Pergamon

Tetrahedron, Vol. 53, No. 37, pp. 12319-12338, 1997

0040-4020/97 $17.00 + 0.00

PII: S0040-4020(97)00769-2

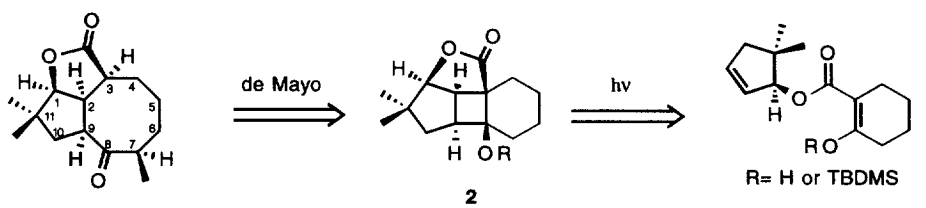
A Concise Synthesis of 7-Desmethylasteriscanolide and the Discovery of an Unusual Fragmentation Reaction to the Related Asteriscunolide Skeleton

Kevin I. Booker-Milburn*, Justin K. Cowell and (in part) Laurence J. Harris

School of Chemical Sciences, University of East Anglia, Norwich, Norfolk, England, NR4 7TJ, UK.

Abstract: A concise synthesis of 7-desmethylasteriscanolide is described. The key features include an efficient intramolecular [2+2] photocycloaddition of the α,β-unsaturated acid-ether **29** followed by a Curtius rearrangement/ ruthenium tetroxide/ fragmentation sequence to yield the cyclooctane lactones **32** and **33**. Attempted methylation of **32** uncovered an interesting retro-Michael type fragmentation to the related naturally occuring asteriscunolide skeleton. © 1997 Elsevier Science Ltd.

Asteriscanolide **1** is a cyclooctane sesquiterpene isolated from *Asteriscus aquaticus* L and was characterised in 1985 by San Feliciano *et al.*[1] The skeleton contains an number of interesting features such as the [6.3.0] carbocyclic system bridged by a butyrolactone ring and thus presents a considerable challenge to the synthetic organic chemist. An enantioselective total synthesis of **1** was described in 1988 by Wender *et al*[2] and employed an elegant Ni^0-catalysed [4+4] cycloaddition as the pivotal step in the construction of the [6.3.0] bicyclic core. Described herein are the full experimental details of our earlier model studies[3a,b] towards asteriscanolide, leading to the concise synthesis of 7-desmethylasteriscanolide. Also described are some interesting retro-Michael type fragmentation reactions leading to the related asteriscunolide skeleton. Our initial approach investigated the possibility of constructing the skeleton of asteriscanolide *via* a de Mayo[4] type fragmentation of the photoadduct **2** (Scheme 1).



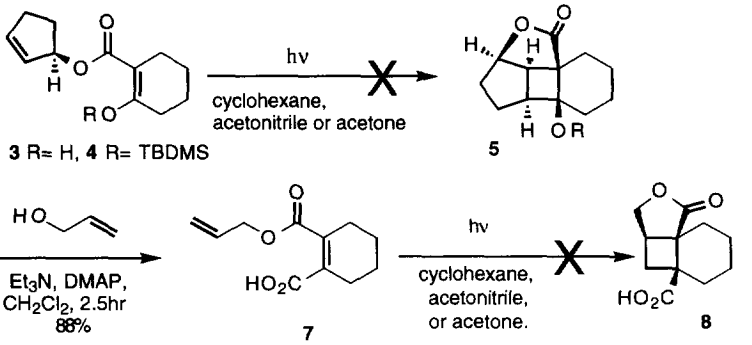
(+)-Asteriscanolide 1 **2**

Scheme 1

This strategy was soon abandoned, however, as we found that the esters **3** and **4** were inert to photolysis under a variety of conditions and none of the photoadduct **5** was ever obtained. The failure of **3/4** to undergo intramolecular [2+2] photocycloaddition was initially rationalised on electronic grounds and therefore the photochemistry of the more electron deficient acid-ester **7** was investigated. Treatment of tetrahydrophthalic anhydride (THPA, **6**) with allyl alcohol under basic conditions gave **7** in 88% yield, however, this also proved inert to photolysis and none of the photoadduct **8** was ever obtained (Scheme 2). The failure of **3,4** and **7** to undergo an intramolecular cycloaddition may be partly explained by the argument that esters have a conformational preference (cisoid) which is governed by stereoelectronic[5] factors and that this prevents **3,4** and

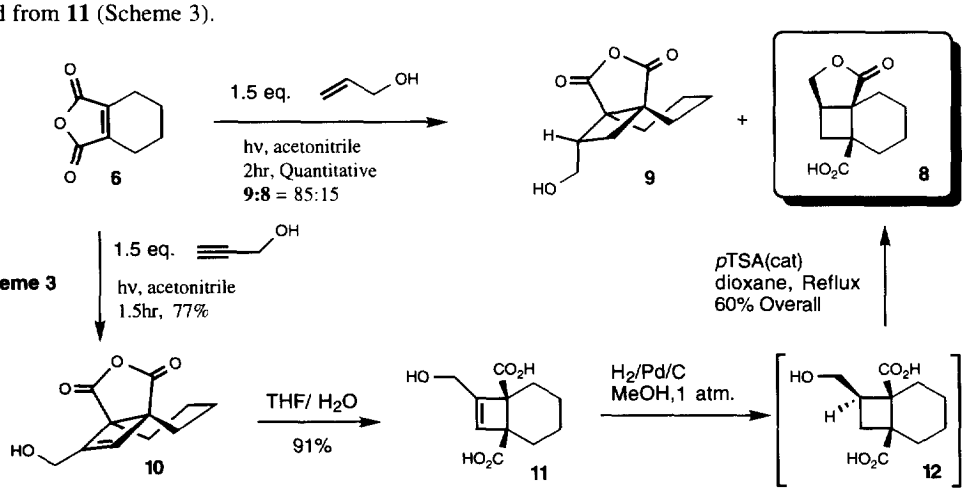
7 from adopting the conformation necessary for intramolecular cycloaddition. Both Pirrung[6] and Boeckman[7] have used similar arguments to explain the failure of related cycloadditions.

Scheme 2



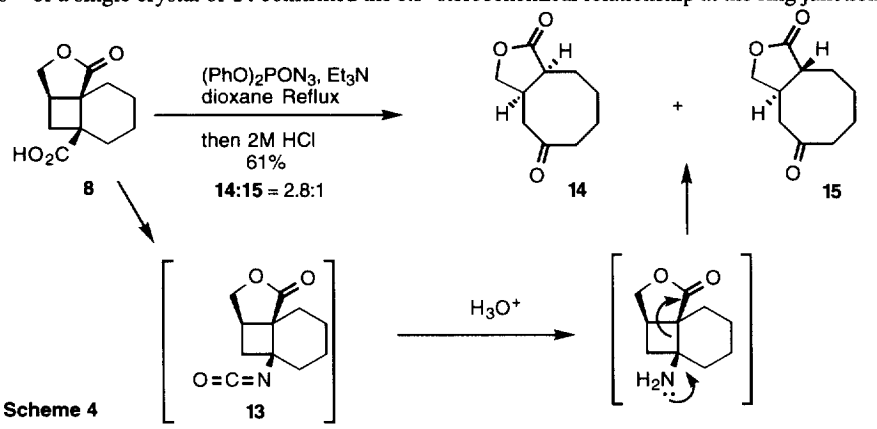
In the course of synthesising **7** it was observed that there was no ester formation between THPA and allyl alcohol under neutral conditions. It was therefore decided to investigate the intermolecular [2+2] photocycloaddition between THPA and allyl alcohol as a strategy towards the acid lactone **8**. Irradiation of an acetonitrile solution of THPA with 1.5 equivalents of allyl alcohol for just 2h gave an essentially quantitative yield[8] of a mixture of the hydroxy anhydride **9** and the desired acid lactone **8** in a ratio of 85:15 (NMR) respectively. Although this was a significant result the low isolable yield (~10%) meant that an alternative synthetic route for the multigram production of **8** had to be devised. Irradiation of THPA with propargyl alcohol gave the slightly unstable cyclobutene-anhydride **10** which could be isolated in good yield (77%) by rapid flash chromatography. This could be subsequently stored in a freezer for a few weeks without any significant polymerisation. Hydrolysis of **10** in aqueous THF gave the stable crystalline diacid **11** in 91% yield. Hydrogenation of **11** followed by *p*TSA catalysed cyclisation of the resulting crude hydroxy-diacid **12** gave the requisite acid-lactone **8** in 60% overall yield from **11** (Scheme 3).

Scheme 3



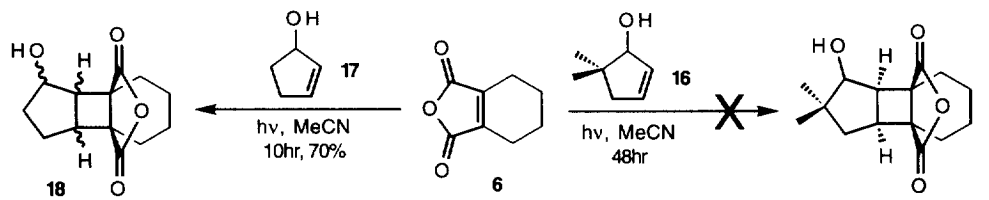
We were now at a stage where we could investigate a novel aza de Mayo fragmentation[9] by subjecting **8** to Curtius rearrangement. This was conveniently achieved with diphenylphosphoryl azide[10] which smoothly converted **8** to the corresponding isocyanate **13** (ν_{max} 2265cm^{-1}), this was not isolated but hydrolysed *in situ* to

give the fragmented *cis/trans* cyclooctanone-lactones **14** and **15** as a 2.8/1 mixture respectively (61%). X-ray analysis[3a] of a single crystal of **14** confirmed the *cis* -stereochemical relationship at the ring junction (Scheme 4).

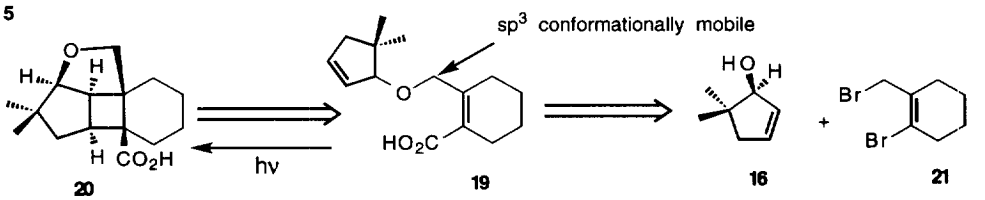


Scheme 4

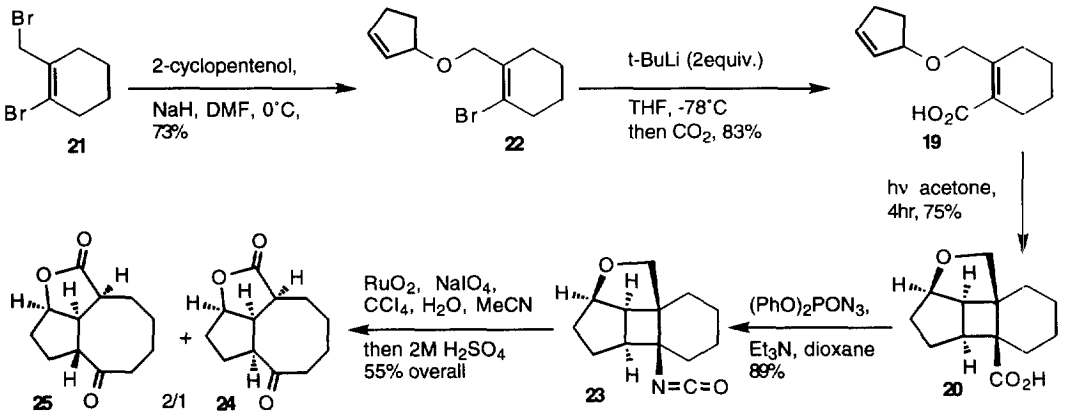
Attempts to extend this strategy towards a synthesis of the natural product by photolysis of THPA with 5,5-dimethylcyclopent-2-enol **16**[11] were unsuccessful and no intermolecular [2+2] photocycloaddition products were observed. We believe that this is probably a result of unfavourable steric interactions involving the *gem*-dimethyl moiety present in **16**, rather than failure of the photoreaction itself. This supposition was partially substantiated as we found that THPA and 2-cyclopentenol **17** readily underwent photolysis to give the photoadduct **18**. This was of limited synthetic value, however, as **18** was obtained as a complex mixture of stereoisomers. At this point it was decided to return to an intramolecular photocycloaddition route and concentrate on the synthesis of the acid-ether **20**. As stated above we believed that intramolecular cycloaddition of **3,4** and **7** was thwarted by the stereoelectronic preference of esters to adopt a *cisoid* geometry and we therefore decided to investigate the photocycloaddition of **19**→**20**. Since the carbonyl group is now absent in the acid-ether **19**, the sp^3 centre should allow a much greater degree of conformational mobility during the cycloaddition. The lactone carbonyl could then be reintroduced, after cycloaddition, by RuO_4 oxidation of the cyclised acid-ether **20** (Scheme 5). Disconnection of **19** leads to **16** and the known[12] allylic-bromide **21**.



Scheme 5

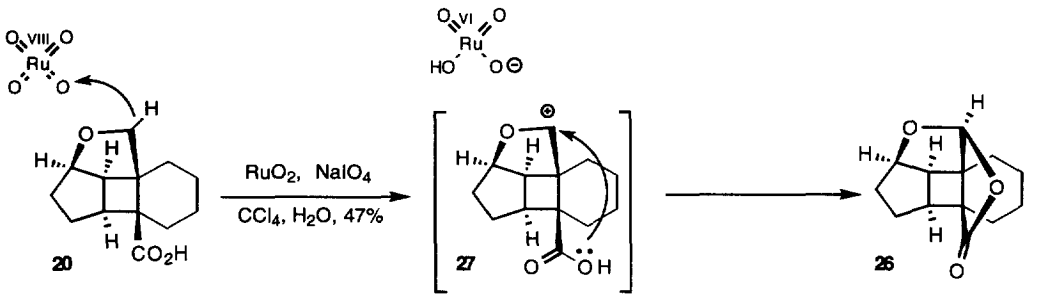


In order to test the above scheme we initially used 2-cyclopentenol rather than the less readily available **16**. Treatment of **21** with the sodium alkoxide of 2-cyclopentenol gave the ether **22** in 73% yield. Metal-halogen exchange with t-BuLi followed by quenching of the resulting vinyllithium with CO_2 gave the acid-ether **19** in excellent yield (83%). Photolysis of **19** in acetone gave the cyclobutane **20** in good yield (75%), thus rather gratifyingly supporting the above conformational arguments. Curtius rearrangement of **20** with DPPA gave the isocyanate **23** in an 89% isolated yield. This isocyanate proved to be remarkably stable to both chromatography and acid hydrolysis and because of this we decided to use it as a rather unconventional protecting group in the subsequent ruthenium tetroxide oxidation step. Thus, oxidation[13] of **23** with ruthenium tetroxide gave a rapid (1.5hr) and clean conversion to the corresponding (labile) isocyanate-lactone which, without purification, was immediately subjected to our aza de Mayo fragmentation by hydrolysis in aqueous acid followed by basification. This yielded the target cyclooctanone-lactone **24** and the C9-epimer **25**, as a 1/2 mixture respectively, in 55% overall yield from **23** (Scheme 6). Although the epimeric ratio was initially disappointing, we have subsequently shown that the two epimers are actually in equilibrium as we found that treatment of pure **25** with 2M H_2SO_4 resulted in a conversion back to the 1/2 mixture of **24** and **25** respectively. The structure and stereochemistry of both epimers was elucidated by a combination of nOe and X-ray crystallography.[14]



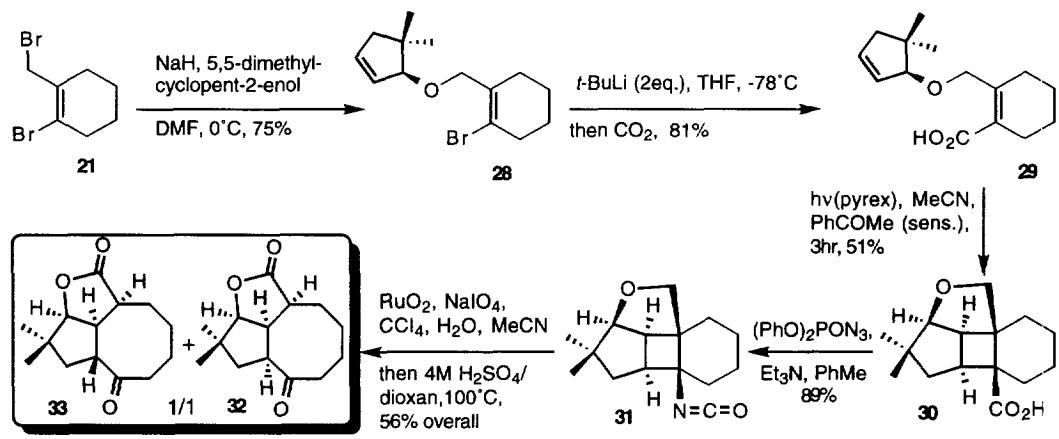
Scheme 6

The reason for subjecting **20** to the Curtius rearrangement prior to oxidation was because we found that treatment of **20** with ruthenium tetroxide resulted in the exclusive formation (47%) of the rather unusual acetal-lactone **26** rather than the expected acid-lactone (Scheme 7). Van den Engh[15] has proposed a mechanism for this type of oxidation which proceeds *via* hydride abstraction to give an intermediate carbocation (eg **27**), which then undergoes further reaction with a reduced Ru^{VI} oxide species to generate the lactone carbonyl. In our system we believe that if the carbocation **27** is formed it is likely to be intercepted by the carboxylic-OH before the Ru^{VI} species can react further, thus resulting in the formation of **26**. This intriguing result would seem to provide good evidence that the ruthenium tetroxide oxidation of ethers does proceed by a carbocation mechanism as proposed by Van den Engh. Further studies of this cyclisation with simpler substrates are in progress.



Scheme 7

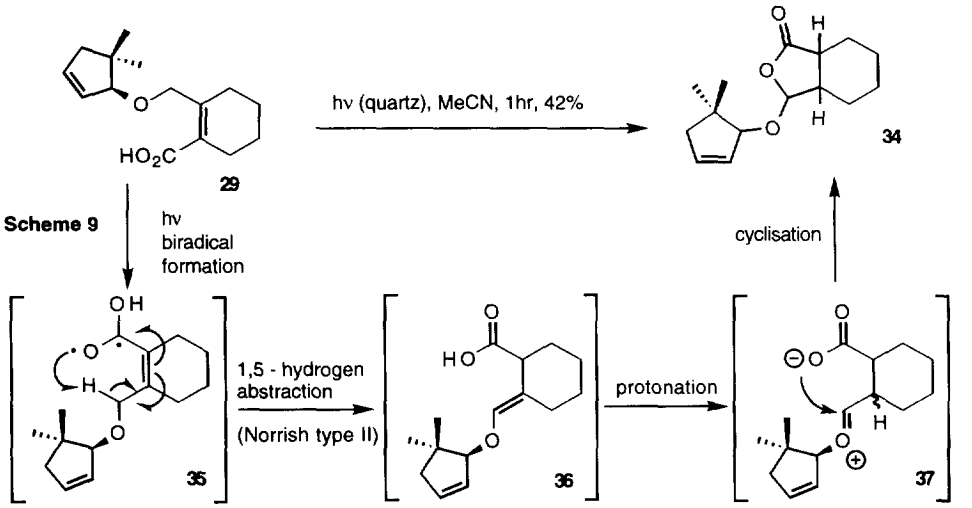
We were now at a stage where we were able to investigate the use of 5,5-dimethylcyclopent-2-enol in the synthesis of asteriscanolide using the above route. Treatment of the dibromide **21** with the sodium alkoxide of 5,5-dimethylcyclopent-2-enol gave the ether **28** (75%). Metal-halogen exchange with *t*-butyllithium followed by quenching with carbon dioxide furnished the α,β-unsaturated carboxylic acid **29** in good yield (81%). After optimisation the [2+2] photocycloaddition was found to proceed in acceptable yield (51%) by irradiation in acetonitrile using acetophenone as sensitiser. Curtius rearrangement of the resulting cycloadduct **30** with diphenylphosphoryl azide in toluene gave the stable isocyanate **31** in excellent yield (89%). Oxidation with ruthenium tetroxide followed by hydrolysis of the resulting isocyanate-lactone gave 7-desmethylasteriscanolide **32** and the 9-H epimer **33** as a separable 1:1 mixture in 56% overall yield from **31** (Scheme 8). The epimeric ratio was a distinct improvement on that obtained in the above model studies where the undesired epimer predominated.



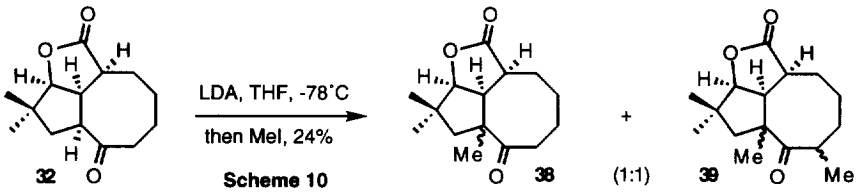
Scheme 8

Although the photocycloaddition **29**→**30** could be carried out on a reasonable scale (2.5-3g), yields were consistently in the region of 50% under sensitised conditions (acetophenone or acetone). The major UV

absorption of **29** is at 219nm which is typical of an α,β-unsaturated acid. Sensitised conditions were required because the key absorption of **29** is below the cut-off point for the pyrex filtered UV source used. In order to increase the yield of **30** we attempted to carry out the photocycloaddition of **29** using quartz glassware which should have, in principle, allowed the desired excitation to take place directly so that the α,β-unsaturated double bond would then undergo the requisite [2+2] photocycloaddition to **30**. However, irradiation of **29** in a quartz immersion well apparatus gave rise to a diastereomeric mixture of the furanones **34** rather than the expected cycloadduct **30**. We believe this unusual result can be explained by assuming **29** undergoes n→π* excitation to give the singlet biradical **35** which then undergoes a 1,5-hydrogen abstraction (Norrish type II) to give, after tautomerisation, the isomerised acid-enol ether **36**. Such Norrish type II isomerisations of α,β-unsaturated carbonyl compounds are well documented in the photochemical literature.[16] Intramolecular protonation of the acid-enol ether **36** would give the oxonium ion **37** which would then cyclise to the observed product. Studies are currently underway with other substrates to test whether this is a general reaction for the formation of butyrolactones from γ-alkoxy-α,β-unsaturated acids (Scheme 9).

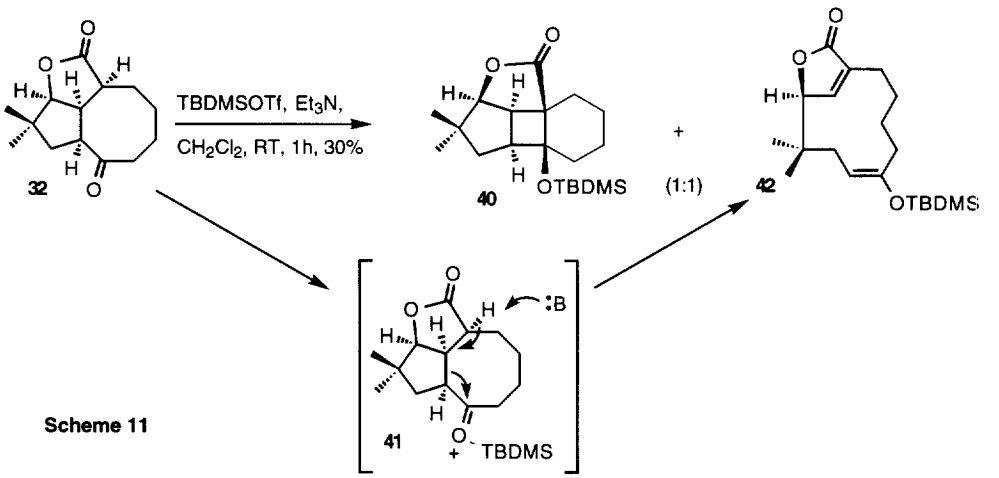


All that remained in order to complete the synthesis of asteriscanolide was the introduction of a methyl group at C-7 which was initially attempted using standard enolate protocol. However, treatment of **32** with LDA followed by alkylation with methyl iodide gave a poor yield (24%) of a 1:1 mixture of compounds which were identified as the monomethyl product **38** and what appeared to be the dimethylated product **39**. Despite various attempts this proved to be the optimum result and the poor mass balances obtained indicated that **32** was very labile under basic conditions. Deprotonation of **32** probably proceeds to give the more substituted enolate at C-9, which undergoes methylation to **38**, rather than formation of the presumed kinetic enolate at C-7. The dimethyl product **39** presumably arises from further alkylation of **38**. Attempted alkylation of the epimer **33** under the same conditions gave a poor yield of a complex reaction mixture with no evidence (NMR) of C-7 alkylation. Thus it would appear that the asteriscanolide skeleton undergoes preferential deprotonation and subsequent alkylation at C-9 rather than C-7 (*vide infra*). Attempts to introduce the C-7 methyl group *via* enamine chemistry were equally unsuccessful and either starting ketones or complex reaction mixtures were obtained (Scheme 10).



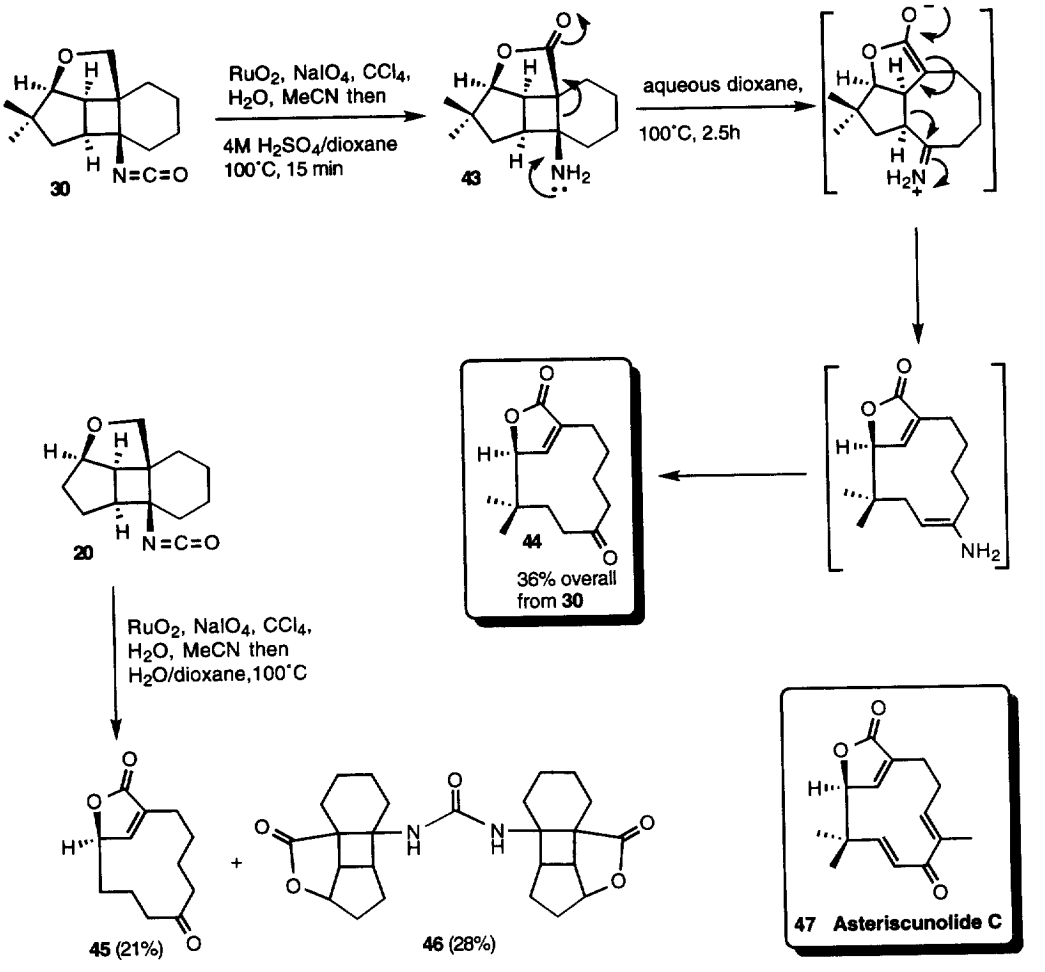
Scheme 10

In another strategy towards **1** we attempted to prepare the TBDMS enol ether of **32** with a view to introducing the methyl group *via* a less direct method such as cyclopropanation/hydrolysis. To this end **32** was treated with TBDMSOTf under basic conditions,[17] however, neither of the expected enol ethers were formed and the only products isolated were the cyclobutane **40** and the fragmented enol ether **42** as a 1:1 mixture in 30% yield. The formation of **40**, which presumably arises by transannular cyclisation[18] of the activated ketone **41**, is ironic as it is exactly the reverse of the key fragmentation used to construct **32** and **33**. The formation of **42** is likely to be a result of the intermediate **41** undergoing the base catalysed retro-Michael fragmentation shown in Scheme 11.



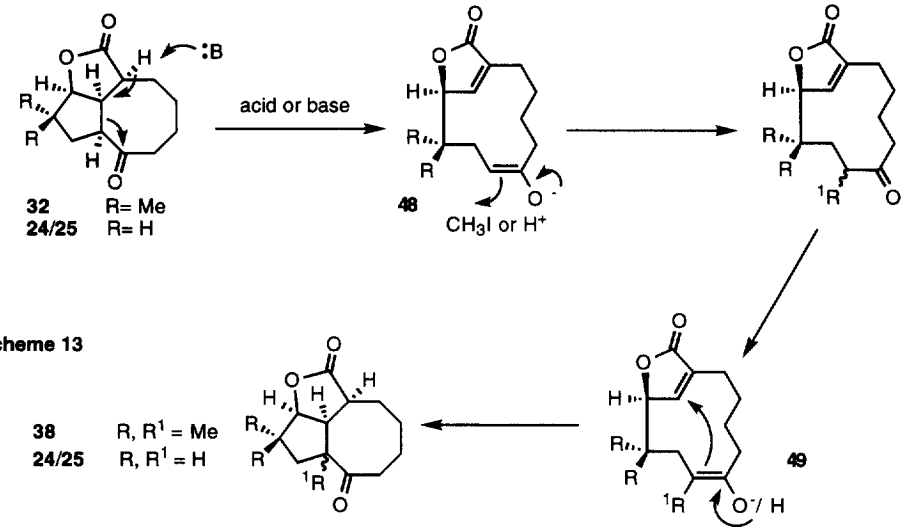
Scheme 11

A related fragmentation was also observed during the oxidation/hydrolysis of **30**. For example it was found that if, after oxidation of **30** with ruthenium tetroxide, the acid hydrolysis step was terminated after 15min an unstable polar compound was formed which was tentatively identified as the cyclobutylamine-lactone **43**. Heating crude **43** in aqueous 1,4-dioxane gave the fragmented keto-lactone **44** (36% from **30**) by the retro-Michael mechanism proposed in Scheme 11. Similarly in the model system it was also found that oxidation of the acid-ether **20** followed by hydrolysis of the isocyanate under neutral conditions gave the same fragmented ring system **45** (22%) along with substantial amounts of the urea **46** (28%) formed from dimerisation of hydrolysed amine with isocyanate. These fragmentations are extremely interesting as they give rise to the same butenolide fused undecane skeleton found in the naturally occurring asteriscunolide C **47**. Furthermore as structures related to asteriscanolide have been isolated[19] from the same natural source as the astericunolides (*Asteriscus graveolens*), it is quite possible that the two skeletons are biosynthetically related *via* the above retro-Michael fragmentation (Scheme 12).



Scheme 12

Finally, as it has been shown that **32** is prone to fragmentation, it is tempting to speculate that attempted methylation *via* enolate formation may be complicated by a competing process involving base catalysed retro-Michael fragmentation to give the enolate **48** (Scheme 13, R=Me) which then undergoes alkylation followed by transannular cyclisation back to **38** (R, R^1=Me). This would help explain why mono-alkylation at C-9 was observed rather than at C-7. A similar mechanism can be argued for the facile, acid catalysed equilibration of the epimers **24** and **25** *via* a sequence involving acid catalysed fragmentation to the enol equivalent of **49** (R, R^1=H) followed by cyclisation back to the respective C-9 epimer (R, R^1=H) (Scheme 13).



Scheme 13

In summary, a short (5 step) synthesis of 7-desmethylasteriscanolide has been described which highlights the use of an intramolecular [2+2] photocycloaddition-fragmentation (aza deMayo) sequence. Unfortunately completion of the synthesis of asteriscanolide itself by methylation at C-7 was frustrated by problems with methylation at C-9 and dimethylation. Present work is concerned with the introduction of the key C-7 methyl group at an earlier stage in the synthetic route (*ie* the 6-methyl analogue of **21**). The above studies have also highlighted the propensity of the asteriscanolide ring system towards retro-Michael type fragmentation. Indeed a double fragmentation sequence involving **30**→**43**→**44** may prove useful as a powerful strategy in a concise synthesis of asteriscunolide C (**47**), and current studies towards this end are in progress.

Acknowledgements: We would like to thank the EPSRC for a studentship (JKC) and financial support of this work (GR/K15985). We also thank the Strategic Research Committee at Zeneca Pharmaceuticals for the provision of an unrestricted research grant to KBM.

EXPERIMENTAL SECTION

All reactions were carried out under an atmosphere of oxygen free nitrogen. ^{1}H NMR spectra were obtained in deuteriochloroform (unless otherwise stated), with chemical shifts measured downfield from TMS (^{1}H) or referenced to the residual solvent resonance (^{13}C) using a Jeol PMX 60, a Jeol EX 270 FT or a Bruker AC 300 spectrometer. ^{13}C spectral assignments were made 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 (Kratos MS25) and elemental microanalyses (Carlo Erba EA 1108) were carried out by Mr A. W. R. Saunders at the University of East Anglia. High resolution mass spectra were run at the University of Manchester on a Kratos Concept 1-S instrument. Flash chromatography was carried out using either Matrex silica 60 (70-200 μm) or Merck silica 60 (40-63 μm) eluting with the solvents stated. Tlc analyses were performed using Camlab polygram® SIL G/UV$_{254}$ plastic backed plates (0.25 mm layer of silica) and were visualised using UV (254 nm), alkaline potassium manganate(VII) solution or acidic cerium(IV) sulfate solution. Short path

distillation was performed using a Büchi GKR-50 kugelröhr (quoted boiling points refer to the oven temperature). Melting points were obtained using a Köpfler hot stage apparatus and are uncorrected. All solutions were dried over anhydrous magnesium sulfate unless otherwise stated. Triethylamine and diisopropylamine were distilled from calcium hydride and stored over potassium hydroxide. Various solvents were dried as follows; THF and diethyl ether were distilled from sodium and benzophenone; acetonitrile, dichloromethane (DCM), toluene, 2-methoxyethyl ether (diglyme), hexane and petroleum ether (PE; bp 40-60 ^{o}C) were distilled from calcium hydride; chloroform was distilled from phosphorus(V) oxide; nitromethane, carbon tetrachloride and 1,4-dioxane were dried by standing over activated 4Å molecular sieves. Dimethylformamide (DMF) was also dried using activated 4Å molecular sieves (for 24h) prior to distillation under reduced pressure. All compounds were formed as racemic mixtures but for clarity have been represented as single enantiomers, with the same configuration as (+)-asteriscanolide. The use of *R** and *S** relates to relative stereochemistry only.

Photochemical reactions were carried out in a 150 mL standard reaction flask using either a pyrex or quartz glass immersion well. The reaction mixture was initially degassed by passage of a stream of nitrogen through the solution for 15 min and then irradiated under an atmosphere of nitrogen for the time stated. The radiation source was a water cooled, 125W medium pressure mercury discharge lamp with a 30 mm arc length. These lamps were obtained from 125W Osram HQL (MBF-U) bulbs by puncturing the outer glass envelope with a heated glass rod and removing the mercury lamp from inside by cutting the two copper electrodes as close to the screw thread as possible. These were then used as normal with a standard 125W power supply. Lamps prepared in this way were inexpensive and on average had a lifetime in excess of 200h. Both the power supply and the quartz glass immersion well were obtained from Photochemical Reactors Ltd, Reading.

Cyclohex-1-ene-1,2-dicarboxylic acid monoallyl ester (7) To a solution of 3,4,5,6-tetrahydrophthalic anhydride (THPA, Aldrich), (0.5 g, 3.29 mmol) in CH_2Cl_2 (30 mL) was added allyl alcohol (0.23 mL. 3.29 mmol), triethylamine (1.0 mL, 8.23 mmol) and DMAP (40 mg, 0.33 mmol) and the resulting mixture stirred at room temperature for 2.5h. The reaction mixture was poured onto CH_2Cl_2 (40 mL) and washed with 2M HCl (50 mL), brine (2 x 50 mL) and the organic phase dried and concentrated under reduced pressure to give a viscous yellow oil. Flash chromatography with EtOAc/ PE (1/1) containing 1% acetic acid gave the title product as a yellow oil (0.609g, 88%) which slowly cyclises back to THPA on prolonged standing at room temperature. ν_{max}/cm^{-1} (neat): 3300 (broad), 1770, 1694, 1646; δH (270 MHz): 5.95-5.83 (1H, m, CH-vinyl), 5.37-5.29 (2H, m, CH_2-vinyl), 4.62 (2H, d, *J*=6.75Hz, CH_2-allyl), 2.48-2.23 (4H, m, CH_2-3 and CH_2-6), 1.74-1.58 (4H, m, CH_2-4 and CH_2-5); HRMS: *m/z* (CI, NH_3) Found: 228.1229 (M + NH_4^+), $C_{11}H_{18}NO_4$ requires: 228.1236.

(1*S, 6*R**)-7-Hydroxymethyl-bicyclo[4.2.0]oct-7-ene-1,6-dicarboxylic acid anhydride (10)** A solution of THPA (1g, 6.57mmol) and propargyl alcohol (0.58 mL, 9.86 mmol) in dry acetonitrile (100 mL) was irradiated for 90min in a pyrex immersion well photo-reactor. The solvent was removed under reduced pressure to give a pale yellow oil which was immediately purified by flash chromatography (30% EtOAc/PE) to give the title compound as a clear oil (1.05g, 77%). This slowly polymerised on standing at room temperature but could be stored indefinitely in the freezer: ν_{max}/cm^{-1} (neat): 3420 (OH), 1844 and 1772 (CO anhydride); δH (270 MHz): 6.32 (1H, t, *J*=1.65Hz, CH-8), 4.26 (2H, d, *J*= 1.65, -C**H**$_2$OH), 2.89 (1H, br, O**H**), 2.12-1.88 (4H,

m, 2x CH_2), 1.68-1.36 (4H, m, 2x CH_2); δC (67.8 MHz): 172.21(C=O), 171.77 (C=O), 153.91 (C), 133.70 (CH), 58.18 (CH_2), 53.85 (C), 51.09 (C), 24.99 (CH_2), 24.17 (CH_2), 19.21 (CH_2), 19.13 (CH_2); MS: *m/z* 208 (M^+, 26.25%), 190 (18.93%), 180 (47.59%), 136 (76.89%).

(1*S, 6*R**)-7-Hydroxymethyl-bicyclo[4.2.0]oct-7-ene-1,6-dicarboxylic acid (11)** A solution of (1*S**, 6*R**)-7-hydroxymethyl-bicyclo[4.2.0]oct-7-ene-1,6-dicarboxylic acid anhydride **10** (2.6g, 12.5mmol) in 10% aqueous THF (100mL) was stirred at RT for 18h after which the solvent was removed under reduced pressure to give a sticky yellow solid. Purification by flash chromatography (20% MeOH/Et_2O) gave the title compound as a white solid (2.57g, 91%); mp 161-163°C. Found: C, 58.40; H, 6.20. $C_{11}H_{14}O_5$ requires: C, 58.41; H, 6.19; ν_{max}/cm^{-1} ($CHCl_3$): 3400 (OH alcohol), 3250-2230 (OH acid) and 1685 (CO acid);δH (270 MHz, DMSOd_6): 12.10 (2H, br, 2 x CO_2H), 6.17 (1H,s, CH-vinyl), 4.88 (1H, br, -CH_2**OH**), 4.21 (1H, d, J_{gem}=15.98Hz, -**CH$_2$**OH), 4.11 (1H, d, J_{gem}=16.17Hz, -**CH$_2$**OH), 2.15-1.98 (2H, m, CH_2), 1.9-1.72 (2H, m, CH_2), 1.65-1.34 (4H, m, 2xCH_2); δC (67.8 MHz): 174.71(C=O), 174.25 (C=O), 151.43 (C), 129.78 (CH), 57.50 (CH_2), 56.05 (C), 53.87 (C), 26.09 (CH_2), 25.68 (CH_2), 15.67 (CH_2), 15.58 (CH_2); HRMS: *m/z* (CI, NH_3) Found: 227.0918 (M + H^+), $C_{11}H_{15}O_5$ requires: 227.0919.

1-Oxo-hexahydro-2-oxa-cyclopenta[1,4]cyclobuta[1,2]benzene-4a-carboxylic acid (8) A suspension of (1*S**, 6*R**)-7-hydroxymethyl-bicyclo[4.2.0]oct-7-ene-1,6-dicarboxylic acid **11** (0.606 g, 2.68 mmol) and 10% Pd/C (60 mg) were stirred together under a hydrogen atmosphere (1atm) at RT for 16h. The reaction mixture was filtered and the solvent removed under reduced pressure to give **12** as a viscous oil. A solution of **12** and *p*-TSA (10 mg) in dry dioxane (20 mL) was heated at reflux for 1h, cooled and the solvent removed under reduced pressure to give a yellow oil. Flash chromatography (70% Et_2O/PE) gave the title product as a white solid (0.338 g, 60%); mp 139-140°C: ν_{max}/cm^{-1} ($CHCl_3$): 3230-2445 (OH acid), 1756 (C=O lactone), 1695 (C=O, acid); δH (300 MHz): 11.01 (1H, br, OH), 4.22-4.14 (2H, m, CH_2 lactone), 3.07-3.00 (1H, m, CH cyclobutane), 2.48-2.35 (2H, m, CH_2 cyclobutane), 1.92- 1.23 (8H, m, 4 x CH_2 cyclohexane); δC (75.47 MHz), 179.91 (CO), 178.60 (CO), 70.85 (CH_2), 51.43 (C), 43.87 (C), 33.97 (CH_2), 33.43 (CH), 32.67 (CH_2), 26.22 (CH_2), 21.71 (CH_2), 21.01 (CH_2); HRMS: *m/z* (CI, NH_3) Found: 228.1236 (M + NH_4^+), $C_{11}H_{18}NO_4$ requires: 228.1236.

(1*S, 5*R**)-3-oxabicyclo[6.3.0]undeca-2,7,-dione (14) and (1*R**, 5*R**)-3-oxabicyclo[6.3.0] undeca-2,7,-dione (15)** A solution of 1-oxo-hexahydro-2-oxa-cyclopenta[1,4]cyclobuta[1,2]benzene-4a-carboxylic acid **8** (1 g, 4.76 mmol), DPPA (1.13 mL, 5.24 mmol) and triethylamine (0.73 mL, 5.24 mmol) were heated at reflux in dry dioxane (10 mL) for 2h. 2M HCl (5 mL) was added and the reaction mixture heated at 100°C for a further 2h after which it was poured onto sat. bicarb. (100 mL) and extracted with EtOAc (2 x 100 mL). The extracts were dried and the solvent removed under reduced pressure to give a pale brown liquid. Purification by Flash chromatography (10%PE/Et_2O) allowed the partial separation of the title componds for analysis (0.529 g in total, 61%, **14/15**= 2.8/1). The first product eluted was (1*R**, 5*R**)-3-oxabicyclo[6.3.0]undeca-2,7,-dione **15**: ν_{max}/cm^{-1} ($CHCl_3$) 1770 (C=O lactone) and 1695 (C=O ketone); δH(300MHz, $CDCl_3$) 4.38 (t, 1H, J= 7.86Hz), 3.74 (t, 1H, J= 9.46), 2.68-2.38 (m, 4H), 2.39-2.26 (dquin.,1H), 2.23-2.12 (dq,1H), 2.05-1.72 (m, 3H), 1.61-1.44 (m, 2H), 1.39-1.2 (m, 1H); δC(75.47 MHz) δ 212.47 (C=O), 177.95 (C=O), 69.93 (CH_2), 45.19 (CH), 44.08 (CH_2), 41.95 (CH), 41.13 (CH_2), 26.51

(CH_2), 26.17 (CH_2), 24.77 (CH_2); HRMS (CI) found: $M^+(+NH_4^+)$ 200.1285, $C_{10}H_{14}O_3NH_4$ requires 200.1287. Further elution gave (1*S**, 5*R**)-3-oxabicyclo[6.3.0]undeca-2,7-dione **14** : ν_{max}/cm^{-1} ($CHCl_3$) 1765 (C=O lactone) and 1695 (C=O ketone); ^1H NMR (300MHz, $CDCl_3$) δ 4.34 (dd,1H, J_{gem}= 9.23, J_{vic}= 5.94Hz), 4.01(dd,1H, J_{gem}= 9.22, J_{vic}= 3.2Hz), 3.3-3.12 (m, 1H), 2.9-2.27 (m, 5H), 2.23-1.9 (m, 3H), 1.88-1.67 (m, 1H), 1.52-1.18 (m, 2H); ^{13}C NMR (75.47 MHz) δ 212.91 (C=O), 177.63 (C=O), 71.03 (CH_2), 44.92 (CH), 42.82 (CH_2), 41.38 (CH_2), 36.24 (CH), 27.17 (CH_2), 26.83 (CH_2), 23.67 (CH_2); HRMS (CI) found: $M^+(+NH_4^+)$ 200.1291, $C_{10}H_{14}O_3NH_4$ requires 200.1287.

1-Bromo-2-(bromomethyl)cyclohex-1-ene (21)[12(b)] A solution of 2-bromocyclohex-1-ene-1-carboxaldehyde[12(a)] (1.86 g, 9.84 mmol) in methanol (25 mL) was stirred vigorously as sodium borohydride (0.372 g, 9.84 mmol) was added in small portions over 2 min. When addition was complete the mixture was stirred for a further 2 min, until effervescence had ceased. The solution was quenched with water (50 mL) and then extracted with ether (3 x 50 mL). The combined organic layers were washed with brine (50 mL), dried and concentrated under reduced pressure to give 1-bromo-2-(hydroxymethyl)cyclohex-1-ene as a colourless liquid (1.74 g, 93%, crude); ν_{max}/cm^{-1} (neat): 3316 (br., OH), 1658 (C=C); δH (270 MHz): 4.25 (2H, s, $C\underline{H}_2$-OH), 2.55 (2H, m), 2.25 (2H, m), 2.01 (1H, s, br., OH), 1.75-1.64 (4H, m, CH_2-4 + CH_2-5). A solution of the crude 1-bromo-2-(hydroxymethyl)cyclohex-1-ene (1.74 g, 9.11 mmol) in ether (35 mL) was cooled to 0 °C (ice/salt) and phosphorus(III) bromide (0.90 mL, 9.57 mmol) was added. The resulting brown solution was stirred for 1 h and then the reaction was quenched by pouring onto ice. The resulting mixture was extracted with ether (4 x 50mL) and the combined organic layers were washed with saturated aqueous sodium bicarbonate (50 mL), dried and concentrated under reduced pressure to leave a pale yellow liquid. This was subjected to flash chromatography (20% Et_2O/PE) to give the title compound as a colourless liquid (1.5 g, 65%); ν_{max}/cm^{-1} (neat): 1650 (C=C); δH (270 MHz): 4.11 (2H, s, CH_2-Br), 2.52 (2H, m), 2.30 (2H, m), 1.71 (4H, m, CH_2-4 + CH_2-5); δC (67.8 MHz): 132.47 (C), 124.67 (C), 36.86 (CH_2), 36.62 (CH_2), 29.31 (CH_2), 24.49 (CH_2), 22.25 (CH_2); MS: *m/z* 256 (M^+ (2 x ^{81}Br), 9.0%), 254 (M^+ (^{81}Br, ^{79}Br), 16.5%), 252 (M^+ (2 x ^{79}Br), 9.0%), 175 (62.8%), 173 (63.6%), 93 (100%).

2-(2'-Cyclopentenyloxy)methyl-1-bromo-1-cyclohexene (22) A portion of sodium hydride (60%) (0.52 g, 13 mmol) was washed with dry PE (2 x 30mL), suspended in DMF (5 mL) and then cooled to 0 °C (ice/salt). A solution of cyclopent-2-enol (1.0 g, 12 mmol) in DMF (15 mL) was added slowly to the suspension, keeping the temperature below 0 °C and vigorous effervescence was observed. The resulting dark solution was stirred for a further 1.5 h at 0 °C before a solution of 1-bromo-2-(bromomethyl)cyclohex-1-ene **21** (3.33 g, 13 mmol) in DMF (15 mL) was added, maintaining the temperature at 0 °C. The solution was stirred at 0 °C for a further 0.5 h and then quenched by pouring onto ice/water (50 mL). This mixture was extracted with ether (4 x 50mL) and the combined organic layers were washed with brine (50 mL), dried and concentrated under reduced pressure to leave a pale yellow liquid (3.2 g). Purification by flash chromatography (5% Et_2O/PE) yielded the title compound as a colourless liquid (2.25 g, 73%) which was stored at -20 °C under nitrogen to avoid decomposition; δH (270 MHz): 6.00 (1H, m), 5.85 (1H, m), 4.60 (1H, m, CH-1), 4.15 (2H, s, CH_2-O), 2.50 (3H, m), 2.20 (4H, m), 1.79-1.61 (5H, m); δC(67.8 MHz): 135.56 (CH), 133.58 (C), 130.89 (CH), 121.56 (C), 84.08 (CH), 71.43 (CH_2), 36.77 (CH_2), 31.04 (CH_2), 29.78 (CH_2), 28.99 (CH_2), 24.69 (CH_2), 22.14 (CH_2).

2-(2'-Cyclopentenyloxy)methyl-1-cyclohexene-1-carboxylic acid (19) A solution of **22** (2.0 g, 8.1 mmol) in THF (25 mL) was cooled to -78 °C and *t*-butyllithium (1.7 M in hexanes) (10.5 mL, 17.8 mmol) was added slowly with stirring, keeping the temperature below -60 °C. After addition, the solution was stirred for a further 1 h at -78 °C, followed by 1 h at about -50 °C to produce a brilliant yellow solution. This was then cooled to -78 °C and a large excess of crushed cardice was added in one portion. This produced an immediate exotherm and the solution became colourless. The reaction was then quenched by pouring onto 2 M HCl/ ice (40 mL) and extracted with ether (4 x 50 mL). The combined organic layers were washed with brine (50 mL), dried and concentrated under reduced pressure to leave a pale brown oil (2.66 g). This was subjected to flash chromatography to give the title compound as a waxy, colourless solid (1.51 g, 83%); mp (EtOAc) 30-33 °C; (Found: C, 70.33; H, 8.34. $C_{13}H_{18}O_3$ requires: C, 70.27; H, 8.11); ν_{max}/cm^{-1} (DCM thin film): 3300-2500 (br., OH), 1685 (CO), 1621 (C=C); δH (270 MHz): 6.10 (1H, m), 5.85 (1H, m), 4.60 (1H, br., CH-1'), 4.35 (2H, s, CH_2-O), 2.58-2.42 (1H, m), 2.40-2.23 (5H, m), 2.19-2.05 (1H, m), 1.86-1.75 (1H,m), 1.72-1.57 (4H, m); δC (67.8 MHz): 172.96 (C), 148.36 (C), 136.08 (CH), 130.46 (CH), 126.79 (C), 84.89 (CH), 69.02 (CH_2), 31.05 (CH_2), 29.60 (CH_2), 28.91 (CH_2), 26.47 (CH_2), 21.91 (CH_2), 21.78 (CH_2); MS: *m/z* 222 (M^+, 0.80%), 155 (33.3%), 137 (72.2%), 109 (61.5%), 67 (100%).

(1*R, 2*S**, 3*R**, 6*S**, 7*S**)-3,1-(epoxymethano)tricyclo[5.4.0.0^{2,6}]undecane-7-carboxylic acid (20)** The acid **19** (0.415 g, 1.96 mmol) was dissolved in acetone (distol) (100 mL) and irradiated for 4 h, after which time all the starting material had been consumed (tlc control). The lamp was switched off and the solvent removed under reduced pressure to leave a pale yellow oil. This was subjected to flash chromatography (40% EtOAc/PE) to furnish the title compound as a colourless oil which slowly solidified to give a colourless solid (0.311 g, 75%); mp (PE) 86-89 °C; (Found: C, 70.22; H, 8.16. $C_{13}H_{18}O_3$ requires: C, 70.27; H, 8.11); ν_{max}/cm^{-1} (neat): 3450-2500 (OH), 1701 (CO); δH (270 MHz): 10.2-9.3 (1H, br., COOH) 4.60 (1H, dd, *J'*=3.63Hz, *J''*=1.32Hz, CH-3), 4.30 (1H, d, *J*=9.90Hz, CH_2-O), 3.56 (1H, d, *J*=9.90Hz, CH_2-O), 2.93 (1H, m, CH-2), 2.46 (1H, dd, *J'*=8.91Hz, *J''*=7.59Hz, CH-6), 2.41-1.30 (12H, m); δC (67.8 MHz): 181.2 (C), 85.41 (CH), 80.25 (CH_2), 50.89 (C), 48.07 (CH), 47.22 (C), 46.11 (CH), 37.27 (CH_2), 36.93 (CH_2), 29.54 (CH_2), 27.37 (CH_2), 22.05 (CH_2), 20.13 (CH_2); MS: *m/z* 222 (M^+, 100%), 223 (14.5%).

(1*R,2*S**,3*R**,6*S**,7*S**)-3,1-(epoxymethano)tricyclo-[5.4.0.0^{2,6}]-undecane-7-isocyanate (23)** Triethylamine (0.14 mL, 1.0 mmol) and diphenylphosphoryl azide (DPPA) (0.19 mL, 0.9 mmol) were added to a solution of **20** (200 mg, 0.9 mmol) in 1,4-dioxane (2.1 mL) and the mixture was heated to reflux for 0.5 h. After cooling, the solution was diluted with DCM (20 mL) and the solvent was removed under reduced pressure. The crude residue was subjected to flash chromatography (20% EtOAc/PE) to provide the title compound as a colourless oil (175 mg, 89%); ν_{max}/cm^{-1} (neat): 2261 (NCO); δH (270 MHz): 4.54 (1H, m, CH-3), 4.07 (1H, d, *J*=9.9Hz, CH_2-O), 3.36 (1H, d, *J*=9.9Hz, CH_2-O), 2.69-2.59 (2H, m), 2.12-1.84 (3H, m), 1.80-1.45 (9H, m); δC (67.8 MHz): 121.8 (C), 85.80 (CH), 77.29 (CH_2), 59.19 (C), 52.53 (C), 48.99 (CH), 45.30 (CH), 36.44 (CH_2), 34.54 (CH_2), 25.18 (CH_2), 24.06 (CH_2), 18.64 (CH_2), 17.31 (CH_2); MS: *m/z* 219 (M^+, 0.80%), 153 (100%); HRMS: *m/z* (CI, NH_3) Found: 237.1611, $C_{13}H_{17}NO_2$ (M + NH_4^+) requires: 237.1603.

(1*R, 2*R**, 3*S**, 9*S**)-8-oxobicyclo[6.3.0] undecane-1,3-carbolactone (24) and 9H-epimer (25)** A portion of ruthenium(IV) oxide hydrate (15 mg, 0.13 mmol) was added to a solution of sodium periodate (686 mg, 3.2 mmol) in a triphasic solvent mixture of water (4 mL), carbon tetrachloride (4 mL) and acetonitrile (1 mL). This mixture was stirred vigorously for 10 min until a bright yellow colour appeared in the organic layer. A solution of **23** (175 mg, 0.799 mmol) in acetonitrile (5.5 mL) was added over 5 min to the vigorously stirred mixture to produce a cloudy yellow suspension. After stirring for a further 1.5 h the mixture was diluted with DCM (100 mL) and a black precipitate was produced. Anhydrous magnesium sulfate was added to the mixture to remove the water and after filtration through celite the solution was dried again and the solvent removed under reduced pressure to leave the isocyanate-lactone as a dark liquid (240 mg); ν_{max}/cm^{-1} (neat): 2265 (NCO), 1775 (CO). The crude isocyanate-lactone (240 mg) was dissolved in 1,4-dioxane (25 mL) and treated with 2 M H_2SO_4 (3 mL). The mixture was heated to reflux for 1.5 h, allowed to cool and then neutralised (indicator paper) by addition of saturated aqueous sodium bicarbonate. After extraction with EtOAc (4 x 30 mL) the combined organic layers were dried and concentrated under reduced pressure to leave a light brown oil (170 mg). This was subjected to flash chromatography (40% EtOAc/PE) to separate the two major products present. The first component of the mixture was isolated as a colourless, crystalline solid and was shown by analysis to be **25** (61 mg, 37% from **23**); mp (EtOAc/PE) 60-61.5 ^{o}C; ν_{max}/cm^{-1} (DCM thin film): 1764 (CO), 1696 (CO); δH (270 MHz): 4.88 (1H, m, CH-1), 2.99-2.81 (3H, m), 2.59-1.55 (12H, m); δC (67.8 MHz): 212.3 (C), 178.1 (C), 84.55 (CH), 51.11 (CH), 48.91 (CH), 44.42 (CH), 41.94 (CH_2), 31.54 (CH_2), 27.26 (CH_2), 27.14 (CH_2), 25.77 (CH_2), 24.67 (CH_2); MS: *m/z* 208 (M^+, 79.2%), 209 (10.8%), 180 (36.8%), 67 (100%); HRMS: *m/z* (CI, NH_3) Found: 226.1450, $C_{12}H_{16}O_3$ ($M + NH_4^+$) requires: 226.1443. Further elution gave the title compound **24** as colourless needles; (30.5 mg 18% from (**23**)); mp (EtOAc/PE) 133-136 ^{o}C; ν_{max}/cm^{-1} (DCM thin film): 1751 (CO), 1683.5 (CO); δH (270 MHz): 4.97 (1H, t, *J*=5.12Hz, CH-1), 3.71 (1H, m, CH-2), 2.88 (1H, m, CH-9), 2.73 (1H, m, CH-3), 2.62-2.53 (1H, m), 2.49-2.37 (1H, m), 2.21-1.38 (10H, m); δC (67.8 MHz): 212.2 (C), 178.1 (C), 84.33 (CH), 54.46 (CH), 44.76 (CH), 43.92 (CH_2), 43.40 (CH), 30.89 (CH_2), 27.39 (CH_2), 25.28 (CH_2), 23.38 (CH_2), 22.59 (CH_2); MS: *m/z* 208 (M^+, 51.3%), 209 (7.4%), 180 (24.8%), 67 (100%); HRMS: *m/z* (CI, NH_3) Found: 226.1444, $C_{12}H_{16}O_3$ ($M + NH_4^+$) requires: 226.1443.

Attempted preparation of (1*R, 2*S**, 3*R**, 6*S**, 7*S**)-7-carboxytricyclo[5.4.0.$0^{2,6}$]undecane -1,3-carbolactone.** A portion of sodium periodate (0.52 g, 2.43 mmol) was dissolved in a biphasic solvent system of water (10 mL) and carbon tetrachloride (10 mL). The solution was stirred vigorously as a portion of ruthenium(IV) oxide hydrate (0.02 g, 0.15 mmol) was added. Stirring was continued for a further 10 min until a deep yellow colour was produced in the organic layer. To this a solution of **20** (0.141 g, 0.665 mmol) in carbon tetrachloride (3 mL) was added, slowly with vigorous stirring. The resulting black suspension was stirred for 14 h and then filtered through celite to furnish a bright yellow solution. The aqueous layer was separated, saturated with sodium chloride and extracted with DCM (4 x 30 mL). The combined organic extracts were treated with isopropyl alcohol (0.25 mL) and vigorously shaken for 5 min. Finally the dark solution was dried and filtered through celite again to leave a clear yellow solution. The solvent was removed under reduced pressure to leave a bright red, oily residue which was subjected to flash chromatography (30% EtOAc/PE). The major component was isolated as a pale yellow, oily solid. Trituration with ether gave a colourless, granular solid that was shown by detailed analysis to be the lactone-acetal **26** (61 mg, 47%); mp 120-122 ^{o}C; (Found: C, 70.57; H, 7.17. $C_{13}H_{16}O_3$ requires: C, 70.90; H, 7.27); ν_{max}/cm^{-1} (nujol): 1762 (CO); δH (270 MHz): 5.58 (1H, s, O-C<u>H</u>-

O(CO)), 4.97 (1H, m, CH-3), 2.98 (1H, dd, *J'*=5.93Hz, *J''*=2.64Hz, CH-2), 2.60-2.51 (1H, m, CH-6), 2.36 (1H, m), 2.08 (1H, m), 1.97-1.83 (2H, m), 1.75-1.10 (8H, m); δC (67.8 MHz): 179.03 (C), 114.86 (CH, d, *J*=170Hz), 91.57 (CH, d, *J*=145Hz), 51.95 (C), 48.12 (CH), 46.16 (CH), 44.19 (C), 36.30 (CH_2), 29.94 (CH_2), 27.39 (CH_2), 26.34 (CH_2), 20.90 (CH_2), 20.52 (CH_2); MS: *m/z* 220 (M^+, 0.23%), 176 (30%), 148 (100%); HRMS: *m/z* (CI, NH_3) Found: 238.1446, $C_{13}H_{16}O_3$ ($M+NH_4^+$) requires: 238.1443.

2-(5',5'-Dimethyl-2'-cyclopentenyloxy)methyl-1-bromo-1-cyclohexene (28) A portion of sodium hydride (60%) (0.21 g, 5.13 mmol) was washed with dry PE (2 x 10 mL), suspended in DMF (4 mL) and cooled to 0 °C (ice/salt). A solution of 5,5-dimethyl-2-cyclopentenol **16** (0.5 g, 4.46 mmol) in DMF (4 mL) was added slowly to the suspension, keeping the temperature between -5 and 0 °C. The resulting brown solution was stirred for a further 50 min at 0 °C before a solution of 1-bromo-2-(bromomethyl)cyclohex-1-ene **21** (1.13 g, 4.46 mmol) in DMF (4 mL) was added, still maintaining the temperature at 0 °C. The solution was stirred at 0 °C for a further 2 h and then allowed to warm to RT. After 15 min the reaction mixture was quenched by pouring onto ice/water (50 mL) and then extracted with ether (4 x 50 mL). The combined organic layers were washed with brine (50 mL), dried and concentrated under reduced pressure to leave a pale yellow liquid (2.1 g). This was subjected to flash chromatography (1% Et_2O/PE) to yield the title compound as a colourless liquid (0.95 g, 75%); ν_{max}/cm^{-1} (neat): 1663 (w, C=C), 1615 (vw, C=C); δH (270 MHz): 5.87 (1H, m), 5.79 (1H, m), 4.19 (2H, s, CH_2-O), 3.90 (1H, s, CH-1), 2.51 (2H, br.), 2.24 (3H, m), 2.04 (1H, m), 1.69 (4H, m), 1.10 (3H, s, CH_3), 1.08 (3H, s, CH_3); δC (67.8 MHz): 133.98 (C), 133.91 (CH), 130.53 (CH), 121.06 (C), 90.85 (CH), 72.78 (CH_2), 47.04 (CH_2), 41.78 (C), 36.82 (CH_2), 29.17 (CH_3), 28.81 (CH_2), 24.82 (CH_2), 22.91 (CH_3), 22.23 (CH_2); MS: *m/z* 286 ($M^+(^{81}Br)$, 3.08%), 284 ($M^+(^{79}Br)$, 3.26%), 112 (100%).

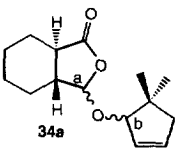
2-(5',5'-Dimethyl-2'-cyclopentenyloxy)methyl-1-cyclohexene-1-carboxylic acid (29) A solution of **28** (0.95 g, 3.33 mmol) in THF (10 mL) was cooled to -78 °C and *t*-butyllithium (1.7 M in hexanes) (3.92 mL, 6.67 mmol) was added slowly with stirring, keeping the temperature below -60 °C. After addition, the solution was stirred for a further 85 min at -78 °C to produce a brilliant yellow solution. A large excess of crushed cardice was then added in one portion and, after an immediate exotherm, the solution became colourless. The reaction was quenched by pouring onto 2 M HCl/ ice and then extracted with ether (4 x 30 mL). The combined organic layers were washed with brine (50 mL), dried and concentrated under reduced pressure to leave a brown oil (1.03 g). This was subjected to flash chromatography (20% EtOAc/PE) to give the title compound as a waxy solid (0.68 g, 81%); mp 25-28 °C; ν_{max}/cm^{-1} (DCM thin film): 3300-2500 (OH), 1694 (CO), 1622 (w, C=C); δH (270 MHz): 5.89 (1H, m), 5.82 (1H, m), 4.49-4.34 (2H, m, CH_2-O), 3.93 (1H, s, CH-1), 2.34 (4H, m), 2.26 (1H, m), 2.06 (1H, m), 1.63 (4H,m), 1.10 (3H, s, CH_3), 1.08 (3H, s, CH_3); δC (67.8 MHz): 173.14 (C), 149.74 (C), 134.41 (CH), 129.92 (CH), 125.93 (C), 91.57 (CH), 70.35 (CH_2), 46.90 (CH_2), 41.85 (C), 28.97 (CH_3), 28.61 (CH_2), 26.36 (CH_2), 22.86 (CH_3), 21.91 (CH_2), 21.76 (CH_2); MS: *m/z* 250 (M^+, 3%), 155 (42%), 139 (100%); HRMS: *m/z* (CI, NH_3) Found: 268.1919, $C_{15}H_{22}O_3$ ($M + NH_4^+$) requires: 268.1913.

(1*R, 2*S**, 3*S**, 6*S**, 7*S**)-4,4-Dimethyl-3,1-(epoxymethano)tricyclo[5.4.0.0^{2,6}]undecane 7-carboxylic acid (30)**

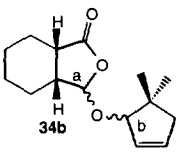
(a) Using acetone sensitisation A solution of **29** (0.49 g, 1.96 mmol) in acetone (distol) (100 mL) was irradiated in a pyrex immersion well for 19 h after which time the starting material had been consumed (tlc control). The solvent was removed under reduced pressure to leave a pale brown oil. This crude material was dissolved in EtOAc (50 mL) and then extracted with saturated aqueous sodium bicarbonate (3 x 100 mL). The combined aqueous layers were neutralised by addition of 2 M HCl (indicator paper) and this was extracted with EtOAc (4 x 75 mL). The combined organic layers were washed with brine (50 mL), dried and concentrated under reduced pressure to leave a pale yellow oil (0.51 g). This was subjected to flash chromatography (20% EtOAc/PE) to give the title compound as a colourless, crystalline solid (0.25 g, 51%); mp 122-124 ^{O}C; (Found: C, 72.03; H, 8.72. $C_{15}H_{22}O_3$ requires: C, 72.00; H, 8.80); ν_{max}/cm^{-1} (DCM thin film): 3441 (br., OH), 1703 (CO); δH (270 MHz): 4.26 (1H, d, *J*=9.90Hz, CH_2-O), 3.92 (1H, d, *J*=5.28Hz, CH-3), 3.59 (1H, d, *J*=9.90Hz, CH_2-O) 3.07 (1H, dd, *J'*=5.28Hz, *J''*=1.98Hz, CH-2) 2.51 (1H, dd, *J'*=8.90Hz, *J''*=7.59Hz, CH-6), 2.39-2.30 (1H, m), 1.77-1.38 (9H, m), 1.09 (3H, s, CH_3), 0.74 (3H, s, CH_3); δC (67.8 MHz): 181.28 (C), 92.69 (CH), 80.47 (CH_2), 50.39 (C), 47.67 (CH), 47.64 (C), 47.37 (C), 45.68 (CH), 40.85 (CH_2), 37.59 (CH_2), 30.21 (CH_2), 25.84 (CH_3), 22.45 (CH_2), 22.32 (CH_3), 20.49 (CH_2); MS: *m/z* 250 (M^+, 100%), 251 (15.5%).

(b) Using acetophenone sensitisation A solution of **29** (2.76 g, 11.0 mmol) and acetophenone (1.5 eq., 16.5 mmol, 2.0 mL) in acetonitrile (100 mL) was irradiated in a pyrex immersion well for 3 h after which time the starting material had been consumed (tlc control). The reaction was worked up as before to give the title compound as a colourless, crystalline solid (1.40 g, 51%). All spectral details concurred with those given in **(a)** above.

(c) Attempted photocycloaddition using quartz immersion well A solution of (**29**) (413 mg, 1.65 mmol) in acetonitrile (100 mL) was irradiated in a quartz immersion well photo-reactor for 1 h after which time all the starting material had been consumed (tlc control). The solvent was removed under reduced pressure to give a yellow oil which was a mixture of two components (tlc). These were separated by flash chromatography (10% EtOAc/PE) and detailed analysis of the spectral data indicated that the two compounds were the diastereomeric lactone-acetals **34a/b**.



34a



34b

Each diastereomer was present as a further inseparable mixture of isomers referred to as **min** (minor) and **maj** (major), although it was not possible to assign whether they were isomeric around the anomeric centre (a) or the cyclopentenyl centre (b). The first component after chromatography was a colourless oil (121.5 mg, 29%); (Found: C, 71.80; H, 8.87. $C_{15}H_{22}O_3$ requires: C, 72.00; H, 8.80); ν_{max}/cm^{-1} (neat): 1775 (CO); δH (270 MHz): 5.97 (1H, m), 5.87 (1.5H, m), 5.79 (2.5H, m), 5.50 (1H, s, O-CH-O(CO)), 5.48 (1.5H, s, OCH-O(CO)), 4.30 (1H, s, br., CH-O), 4.19 (1.5H, s, br., CH-O), 2.63 (2.5H, m), 2.56-2.45 (2.5H, m), 2.27 (1H, dt, *J'*=2.31Hz, *J''*=1.98Hz, CH(CO)), 2.21 (1.5H, dt, *J'*=2.31Hz, *J''*=1.98Hz, CH(CO)), 2.12-1.97 (5H, m), 1.71-1.24 (17.5H, m), 1.10 (4.5H, s, CH_3), 1.09 (3H, s, CH_3), 1.05 (3H, s, CH_3), 1.04 (4.5H, s, CH_3); δC (67.8 MHz): 176.9 (Q, **min+maj**), 136.2 (CH, **min**), 134.2 (CH, **maj**), 130.8 (CH, **maj**), 128.5 (CH, **min**),

106.5 (CH, **maj**), 103.7 (CH, **min**), 94.16 (CH, **maj**), 90.98 (CH, **min**), 46.87 (CH_2, **min**), 46.61 (CH_2, **maj**), 41.73 (Q, **min**), 41.67 (Q, **maj**), 40.60 (CH, **min**), 40.47 (CH, **maj**), 39.23 (CH, **min**), 39.14 (CH, **maj**), 28.82 (CH_3, **maj**), 28.25 (CH_3, **min**), 23.34 (CH_3, **min**), 23.24 (CH_3, **maj**), 23.20 (CH_2, **min+maj**), 22.84 (2 x CH_2, **min+maj**), 21.84 (CH_2, **maj**), 21.74 (CH_2, **min**); MS: *m/z* 250 (M^+, 2.7%), 139 (100%), 112 (30%), 95 (83%). The second component was a colourless oil (52.5 mg, 13%) ν_{max}/cm^{-1} 1784 (CO); δH (270 MHz): 5.97 (1.2H, m), 5.86 (1H, m), 5.79 (1.2H, m), 5.71 (1H, m), 5.13 (1H, s, O-CH-O(CO)), 5.11 (1.2H, s, O-CH-O(CO)), 4.22 (1.2H, s, br., CH-O), 4.17 (1H, s, br., CH-O), 2.92 (2.2H, m, br.), 2.45-2.33 (2.2H, m), 2.27 (1H, m, CH(CO)), 2.21 (1.2H, m, CH(CO)), 2.07 (4.4H, m), 1.86 (2.2H, m, br.), 1.64-1.48 (13.2H, m), 1.10 (3.6H, s, CH_3), 1.07 (3.6H, s, CH_3), 1.04 (3H, s, CH_3), 0.99 (3H, s, CH_3); δC (67.8 MHz): 178.47 (Q, **maj**), 178.35 (Q, **min**), 135.85 (CH, **maj**), 134.34 (CH, **min**), 130.71 (CH, **maj**), 128.77 (CH, **min**), 107.10 (CH, **min**), 105.01 (CH, **maj**), 92.18 (CH, **min**), 89.92 (CH, **maj**), 46.83 (CH_2, **min**), 46.60 (CH_2, **maj**), 41.38 (Q, **min+maj**), 41.33 (CH, **maj**), 41.10 (CH, **min**), 37.76 (CH, **maj**), 37.67 (CH, **min**), 29.02 (CH_3, **maj**), 28.30 (CH_3, **min**), 25.81 (CH_2, **min+maj**), 23.13 (2 x CH_2, **min+maj**), 23.08 (CH_3, **min+maj**), 22.57 (CH_2, **maj**), 22.46 (CH_2, **min**); MS: *m/z* 250 (M^+, 2.5%), 139 (100%), 112 (33%), 95 (94%); HRMS: *m/z* (CI, NH_3) Found: 268.1903, $C_{15}H_{22}O_3$ (M + NH_4^+) requires: 268.1912.

(1*R, 2*S**, 3*S**, 6*S**, 7*S**)-4,4-Dimethyl-3,1-(epoxymethano)tricyclo[5.4.0.$0^{2,6}$]undecane-7-isocyanate (31)** DPPA (0.8 mmol, 0.172 mL) and TEA (1.2 eq., 0.96 mmol, 0.14 mL) were added to a solution of **30** (200 mg, 0.8 mmol) in toluene (3 mL). The mixture was heated at reflux for 0.5 h after which time the reaction was judged complete (tlc and IR control). The cooled reaction mixture was diluted with DCM (10 mL) and then concentrated under reduced pressure to give a pale brown oil (540 mg). This was subjected to flash chromatography (20% Et_2O/PE) to give the title compound as a colourless oil (175 mg, 89%); ν_{max}/cm^{-1} (neat): 2261 (NCO); δH (270 MHz): 4.12 (1H, d, *J*=9.57Hz, CH_2-O), 3.89 (1H, d, *J*=4.61Hz, CH-3), 3.37 (1H, d, *J*=9.57Hz, CH_2-O), 2.79 (1H, m) 2.63 (1H, m), 1.98-1.90 (1H, m), 1.79-1.39 (9H, m) 1.14 (3H, s, CH_3) 0.76 (3H, s, CH_3); δC (67.8 MHz): 121.89 (Q, NCO), 93.10 (CH), 77.68 (CH_2), 59.14 (C), 52.08 (C), 48.61 (CH), 46.58 (C), 45.45 (CH), 37.63 (CH_2), 37.11 (CH_2), 26.27 (CH_3), 25.93 (CH_2), 22.09 (CH_3), 19.21 (CH_2), 17.81 (CH_2); MS: *m/z* 247 (M^+, 7.5%), 248 (1.2%), 153 (100%); HRMS: *m/z* (CI, NH_3) Found: 265.1921, $C_{15}H_{21}NO_2$ (M + NH_4^+) requires: 265.1916.

7-Desmethylasteriscanolide (32) and 9H-epimer (33) A portion of ruthenium(IV) oxide hydrate (15 mg, 0.13 mmol) was added to a solution of sodium periodate (579 mg, 2.7 mmol) in a triphasic solvent mixture of water (3.7 mL), carbon tetrachloride (3.7 mL) and acetonitrile (1.2 mL). The mixture was stirred vigorously for 10 min until a bright yellow colour appeared in the organic layer. A solution of **31** (167 mg, 0.676 mmol) in acetonitrile (4.5 mL) was added over 5 min to the vigorously stirred mixture to produce a cloudy yellow suspension. After a further 1.5 h stirring the mixture was diluted with DCM (100 mL) and a black precipitate was formed. Anhydrous magnesium sulfate was added to the mixture to remove the water and after filtration through celite the solution was dried again and concentrated under reduced pressure to leave a dark liquid (245 mg).This was dissolved in 1,4-dioxane (20 mL) containing 4 M H_2SO_4 (5 mL) and the mixture was heated at reflux for 3.25 h before being allowed to cool. The reaction mixture was neutralised (indicator paper), by pouring into an excess of saturated aqueous sodium bicarbonate and then extracted with EtOAc (4 x 30 mL). The combined organic layers were dried and then concentrated under reduced pressure to leave a light brown oil (170

mg). This was subjected to flash chromatography (40% EtOAc/PE) to separate the two components present. The first component of the mixture, isolated as a colourless, crystalline solid, was shown by analysis to be the 9H-epimer **33**; (46 mg, 29% from **31**); mp (EtOAc/PE) 131.5-133.5 ^{O}C; (Found: C, 71.19; H, 8.47. $C_{14}H_{20}O_3$ requires: C, 71.19; H, 8.50); ν_{max}/cm^{-1} (DCM thin film): 1767.5 (CO), 1699.5 (CO); δH (270 MHz): 4.29 (1H, d, *J*=4.95Hz, CH-1), 3.17-3.04 (2H, m), 2.86 (1H, m), 2.60-2.51 (2H, m), 2.48-2.37 (1H, m), 2.19-2.00 (2H, m), 1.94-1.45 (5H, m), 1.11 (3H, s, CH_3), 1.01 (3H, s, CH_3); δC (67.8 MHz): 211.1 (C), 177.9 (C), 91.61 (CH), 48.41 (CH), 47.14 (CH), 44.51 (CH), 42.23 (C), 42.09 (CH_2), 38.53 (CH_2), 27.35 (CH_2), 27.01 (CH_3), 26.34 (CH_2), 24.40 (CH_2), 23.06 (CH_3); MS: *m/z* 236 (M^+, 37.4%), 237 (6.2%), 95 (100%). Further elution gave 7-desmethylasteriscanolide **32** as a colourless solid (43 mg, 27% from **31**); mp (EtOAc/PE) 147-150 ^{O}C; ν_{max}/cm^{-1} (DCM thin film): 1761.5 (CO), 1695.5 (CO); δH (270 MHz): 4.28 (1H, d, *J*=5.61Hz, CH-1), 3.77 (1H, m, CH-2), 3.15 (1H, m, CH-9), 2.74 (1H, m, CH-3), 2.58-2.01 (5H, m), 1.94-1.40 (5H, m), 1.20 (3H, s, CH_3), 1.00 (3H, s, CH_3); δC (67.8 MHz): 212.4 (C), 177.8 (C), 90.85 (CH), 50.71 (CH), 45.14 (CH), 44.15 (CH_2), 43.25 (CH), 40.43 (C), 38.20 (CH_2), 26.96 (CH_2), 24.44 (CH_3), 22.98 (CH_2), 22.91 (CH_3), 21.49 (CH_2); MS: *m/z* 236 (M^+, 30%), 237 (4.7%), 95(100%); HRMS: *m/z* (CI, NH_3) Found: 254.1757, $C_{14}H_{20}O_3$ ($M + NH_4^+$) requires: 254.1756.

Attempted preparation of asteriscanolide (1) A 1.0 M solution of LDA was prepared by addition of *n*-butyllithium (2.0 M in hexanes) (10 mL, 0.02 mol) to a solution of diisopropylamine (0.02 mol, 2.80 mL) in THF (10 mL) at 0 ^{O}C (ice/ salt). A portion of this LDA (0.224 mL, 0.224 mmol) was cooled to -78 ^{O}C and a cooled solution of 7-desmethylasteriscanolide **32** (52.8 mg, 0.224 mmol) in THF (1.0 mL) was added to produce a bright yellow solution. After stirring at -78 ^{O}C for 45 min methyl iodide (1.0 M in THF) (0.224 mmol, 0.224 mL) was added in one portion. After 5 min the reaction was deemed complete (tlc control) and was quenched by addition of saturated aqueous ammonium chloride (1.0 mL). The reaction mixture was extracted with ether (3 x 5 mL) and the combined organic layers were dried and concentrated under reduced pressure to leave a colourless oil. This was subjected to flash chromatography (25% EtOAc/PE) two components were eluted. The first component isolated as a colourless solid was shown by analysis to be *iso*-asteriscanolide **38** (6.9 mg, 12%); ν_{max}/cm^{-1} (DCM thin film): 1701.5 (CO), 1765 (CO); δH (270 MHz): 4.35 (1H, d, *J*=4.95Hz, CH-1), 3.30 (1H, m), 3.20-3.09 (1H, m), 2.56-2.40 (2H, m), 2.21-2.10 (1H, m), 2.07-1.56 (6H, m), 1.41 (1H, m), 1.28 (3H, s, CH_3), 1.21 (3H, s, CH_3), 0.99 (3H, s, CH_3); δC (67.8 MHz): 212.24 (C), 180.86 (C), 89.92 (CH), 53.21 (CH), 51.27 (CH), 45.50 (C), 44.37 (CH_2), 39.79 (C), 38.28 (CH_2), 28.61 (CH_2), 24.78 (CH_3), 24.33 (CH_3), 23.45 (CH_2), 23.00 (CH_3), 20.99 (CH_2); MS: *m/z* 250 (M^+, 21%), 251 (3.5%), 95 (100%); HRMS: *m/z* (CI, NH_3) Found: 268.1912, $C_{15}H_{22}O_3$ ($M + NH_4^+$) requires: 268.1912. The second component was isolated as an impure colourless solid (7.8 mg) which was tentatively identified as a mixture of dimethylated products (**39**); ν_{max}/cm^{-1} (DCM thin film): 1766 (CO), 1694 (CO); MS: *m/z* 264 (12%), 250 (26.5%), 95 (100%).

Attempted preparation of 8-(*t*-butyldimethylsilyl)oxy-7,8-dehydro-7-desmethylasteriscanolide *t*-Butyldimethylsilyl triflate (0.54 mmol, 0.124 mL) was added dropwise with stirring to a solution of 7-desmethylasteriscanolide (**32**) (116 mg, 0.49 mmol) and TEA (0.735 mmol, 0.10 mL) in DCM (1.5 mL) at RT. As stirring continued the solution became pale brown in colour and after 1 h the reaction was complete (tlc control). The mixture was diluted with DCM (10 mL) and washed with cold saturated

aqueous sodium bicarbonate (5 mL). The organic layer was dried with anhydrous sodium sulfate, filtered and then concentrated under reduced pressure to leave a pale red oil. This residue was subjected to flash chromatography on neutral alumina (20% Et_2O/PE + 1 drop of pyridine) and two components were recovered. The first component, shown by analysis to be the TBDMS enol ether **40**, was isolated as a colourless oil which slowly crystallised to a colourless solid; (21mg, 12%); mp 72.5-74 ^oC; ν_{max}/cm^{-1} (DCM thin film): 1770 (CO); δH (270 MHz, C_6D_6): 3.75 (1H, d, *J*=5.61Hz, CH-1), 2.30-1.85 (5H, m), 1.52-1.15 (7H, m), 1.13 (3H, s, CH_3), 1.06 (9H, s, $SiC(CH_3)_3$), 0.51 (3H, s, CH_3), 0.22 (3H, s, $SiCH_3$), 0.04 (3H, s, $SiCH_3$); δC (67.8 MHz, C_6D_6): 177.34 (C), 88.81 (CH), 71.56 (C), 53.30 (C), 49.69 (CH), 47.18 (C), 42.00 (CH), 39.41 (CH_2), 35.53 (CH_2), 26.40 (CH_2), 26.24 (3 x CH_3), 24.75 (CH_3), 22.43 (CH_3), 20.81 (CH_2), 19.57 (CH_2), 18.77 (C), -1.97 (CH_3), -2.71 (CH_3); MS: *m/z* 293 (M^+-*t*-Bu) (15.7%), 294 (3.4%), 199 (100%); HRMS: *m/z* (CI, NH_3) Found: 351.2347, $C_{20}H_{34}SiO_3$ (M + H^+) requires: 351.2355. The second component, subsequently shown by analysis to be the fragmented enol ether **42**, was isolated as a colourless solid; (21mg, 12%); mp 75-79 ^oC; ν_{max}/cm^{-1} (DCM thin film): 1758 (CO), 1662 (C=C); δH (270 MHz): 7.14 (1H, m, CH-1), 4.55 (1H, m, CH-8), 4.47 (1H, s, CH-11), 2.25 (2H, m), 2.02-1.35 (8H, m), 1.14 (3H, s, CH_3), 1.08 (3H, s, CH_3), 0.89 (9H, s, $SiC(CH_3)_3$), 0.14 (3H, s, $SiCH_3$), 0.08 (3H, s, $SiCH_3$); δC (67.8 MHz): 174.88 (C), 151.37 (C), 147.73 (CH), 133.14 (C), 104.65 (CH), 88.39 (CH), 41.08 (C), 31.48 (CH_2), 29.08 (CH_3), 27.91 (CH_2), 27.05 (CH_2), 25.79 (CH_2), 25.68 (3 x CH_3), 23.74 (CH_2), 22.84 (CH_3), 18.06 (C), -4.26 (CH_3), -4.69 (CH_3); MS: *m/z* 293 (M^+-*t*-Bu) (7.9%), 294 (1.8%), 199 (48%), 84 (100%); HRMS: *m/z* (CI, NH_3) Found: 351.2347, $C_{20}H_{34}SiO_3$ (M + H^+) requires: 351.2355.

(11*R)-10,10-dimethyl-7-oxocycloundec-1-ene-2,11-carbolactone (44)** A portion of **30** (350 mg, 1.42 mmol) was oxidised with ruthenium tetroxide as before to give crude (1*R**, 2*S**, 3*S**, 6*S**, 7*S**)-7-isocyanato-4,4-dimethyltricyclo [5.4.0.$0^{2,6}$]undecane-1,3-carbolactone (520 mg). This was dissolved in 1,4-dioxane (50 mL) containing 4 M H_2SO_4 (7 mL) and the mixture was heated at reflux for 15 min after which time it was allowed to cool to RT. The mixture was then neutralised (universal indicator) by pouring into an excess of saturated aqueous sodium bicarbonate and this was extracted with EtOAc (3 x 50 mL). The combined organic layers were washed with brine (50 mL), dried and concentrated under reduced pressure to leave a brown liquid (605 mg) which appeared to be the crude amine **43**; ν_{max}/cm^{-1} (neat): 3384 and 3327 (NH_2), 1745 (CO), 1622 (NH bend). This was dissolved in 1,4-dioxane (10 mL) and water (2 mL) was added. The solution was heated at reflux for 2.5 h after which time all the intermediate had been consumed (tlc control). The solvent was removed under reduced pressure to leave a yellow/brown solid (348 mg). This was subjected to flash chromatography (30% EtOAc/PE) to give the title compound as a white solid (121 mg, 36% from **30**); mp (EtOAc/PE) 156-158 ^oC; (Found: C, 71.31; H, 8.35. $C_{14}H_{20}O_3$ requires: C, 71.19; H, 8.47); ν_{max}/cm^{-1} (DCM thin film): 1748 (CO), 1702 (CO); δH (270 MHz): 6.93 (1H, m, CH-1), 4.49 (1H, m, CH-11), 2.42-2.32 (4H, m), 2.27-2.13 (2H, m), 2.01-1.74 (6H, m), 1.21 (3H, s. CH_3), 1.11 (3H, s, CH_3); δC (67.8 MHz): 210.19 (C), 173.37 (C), 146.07 (CH), 134.82 (C), 87.40 (CH), 40.38 (CH_2), 38.90 (CH_2), 38.49 (C), 30.28 (CH_3), 28.46 (CH_2), 24.91 (CH_2), 23.04 (CH_2), 22.84 (CH_3), 21.42 (CH_2); MS: *m/z* 236 (M^+, 100%), 237 (16%).

(11*R)-7-oxocycloundec-1-ene-2,11-carbolactone (45)** The crude (1*R**, 2*S**, 3*R**, 6*S**, 7*S**)-7-isocyanatotricyclo[5.4.0.$0^{2,6}$]undecane-1,3-carbolactone (236 mg) obtained from the above ruthenium tetroxide oxidation of **20** was dissolved in a mixture of water (24 mL) and 1,4-dioxane (96 mL) and heated to reflux for

1.5 h, after which time no starting material remained (tlc control). The solution was allowed to cool and the solvent was removed under reduced pressure. The residue was subjected to flash chromatography (50-80% EtOAc/PE) and two components were isolated. The first component was found to be (11*R**)-7-oxocycloundec-1-ene-2,11-carbolactone (**45**) as a colourless solid (37.3 mg, 22% from **20**); mp (Et_2O) 121-123°C; (Found: C, 69.01; H, 7.71 $C_{12}H_{16}O_3$ requires: C, 69.23; H, 7.69); ν_{max}/cm^{-1} (DCM thin film): 1751 (CO), 1706 (CO); δH (270 MHz): 6.79 (1H, m, CH-1), 5.04 (1H, m, CH-11), 2.49-1.56 (14H, m); δC (67.8 MHz): 210.8 (C), 173.8 (C), 148.1 (CH), 134.9 (C), 79.03 (CH), 44.74 (CH_2), 39.50 (CH_2), 32.36 (CH_2), 24.74 (CH_2), 23.40 (CH_2), 21.28 (CH_2), 16.26 (CH_2); MS: *m/z* 208 (M^+, 100%), 209 (14.0%), 150 (75%). Further elution with neat EtOAc furnished another compound as a pale yellow, sticky solid (56.2 mg). This was recrystallised from EtOAc to give the urea **46** as a colourless powder (42 mg, 28%); mp (EtOAc) 271-272 °C; ν_{max}/cm^{-1} (DCM thin film): 3382 (NH), 1742 (CO), 1672 (CO); δH (270 MHz): 5.01 (4H, br., 2 x CH-3 + 2 x NH), 3.04 (2H, m), 2.80 (2H, m), 2.62 (2H, m), 2.16 (2H, m), 1.96 (2H, m), 1.79-1.26 (18H, m); δC (67.8 MHz): 181.1 (C), 153.6 (C), 84.76 (CH), 52.35 (C), 50.08 (C), 48.91 (CH), 44.42 (CH), 37.36 (CH_2), 36.21 (CH_2), 28.14 (CH_2), 22.90 (CH_2), 21.89 (CH_2), 20.06 (CH_2); MS: *m/z* 440 (M^+, 2.53%), 141 (100%); HRMS: *m/z* (CI, NH_3) Found: 441.2387, $C_{25}H_{32}N_2O_5$ ($M + H^+$) requires: 441.2390.

References

1. Isolation: A. San Feliciano, A.F. Barrero, M. Medarde, J.M.M. del Corral and A. Aramburu, *Tetrahedron Lett.*, **1985**, *26* , 2369.
2. Total synthesis: P.A.Wender, N.C.Ihle and C.R.D. Correia, *J. Am. Chem. Soc.*, **1988**, *110*, 5904.
3. (a) K.I. Booker-Milburn, J.K. Cowell and L.J. Harris, *Tetrahedron Lett.*, **1994**, 35, 3883; (b) K.I. Booker-Milburn and J.K. Cowell,*Tetrahedron Lett.*,**1996**, *37*, 2177; (c) Recently Lange and Organ have described a related photochemical based synthesis of *nor*-asteriscanolide: G.L.Lange and M.G.Organ *J.Org.Chem.*, **1996**, *61*, 5358.
4. (a) P.A. de Mayo, *Acc. Chem. Res.* , **1971** ,*4* , 41; (b) M.T. Crimmins, *Chem. Rev.*, **1988**, *88*, 1453. (c) N.A. Petasis and M.A. Patane, *Tetrahedron* , **1992**, *48* , 5757.
5. Stereoelectronic Effects in Organic Chemistry, Chapter 3, P. Deslongchamps, 1983, Pergamon Press Ltd.
6. M.C. Pirrung and S.A. Thomson, *Tetrahedron Lett.* , **1986**, *27* , 2703.
7. R.K. Boeckman, Jr. and D.M. Demko, *J. Org. Chem.*, **1982**, *47* , 1789.
8. The full experimental details of this and other THPA/alkenol photocycloadditions will be published separately.
9. For related reactions using vinylogous amides see: (a) F.M. Schell, P.M. Cook, S.W. Hawkinson, R.E. Cassady and W.E. Thiessen, *J. Org. Chem.*, **1979**, *44*, 1380; (b) C.S. Swindell and P.B. Patel, *J. Org. Chem.*, **1990**, *55*, 3.
10. T. Shioiri, K. Ninomiya and Y. Shun-ichi, *J. Am. Chem. Soc.* , **1972**, *94* , 620.
11. K.R. Kopecky and C. Levine, *Can.J.Chem.*, **1981**, *59*, 3273.
12. (a) R.M. Coates, P.D. Senter and W.R. Baker, *J.Org.Chem.*, **1982**, *47*, 3597; (b) T. Rajamannar and K.K. Balasubramanian,*Tetrahedron Lett.*, **1988**, *29*, 5789.
13. P.H.J. Carlsen, T. Katsuki, V.S. Martin and K.B. Sharpless, *J. Org. Chem.*, **1981**, *46*, 3936. For the oxidation of related cyclobutane containing ethers see: T. Kojima, Y. Inouye and H. Kakisawa, *Chem. Lett.*, **1985**, 323 and also W.F. Berkowitz, A.S. Amarasekara and J.J. Perumattam, *J.Org.Chem.*, **1987**, *52*, 3597.
14. We are grateful Drs A.K. Powell and M. Molinier (UEA) for solving the structure of **24** and **25** by X-ray crystallography, the full details of which will be published separately.
15. D.G. Lee and M. Van den Engh, *Can. J. Chem.*, **1972**, *50*, 3129.
16. N.C. Yang and M.J. Jorgenson, *Tetrahedron Lett.* , **1964**, 1203.
17. L.N. Mander and S.P. Sethi,*Tetrahedron Lett.*,**1984**, *25*, 5953.
18. M.Ihara, T. Taniguchi, M. Yamada, Y. Tokunaga and K. Fukumoto, *Tetrahedron Lett.*, **1995**, *36*, 8071.
19. S. El Dahmy, J. Jakupovic, F. Bohlmann and T.M. Sarg, *Tetrahedron*, **1985**, *41*, 309.

(*Received in USA* 21 *May* 1997; *accepted* 2 *July* 1997)