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β-Lactams (including polycyclic) derived from chromium carbenes

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Abstract

The photolytic reaction of *N*-methylbenzylideneimine with 12-methoxypodocarpane chromium carbenes gave products derived either from carbon monoxide dissociation followed by 12-methoxy ligation or from oxidation of the carbene metal moiety, while the reaction of *N*-methylbenzylideneimine with 12-desmethoxy diterpenoid carbenes gave diterpenoid β-lactams. The relative stereochemistry of two monocyclic 3,4-diaryl β-lactams prepared from a methoxy- or ethylthio-phenylcarbene by photolysis with an imine has been determined by X-ray crystallography. © 2001 Elsevier Science B.V. All rights reserved.

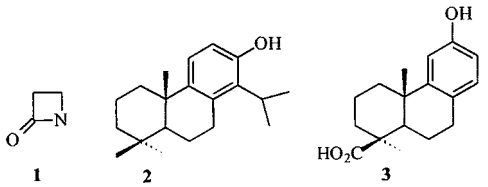
Keywords: Chromium; Fischer carbene; Photochemistry; Diterpenoid; β-Lactam

1. Introduction

Since the serendipitous discovery of penicillin by Fleming, antibiotics containing a β-lactam (azetidin-2-one, **1**) heterocycle have been viewed as miracle drugs due to their ability to eliminate bacteria with minimal harm to host cells. However, the ability of bacteria to acquire resistance genes, either from other bacteria or from viruses infecting bacteria or by mutation, coupled with the misuse of antibiotics due to over-prescription or for the treatment of diseases (viral infections) in which they have no effect, has led to multiple drug resistance in many pathogenic bacteria [1]. This has in turn established a need to develop novel antibacterial agents, including non-classical polycyclic β-lactams [2].

The unique reactivities of transition metal complexes allow the construction of the azetidin-2-one moiety under mild and specific conditions; rhodium [3–5], palladium [6–10], nickel [11], chromium [12], cobalt [13] and iron [14–18] complexes have been used in either stoichiometric or catalytic amounts in the synthesis of β-lactams. Photolysis of certain Fischer carbene complexes with imines has proved to be a general and synthetically useful method for the construction of β-lactams [19–30].

We were interested in synthesising azetidin-2-one substituted podocarpane diterpenoids via the photolytic reaction of imines with diterpenoid chromium carbenes. The potent antibacterial diterpene, totarol (**2**) [31,32], is structurally similar to podocarpic acid (**3**); it was envisaged that a non-classical monocyclic β-lactam incorporating a phenolic diterpenoid could have interesting pharmacological properties. Furthermore, a number of monocyclic azetidin-2-ones possessing diverse aromatic substituents on the four-membered ring [33–35] have been shown to be inhibitors of the human cytomegalovirus (HCMV) which is a serious pathogen in immunocompromised individuals.



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2. Results and discussion

Initial studies focussed on the photolytic behaviour of pentacarbonyl[(methoxy)-13-(12,19-dimethoxypodocarpa-8,11,13-triene)carbene]chromium (**4**) [36] with *N*-methylbenzylideneimine. Formation of β-lactam products was not detected after a variety of photolytic

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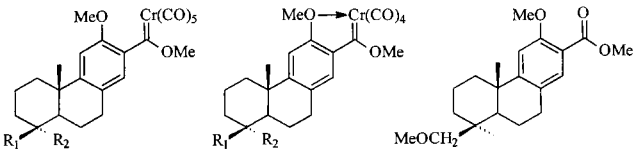
conditions. The only products isolated were the internally ligated alkoxycarbene complex **5** formed from decarbonylation of **4**, and methyl 12,19-dimethoxypodocarpa-8,11,13-trien-13-oate (**6**) derived from oxidation of the carbene moiety (Table 1).



4: $R_1 = MeOCH_2$, $R_2 = Me$ **5**: $R_1 = MeOCH_2$, $R_2 = Me$ **6**
7: $R_1, R_2 = CH_2$ **8**: $R_1, R_2 = CH_2$

Similarly, photolysis of the 4(18)-alkene analogue, pentacarbonyl[(methoxy)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**7**) [36] with *N*-methylbenzylideneimine for 3 h at 3000 Å (Rayonet) gave the tetracarbonyl methoxycarbene complex **8** (20%) and starting material **7** (39%).

Some carbenes which are unreactive towards photolysis have been shown to have a ^{53}Cr linewidth less than 500 Hz in the ^{53}Cr-NMR spectrum, while those which do give β-lactams have a linewidth greater than 1000 Hz [37]. The reason for the relationship between ^{53}Cr linewidth and reactivity towards imines is unknown, but nevertheless this observation offers a useful guide to predict the reactivity of a particular carbene complex. The ^{53}Cr-NMR spectra were not recorded for either of the diterpenoid 13-methoxycarbenes **4** and **7**, but the related *ortho*-methoxy benzenoid complex pentacarbonyl[(2-methoxyphenyl)methoxycarbene]chromium has a ^{53}Cr linewidth of 1900 Hz, well above the empirically derived lower limit for reactivity. Therefore, the failure of **4** and **7** to undergo reaction other than decarbonylation on photolysis in the presence of *N*-methylbenzylideneimine would not be reflected in the ^{53}Cr linewidth expected for these diterpenoid complexes.

Excitation of an electron into the metal to ligand charge transfer (MLCT) band is a formal one electron oxidation of the metal, and photochemically driven insertion of a *cis* carbon monoxide ligand into the metal–carbene bond produces a short lived metal ketene complex (Scheme 1) which can either react with appropriate reagents or deinsert to regenerate the starting complex [19,37].

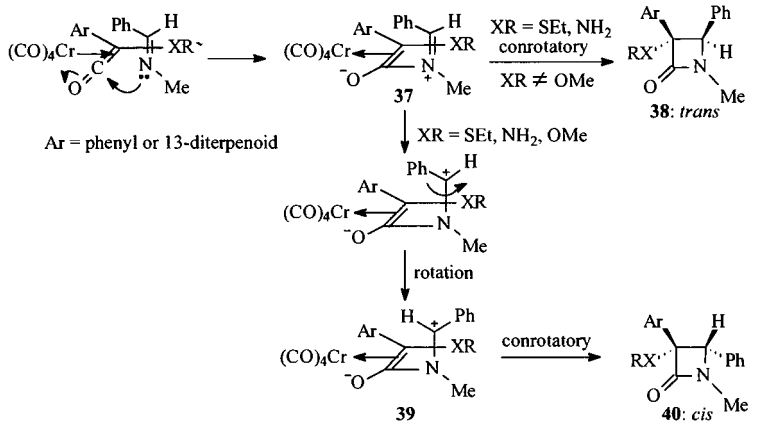
Excitation into the MLCT band does not, however, result in carbon monoxide dissociation [38–40]. The maximum for the $Cr \rightarrow \pi^*$ (spin-allowed MLCT) band of the podocarpane carbenes **4** and **7** occurred at 402 and 403 nm, respectively, consistent with the corresponding band ($\lambda_{max} = 400$ nm) assigned for pentacarbonyl[(2-methoxyphenyl)methoxycarbene]chromium [37]. The electronic spectra of the two diterpenoid alkoxycarbene complexes showed that the ligand field (LF) and MLCT bands overlap each other, and the high energy LF band overlaps with the arene $\pi \rightarrow \pi^*$ transition. Excitation into the lower energy LF band results in the dissociation of the carbene ligand [40,41]. In the present work, however, metal-free diterpenoid carbenes have not been observed and no products which could be ascribed to diterpenoid carbenes were isolated.

The inability of the diterpenoid alkoxycarbene complexes **4** and **7** to react with the imine to give a β-lactam is believed to be due to dissociation of CO as a consequence of photolytic excitation into the high energy LF band [41]. The high energy LF band is overlapped with the $\pi \rightarrow \pi^*$ band of the arene on the higher energy side, and with the low energy LF band and probably the spin-allowed MLCT band on the lower energy side. Although the maximum of the high energy LF absorption could not be determined for the diterpenoid methoxy complexes **4** and **7**, this transition occurs at ~ 334–340 nm in related compounds [37]. Excitation into the high energy LF band populates the $3a_1$ orbital ($d_{x^2-y^2}$) [38,40,41], thereby weakening the *cis* CO–chromium bond; intramolecular coordination of the *ortho*-methoxy group would aid cleavage of this bond, giving the thermodynamically stable methoxy-ligated tetracarbonyl complex. However, this tetracarbonyl complex cannot undergo insertion of CO into the chromium–carbene bond to give the ketene, and therefore a β-lactam cannot arise.

To test the proposition that the potential ligating functionality (OMe) at C(12) was inhibiting the photolytic reaction of these chromium carbenes with *N*-methylbenzylideneimine, it was necessary to synthesise a series of 12-desoxy diterpenoids which retained the bromine substituent at C(13), in order to allow subsequent introduction of the carbene moiety. Reductive desoxygenation of a *para*-bromoaryl triflate without concomitant bromide reduction has been achieved using triethylsilane with catalytic amounts of palladium acetate and 1,3-diphenylphosphinopropane (dppp) in DMF [42]. Therefore, methyl 13-bromo-12-(trifluoromethanesulfonyloxy)podocarpa-8,11,13-trien-19-oate (**10**) was prepared (98%) by addition of triflic anhydride to a solution of the phenol **9**, 2,6-lutidine and DMAP. However, treatment of **10** with Et_3SiH and

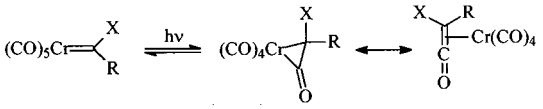
Table 1
Photolysis of methoxycarbene **4** with *N*-methylbenzylideneimine

Wavelength; solvent	**4** (%)	**5** (%)	**6** (%)
Sunlamp, 300 W; hexanes	2	13	17
3000 Å (Rayonet); hexanes	9	64	13
Sunlight; hexanes	0	28	12
2540 Å, 125 W (Hanovia); hexanes	5	54	0
3500 Å (Rayonet); diethyl ether	10	64	7
3500 Å (Rayonet); acetonitrile	9	64	13

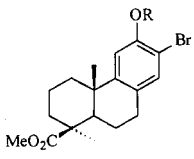


Scheme 1.

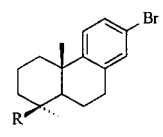
$Pd(OAc)_2$ in the presence of dppp as the stabilising phosphine ligand proved unsatisfactory, leading to loss of both the triflate and the bromide. Extensive variation of the experimental parameters (including the use of either HCOOH or Bu_3SnH or $(Me_3Si)_3SiH$ as the hydride source) led to optimised conditions for the selective detriflation of **10**. Thus, triethylsilane (five molar equivalents) and $Pd(OAc)_2$/1,1′-bis(diphenylphosphino)ferrocene (5 mol% of each) in anhydrous DMF at 7°C gave methyl 13-bromopodocarpa-8,11,13-trien-19-oate (**11**) in high yield (88%) after 40.5 h.



Hydrolysis of the 13-bromo ester **11** with aqueous KOH in DMSO gave the 19-carboxylic acid **12** (85%), which was reduced with $BH_3{\cdot}SMe_2/(MeO)_3B$ [43] to afford the primary alcohol **13** (72%); methylation of **13** gave 13-bromo-19-methoxypodocarpa-8,11,13-triene (**14**) (84%). The analogous 13-bromide **15** in the $\Delta^{4,(18)}$ series was synthesised from **12** via an oxidative decarboxylation sequence [36]. Thus the acid chloride **16** (100%) was treated with the sodium salt of 1-hydroxy-2-pyridinethione, leading to 13-bromo-4α-(2′-pyridylthio)-18-norpodocarpa-8,11,13-triene (**17**) (91%). Oxidation of the sulfide **17** with *m*-chloroperoxybenzoic acid at −78°C afforded a mixture of epimeric sulfoxides which underwent cycloelimination in refluxing benzene to give 13-bromo-19-norpodocarpa-4(18),8,11,13-tetraene (**15**) (87%).



9: R = H
10: R = SO_2CF_3



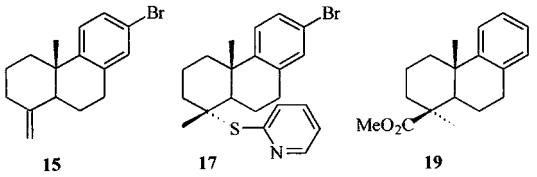
11: R = CO_2Me **14**: R = CH_2OMe
12: R = CO_2H **16**: R = COCl
13: R = CH_2OH

Conversion of the 13-bromide **11** into the required 12-desoxy carbene **18** was achieved via metal–halogen exchange with butyllithium at −78°C. Addition of the resulting 13-lithioarene to $Cr(CO)_6$ at 0°C followed by reaction of the lithio acylate with methyl triflate gave methyl pentacarbonyl[(methoxy)(13-(12-methoxypodocarpa-8,11,13-trien-19-oate))carbene]chromium (**18**) (21%). The molecular ion at m/z 506.1061 in the mass spectrum of **18** corresponded to the molecular formula $C_{25}H_{26}CrO_8$, and fragment ions derived from sequential losses of the CO ligands were observed, leading to the base peak at m/z 366. The aromatic region in the ^{1}H-NMR spectrum showed a broadened singlet at 7.14 due to H(14), a doublet of doublets ($J = 8.3$, 1.7 Hz) at 7.29 due to H(12), and a doublet ($J = 8.3$ Hz) at 7.34 ppm due to H(11). The ^{13}C-NMR spectrum included signals at 216.5 ($C{\equiv}O_{cis}$), 224.1 ($C{\equiv}O_{trans}$) and 348.2 ppm ($C_{carbene}$). As expected, the high energy MLCT band occurred at 419 nm in the UV–vis spectrum. However, an accurate molar absorptivity coefficient could not be determined due to contamination of **18** by some (< 5%) debrominated arene **19** arising from competing protonation of the lithio acylate.

The $\Delta^{4,(18)}$ and 19-CH_2OMe analogues of ester **18**, pentacarbonyl[(methoxy)(13-(19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**20**) and pentacarbonyl[(methoxy)(13 - (19 - methoxypodocarpa - 8,11,13-triene))carbene]chromium (**21**) were synthesised from **15** and **14** (31 and 40%, respectively). In their UV–vis spectrum, the high energy MLCT band was observed at 420 nm ($\log \varepsilon_{max} = 3.85$) for **20** and at 419.5 nm ($\log \varepsilon_{max} = 3.86$) for **21**.

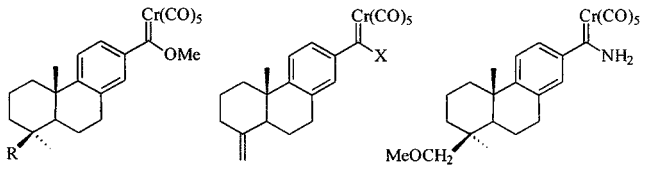
The opportunity was also taken to prepare 12-desoxypodocarpane amino- and thio-carbenes, in order to investigate their photolytic reactivity. Thus, aminolysis of **21** with ammonia produced pentacarbonyl[(dihydroamino)(13-(19-methoxypodocarpa-8,11,13-triene))-carbene]chromium (**22**) (96%). Broad singlets at 8.26 and 8.74 ppm in the ^{1}H-NMR spectrum were assigned

to $NH_{(Z)}$ and $NH_{(E)}$, respectively. The electronic spectrum of **22** showed maxima at 390.5 (spin-allowed MLCT) and 232.5 nm (arene $\pi-\pi^*$). Reaction of pentacarbonyl[(methoxy)(13-(19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**20**) with ethanethiol in the presence of sodium carbonate gave pentacarbonyl[(thioethyl)(13-(19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**23**) (55%). The electronic spectrum of **23** showed maxima at 477 (spin forbidden MLCT), 352 (higher energy LF) and 233 nm (arene $\pi \rightarrow \pi^*$).



15 **17** **19**

With the required 12-desoxy diterpenoid substrates in hand, simple benzenoid analogues were used initially to define the optimum conditions for photolysis. There is an inverse correlation between the yield of a β-lactam and the steric bulk of simple benzylideneimine and carbene precursors [21]. In order to investigate the possibility of synthesising highly crowded β-lactams using sterically more demanding imines, pentacarbonyl-[methoxyphenylcarbene]chromium (**24**) was photolysed (Hanovia medium pressure lamp, CH_3CN, 25 h, ≈ 20°C) with *N*-phenyl(4-methoxybenzylidene)imine; racemic *cis*-3-methoxy-4-(4′-methoxyphenyl)-1-phenyl-3-phenylazetidin-2-one (***rac*-25**) was isolated in 29% yield (100% stereoselective as shown by the ^{1}H-NMR spectrum of the crude photolysate). Single crystal X-ray crystallographic analysis (Fig. 1) confirmed the *cis* relationship between the methoxy group on C(3) and the 4-methoxyphenyl group on C(4) of ***rac*-25**.



18: R = CO_2Me
21: R = CH_2OMe
20: X = OMe
23: X = SEt
22

Under the same conditions but for 48 h a less congested imine, *N*-methylbenzylideneimine, reacted with the (methoxy)phenylcarbene **24** to give racemic *cis*-1-methyl-3-methoxy-3,4-diphenylazetidin-2-one (***rac*-26**) in much higher yield (76%, 100% stereoselective). In contrast, photolysis of the (dihydroamino)-phenylcarbene **27** with *N*-methylbenzylideneimine produced 3-(benzylideneimine)-1-methyl-3,4-diphenylazetidin-2-one (***rac*-28**) in very low (6%) yield. Accurate measurement of the molecular ion in the mass spectrum of ***rac*-28** was correct for the molecular formula $C_{23}H_{20}N_2O$, and the base peak at m/z 193 corresponded

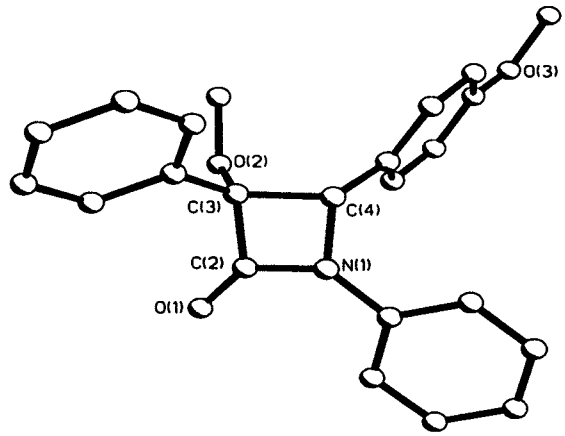


Fig. 1. The atomic arrangement in ***rac*-25**.

to PhCH=N=CPh$^+$. A broad singlet at 8.52 ppm in the ^{1}H-NMR spectrum was assigned to the imine hydrogen. The reaction was not completely stereoselective, as shown by the presence in the ^{1}H-NMR spectrum of singlets at 2.88 and 2.93 ppm due to *N*-methyl groups. In the ^{13}C-NMR spectrum, the chemical shifts for C(4) (71.7, 72.2 ppm) and for *N*-CH_3 (25.7, 26.6 ppm) also indicated two isomers. Although these compounds could be (*E*) and (*Z*) imine isomers, only one signal (169.0 ppm) due to an imine carbon was observed in the ^{13}C-NMR spectrum. Furthermore, imine derivatives of benzaldehydes exist exclusively as the (*E*)-isomers [44]. The two β-lactam products are therefore C(3)–C(4) stereoisomers. The isolation of a 3-(benzylideneimine) rather than of the parent 3-dihydroamino β-lactam was not unexpected, since the latter are known to react with benzaldehyde to give a β-lactam imine [45–47]. Nucleophilic attack by the nitrogen atom of the initial 3-dihydroamino β-lactam on *N*-methylbenzylidineimine, followed by elimination of methylamine, would generate ***rac*-28**.

The photolytic reaction of a thiocarbene with an imine has not been reported. Photolysis of pentacarbonyl[(thioethyl)phenylcarbene]chromium (**29**) with *N*-methylbenzylideneimine in acetonitrile for 17 h gave racemic 1-methyl-3-thioethyl-3,4-diphenylazetidin-2-one (47%) as a mixture (15:85) of *cis* (***rac*-30**) and *trans* (***rac*-31**) isomers (C–I–P priorities). Each of the diastereotopic methylene hydrogens of ***rac*-30** and ***rac*-31** gave a separate signal in the ^{1}H-NMR spectrum, and triplets due to the methyl groups were observed at 0.94 and 1.14 ppm. A singlet at 4.68 ppm was assigned to H(4) of the major isomer; this signal showed a weak nOe to the methylene group of the thioethyl substituent, suggesting *trans* C(3)–C(4) stereochemistry. The *trans* stereochemistry was determined by the X-ray crystal structure (Fig. 2); a portion of the same crystal was analysed by ^{1}H-NMR spectroscopy in order to confirm that it was in fact the major isomer, ***rac*-31**.

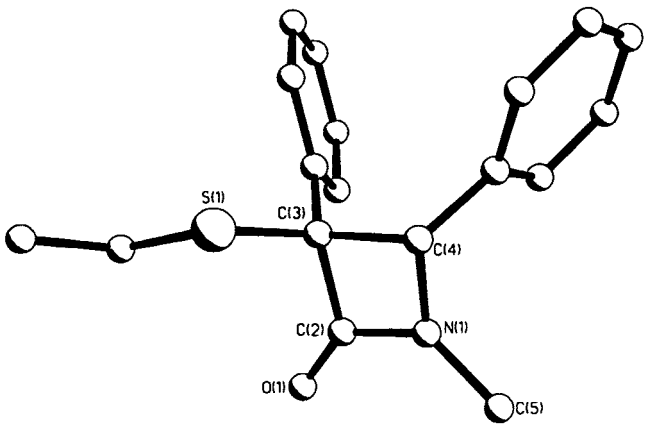
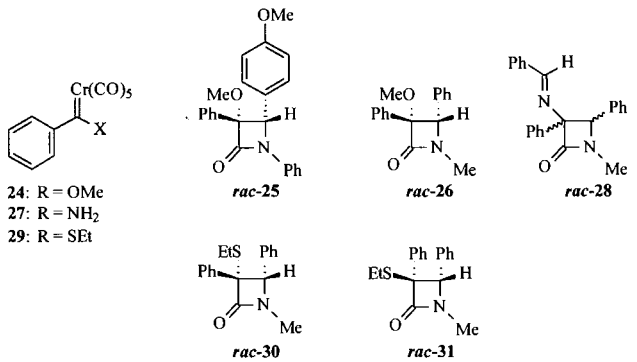


Fig. 2. The atomic arrangement in ***rac*-31**.

Having successfully demonstrated the synthesis of β-lactams from benzenoid alkoxy-, amino- and thiocarbene substrates, attention was turned to the corresponding chiral 12-desoxypodocarpane analogues. A solution of the methoxycarbene **18** and *N*-methylbenzylideneimine in acetonitrile was photolysed (Hanovia medium pressure) for 24 h. Pleasingly, *cis*-1-methyl-3ζ-methoxy-4ζ-phenyl-3-(13′-(podocarpa-8′,11′,13′-triene))-azetidin-2-one (**32**) was isolated in 58% yield. This reaction was also 100% stereoselective, giving only the two diastereoisomers having the methoxy *syn* to the phenyl group on the β-lactam ring. Singlets at 2.84(6) and 2.84(8) ppm in the ^{1}H-NMR spectrum were assigned to the *N*-methyl group in each diastereoisomer. Integration of these signals showed that the ratio of diastereoisomers was 1:1, and hence there had been no diastereofacial discrimination when the imine reacted with the chiral diterpenoid ketene. The presence of the β-lactam carbonyl was confirmed by a signal at 168.3 ppm in the ^{13}C-NMR spectrum and by a strong peak at 1755 cm^{-1} in the infrared spectrum.

Photolysis of the corresponding $\Delta^{4(18)}$ methoxycarbene **20** with *N*-benzylideneimine gave *cis*-1-methyl-3ζ-methoxy-4ζ-phenyl-3-(13′-(19′-norpodocarpa-4′(18′),8′,11′,13′-tetraene))-azetidin-2-one (**33**) (86%). The β-lactam **33** was also a 1:1 mixture of two diastereoisomers, and again the reaction was 100% stereoselective, only the isomers with the methoxy *syn* to the phenyl group on the heterocycle being produced. A signal at 168.3 in the ^{13}C-NMR spectrum was assigned to the carbonyl group of the β-lactam, whose quaternary carbon was observed at 92.4(5) ppm. The lactam methine carbon [C(4)] showed different chemical shifts (70.5(2) and 70.5(6) ppm) in each diastereoisomer. Separate singlets were also observed for H(4) in the ^{1}H-NMR spectrum, at 4.64(3) and 4.63(5) ppm.

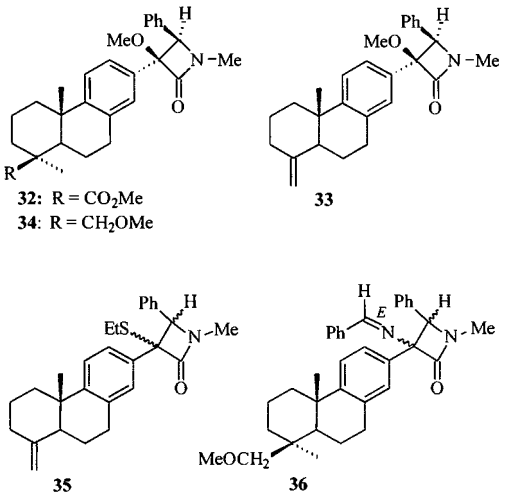
Photolysis of the 19-methoxy carbene **21** with *N*-methylbenzylideneimine in acetonitrile for 21 h gave 1-methyl-3ζ-methoxy-4ζ-phenyl-3-(13′-(19′-methoxypodocarpa-8′,11′,13′-triene))azetidin-2-one (**34**) (71%). This reaction was also 100% stereoselective, again giving a 1:1 mixture of *cis* diastereoisomers. The formation of the β-lactam was confirmed by the presence of a carbonyl signal at 168.3 ppm in the ^{13}C-NMR spectrum and by a strong peak at 1756 cm^{-1} in the infrared. The mass spectrum of **34** gave the molecular ion at *m*/*z* 447.2772 consistent with the formula $C_{29}H_{37}NO_3$. Fragment ions corresponding to loss of MeN=C=O and PhCH=NMe (retro-lactam) were evident, and further loss of a methoxy radical gave a ketene cation as the base peak. The mass spectrum of the diterpenoid β-lactams **32** and **33** showed analogous fragmentation sequences.



Photolysis of pentacarbonyl[(thioethyl)(13-(19-norpodocarpa-4(18),8,11,13-tetraene))-carbene]chromium (**23**) in the presence of *N*-methylbenzylideneimine gave 1-methyl-3-thioethyl-4-phenyl-3-(13′-(19′-norpodocarpa-4′(18′),8′,11′,13′-tetraene))azetidin-2-one (**35**) (42%). Mass spectroscopy gave the molecular ion at *m*/*z* 431.2279 ($C_{28}H_{33}NOS$), the fragment ion at *m*/*z* 374 corresponding to the loss of MeN=C=O and the base peak at *m*/*z* 255 being indicative of $ArC{\equiv}S^{+}$. The characteristic carbonyl stretching frequency occurred at 1759 cm^{-1} in the infrared spectrum. Lactam carbonyl signals were observed at 168.9(5) ($C{=}O_{trans}$) and 169.2 ($C{=}O_{cis}$) ppm in the ^{13}C-NMR spectrum, and signals due to $C(3)_{cis}$ and $C(3)_{trans}$ were present at 63.9 and 68.1 ppm. Four signals due to NCH_3 were detected in the ^{1}H-NMR spectrum, indicating that all four isomers of the β-lactam had been produced, although the ratios could not be determined. However, comparison of the NMR data with that of the monocyclic thio-β-lactam ***rac*-31** indicated that the *trans* isomer(s) (EtS and Ph *trans*) were the predominant diterpenoid products; integration of the signals at 0.96 ($SCH_2CH_{3(cis)}$) and 1.19 ppm ($SCH_2CH_{3(trans)}$) gave a *cis*/*trans* ratio of ca. 1:3.

Photolysis of the 12-desoxy dihydroaminocarbene (**22**) with *N*-methylbenzylideneimine was less successful, 3-(benzylideneimine)-1-methyl-4-phenyl-3-(13′-(19′-methoxypodocarpa-8′,11′,13′-triene))-β-azetidinone (**36**) being isolated in only 5% yield. The molecular ion at *m*/*z* 520.3071 in the mass spectrum indicated the molecular formula $C_{35}H_{40}N_2O_2$, the base peak at *m*/*z* 373

being assigned to ArC=N=CHPh$^+$, confirming the occurrence of the secondary reaction to generate the imine derivative. As with the diterpenoid ethylthio-β-lactam **35**, all four possible isomers of **36** were formed, signals due to imine hydrogen being observed at 8.46, 8.48, 8.53 and 8.54 ppm in the ^{1}H-NMR spectrum. However, the relative stereochemistry of the lactam ring substituents could not be deduced. The imine carbon was observed as a broad signal at 161.0 in the ^{13}C-NMR spectrum, while the quaternary carbon of the heterocycle [C(4)] resonated at 71.5 ppm. The low yield of **36** shows that (aryl)dihydroaminocarbenes are not suitable substrates, even though the ^{53}Cr-NMR linewidths of similar aminocarbene complexes [37] had suggested that they would be amenable to photolytically induced β-lactam formation.



The reactions of *N*-methylbenzylideneimine with the methoxycarbenes were 100% stereoselective, giving β-lactams with the C(3)-methoxy group and the C(4)-phenyl group *syn* (*cis* isomer). In contrast, the photolytic reaction of the imine with an aminocarbene or the thiocarbenes afforded both *cis* and *trans* isomers. This lack of stereoselectivity implies that β-lactam formation is not a formal [2 + 2] cycloaddition; rather, it progresses through zwitterionic intermediates [48]. The imine nitrogen of (*E*)-*N*-methylbenzylideneimine is proposed to attack the LUMO of the ketene carbonyl group, which is coplanar with the ketene substituent, giving zwitterionic intermediate **37** (Scheme 1) [49]. Rotation of the imine into the plane in concert with conrotatory ring closure gives the *trans* β-lactam **38**, which is the product derived from kinetic control. The *cis* β-lactam is the thermodynamically stable isomer, having the sterically encumbered C(3)-aryl [phenyl or -(13-podocarpanyl)] and C(4)-phenyl groups *trans* to each other. If intermediate **37** isomerises by rotation to **39** before conrotatory ring closure, the *cis* β-lactam **40** can form [48]. The major cycloadduct isolated from photolysis of both of the thiocarbenes was *trans*, whereas only *cis* isomers were isolated from photolyses of all of the methoxycarbenes. This implies that the zwitterionic intermediate formed from a methoxycarbene is more stable than that formed from a thiocarbene or an aminocarbene. Therefore, intermediate **37** (XR = OMe) can isomerise before ring closure and lead to the thermodynamically favoured *cis* azetidin-2-one. In contrast, the kinetic and thermodynamic pathways are competitive for the thio- and amino-carbenes, leading to both *trans* and *cis* β-lactams.

2.1. Summary

The reaction of *N*-methylbenzylideneimine with 12-methoxypodocarpane chromium carbenes gave products derived either from carbon monoxide dissociation followed by 12-methoxy ligation, or from oxidation of the carbene metal moiety. In contrast, the reaction of *N*-methylbenzylideneimine with 12-desmethoxypodocarpane carbenes gave β-lactams. Both the 12-methoxy- and 12-desmethoxy-carbenes show similar UV–vis spectra, and therefore the difference in reactivity cannot be attributed to a possible difference in electronic excited states. Although excitation into the MLCT band to give a ketene followed by reaction of the metal-bound ketene with an imine is possible for both 12-methoxy- and 12-desmethoxy-diterpenoid carbenes, the failure of the podocarpane 12-methoxycarbenes to give β-lactams indicates that this process is not competitive with dissociation of CO. To reiterate the points discussed earlier: irradiation into the MLCT band leads to ketene formation; irradiation into the low energy LF band induces loss of the Cr(CO)$_5$ moiety; irradiation into the high energy LF band induces dissociation of a *cis* CO ligand; these bands are overlapped substantially in the ultraviolet spectra; and all of the photolysis sources used in the present work emitted radiation of a wavelength suitable for excitation of an electron into the high energy LF band. Dissociation of a *cis* CO ligand from a 12-methoxypodocarpane methoxycarbene complex (**4** or **7**) (Scheme 2) would lead to coordination of the 12-methoxy group to chromium, giving a thermodynamically stable chelated tetracarbonyl complex. Subsequent formation of a ketene (leading to a β-lactam) is not favoured, since this would require the breaking the intramolecular MeO–Cr bond. That is, decarbonylation of the 12-methoxy pentacarbonylcarbene leads irreversibly to **5** or **8**, which does not undergo ketene formation, and consequently a β-lactam cannot be formed. Re-coordination of CO to regenerate **4** or **7** is possible, but only in the presence of carbon monoxide and in the absence of either thermolysis or photolysis. That is, photolysis is required for formation of a ketene but it also induces rapid dissociation of CO to give a tetracarbonyl complex which cannot undergo ketene formation. In contrast, decarbonylation of a 12-desmethoxy pentacarbonylcarbene cannot lead to

intramolecular chelation as the 12-methoxy group is absent. Dissociation of CO is therefore reversible, or alternatively solvent acetonitrile could coordinate to the unsaturated chromium (Scheme 3). Although decarbonylation does occur, it leads to complex(es) which can still undergo ketene formation upon irradiation into the MLCT band, the formation of β-lactams then being irreversible. Overall, therefore, β-lactam formation is inhibited in a carbene possessing a substituent which can ligate intramolecularly to chromium following dissociation of CO.

2.2. X-ray crystal structures of **25** and **31**

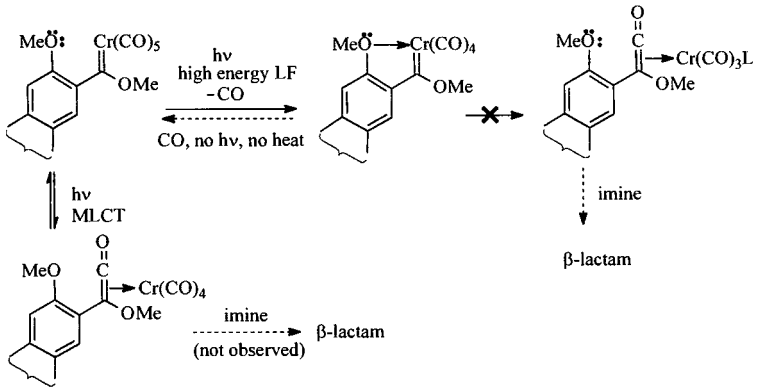
Data were collected on a Siemens SMART area detector diffractometer using 0.3° frames and profile fitting. Lorentz, polarisation and absorption corrections [50] were applied and equivalent reflections averaged to give 4231 unique data for ***rac*-25** and 3800 unique data for ***rac*-31**. Unit cell parameters were obtained by least-squares fit to all data with $I > 10\sigma(I)$. The structures were solved by direct methods [51] and refined by full-matrix least-squares on F^2 [52]. Hydrogen atoms were placed geometrically and refined with a riding model, including free rotation for methyl groups, with thermal parameter 20% (50% for methyl groups) greater than U_{iso} of the carrier atom. All non-hydrogen atoms were refined with anisotropic thermal parameters. Refinement converged to R_1 (observed data) 0.0457 for ***rac*-25** and 0.0635 for ***rac*-31**. Crystal data and refinement parameters are given in Table 2 and the structures are shown in Figs. 1 and 2.

3. Experimental

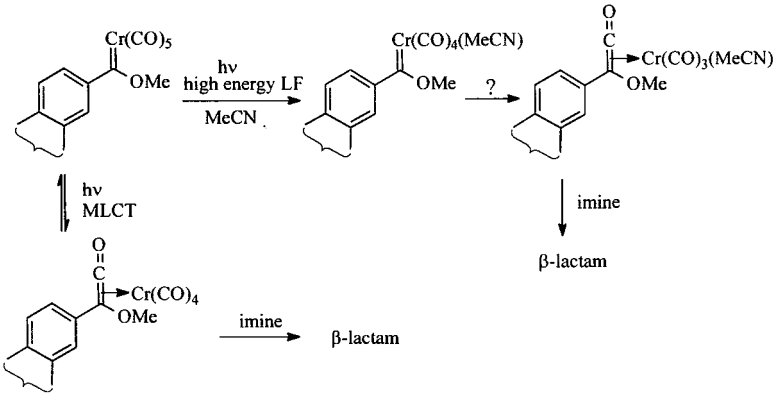
3.1. Photolysis of pentacarbonyl[(methoxy)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (**4**) with N-methylbenzylideneimine

3.1.1. Wotan sunlamp

A solution of *N*-methylbenzylideneimine (49 mg, 0.41 mmol) in hexanes (5 ml) was added to pentacarbonyl[(methoxy)(13 - (12,19 - dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**4**) (0.201 g, 0.385 mmol) [36] in hexanes (15 ml) under nitrogen. Photolysis using a Wotan (Ultra)Vitalux (GUR 53 AC, 300 W) for 2.5 h gave a brown heterogeneous mixture which was quickly filtered followed by freeze–pump–thaw cycling to remove small amounts of heterogeneous impurities. Photolysis for a further 5.5 h and PLC (hexanes–ether, 8:2) gave: (i) a mixture (4:1) (19 mg, 2%) of



Scheme 2.



Scheme 3.

benzaldehyde and **4**; (ii) tetracarbonyl[(methoxy)(13-(12,19 - dimethoxypodocarpa - 8,11,13 - triene))carbene-C^{13},O^{12}]chromium (**5**) (63 mg, 33%) [36]; and (iii) methyl 12,19-dimethoxypodocarpa-8,11,13-trien-13-oate (**6**) (23 mg, 17%) as colourless crystals, m.p. 79–80°C. Found: 346.2154 [$M^{+\bullet}$]. Calc. for $C_{21}H_{30}O_4$: 346.2144. IR (Nujol, ν_{max}, cm^{-1}): 1700 (s, C=O), 1613 (sh, C=C), 1257 (s, C–O–C_{anti}), 1114 (s, C–O–C_{syn}). ^{1}H-NMR: δ 1.02 (ddd, $J = 13.6$, 13.6, 4.2 Hz, H(3ax)); 1.04 (s, H(18)); 1.20 (s, H(20)); 1.41 (dd, $J = 12.6$, 1.5 Hz, H(5)); 1.45 (ddd, $J = 13.0$, 13.0, 3.8 Hz, H(1ax)); 1.61–1.77 (m, H(2ax), H(2eq), H(6ax)); 1.88 (bd, $J = 13.5$ Hz, H(3eq)); 1.99 (bdd, $J = 13.2$, 7.2 Hz, H(6eq)); 2.28 (bd, $J = 12.8$ Hz, H(1eq)); 2.75 (ddd, $J = 17.2$, 11.4, 7.2 Hz, H(7ax)); 2.88 (bdd, $J = 16.4$, 6.1 Hz, H(7eq)); 3.25 (d, $J = 9.1$ Hz, H(19)); 3.33 (s, 19-OMe); 3.51 (s, $J = 9.1$ Hz, H(19)); 3.86 (s, 12-OMe); 3.87 (s, $COOCH_3$); 6.85 (s, H(11)); 7.49 (s, H(14)). ^{13}C-NMR: δ 19.1 (C(2)); 19.2 (C(6)); 25.4 (C(20)); 27.6 (C(18)); 29.9 (C(7)); 35.9 (C(3)); 38.1 (C(10)); 38.4 (C(4)); 38.8 (C(1)); 50.9(5) ($COOCH_3$); 51.8(5) (C(5)); 56.1 (12-OMe); 59.4 (19-OMe); 75.9 (C(19)); 108.4 (C(11)); 117.2 (C(13)); 127.0 (C(8)); 132.3 (C(14)); 155.8 (C(9)); 157.3 (C(12)); 166.7 (C=O). MS; m/z: 346 (100, M^+), 331 (10, M – $Me^{\bullet}$), 315 (12, M – $^{\bullet}$OMe), 255 (37, M – MeOH – $^{\bullet}CO_2Me$), 219 (75).

3.1.2. Rayonet photochemical reactor

A solution of *N*-methylbenzylideneimine (28 mg, 0.23 mmol) in hexanes (1 ml) was added to a solution of **4** (97 mg, 0.19 mmol) in hexanes (8 ml) under nitrogen. Photolysis using a Rayonet photochemical reactor (3000 Å) for 3 h gave a brown heterogeneous mixture. Filtration and PLC gave: (i) a mixture (4:3) (32 mg, 14%) of benzaldehyde and **4**; (ii) (**5**) (35 mg, 38%); and (iii) (**6**) (11 mg, 17%).

3.1.3. Rayonet photochemical rector

A solution of *N*-methylbenzylideneimine (16.2 mg, 0.135 mmol) and pentacarbonyl [(methoxy)(13-(12-methoxypodocarpa-8,11,13-triene))carbene]chromium (**4**) (58 mg, 0.111 mmol) in MeCN (4 ml) under nitrogen was photolysed using a Rayonet photochemical reactor (3500 Å) for 5 h. The brown heterogeneous mixture was filtered and PLC (hexanes–ether, 9:1) gave: (i) **4** (5 mg, 9%); (ii) **5** (35 mg, 64%); and (iii) **6** (5 mg, 13%).

Table 2
X-ray data collection and processing parameters

	***rac*-25**	***rac*-31**
Formula	$C_{23}H_{21}NO_3$	$C_{18}H_{19}NOS$
Molecular weight	359.41	297.40
Temperature (K)	203(2)	293(2)
Wavelength (Å)	0.71073	0.71073
Crystal system	Monoclinic	Orthorhombic
Space group	*C*2/*c*	*Pbca*
Unit cell dimensions		
a (Å)	36.5673(11)	9.69520(10)
b (Å)	6.3405(2)	14.10580(10)
c (Å)	19.1930(6)	24.44100(10)
β (°)	121.66	
V (Å^3)	3787.8(2)	3342.52(4)
Z	8	8
D_{calc} (g cm^{-3})	1.261	1.182
μ (mm^{-1})	0.083	0.192
F(000)	1520	1264
Crystal size (mm)	$0.79 \times 0.29 \times 0.25$	$0.75 \times 0.58 \times 0.35$
2θ Range (°)	1.31–27.51	1.67–28.24
Reflections collected	33 672	19 933
Observed data	3431	2827
Independent reflections	4231 [$R_{int} = 0.0344$]	3800 [$R_{int} = 0.0309$]
A (min/max)	0.9795, 0.9371	0.9358, 0.8693
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
R_1 (observed data)	0.0457, $wR^2 = 0.1245$	0.0635, $wR^2 = 0.1620$
wR_2 (all data)	0.0583, $wR^2 = 0.1353$	0.0853, $wR^2 = 0.1756$
Goodness-of-fit on F^2	1.028	1.102
Weighting scheme	Calc $w = 1/[\sigma^2(F_o^2) + (0.0676P)^2 + 1.6393P]$ where $P = (F_o^2 + 2F_c^2)/3$	Calc $w = 1/[\sigma^2(F_o^2) + (0.0599P)^2 + 1.6959P]$ where $P = (F_o^2 + 2F_c^2)/3$
Difference map (min/max) (e Å^{-3})	+0.246, −0.204	+0.224, −0.292

3.1.4. Rayonet photochemical reactor

A solution of *N*-methylbenzylideneimine (17.1 mg, 0.143 mmol) and **4** (61 mg, 0.117 mmol) in ether (4 ml) under nitrogen was photolysed using a Rayonet photochemical reactor (3500 Å) for 5 h. The mixture was filtered and PLC (hexanes–ether, 9:1) gave: (i) **4** (6 mg); (ii) **5** (37 mg, 64%); and (iii) **6** (3 mg, 7%).

3.1.5. Sunlight

A solution of *N*-methylbenzylideneime (55 mg, 0.46 mmol) in hexanes (5 ml) was added to **4** (0.183 g, 0.35 mmol) in hexanes (15 ml) under nitrogen. Photolysis on the roof of the Chemistry Department of The University of Auckland for 5 days followed by PLC gave: (i) **5** (51 mg, 28%) and (ii) **6** (12%).

3.1.6. Hanovia medium pressure lamp

A solution of *N*-methylbenzylideneimine (28 mg, 0.23 mmol) in hexanes (1 ml) was added to **4** (98 mg, 0.19 mmol) in hexanes (8 ml) under nitrogen. Photolysis using a 125 W Hanovia medium pressure lamp for 3 h 15 min gave a brown heterogeneous mixture. PLC (hexanes–ether, 95:5) gave: (i) a mixture (4:3) (5%) of benzaldehyde and **4**; and (ii) **5** (50 mg, 54%).

*3.2. Photolysis of N-methylbenzylideneimine with pentacarbonyl[(methoxy)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]-chromium (**7**)*

A solution of *N*-methylbenzylideneimine (28 mg, 0.23 mmol) in hexanes (1 ml) was added to a solution of **7** (99 mg, 2.1 mmol) [36] in hexanes (8 ml) under nitrogen. Photolysis using a Rayonet photochemical reactor (3000 Å) for 3 h followed by PLC gave: (i) **7** (39 mg, 39%) and (ii) tetracarbonyl[(methoxy)(13-(12-methoxypodocarpa-4(18),8,11,13-tetraene))carbene-C^{13},O^{12}]-chromium (**8**) (19 mg, 20%) [36].

*3.3. Methyl 13-bromo-12-(trifluoromethanesulfonyloxy)podocarpa-8,11,13-trien-19-oate (**10**)*

A solution of methyl 13-bromo-12-hydroxypodocarpa-8,11,13-trien-19-oate (**9**) (3.825 g, 10.4 mmol) [53], 2,6-lutidine (1.95 ml, 16.7 mmol) and 4-*N*,*N*-dimethylaminopyridine (0.244 g, 1.98 mmol) in CH_2Cl_2 (80 ml) was cooled to −78°C. Triflic anhydride (2.40 ml, 14.2 mmol) was added slowly and the solution was warmed to room temperature (r.t.). After 16.5 h, the solution was washed with HCl (2 mol l^{-1}), and brine, and dried. Column chromatography (hexanes–ether, 3:1) gave methyl 13-bromo-12-(trifluoromethanesulfonyloxy)-podocarpa-8,11,13-trien-19-oate (**10**) (5.068 g, 98%) as a colourless oil which solidified to a white solid, m.p. 53–55°C. Found: 500.0304 [$M^{+\bullet}$]. Calc. for $C_{19}H_{22}^{81}BrF_3O_5S$: 500.0303. Found: 498.0316 [$M^{+\bullet}$]. Calc. for $C_{19}H_{22}^{79}BrF_3O_5S$: 498.0323. IR ($\nu_{max}$, cm^{-1}): 1728 (s, C=O), 1214 ($CF_{3(assym)}$), 1141 ($CF_{3(sym)}$). ^{1}H-NMR: δ 1.01 (s, H(20)); 1.09 (ddd, J = 13.6, 13.6, 4.2 Hz, H(3ax)); 1.28 (s, H(18)); 1.40 (ddd, J = 13.3, 13.3, 4.1 Hz, H(1ax)); 1.49 (dd, J = 12.3, 1.7 Hz, H(5)); 1.66 (dp, J = 14.3, 1.2 Hz, H(2eq)); 1.92–2.05 (m, H(2ax), H(6ax)); 2.13 (bd, J = 12.8 Hz, H(3eq)); 2.21 (ddt, J = 14.0, 6.2, 1.7 Hz, H(6eq)); 2.30 (bd, J = 13.6 Hz, H(1eq)); 2.77 (ddd, J = 16.4, 12.6, 6.2 Hz, H(7ax)); 2.91 (ddd, J = 16.4, 5.5, 1.2 Hz, H(7eq)); 3.69 (s, 19-OMe); 7.18 (s, H(11)); 7.34 (s, H(14)). ^{13}C-NMR: δ 19.7 (C(2)); 20.4 (C(6)); 22.9 (C(20)); 28.4 (C(18)); 31.1 (C(7)); 37.3 (C(3)); 38.6 (C(10)); 39.0 (C(1)); 43.9 (C(4)); 51.4 (19-OMe); 51.8 (C(5)); 111.9 (C(13)); 118.6(5) (q, J = 318 Hz, CF_3); 120.1 (C(11)); 134.2 (C(14)); 137.8 (C(9)); 145.1 (C(8)); 149.8 (C(12)); 177.4 (C(19)).MS; m/z: 500 (16, M^+), 498 (16, M^+), 485 (16, $M - Me^{\bullet}$), 483 (16, $M - Me^{\bullet}$), 425 (100), 423 (85).

*3.4. Methyl 13-bromopodocarpa-8,11,13-trien-19-oate (**11**)*

A mixture of methyl 13-bromo-12-(trifluoromethanesulfonyloxy)podocarpa-8,11,13-trien-19-oate (**10**) (1.0 g, 2.0 mmol), palladium(II) acetate (44 mg, 0.20 mmol) and dppf (0.116 g, 0.209 mmol) in DMF (15 ml, dried over CaH_2) was purged with nitrogen for 5 min. Triethylsilane (1.8 ml, 11.3 mmol) was added and the mixture was stirred at 7°C for 40.5 h. Workup followed by column chromatography (hexanes–ether, 9:1) gave methyl 13-bromopodocarpa-8,11,13-trien-19-oate (**11**) (0.616 g, 88%) as colourless crystals, m.p. 154–154.5°C. Found: 352.0862 [$M^{+\bullet}$]. Calc. for $C_{18}H_{23}^{81}BrO_2$: 352.0861. Found: 350.0873 [$M^{+\bullet}$]. Calc. for $C_{18}H_{23}^{79}BrO_2$: 350.0881. IR (ν_{max}, cm^{-1}, CH_2Cl_2): 1718 (C=O), 1190, 1031, 815, 723. ^{1}H-NMR: δ 1.00 (s, H(20)); 1.08 (ddd, J = 13.6, 13.6, 4.2 Hz, H(3ax)); 1.28 (s, H(18)); 1.35 (ddd, J = 13.3, 13.3, 4.2 Hz, H(1ax)); 1.50 (dd, J = 12.3, 1.7 Hz, H(5)); 1.62 (dp, J = 14.3, 1.2 Hz, H(2eq)); 1.90–2.05 (m, H(2ax), H(6ax)); 2.17 (ddt, J = 13.9, 6.0, 1.7 Hz, H(6eq)); 2.22 (bd, J = 13.8 Hz, H(1eq)); 2.28 (bd, J = 11.0, 2.5 Hz, H(3eq)); 2.76 (ddd, J = 17.0, 12.4, 6.1 Hz, H(7ax)); 2.87 (ddd, J = 17.0, 5.5, 1.5 Hz, H(7eq)); 3.66 (s, 19-OMe); 7.12 (d, J = 8.5 Hz, H(11)); 7.18 (bd, J = 2.0 Hz, H(14)); 7.23 (dd, J = 8.5, 2.1 Hz, H(12)). ^{13}C-NMR: δ 19.8 (C(2)); 20.7 (C(6)); 22.9 (C(20)); 28.5 (C(18)); 31.8 (C(7)); 37.5 (C(3)); 38.3 (C(10)); 39.2 (C(1)); 43.9 (C(4)); 51.3 (19-OMe); 52.5 (C(5)); 119.0 (C(13)); 127.5 (C(12)); 128.8 (C(11)); 131.6 (C(14)); 137.9 (C(9)); 147.1 (C(8)); 177.7 (C(19)). MS; m/z: 352 (22, M^+), 350 (22, M^+), 337 (40, $352 - Me^{\bullet}$), 335 (40, $350 - Me^{\bullet}$), 277 (100, $337 - HCO_2Me$), 275 (92, $335 - HCO_2Me$).

*3.5. 13-Bromopodocarpa-8,11,13-trien-19-oic acid (**12**)*

Potassium hydroxide (0.632 g, 11.3 mmol) dissolved in water (2 ml) was added to a slurry of methyl 13-bro-

mopodocarpa-8,11,13-trien-19-oate (**11**) (0.470 g, 1.34 mmol) in Me_2SO (25 ml) and the mixture was heated to 100°C for 41.5 h. The yellow solution was poured onto ice (150 g) containing HCl (10 ml, 11 mol l^{-1}), extracted with Et_2O (3 × 50 ml) and the extract was washed with water and dried. Flash column chromatography (hexanes–ether, 4:1) gave 13-bromopodocarpa-8,11,13-trien-19-oic acid (**12**) (0.384 g, 85%) as a white solid, m.p. 190–193°C. Found: 338.0701 [$M^{+\bullet}$]. Calc. for $C_{17}H_{21}^{81}BrO_2$: 338.0704. Found: 336.0722 [$M^{+\bullet}$]. Calc. for $C_{17}H_{21}^{79}BrO_2$: 336.0725. IR (ν_{max}, cm^{-1}): 3200–2700 (br, OH), 1694 (s, C=O). ^{1}H-NMR: δ 1.08 (ddd, J = 13.0, 13.0, 4.1 Hz, H(3ax)); 1.09 (s, H(20)); 1.33 (s, H(18)); 1.36 (ddd, J = 13.5, 13.5, 4.0 Hz, H(1ax)); 1.53 (dd, J = 12.2, 1.7 Hz, H(5)); 1.62 (dp, J = 14.5, 4.1 Hz, H(2eq)); 1.95–2.10 (m, H(6ax), H(2ax)); 2.15–2.29 (m, H(1eq), H(6eq), H(3eq)); 2.77 (ddd, J = 16.6, 12.5, 6.0 Hz, H(7ax)); 2.79 (bdd, J = 16.6, 4.5 Hz, H(7eq)); 7.11 (d, J = 8.5 Hz, H(11)); 7.18 (bd, J = 2.2 Hz, H(14)); 7.22 (dd, J = 8.5, 2.2 Hz, H(12)); COOH not observed. ^{13}C-NMR: δ 19.7(5) (C(2)); 20.6 (C(6)); 23.1 (C(20)); 28.6 (C(18)); 31.7 (C(7)); 37.2 (C(3)); 38.5 (C(10)); 39.1 (C(4)); 43.8 (C(1)); 52.4(5) (C(5)); 119.1 (C(13)); 125.8 (C(12)); 127.5 (C(11)); 128.8(5) (C(14)); 131.8 (C(9)); 147.0 (C(8)); 183.8 (C(19)). MS; m/z: 338 (38, M^+), 336 (38, M^+), 323 (100, $M - Me^{\bullet}$), 321 (100, $M - Me^{\bullet}$), 277 (95, $M - Me^{\bullet} - HO_2CH$), 275 (95, $M - Me^{\bullet} - HO_2CH$).

3.6. 13-Bromopodocarpa-8,11,13-trien-19-ol (13)

A solution of 13-bromopodocarpa-8,11,13-trien-19-oic acid (**12**) (0.704 g, 2.09 mmol) in THF (10 ml) was added via cannula to a solution of $BH_3{\cdot}SMe_2$ (10 mol l^{-1}, 0.63 ml, 6.3 mmol) and trimethyl borate (0.71 ml, 6.25 mmol) in THF (10 ml) cooled to 0°C under nitrogen. The solution was stirred at r.t. for 21 h, then MeOH was added cautiously until gas evolution ceased, and the solvents were removed in vacuo. The residual oil was dissolved in MeOH and the solvent was again removed; this procedure was repeated three times. Flash column chromatography (hexanes–ether, 1:1) gave 13-bromopodocarpa-8,11,13-trien-19-ol (**13**) (0.486 g, 72%) as a white solid, m.p. 110–111°C. Found: 324.0912 [$M^{+\bullet}$]. Calc. for $C_{17}H_{23}^{81}BrO$: 324.0906. Found: 322.0932 [$M^{+\bullet}$]. Calc. for $C_{17}H_{23}^{79}BrO$: 322.0921. IR (ν_{max}, cm^{-1}): 3478 (br, OH), 1109 (C–O). ^{1}H-NMR: δ 1.02 (ddd, J = 13.0, 13.0, 4.0 Hz, H(3ax)); 1.05 (s, H(18)); 1.15 (s, H(20)); 1.40 (ddd, J = 12.9, 12.9, 4.1 Hz, H(1ax)); 1.46 (dd, J = 12.8, 2.0 Hz, H(5)); 1.52 (bs, 19-OH); 1.58–1.77 (m, H(2ax), H(2eq), H(6ax)); 1.89 (bdd, J = 13.7, 1.3 Hz, H(3eq)); 1.98 (ddt, J = 13.4, 7.2, 1.9 Hz, (6eq)); 2.28 (bd, J = 12.8 Hz, H(1eq)); 2.80 (ddd, J = 17.0, 11.4, 6.1 Hz, H(7ax)); 2.89 (bdd, J = 17.0, 6.8 Hz, H(7eq)); 3.55 (d, J = 9.0 Hz, H(19)); 3.84 (d, J = 9.0 Hz, H(19)); 7.11 (d, J = 8.5 Hz, H(11)); 7.16 (d, J = 2.0 Hz, H(14)); 7.22 (dd, J = 8.5, 2.0 Hz, H(12)). ^{13}C-NMR: δ 18.8(6) (C(2)); 18.9(1) (C(6)); 25.6 (C(20)); 26.8 (C(18)); 30.7 (C(7)); 35.1 (C(3)); 37.6 (C(10)); 38.7 (C(4)); 38.8 (C(1)); 50.9 (C(5)); 65.2 (C(19)); 118.9(5) (C(13)); 125.5 (C(12)); 128.7 (C(11)); 131.6 (C(14)); 137.4 (C(9)); 148.7 (C(8)). MS; m/z: 324 (58, M^+), 322 (58, M^+), 309, (100, $324 - Me^{\bullet}$), 307 (100, $322 - Me^{\bullet}$), 291 (60, $309 - H_2O$), 289 (50, $307 - H_2O$), 221 (45), 211 (73), 209 (80), 141 (42), 128 (58), 115 (40).

3.7. 13-Bromo-19-methoxypodocarpa-8,11,13-triene (14)

A solution of 13-bromopodocarpa-8,11,13-trien-19-ol (**13**) (0.662 g, 2.05 mmol) in THF (14 ml) was added to imidazole (6 mg, 0.09 mmol) and NaOH (0.215 g, 4.5 mmol, 50% dispersion in oil, washed with hexanes). The mixture was refluxed under nitrogen for 2 h then cooled to r.t. Iodomethane (0.50 ml, 8.0 mmol) was added and the mixture was refluxed for 2 h. Workup and flash chromatography (hexanes–ether, 9:1) gave 13-bromo-19-methoxypodocarpa-8,11,13-triene (**14**) (0.582 g, 84%) as colourless crystals, m.p. 85–86°C. Found: 338.1065 [$M^{+\bullet}$]. Calc. for $C_{18}H_{25}^{81}BrO$: 338.1068. Found: 336.1090 [$M^{+\bullet}$]. Calc. for $C_{18}H_{25}^{79}BrO$: 336.1089. IR (ν_{max}, cm^{-1}): 1110 (C–O–C). ^{1}H-NMR: δ 1.01 (ddd, J = 13.6, 13.6, 4.0 Hz, H(3ax)); 1.03 (s, H(18)); 1.16 (s, H(20)); 1.38 (ddd, J = 13.0, 13.0, 4.0 Hz, H(1ax)); 1.39 (dd, J = 12.7, 2.0 Hz, H(5)); 1.58–1.77 (m, H(2ax), H(2eq), H(6ax)); 1.86 (bdd, J = 13.5, 1.1 Hz, H(3eq)); 1.97 (ddt, J = 13.4, 7.1, 1.7 Hz, H(6eq)); 2.26 (bd, J = 12.8 Hz, H(1eq)); 3.25 (d, J = 9.1 Hz, H(19)); 3.33 (s, 19-OMe); 3.50 (d, J = 9.1 Hz, H(19)); 7.11 (d, J = 8.5 Hz, H(11)); 7.16 (d, J = 1.9 Hz, H(14)); 7.22 (dd, J = 8.4, 2.1 Hz, H(12)). ^{13}C-NMR: δ 19.0(5) (C(2), C(6)); 25.6 (C(20)); 27.6 (C(18)); 30.7 (C(7)); 36.0 (C(3)); 37.6 (C(10)); 38.0 (C(4)); 38.9 (C(1)); 51.1 (C(5)); 59.4 (19-OMe); 75.9 (C(19)); 118.9 (C(13)); 126.5 (C(12)); 128.7 (C(11)); 131.6 (C(14)); 137.6 (C(9)); 148.9 (C(8)). MS; m/z: 338 (39, M^+), 336 (39, M^+), 323 (55, $M - Me^{\bullet}$), 321 ($M - Me^{\bullet}$), 291 (43, $M - MeOCH_2^{\bullet}$), 289 (38, $M - MeOCH_2^{\bullet}$), 221 (40), 211 (90), 209, (100).

3.8. 13-Bromopodocarpa-8,11,13-trien-19-oyl chloride (16)

A solution of 13-bromopodocarpa-8,11,13-trien-19-oic acid (**12**) (72 mg, 0.21 mmol) and thionyl chloride (0.20 ml, 2.8 mmol) in benzene (2 ml) was refluxed for 1.3 h. Removal of solvent in vacuo gave 13-bromopodocarpa-8,11,13-trien-19-oyl chloride (**16**) (76 mg, 100%) as a colourless oil. IR (ν_{max}, cm^{-1}): 1798 (C=O).

3.9. 13-Bromo-4α-(2′-pyridylthio)-18-norpodocarpa-8,11,13-triene (17)

A solution of 13-bromopodocarpa-8,11,13-trien-19-oyl chloride (**16**) (1.065 g, 3.00 mmol) in benzene (15 ml) was added to sodium 1-hydroxy-2-pyridinethione

(0.493 g, 3.31 mmol) and 4-*N*,*N*-dimethylaminopyridine (20 mg, 0.16 mmol). The mixture was refluxed under nitrogen for 2.5 h, then cooled and filtered through Celite. Removal of the solvent followed by flash chromatography (hexanes–ether, 8:2) gave 13-bromo-4α-(2′-pyridylthio)-18-norpodocarpa-8,11,13-triene (**17**) (1.090 g, 90.5%) as a colourless oil. Found: 403.0800 [$M^{+\bullet}$]. Calc. for $C_{21}H_{24}^{81}BrNS$: 403.0792. Found: 401.0810 [$M^{+\bullet}$]. Calc. for $C_{21}H_{24}^{79}BrNS$: 401.0813. IR (ν_{max}, cm^{-1}): 1574 (s, C=C), 1557 (s, C=C), 1480, 1449, 1413, 1120, 1092, 759, 724. ^{1}H-NMR: δ 1.20 (s, H(20)); 1.35 (ddd, $J = 13.1$, 13.1, 4.0 Hz, H(1ax)); 1.45 (s, H(19)); 1.59–1.90 (m, H(2ax), H(2eq), H(6ax)); 1.97 (dd, $J = 12.3$, 1.8 Hz, H(5)); 2.08 (dtd, $J = 13.2$, 3.2, 1.4 Hz, H(3eq)); 2.19 (dd, $J = 13.2$, 4.1 Hz, H(1eq)); 2.23 (ddd, $J = 13.2$, 5.1 Hz, H(3ax)); 2.55 (ddt, $J = 13.2$, 7.2, 1.8 Hz, H(6eq)); 2.79 (ddd, $J = 16.6$, 11.2, 7.0 Hz, H(7ax)); 2.88 (bdd, $J = 16.6$, 5.9 Hz, H(7eq)); 7.06 (d, $J = 8.5$ Hz, H(11)); 7.09 (ddd, $J = 7.5$, 4.9, 1.1 Hz, H(4′)); 7.16 (d, $J = 2.1$ Hz, H(14)); 7.19 (dd, $J = 8.4$, 2.2 Hz, H(12)); 7.39 (dd, $J = 7.7$, 0.9 Hz, H(6′)); 7.52 (td, $J = 7.7$, 1.9 Hz, H(5′)); 8.50 (ddd, $J = 4.8$, 1.9, 1.0 Hz, H(3′)). ^{13}C-NMR: δ 19.8(2) (C(2)); 19.8(7) (C(6)); 21.6 (C(20)); 25.4 (C(19)); 29.7 (C(7)); 37.8 (C(3)); 39.3 (C(10)); 40.3 (C(1)); 47.3 (C(5)); 57.6 (C(4)); 119.0 (C(13)); 121.7 (C(4′)); 126.3 (C(12)); 128.6 (C(11)); 129.7 (C(6′)); 131.7 (C(14)); 136.1 (C(5′)); 137.8(5) (C(9)); 148.4 (C(8)); 149.8 (C(3′)); 157.0 (C(1′). MS; *m*/*z*: 403 (1, M^+), 401 (1, M^+), 370, (1, 403-$SH^{\bullet}$), 368 (1, $401 - SH^{\bullet}$), 322 (1, $M - Br^{\bullet}$), 277 (7, $403 - Me^{\bullet} - C_5H_5NS$), 275 (7, $401 - Me^{\bullet} - C_5H_5NS$), 221 (9), 211 (20), 209 (20), 112 (100, $C_5H_6NS^+$).

3.10. 13-Bromo-19-norpodocarpa-8,11,13-tetraene (**15**)

A suspension of *m*-chloroperoxybenzoic acid (85% w/w, 0.542 g, 2.68 mmol) in CH_2Cl_2 (15 ml) was added slowly to a cooled (−78°C) and stirred solution of 13-bromo-4α-(2′-pyridylthio)-18-norpodocarpa-8,11,13-triene (**17**) (1.076 g, 2.68 mmol) in CH_2Cl_2 (10 ml) under an atmosphere of nitrogen. After 1 h the suspension was allowed to come to r.t. and added dropwise to dry benzene (100 ml) at reflux. After 1 h the solution was cooled to r.t. Flash chromatography (hexanes–ether, 9:1) gave 13-bromo-19-norpodocarpa-8,11,13-tetraene (**15**) (0.679 g, 87%) as a colourless oil. Found: 292.0647 [$M^{+\bullet}$]. Calc. for $C_{16}H_{19}^{81}Br$: 292.0650. Found: 290.0659 [$M^{+\bullet}$]. Calc. for $C_{16}H_{19}^{79}Br$: 290.0670. IR (ν_{max}, cm^{-1}): 1648 (s, C=C), 1480, 1440, 1090. ^{1}H-NMR: δ 0.98 (s, H(20)); 1.53 (ddd, $J = 13.0$, 13.0, 4.6 Hz, H(1ax)); 1.65–1.87 (m, H(2eq), H(2ax), H(6ax), H(6eq)); 2.05 (ddd, $J = 13.1$, 13.1, 4.5 Hz, H(3ax)); 2.18 (dd, $J = 12.0$, 1.1 Hz, H(5)); 2.23 (bd, $J = 12.8$ Hz, H(1eq)); 2.38 (ddd, $J = 13.1$, 4.3, 2.2 Hz, H(3eq)); 2.88 (4 lines, H(7ax), H(7eq)); 4.60 (d, $J = 1.5$ Hz, H(18)); 4.86 (d, $J = 1.5$ Hz, H(18)); 7.16 (d, $J = 9.4$ Hz, H(11)); 7.22–7.26 (m, H(12), H(14)). ^{13}C-NMR: δ 21.0 (C(6)); 22.7 (C(20)); 23.6 (C(2)); 29.6 (C(7)); 36.2 (C(3)); 38.2 (C(1)); 39.2(5) (C(10)); 47.5 (C(5)); 106.7(5) (C(18)); 119.1 (C(13)); 127.4 (C(12)); 128.7 (C(11)); 131.8 (C(14)); 137.7 (C(9)); 146.3 (C(4)); 150.0 (C(8)). MS; *m*/*z*: 292 (25, M^+), 290 (25, M^+), 277 (28, $292 - Me^{\bullet}$), 275 (28, $290 - Me^{\bullet}$), 196 ($M - Me^{\bullet} - Br^{\bullet}$).

3.11. Methyl pentacarbonyl[(methoxy)(13-(podocarpa-8,11,13-trien-19-oate))carbene]chromium (**18**)

Butyllithium (0.84 ml, 2.5 mol l^{-1}) was added to a solution of methyl 13-bromo-podocarpa-8,11,13-trien-19-oate (**11**) (0.741 g, 2.11 mmol) in THF (15 ml) at −78°C under nitrogen. The solution was stirred at −78°C for 2 min then added to a slurry of $Cr(CO)_6$ (0.487 g, 2.21 mmol) in ether (15 ml) at 0°C. After 45 min, methyl triflate (0.35 ml, 3.09 mmol) was added and the solution was stirred for 2 h at r.t. The mixture was diluted with ether (and the extracts were washed with water and dried. Radial chromatography (hexanes–ether, 9:1) gave methyl pentacarbonyl[(methoxy)(13-(podocarpa-8,11,13-trien-19-oate))carbene]chromium (**18**) (0.221 g, 21%) as a red oil. Attempts to obtain an analytically pure sample of **18** using preparative TLC were unsuccessful, small amounts of methyl podocarpa-8,11,13-trien-19-oate being present. Found: 506.1061 [$M^{+\bullet}$]. Calc. for $C_{25}H_{26}CrO_8$: 506.1033. IR (ν_{max}, cm^{-1}): 2059 (s, C≡O), 1983 (sh, C≡O), 1932 (br, C≡O). λ_{max}, nm: 419, 234. ^{1}H-NMR: δ 1.03 (s, H(20)); 1.10 (ddd, $J = 13.6$, 13.6, 4.3 Hz, H(3ax)); 1.29 (s, H(18)); 1.39 (ddd, $J = 13.4$, 13.4, 3.6 Hz, H(1ax)); 1.55 (d, $J = 10.7$ Hz, H(5)); 1.65 (dp, $J = 14.0$, 3.3 Hz, H(2eq)); 1.91–2.06 (m, H(2ax), H(6ax)); 2.15–2.31 (m, H(1eq), H(3eq), H(6eq)); 2.81 (ddd, $J =$ 16.9, 12.2, 6.2 Hz, H(7ax)); 2.95 (bdd, $J =$ 16.9, 5.1 Hz, H(7eq)); 3.66 (s, 19-OMe); 4.76 (s, $OMe_{carbene}$); 7.11 (bs, H(14)); 7.26–7.31 (m, H(11), H(12)). ^{13}C-NMR: δ 19.8(5) (C(2)); 20.8 (C(6)); 22.8 (C(20)); 28.5 (C(18)); 30.1 (C(7)); 37.5 (C(3)); 38.8 (C(10)); 39.1 (C(1)); 44.0 (C(4)); 51.3 (19-OMe); 52.4 (C(5)); 67.1(5) ($OMe_{carbene}$); 122.7 (C(12)); 125.1 (C(11)); 125.4 (C(14)); 135.2 (C(13)); 150.7 (C(8)); 151.9 (C(9)); 177.7 (C(19)); 216.5 ($C{\equiv}O_{cis}$); 224.1 ($C{\equiv}O_{trans}$); 348.2 ($C_{carbene}$). MS; *m*/*z*: 506 (2, M^+), 478 (5, M − CO), 450 (3, M − 2CO), 422 (6, M − 3CO), 394 (18, M − 4CO), 366 (100, M − 5CO).

3.12. Pentacarbonyl[(methoxy)(13-(19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**20**)

Butyllithium (0.93 ml, 2.5 mol l^{-1}, 2.33 mmol) was added to a solution of 13-bromo-19-norpodocarpa-4(18),8,11,13-tetraene (**15**) (0.679 g, 2.33 mmol) in THF (10 ml) cooled to −78°C. The solution was stirred at −78°C for 2 min then added via cannula to a slurry of $Cr(CO)_6$ (0.541 g, 2.46 mmol) in ether (15 ml) at 0°C.

The yellow–brown solution was stirred for 1 h then methyl triflate (0.4 ml, 3.53 mmol) was added and the resulting red solution was stirred at r.t. for 1 h. The solution was diluted with ether (50 ml) and the organic extract was washed with aqueous sodium hydrogencarbonate, and water, and dried. Flash chromatography followed by radial chromatography (hexanes–ether, 9:1) gave pentacarbonyl[(methoxy)(13-(19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**20**) (0.308 g, 31%) as a red solid, m.p. 81–83°C. Found: 446.0807 [$M^{+\bullet}$]. Calc. for $C_{23}H_{22}CrO_6$: 446.0821. IR (ν_{max}, cm^{-1}): 2059 (s, C≡O), 1981 (sh, C≡O), 1942 (br, C≡O). λ_{max}, nm ($\log_{10}\varepsilon$): 239.5 (4.50), 420.0 (3.85). ^{1}H-NMR: δ 1.01 (s, H(20)); 1.57 (ddd, J = 13.0, 13.0, 4.6 Hz, H(1ax)); 1.66–1.92 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 2.07 (ddd, J = 13.0, 13.0, 5.4 Hz, H(3ax)); 2.22 (dd, J = 12.3, 1.4 Hz, H(5)); 2.28 (bd, J = 13.0 Hz, H(1eq)); 2.39 (ddd, J = 13.0, 4.2, 2.0 Hz, H(3eq)); 2.92–2.96 (m, H(7ax), H(7eq)); 4.62 (d, J = 1.4 Hz, H(18)); 4.78 (s, $OMe_{carbene}$); 4.88 (d, J = 1.4 Hz, H(18)); 7.14 (b, H(14)); 7.29 (dd, J = 8.3, 1.7 Hz, H(12)); 7.34 (d, J = 8.3 Hz, H(11)). ^{13}C-NMR: δ 21.1 (C(6)); 22.6 (C(20)); 23.5 (C(2)); 30.0 (C(7)); 36.2 (C(3)); 38.0 (C(1)); 39.7 (C(10)); 47.4 (C(5)); 67.2 ($OMe_{carbene}$); 106.8(5) (C(18)); 122.9 (C(12)); 125.3 (C(11), C(14)); 135.0 (C(13)); 150.0 (C(8)); 150.7 (C(4)); 151.2 (C(9)); 216.5 ($C{\equiv}O_{cis}$); 224.1 ($C{\equiv}O_{trans}$); 348.2 ($C_{carbene}$). MS; m/z: 446 (4, M^+), 418 (5, M − CO), 390 (5, M − 2CO), 362 (3, M − 3CO), 334 (22, M − 4CO), 306 (100, M − 5CO), 263 (32), 52 (50, $Cr^{+\bullet}$).

3.13. Pentacarbonyl[(methoxy)(13-(19-methoxy-podocarpa-8,11,13-triene))carbene]chromium (21)

Butyllithium (1.10 ml, 2.15 mol l^{-1}, 2.37 mmol) was added to a solution of 13-bromo-19-methoxypodocarpa-8,11,13-triene (**14**) (0.757 g, 2.34 mmol) in THF (10 ml), cooled to −78°C and the solution was allowed to stir for 4 min at −78°C before being added to a slurry of $Cr(CO)_6$ (0.524 g, 2.38 mmol) in ether (15 ml) at 0°C. The yellow–brown solution was stirred for 1 h then methyl triflate (0.4 ml, 3.53 mmol) was added and the resulting red solution was stirred at r.t. for 1 h. The solution was diluted with ether, washed with aqueous sodium hydrogencarbonate, and water, and dried. Radial chromatography (hexanes–ether, 9:1) gave pentacarbonyl[(methoxy)(13 - (19 - methoxypodocarpa-8,11,13-triene))carbene]chromium (**21**) (0.458 g, 40%) as a red oil. Found: 494.1392 [$M^{+\bullet}$ + 2H]. Calc. for $C_{25}H_{30}CrO_7$: 494.1397. IR (ν_{max}, cm^{-1}): 2059 (s, C≡O), 1981 (sh, C≡O), 1942 (br, C≡O). λ_{max}, nm ($\log_{10}\varepsilon$): 239.5 (4.50), 419.5 (3.86). ^{1}H-NMR: δ 1.05 (ddd, J = 13.6, 13.6, 4.1 Hz, H(3ax)); 1.08 (s, H(18)); 1.22 (s, H(20)); 1.46 (ddd, J = 12.9, 12.9, 3.7 Hz, H(1ax)); 1.46 (dd, J = 12.5, 1.7 Hz, H(5)); 1.60–1.82 (m, H(2ax), H(2eq), H(6ax)); 1.90 (bd, J = 13.5 Hz, H(3eq)); 2.05 (bdd, J = 13.3, 7.3 Hz, H(6eq)); 2.34 (bd, J = 12.6 Hz, H(1eq)); 2.88 (ddd, J = 17.1, 11.3, 7.3 Hz, H(7ax)); 2.99 (bdd, J = 17.1, 6.0 Hz, H(7eq)); 3.30 (d, J = 9.1 Hz, H(19)); 3.36 (s, 19-OMe); 3.54 (d, J = 9.1 Hz, H(19)); 4.76 (s, $OMe_{carbene}$); 7.13 (b, H(12)); 7.32 (b, H(11), H(14)). ^{13}C-NMR: δ 19.0(5) (C(2)); 19.2 (C(6)); 25.4 (C(20)); 27.6 (C(18)); 31.0(5) (C(7)); 35.9(5) (C(3)); 38.0(4) (C(10)); 38.0(8) (C(4)); 38.7 (C(1)); 50.9 (C(5)); 59.4 (19-OMe); 67.1 ($OMe_{carbene}$); 76.0 (C(19)); 123.0 (C(12)); 124.4 (C(11)); 125.1 (C(14)); 134.8(5) (C(13)); 150.6 (C(8)); 153.8 (C(9)); 216.5 ($C{\equiv}O_{cis}$); 224.1 ($C{\equiv}O_{trans}$); 347.9 ($C_{carbene}$). FABMS; m/z: 494 (5, $M^{+\bullet}$ + 2H), 466 (10, 494 − CO), 410 (100, 494 − 3CO), 382 (100, 494 − 4CO), a weak molecular ion (492) was seen in an early scan.

3.14. Pentacarbonyl[(dihydroamino)(13-(19-methoxy-podocarpa-8,11,13-triene))carbene]chromium (22)

Anhydrous NH_3 was condensed into a solution of pentacarbonyl[(methoxy)(13 - (19 - methoxypodocarpa-8,11,13-triene))carbene]chromium (**21**) (49.4 mg, 0.100 mmol) until the colour of the solution had changed from red to yellow. Removal of solvent followed by radial chromatography (hexanes–ether, 1:1) gave pentacarbonyl[(dihydroamino)(13 - (19 - methoxypodocarpa-8,11,13-triene))carbene]chromium (**22**) (45.9 mg, 96%) as a yellow foam. Found: 477.1240 [$M^{+\bullet}$]. Calc. for $C_{24}H_{27}CrNO_6$: 477.1243. IR (ν_{max}, cm^{-1}): 2055 (s, C≡O), 1973 (sh, C≡O), 1925 (br, C≡O). λ_{max}, nm ($\log_{10}\varepsilon$): 232.5 (4.42), 390.5 (3.65). ^{1}H-NMR: δ 1.01 (ddd, J = 13.5, 13.5, 4.2 Hz, H(3ax)); 1.05 (s, H(18)); 1.19 (s, H(20)); 1.41 (ddd, J = 13.1, 13.1, 4.3 Hz, H(1ax)); 1.42 (dd, J = 12.7, 1.9 Hz, H(5)); 1.60–1.79 (m, H(2ax), H(2eq), H(6ax)); 1.87 (bd, J = 13.5 Hz, H(3eq)); 2.02 (ddt, J = 13.6, 7.1, 1.7 Hz, H(6eq)); 2.31 (bd, J = 12.7 Hz, H(1eq)); 2.85 (ddd, J = 16.8, 11.2, 7.3 Hz, H(7ax)); 2.95 (bdd, J = 16.8, 6.4 Hz, H(7eq)); 3.27 (d, J = 9.1 Hz, H(19)); 3.33 (s, 19-OMe); 3.51 (d, J = 9.1 Hz, H(19)); 6.87 (b, H(14)); 7.05 (dd, J = 8.2, 1.8 Hz, H(12)); 7.30 (d, J = 8.2 Hz, H(11)); 8.26 (bs, NH_Z); 8.74 (bs, NH_E). ^{13}C-NMR: δ 19.0(9) (C(2)); 19.1(5) (C(6)); 25.5 (C(20)); 27.7 (C(18)); 31.1 (C(7)); 36.0 (C(3)); 38.0(5) (C(10), C(4)); 38.8(5) (C(1)); 51.1 (C(5)); 59.4 (19-OMe); 76.0 (C(19)); 120.9 (C(12)); 122.9 (C(11)); 125.0 (C(14)); 135.6 (C(13)); 149.4 (C(8)); 152.3 (C(9)); 217.3 ($C{\equiv}O_{cis}$); 223.2 ($C \equiv O_{trans}$); 268.7 ($C_{carbene}$). FABMS; m/z: 477 (13, M^+), 449, (31, M − CO), 421 (7, M − 2CO), 393 (7, M − 3CO), 365 (95, M − 4CO), 337 (100, M − 5CO).

3.15. Pentacarbonyl[(ethylthio)(13-(19-norpodocarpa-4-(18),8,11,13-tetraene))carbene]chromium (23)

Ethanethiol (15 μl, 0.20 mmol) was added to anhydrous Na_2CO_3 (26 mg, 0.25 mmol) and pentacarbonyl[(methoxy)(13-(19-norpodocarpa-4(18),8,11,13-

tetraene))carbene]chromium (**20**) (60.4 mg, 0.135 mmol) in isopropanol (2 ml) cooled to 0°C under a nitrogen atmosphere. The solution was stirred at r.t. for 2 h, then diluted with ether. The ether extract was washed with water, dried and the solvent was evaporated under a stream of nitrogen. Radial chromatography (hexanes) gave pentacarbonyl[(ethylthio)(13-(19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**23**) (35.3 mg, 55%) as a viscous red–black oil. Found: 476.0770 [$M^{+\bullet}$]. Calc. for $C_{24}H_{24}CrO_5S$: 476.0750. IR (ν_{max}, cm^{-1}): 2056 (s, C≡O), 1990 (sh, C≡O), 1935 (br, C≡O). λ_{max}, nm: 233, 353, 477. ^{1}H-NMR: δ 1.02 (s, H(20)); 1.14 (t, $J = 7.6$ Hz, SCH_2CH_3); 1.59 (ddd, $J = 12.9$, 12.9, 4.2 Hz, H(1ax)); 1.68–1.92 (m, H(2ax), H(2eq), H(6eq), H(6ax)); 2.08 (ddd, $J = 12.6$, 12.6, 5.2 Hz, H(3ax)); 2.24–2.30 (3 lines, H(5), H(1eq)); 2.40 (bd, $J = 11.9$ Hz, H(3eq)); 2.78 (q, $J = 7.6$ Hz, SCH_2CH_3); 2.88–2.97 (m, H(7ax), H(7eq)); 4.62 (b, H(18)); 4.88 (b, H(18)); 6.38 (b, H(14)); 6.46 (bd, $J = 7.8$ Hz, H(12)); 7.32 (d, $J = 7.8$ Hz, H(11)). ^{13}C-NMR: δ 12.6 (SCH_2CH_3); 21.2 (C(6)); 22.8 (C(20)); 23.6(5) (C(2)); 30.0 (C(7)); 36.3 (C(3)); 38.2 (C(1)); 38.8(5) (SCH_2CH_3); 39.4 (C(10)); 47.6 (C(5)); 106.7 (C(18)); 115.2 (C(12)); 117.7 (C(11)); 125.2 (C(14)); 135.0 (C(13)); 146.6 (C(8)); 150.2 (C(4)); 154.7 (C(9)); 215.8 ($C \equiv O_{cis}$); 228.7 ($C \equiv O_{trans}$); 363.3 ($C_{carbene}$). FABMS; m/z: 476 (2, M^+), 448 (1, M − CO), 420 (3, M − 2CO), 392 (2, M − 3CO), 364 (2, M − 4CO), 336 (3, M − 5CO), 239 (100, ArCOSEt impurity? M^+ − SEt).

3.16. N-Phenyl(4-methoxy)benzylideneimine

4-Methoxybenzaldehyde (1.993 g, 14.6 mmol) and aniline (1.33 ml, 14.6 mmol) were mixed in a round-bottomed flask for 3 min, giving a cloudy mixture. Water was distilled from the mixture using a Kugelrohr apparatus (50°C, 0.4 mmHg). The clear oil was then distilled (0.4 mmHg, 175°C) to give *N*-phenyl(4-methoxy)benzylideneimine (2.821 g, 91%) as a colourless oil which gradually solidified, m.p. 63–64°C (lit. m.p. 63°C [54]).

3.17. 3-Methoxy-4-(4′-methoxyphenyl)-1-phenyl-3-phenylazetidin-2-one (*rac*-25)

A solution of pentacarbonyl(methoxyphenylcarbene)chromium (**24**) (0.151 g, 0.484 mmol) [55] and *N*-phenyl(4-methoxy)benzylideneimine (0.116 g, 0.549 mmol) in MeCN (12 ml) was freeze–pump–thaw cycled three times and then flushed with nitrogen. The solution was photolysed using a Hanovia medium pressure lamp (125 W) for 25 h, keeping the solution temperature below 20°C. The solvent was removed and the residual oil was dissolved in hexanes–ether and exposed to sunlight until the solution became colourless. PLC (hexanes–ether, 4:1) gave an impure yellow solid which was recrystallised from hexanes to give 3-methoxy-4-(4′-methoxyphenyl)-1-phenyl-3-phenylazetidin-2-one (*rac*-**25**) (50 mg, 29%) as colourless needles, m.p. 149–151°C. Found: 359.1521 [$M^{+\bullet}$]. Calc. for $C_{23}H_{21}NO_3$: 359.1521. IR (ν_{max}, cm^{-1}): 1748 (s, C=O), 1613 (s, C=C), 1599 (s, C=C). ^{1}H-NMR: δ 3.26 (s, OMe_{lactam}); 3.82 (s, OMe_{aryl}); 5.10 (s, H(4)); 6.94 (dt, $J = 8.8$, 2.1, 1.1 Hz, H(15)); 7.08 (tt, $J = 7.5$, 1.1 Hz, H(8)); 7.26 (t, $J = 7.4$ Hz, H(7)); 7.35 (bd, $J = 8.6$ Hz, H(14), H(6)); 7.39–7.47 (m, H(9), H(10)); 7.58 (dt, $J = 6.6$, 1.6 Hz, H(11)). ^{13}C-NMR: δ 54.3 (OMe_{lactam}); 55.2 (OMe_{aryl}); 68.7 (C(4)); 90.9 (C(3)); 114.0 (C(15)); 117.7 (C(6)); 124.3 (C(8)); 125.2(5) (C(5)); 127.0 (C(11)); 128.9 (C(9), C(10)); 129.0 (C(7)); 129.3 (C(14)); 136.5 (C(13)); 127.0(5) (C(12)); 137.0(5) (C(16)); 165.3 (C(2). MS; m/z: 359 (35, M^+), 240 (35, M − PhNCO), 211 (100, M − Ph(OMe)C=C=O), 105 (75, $PhCO^+$), 77 (Ph^+).

3.18. 1-Methyl-3-methoxy-3,4-diphenylazetidin-2-one (*rac*-26)

A solution of pentacarbonyl[methoxyphenylcarbene]chromium (**24**) (0.171 g, 0.548 mmol) in MeCN (12 ml) in a sealed pressure vessel was freeze–pump–thaw cycled three times and then flushed with nitrogen. *N*-Methylbenzylideneimine (71 μl, 0.58 mmol) was added and the solution was photolysed using a Hanovia medium pressure lamp (125 W) for 48 h, keeping the solution temperature less than 20°C. The solvent was removed and the residue was dissolved in ether–hexanes and exposed to sunlight until the solution was colourless. Filtration and removal of solvent gave 1-methyl-3-methoxy-3,4-diphenylazetidin-2-one (*rac*-**26**) (0.111 g, 76%) as a white solid. Recrystallisation of a small portion from pentane gave colourless crystals, m.p. 95–96°C (lit. m.p. 91–92°C [21]). Found: 267.1253 [$M^{+\bullet}$]. Calc. for $C_{17}H_{17}NO_2$: 267.1259. IR (ν_{max}, cm^{-1}, CH_2Cl_2): 1756 (s, C=O), 1603 (s, C=C), 774, 700, 625. ^{1}H-NMR: δ 2.86 (s, NCH_3); 3.18 (s, OMe); 4.63 (s, CH_{lactam}); 7.33–7.57 (m, Ph). ^{13}C-NMR: δ 26.2 (NCH_3); 54.1 (OMe); 70.5 (C(3)); 92.5 (C(4)); 127.0 (CH); 128.2 (CH); 128.4 (CH); 128.6 (CH); 128.7 (CH); 133.7 (C(4′)); 136.6 (C(8′)); 168.0 (C(2)). MS; m/z: 267 (8, M^+), 210 (90, M − MeNCO$^\bullet$), 105 (100, $PhCO^+$), 77 (33, Ph^+).

3.19. 3-(Benzylideneimine)-1-methyl-3,4-dipheny-azetidin-2-one (*rac*-28)

A solution of pentacarbonyl[(dihydroamino)phenylcarbene]chromium (**27**) (0.164 g, 0.552 mmol) [56] in MeCN (5 ml) in a sealed pressure vessel was freeze–pump–thaw cycled three times and then flushed with nitrogen. *N*-Methylbenzylideneimine (482, 136 μl, 1.10 mmol) was added and the solution was photolysed for 51 h using a Hanovia medium pressure lamp (125 W),

keeping the solution temperature below 20°C. The solvent was removed and the residue was dissolved in hexanes–ether (1:1) and the solution was exposed to sunlight until it was colourless. PLC (hexanes–ether, 2:1) gave 3-(benzylideneimine)-1-methyl-3,4-diphenylazetidin-2-one (***rac*-28**) (11.4 mg, 6%) as a colourless oil. Found: 340.1578 [$M^{+\bullet}$]. Calc. for $C_{23}H_{20}N_2O$: 340.1576. IR (ν_{max}, cm^{-1}): 1749 (C=O), 1644 (C=N). ^{1}H-NMR: δ 2.88 (s, NMe_{min}); 2.93 (s, NMe_{maj}); 4.98 (s, H(4)); 7.23–7.43 (m, 11H, Ph); 7.47 (t, $J = 7.3$ Hz, H_{para}); 7.56 (dd, $J = 8.6$, 1.5 Hz, 2H, H_{ortho}); 8.48 (dd, $J = 7.8$, 1.4 Hz, H_{ortho}); 8.52 (bs, CH_{imine}). ^{13}C-NMR: δ 25.7 (NMe_{min}); 26.6 (NMe_{maj}); 71.7 ($C(4)_{min}$); 72.2 ($C(4)_{maj}$); 85.2 (C(4)); 125.8 (CH_{maj}); 126.1 (CH_{min}); 126.8 (2C, CH_{maj}); 127.0 (CH_{min}); 128.0 (CH); 128.3 (b, 6C, CH); 128.6 (2C, CH); 128.8 (CH); 129.2(7) (CH_{maj}); 129.3(2) (CH_{min}); 130.8 (CH); 132.7 (C_{quat}); 134.6 (C_{quat}); 136.1(5) (C_{quat}); 139.5(5) (C_{quat}); 161.8 (CH_{imine}); 169.0 (C(2)). MS; *m*/*z*: 340 (40, M^+), 325 (1, M − Me), 283 (30, M − MeNCO), 206 (30, 283 − Ph), 193 (100, PhCH=N=CPh$^+$), 105 (77, PhCH=NH$^+$), 90 (23, PhCH$^{+\bullet}$), 77 (35, Ph).

3.20. 1-Methyl-3-ethylthio-3,4-diphenylazetidin-2-one

A solution of pentacarbonyl[(ethylthio)phenylcarbene]chromium (**29**) (0.203 g, 0.593 mmol) [57] in MeCN (15 ml) was freeze–pump–thaw cycled three times and then flushed with nitrogen in a sealed pressure vessel containing glass beads to facilitate light transmission. *N*-Methylbenzylideneimine (80 μl, 0.65 mmol) was added and the solution was photolysed using a Hanovia medium pressure lamp (125 W) for 17 h, keeping the solution temperature less than 20°C. The solvent was removed and the yellow–green oil was dissolved in ether and exposed to sunlight until it was colourless. Filtration followed by PLC (hexanes–ether, 1:1) gave a mixture (15:85) of *cis* (***rac*-30**) and *trans* (***rac*-31**) isomers of 1-methyl-3-ethylthio-3,4-diphenylazetidin-2-one (83.0 mg, 47%) as an oil which became a white solid. Crystallisation by evaporation of $CDCl_3$ from the NMR sample gave pure *trans*-1-methyl-3-thioethyl-3,4-diphenylazetidin-2-one (***rac*-31**) as colourless needles, m.p. 66–68°C. Found: 297.1192 [$M^{+\bullet}$]. Calc. for $C_{18}H_{19}NOS$: 297.1187. IR (ν_{max}, cm^{-1}): 1755 (C=O). ^{1}H-NMR: δ 0.94 (t, $J = 7.5$ Hz, $SCH_2CH_{3(cis)}$); 1.14 (t, $SCH_2CH_{3(trans)}$); 2.09 (dq, $J = 12.0$, 7.5 Hz, $SCH_2CH_{3(cis)}$); 2.40 (dq, $J = 12.1$, 7.5 Hz, $SCH_2CH_{3(trans)}$); 2.52 (dq, $J = 12.0$, 7.4 Hz, $SCH_2CH_{3(cis)}$); 2.80 (dq, $J = 12.1$, 7.5 Hz, $SCH_2CH_{3(trans)}$); 2.86 (s, NMe_{trans}); 2.89 (s, NMe_{cis}); 4.68 (s, $H(4)_{trans}$); 4.80 (s, $H(4)_{trans}$); 6.94 (dd, $J = 7.4$, 2.2 Hz, $H_{ortho(trans)}$); 7.03 (3 lines, $H_{meta(trans)}$, $H_{para(trans)}$); 7.13 (3 lines, $H_{meta(trans)}$, $H_{para(trans)}$); 7.20 (dd, $J = 7.4$, 2.2 Hz, $H_{ortho(trans)}$); 7.33 (t, $J = 7.4$ Hz, $H_{para(cis)}$); 7.40–7.50 (m, $H_{meta(cis)}$, $H_{meta(cis)}$, $H_{para(cis)}$, $H_{ortho(cis)}$); 7.67 (d, $J = 7.2$ Hz, $H_{ortho(cis)}$). ^{13}C-NMR: δ 14.1(5) ($SCH_2CH_{3(cis)}$); 14.2 ($SCH_2CH_{3(trans)}$); 23.6(5) ($SCH_2CH_{3(cis)}$); 24.2 ($SCH_2CH_{3(trans)}$); 26.9(5) (NMe_{cis}); 27.2 (NMe_{trans}); 68.2 (C(3)); 69.7 ($C(4)_{cis}$); 69.9 ($C(4)_{trans}$); 127.2(4) ($CH_{para(trans)}$); 127.2(8) (CH_{cis}); 127.6 ($CH_{ortho(trans)}$); 127.7 ($CH_{meta(trans)}$); 128.1 (CH_{cis}); 128.2 ($CH_{meta(trans)}$); 128.3 (CH_{para}); 128.5 (CH_{trans}); 128.6 (CH_{cis}); 128.9 (CH_{cis}); 133.5 ($C_{ipso(cis)}$); 134.0 ($C_{ipos(trans)}$); 134.7 ($C_{ipso(trans)}$); 139.1 ($C_{ipos(cis)}$); 168.8 ($C(2)_{trans}$); 168.9 ($C(2)_{cis}$). MS; *m*/*z*: 297 (8, M^+), 268 (15, M − Et)); 240 (14, M − MeNCO), 211 (23, 240 − Et), 178 (58, 240 − H − SEt), 121 (100, PhCS$^+$), 77, (18, Ph$^+$).

3.21. Methyl 1-methyl-3ζ-methoxy-4ζ-phenyl-3-(13′-(podocarpa-8′,11′,13′-trien-19′-oate))-azetidin-2-one (*32*)

A solution of methyl pentacarbonyl[(methoxy)(13-(podocarpa-8,11,13-triene))carbene] chromium (**18**) (36.9 mg, 0.0729 mmol) in MeCN (1 ml) in a sealed pressure vessel was freeze–pump–thaw cycled three times and then flushed with nitrogen. *N*-Methylbenzylideneimine (10 μl, 0.081 mmol) was added and the solution was photolysed for 24 h using a Hanovia medium pressure lamp (125 W), keeping the solution temperature below 20°C. The solvent was removed and the residual greenish oil was dissolved in hexanes–ether (1:1) and exposed to sunlight until it was colourless. Filtration followed by PLC gave methyl 1-methyl-3ζ-methoxy-4ζ-phenyl-3-(13′-(podocarpa-8′,11′,13′-trien-19′-oate))azetidin-2-one (**32**) (19.6 mg, 58%) as a colourless foam. Found: 461.2563 [$M^{+\bullet}$]. Calc. for $C_{29}H_{35}NO_4$: 461.2566. IR (ν_{max}, cm^{-1}): 1753 (s, $C{=}O_{lactam}$), 1723 ($C{=}O_{ester}$). ^{1}H-NMR: δ 1.05 (s, H(20′)); 1.09(9) (ddd, $J = 13.6$, 13.6, 4.1 Hz, H(3ax′)); 1.10(1) (ddd, $J = 13.6$, 13.6, 4.1 Hz, H(3ax′)); 1.28(7) (s, H(18′)); 1.28(9) (H(18′)); 1.40 (ddd, $J = 13.4$, 13.4, 4.4 Hz, H(1ax′)); 1.56 (bd, $J = 12.2$ Hz, H(5′)); 1.60–2.05 (m, H(2ax′), H(2eq′), H(6ax′)); 2.21 (bdd, $J = 13.7$, 6.1 Hz, H(6eq′)); 2.28 (b, H(1eq′), H(3eq′)); 2.80–2.98 (m, H(7ax′), H(7eq′)); 2.84(6) (NMe); 2.84(8) (NMe); 3.15(5) (s, OMe_{lactam}); 3.15(8) (s, OMe_{lactam}); 3.67 (s, 19′-OMe); 4.63 (s, H(4)); 7.22–7.45 (m, H(11′), H(12′), H(14′), Ph). ^{13}C-NMR: δ 19.9 (C(2′)); 20.9 (C(6′)); 23.0 (C(20′)); 26.3 (NMe); 28.5 (C(18′)); 32.1 (C(7′)); 37.6 (C(3′)); 38.5 (C(10′)); 39.3 (C(1′)); 44.0 (C(4′)); 51.2(0) (19′-OMe); 51.2(4) (19′-OMe); 52.6(8) (C(5′)); 52.7(1) (C(5′)); 54.2 (OMe_{lactam}); 70.5(0) (C(4)); 70.5(3) (C(4)); 92.4 (C(3)); 124.5 (C(12′)); 126.1 (C_{para}); 127.6 (C(11′)); 128.3 (C(14′)); 128.4 (C_{ortho}); 128.6 (C_{meta}); 133.4 (C(13′)); 134.0 (C(9′)); 135.8(0) (C_{ipso}); 135.8(5) (C_{ipso}); 148.6 (C(8′)); 168.3 (C(2)); 177.8 (C(19′). MS; *m*/*z*: 461 (9, M^+), 446 (2, M − Me), 404 (22, M − MeNCO), 342 (9, M − PhCH=NMe$^+$), 329 (7), 315 (14), 299 (100, ArC=C=O$^+$).

3.22. 1-Methyl-3ζ-methoxy-4ζ-phenyl-3-(13′-(19-norpodocarpa-4′(18′),8′,11′,13′-tetraene))-azetidin-2-one (33)

A solution of pentacarbonyl[(methoxy)(13-(19-norpodocarpa-4(18),8,11,13-tetraene)) carbene]chromium (**20**) (0.120 g, 0.269 mmol) in MeCN (5 ml) in a sealed pressure vessel was freeze–pump–thaw cycled three times and then flushed with nitrogen. *N*-Methylbenzylideneimine (37 μl, 0.30 mmol) was added and the solution was photolysed for 21 h using a Hanovia medium pressure lamp (125 W), keeping the solution temperature below 20°C. The solvent was removed and the greenish-yellow solid was dissolved in hexanes–ether (1:1) and exposed to sunlight until it was colourless. Filtration followed by PLC (hexanes–ether, 9:1) gave 1-methyl-3ζ-methoxy-4ζ-phenyl-3-(13′-(19′-norpodocarpa-4′(18′),8′,11′,13′-tetraene)azetidin-2-one (**33**) (92.8 mg, 86%) as a colourless foam. Found: 401.2355 [$M^{+\bullet}$]. Calc. for $C_{27}H_{31}NO_2$: 401.2355. IR (ν_{max}, cm^{-1}): 1753 (C=O). ^{1}H-NMR: δ 1.02 (s, H(20′)); 1.58 (ddd, $J = 12.8$, 12.8, 4.4 Hz, H(1ax′)); 1.68–1.90 (m, H(2ax′), H(2eq′), H(6ax′), H(6eq′)); 2.07 (ddd, $J = 12.6$, 12.6, 5.7 Hz, H(3ax′)); 2.23 (bd, $J = 12.0$ Hz, H(5′)); 2.30 (bd, $J = 12.5$ Hz, H(1eq′)); 2.39 (ddd, $J = 13.0$, 4.2, 1.7 Hz, H(3eq′)); 2.85 (s, NMe); 2.91–2.96 (m, H(7ax), H(7eq)); 3.16(9) (s, OMe); 3.17(2) (s, OMe); 4.62 (bs, H(18′)); 4.64(3) (s, H(4)); 4.63(5) (s, H(4)); 4.87 (d, $J = 1.2$ Hz, H(18′)); 7.25–7.47 (m, H(11′), H(12′), H(14′), Ph). ^{13}C-NMR: δ 22.2 (C(6′)); 22.7 (C(20′)); 23.6(5) (C(2′)); 26.3 (NMe); 30.0 (C(7′)); 36.3 (C(3′)); 38.3 (C(1′)); 39.4 (C(10′)); 47.7 (C(5′)); 54.2 (OMe); 70.5(2) (C(4)); 70.5(6) (C(4)); 92.4(5) (C(3)); 106.6 (C(18′)); 124.3(8) (C(12′)); 124.4(1) (C(12′)); 125.9 (C_{para}); 127.8 (C(11′)); 128.4 (C_{ortho}); 128.6 (C_{meta}); 133.5 (C(13′)); 134.0 (C(9′)); 135.6 (C_{ipso}); 147.8 (C(8′)); 150.3 (C(4′)); 168.3 (C(2)). MS; m/z: 401 (11, M^+), 386 (2, $M - Me^{\bullet}$)); 344 (27, M − MeNCO), 329 (2, 344 − $Me^{\bullet}$), 297 (8, M − PhCH=$N^{\bullet}$), 282 (13, M − PhCH=NMe), 239 (100, ArC=C=O^+).

3.23. 1-Methyl-3ζ-methoxy-4ζ-phenyl-3-(13′-(19′-methoxypodocarpa-8′,11′,13′-triene))-azetidin-2-one (34)

A solution of pentacarbonyl[(methoxy)(13-(19-methoxypodocarpa-8,11,13-triene))carbene]chromium (**21**) (0.1732 g, 0.352 mmol) in MeCN (5 ml) in a sealed pressure vessel was freeze–pump–thaw cycled three times and then flushed with nitrogen. *N*-Methylbenzylideneimine (46 μl, 0.37 mmol) was added and the solution was photolysed for 19 h using a Hanovia medium pressure lamp (125 W), keeping the solution temperature below 20°C. The solvent was removed and the greenish oil was dissolved in hexanes–ether and was exposed to sunlight until it was colourless. Filtration followed by PLC gave 1-methyl-3ζ-methoxy-4ζ-phenyl-3 - (13′ - (19′ - methoxypodocarpa - 8′,11′,13′ - triene))-azetidin-2-one (**34**) (0.1119 g, 71%) as a colourless foam. Found: 447.2772 [$M^{+\bullet}$]. Calc. for $C_{29}H_{37}NO_3$: 447.2773. IR (ν_{max}, cm^{-1}): 1756 (C=O). ^{1}H-NMR: δ 1.01 (ddd, $J = 13.4$, 13.4, 4.4 Hz, H(3ax′)); 1.05(0) (s, H(18′)); 1.05(2) (s, H(18′)); 1.21 (bs, H(20′)); 1.44 (ddd, $J = 12.8$, 12.8, 3.5 Hz, H(1ax′)); 1.45 (bd, $J = 12.4$ Hz, H(5′)); 1.61–1.79 (m, H(2ax′), H(2eq′), H(6ax′)); 1.89 (bd, $J = 13.4$ Hz, H(3eq′)); 2.01 (bdd, $J = 13.3$, 6.9 Hz, H(6eq′)); 2.33 (bd, $J = 12.8$ Hz, H(1eq′)); 2.84 (s, NMe); 2.80–3.01 (m, H(7ax′), H(7eq′)); 3.15 (s, OMe_{lactam}); 3.16 (OMe_{lactam}); 3.27 (d, $J = 9.1$ Hz, H(19′)); 3.34 (s, 19′-OMe); 3.54 (d, $J = 9.1$ Hz, H(19′)); 4.62 (s, H(4)); 4.63 (s, H(4)); 7.20–7.45 (m, H(11′), H(12′), H(14′), Ph). ^{13}C-NMR: δ 19.1 (C(2′)); 19.2 (C(6′)); 25.6 (C(20′)); 26.3 (NMe); 27.6 (C(18′)); 31.0 (C(7′)); 36.0 (C(3′)); 37.8 (C(10′)); 38.0 (C(4′)); 38.9 (C(1′)); 51.2(0) (C(5′)); 51.2(4) (C(5′)); 54.2 (OMe_{lactam}); 59.4 (19′-OMe); 70.5(0) (C(4)); 70.5(3) (C(4)); 92.5 (C(3)); 124.4 (C(12′)); 125.1 (C_{para}); 127.5(4) (C(11′)); 127.5(8) (C(11′)); 128.3(4) (C_{ortho}); 128.3(8) (C_{meta}); 128.6 (C(14′)); 133.3 (C(13′)); 134.0 (C(9′)); 135.5 (C_{ipso}); 150.5 (C(8′)); 168.3 (C(2)). MS; m/z: 447 (10, M^+), 432 (2, M − Me), 390 (21, M − MeNCO), 343 (3, M − PhCH=$N^{\bullet}$), 328 (11, M − PhCH=NMe), 285 (100, ArC=C=O^+).

3.24. 1-Methyl-3-ethylthio-4-phenyl-3-(13′-(19′-norpodocarpa-4′(18′),8′,11′,13′-tetraene))-azetidin-2-one (35)

A solution of pentacarbonyl[(ethylthio)(13-(19-norpodocarpa - 4(18),8,11,13 - tetraene))carbene]chromium (**23**) (26.6 mg, 0.0558 mmol) in MeCN (3 ml) in a sealed pressure vessel was freeze–pump–thaw cycled three times. *N*-Methylbenzylideneimine (8 μl, 0.06 mmol) was added and the solution was photolysed for 15 h using a Hanovia medium pressure lamp (125 W), keeping the solution temperature below 20°C. The solvent was removed and the residue was dissolved in hexanes–ether and exposed to sunlight until it was colourless. PLC hexanes–ether (1:1) gave 1-methyl-3-ethylthio-4-phenyl - 3 - (13′ - (19′ - norpodocarpa - 4′(18′),8′,11′,13′-tetraene))azetidin-2-one (**35**) (10.4 mg, 42%) as a colourless oil. Found: 431.2279 [$M^{+\bullet}$]. Calc. for $C_{28}H_{33}NOS$: 431.2283. IR (ν_{max}, cm^{-1}): 1759 (s (C=O). ^{1}H-NMR: δ 0.96 (t, $J = 7.5$ Hz, SCH_2CH_3(*cis*)); 1.01(8) (s, H(20′)); 1.02(2) (s, H(20′)); 1.19 (t, $J = 7.5$ Hz, SCH_2CH_3(*trans*)); 1.50–1.90 (m, H(1′ax), H(2′ax), H(2′eq), H(6′ax), H(6′eq)); 2.01 (ddd, $J = 13.0$, 13.0, 5.3 Hz, H(3′ax)); 2.10 (dd, $J = 11.9$, 1.5 Hz, H(5′)); 2.12 (dd, $J = 12.0$, 1.5 Hz, H(5′)); 2.20–2.30 (m, H(1′eq)); 2.30–2.40 (m, H(3′eq)); 2.44 (dq, $J = 12.0$, 7.5 Hz, SCH_2CH_3); 2.45 (dq, $J = 12.0$, 7.5 Hz, SCH_2CH_3); 2.55 (dq, $J = 12.0$, 7.5 Hz, SCH_2CH_3); 2.69 (ddd, $J = 17.2$, 11.3, 7.1 Hz, H(7′ax)); 2.83 (bdd, $J = 17.2$, 4.8, Hz, H(7′eq)); 2.85 (s, NMe); 2.87 (s, NMe); 2.88 (s, NMe);

2.89 (s, NMe); 4.53(4) (d, $J = 1.7$ Hz, H(18′)); 4.54 (d, $J = 1.5$ Hz, H(18′)); 4.62 (bs, C(4)); 4.64 (d, $J = 1.7$ Hz, H(18′)); 4.79 (s, H(4)); 4.82 (d, $J = 1.3$ Hz, H(18′)); 4.87 (d, $J = 1.4$ Hz, H(18′)); 6.77 (s, H(14′)); 6.82 (s, H(14′)); 6.83 (s, H(14′)); 6.89 (dd, $J = 7.0$, 1.7 Hz, H_{ortho}); 6.91 (dd, $J = 8.4$, 1.0 Hz, H_{ortho}); 7.07–7.12 (m, H(12′), H_{meta}); 7.13–7.17 (m, H(12′), H_{meta}); 7.36 (t, $J = 8.3$ Hz, H_{para}); 7.37 (t, $J = 8.3$ Hz, H_{para}); 7.40 (d, $J = 8.4$ Hz, H(11′)); 7.46 (d, $J = 8.4$ Hz, H(11′). ^{13}C-NMR: δ 14.1(5) (SCH_2CH_3); 14.3 (SCH_2CH_3); 20.9 (C(6′)); 21.1 (C(6′)); 22.6(6) (C(20′)); 22.7(6) (C(20′)); 23.5(5) (C(2′)); 23.6 (C(2′)); 23.6(5) (SCH_2CH_3); 23.8 (SCH_2CH_3); 24.3 (SCH_2CH_3); 26.9 (NMe_{cis}); 27.0 (NMe_{cis}); 27.2 (NMe_{trans}); 29.5 (C(7′)); 29.7 (C(7′)); 30.0 (C(7′)); 36.2 (C(3′)); 36.3 (C(3′)); 38.0 (C(1′)); 38.1 (C(1′)); 38.2 (C(1′)); 39.1 (C(10′)); 39.2 (C(10′)); 39.4 (C(10′)); 40.4 (C(10′)); 47.4 (C(5′)); 47.6 (C(5′)); 47.7 (C(5′)); 63.9 ($C(3)_{trans}$); 68.1 ($C(3)_{cis}$); 69.7 ($C(4)_{cis}$); 70.0 ($C(4)_{trans}$); 106.4 (C(18′)); 106.6 (C(18′)); 124.7 (C(12′)); 124.7(5) (C(12′)); 125.6 (C_{para}); 125.7 (C_{para}); 125.7(5) (C_{para}); 125.8(5) (C_{para}); 127.6(6) (C(11′)); 127.7 (C(11′)); 127.7(9) (C(11′)); 127.9(5) (C(11′)); 128.1 (C(14′)); 128.1(8) (C(14′)); 128.2(4) (C(14′)); 128.3 (C(14′)); 128.6 (C_{ortho}); 128.9 (C_{ortho}); 129.1 (C_{ortho}); 129.2 (C_{ortho}); 129.4 (131.2 (C_{meta}); 131.3 (C_{meta}); 133.6 (C(13′)); 133.6(5) (C(13′)); 133.8 (C(13′)); 134.3 (C(9′)); 134.4 (C(9′)); 135.4 (C_{ipso}); 135.5 (C_{ipso}); 135.8 (C_{ipso}); 135.8(5) (C_{ipso}); 146.4 (C(8′)); 146.9 (C(8′)); 147.8 (C(8′)); 150.1 (C(4′)); 150.3 (C(4′)); 150.5 (C(4′)); 168.9(5) ($C{=}O_{trans}$); 169.2 ($C{=}O_{cis}$). MS; m/z: 431 (5, M^+), 402 (15, $M - Et^{\bullet}$), 374 (10, M − MeN=C=O), 312 (71, 374 − $HSCH_2CH_3$), 255 (100, $ArC{\equiv}S^+$).

3.25. 3-(Benzylideneimine)-1-methyl-4-phenyl-3-(13′-(19′-methoxypodocarpa-8′,11′,13′-triene-))-azetidin-2-one (36)

A solution of pentacarbonyl[(dihydroamino)(13-(19-methoxypodocarpa-8,11,13-triene))-carbene]chromium (**22**) (45.9 mg, 0.0961 mmol) in MeCN (4 ml) in a sealed pressure vessel was freeze–pump–thaw cycled three times and then flushed with nitrogen. *N*-Methylbenzylideneimine (24 μl, 0.20 mmol) was added and the solution was photolysed for 15.5 h, keeping the solution temperature below 20°C. The solvent was removed and the residue was dissolved in hexanes–ether (1:1) and the solution was exposed to sunlight until it was colourless. PLC (hexanes–ether, 1:1) gave 3-(benzylideneimine)-1-methyl-4-phenyl-3-(13′-(19′-methoxypodocarpa-8′,11′,13′-triene))azetidin-2-one (**36**) (2.7 mg, 5%) as a colourless oil. Found: 520.3071 [$M^{+\bullet}$]. Calc. for $C_{35}H_{40}N_2O_2$: 520.3090. IR (ν_{max}, cm^{-1}): 1752 (s, C=O). ^{1}H-NMR: δ 1.00 (ddd, $J = 13.0$, 13.0, 5.4 Hz, H,3′ax)); 1.03 (s, H(18′)); 1.04 (s, H(18′)); 1.17 (s, H(18′)); 1.19 (s, H(18′)); 1.25 (s, H(20′)); 1.28 (s, H(20′)); 1.30–1.40 (m, H(1′ax)); 1.43 (bd, $J = 12.6$ Hz, H(5′)); 1.50–1.75 (m, H(2′ax), H(2′eq), H(6′ax)); 1.87 (bd, $J = 13.1$ Hz, H(3′eq)); 2.00 (m, H(6′eq)); 2.30–2.40 (m, H(1′eq)); 2.70–2.95 (m, H(7′ax), H(7′eq)); 2.89(5) (s, NMe); 2.91 (s, NMe); 3.24 (d, $J = 8.9$ Hz, H(19′)); 3.26 (d, $J = 9.1$ Hz, H(19′)); 3.32 (s, 19′-OMe); 3.33 (s, 19′-OMe); 3.34 (s, 19′-OMe); 3.50–3.55 (m, H(19′)); 4.79 (s, H(4)); 4.97 (s, H(4)); 4.99 (s, H(4)); 7.15–7.42 (m, Ph, H(12′), H(14′)); 7.48 (d, $J = 7.6$ Hz, H(11′)); 7.51 (d, $J = 7.6$ Hz, H(11′)); 8.46 (s, H_{imine}); 8.48 (s, H_{imine}); 8.53 (s, H_{imine}); 8.54 (s, H_{imine}). ^{13}C-NMR: δ 19.1 (C(2′)); 19.2 (C(6′)); 24.7 (C(20′)); 25.6 (NMe); 26.2 (NMe); 27.6 (C(18′)); 31.1 (C(7′)); 36.0 (C(3′)); 37.7 (C(10′)); 38.0 (C(4′)); 38.9 (C(1′)); 51.3 (C(5′)); 59.4 (19-OMe); 71.5 (C(4)); 75.9 (C(19′)); 123.5, 125.2, 126.5, 127.0, 128.2(5) (>1C); 128.3, 128.6, 129.2 ($C_{aromatic}$); 161.0 (C_{imine}); C=O, C(8′), C(9′), C(13′), C_{ipso}; C(3) not observed. MS; m/z: 520 (58, $M^{+\bullet}$), 463 (24, M − MeN=C=O), 373 (100, $ArC{=}N{=}CHPh^+$).

4. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC nos. 157422 and 157423 for ***rac*-25** and ***rac*-31**, respectively. Copies of this information may be obtained free of charge from The Director, CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (Fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk or www: http://www.ccdc.cam.ac.uk).

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