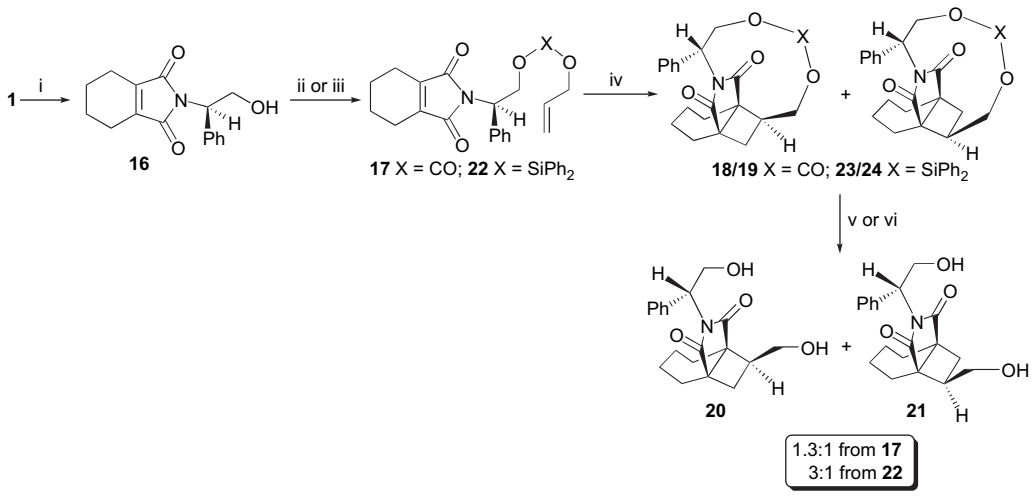
2.2. (*R*)-(−)-2-Phenylglycinol tether

Tethered chiral ethanolamines were then investigated as the diastereoselective control element of the *endo* selective cycloadditions as postulated in Scheme 1. Treatment of THPA with (*R*)-(−)-2-phenylglycinol gave the corresponding tetrahydrophthalimide **16** in excellent yield (99%). Reaction of this with allyl chloroformate gave the carbonate **17** (56%),[13] which upon irradiation gave an excellent yield (98%) of the photocycloadducts **18** and **19**. Hydrolysis was very capricious and afforded (34%) an inseparable mixture of the diols **20** and **21** in a poor diastereomeric ratio of 1.3:1 (13% de). To improve the diastereoselectivity of the photocyclisation leading to **20** and **21**, the alternative $SiPh_2$ linkage was studied. It was argued that the bulkier diphenylsilane unit would afford less conformational mobility in the putative exited state (cf. **5**, Scheme 1). Treatment of **16** with Cl_2SiPh_2 in MeCN followed by an excess of allyl alcohol gave the corresponding diphenylsilane-linked tetrahydrophthalimide **22** in 46% overall yield. When **22** was irradiated in MeCN, two diastereomeric cycloadducts **23** and **24** were isolated in excellent yield (89%). TBAF cleavage of the $SiPh_2$ linkage afforded the diastereomeric diols **20** and **21** in excellent yield (93%) and in a greatly improved 3:1 ratio (Scheme 3).

The diastereoselectivity obtained in the formation of **20** and **21** from **22** (50% de), although good compared to the



Scheme 2. Reagents and conditions: (i) ethanolamine, toluene, heat, 98%; (ii) allyl chloroformate, pyridine, THF, 0 °C, 95% for **9**; (iii) $Cl_2Si^iPr_2$, Et_3N, CH_2Cl_2, rt, then allyl alcohol, 53% for **12**; (iv) Cl_2SiPh_2, Et_3N, DMF, rt, then allyl alcohol, 54% for **14**; (v) *hν*, MeCN, 95% for **10**, 74% for **13**, 91% for **15**; (vi) NaOH, THF/H_2O, rt, 75% from **10**; (vii) Bu_4NF, THF, rt, 82% from **13**, 95% from **15**.

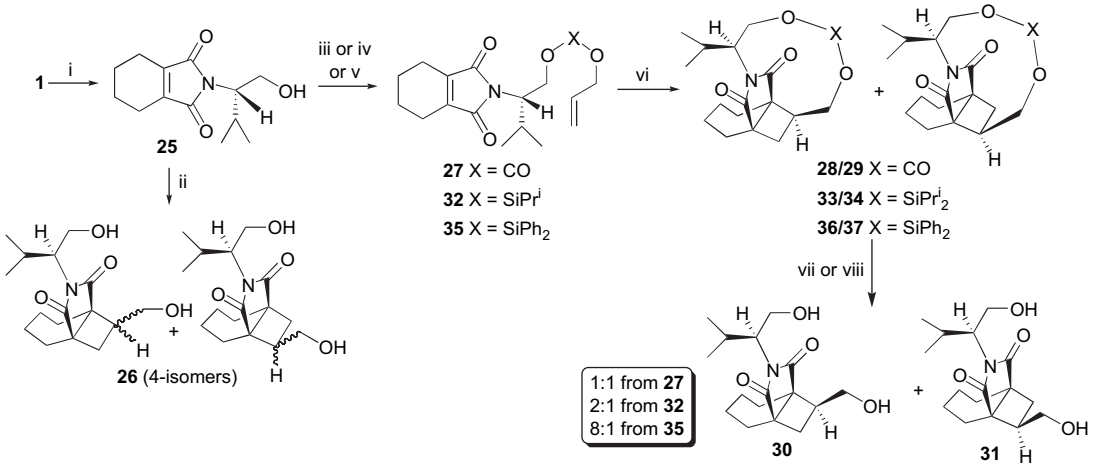


Scheme 3. Reagents and conditions: (i) (*R*)-(−)-2-phenylglycinol, toluene, heat, 99%; (ii) allyl chloroformate, pyridine, THF, 0 °C, 56% for **17**; (iii) Cl_2SiPh_2, Et_3N, MeCN, rt, then allyl alcohol, 46% for **22**; (iv) *hν*, MeCN, 98% for **18/19**, 89% for **23/24**; (v) NaOH, THF/H_2O (1:1), rt, 34% from **18/19**; (vi) Bu_4NF, THF, rt, 93% from **23/24**.

carbonate tether in **17**, falls short of the standards expected for a modern chiral auxiliary. This suggested to us that (*R*)-(−)-2-phenylglycinol was not optimal and alternative readily available auxiliaries were explored.

2.3. L-(+)-Valinol as a tether

Anhydride **1** was treated with L-(+)-valinol[14] to afford the corresponding tetrahydrophthalimide **25** in excellent yield (95%). As an aside, irradiation of **25** with allyl alcohol in an intermolecular cycloaddition was investigated. This provided a complex mixture (75%) of four cycloadducts,[11] whose ^{1}H NMR spectroscopy indicated a mixture of various *exo* and *endo* diastereoisomers of **26**. This result clearly shows the poor stereocontrol exerted by the auxiliary in an intermolecular reaction. Reaction of **25** with allyl chloroformate as before gave the carbonate **27** (61%).[13] Irradiation of **27** led efficiently (90%, 40 min) to two diastereomeric cycloadducts **28** and **29**. Hydrolysis afforded the two inseparable diastereomeric diols **30** and **31** in good yield (79%) but in a ratio of 1:1. Although this result is disappointing in terms of asymmetric induction (on changing from Ph to ^{i}Pr), the yield of these photocycloaddition steps was high and the irradiation times were short, thus indicating that the basic photocycloaddition was not hampered by the introduction of either phenyl or isopropyl groups in the ethanolamine tether. Attention was then focussed on a silicon linkage. Synthesis of the Si^iPr_2-linked variant was carried out as before to **32** in 71% overall yield. Irradiation (90 min) of **32** gave a mixture of the cycloadducts **33** and **34** (74%), which upon treatment with TBAF gave the diols **30/31** as an inseparable mixture of diastereoisomers (87%) with moderate selectivity (2:1). Treatment of **25** with Cl_2SiPh_2 in DMF followed by treatment with an excess of allyl alcohol gave the $SiPh_2$-tethered variant **35** (60%). Irradiation of **35** gave an excellent yield (86%) of the cycloadducts **36/37**. Removal of the silicon linkage gave the diastereomeric diols **30** and **31** (99%) in a much improved ratio of 8:1 (Scheme 4).[2,5,6]



Scheme 4. Reagents and conditions: (i) L-(+)-valinol, toluene, heat, 95%; (ii) *hν*, allyl alcohol, MeCN, 6 h, 75%; (iii) allyl chloroformate, pyridine or 2,6-lutidine, THF, 0 °C, 61% for **27**; (iv) $Cl_2Si^iPr_2$, Et_3N, CH_2Cl_2, rt, then allyl alcohol, 71% for **32**; (v) Cl_2SiPh_2, Et_3N, DMF, rt, then allyl alcohol, 60% for **35**; (vi) *hν*, MeCN, 90% for **28/29**, 74% for **33/34**, 86% for **36/37**; (vii) KOH, THF/H_2O (1:1), 79% from **28/29**; (viii) Bu_4NF, THF, rt, 87% from **33/34**, 99% from **36/37**.

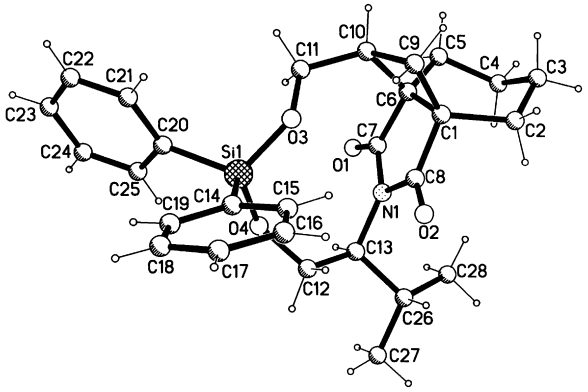


Figure 2. X-ray structure of diastereomeric cycloadduct **36**.

The direct absolute assignment of the stereochemistry of **30/31** formed from these cycloadditions proved extremely difficult as even the 8:1 mixture was an oil and inseparable by chromatographic methods. Attempts to carry out a direct NOE analysis of this mixture did not yield conclusive results. Fortunately, although inseparable by chromatography, recrystallisation of the 8:1 mixture of **36/37** from Et_2O yielded a pure sample (by ^1H and ^{13}C NMR spectroscopy) of the major diastereoisomer (**36**), which was then slowly crystallised to afford a single crystal of **36** of suitable quality for X-ray analysis (Fig. 2), thus establishing the major diastereoisomer formed in these photocycloadditions.

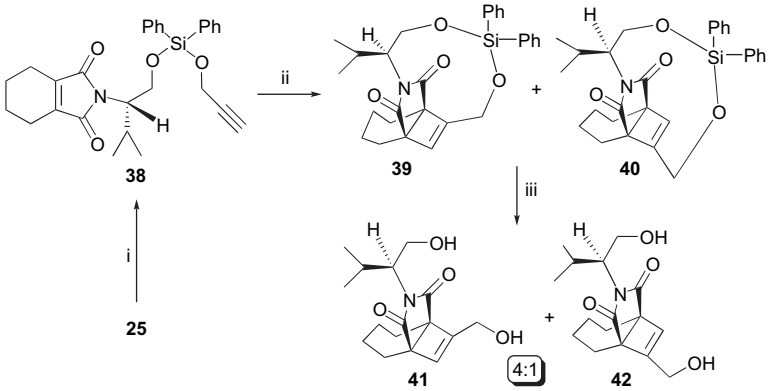
At the start of this study the conformation depicted for **5** in Scheme 1 was only tentatively proposed to confer stereocontrol during cycloaddition and was considered as an adventurous but plausible model. It is intriguing therefore that in light of the results confirmed by X-ray crystallography this now serves as a useful explanation of the origin of the major diastereomer **36** formed during the cycloaddition of **35**.

In an attempt to explore the possibilities for the selective synthesis of cyclobutenes, the valinol derivative **25** was treated with Cl_2SiPh_2 followed by an excess of propargyl alcohol to afford the $SiPh_2$-tethered alkynol variant **38** (58%). Irradiation of **38** lead to the corresponding cyclobutenes **39** and **40** in only moderate yield (49%). Desilylation with TBAF gave the diastereomeric diols **41** and **42** (81%) in the ratio 4:1. Although this ratio was not as good as in the allyl alcohol case **36/37**, it is, to our knowledge, the first reported example of this type of diastereoselective cyclobutene formation (Scheme 5).

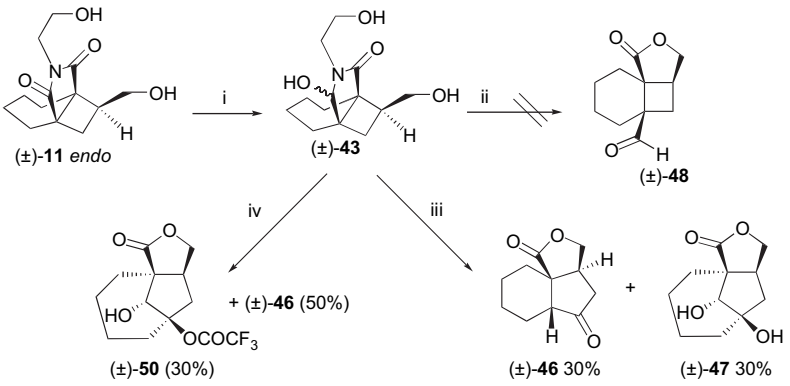
2.4. Tether cleavage

Although cleavage of the silicon/carbonate linkages was straightforward, cleavage of the imide bound linkers was much more difficult and was found to be not possible under direct hydrolytic cleavage with aqueous hydroxide or mineral acid. Ganem and co-workers[15] reported an easy and near-neutral method for removing the amine group from *N*-alkyl substituted phthalimides involving partial reduction with $NaBH_4$[15–17] followed by hydrolysis of the hydroxypyrrolidone with glacial acetic acid resulting in lactone formation. Subjecting **11** to the same reaction conditions gave the hydroxypyrrolidone derivative **43**, in good yield (80%), as a mixture of epimers (3:1) presumably arising from the reduction of this least sterically encumbered imide carbonyl. However, despite numerous attempts the hydroxypyrrolidone derivative **43** failed to lactonise to **48** in glacial acetic acid at reflux and gave only the recovered starting material (Scheme 6). Heating **43** in 4 M H_2SO_4 at 80 °C for 12 h gave the rather unexpected and appealing formation of the tricyclic keto-lactone **46** in 30% yield and tricyclic 1,2-diol-lactone **47** in 30% yield (Scheme 6).[18,19] The same acid-catalysed rearrangement was carried out using trifluoroacetic acid instead of H_2SO_4. This gave the tricyclic lactone **46** in higher isolated yield (50%) along with the hydroxy-trifluoroacetate **50** in 30% yield (Scheme 6).

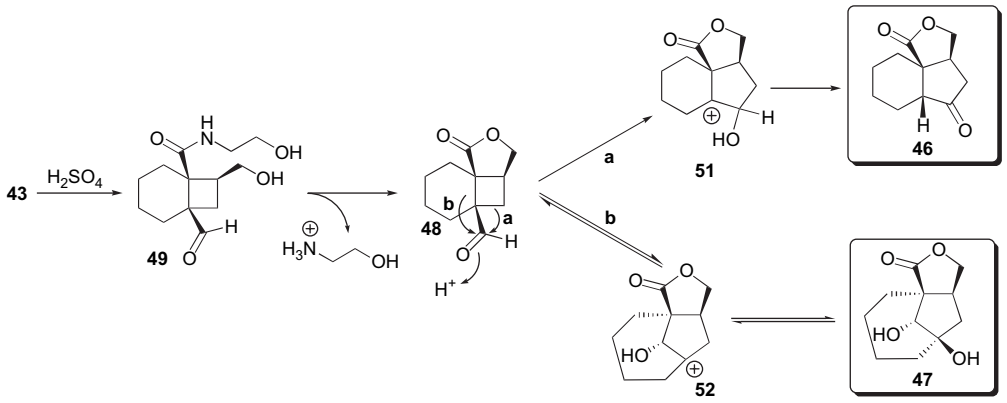
Plausible mechanisms leading to the formation of **46** and **47** and other products are illustrated in Scheme 7. It is likely that ring opening of the hydroxypyrrolidone in **43** leads to the amide aldehyde **49**, which undergoes lactonisation with loss of ethanolamine. The reverse of this is probably suppressed under the strongly acidic conditions by capture of the ethanolamine by protonation. The resulting lactone-aldehyde **48** then undergoes acid-catalysed cyclobutane ring expansion by two classic Wagner–Meerwein type pathways. Pathway 'a' leads to the cation **51**, which upon proton loss and tautomerization gives the keto-lactone **46**. The alternative pathway 'b' leads to the cation **52**, which upon solvolysis yields the diol **47**. Solvolysis of **52** with trifluoroacetate accounts for the formation of **49** observed during the reaction of **43** in neat TFA.



Scheme 5. Reagents and conditions: (i) Cl_2SiPh_2, Et_3N, MeCN, rt, then prop-2-yn-1-ol, 58%; (ii) *hν*, MeCN, 49%; (iii) Bu_4NF, THF, rt, 81%.



Scheme 6. Reagents and conditions: (i) $NaBH_4$, 2-propanol/H_2O, rt, 80%; (ii) CH_3COOH (glacial), heat; (iii) 4 M H_2SO_4 at 80 °C for 12 h; (iv) TFA, reflux, 12 h.



Scheme 7.

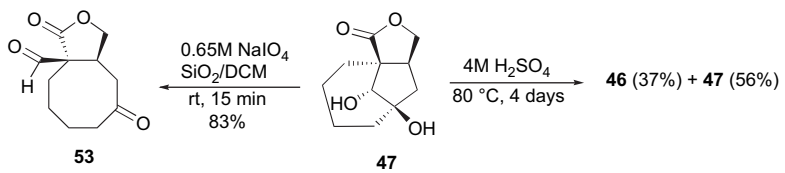
Assignment of **47** was further supported by the typical reactions of 1,2-diols such as the pinacol rearrangement and oxidative cleavage. The pinacol rearrangement of **47** was carried out in 4 M H_2SO_4 at 80 °C and after four days gave the rearranged keto-lactone **46** in 37% yield and recovered the starting diol **47** (56%). This result clearly suggests that the aldehyde **48** and diol **47** are actually in equilibrium during the reaction as outlined in Scheme 7. Subjecting pure keto-lactone **46** to the same conditions did not give any evidence of reversibility. Pleasingly, the oxidative cleavage of **47** using a sodium periodate/wet silica gel protocol[20] afforded the desired eight-membered keto-aldehyde **53** in excellent yield (Scheme 8). Final confirmation of the structures **46** and **47** was obtained by X-ray crystallography (Fig. 3).

In summary, the intramolecular photocycloaddition of alkenols attached via a temporary carbonate or silicon linkage to ethanolamine-linked tetrahydrophthalimide derivatives has been investigated. The cycloadditions have been shown to proceed in excellent overall yields with complete control of *endo* selectivity in contrast to the *exo*-selective intermolecular reaction. Further studies using chiral, amino acid derived tethers demonstrate that the valinol derived tetrahydrophthalimide unit is superior to phenylglycinol in controlling diastereoselectivity during photocycloaddition. With the valinol tether, de as high as 78% was observed; an impressive result compared to the corresponding intermolecular equivalent, which afforded no observable stereocontrol. Further synthetic studies on the cycloadducts have shown that they can undergo useful synthetic transformations. The resulting cleaved and partially reduced diol products undergo Wagner–Meerwien ring expansion reactions yielding further polycyclic products as well as providing unique access to an 8,5-fused keto-lactone ring system.

3. Experimental section

3.1. General

NMR spectra were recorded using a Jeol JNM-EX 270 and Varian NMR Gemini 300 spectrometers. Samples were dissolved in deuterochloroform (unless otherwise noted) using



Scheme 8.

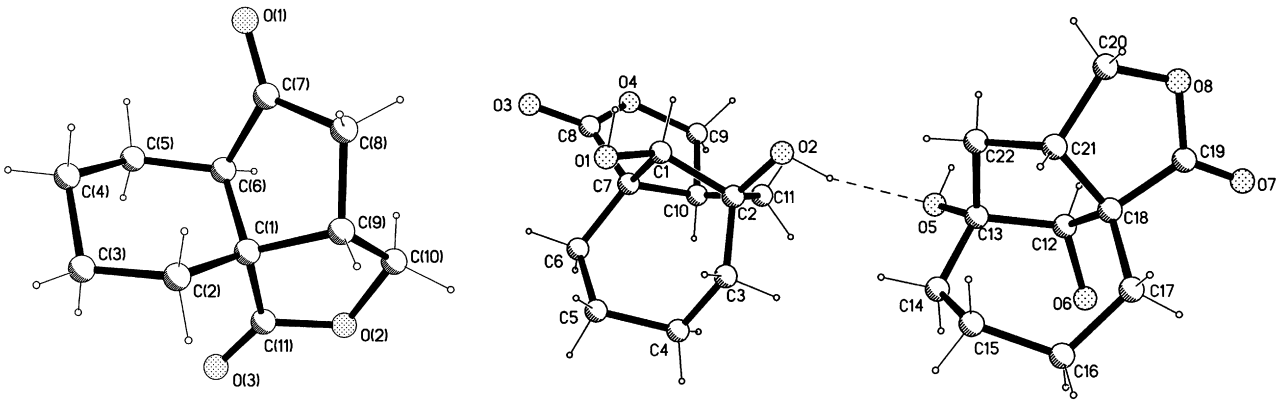


Figure 3. X-ray structures of tricyclic keto-lactone **46** and 1,2-diol **47** (H-bonded pair in unit cell).

tetramethylsilane (TMS) as an internal reference. All carbon-13 spectra were assigned with the aid of DEPT experiments. Infrared spectra were recorded on a Perkin–Elmer 1720 X FT spectrometer using sodium chloride plates. Low-resolution electron impact mass spectra were run on Kratos MS 25 and elemental microanalyses were carried out on a Carlo Erba EA 1108. Optical rotations were measured on Perkin–Elmer 141 Polarimeter. Flash chromatography was carried out using Matrix silica 60 (70–200 μm). Camlab polygram® SIL G/UV_{254} plastic backed plates (0.25 mm layer of silica) were used for TLC analyses. Chromophoric compounds were visualised by UV light (254 nm) and subsequent staining with alkaline potassium permanganate solution or iodine. Melting points were obtained using a Köpfler hot stage apparatus and are uncorrected. All reactions were carried out under an atmosphere of oxygen-free nitrogen. Petroleum ether refers to light petroleum (bp 40–60 °C). Evaporation of solvents was carried out on a Büchi rotary evaporator. Toluene, acetonitrile, dichloromethane and petroleum ether were distilled from calcium hydride; THF and diethyl ether were distilled from sodium and benzophenone; DMF was initially dried using activated 4 Å molecular sieves overnight followed by distillation under reduced pressure. Photochemical reactions were carried out in a 100 mL Pyrex immersion well photoreactor. The reaction mixture was initially degassed by passage of nitrogen for 10 min and then irradiated for the specified length of time under an atmosphere of nitrogen. The radiation source was a 125 W medium pressure, water cooled, mercury discharge lamp (Osram HQL (MBF-U) bulbs).

3.2. General procedure 1, imide formation

To a solution of 3,4,5,6-tetrahydrophthalic anhydride (THPA, **1**) in toluene was added the amine (1 equiv). The reaction flask was fitted with a condenser via a Dean–Stark trap and heated at reflux for 3 h and then the solvent was concentrated under reduced pressure. The crude product was subjected to flash chromatography (petrol/ethyl acetate) to afford the imide.

3.3. General procedure 2, carbonate formation

To a stirred solution of the imido-alcohol in THF was added pyridine at 0 °C. After stirring for 20 min allyl chloroformate was added dropwise at 0 °C and a white precipitate formed after completion of addition. The white reaction mixture was stirred for 30 min at 0 °C and then for 3 h at rt, then the solution filtered and the solvent removed under reduced pressure. Et_2O was added and the solution filtered again, washed with H_2O and brine and dried over anhydrous $MgSO_4$. Filtration and concentration under reduced pressure followed by purification via flash chromatography (petrol/ethyl acetate) gave the carbonate product.

3.4. General procedure 3, silicon-tethered compounds

Part 1: to a stirred solution of the imido-alcohol in the specified solvent was added Et_3N and the mixture allowed to stir at rt for 20 min, after which time the dichlorosilane was added dropwise. The reaction mixture was stirred overnight at rt and then the solvent was concentrated under reduced pressure to leave the crude product, which was used immediately in *part 2* without purification.

Part 2: a mixture of allyl or propargyl alcohol and Et_3N in the solvent was added dropwise to a solution of the crude product in the solvent. The resulting reaction mixture was stirred overnight at rt and then the solvent was concentrated under reduced pressure to leave a brown solid, which was dissolved in saturated aqueous sodium bicarbonate, extracted with EtOAc, dried over $MgSO_4$ and then concentrated under reduced pressure to afford a brown oil. The residue was purified by flash chromatography (petrol/ethyl acetate) to afford the silicon-tethered products.

3.4.1. 2-(2-Hydroxyethyl)-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 8. Following *general procedure 1*, using THPA (3.51 g, 23.07 mmol), ethanolamine (1.39 mL, 23.07 mmol) and toluene (70 mL), afforded **8** as a pale yellow oil, which slowly solidified to a white solid (4.40 g, 98%); mp 50–52 °C. IR (DCM thin film): 3460, 1770, 1715 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 3.73–3.60 (4H, m), 2.70 (1H, m), 2.34–2.25 (4H, m), 1.80–1.69 (4H, m); ^{13}C NMR ($CDCl_3$, 67.80 MHz): δ 171.6, 141.8, 61.2, 40.4, 21.3, 20.0; LRMS (EI): *m/z* 195 (18.6%, M^+), 164 (100), 152 (15.4), 135 (5.6), 107 (11.6), 79 (16.2); Anal. Calcd for $C_{10}H_{13}O_3N$: C, 61.52; H, 6.71; N, 7.17. Found. C, 61.34; H, 6.71; N, 7.12.

3.4.2. Carbonic acid-2-(1,3-dioxo-1,3,4,5,6,7-hexahydro-2*H*-isoindole-2-yl)ethyl-2-propenyl ester 9. Following

general procedure 2, using **8** (2.20 g, 11.27 mmol), THF (50 mL), pyridine (1.12 mL, 13.85 mmol), allyl chloroformate (1.47 mL, 13.85 mmol), afforded **9** as a pale yellow oil (2.98 g, 95%). IR (neat): 1760, 1714, 1649 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 6.00–5.80 (1H, m), 5.40 (1H, dq, J=17.3, 1.5 Hz), 5.30 (1H, dq, J=10.5, 1.4 Hz), 4.65 (2H, dt, J=5.7, 1.5 Hz), 4.29 (2H, t, J=5.6 Hz), 3.89 (2H, t, J=5.6 Hz), 2.34 (4H, m), 1.76 (4H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 170.8, 154.7, 141.7, 131.5, 118.8, 68.5, 64.9, 36.2, 21.1, 19.8; LRMS (EI): *m/z* 279 (0.8%, M^+), 177 (100), 164 (70.9), 107 (10.8), 77 (12.4), 41 (20.8); Anal. Calcd for $C_{14}H_{17}O_5N$: C, 60.20; H, 6.13; N, 5.01. Found: C, 60.42; H, 6.13; N, 5.18.

3.4.3. (2*R,8a*S**,9a*R**,13a*S**)-Octahydro-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobuta[1,2-*h*][1,3,6]-dioxazecine-1,6,14-trione 10.** A solution of **9** (2.40 g, 8.59 mmol) in acetonitrile (100 mL) was irradiated for 2 h. The solvent was removed under reduced pressure and the white solid residue was purified by flash chromatography (petrol/ethyl acetate 1:1) to afford **10** as a white solid (2.29 g, 95%); mp 156.5–165 °C. IR (DCM thin film): 1764, 1699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 4.60 (2H, m), 4.30 (1H, m), 4.11 (2H, m), 3.80 (1H, m), 2.75 (1H, m), 2.56 (1H, dd, J=13.3, 10.8 Hz), 2.46 (1H, dd, J=13.3, 6.3 Hz), 2.30 (1H, m), 1.85 (1H, m), 1.80–1.50 (4H, m), 1.50–1.00 (2H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 182.5, 181.6, 151.9, 68.0, 66.7, 47.2, 43.1, 42.2, 40.1, 30.3, 27.8, 27.1, 19.5, 19.4; LRMS (EI): *m/z* 279 (6.9%, M^+), 177 (10.3), 61 (21.4), 43 (100); Anal. Calcd for $C_{14}H_{17}O_5N$: C, 60.20; H, 6.13; N, 5.01. Found: C, 59.96; H, 6.12; N, 4.84.

3.4.4. 2-[2-[[Bis(1-methylethyl)(2-propenyloxy)silyl]-oxy]ethyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 12. Following *general procedure 3*, using in *part 1*; **8** (0.35 g, 1.79 mmol), DCM (30 mL), Et_3N (0.50 mL, 3.59 mmol) and diisopropyldichlorosilane (0.64 mL, 3.59 mmol). Then in *part 2*, allyl alcohol (0.90 mL, 13.26 mmol), Et_3N (1.85 mL, 13.26 mmol), DCM (10 mL) and the crude product in DCM (60 mL) were used to afford **12** (0.345 g, 53%) as a pale yellow oil. IR (neat): 1770, 1710, 1647 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 5.96–5.82 (1H, m), 5.30 (1H, dq, J=17.2, 2.0 Hz), 5.20 (1H, dq, J=10.7, 2.0 Hz), 4.20 (2H, m), 3.85 (2H, t, J=6.0 Hz), 3.65 (2H, t, J=6.0 Hz), 2.30 (4H, m), 1.80 (4H, m), 1.00 (14H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 171.1, 141.5, 137.1, 113.9, 63.6, 60.0, 39.5, 21.4, 20.0, 17.2, 12.0; LRMS (EI): *m/z* 322 (100%, $M^+-CH(CH_3)_2$), 296 (10.0), 134 (11.4), 99 (19.2), 41 (20.4); Anal. Calcd for $C_{19}H_{31}O_4NSi$: C, 62.43; H, 8.54; N, 3.83. Found: C, 62.04; H, 8.77; N, 3.75.

3.4.5. (2*R,8a*S**,9a*R**,13a*S**)-6,6-Bis(1-methylethyl)-octahydro-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobuta[1,2-*h*][1,3,6,2]dioxazasilecine-1,14-dione 13.** A solution of **12** (0.175 g, 0.48 mmol) in acetonitrile (100 mL) was irradiated for 1.5 h. The solvent was concentrated under reduced pressure and the yellow liquid residue was subjected to flash chromatography (petrol/ethyl acetate 17:3) to afford **13** as a pink solid (0.13 g, 74%); mp 91–95 °C. IR (DCM thin film): 1763, 1694 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 4.06 (4H, m), 3.81 (1H, dd, J=6.8, 3.8 Hz), 3.75 (1H, dd, J=6.6, 4.5 Hz), 3.70 (1H, m), 3.65 (1H, m), 3.57 (1H, m), 2.55 (1H, m), 2.30 (1H, m), 1.90–1.40 (6H, m), 1.00 (14H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 183.0, 180.9, 61.6, 60.3, 46.6, 44.7, 42.0, 41.6, 28.6, 27.8, 26.4, 19.7, 19.4, 17.5, 17.1, 12.3, 11.2; LRMS (EI): *m/z* 365 (0.5%, M^+), 322 (100), 249 (3.4), 149 (5.9), 41 (16.2); Anal. Calcd for $C_{19}H_{31}O_4NSi$: C, 62.43; H, 8.54; N, 3.83. Found: C, 62.43; H, 8.67; N, 3.71.

3.4.6. 2-[2-[[(Diphenyl)(2-propenyloxy)silyl]oxy]ethyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 14. Following *general procedure 3*, using in *part 1*; **8** (5.23 g, 26.8 mmol), DMF (70 mL), Et_3N (7.45 mL, 53.6 mmol) and diphenyldichlorosilane (11.23 mL, 53.6 mmol). Then in *part 2*, allyl alcohol (16 mL, 236 mmol), Et_3N (33 mL, 236 mmol), DMF (20 mL) and the crude product in DMF (140 mL) were used to afford **14** (6.28 g, 54%) as a yellow oil. IR (neat): 1768, 1700, 1647 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 7.64 (4H, m), 7.35 (6H, m), 5.95 (1H, m), 5.35 (1H, dq, J=17.2, 1.3 Hz), 5.13 (1H, dq, J=10.2, 1.7 Hz), 4.30 (2H, dt, J=4.6, 1.7 Hz), 3.95 (2H, t, J=5.6 Hz), 3.70 (2H, t, J=5.6 Hz), 2.35 (4H, m), 1.73 (4H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 171.0, 141.4, 136.4, 134.9, 132.2, 130.4, 127.8, 114.7, 63.9, 60.4, 39.4, 21.3, 19.9; LRMS (EI): *m/z* 433 (2.7%, M^+), 356 (80.8), 179 (100), 139 (94.5); Anal. Calcd for $C_{25}H_{27}O_4NSi$: C, 69.25; H, 6.27; N, 3.23. Found: C, 69.29; H, 6.10; N, 2.84.

3.4.7. (2*R,8a*S**,9a*R**,13a*S**)-6,6-Diphenyloctahydro-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobuta[1,2-*h*][1,3,6,2]-dioxazasilecine-1,14-dione 15.** A solution of **14** (1.48 g, 3.41 mmol) in acetonitrile (100 mL) was irradiated for 7 h. The solvent was concentrated under reduced pressure to afford a white solid. This was subjected to flash chromatography (petrol/ethyl acetate 7:3) to afford **15** as a white solid (1.35 g, 91%); mp 45–46 °C. IR (DCM thin film): 1766, 1699 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.60 (4H, m), 7.40 (6H, m), 4.15 (2H, m), 3.95 (2H, m), 3.65 (1H, dd, J=11.5, 4.0 Hz), 3.56 (1H, m), 2.75 (1H, dd, J=12.2, 5.3 Hz), 2.55 (1H, m), 2.36 (1H, m), 2.34 (1H, m), 1.92–1.20 (7H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 183.4, 181.3, 135.4, 135.3, 132.5, 131.1, 130.8, 128.2, 128.1, 62.5, 61.3, 46.9, 44.3, 42.2, 41.2, 28.6, 27.7, 26.8, 19.5, 19.2; LRMS (EI): *m/z* 356 (10.1%, $M^+-C_6H_5$), 216 (51.9), 139 (100), 88 (7.8).

3.4.8. (3aα,7aα,8*S)-3a,7a-Ethano-2-(2-hydroxyethyl)-8-(hydroxymethyl)-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 11.** *Method 1*: the photocycloadduct **10** (1.33 g, 4.76 mmol) was dissolved in a mixture of THF (35 mL) and H_2O (15 mL) and then treated with NaOH (0.38 g, 9.52 mmol). After stirring for 3 h at rt, the reaction mixture was neutralised by addition of 2 M HCl and the solvent concentrated under reduced pressure to leave a white solid. The crude product was dissolved in hot EtOH (200 mL), the solution filtered and concentrated under reduced pressure to leave a yellow liquid, which was purified by flash chromatography (ethyl acetate/ethyl alcohol 9:1) to give **11** as a pale yellow oil (0.90 g, 75%).

Method 2: to a stirred solution of **13** (93.7 mg, 0.256 mmol) in THF (15 mL) was added, dropwise, Bu_4NF (0.15 mL, 0.51 mmol) at rt. After 30 min all starting material had been consumed. The solvent was concentrated under reduced pressure to leave a pale yellow liquid. This was

purified by flash chromatography (ethyl alcohol/ethyl acetate 3:17) to give **11** as a pale yellow oil (53 mg, 82%).

Method 3: to a solution of **15** (2.90 g, 6.7 mmol) in THF (60 mL) was added, dropwise, Bu_4NF (3.90 mL, 13.40 mmol) and then the deep yellow reaction mixture was stirred for 30 min at rt. The solvent was concentrated under reduced pressure to leave a yellow oil. The yellow oil residue was subjected to flash chromatography (pure EtOAc) to give **11** as a pale yellow oil (1.60 g, 95%).

IR (neat): 3434, 1765, 1700 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 3.75 (5H, m), 3.60 (1H, dd, J=12.0, 7.6 Hz), 3.0 (2H, br s), 2.85 (1H, m), 2.35 (1H, m), 2.16 (1H, dd, J=13.9, 9.2 Hz), 2.10 (1H, m), 2.00 (1H, m), 1.65 (2H, m), 1.55 (3H, m), 1.10 (1H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 183.2, 182.5, 62.6, 60.1, 47.1, 42.2, 41.5, 39.1, 32.4, 28.5, 27.6, 20.9, 20.2; LRMS (EI): *m/z* 253 (0.3%, M^+), 210 (100), 165 (33.7), 121 (34.0), 84 (52.4); Anal. Calcd for $C_{13}H_{19}O_4N$: C, 61.64; H, 7.56; N. 5.53. Found: C, 61.34; H, 7.64; N, 5.37.

3.4.9. (2*R*)-2-[1-(Hydroxymethyl)-2-phenyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 16. Following *general procedure 1*, using THPA (0.50 g, 3.3 mmol), (*R*)-(−)-2-phenylglycinol (0.49 g, 3.6 mmol) and toluene (20 mL), afforded **16** as a yellow oil (0.88 g, 99%). IR (neat): 3458, 1768, 1696, 1652 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.20–7.40 (5H, m), 5.20 (1H, dd, J=8.9, 5.0 Hz), 4.50 (1H, dd, J=11.6, 8.6 Hz), 4.10 (1H, dd, J=11.6, 5.0 Hz), 2.30 (5H, m), 1.70–1.80 (4H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 171.9, 142.0, 137.5, 128.9, 128.2, 128.0, 62.7, 57.2, 21.3, 20.0; LRMS (EI): *m/z* 253 (0.5%, M^+-H_2O), 241 (48.7, M^+-CH_2O), 240 (100, M^+-CH_2OH), 107 (8.6), 77 (14.9), 43 (23.6); Anal. Calcd for $C_{16}H_{17}O_3N$: C, 70.83; H, 6.31; N, 5.16. Found: C, 70.40; H, 6.39; N, 5.06.

3.4.10. Carbonic acid-2-(1,3-dioxo-1,3,4,5,6,7-hexahydro-2*H*-isoindole-2-yl)-(1*R*)-phenylethyl-2-propenyl ester 17. Following *general procedure 2*, using **16** (0.75 g, 2.8 mmol), THF (45 mL), pyridine (0.28 mL, 3.46 mmol) and allyl chloroformate (0.37 mL, 3.46 mmol) afforded **17** as a yellow oil (0.55 g, 56%). IR (neat): 1752, 1702, 1649 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.45 (2H, m), 7.35 (3H, m), 5.70 (1H, m), 5.40 (1H, dd, J=10.5, 5.3 Hz), 5.30 (1H, dq, J=17.2, 1.4 Hz), 5.25 (1H, dq, J=10.3, 1.3 Hz), 5.10 (1H, t, J=11.0 Hz), 4.70 (1H, dd, J=11.0, 5.3 Hz), 4.60 (2H, dt, J=5.9, 1.3 Hz), 2.3 (4H, m), 1.8 (4H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 171.1, 154.8, 141.9, 136.5, 131.6, 129.0, 128.6, 128.2, 119.3, 68.8, 65.9, 53.4, 21.3, 20.0; LRMS (EI): *m/z* 254 (17.7%, $M^+-C_4H_5O_3$), 253 (46.8), 240 (100), 103 (8.0), 77 (12.1); Anal. Calcd for $C_{20}H_{21}O_5N$: C, 67.59; H, 5.95; N, 3.94. Found: C, 67.71; H, 5.94; N, 4.0.

3.4.11. (2*R*,8a*S*,9a*R*,13a*S*)-Octahydro-3-phenyl-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobuta[1,2-*h*][1,3,6]dioxazecine-1,6,14-trione 18 and isomer 19. A solution of **17** (0.85 g, 2.4 mmol) in acetonitrile (100 mL) was irradiated for 6 h. The solvent was concentrated under reduced pressure to leave a pale yellow oil. The residue was then subjected to flash chromatography (petrol/ethyl acetate 7:3) to give a white solid (0.83 g, 98%); mp 44.5–54.1 °C. This photocycloadduct was shown to be a mixture of two diastereoisomers **18** and **19** in a 1.3:1 ratio as shown by integration of signals in the ^1H NMR spectrum.

Major isomer **18**. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.40 (2H, m), 7.35 (3H, m), 5.65 (1H, m), 4.65 (1H, dd, J=11.9, 2.2 Hz), 4.20 (2H, m), 4.00 (1H, dd, J=11.8, 1.8 Hz), 2.70 (1H, m), 2.62 (1H, m), 2.45 (2H, m), 2.20 (2H, m), 1.70 (1H, m), 1.60 (2H, m), 1.50 (2H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 181.3, 180.9, 152.5, 134.8, 129.1, 128.9, 128.8, 128.6, 68.6, 66.6, 57.2, 46.7, 43.4, 41.9, 31.8, 28.5, 26.7, 19.6, 18.9.

Minor isomer **19**. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.38 (5H, m), 5.70 (1H, m), 5.55 (1H, dd, J=13.0, 7.8 Hz), 4.76 (1H, m), 4.51 (1H, d, J=12.8 Hz), 4.40 (1H, m), 2.80 (1H, m), 2.52 (2H, m), 2.42 (2H, m), 1.85 (2H, m), 1.75 (2H, m), 1.60 (2H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 183.6, 181.1, 151.8, 135.7, 128.3, 128.2, 128.1, 128.0, 69.0, 66.4, 56.2, 47.4, 43.6, 41.8, 31.8, 28.6, 27.2, 20.0, 18.9.

For the mixture. IR (DCM thin film): 1761, 1701 cm^{-1}; LRMS (EI): *m/z* 355 (3.6%, M^+), 253 (4.7), 84 (94.6), 43 (100).

3.4.12. (1*R*)-2-[1-Phenyl-2-[[diphenyl(2-propenyloxy)-silyl]oxy]ethyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 22. Following *general procedure 3*, using in *part 1*; **16** (0.37 g, 1.36 mmol), MeCN (25 mL), Et_3N (0.38 mL, 2.73 mmol) and diphenyldichlorosilane (0.57 mL, 2.73 mmol). Then in *part 2*, allyl alcohol (1.21 mL, 17.8 mmol), Et_3N (2.48 mL, 17.8 mmol), MeCN (10 mL) and the crude product in MeCN (50 mL) were used to afford **22** (0.32 g, 46%) as a pale yellow oil. IR (neat): 1770, 1710, 1647 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 7.60–7.20 (15H, m), 5.99 (1H, m), 5.35 (2H, m), 5.14 (1H, dq, J=10.6, 1.7 Hz), 4.70 (1H, t, J=10.2 Hz), 4.30 (2H, dd, J=6.0, 1.3 Hz), 4.25 (1H, m), 2.25 (4H, m), 1.71 (4H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 171.2, 141.4, 137.2, 136.4, 134.8, 134.6, 132.2, 130.4, 128.5, 128.2, 127.8, 114.7, 64.0, 61.94, 56.4, 21.3, 19.9.

3.4.13. (2*R*,8a*S*,9a*R*,13a*S*)-Octahydro-3,6,6-triphenyl-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobuta[1,2-*h*][1,3,6,2]-dioxazasilecine-1,14-dione 23 and isomer 24. A solution of **22** (0.785 g, 1.54 mmol) in acetonitrile (100 mL) was irradiated for 5 h. The solvent was removed under reduced pressure to leave a pale yellow solid. The residue was then subjected to flash chromatography (petrol/ethyl acetate 7:3) to give a pale yellow solid (0.70 g, 89%), mp 71.2–73.8 °C, which was shown to be a mixture of two diastereoisomers **23** and **24** in a 3:1 ratio as shown by integration of signals in the ^1H NMR spectrum.

Major isomer **23**. ^1H NMR ($CDCl_3$, 270 MHz): δ 7.60 (4H, m), 7.40 (6H, m), 7.10 (5H, m), 5.70 (1H, dd, J=10.9, 3.3 Hz), 5.06 (1H, t, J=11.2 Hz), 4.22 (1H, dd, J=11.6, 3.3 Hz), 3.95 (1H, m), 3.61 (1H, dd, J=11.6, 4.0 Hz), 2.47 (1H, m), 2.06 (2H, m), 1.50 (2H, m), 1.25 (4H, m), 0.99 (2H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 183.2, 179.9, 136.0, 135.2, 135.0, 134.6, 134.3, 131.7, 130.9, 130.5, 130.3, 127.9, 127.8, 127.5, 62.4, 61.9, 56.8, 47.9, 44.9, 42.5, 29.6, 27.8, 24.6, 20.7, 19.9.

Minor isomer **24**. ^{1}H NMR ($CDCl_3$, 270 MHz): δ 7.70 (4H, m), 7.50 (6H, m), 7.20 (5H, m), 5.60 (1H, dd, J=11.22, 4.0 Hz), 5.30 (1H, t, J=11.2 Hz), 4.15 (1H, m), 4.07 (1H, dd, J=11.6, 4.0 Hz), 3.91 (1H, m), 2.79 (1H, m), 2.62 (1H, m), 2.55 (2H, m), 2.47 (1H, m), 1.78 (2H, m), 1.40 (2H, m), 1.10 (2H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 183.1, 180.40, 136.5, 135.2, 134.8, 134.5, 133.8, 132.4, 131.2, 130.7, 130.4, 130.3, 128.6, 128.4, 62.7, 62.6, 58.3, 46.4, 44.9, 43.4, 28.3, 28.0, 25.8, 21.0, 20.1.

For the mixture. IR (DCM thin film): 1770, 1700 cm^{-1}; LRMS (EI): *m/z* 509 (19.5%, M$^+$), 432 (100), 390 (55.0), 199 (21.9), 91 (29.0); Anal. Calcd for $C_{31}H_{31}O_4NSi$: C, 73.05; H, 6.13; N, 2.74. Found: C, 72.69; H, 6.12; N, 2.47.

3.4.14. (3a*R*,7a*S*,8*S*)-3a,7a-Ethano-8-(hydroxymethyl)-2-(2-hydroxy-1-phenylethyl)-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 20 and isomer 21. *Method 1*: a mixture of the diastereoisomers **18** and **19** (0.32 g, 0.9 mmol) was dissolved in THF (15 mL), and then H_2O (15 mL) and NaOH (0.072 g, 1.8 mmol) were added to the solution. It was stirred at rt for 2.5 h followed by treatment with 2 M HCl until neutral. The solvent was concentrated in vacuo to leave a pale yellow solid. Hot EtOH (150 mL) was poured into the crude mixture, which was filtered and concentrated to afford a yellow oil. The residue was then subjected to flash chromatography (petrol/ethyl acetate 3:7) to give a pale yellow oil (99.5 mg, 34%). This compound was shown to be a mixture of two diastereoisomers **20** and **21** in a 1.3:1 ratio as shown by integration of signals in the ^{1}H NMR spectrum.

Method 2: to a solution of **23** and **24** (0.44 g, 0.86 mmol) in THF (20 mL) under a nitrogen atmosphere at rt was added, dropwise, Bu_4NF (0.49 mL, 1.73 mmol). The brown mixture was stirred at rt for 1 h. The solvent was removed in vacuo to leave a brown oil, which was purified by flash chromatography (EtOAc) to afford a mixture of **20** and **21** in a 3:1 ratio as a pale yellow oil (0.26 g, 93%).

Major isomer **20**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.40 (5H, m), 5.30 (1H, m), 4.10 (1H, dd, J=11.4, 4.9 Hz), 4.02 (1H, dd, J=11.5, 4.9 Hz), 3.75 (1H, dd, J=11.9, 4.1 Hz), 3.65 (1H, dd, J=12.0, 5.1 Hz), 3.40 (2H, br s), 2.70 (1H, m), 2.10 (2H, m), 1.90 (2H, m), 1.64 (2H, m), 1.58 (2H, m), 1.50 (2H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 183.4, 182.5, 136.8, 128.4, 128.3, 127.8, 63.1, 61.5, 58.1, 46.7, 42.1, 38.8, 32.0, 28.5, 27.6, 20.8, 20.0.

Minor isomer **21**. ^{1}H NMR ($CDCl_3$, 300 MHz): δ 7.35 (5H, m), 5.40 (1H, m), 4.70 (1H, m), 4.60 (1H, m), 3.51 (1H, m), 3.49 (1H, m), 3.40 (2H, br s), 2.80 (1H, m), 2.30 (2H, m), 2.00 (2H, m), 1.85 (2H, m), 1.60 (2H, m), 1.45 (2H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 183.4, 182.5, 136.6, 128.9, 127.9, 126.7, 62.2, 61.3, 57.9, 47.2, 42.0, 38.3, 32.7, 28.6, 27.5, 20.9, 20.1.

For the mixture. IR (neat): 3444, 1765, 1740, 1697 cm^{-1}; LRMS (EI): *m/z* 299 (1.0%, M$^+$−CH_2O), 84 (63.8), 61 (18.0), 42 (100).

3.4.15. (2*S*)-2-[1-(Hydroxymethyl)-2-methylpropyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 25. Following *general procedure 1*, using THPA (1.34 g, 8.8 mmol), L-(+)-valinol[14] (0.91 g, 9.68 mmol) and toluene (85 mL), afforded **25** [(1.98 g, 95%), $[\alpha]_D$ +1.27±2 (*c* 1, C_2H_5OH at 20 °C)] as a yellow oil. IR (neat): 3448, 1767, 1699, 1640 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz): δ 4.00 (1H, dd, J=11.9, 7.25 Hz), 3.80–3.70 (2H, m), 3.00 (1H, br s), 2.30 (5H, m), 1.70 (4H, m), 1.00 (3H, d, J=6.6 Hz), 0.80 (3H, d, J=6.6 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 172.1, 141.4, 62.3, 59.5, 27.2, 21.4, 20.2, 20.1, 20.0; LRMS (EI): *m/z* 237 (4.0%, M$^+$), 206 (100), 152 (15.2), 134 (4.4); Anal. Calcd for $C_{13}H_{19}O_3N$: C, 65.80; H, 8.07; N, 5.90. Found: C, 65.82; H, 8.00; N, 5.97.

3.4.16. (2S)-Carbonic acid-2-(1,3-dioxo-1,3,4,5,6,7-hexahydro-2*H*-isoindole-2-yl)-3-methylbutyl-2-propenyl ester 27. Following *general procedure 2*, using **25** (0.50 g, 2.1 mmol), THF (20 mL), pyridine (0.21 mL, 2.64 mmol) and allyl chloroformate (0.28 mL, 2.64 mmol), afforded **27** as a pale yellow oil (0.41 g, 61%). IR (neat): 1751, 1706, 1649 cm^{-1}; ^{1}H NMR ($CDCl_3$, 270 MHz): δ 5.80–6.00 (1H, m), 5.30 (1H, dq, J=17.2, 1.3 Hz), 5.20 (1H, dd, J=17.1, 1.3 Hz), 4.58 (2H, dt, J=5.6, 1.3 Hz), 4.45 (2H, m), 3.99 (1H, m), 2.30 (5H, m), 1.70 (4H, m), 1.00 (3H, d, J=6.6 Hz), 0.80 (3H, d, J=6.6 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 171.2, 154.8, 141.2, 131.8, 118.6, 68.5, 65.9, 56.3, 27.9, 21.5, 20.2, 20.1, 20.0; LRMS (EI): *m/z* 321 (4.0%, M$^+$), 206 (100), 164 (19.0); Anal. Calcd for $C_{17}H_{23}O_5N$: C, 63.53; H, 7.21; N, 4.36. Found: C, 63.61; H, 7.22; N, 4.38.

3.4.17. (2*R*,8a*S*,9a*R*,13a*S*)-3-(1-Methylethyl)octahydro-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobuta[1,2-*h*][1,3,6]-dioxazecine-1,6,14-dione 28 and isomer 29. A solution of **27** (0.26 g, 0.82 mmol) in acetonitrile (100 mL) was irradiated for 40 min. The solvent was concentrated under reduced pressure to leave a yellow liquid. The liquid was purified by flash chromatography (petrol/ethyl acetate 7:3) to give a white solid (0.234 g, 90%); mp 108–116 °C. It was shown to be a mixture of two diastereoisomers **28** and **29** in a 1:1 ratio as shown by integration of signals in the ^{1}H NMR spectrum.

For the mixture. IR (DCM thin film): 1761, 1695 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz): δ 5.00 (2H, dd, J=13.3, 7.6 Hz), 4.62 (2H, dd, J=11.7, 2.1 Hz), 4.15 (2H, m), 4.00 (2H, m), 2.75 (2H, m), 2.55 (2H, m), 2.47 (2H, m), 2.41 (2H, m), 2.00–1.80 (8H, m), 1.60–1.40 (8H, m), 1.30 (2H, m), 1.08 (2×3H, 2×d, J=6.6 Hz), 0.80 (2×3H, 2×d, J=6.8 Hz); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 183.5, 182.4, 181.3, 154.5, 151.6, 68.2, 67.8, 61.2, 56.8, 47.4, 46.7, 43.0, 41.6, 31.5, 29.0, 28.0, 27.3, 26.8, 26.5, 26.2, 20.7, 20.4, 20.1, 19.8, 19.6, 19.3, 18.5; LRMS (EI): *m/z* 321 (47.6%, M$^+$), 219 (65.5), 121 (67.0), 85 (100); Anal. Calcd for $C_{17}H_{23}O_5N$: C, 63.53; H, 7.21; N. 4.36. Found: C, 63.55; H, 7.29; N, 4.07.

3.4.18. (2*S*)-2-[1-[[Bis(1-methylethyl)(2-propenyloxy)-silyl]oxy]methyl-2-methylpropyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 32. Following *general procedure 3*, using in *part 1*; **25** (0.53 g, 2.25 mmol), DCM (30 mL), Et_3N (0.63 mL, 4.5 mmol) and diisopropyldichlorosilane (0.79 mL, 4.5 mmol). Then in *part 2*, allyl alcohol (1.13 mL, 16.6 mmol), Et_3N (2.31 mL, 16.6 mmol), DCM (10 mL) and the crude product in DCM (60 mL) were added

to afford **32** (0.65 g, 71%) as a pale yellow oil. IR (neat): 1769, 1709, 1647 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 5.90 (1H, m), 5.30 (1H, dq, J=17.2, 2.0 Hz), 5.00 (1H, dd, J=10.6, 1.7 Hz), 4.30 (2H, m), 4.10 (1H, m), 4.00 (1H, dd, J=10.23, 5.0 Hz), 3.80 (1H, td, J=21.0, 10.2, 5.0 Hz), 2.30 (5H, m), 1.70 (4H, m), 1.00 (17H, m), 0.85 (3H, d, J=6.9 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 171.9, 141.0, 137.1, 113.8, 63.5, 61.0, 59.4, 27.7, 21.5, 20.3, 20.2, 20.0, 17.2, 12.1; LRMS (EI): *m/z* 365 (10.0%, $M^+-C(CH_3)_2$), 364 (38.6, $M^+-CH(CH_3)_2$), 275 (100), 191 (20.5), 135 (10.6); Anal. Calcd for $C_{22}H_{37}O_4NSi$: C, 64.82; H, 9.15; N, 3.44. Found: C, 64.96; H, 9.14; N, 3.43.

3.4.19. (2*R*,8a*S*,9a*R*,13a*S*)-Octahydro-3,6,6-tris(1-methyl)-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobuta[1,2-*h*][1,3,6,2]dioxazasilecine-1,14-dione 33 and isomer 34. A solution of **32** (0.41 g, 1.00 mmol) in acetonitrile (100 mL) was irradiated for 1 h. The solvent was removed in vacuo to leave a pale yellow crystalline solid. The residue was then subjected to flash chromatography (petrol/ethyl acetate 8:2) to afford a white solid (0.305 g, 74%), mp 102–107 °C, which was shown to be a mixture of two diastereoisomers **33** and **34** in a 2:1 ratio as shown by integration of the ^1H NMR signals.

Major isomer **33**. ^1H NMR ($CDCl_3$, 270 MHz): δ 4.50 (1H, t, J=10.9 Hz), 4.00 (1H, m), 3.88 (1H, m), 3.70 (1H, dd, J=11.2, 4.6 Hz), 2.60 (2H, m), 2.45 (2H, m), 2.33 (4H, m), 1.65 (3H, m), 1.10–0.70 (22H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 183.9, 180.7, 61.6, 61.4, 61.0, 47.3, 45.0, 41.9, 30.1, 28.4, 25.4, 24.5, 20.8, 20.7, 20.3, 20.1, 17.5, 17.3, 12.0, 11.7.

Minor isomer **34**. ^1H NMR ($CDCl_3$, 270 MHz): δ 4.63 (1H, t, J=10.9 Hz), 4.05 (1H, m), 3.93 (2H, m), 2.65 (2H, m), 2.50 (2H, m), 2.33 (2H, m), 1.98 (2H, m), 1.60 (4H, m), 1.10–0.70 (21H, m); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 183.9, 180.7, 62.0, 60.7, 60.5, 47.3, 45.2, 41.9, 30.1, 28.9, 27.1, 26.0, 20.7, 20.4, 20.0, 19.8, 17.5, 17.1, 12.4, 10.6.

For the mixture. IR (DCM thin film): 1765, 1702 cm^{-1}; LRMS (EI): *m/z* 365 (26.3%, $M^+-C(CH_3)_2$), 364 (100, $M^+-CH(CH_3)_2$), 275 (8.8); Anal. Calcd for $C_{22}H_{37}O_4SiN$: C, 64.82; H, 9.15; 3.44. Found: C, 64.80; H, 9.25; N, 3.32.

3.4.20. (2*S*)-2-[1-[[(Diphenyl)(2-propenyloxy)silyl]oxy]-methyl-2-methylpropyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 35. Following *general procedure 3*, using in *part 1*; **25** (1.69 g, 7.12 mmol), DMF (40 mL), Et_3N (1.97 mL, 14.2 mmol) and diphenyldichlorosilane (2.45 mL, 14.2 mmol). Then in *part 2*, allyl alcohol (4.2 mL, 52.8 mmol), Et_3N (7.36 mL, 52.8 mmol), DMF (10 mL) and the crude product in DMF (80 mL) were used to afford **35** (2.01 g, 60%) as a pale yellow oil. IR (neat): 1768, 1704, 1647 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 7.63 (4H, m), 7.30 (6H, m), 5.95 (1H, m), 5.34 (1H, dq, J=17.0, 1.8 Hz), 5.12 (1H, dq, J=10.3, 2.0 Hz), 4.25 (2H, m), 4.21 (1H, m), 4.01 (1H, dd, J=10.3, 4.6 Hz), 3.85 (1H, td, J=20.1, 10.0, 4.5 Hz), 2.30 (5H, m), 1.72 (4H, m), 0.90 (3H, d, J=6.6 Hz), 0.83 (3H, d, J=6.6 Hz); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 172.1, 141.3, 136.7, 134.9, 132.6, 130.6, 128.0, 114.8, 64.0, 61.4, 59.5, 27.6, 21.4, 20.3, 20.0; LRMS (EI): *m/z* 475 (7.6%, M^+), 398 (100), 206 (75.2), 161 (25.5); Anal. Calcd for $C_{28}H_{33}O_4NSi$: C, 70.70; H, 6.99; N, 2.94. Found: C, 70.61; H, 6.97; N, 2.86.

3.4.21. (2*R*,8a*S*,9a*R*,13a*S*)-6,6-Diphenyl-3-(1-methylethyl)octahydro-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobuta[1,2-*h*][1,3,6,2]dioxazasilecine-1,14-dione 36 and isomer 37. A solution of **35** (0.71 g, 1.50 mmol) in acetonitrile (100 mL) was irradiated for 2 h. The solvent was concentrated in vacuo to leave a pale yellow oil. The oil was purified by flash chromatography (petrol/ethyl acetate 17:3) to afford a white crystalline solid (0.61 g, 86%); mp 53.2–62.8 °C; $[\alpha]_D$ +4.3±2 (*c* 1, C_2H_5OH at 20 °C). It was shown to be a mixture of two diastereoisomers **36** and **37** in a 8:1 ratio as shown by comparison of the signals in the ^1H NMR spectrum. Recrystallisation from Et_2O gave a pure sample of **36**, which was slowly crystallised from Et_2O/petroleum ether to give a suitable single crystal for X-ray diffraction.

Major isomer **36**. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.62 (4H, m), 7.30 (6H, m), 4.39 (1H, dd, J=11.4, 10.4 Hz), 4.15 (1H, m), 3.99 (1H, m), 3.91 (1H, m), 3.57 (1H, dd, J=11.4, 3.9 Hz), 2.55 (2H, m), 2.45 (2H, m), 1.90 (3H, m), 1.61–1.47 (5H, m), 1.00 (3H, d, J=6.6 Hz), 0.80 (3H, d, J=6.6 Hz); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 184.1, 181.0, 135.3, 135.2, 130.7, 128.1, 62.0, 62.0, 61.3, 47.7, 45.1, 42.2, 30.4, 28.6, 27.2, 25.2, 24.6, 21.0, 20.7, 20.5, 20.2, 20.0.

Minor isomer **37**. ^1H NMR ($CDCl_3$, 300 MHz): δ 7.50 (4H, m), 7.43 (6H, m), 4.65 (1H, dd, J=11.4, 9.6 Hz), 4.20–4.10 (1H, m), 3.96 (1H, dd, J=11.4, 2.9 Hz), 3.93 (1H, m), 3.80 (1H, dd, J=11.6, 7.6 Hz), 2.78 (2H, m), 2.55 (2H, m), 2.41 (2H, m), 2.32 (2H, m), 1.95 (3H, m), 1.61–1.47 (4H, m), 1.00 (3H, d, J=6.6 Hz), 0.80 (3H, d, J=6.6 Hz); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 184.1, 181.0, 135.5, 135.1, 132.2, 131.5, 62.8, 62.0, 60.6, 46.1, 44.8, 43.2, 30.9, 30.5, 28.4, 28.4, 26.4, 20.9, 20.8, 20.6, 20.2, 20.1.

For the mixture. IR (DCM thin film): 1765, 1702 cm^{-1}; LRMS (EI): *m/z* 475 (1.7%, M^+), 398 (100), 390 (30.4), 199 (15.5), 78 (14.3); Anal. Calcd for $C_{28}H_{33}O_4NSi$: C, 70.70; H, 6.99; N, 2.94. Found: C, 70.64; H, 6.95; N, 3.02.

3.4.22. (3a*R*,7a*S*,8*S*)-3a,7a-Ethano-8-(hydroxymethyl)-2-[1-(hydroxymethyl)-2-methylpropyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 30 and isomer 31. *Method 1*: the photocycloadducts **28** and **29** (0.18 g, 0.57 mmol) were dissolved in a mixture of EtOH (15 mL) and water (15 mL) and treated with KOH (0.064 g, 1.14 mmol). After stirring at rt for 3 h, the reaction mixture was neutralised by the addition of 2 M HCl. The solvent was concentrated in vacuo to leave a brown oil. The oil was purified by flash chromatography (ethyl alcohol/ethyl acetate 1:9) to afford a pale yellow oil (0.13 g, 79%). It was shown to be a mixture of two diastereoisomers **30** and **31** in a 1:1 ratio as shown by integration of signals in the ^1H NMR spectrum.

Method 2: to a solution of **33** and **34** (0.27 g, 0.67 mmol) in THF (25 mL) was added, dropwise, Bu_4NF (0.39 mL, 1.34 mmol) at rt. The reaction mixture was then stirred for 20 min at rt. The solvent was concentrated under reduced pressure to leave a yellow oil. This was subjected to flash chromatography (petrol/ethyl acetate 8:2) to give a pale

yellow oil (0.169 g, 87%), which was shown to be a mixture of two diastereoisomers **30** and **31** in a 2:1 ratio.

Method 3: to a solution **36** and **37** (0.18 g, 0.38 mmol) in THF (25 mL) was added, dropwise, Bu_4NF (0.22 mL, 0.76 mmol) and then the reaction mixture was stirred at rt for 30 min. The solvent was concentrated in vacuo to leave a yellow oil. The oil was then subjected to flash chromatography (petrol/ethyl acetate 7:3) to provide a pale yellow oil (0.109 g, 99%), which was shown to be mixture of two diastereoisomers **30** and **31** in a 8:1 ratio. $[\alpha]_D$ +2.6±2 (*c* 1, C_2H_5OH at 20 °C).

For the mixture. IR (neat): 3439, 1764, 1700 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 4.20 (2H, m), 3.90 (2H, m), 3.75 (1H, m), 3.73 (1H, m), 3.65–3.40 (8H, m), 2.80 (1H+1H, m), 2.40 (2H, m), 2.35 (2H, m), 2.14 (4H, m), 2.00 (2H, m), 1.70 (4H, m), 1.60 (2H, m), 1.55 (2H, m), 1.50 (4H, m), 1.00 (2×3H, 2×d, *J*=6.9 Hz), 0.82 (2×3H, d, *J*=6.6 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 184.1, 183.1, 182.9, 63.2, 62.6, 61.4, 61.3, 61.0, 47.2, 46.6, 42.1, 41.8, 38.7, 38.6, 32.0, 32.7, 29.7, 29.1, 28.9, 28.0, 27.8, 26.6, 26.2, 21.2, 21.2, 20.3, 20.1, 20.0, 20.0, 19.9; LRMS (EI): *m/z* 295 (2.1%, M^+), 210 (50.6), 165 (13.1), 121 (7.3), 84 (100); Anal. Calcd for $C_{16}H_{25}O_4N$: C, 65.06, H, 8.53; N, 4.74. Found: C, 64.99; H, 8.14; N, 4.29.

3.4.23. (2*S*)-2-[1-[[[Diphenyl(2-propynyloxy)silyl]oxy]-methyl]-2-methylpropyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 38. Following *general procedure 3*, using in *part 1*; **25** (1.11 g, 4.67 mmol), MeCN (40 mL), Et_3N (1.3 mL, 9.35 mmol) and diphenyldichlorosilane (1.96 mL, 9.33 mmol). Then in *part 2*, propargyl alcohol (2.43 mL, 41.8 mmol), Et_3N (5.83 mL, 41.8 mmol), MeCN (10 mL) and the crude product in MeCN (80 mL) were used to afford **38** (1.28 g, 58%) as a pale yellow oil. IR (neat): 3289, 2125, 1770, 1705 cm^{-1}; ^1H NMR ($CDCl_3$, 270 MHz): δ 7.50 (4H, m), 7.30 (6H, m), 4.40 (2H, s), 4.20 (1H, s), 4.05 (2H, m), 3.83 (1H, td, *J*=20.1, 9.9, 4.6 Hz), 2.35 (5H, m), 1.70 (4H, m), 0.85 (3H, d, *J*=6.6 Hz), 0.77 (3H, d, *J*=6.6 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 171.0, 141.0, 134.9, 132.0, 130.5, 127.9, 82.0, 73.3, 61.5, 59.4, 51.5, 27.6, 21.4, 20.3, 20.0; LRMS (EI): *m/z* 473 (1.1%, M^+), 206 (100), 152 (24.9), 139 (37.6).

3.4.24. (2*R*,8a*S*,9a*R*,13a*S*)-6,6-Diphenyl-3-(1-methylethyl)octahydro-1*H*,8*H*-2,9a-methanobenzo[1,4]cyclobutene[1,2-*h*][1,3,6,2]dioxazasilecine-1,14-dione 39 and isomer 40. A solution of **38** (0.865 g, 1.82 mmol) in acetonitrile (100 mL) was irradiated for 6 h. The solvent was removed under reduced pressure to leave a yellow solid. The solid residue was subjected to flash chromatography (petrol/ethyl acetate 9:1) to afford a white solid (0.42 g, 49%); mp 42–47 °C, which was shown to be a mixture of two diastereoisomers **39** and **40** in a 4:1 ratio as shown by integration of signals in the ^1H NMR spectrum.

Major isomer **39**. ^1H NMR ($CDCl_3$, 270 MHz): δ 7.50 (4H, m), 7.20 (6H, m), 5.90 (1H, s), 4.30 (4H, m), 2.40–2.20 (6H, m), 1.20 (4H, m), 0.80 (6H, d, *J*=6.6 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 179.7, 178.2, 156.3, 137.0, 135.1, 135.0, 134.8, 132.7, 131.9, 130.5, 127.9, 60.8, 59.1, 59.1, 52.5, 51.4, 27.4, 25.6, 23.4, 21.4, 20.4, 20.2, 19.9.

Minor isomer **40**. ^1H NMR ($CDCl_3$, 270 MHz): δ 7.60 (4H, m), 7.30 (6H, m), 6.20 (1H, s), 4.00 (4H, m), 2.50–2.00 (6H, m), 1.80 (4H, m), 0.90 (6H, d, *J*=6.6 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 179.7, 178.2, 156.3, 136.9, 135.2, 135.0, 134.7, 132.7, 131.9, 130.5, 127.9, 60.8, 59.1, 59.0, 52.5, 51.4, 27.3, 25.6, 23.4, 21.4, 20.4, 20.2, 19.9.

For the mixture. IR (DCM thin film): 1765, 1700, 1652 cm^{-1}.

3.4.25. (2*S*)-3a,7a-Ethano-8-(hydroxymethyl)-2-[1-(hydroxymethyl)-2-methylpropyl]-4,5,6,7-tetrahydro-1*H*-isoindole-1,3(2*H*)-dione 41 and isomer 42. To a solution of **39** and **40** (0.30 g, 0.634 mmol) in THF (25 mL) was added, dropwise, Bu_4NF (0.36 mL, 1.26 mmol) and the resulting brown solution was stirred at rt for 20 min. The solvent was concentrated in vacuo to leave a brown liquid. The residue was purified by flash chromatography (petrol/ethyl acetate 6:4) to afford a colourless oil (0.15 g, 81%). It was shown to be a mixture of two diastereoisomers **41** and **42** in a 4:1 ratio as shown by integration signals in the ^1H NMR spectrum.

Major isomer **41**. ^1H NMR ($CDCl_3$, 270 MHz): δ 6.20 (1H, s), 4.20 (2H, s), 4.00 (1H, m), 3.80 (2H, m), 3.20 (2H, br s), 2.45 (1H, m), 1.90 (4H, m), 1.60 (2H, m), 1.35 (2H, m), 1.00 (3H, d, *J*=6.6 Hz), 0.85 (3H, d, *J*=6.6 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 180.0, 179.3, 154, 134.1, 61.7, 59.8, 58.4, 53.4, 50.6, 26.2, 25.2, 24.7, 24.2, 19.8, 19.6, 19.5.

Minor isomer **42**. ^1H NMR ($CDCl_3$, 270 MHz): δ 6.10 (1H, s), 4.10 (2H, s), 4.00 (1H, m), 3.70 (2H, m), 2.40 (3H, br m), 2.00 (4H, m), 1.50 (2H, m), 1.40 (2H, m), 0.90 (3H, d, *J*=6.6 Hz), 0.80 (3H, d, *J*=6.6 Hz); ^{13}C NMR ($CDCl_3$, 67.8 MHz): δ 180.0, 179.3, 154.6, 134.1, 61.7, 59.8, 58.3, 53.42, 50.6, 26, 25.12, 24.7, 24.2, 19.8, 19.6, 19.5.

For the mixture. IR (neat): 3426, 1761, 1682, 1634 cm^{-1}; LRMS (EI): *m/z* 293 (3.3%, M^+), 208 (83), 119 (100), 84 (28.4).

3.4.26. (3aα,7aα,8*S)-3a,7a-Ethano-3-hydroxy-2-(2-hydroxyethyl)-8-(hydroxymethyl)-1-one-4,5,6,7-tetrahydro-1*H*-isoindole 43.** To a stirred solution of **11** (0.45 g, 1.77 mmol) in 90% aqueous 2-propanol (10 mL) was added $NaBH_4$ (0.10 g, 2.63 mmol) in one portion. After stirring overnight at rt, TLC indicated complete consumption of the starting material. Excess $NaBH_4$ was decomposed by careful addition of glacial acetic acid. The mixture was concentrated, diluted with water (10 mL), extracted with Et_2O (3×25 mL), dried over Na_2SO_4 and concentrated under reduced pressure. The resulting yellow oil was purified by flash chromatography (ethyl alcohol/ethyl acetate 1:9) to afford the product **43** as a pale yellow oil (0.36 g, 80%). It was shown to be a mixture of diastereoisomers in a 1:2 ratio as shown by integration of the ^1H NMR signals.

For the mixture. IR (neat): 3322, 1739, 1653 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 5.45 (2H, br s), 5.01 (1H, s, minor isomer), 4.96 (1H, s, major isomer), 4.40 (1H, br s), 3.8 (4H, m), 3.65 (4H, m), 3.55 (2H, m), 3.40 (2H, m), 2.65 (2H, m), 2.00 (4H, m), 1.70 (6H, m), 1.50 (8H, m), 1.05 (2H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 179.0, 178.4, 86.3, 84.6, 62.9, 60.3,

60.2, 59.8, 47.4, 46.7, 43.0, 42.5, 42.0, 39.9, 36.0, 34.3, 29.4, 28.7, 27.5, 26.7, 26.7 23.6, 21.1, 20.3, 20.2, 19.8; LRMS (EI): *m/z* 255 (6.5%, M^+), 237 (64.9), 206 (100), 194 (80.0), 180 (59.7).

3.4.27. (1*S,6*R**,9*R**)-7-Oxobicyclo[4.3.0]nonane-1,9-carbolactone 46 and (1*R**,6*S**,8*R**,9*R**)-6,9-dihydroxybicyclo[4.2.1]nonane-1,8-carbolactone 47.** A stirred solution of **43** (0.19 g, 0.74 mmol) in 4 M H_2SO_4 (5 mL) was heated at 80 °C for 12 h. The reaction mixture was cooled to rt and neutralised by the addition of 2 M NaOH. The mixture was concentrated under reduced pressure to leave a pale yellow solid. The residue was dissolved in hot EtOH (100 mL) and then filtered to remove Na_2SO_4. The solvent was concentrated under reduced pressure to afford a yellow oil, which was purified by flash chromatography (petrol/ethyl acetate 1:1) to afford **46** as a pale yellow solid (43 mg, 30%), mp 85 °C, and **47** as a pale yellow solid (48 mg, 30%), mp 100 °C.

Carbolactone **46**. IR (DCM thin film): 1770, 1746 cm^{-1}; ^1H NMR ($CDCl_3$, 300 MHz): δ 4.45 (1H, dd, *J*=9.6, 7.3 Hz), 4.07 (1H, dd, *J*=9.6, 6.2 Hz), 2.99 (1H, m), 2.70 (1H, dd, *J*=19.7, 9.0 Hz), 2.50 (1H, t, *J*=6.4 Hz), 2.30 (1H, ddd, *J*=19.8, 4.1, 1.0 Hz), 1.90 (2H, m), 1.75 (2H, m), 1.50 (4H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 214.4, 179.83, 70.8, 49.4, 48.7, 39.6, 39.4, 28.5, 22.5, 22.5, 21.2; LRMS (EI): *m/z* 194 (100%, M^+), 166 (30.3), 139 (26.9), 79 (16.9); Anal. Calcd for $C_{11}H_{14}O_3$: C, 68.03; H, 7.26. Found: C, 68.20; H, 7.38.

Carbolactone **47**. IR (DCM thin film): 3426, 1757; ^1H NMR ($CDCl_3$, 300 MHz): δ 4.56 (1H, t, *J*=9.6 Hz), 4.16 (1H, d, *J*=4.0 Hz), 4.01 (1H, dd, *J*=9.3, 6.9 Hz), 3.20 (1H, d, *J*=4.0 Hz), 2.70 (1H, m), 2.50 (1H, s), 2.40 (1H, m), 2.26 (1H, dd, *J*=13.9, 9.90 Hz), 2.00 (2H, m), 1.70 (4H, m), 1.45 (2H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 182.1, 83.7, 82.5, 74.9, 52.9, 41.8, 40.6, 37.7, 31.9, 24.6, 22.1; LRMS (EI): *m/z* 212 (8.1%, M^+), 194 (17.9), 91 (20.5), 79 (28.0), 43 (100).

3.4.28. Preparation of pinacol rearrangement product from (1*R,6*S**,8*R**,9*R**)-6,9-dihydroxybicyclo[4.2.1]-nonane-1,8-carbolactone 47.** A stirred solution of **47** (90 mg, 0.42 mmol) in 4 M H_2SO_4 (5 mL) was heated at 80 °C for four days. The reaction mixture was cooled to rt and neutralised by addition of 2 M NaOH. The mixture was concentrated under reduced pressure to leave a pale yellow solid, which was dissolved in hot EtOH (80 mL) and filtered to remove Na_2SO_4. The solvent was concentrated under reduced pressure to leave a yellow oil. This was subjected to flash chromatography (petrol/ethyl acetate 1:1) to give product **46** (30 mg, 37%) as a pale yellow solid and also **47** (50 mg, 56%) was recovered as a pale yellow solid. Data matched that reported above.

3.4.29. (1*S,8*R**)-8-Formyl-10-oxa-9-oxobicyclo[6.3.0]-undecane 53.** To a vigorously stirred suspension of chromatographic grade silica gel (1.0 g) in DCM (5 mL) at rt, was added a 0.65 M aqueous solution of $NaIO_4$ (1 mL), dropwise with stirring, at this time a flaky suspension was formed. Carbolactone **47** (17 mg, 0.08 mmol) in DCM (3 mL) was then added. After 15 min the mixture was filtered and the silica thoroughly washed with DCM (2×15 mL). The solvent was concentrated under reduced pressure to afford a yellow oil. Purification was carried out by flash chromatography (ethyl alcohol/ethyl acetate 1:9) to give **53** as a yellow oil (14 mg, 83%). IR (neat): 1777, 1710, 1698; ^1H NMR ($CDCl_3$, 300 MHz): δ 9.49 (1H, d, *J*=2.2 Hz), 4.45 (1H, m), 4.17 (1H, dd, *J*=11.2, 8.5 Hz), 3.20 (1H, m), 2.90 (1H, m), 2.73 (1H, m), 2.53 (1H, dd, *J*=14.0, 3.8 Hz), 2.37 (2H, m), 2.13 (1H, m), 1.89 (2H, m), 1.69 (2H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 211.2, 197.0, 173.1, 69.0, 61.6, 41.0, 40.8, 38.9, 29.3, 27.4, 22.2; LRMS (EI): *m/z* 210 (0.7%, M^+), 182 (15.3), 84 (100), 67 (26).

3.4.30. (1*S,6*R**,9*R**)-7-Oxobicyclo[4.3.0]nonane-1,9-carbolactone 46 and (1*R**,6*R**,8*R**,9*R**)-9-hydroxy-6-trifluoroacetoxybicyclo[4.2.1]nonane-1,8-carbolactone 50.** A stirred yellow solution of **43** (0.20 g, 0.78 mmol) in anhydrous TFA (10 mL) was heated at reflux for 12 h. The reaction mixture was cooled to rt and then the acid concentrated under reduced pressure to leave a brown oil. H_2O (10 mL) was added to the residue, which was then extracted with Et_2O (3×25 mL), the combined extracts washed with saturated aqueous $NaHCO_3$ solution (30 mL), dried over Na_2SO_4, filtered and concentrated to give a pale brown oil. This was subjected to flash chromatography (petrol/ethyl acetate 1:1) to afford **46** as a pale yellow solid (76 mg, 50%) and **50** as a pale yellow solid (73 mg, 30%); mp 80 °C. Data matched that reported above. IR (DCM thin film): 3452, 1761, 1700, 1221–1163; ^1H NMR ($CDCl_3$, 300 MHz): δ 4.50 (2H, m), 3.90 (1H, dd, *J*=9.6, 6.3 Hz), 2.80 (2H, m), 2.40 (1H, m), 2.20 (2H, m), 1.85 (2H, m), 1.95 (1H, m), 1.70 (1H, m), 1.50 (2H, m), 1.41 (1H, m); ^{13}C NMR ($CDCl_3$, 75.45 MHz): δ 179.9, 157.0, 110.0–120.0 (very weak, CF_3), 97.3, 79.8, 73.6, 51, 41.5, 38.4, 32.0, 31.1, 23.9, 21.5; ^{19}F NMR (254 MHz, $CDCl_3$): δ −74.6 (3F, s); LRMS (EI): *m/z* 306 (6.3%, $M^+-2\times H$), 290 (14.7, M^+-H_2O), 280 (30.8), 246 (27.3), 194 (59.1), 176 (78.7), 69 (100); Anal. Calcd for $C_{13}H_{15}O_5F_3$: C, 50.66; H, 4.90. Found: C, 50.78; H, 4.74.

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References and notes

1. (a) Pirrung, M. C. *J. Am. Chem. Soc.* **1981**, *103*, 82–87; (b) Crimmins, M. T. *Chem. Rev.* **1988**, *88*, 1453–1473; (c) Winkler, J. D.; Bowen, C. M.; Liotta, F. *Chem. Rev.* **1995**, *95*, 2003–2020; (d) Samajdar, S.; Ghatak, A.; Ghosh, S. *Tetrahedron Lett.* **1999**, *40*, 4401–4402; (e) Lange, L. G.; Gottarado, C.; Merica, A. *J. Org. Chem.* **1999**, *64*, 6738–6744; (f) Randall, M. L.; Lo, P. *J. Am. Chem. Soc.* **1999**, *121*, 4534–4535; (g) Lo, P. C.-K.; Snapper, M. L. *Org. Lett.* **2001**, *3*, 2819–2821; (h) Inoue, M.; Sato, T.; Hirama, M. *J. Am. Chem. Soc.* **2003**, *125*, 10772–10773; (i) Padwa, A.; Lipka, H.; Watterson, S. H.; Murphree, S. S. *J. Org. Chem.* **2003**, *68*, 6238–6250.

2. Hutchinson, J. H.; Daynard, T. S.; Gillard, J. W. *Tetrahedron Lett.* **1991**, *32*, 573–576.
3. Shea, K. J.; Staab, A. J.; Zandi, K. S.; Kathleen, S. *Tetrahedron Lett.* **1991**, *32*, 2715–2718.
4. (a) Bergens, S. H.; Noheda, P.; Whelan, J.; Bosnich, B. *J. Am. Chem. Soc.* **1992**, *114*, 2121–2128; (b) Hale, M. R.; Hoveyda, A. H. *J. Org. Chem.* **1992**, *57*, 1643–1645.
5. (a) Fleming, S. A.; Ward, S. C. *Tetrahedron Lett.* **1992**, *33*, 1013–1016; (b) Bradford, C. L.; Fleming, S. A.; Ward, S. C. *Tetrahedron Lett.* **1995**, *36*, 4189–4192.
6. Crimmins, M. T.; Guise, L. E. *Tetrahedron Lett.* **1994**, *35*, 1657–1660.
7. Penkett, C. S.; Byrne, P. W.; Teobald, B. J.; Rola, B.; Ozanne, A.; Hitchcock, P. B. *Tetrahedron* **2004**, *60*, 2771–2784.
8. (a) Fensterbank, L.; Malacria, M.; Sieburth, S. M. *Synthesis* **1997**, 813–854; (b) Gauthier, D. R.; Zandi, K. S.; Shea, K. J. *Tetrahedron* **1998**, *54*, 2289–2338.
9. (a) Green, B. S.; Rabinsohn, Y.; Retjö, M. *Carbohydr. Res.* **1975**, *45*, 115–126; (b) Green, B. S.; Hagler, A. T.; Rabinsohn, Y.; Retjö, M. *Isr. J. Chem.* **1976/77**, *15*, 124–130; (c) Lange, G. L.; Decicco, C.; Lee, M. *Tetrahedron Lett.* **1987**, *28*, 2833–2836; (d) Meyers, A. I.; Fleming, S. A. *J. Am. Chem. Soc.* **1986**, *108*, 306–307; (e) Herzog, H. D.; Scharf, H. D.; Runsink, J. *Tetrahedron* **1986**, *42*, 3547–3558; (f) Demuth, M.; Palomer, A.; Sluma, H. D.; Dey, A. K.; Kruger, C.; Tsay, Y. H. *Angew. Chem., Int. Ed. Engl.* **1986**, *25*, 1117–1119; (g) Sato, M.; Takayama, K.; Abe, Y.; Furuya, T.; Inukai, N.; Kaneko, C. *Chem. Pharm. Bull.* **1990**, *38*, 336–339; (h) Haag, D.; Scharf, H. D. *J. Org. Chem.* **1996**, *61*, 6127–6135; (i) Crimmins, M. T.; Reinhold, T. L. *Org. React.* **1993**, *44*, 297–588.
10. (a) Faure, S.; Piva-Le Blanc, S.; Piva, O.; Pete, J.-P. *Tetrahedron Lett.* **1997**, *38*, 1045–1048; (b) Piva-Le Blanc, S.; Piva, O.; Pete, J.-P. *Chem. Commun.* **1998**, 235–236; (c) Faure, S.; Piva, O. *Tetrahedron Lett.* **2001**, *42*, 255–259; (d) Faure, S.; Piva-Le Blanc, S.; Bertrand, C.; Pete, J.-P.; Piva, O. *J. Org. Chem.* **2002**, *67*, 1061–1070.
11. Booker-Milburn, K. I.; Gulten, S.; Sharpe, A. *Chem. Commun.* **1997**, 1385–1386.
12. (a) Booker-Milburn, K. I.; Cowell, J. K.; Harris, L. J. *Tetrahedron Lett.* **1994**, *35*, 3883–3886; (b) Booker-Milburn, K. I.; Delgado Jimènez, F.; Sharpe, A. *Synlett* **1995**, 735–736; (c) Booker-Milburn, K. I.; Cowell, J. K.; Sharpe, A.; Delgado Jiménez, F. *Chem. Commun.* **1996**, 249–251; (d) Booker-Milburn, K. I.; Cowell, J. K.; Harris, L. J. *Tetrahedron* **1997**, *53*, 12319–12338; (e) Booker-Milburn, K. I.; Costin, N. J.; Dainty, R. F.; Patel, D.; Sharpe, A. *Tetrahedron Lett.* **1998**, *39*, 7423–7426; (f) Booker-Milburn, K. I.; Cowell, J. K.; Delgado Jiménez, F.; Sharpe, A.; White, A. J. *Tetrahedron* **1999**, *55*, 5875–5888; (g) Booker-Milburn, K. I.; Delgado Jiménez, F.; Sharpe, A. *Tetrahedron* **1999**, *55*, 5889–5902; (h) Booker-Milburn, K. I.; Anson, C. E.; Clissold, C.; Costin, N. J.; Dainty, R. F.; Murray, M.; Patel, D.; Sharpe, A. *Eur. J. Org. Chem.* **2001**, 1473–1482.
13. Corey, E. J.; Sugss, J. W. *J. Org. Chem.* **1973**, *38*, 3223–3224.
14. Meyers, A. I.; Dickman, D. A.; Bailey, T. R. *J. Am. Chem. Soc.* **1985**, *107*, 7974–7978.
15. (a) Uhle, F. C. *J. Org. Chem.* **1961**, *26*, 2998–3001; (b) Osby, J. O.; Martin, M. G.; Ganem, B. *Tetrahedron Lett.* **1984**, *25*, 2093–2096.
16. (a) Hubert, J. C.; Wijnberg, J. B. P. A.; Speckamp, W. N. *Tetrahedron* **1975**, *31*, 1437–1441; (b) Wijnberg, J. B. P. A.; Schoemaker, H. E.; Speckamp, W. N. *Tetrahedron* **1978**, *34*, 179–187.
17. (a) Horii, Z.-I.; Iwata, C.; Tamura, Y. *J. Org. Chem.* **1961**, *26*, 2273–2276; (b) Dener, J. M.; Hart, D. J.; Ramesh, S. *J. Org. Chem.* **1988**, *53*, 6022–6030; (c) Micouin, L.; Quirion, J.-C.; Husson, H.-P. *Synth. Commun.* **1996**, *26*, 1605–1612.
18. Mukaiyama, T.; Yamashita, H.; Asami, M. *Chem. Lett.* **1983**, 385–388.
19. Kang, J.; Lee, J. W.; Kim, J. I.; Pyun, C. *Tetrahedron Lett.* **1995**, *36*, 4265–4268.
20. Daumas, M.; Vo-Quang, Y.; Vo-Quang, L.; Goffic, F. L. *Synthesis* **1989**, 64–65.