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Journal of Organometallic Chemistry 628 (2001) 155–168

Journal of Organometallic Chemistry

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Insertion reactions of alkenes with diterpenoid chromium aminocarbenes

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Received 22 January 2001; accepted 5 March 2001

Abstract

Insertion reactions of electron-deficient alkenes with chromium aminocarbenes derived from podocarpic acid generally give aryl ketone products derived from ring opening of an aminocyclopropane and subsequent enamine hydrolysis, the exception being alkenyl sulphones which give products derived from insertion of the carbene into the β-CH bond of the alkene. Increasing steric hindrance due to the substituents on the aminocarbene nitrogen appears to result in higher yields of the insertion products. However, other factors such as stabilisation of the intermediate tetracarbonylaminocarbene may explain why morpholinocarbenes give superior yields of the insertion products. Propenoic acid, propenal or nitropropene give a 13-formyl-substituted diterpenoid. Electron-rich alkenes do not undergo insertion reactions with these aminocarbenes at 110°C.

Keywords: Chromium; Aminocarbene; Diterpenoid; Alkene; Aryl ketone

1. Introduction

The synthesis of cyclopropane derivatives by insertion of electron deficient alkenes [1–10] and dienes [11,12] into alkoxycarbenes has been widely studied. In contrast, literature reports of insertion of an alkene into a chromium aminocarbene are rare. Reissig reported that a phenyl dialkylaminocarbene reacted with propenenitrile at 140°C to give impure 4-oxo-4-phenylbutanenitrile in 28% yield [4]. Barluenga obtained good yields of vinyl cyclopropylketones by heating vinyl(dialkylamino)carbenes with electron deficient alkenes [13]. In the case of a molybdenum aminocarbene, subsequent Cope rearrangement of the vinyl cyclopropylketone product gave a hydroazulene derivative. Heating pentacarbonyl[(*N*,*N*-dimethylamino)methylene]chromium with either methyl propenoate or propenenitrile gave a 1,2,4-trisubstituted cyclopentane resulting from a formal [2 + 2 + 1] cycloaddition reaction [14], while dimethyl fumarate or diethyl maleate gave enamine products resulting from formal CH insertion. In contrast, an alkyl(dialkylamino)carbene gave only insertion/hydrolysis products [14] analogous to the example described by Reissig [4]. Hegedus [15] has shown that pyrrolocarbene complexes exhibit reactivity similar to that of alkoxycarbene complexes, thermolysis with an electron deficient alkene giving pyrrolocyclopropanes as well as the enamine products derived from cyclopropane ring opening. Reaction of chromium aminocarbenes with electron-deficient alkenes can also be promoted at room temperature, in the presence of palladium chloride, leading to cyclopropanation and then ring opening; the reactive species is presumed to be a palladium aminocarbene formed by transmetallation [16].

Insertion of a variety of alkenes into a diterpenoid chromium aminocarbene would allow the construction of various substituted ketonic side chains having an electron withdrawing group on the β-carbon, further modification of which could allow the synthesis of potentially valuable ring-C aromatic steroidal compounds [17–22]. We sought to optimise the yields of the insertion/hydrolysis products, either by variation of the amino substituent on the carbene or by changing the reaction solvent. Furthermore, given the wide variety of electron deficient alkenes which have been used in the

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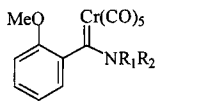
0022-328X/01/$ - see front matter
PII: S0022-328X(01)00803-8

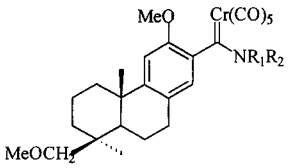
cyclopropanation reaction with alkoxycarbenes, the scope of the reaction with aminocarbenes warranted investigation.

2. Results and discussion

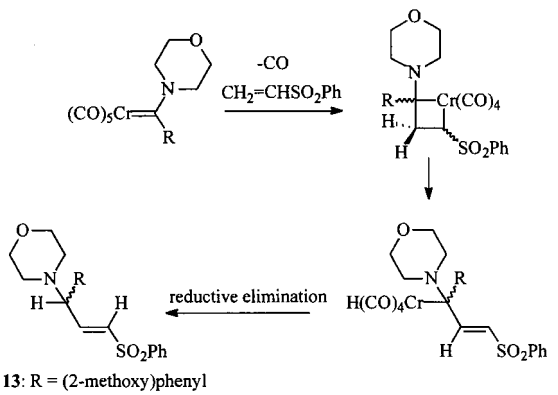
Initial studies focussed on the reactivity of the (2-methoxyphenyl)aminocarbenes **1**–**6** as model systems, in order to define the parameters for optimisation of the cyclopropanation reaction of 13-methoxy diterpenoid chromium aminocarbene complexes **7**–**12** [23] with electron deficient alkenes.



1: $R_1 = R_2 = H$
2: $R_1 = H$, $R_2 = Me$
3: $R_1 = R_2 = Me$
4: $R_1, R_2 = (CH_2)_2$
5: $R_1, R_2 = (CH_2)_4$
6: $R_1, R_2 = (CH_2)_2O(CH_2)_2$



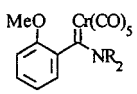
7: $R_1 = R_2 = H$
8: $R_1 = H$, $R_2 = Me$
9: $R_1 = R_2 = Me$
10: $R_1, R_2 = (CH_2)_2$
11: $R_1, R_2 = (CH_2)_4$
12: $R_1, R_2 = (CH_2)_2O(CH_2)_2$

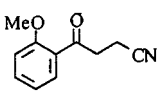


13: R = (2-methoxy)phenyl

Scheme 1.

Table 1
Reaction of an aminocarbene with propenenitrile



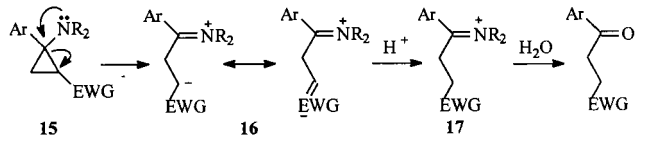


R_2	Yield (%) (**14**)
H_2 (**1**)	0
H,Me (**2**)	16
Me_2 (**3**)	36
$(CH_2)_2$ (**4**)	11
$(CH_2)_4$ (**5**)	20
$(CH_2)_2O(CH_2)_2$ (**6**)	64

Phenyl vinyl sulphone was selected as the electron poor alkene, since its reaction with the alkoxy carbene pentacarbonyl[(methoxy)phenylcarbene]chromium is known to afford cyclopropane and enol ether products [4], and compounds arising from CH insertion were not observed. Thus, pentacarbonyl[(morpholino)(2-methoxyphenyl)carbene]chromium (**6**) was heated with phenyl vinyl sulphone (1.1 molar equivalents) in refluxing toluene (b.p. 111°C) for 22.5 h; (*E*)-2-methoxy-1-(morpholino-3′-phenylsulphonylprop-2-enyl)benzene (**13**) was the only product isolated, albeit in low yield (10%). Signals in the ^{1}H-NMR spectrum of **13** at 4.50 (d, $J = 7.6$ Hz), 6.57 (dd, J=15.2, 1 Hz) and 6.95 ppm (J=15.2, 7.6 Hz) confirmed the presence of an (*E*)-1,3-disubstituted prop-2-enyl side chain. The β-CH insertion reaction is postulated to proceed via *syn* elimination of a β-hydrogen from an intermediate chromacyclobutane, followed by the reductive elimination of $Cr(CO)_4$ [24] (Scheme 1). Only the *E* stereoisomer of the alkene **13** [R=(2-methoxy)phenyl] was isolated, indicating that the sterically demanding sulphone group rotates away from the $Cr(CO)_4$ moiety in the transition state for the *syn* elimination.

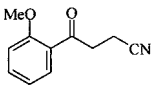
A reaction temperature higher than 110°C is usually required to induce decarbonylation of aminocarbene complexes [25], although those which undergo insertion of an alkene or alkyne intramolecularly can lose CO at a lower temperature (~ 85°C) [26]. Chemical activation can offer a milder alternative to thermally induced decarbonylation. For example, trimethylamine *N*-oxide has been used to decarbonylate organoiron [27,28], organomanganese [29] and organocobalt [30] complexes. A reasonable correlation has been observed between the reactivity of an amine *N*-oxide with a metal carbonyl [31] and the stretching force constants [32]; it has been proposed empirically that the stretching frequency of a CO ligand in the infrared should be higher than 2000 cm^{-1} in order for such decarbonylation to occur [31,33]. Since the morpholinocarbene complex **6** shows an absorption at 2055 cm^{-1}, on this basis it should be amenable to chemically-induced decarbonylation. However, refluxing **6** with Me_3NO (1.6 molar equivalents) and phenyl vinyl sulphone in dichloromethane did not lead to the formation of insertion products, and carbene starting material was returned (30%). Moreover, repeating the thermolysis reaction of phenyl vinyl sulphone with either the methylaminocarbene **2** or the dimethylaminocarbene **3** in refluxing toluene failed to give any insertion products.

Propenenitrile was therefore chosen for subsequent insertion reactions. Heating each of the aminocarbenes **1**–**6** with this electron deficient alkene in refluxing toluene gave 4-(2-methoxyphenyl)-4-oxobutanenitrile (**14**). The highest yield (64%) (Table 1) arose from the morpholinocarbene **6**. Triplets at 2.72 (J=7.6 Hz) and



Scheme 2.

3.40 ppm (J=7.6 Hz) in the ^{1}H-NMR spectrum were assigned to the methylene hydrogens adjacent to the nitrile and carbonyl groups, respectively. The carbonyl carbon was observed at 196.7 ppm in the ^{13}C-NMR spectrum while the nitrile carbon was evident at 119.7 ppm. Thermolysis of **6** with propenenitrile in refluxing *p*-xylene (b.p. 138°C) gave **14** in lower yield (35%).



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Cyclopropylamines bearing an electron withdrawing group on the adjacent carbon undergo facile ring opening due to stabilisation of the developing negative charge. The presence of a sulphide (rather than a sulphone) inhibits ring opening, and fission of the cyclopropylamine is dependent on the presence of the lone pair of electrons on nitrogen, cationic aminocyclopropanes failing to undergo cleavage [34]. The formation of an aryl ketone (e.g. **14**) from an (aryl)aminocarbene involves initial formation and then ring opening (Scheme 2) of a 1-aryl-1-aminocyclopropane **15** to give a zwitterionic intermediate **16**, the negative charge being stabilised by the electron withdrawing group from the alkene. Protonation of the carbanion gives the iminium cation **17** which hydrolyses on workup [4,13,34,35]. Overall, therefore, a chromium aminocarbene can act as an acyl synthon.

An intriguing result from the present work was that thermolysis of the morpholinocarbene **6** with phenyl vinyl sulphone gave the β-CH insertion product **13**, while propenenitrile gave the product **14** derived from the initial formation of an aminocyclopropane. Solvent effects are known to affect the product distribution, the formation of β-CH insertion products being more favourable in either cyclohexane or 1,2-dichloroethane than in polar solvents such as acetonitrile [24]. However, since both reactions in the present work were carried out in toluene the difference in product structure should not reflect a solvent bias. The reason for the selection between the cyclopropanation pathway or the CH-insertion pathway remains unknown, although it appears that CH-insertion is favoured when either more sterically hindered alkenes [24] or alkenes bearing one highly electron withdrawing group or two electron withdrawing groups are used.

The thermolysis reactions of propenenitrile with some of the (2-methoxyphenyl)aminocarbenes **1**–**6** had afforded the aryl ketone **14** in sufficiently good yield to warrant studies using the analogous 13-methoxy diterpenoid complexes. The parent podocarpane-derived (dihydroamino)carbene **7** did not give any insertion products in toluene as solvent. However, the alkylaminocarbenes **8**–**12** reacted with propenenitrile in refluxing toluene to give 12,19-dimethoxy-13-(4-oxobutanenitrile)podocarpa-8,11,13-triene (**18**) and either 13-cyano-12,19-dimethoxypodocarpa-8,11,13-triene (**19**) or 12,19-dimethoxypodocarpa-8,11,13-trien-13-oic acid (**20**) (Table 2).

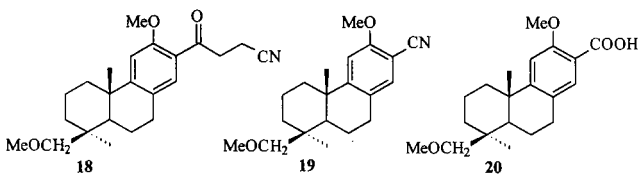
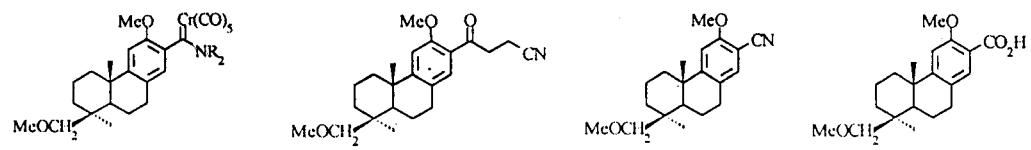


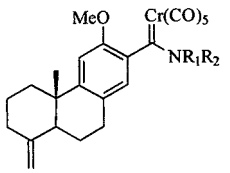
Table 2
Products from reaction of propenenitrile with diterpenoid aminocarbenes **7**–**12**



R_2	Yield (%) **18**	Yield (%) **19**	Yield (%) **20**
H_2 (**7**)	–	–	–
H,Me (**8**)	5	8	–
Me_2 (**9**)	31	–	–
$(CH_2)_2$ (**10**)	5	20	–
$(CH_2)_4$ (**11**)	35	7	–
$(CH_2)_2O(CH_2)_2$ (**12**)	57	–	2

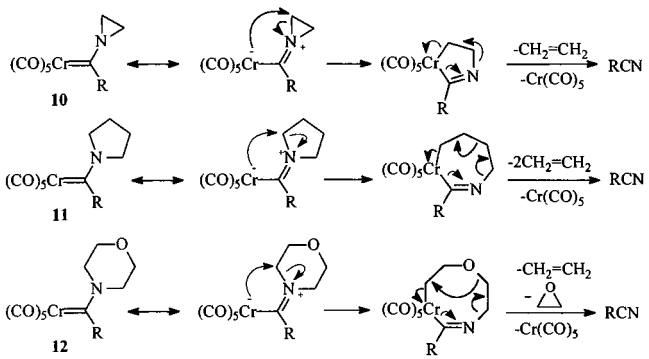
The infrared spectrum of **18** showed strong absorption due to a nitrile group at 2225 cm^{-1} and an intense peak characteristic of an aryl ketone at 1673 cm^{-1}. In the ^{1}H-NMR spectrum a triplet at 2.68 (CH_2CN; J=7.4 Hz) and triplets at 3.34 and 3.35 ppm ($ArCOCH_2$; J=7.5 Hz) were indicative of the side chain methylene protons. Signals at 119.8 and 196.2 ppm in the ^{13}C-NMR spectrum were assigned to the nitrile and carbonyl carbons, respectively. Similarly, benzonitrile **19** showed peaks at 2225 cm^{-1} in the infrared spectrum and at 99.0 ppm in the ^{13}C-NMR spectrum.

A study of the yields (Tables 1 and 2) from the reactions of propenenitrile with the (2-methoxyphenyl) and diterpenoid aminocarbenes reveals similarities. The order for the monocyclic complexes in terms of the yield of insertion products is morpholino > NMe_2 > pyrrolidinyl > NHMe > aziridinyl > NH_2, while the order for the diterpenoid analogues is morpholino > pyrrolidinyl > NMe_2 > aziridinyl > NHMe > NH_2. The yields of products derived from insertion of an alkyne into some related aminocarbenes decrease in the order morpholino > > pyrrolidinyl > NMe_2, although this pattern has not been explained [25,36]. It is possible that the different electronic properties of each amino group could influence the reactivity of the chromium carbene. Although the X-ray crystal structures [23] of the 19-methoxy morpholinocarbene **12** and the $\Delta^{4(18)}$ (dihydroamino)carbene (**21**) show bond lengths for $C_{carbene}$–Cr and $C_{carbene}$–N that the same are



21: $R_1 = R_2 = H$
35: $R_1 = R_2 = (CH_2)_2O(CH_2)_2$

within the experimental error, **12** gave the highest yields of alkene insertion products while the 19-methoxy (dihydroamino)carbene **7** gave zero yields. Therefore, electronic effects are probably not important, although the species active in the insertion step is a tetracarbonyl



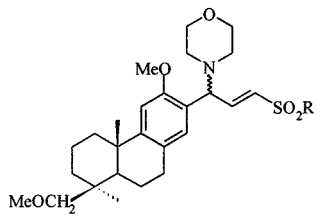
Scheme 3.

derivative and not the pentacarbonylcarbene parent. At this stage, therefore, correlation between the yields of alkene insertion product and the electronic effects of the amino substituent(s) remains uncertain. As an empirical guide, good yields of the alkene insertion products were obtained when the solution remained clear orange throughout the reaction, while poor yields were obtained when the solution changed to a cloudy orange–brown colour, uncontrollable metal loss followed by polymerisation of the alkene appearing to have occurred. This led to the suggestion that steric shielding of the chromium by the nitrogen substituent(s) inhibits decomposition; indeed, the increasing yield of alkene insertion products derived from the diterpenoid aminocarbenes parallels the increasing steric bulk of the amino group. In this regard, increasing the size of the substituent(s) on a (phenyl)aminocarbene nitrogen atom results in steric inhibition of the orbital co-linearity required for efficient (and stabilising) π-overlap between nitrogen and the carbene carbon, as shown by a downfield shift of the ^{53}Cr-NMR signal [37].

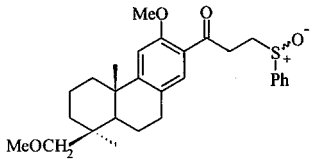
The 13-nitrile **19** was isolated from reactions of the diterpenoid chromium aminocarbenes **8**, **10** and **11** with propenenitrile, while **12** gave the hydrolysis product, 13-carboxylic acid **20**. It was thought initially that the 13-cyano group may be derived from propenenitrile. However, any reaction mechanism postulated to account for such a route would require cleavage of the bond between C(13) and the carbene carbon. Since thermolysis of the aziridinyl aminocarbene **10** in the absence of propenenitrile also gave the 13-cyano derivative **19** (50%), the nitrile group includes the aminocarbene nitrogen and the carbene carbon. The formation of a nitrile derivative from an aziridinyl aminocarbene has been observed previously in Refs. [38,39], and is believed to proceed via electrocyclic ring expansion to give a chromacycle, which can undergo further rearrangement to expel ethylene (and oxirane in the case of **12**) and give a metal-coordinated nitrile (Scheme 3). In contrast, formation of the nitrile from the methylaminocarbene is probably initiated by demethylation.

The scope of the insertion reaction was investigated using some other electron deficient alkenes. Thus, thermolysis of the morpholino carbene **12** with phenyl vinyl sulphone in refluxing toluene gave (*E*)-12,19-dimethoxy-13-(1-morpholino-3-phenylsulphonylprop-2-enyl)podocarpa-8,11,13-triene (**22**) (49%; cf. only 10% of **13** from the benzenoid carbene **6**), and methyl vinyl sulphone gave (*E*)-12,19-dimethoxy-13-(1-morpholino-3-methylsulphonylprop-2-enyl)podocarpa-8,11,13-triene (**23**) (46%), each as a mixture (1:1) of epimers.

The diterpenoid vinyl sulphones **22** and **23** are derived from insertion of the morpholinocarbene **12** into the β-CH bond of the alkene. Since alkenyl sulphoxides are less electron deficient than the corresponding sulphones, phenyl vinyl sulphoxide was used



22: R = Ph
23: R = Me



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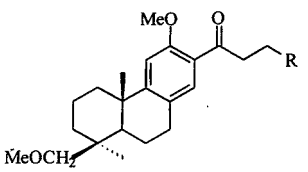
to determine if an analogous product would form. Thermolysis of **12** with phenyl vinyl sulphoxide gave 12,19-dimethoxy-13-(phenyl-4-oxopropanesulphoxide)-podocarpa-8,11,13-triene (**24**) (14%). A weak molecular ion (1%) in the mass spectrum confirmed the molecular formula of **24** ($M^{+\bullet}$ 468.2320, $C_{28}H_{36}O_4S$), expulsion of an oxygen atom giving the fragment at m/z 452 (30%). The ketone carbonyl was indicated by a strong absorption at 1668 cm^{-1} in the infrared spectrum and by a signal at 199.7 ppm in the ^{13}C-NMR spectrum, in which resonances at 28.3 and 43.4 ppm were assigned to the methylene groups adjacent to the carbonyl group and the sulphoxide, respectively. The low yield of **24** may be attributed to oxidation of the aminocarbene by the sulphoxide [4]. No products due to β-CH insertion were isolated, only phenyl vinyl sulphoxide and starting aminocarbene (4%) being also recovered. The results of the reactions of the diterpenoid aminocarbene **12** with either phenyl vinyl sulphoxide or phenyl vinyl sulphone indicate that increased electron deficiency in the alkene favours products arising from the β-CH insertion.

Thermolysis of **12** with but-3-en-2-one in refluxing toluene for 3 h gave 12,19-dimethoxy-13-(1,4-dioxopentyl)podocarpa-8,11,13-triene (**25**) in good yield (81%). The infrared spectrum of **25** showed the peaks at 1717 and 1668 cm^{-1} due to a dialkyl- and arylalkyl-ketone, respectively, and the ^{13}C-NMR spectrum confirmed the presence of two carbonyl groups, at 199.9 (aryl ketone) and 207.9(5) ppm (alkyl ketone).

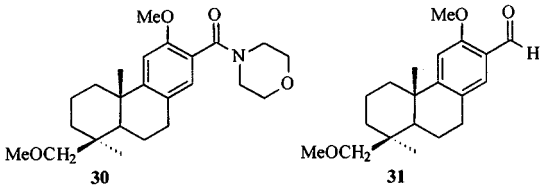


25: R = COMe
26: R = COOMe
27: R = COOtBu
28: R = COSPh
29: R = $CONH_2$
32: R = NO_2
33: R = COOH
34: R = CHO

α,β-Unsaturated esters have been used widely as the electron deficient alkene component [13,14]. Thermolysis of the morpholinocarbene **12** with methyl propenoate in toluene for 4.5 h gave 12,19-dimethoxy-13-(methyl 4-oxobutanoate)podocarpa-8,11,13-triene (**26**) in high yield (93%). The ester carbonyl was evident in the ^{13}C-NMR spectrum at 173.8, and the ketone carbonyl at 199.4 ppm. The ^{1}H-NMR spectrum showed characteristic side-chain triplets at 2.69 (J=6.6 Hz, CH_2CO_2Me) and 3.30 ppm (J=6.6 Hz, CH_2COAr), while a singlet at 3.69 ppm was assigned to the ester methyl group. Similarly, 12,19-dimethoxy-13-(*tert*-butyl 4-oxobutanoate)podocarpa-8,11,13-triene (**27**) was synthesised (49%) by thermolysis of **12** with *tert*-butyl propenoate. Characteristic ester and ketone carbonyl absorptions were observed at 1737 and 1671 cm^{-1} in the infrared spectrum. Signals in the ^{13}C-NMR spectrum at 29.8 [$(CH_3)_3C$] and 80.2 ppm [$(CH_3)_3C$] confirmed the incorporation of the *tert*-butyl group. In the mass spectrum, loss of a *tert*-butoxy radical from the molecular ion ($M^{+\bullet}$ 444.2875, $C_{27}H_{40}O_5$) gave rise to a relatively weak fragment ion at m/z 371.

Since α,β-unsaturated esters had given good yields of diterpenoid 13-(4-oxobutanoate) derivatives, α,β-unsaturated thioesters would be expected to give the analogous oxobutanethioate products. Thermolysis of phenyl propenethioate [40] with the morpholinocarbene **12** in refluxing toluene for 1 h gave 12,19-dimethoxy-13-(phenyl 4-oxobutanethioate)podocarpa-8,11,13-triene (**28**) (83%). In contrast to the carboxylic ester derivatives **26** and **27** for which the base peak in the mass spectrum corresponded to $ArCO^+$, the base peak (m/z 371) for the phenylthio ester **28** arose from loss of the phenylsulphide radical from the molecular ion ($M^{+\bullet}$ 480.2307, $C_{29}H_{36}O_4S$).

N,*N*-(Dialkyl)propenamides are known to react with (phenyl)methoxycarbene to give a cyclopropylcarboxamide in good yield, together with small amounts of acyclic enol ether and β-CH insertion products [4]. The reaction of propenamides with aminocarbenes, however, has not been reported. Thermolysis of **12** with propenamide (2.3 molar equivalents) in toluene for 3 h gave 12,19-dimethoxy-13-(4-oxobutanamide)podocarpa-8,11,13-triene (**29**) (11%). High resolution mass spectroscopy of **29** indicated the molecular ion at m/z 387.2405 ($C_{23}H_{33}NO_4$), the base peak at m/z 315 corresponding to $ArCO^+$. Although the signal due to the methylene group adjacent to the primary amide carbonyl was obscured in the ^{1}H-NMR spectrum, a triplet at 3.34 ppm (J=6.5 Hz) was assigned to the methylene group adjacent to the aryl ketone. In addition, broad signals at 5.39 and 5.88 ppm were assigned to $NH_{(Z)}$ and $NH_{(E)}$, respectively. The presence of an amide was confirmed by a carbonyl signal at 175.1 in the ^{13}C-NMR spectrum, in which the signal for the ketone carbonyl occurred at 200.3 ppm. The low yield of **29** was attributed to competitive polymerisation of propenamide. In an attempt to improve the yield, the reaction was repeated using 4.7 molar equivalents of the primary amide, and the reaction time was extended to 15.5 h. However, only *N*-morpholino-12,19-dimethoxypodocarpa-8,11,13-triene-13-carboxamide (**30**) and traces of propenamide were recovered.



Reaction of a diterpenoid aminocarbene with propenoyl chloride might give a 13-(4-oxobutanoyl chloride), which would lead to a D-homoandrostane derivative via intramolecular Friedel–Crafts acylation. Perhaps not unexpectedly, however, treatment of **12** with propenoyl chloride (2 molar equivalents) in refluxing toluene for 30 min gave only intractable material. Surprisingly, thermolysis of **12** with propenoic acid gave only 13-formyl-12,19-dimethoxypodocarpa-8,11,13-triene (**31**) (73%) [29]. The mass spectrum of **31** included the molecular ion at m/z 316.2033 ($C_{20}H_{28}O_3$), and a singlet at 10.37 ppm in the ^{1}H-NMR spectrum together with a methine carbon signal at 189.7 ppm in the ^{13}C-NMR spectrum confirmed the presence of an aldehyde. The 13-formyl diterpenoid **31** (15%) was the only product isolated from reaction between **12** and propenal. Thermolysis of **12** with nitroethene in refluxing toluene for 40 min also gave **31** (19%), together with carboxamide **30** (36%) and starting carbene (18%). Low yield of the **31** is attributed to rapid polymerisation of nitroethene, probably in a radical chain process with a chromium species being the initiator. The carboxamide **30** is believed to arise via oxidation of the morpholinocarbene by the nitro group in nitroethene [4].

We speculated that the 13-formyl diterpenoid **31** could arise via abstraction of a hydrogen atom from solvent toluene by a 13-acyl radical. This radical could be generated by loss of a nitro radical from **32**, followed by expulsion of ethene. Related routes are available by abstraction of a hydrogen atom from the β-keto acid **33** or the β-keto aldehyde **34**, followed by loss of either CO_2 or CO, respectively, and then of ethene. Although such pathways appear reasonable, experimental evidence does not support them. Thus, refluxing the carboxylic acid **33** (from saponification of the *tert*-butyl ester **27**) with $Cr(CO)_6$ in toluene returned starting material, and repeating this reaction also in the presence of morpholine and propenoic acid similarly failed to give **31**. Hence, the carboxylic acid **33** is apparently not an intermediate in the formation of the 13-formyl compound **31**. Thermolysis of the morpholinocarbene **12** with propenoic acid in toluene-d_8 gave aldehyde **31** (55%), but incorporation of deuterium was not detected by mass spectroscopy, the (M + 1) peak at m/z 317 being due only to the carbon-13 isotopomer of the molecular ion. Therefore, toluene was not involved in formation of the aldehyde. Furthermore, small amounts of **31** were also isolated from reaction between the $\Delta^{4(18)}$ morpholinocarbene **35** and an alkyne (ethyl 4,4-dimethylpentynoate) in dmf at 125°C [41]. In all of the experiments which gave **31**, decomposition of the carbene **12** was rapid ($\sim$10 min) relative to reactions which gave 'cyclopropanation' products, implying that the 13-formyl compound may be derived from the reduction of the morpholinocarboxamide **30,** possibly by a chromium hydride species [42].

Fischer carbenes undergo facile cyclopropanation with electron-rich alkenes [43]. Since all of the alkenes which had been studied in the present work are electron deficient, the potential use of electron rich alkenes was investigated briefly. Thermolysis of the morpholinocarbene with phenylethene in refluxing toluene returned only **12** (48%), the low recovery being attributed to uncontrollable loss of the $Cr(CO)_5$ moiety associated with polymerisation of the alkene. Thermolysis of the morpholinocarbene with either trimethylsilylethene or triethoxysilylethene in refluxing toluene also returned only **12** (81 and 85%, respectively). The failure of these alkenes to undergo an insertion reaction with **12** was not surprising, since treatment of [(dimethylamino)methylcarbene]chromium with phenylethene returned carbene starting material [14], and thermolysis of an alkoxycarbene with phenylethene also failed to give cyclopropane derivatives [4], only phenylethene-derived polymers being formed. Insertion of electron-rich alkenes into heteroatom-stabilised carbenes generally requires forcing conditions and the product distribution is strongly dependent on carbon monoxide concentration [44]. High carbon monoxide pressure favours cyclopropane derivatives while performing the reaction without CO, as in the current work, generally gives metathesis products or mixtures of cyclopropane and metathesis products [43–46]. No metathesis products were isolated from the present reactions, perhaps because their formation would require the co-production of a highly unstable hydridocarbene [47].

We have shown that the chromium morpholinocarbene **12** derived from podocarpic acid reacts with a range of simple electron-deficient alkenes to give aryl ketones derived from ring opening of an aminocyclopropane followed by enamine hydrolysis; vinyl sulphones react differently, giving products derived from insertion of the carbene into the β-CH bond of the alkene. The availability in generally good yield of the 13-(4-oxobutanoyl) derivatives **18**, **25–29**, **33** and **34** by this thermally-promoted chemistry provides an alternative to their preparation by acylation procedures involving Lewis acid catalysts, which are known to cause unwanted side reactions such as dealkylation/re-alkylation of the aromatic ring at C(9), leading to loss of stereochemistry across the A/B ring junction.

3. Experimental

Structures were assigned using HRMS ($\Delta < 5$ ppm) for the molecular formula, in combination with complete assignment of the ^{1}H- and ^{13}C-NMR spectra and selected infrared data.

All of the chromium aminocarbenes were synthesised according to a literature procedure [23].

*3.1. Reaction of pentacarbonyl[(morpholino)-(2-methoxyphenyl)carbene]chromium (**6**) with phenyl ethenyl sulphone*

3.1.1. Thermolysis in $C_6H_5CH_3$

A solution of pentacarbonyl[(morpholino)(2-methoxyphenyl)carbene]chromium (**6**) (0.215 g, 0.541 mmol) and phenyl ethenyl sulphone (0.130 g, 0.612 mmol) in $C_6H_5CH_3$ (3 ml) in a sealed pressure vessel was refluxed under nitrogen for 22.5 h. Removal of solvent followed by p.l.c. (hexanes–Et_2O, 1:1) gave: (i) carbene starting material (7 mg); and (ii) (*E*)-2-methoxy-(1′-morpholino-3′-phenylsulphonylprop-2-enyl)benzene (**13**) (20 mg, 10%) as a colourless oil. Anal. Found: $M^{+\bullet}$ 373.1346. Calc. for $C_{20}H_{23}NO_4S$: 373.1348%. IR (cm^{-1}) ν_{max} ($CH_{aromatic}$) 3061, (C=C) 1598, (SO_{2sym}) 1318, (SO_{2anti}) 1147. ^{1}H-NMR $\delta = 2.39$ (m, NCH_2), 3.67 (t, $J = 4.7$ Hz, OCH_2), 3.70 (s, OMe), 4.50 (d, $J = 7.6$ Hz, C*H*CH=CHSO$_2$), 6.57 (dd, $J =$ 15.2, 1 Hz, CHCH=C*H*SO$_2$), 6.83 (dd, $J = 8.3$, 0.6 Hz, H(6)), 6.94(5) (td, $J = 7.6$, 1.0 Hz, H(4)), 6.95 (dd, $J = 15.2$, 7.6 Hz, CHC*H*=CHSO$_2$), 7.25 (ddd, $J = 8.3$, 7.6, 1.8 Hz, H(5)), 7.33 (dd, $J = 7.5$, 1.5 Hz, H(3)), 7.50 (t, $J = 7.9$ Hz, H_{meta}), 7.59 (tt, $J = 7.4$, 2.1 Hz, H_{para}), 7.79 (dd, 7.9, $J = 1.4$ Hz, H_{ortho}). ^{13}C-NMR $\delta = 51.7$ (NCH_2), 55.3 (OMe), 63.2 (*C*HCH=CHSO$_2$), 67.0 (OCH_2), 110.9 (C(6)), 120.9 (C(4)), 125.2 (C(2)), 127.5 (C_{ortho}), 129.0 (C_{meta}), 129.1 (C(3)), 129.2 (C(5)), 130.4 (CHCH=*C*HSO$_2$), 133.2 (C_{para}), 140.6 (C_{ipso}), 146.7 (CH*C*H=CHSO$_2$), 157.2 (C(1)). MS; *m*/*z*: 373 (23, M^+), 232 (90, $M - PhSO_2^{\bullet}$), 206 (48), 145 (100, 232-C_8H_9NO).

3.1.2. Me_3NO activation

Anhydrous trimethylamine-*N*-oxide (59 mg, 0.79 mmol) was added to a solution of **6** (0.199 g, 0.501 mmol) and phenyl ethenyl sulphone (93 mg, 0.55 mmol) in CH_2Cl_2 (4 ml) under nitrogen and the solution was refluxed for 4.5 h. Workup followed by p.l.c. (hexanes–Et_2O, 1:1) returned only carbene starting material **6** (59 mg).

*3.2. Reaction of pentacarbonyl[(methylamino)-(2-methoxyphenyl)carbene]chromium (**2**) with phenyl ethenyl sulphone*

A solution of pentacarbonyl[(methylamino)(2-methoxyphenyl)carbene]chromium (**2**) (0.197 g, 0.578 mmol) and phenyl ethenyl sulphone (0.105 g, 0.642 mmol) in $C_6H_5CH_3$ (6 ml) was refluxed under nitrogen for 23 h. Workup followed by p.l.c. (hexanes–Et_2O, 1:1) failed to give any product.

*3.3. Reaction of pentacarbonyl[(dimethylamino)-(2-methoxyphenyl)carbene] (**3**) chromium with phenyl ethenyl sulphone*

A solution of pentacarbonyl[(dimethylamino)(2-methoxyphenyl)carbene]chromium (**3**) (0.219 g, 0.616 mmol) and phenyl ethenyl sulphone (0.112 g, 0.666 mmol) in $C_6H_5CH_3$ (6 ml) was refluxed under nitrogen for 17.5 h. The solution was diluted with Et_2O (30 ml), washed with water, HCl (1 mol l^{-1}) and brine, and dried. Removal of solvent followed by p.l.c. gave carbene starting material (**3**) (31.1 mg).

*3.4. Reaction of pentacarbonyl[(dihydroamino)-(2-methoxyphenyl)carbene]chromium (**1**) with propenenitrile*

A solution of pentacarbonyl[(dihydroamino)(2-methoxyphenyl)carbene]chromium (**1**) (0.169 g, 0.516 mmol) and propenenitrile (42 μl, 0.64 mmol) in $C_6H_5CH_3$ (3 ml) in a sealed pressure vessel was refluxed under nitrogen for 2 h. Propenenitrile (32 μl, 0.49 mmol) was added and the solution was heated for 2 h; more propenenitrile (32 μl, 0.49 mmol) was added and the solution was heated for a further 2.5 h. Removal of solvent followed by p.l.c. gave a complicated mixture of products, but none of the desired ketone.

*3.5. Reaction of pentacarbonyl[(methylamino)-(2-methoxyphenyl)carbene]chromium (**2**) with propenenitrile*

A solution of pentacarbonyl[(methylamino)(2-methoxyphenyl)carbene]chromium (**2**) (0.170 g, 0.499 mmol) and propenenitrile (42 μl, 0.64 mmol) in $C_6H_5CH_3$ (3 ml) in a sealed pressure vessel was refluxed under nitrogen. Propenenitrile (32 μl, 0.49 mmol) was added and the solution was heated for 2.5 h; more propenenitrile (32 μl, 0.49 mmol) was added and the solution was heated for a further 2.5 h. Removal of solvent followed by p.l.c. (hexanes–Et_2O, 1:1) gave 4-(2-methoxyphenyl)-4-oxobutanenitrile (**14**) (15 mg, 16%) as an oil. Anal. Found: $M^{+\bullet}$ 189.0786. Calc. for $C_{11}H_{11}NO_2$: 189.0790. IR (cm^{-1}) ν_{max} (C≡O) 2252, (C=O) 1673. ^{1}H-NMR $\delta = 2.72$ (t, $J = 7.6$ Hz, CH_2CN), 3.40 (t, $J = 7.6$ Hz, CH_2CO), 3.94 (s, OCH_3), 7.00 (d, $J = 8.2$ Hz, H(3)), 7.03 (t, $J = 7.8$ Hz, H(5)), 7.52 (ddd, $J = 8.2$, 7.8, 1.8 Hz, H(4)), 7.83 (dd, $J = 7.8$, 1.8 Hz, H(6). ^{13}C-NMR $\delta = 12.0$ (CH_2CN), 39.4 (CH_2CO), 55.5 (OCH_3), 111.6 (C(3)), 119.7 (C≡N), 120.8 (C(5)),

125.9(5) (C(1)), 130.8 (C(6)), 134.6 (C(4)), 159.2 (C(2)), 196.7 (C=O). MS; *m*/*z*: 189 (11, M^+), 135 (100, $M - NCCH_2CH_2^{\bullet}$), 77 (23, Ph^+).

3.6. Reaction of pentacarbonyl[(dimethylamino)-(2-methoxyphenyl)carbene]chromium (3) with propenenitrile

A solution of pentacarbonyl[(dimethylamino)(2-methoxyphenyl)carbene]chromium (**3**) (0.171 g, 0.481 mmol) and propenenitrile (42 μl, 0.64 mmol) in $C_6H_5CH_3$ (3 ml) in a sealed pressure vessel was refluxed under nitrogen for 2 h. Propenenitrile (32 μl, 0.49 mmol) was added and the solution was heated for 2.5 h; more propenenitrile (32 μl, 0.49 mmol) was added and the solution was heated for a further 2.5 h. Removal of solvent and p.l.c. gave: (i) η^6-(methylbenzene)tricarbonylchromium (21 mg); and (ii) **14** (33 mg, 36%).

3.7. Reaction of pentacarbonyl[(aziridinyl)-(2-methoxyphenyl)carbene]chromium (4) and propenenitrile

A solution of pentacarbonyl[(aziridinyl)(2-methoxyphenyl)carbene]chromium (**4**) (0.172 g, 0.487 mmol) and propenenitrile (42 μl, 0.65 mmol) in $C_6H_5CH_3$ (3 ml) in a sealed pressure vessel was refluxed under nitrogen for 2 h. Propenenitrile (32 μl, 0.49 mmol) was added and the solution was heated for 2 h; propenenitrile (32 μl, 0.49 mmol) was added and the solution was heated for a further 3 h. Removal of solvent followed by p.l.c. (hexanes–Et_2O, 1:1) gave: (i) tricarbonyl(η^6-methylbenzene)chromium (46 mg); and (ii) **14** (10 mg, 11%).

3.8. Reaction of pentacarbonyl[(pyrrolidinyl)-(2-methoxyphenyl)carbene]chromium (5) with propenenitrile

A solution of pentacarbonyl[(pyrrolidinyl)(2-methoxyphenyl)carbene]chromium (**5**) (0.152 g, 0.399 mmol) and propenenitrile (33 μl, 0.50 mmol) in $C_6H_5CH_3$ (2.5 ml) in a sealed pressure vessel was refluxed under nitrogen for 2.5 h. Propenenitrile (26 μl, 0.43 mmol) was added and the solution was heated for 2 h; more propenenitrile (26 μl, 0.43 mmol) was added and the solution was heated for a further 2.5 h. Removal of solvent followed by p.l.c. gave **14** (15 mg, 20%).

3.9. Reaction of pentacarbonyl[(morpholino)-(2-methoxyphenyl)carbene]chromium (6) with propenenitrile

3.9.1. In $C_6H_5CH_3$

A solution of pentacarbonyl[(morpholino)(methoxyphenyl)carbene]chromium (**6**) (0.132 g, 0.332 mmol) and propenenitrile (28 μl, 0.43 mmol) in $C_6H_5CH_3$ (2.5 ml) in a sealed pressure vessel was refluxed under nitrogen for 2 h. More propenenitrile (20 μl, 0.30 mmol) was added and the solution was heated for 2 h; more propenenitrile (20 μl, 0.30 mmol) was then added and the solution was heated for a further 19 h. Removal of solvent followed by p.l.c. gave **14** (0.040 g, 64%).

3.9.2. In *p*-xylene

A solution of **6** (0.200g, 0.503 mmol) and propenenitrile (50 μl, 0.76 mmol) in *p*-xylene (2.5 ml) was refluxed under nitrogen in a sealed pressure tube for 3 h. Removal of the solvent followed by p.l.c. gave: (i) η^6-(1,4-dimethylbenzene)tricarbonylchromium (62 mg); and (ii) **14** (33 mg, 35%).

3.10. Reaction of pentacarbonyl[(dihydroamino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (7) with propenenitrile in $C_6H_5CH_3$

A solution of pentacarbonyl[(dihydroamino)(13-(12,19 - dimethoxypodocarpa - 8,11,13 - triene))carbene]-chromium (**7**) (0.203 g, 0.400 mmol) and propenenitrile (20 μl, 0.30 mmol) in $C_6H_5CH_3$ (2.5 ml) in a sealed pressure vessel was refluxed for 1 h under nitrogen. 2-Propenenitrile (20 μl, 0.40 mmol) was added and the solution was heated for 1 h. Removal of solvent followed by p.l.c. (hexanes–Et_2O, 1:1) gave no insertion products.

3.11. Reaction of pentacarbonyl[(methylamino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (8) with propenenitrile

A solution of pentacarbonyl[(methylamino)(13-(12,19 - dimethoxypodocarpa - 8,11,13 - triene))carbene]-chromium (**8**) (0.205 g, 3.93 mmol) and propenenitrile (28 μl, 0.43 mmol) in $C_6H_5CH_3$ (2 ml) in a sealed pressure tube was refluxed under nitrogen for 1 h. Propenenitrile (20 μl, 0.3 mmol) was added and the solution was heated for 1 h. Removal of solvent followed by p.l.c. gave (i) 13-cyano-12,19-dimethoxypodocarpa-8,11,13-triene (**19**) (8 mg, 8%) as white flaky crystals, m.p. 108–110°C. Anal. Found: 313.2037. Calc. for $C_{20}H_{27}NO_2$: 313.2042. IR (cm^{-1}) ν_{max} (s, C≡N) 2225, (s, C=C) 1609, (s, C–O–C_{sym}) 1109. ^{1}H-NMR $\delta = 1.02$ (ddd, $J = 13.6$, 4.2 Hz, H(3ax)), 1.04 (s, H(18)), 1.20 (s, H(20)), 1.38 (dd, $J = 12.7$, 1.8 Hz, H(5)), 1.43 (ddd, $J = 12.9$, 3.9 Hz, H(1ax)), 1.60–1.80 (m, H(2ax), H(2eq), H(6ax)), 1.88 (bd, $J = 13.7$ Hz, H(3eq)), 2.00 (bdd, $J = 13.6$, 7.4 Hz, H(6eq)), 2.27 (bd, $J = 12.9$, H(1eq)), 2.73 (ddd, $J = 16.8$, 11.6, 7.4 Hz,

H(7ax)), 2.86 (bdd, $J = 16.8$, 6.0 Hz, H(7eq)), 3.26 (d, $J = 9.1$ Hz, H(19)), 3.33 (s, 19-OMe), 3.49 (d, $J = 9.1$ Hz, H(19)), 3.88 (s, 12-OMe), 6.83 (s, H(11)), 7.21 (s, H(14). ^{13}C-NMR $\delta = 18.9(6)$ (C(2)), 19.0(0) (C(6)), 25.3 (C(20)), 27.7 (C(18)), 29.7 (C(7)), 35.8(5) (C(3)), 38.0 (C(10)), 38.7 (C(4)), 38.8 (C(1)), 50.7 (C(5)), 55.8(5) (12-OMe), 59.4 (19-OMe), 75.9 (C(19)), 99.0 (C≡N), 107.3 (C(11)), 116.9 (C(13)), 128.0 (C(8)), 134.0 (C(14)), 156.9 (C(9)), 159.2 (C(12)). MS; m/z: 313 (39, M^+), 186 (100); and (ii) 12,19-dimethoxy-13-(4-oxobutanenitrile)podocarpa-8,11,13-triene (**18**) (6.7 mg, 5%) as white flaky crystals, m.p. 102–103°C. Anal. Found: $M^{+\bullet}$ 369.2304. Calc. for $C_{23}H_{31}NO_3$: 369.2302. IR (cm^{-1}) ν_{max} (s, C≡N) 2225, (s, C=C) 1609, (s, C–O–C_{sym}) 1109. ^{1}H-NMR $\delta = 0.99$ (ddd, $J = 13.6$, 4.0 Hz, H(3ax)), 1.02 (s, H(18)), 1.19 (s, H(20)), 1.38 (dd, $J = 12.7$, 1.8 Hz, H(5)), 1.44 (ddd, $J = 12.9$, 3.8 Hz, H(1ax)), 1.59–1.79 (m, H(2ax), H(2eq), H(6ax)), 1.87 (bd, $J = 13.6$ Hz, H(3eq)), 1.97 (ddt, $J = 13.4$, 7.4, 1.7 Hz, H(6eq)), 2.27 (bd, $J = 12.4$ Hz, H(1eq)), 2.68 (t, $J = 7.4$ Hz, CH_2CN; 2.74 (ddd, $J = 16.8$, 11.5, 7.6 Hz, H(7ax)), 2.88 (bdd, $J = 16.8$, 6.1 Hz, H(7eq)), 3.23 (d, $J = 9.1$ Hz, H(19)), 3.31 (s, 19-OMe), 3.34 (t, $J = 7.5$ Hz, ArCOCH), 3.35 (t, $J = 7.5$ Hz, ArCOCH), 3.49 (d, $J = 9.1$ Hz, H(19)), 3.88 (s, 12-OMe), 6.83 (s, H(11)), 7.50 (s, H(14)).^{13}C-NMR $\delta = 12.0$ (CH_2CN), 19.0(2) (C(2)), 19.0(8) (C(6)), 25.3 (C(20)), 27.6 (C(18)), 29.7(5) (C(7)), 35.8 (C(3)), 38.0 (C(10)), 38.5 (C(1)), 39.2 ($ArCOCH_2$), 50.8 (C(5)), 55.4 (12-OMe), 59.4 (19-OMe), 75.8(5) (C(19)), 107.5(5) (C(11), 119.8 (C≡N), 123.4 (C(13)), 127.7 (C(8)), 131.3 (C(14)), 157.2 (C(9)), 157.4 (C(12), 196.2 (C=O). MS; m/z: 369 (95, M^+), 324 (15, $M - MeOCH_2^{\bullet}$), 322 (28, 324-2H$^{\bullet}$), 315 (57, $ArCO^+$), 254 (20), 242 (100, 324-NC$(CH_2)_2$CO$^{\bullet}$).

3.12. Reaction of pentacarbonyl[(dimethylamino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (9) with propenenitrile

A solution of pentacarbonyl[(dimethylamino)(13-(12,19 - dimethoxypodocarpa - 8,11,13 - triene))carbene]-chromium (**9**) (0.217 g, 0.407 mmol) and propenenitrile (28 μl, 0.43 mmol) in $C_6H_5CH_3$ (2 ml) in a sealed pressure tube was refluxed under nitrogen for 1 h. Propenenitrile (20 μl, 0.30 mmol) was added and the solution was heated for 2 h. Removal of solvent followed by p.l.c. gave **18** (47 mg, 31%).

3.13. Reaction of pentacarbonyl[(aziridinyl)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (10) with propenenitrile

A solution of pentacarbonyl[(aziridinyl)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**10**) (0.211 g, 0.396 mmol) and propenenitrile (28 μl, 0.43 mmol) in $C_6H_5CH_3$ (2 ml) in a sealed tube was refluxed under nitrogen for 1 h. Propenenitrile (20 μl, 0.30 mmol) was added and the solution was heated for 1 h followed by the addition of more 2-propenenitrile (20 μl, 0.30 mmol) and heating for a further 1 h. Removal of the solvent followed by p.l.c. gave: (i) **19** (24.4 mg, 20%); and (ii) **18** (7.7 mg, 5%).

3.14. Reaction of pentacarbonyl[(pyrrolidinyl)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (11) with propenenitrile in $C_6H_5CH_3$

A solution of pentacarbonyl[(pyrrolidinyl)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**11**) (0.191 g, 0.340 mmol) and propenenitrile (28 μl, 0.54 mmol) in $C_6H_5CH_3$ (2 ml) was refluxed under nitrogen for 1 h. Propenenitrile (23 μl, 0.35 mmol) was added and the solution was heated for a further 1.5 h. Removal of solvent followed by p.l.c. (hexanes–Et_2O, 1:1) gave: (i) **19** (7.9 mg, 7%); and (ii) **18** (43.5 mg, 35%).

3.15. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (12) with propenenitrile

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-))trienecarbene]chromium (**12**) (0.238 g, 0.412 mmol) and propenenitrile (28 μl, 0.425 mmol) in $C_6H_5CH_3$ (2.5 ml) in a sealed pressure vessel was refluxed under nitrogen for 1 h. Propenenitrile (20 μl, 0.30 mmol) was added and the solution was heated for a further 40 min. Removal of solvent followed by p.l.c. gave: (i) 12,19-dimethoxypodocarpa-8,11,13-triene-13-carboxylic acid (**20**) (3.3 mg, 2%) [32]; and (ii) **18** (87.1 mg, 57%).

3.16. Thermolysis of pentacarbonyl[(aziridinyl)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (10)

A solution of pentacarbonyl[(aziridinyl)(13 - (12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**10**) (0.278 g, 0.521 mmol) in $C_6H_5CH_3$ (10 ml) was refluxed under nitrogen for 16 h. Removal of solvent followed by p.l.c. gave **19** (50%).

3.17. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (12) with phenyl ethenyl sulphone

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.540 g, 0.935 mmol) and phenyl ethenyl sulphone (0.241 g, 1.43 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed

pressure vessel was refluxed under nitrogen for 3 h. The product was adsorbed onto silica gel and exposed to air for 4 days. P.l.c. (hexanes–Et_2O, 1:1) gave (*E*)-12,19-dimethoxy-13-(1′-morpholino-3′-phenylsulphonylprop-2′-enyl)podocarpa-8,11,13-triene (**22**) (0.236 g, 46%) as a colourless foam. Anal. Found: 553.2864. Calc. for $C_{32}H_{43}NO_5S$: 553.2862. IR (cm^{-1}) ν_{max} ($CH_{aromatic}$) 3057, (C=C) 1609, ($SO_{2(sym)}$) 1320, ($SO_{2(anti)}$) 1147. ^{1}H-NMR $\delta = 1.00$ (ddd, $J = 13.6$, 13.6, 4.0 Hz, H(3ax)), 1.04 (s, H(18)), 1.05 (s, H(18)), 1.18 (s, H(20)), 1.20 (s, H(20)), 1.39–1.46 (m, H(5), H(1ax)), 1.59–1.78 (m, H(2ax), H(2eq)), H(6ax)), 1.89 (bd, $J = 13.5$ Hz, H(3eq)), 1.98 (bdd, $J = 13.2$, 7.0 Hz, H(6eq)), 2.29 (bd, $J = 13.5$ Hz, H(1eq)), 2.38–2.43 (NCH_2), 2.73 (ddd, $J = 16.7$, 11.4, 7.0 Hz, H(7ax)), 2.81 (bdd, $J = 16.7$, 6.3 Hz, H(7eq)), 3.24 (d, $J = 9.1$ Hz, H(19)), 3.33 (s, 19-OMe), 3.34 (s, 19-OMe), 3.53 (d, $J = 9.1$ Hz, H(19)), 3.54 (d, $J = 9.1$ Hz, H(19)), 3.64–3.68 (m, OCH_2), 3.66 (s, 12-OMe), 4.40(7) (dd, $J = 7.0$, 0.9 Hz, C*H*CH=CHSO$_2$), 4.41 (dd, $J = 7.4$, 0.9 Hz, C*H*CH=CHSO$_2$), 6.55(5) (dd, $J = 15.2$, 0.9 Hz, CHCH=C*H*SO$_2$), 6.56 (dd, $J = 15.2$, 0.9 Hz, CHCH=C*H*SO$_2$), 6.69 (s, H(11)), 6.87 (s, H(14)), 6.88 (s, H(14)), 6.94 (dd, $J = 15.2$, 7.4 Hz, CHC*H*=CHSO$_2$), 6.95 (dd, $J = 15.2$, 7.4 Hz, CHC*H*=CHSO$_2$), 7.49(6) (t, $J = 8.0$ Hz, H_{meta}), 7.50 (t, $J = 8.0$ Hz, H_{meta}), 7.60 (m, H_{para}), 7.79(8) (d, $J = 8.0$ Hz, H_{ortho}), 7.80(1) (d, $J = 8.0$ Hz, H_{ortho}). ^{13}C-NMR $\delta = 19.1$ (C(2)), 19.2 (C(6)), 25.5(5) (C(20)), 25.6 (C(20)), 27.6 (C(18)), 30.1(5) (C(7)), 35.9 (C(3)), 38.0 (C(10), C(4)), 39.0 (C(1)), 51.1(6) (C(5)), 51.2 (NCH_2), 51.6 (NCH_2), 55.3 (12-OMe), 59.4 (19-OMe), 62.9 (*C*HCH=CHSO$_2$), 63.0 (*C*HCH=CHSO$_2$), 66.9 (CH_2O), 75.8 (C(19)), 106.9 (C(11)), 122.1 (C(13)), 127.4 (C_{ortho}), 129.0 (C(8)), 129.1 (C_{meta}), 129.3 (C(14)), 129.3(5) (C(14)), 129.7 (CHCH=*C*HSO$_2$), 129.9 (CHCH=*C*HSO$_2$), 130.0(5) (CHCH=*C*HSO$_2$), 133.1(5) (C_{para}), 140.7 (C_{ipso}), 147.0 (CH*C*H=CHSO$_2$), 147.2 (CH*C*H=CHSO$_2$), 150.7 (C(9)), 155.4 (C(12)). MS; *m*/*z*: 553 (4, M^+), 522 (1, $M - Me^{\bullet}$), 467 (5, $M - PhSO_2^{\bullet}$), 412 (32), 325 (21), 218 (21), 141 (78, $PhSO_2^+$), 125 (28, $PhSO^+$), 77 (100, Ph^+).

*3.18. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (**12**) with methyl ethenyl sulphone*

A solution of pentacarbonyl[(morpholino)13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.142 g, 0.246 mmol) and methyl ethenyl sulphone (45 μl, 0.51 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure vessel was refluxed under nitrogen for 3.5 h. Removal of solvent followed by p.l.c. (Et_2O–EtOH, 9:1) gave (*E*)-12,19-dimethoxy-13-(1′-morpholino-3′-methylsulphonylprop-2′-enyl)podocarpa-8,11,13-triene (**23**) (55 mg, 46%) as a colourless oil. Anal. Found: $M^{+\bullet}$ 491.2707. Calc. for $C_{27}H_{41}NO_5S$: 491.2705. IR (cm^{-1}) ν_{max} ($CH_{aromatic}$) 3057, (C=C) 1609, ($SO_{2(sym)}$) 1320, ($SO_{2(anti)}$) 1147. ^{1}H-NMR $\delta = 1.00(5)$ (td, $J = 13.7$, 3.8 Hz, H(3ax)), 1.01 (td, $J = 13.7$, 3.8 Hz, H(3ax)), 1.03(9) (s, H(18)), 1.04 (s, H(18)), 1.19 (s, H(20)), 1.41 (bd, $J = 12.6$ Hz, H(5)), 1.43 (bt, $J = 12.9$ Hz, H(1ax)), 1.59–1.75 (m, H(2ax), H(2eq), H(6ax)), 1.88 (bdd, $J = 13.4$, 2.5 Hz, H(3eq)), 1.97 (bdd, $J = 13.3$, 7.2 Hz, H(6eq)), 2.27 (bd, $J = 12.5$ Hz, H(1eq)), 2.41 (m, NCH_2), 2.73 (ddd, $J = 17.5$, 11.7, 7.3 Hz, H(7ax)), 2.84 (bdd, $J = 17.5$, 6.1 Hz, H(7eq)), 2.96 (s, SO_2Me), 3.23 (d, $J = 9.1$ Hz, H(19)), 3.24 (d, $J = 9.1$ Hz, H(19)), 3.36 (s, 19-OMe), 3.53 (d, $J = 9.1$ Hz, H(19)), 3.54 (d, $J = 9.1$ Hz, H(19)), 3.69 (dd, $J = 9.0$, 4.5 Hz, OCH_2; 3.78 (s, 12-OMe), 4.43 (d, $J = 7.5$ Hz, CHCH=CHSO$_2$), 4.45 (d, $J = 7.5$ Hz, CHCH=CHSO$_2$), 6.47 (d, $J = 16.5$ Hz, CHCH=CHSO$_2$), 6.73(6) (s, H(11)), 6.74(2) (s, H(11)), 6.75 (dd, $J = 16.5$, 7.5 Hz, CHCH=CHSO$_2$), 6.93(0) (s, H(14)), 6.93(7) (s, H(14)). ^{13}C-NMR $\delta = 19.1$ (C(2)), 19.2 (C(6)), 25.5 (C(20)), 27.6 (C(18)), 30.1 (C(7)), 35.8 (C(3)), 38.0 (C(10), C(4)), 39.0 (C(1)), 42.2 (SO_2Me), 42.7(5) (SO_2Me), 51.1 (C(5)), 51.2 (NCH_2), 51.6 (NCH_2), 55.4(5) (12-OMe), 59.3(5) (19-OMe), 62.9(3) (CHCH=CHSO$_2$), 63.0(3) (CHCH=CHSO$_2$), 66.9(5) (OCH_2), 75.7 (C(19)), 107.0 (C(11)), 122.1 (C(13)), 127.4 (C(8)), 129.2 (C(14)), 129.3 (CHCH=CHSO$_2$), 148.3 (CHCH=CHSO$_2$), 150.7 (C(9)), 155.4 (C(12)). MS; *m*/*z*: 491, (19, M^+), 476, (4, $M - Me^{\bullet}$), 412, (100, $M - SO_2Me^{\bullet}$), 405, (32, $M - C_4H_8NO^{\bullet}$), 386, (20, $M - MeSO_2CH{=}CH^{\bullet}$), 325, (71, 412-$C_4H_9NO$).

*3.19. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxy-podocarpa-8,11,13-triene))-carbene]chromium (**12**) with phenyl ethenyl sulphoxide*

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.144 g, 0.249 mmol) and phenyl ethenyl sulphoxide (70 μl, 0.52 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure vessel was refluxed for 3.5 h. Removal of solvent followed by p.l.c. gave (i) 12,19-dimethoxy-13-(4-oxo-1-(phenylsulphoxide))podocarpa-8,11,13-triene (**24**) (16 mg, 14%) as a colourless oil. Anal. Found: $M^{+\bullet}$ 468.2320. Calc. for $C_{28}H_{36}O_4S$: 468.2334%. IR (cm^{-1}) ν_{max} (C=O) 1668, (C=C) 1606, (C–O–C_{sym}) 1108, (bdd, $J = 13.4$, 7.3 Hz, H(6eq)), 2.27 (bd, $J = 12.4$ Hz, H(1eq)), 2.74 (ddd, $J = 17.2$, 11.4, 7.4 Hz, H(7ax)), 2.88 (bdd, $J = 16.8$, 5.9 Hz, H(7eq)), 3.23–3.31 (m, ArCOC*H*$_2$, C*H*$_2$SOPh, H(19)), 3.33 (s, 19-OMe), 3.51 (d, $J = 9.1$ Hz, H(19)), 3.80 (s, 12-OMe), 6.80 (s, H(11)), 7.17 (tt, $J = 7.4$, 1.2 Hz, H_{para}), 7.28 (ddt, $J = 8.1$, 7.5, 1.2 Hz, H_{meta}), 7.36 (dt, $J = 8.1$, 1.2 Hz, H_{ortho}), 7.41 (s, H(14)). ^{13}C-NMR $\delta = 19.0(6)$ (C(2)), 19.1(3) (C(6)), 25.4 (C(20)), 27.6 (C(18)), 28.3 (ArCO*C*H$_2$), 29.8 (C(7)), 35.8 (C(3)), 38.0(5) (C(10)),

38.4 (C(4)), 38.9 (C(1)), 43.4 (CH_2SOPh), 50.9 (C(5)), 55.4 (12-OMe) 59.4 (19-OMe), 75.8(5) (C(19)), 107.5 (C(11)), 125.0 (C(13)), 125.9 (C_{para}), 127.5 (C(8)), 128.8 (C_{ortho}), 129.2(5) (C_{meta}), 131.0 (C(14)), 136.4 (C_{ipso}), 156.2(5) (C(9)), 157.0 (C(12)), 199.7 (C=O). MS; *m/z*: 468 (1, M^+), 452 (30, M − O), 343 (100, M − PhSO$^\bullet$), 315 (95, $ArCO^+$), 175 (39); (ii) starting material **12** (5.6 mg, 4%); and (iii) phenyl ethenylsulphoxide (51 mg).

3.20. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (12) with but-3-en-2-one

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.137 g, 0.237 mmol) and but-3-en-2-one (44 μl, 0.53 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure tube was refluxed under nitrogen for 3 h. The solvent and $Cr(CO)_6$ was removed in vacuo and p.l.c. of the green residue gave 12,19-dimethoxy-13-(1,4-dioxopentyl)-podocarpa-8,11,13-triene (**25**) (74 mg, 81%) as a colourless oil. Anal. Found: $M^{+\bullet}$ 86.2456. Calc. for $C_{24}H_{34}O_4$: 386.2457. IR (cm^{-1}) ν_{max} (s, C=O alkyl) 1717, (s, C=O aryl) 1668, (C=C) 1606, (s, C–O–C_{anti}) 1257, (C–O–C_{sym}) 1108. ^{1}H-NMR $\delta = 1.01$ (ddd, $J = 13.7$, 4.0 Hz, H(3ax)), 1.04 (s, H(18)), 1.20 (s, H(20)), 1.41 (dd, $J = 12.7$, 1.9 Hz, H(5)), 1.44 (ddd, $J = 12.9$, 3.8 Hz, H(1ax)), 1.60–1.80 (m, H(2ax), H(2eq), H(6ax)), 1.88 (bd, $J = 13.6$ Hz, H(3eq)), 1.98 (bdd, $J = 13.4$, 7.3 Hz, H(6eq)), 2.23 (s, $COCH_3$), 2.29 (bd, $J = 12.3$ Hz, H(1eq)), 2.73 (ddd, $J = 16.6$, 11.8, 7.4 Hz, H(7ax)), 2.80 (t, $J = 6.4$ Hz, CH_2COCH_3), 2.88 (bdd, $J = 16.6$, 6.4 Hz, H(7eq)), 3.23 (d, $J = 9.1$ Hz, H(19)), 3.26 (t, $J = 6.4$ Hz, ArCOC*H*), 3.27 (t, $J = 6.4$ Hz, ArCOC*H*), 3.33 (s, 19-OMe), 3.52 (d, $J = 9.1$ Hz, H(19)), 3.87 (s, 12-OMe), 6.83 (s, H(11)), 7.43 (s, H(14)). ^{13}C-NMR $\delta = 19.0(7)$ (C(2)), 19.1(4) (C(6)), 25.4 (C(20)), 27.6 (C(18)), 29.8 (C(7)), 30.1 ($COCH_3$), 35.8 (C(3)), 37.6 (CH_2CO), 37.8 (CH_2CO), 38.0(5) (C(10)), 38.4 (C(4)), 38.9 (C(1)), 50.9(5) (C(5)), 55.4(5) (12-OMe) 59.4 (19-OMe), 75.8 (C(19)), 107.6 (C(11)), 124.9 (C(13)), 127.4 (C(8)), 131.0 (C(14)), 156.1 (C(9)), 157.1 (C(12)), 199.9 (C=O (aryl ketone)), 207.9(5) C=O (alkyl ketone)). MS; *m/z*: 386 (30, M^+), 315 (100, $ArCO^+$), 99 (25, CH_3CO-$(CH_2)_2CO^+$).

3.21. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (12) with methyl propenoate

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.149 g, 0.258 mmol) and methyl propenoate (50 μl, 0.56 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure tube was refluxed under nitrogen for 4.5 h. Removal of solvent and $Cr(CO)_6$ in vacuo followed by p.l.c. (hexanes–Et_2O, 1:1) gave 12,19-dimethoxy-13-(methyl 4-oxobutanoate)podocarpa-8,11,13-triene (**26**) (97 mg, 93%) as colourless needles, m.p. 112.5–113.5°C. Anal. Found: $M^{+\bullet}$ 402.2404. Calc. for $C_{24}H_{24}O_5$: 402.2406. IR (cm^{-1}) ν_{max} (s, C=O ester) 1737, (s, C=O ketone) 1671, (s, C=C) 1606, (s, C–O–C_{sym}) 1107. ^{1}H-NMR $\delta = 1.01$ (ddd, $J = 13.7$, 13.7, 4.0 Hz, H(3ax)), 1.04 (s, H(18)), 1.20 (s, H(20)), 1.35 (d, $J = 13.1$ Hz, H(5)), 1.46 (ddd, $J = 12.9$, 3.3 Hz, H(1ax)), 1.60–1.79 (m, H(2ax), H(2eq), H(6ax)), 1.89 (bd, $J = 13.2$ Hz, H(3eq)), 1.98 (bdd, $J = 13.0$, 7.2 Hz, H(6eq)), 2.29 (bd, $J = 12.3$ Hz, H(1eq)), 2.69 (t, $J = 6.6$ Hz, CH_2CO_2Me), 2.75 (ddd, $J = 16.8$, 11.3, 7.5 Hz, H(7ax)), 2.89 (dd, $J = 16.8$, 6.2 Hz, H(7eq)), 3.24 (d, $J = 9.2$ Hz, H(19)), 3.30 (t, $ArCOCH_2$), 3.33 (s, 19-OMe), 3.52 (d, $J = 9.2$ Hz, H(19)), 3.69 (s, CO_2Me), 3.88 (s, 12-OMe), 6.83 (s, H(11)), 7.46 (s, H(14)). ^{13}C-NMR $\delta = 19.0(8)$ (C(2)), 19.1(5) (C(6)), 25.4 (C(20)), 27.6 (C(18)), 28.5 (CH_2CO_2Me), 29.8 (C(7)), 35.8 (C(3)), 38.1 (C(10)), 38.4 (C(4)), 38.6 ($ArCOCH_2$), 38.9 (C(1)), 51.0 (C(5)), 51.7 (CO_2Me), 55.5 (12-OMe), 59.4 (19-OMe), 75.9 (C(19)), 107.6 (C(11)), 124.7 (C(13)), 127.4 (C(8)), 131.1 (C(14)), 156.2 (C(9)), 157.2 (C(12)), 173.8 (C=O (ester)), 199.4 (C=O (ketone)). MS; *m/z*: 402 (28, M^+), 315 (100, $ArCO^+$), 115 (17, $MeO_2C(CH_2)_2CO^+$).

3.22. Reaction of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (12) with tert-butyl propenoate

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.685 g, 1.19 mmol) and *tert*-butyl propenoate (260 μl, 1.77 mmol) in $C_6H_5CH_3$ (10 ml) was refluxed in a sealed pressure vessel under nitrogen for 1 h. The solution was cooled, *tert*-butyl propenoate (0.200 ml, 1.36 mmol) was added, and the solution was heated under nitrogen for 2 h. The solution was adsorbed onto silica and exposed to air for 48 h. Extraction with Et_2O followed by p.l.c. (hexanes–Et_2O, 1:1) gave 12,19-dimethoxy-13-(*tert*-butyl 4-oxobutanoate)podocarpa-8,11,13-triene (**27**) (0.259 g, 49%) as a colourless oil. Anal. Found: $M^{+\bullet}$ 444.2875. Calc. for $C_{27}H_{40}O_5$: 444.2876. IR (cm^{-1}) ν_{max} (s, C=O ester) 1730, (C=O aryl ketone) 1673, (C=C) 1607, (C–O–C_{assym}) 1257,(C–O–C_{sym}) 1107. ^{1}H-NMR $\delta = 1.01$ (ddd, $J =$ 13.7, 4.1 Hz, H(3ax)), 1.04 (s, H(18)), 1.20 (s, H(20)), 1.40 (dd, $J = 12.8$, 1.9 Hz, H(5)), 1.45 (s, $(CH_3)_3C$), 1.45 (obscured) (ddd, $J = 12.9$, 4.1 Hz, H(1ax)), 1.60–1.79 (m, H(2ax), H(2eq), H(6eq)), 1.88 (bd, $J = 13.5$ Hz, H(3eq)), 1.98 (bdd, $J = 13.4$, 7.3 Hz, H(6eq)), 2.28 (bd, $J = 12.5$ Hz, H(1eq)), 2.59 (t, $J = 6.8$ Hz, CH_2CO_2t-Bu), 2.74 (ddd, $J = 16.8$, 11.6, 7.2 Hz, H(7ax)), 2.88 (bdd, $J = 16.8$, 6.0 Hz, H(7eq)), 3.24 (t, $J = 6.6$ Hz, $ArCOCH_2$), 3.24 (d, $J = 9.1$ Hz, H(19)), 3.33 (s, 19-OMe), 3.52 (d, $J = 9.1$ Hz, H(19)), 3.87 (s, 12-OMe),

6.82 (s, H(11)), 7.43 (s, H(14)). ^{13}C-NMR $\delta = 19.0(8)$ (C(2)), 19.1(6) (C(6)), 25.4 (C(20)), 27.6 (C(18)), 28.1, $(CH)_3C$), 29.8 (C(7)), 29.9 (CH_2CO_2t-Bu), 35.8 (C(3)), 38.1 (C(10), 38.4 (C(4)), 38.7 (ArCOCH_2), 38.9 (C(1)), 51.0 (C(5)), 55.4 (12-OMe), 59.4 (19-OMe), 75.8(5) (C(19)), 80.2 ($(CH)_3C$), 107.6 (C(11)), 125.1 (C(13)), 127.4 (C(8)), 131.0 (C(14)), 155.9 (C(9)), 157.1 (C(12)), 172.6 (C=O (ester)), 199.8 (C=O (ketone)). MS; m/z: 444 (23, M^+), 371 (12, $M - t$-BuO$^\bullet$), 315 (100, $ArCO^+$).

3.23. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (12) with phenyl propenethioate

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.110 g, 1.90 mmol) and phenyl propenethioate (0.102 g, 0.621 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure vessel was refluxed under nitrogen for 1 h. Removal of solvent followed by p.l.c. (hexanes–Et_2O, 2:1) gave 12,19-dimethoxy-13-(phenyl 4-oxobutanethioate)podocarpa-8,11,13-triene (**28**) (76 mg, 83%) as a colourless oil which slowly solidified, m.p. 90–93°C. Anal. Found: $M^{+\bullet}$ 480.2307. Calc. for $C_{29}H_{36}O_4S$: 480.2334. IR (cm^{-1}) ν_{max} (C=O ester) 1717, (C=O aryl ketone) 1657, (C=C) 1603, (C–O–C_{sym}) 1107. ^{1}H-NMR $\delta = 1.01$ (ddd, $J = 13.5$, 4.1 Hz, H(3ax)), 1.04 (s, H(18)), 1.20 (s, H(20)), 1.39 (dd, $J = 12.7$, 1.9 Hz, H(5)), 1.45 (ddd, $J = 13.0$, 3.9 Hz, H(1ax)), 1.60–1.80 (m, H(2ax), H(2eq), H(6ax)), 1.88 (bd, $J = 13.6$ Hz, H(3eq)), 1.98 (bdd, $J = 13.5$, 7.4 Hz, H(6eq)), 2.28 (bd, $J = 12.5$ Hz, H(1eq)), 2.74 (ddd, $J = 16.9$, 11.5, 7.5 Hz, H(7ax)), 2.88 (bdd, $J = 16.8$, 6.0 Hz, H(7eq)), 3.06 (t, $J = 6.7$ Hz, CH_2COSPh), 3.24 (d, $J = 9.1$ Hz, H(19)), 3.33 (s, 19-OMe), 3.36 (td, $J = 6.7$, 1.6 Hz, CH_2COAr), 3.52 (d, $J = 9.1$ Hz, H(19)), 3.86 (s, 12-OMe), 6.82 (s, H(11)), 7.37–7.45 (m, Ph), 7.46 (s, H(14)). ^{13}C-NMR $\delta = 19.0(6)$ (C(2)), 19.1(3) (C(6)), 25.4 (C(20)), 27.6 (C(18)), 29.8 (C(7)), 35.8 (C(3)), 38.0 (C(10), CH_2COSPh), 38.4 (C(4)), 38.7(8) (CH_2COAr), 38.8(6) (C(1)), 50.9 (C(5)), 55.4 (12-OMe), 59.4 (19-OMe), 75.8 (C(19)), 107.5 (C(11)), 124.5 (C(13)), 127.5 (C(8)), 127.9 (C_{ipso}0, 129.1 (C_{ortho}), 129.2 (C_{para}), 131.2 (C(14)), 134.5 (C_{meta}), 156.3 (C(9)), 157.2 (C(12)), 197.0 (C=O (ester)), 198.7 (C=O (ketone)). MS; m/z: 480 (1, M^+), 371 (100, $M - PhS^\bullet$)), 315 (9, $ArCO^+$), 110 (17, $PhSH^{+\bullet}$).

3.24. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (12) with propenamide

3.24.1. For 3 h

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene)carbene]chromium (**12**) (0.086 g, 0.15 mmol) and propenamide (0.025 g, 0.35 mmol) in $C_6H_5CH_3$ (2 ml) in a sealed pressure vessel was refluxed under nitrogen for 3 h. The orange suspension was filtered and the solvent removed from the filtrate in vacuo. P.l.c. (Et_2O–EtOH, 9:1) gave 12,19-dimethoxy-13-(4-oxobutanamide)podocarpa-8,11,13-triene (**29**) (7.5 mg, 11%) as a pale yellow gum. Anal. Found: $M^{+\bullet}$ 387.2405. Calc. for $C_{23}H_{33}NO_4$: 387.2410. IR (cm^{-1}) ν_{max} (b, NH) 3347, (b, NH) 3206, (b, $C{=}O_{ketone}$, $C{=}O_{amide}$) 1669. ^{1}H-NMR $\delta = 1.01$ (ddd, $J = 13.6$, 4.1 Hz, H(3ax)), 1.04 (s, H(18)), 1.20 (s, H(20)), 1.40 (dd, $J = 12.7$, 1.9 Hz, H(5)), 1.50 (ddd, $J = 13.0$, 3.9 Hz, H(1ax)), 1.61–1.79 (m, H(2ax), H(2eq), H(6ax)), 1.88 (bd, $J = 13.6$ Hz, H(3eq)), 1.99 (ddt, $J = 13.4$, 7.3, 1.8 Hz, H(6eq)), 2.23–2.30 (m, H(1eq), CH_2CONH$_2$), 2.75 (ddd, $J = 17.0$, 11.4, 7.4 Hz, H(7ax)), 2.88 (dd, $J = 16.8$, 5.9 Hz, H(7eq)), 3.24 (d, $J = 9.1$ Hz, H(19)), 3.33 (s, 19-OMe), 3.34 (t, $J = 6.5$, 1.7 Hz, ArCOCH), 3.35 (t, $J = 6.5$ Hz, ArCOCH), 3.52 (d, $J = 9.1$ Hz, H(19)), 3.87 (s, 12-OMe), 5.39 (s, $NH_{(Z)}$), 5.88 (s, $NH_{(E)}$), 6.83 (s, H(11)), 7.46 (s, H(14)). ^{13}C-NMR $\delta =$ 19.0(7) (C(2)), 19.1(5) (C(6)), 25.4 (C(20)), 27.6 (C(18)), 29.8 (C(7)), 30.1(5) (CH_2CONH$_2$), 35.8 (C(3)), 38.1 (C(10)), 38.5 (C(4)), 38.9 (C(1)), 39.3 (CH_2COAr), 50.9 (C(5)), 55.4 (12-OMe), 59.4 (19-OMe), 75.9 (C(19)), 107.6 (C(11)), 124.6 (C(13)), 127.4 (C(8)), 131.1 (C(14)), 156.5 (C(9)), 157.3 (C(12)), 175.1 (C=O (amide)), 200.3 (C=O (ketone)). MS; m/z: 387 (33, M^+), 369 (30, $M - H_2O$), 315 (100, $ArCO^+$).

3.24.2. For 15.5 h

A solution of **12** (0.139 g, 0.241 mmol) and propenamide (0.100 g, 1.14 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure vessel was refluxed under nitrogen for 15.5 h. Removal of solvent followed by p.l.c. (Et_2O) gave *N*-morpholino-12,19-dimethoxypodocarpa-8,11,13-triene-13-carboxamide (**30**) (18 mg, 19%).

3.25. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (12) with propenoyl chloride

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.149 g, 0.258 mmol) and propenoyl chloride (44 μl, 0.54 mmol) in $C_6H_5CH_3$ (6 ml) in a sealed pressure vessel was refluxed under nitrogen for 30 min. A large amount of an orange precipitate formed after 5 min, and t.l.c. (Et_2O–$(CH_3)_2CO$, 9:1) of the reaction mixture indicated only highly coloured baseline material.

3.26. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (12) with propenoic acid

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium

(**12**) (0.197 g, 0.341 mmol) and propenoic acid (70 μl, 0.71 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure vessel was refluxed under nitrogen for 15 min, producing a cloudy green solution. Removal of solvent followed by p.l.c. (hexanes–Et_2O, 1:1) gave 13-formyl-12,19-dimethoxypodocarpa-8,11,13-triene (**31**) (79 mg, 73%) [29].

*3.27. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (**12**) with nitroethene*

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.087 g, 0.151 mmol) and nitroethene (125 μl, 20% sol. in Et_2O, 0.343 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure vessel was refluxed under nitrogen for 40 min. A white suspension formed, indicating that polymerisation of the nitroethene had occurred. P.l.c. (hexanes–Et_2O, 1:1) gave: (i) 13-formyl-12,19-dimethoxypodocarpa-8,11,13-triene (**31**) (8.9 mg, 19%); (ii) starting material **12** (15.8 mg, 18%); and (iii) the amide **30** (22.0 mg, 36%).

*3.28. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (**12**) with propenal*

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.147 g, 0.255 mmol) and propenal (80 μl, 1.3 mmol) in $C_6H_5CH_3$ (5 ml) in a sealed pressure vessel was refluxed under nitrogen for 4 h. P.l.c. (hexanes–Et_2O, 1:1) gave 13-formyl-12,19-dimethoxypodocarpa-8,11,13-triene (**31**) (18 mg, 15%).

*3.29. 12,19-Dimethoxy-13-(4-oxobutanoic acid)podocarpa-8,11,13-triene (**33**)*

A solution of NaOH (60 mg, 1.5 mmol) in water (0.6 ml) was added to a solution of 12,19-dimethoxy-13-(*tert*-butyl 4-oxobutanoate)podocarpa-8,11,13-triene (**27**) (0.136 g, 0.306 mmol) in Me_2SO (8 ml) and the solution was refluxed for 26.5 h. The solution was poured onto ice ($\sim$50 ml) containing HCl (2 mol l^{-1}, 20 ml), giving a white solid. The suspension was extracted with Et_2O, and the combined Et_2O layers were washed with water and dried ($MgSO_4$). Column chromatography (Et_2O) gave 12,19-dimethoxy-13-(4-oxobutanoic acid)podocarpa-8,11,13-triene (**33**) (83 mg, 70%) as a colourless oil. Anal. Found: $M^{+\bullet}$ 388.2250. Calc. for $C_{23}H_{32}O_5$: 388.2250. IR (cm^{-1}) ν_{max} (br, OH) 3222, (s, C=O_{acid}) 1712, (s, C=O_{ketone}) 1671, (C=C) 1606, (C–O–C) 1257, (C–O–C) 1109. ^{1}H-NMR $\delta = 1.01$ (ddd, $J = 13.6, 13.6, 4.1$ Hz, H(3ax)), 1.04 (s, H(18)), 1.21 (s, H(20)), 1.40 (dd, $J = 12.7, 1.9$ Hz, H(5)), 1.46 (ddd, $J = 12.9, 12.9, 3.9$ Hz, H(1ax)), 1.61–1.77 (m, H(2ax), H(2eq), H(6ax)), 1.88 (bd, $J = 13.5$ Hz, H(3eq)), 1.98 (bdd, $J = 13.4, 7.3$ Hz, H(6eq)), 2.28 (bd, $J = 12.5$ Hz, H(1eq)), 2.72 (t, $J = 6.7$ Hz, CH_2COOH), 2.75 (ddd, $J = 16.8, 11.5, 7.5$ Hz, H(7ax)), 2.87 (bdd, $J = 16.8, 6.5$ Hz, H(7eq)), 3.25 (d, $J = 9.1$ Hz, H(19)), 3.30 (td, $J = 6.8, 0.7$ Hz, CH_2COAr), 3.33 (s, 19-OMe; 3.52 (d, $J = 9.1$ Hz, H(19)), 3.88 (s, 12-OMe; 5.20 (bs, COOH; 6.83 (s, H(11)), 7.47 (s, H(14)). ^{13}C-NMR $\delta = 19.1$ (C(2)), 19.1(5) (C(6)), 25.4 (C(20)), 27.6 (C(18)), 28.6 (CH_2COOH), 29.8 (C(7)), 35.9 (C(3)), 38.1 (C(3)), 38.4(7), C(4)), 38.4(9) (CH_2COAr), 38.9 (C(1)), 50.9(5) (C(5)), 55.5 (12-OMe), 59.4 (19-OMe), 75.9 (C(19)), 107.6 (C(11)), 124.5 (C(13)), 127.5 (C(8)), 131.2 (C(14)), 156.4(5) (C(9)), 157.3 (C(12)), 177.9 (C=O_{acid}), 199.4 (C=O_{ketone}). MS; m/z: 388 (37, M^+), 315 (100, $M - HO_2CCH_2CH_2^{\bullet}$).

*3.30. Attempted conversion of 12,19-dimethoxy-13-(4-oxobutanoic acid)podocarpa-8,11,13-triene (**33**) into 12,19-dimethoxy-13-formylpodocarpa-8,11,13-triene (**31**)*

A solution of $Cr(CO)_6$ (29 mg, 0.13 mmol) and 12,19-dimethoxy-13-(4-oxobutanoic acid)podocarpa-8,11,13-triene (**33**) (50 mg, 0.13 mmol) in $C_6H_5CH_3$ (2 ml) was refluxed for 2 h; t.l.c. indicated that no reaction had occurred. The solution was cooled and morpholine (22 μl, 0.25 mmol) and propenoic acid (26 μl, 0.38 mmol) were added. The solution was refluxed for a further 2 h, removal of the solvent and p.l.c. gave **33** (45 mg, 90%); no 12,19-dimethoxy-13-formylpodocarpa-8,11,13-triene (**31**) was present.

*3.31. Reaction of pentacarbonyl[(morpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (**12**) with propenoic acid in $C_6H_5CH_3$-d_8*

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (20 mg, 34.6 μmol) and propenoic acid (7.0 μl, 0.10 mmol) in $C_6H_5CH_3$-d_8 (0.5 ml) was refluxed for 15 min. Removal of solvent followed by p.l.c. gave 12,19-dimethoxy-13-formylpodocarpa-8,11,13-triene (**31**) (6.0 mg, 55%). Anal. Found: $M^{+\bullet}$ 316.2038. Calc. for $C_{20}H_{28}O_3$: 316.2059. Anal. Found: $M^{+\bullet}$, 317.2072. Calc. for $C^{13}_{19}CH_{28}O_3$: 317.2065.

*3.32. Attempted reaction of pentacarbonyl-[(morpholino)(13-(12,19-dimethoxy podocarpa-8,11,13-triene))carbene]chromium (**12**) with triethoxyvinylsilane*

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium

(**12**) (0.250 g, 0.433 mmol) and triethoxyvinylsilane (182 μl, 0.864 mmol) in $C_6H_5CH_3$ (5 ml) was refluxed in a sealed pressure vessel under nitrogen for 5 h. Removal of solvent followed by p.l.c. returned **12** (85%).

*3.33. Attempted reaction of pentacarbonyl-[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) with trimethylvinylsilane*

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (0.124 g, 0.215 mmol) and trimethylvinylsilane (70 μl, 0.45 mmol) in $C_6H_5CH_3$ (2.5 ml) was refluxed in a sealed pressure vessel under nitrogen for 4.5 h. Removal of the solvent followed by p.l.c. (hexanes–Et_2O, 2:1) returned **12** (81%).

*3.34. Attempted reaction of pentacarbonyl-[morpholino)(13-(12,19-dimethoxy podocarpa-8,11,13-triene))carbene]chromium (**12**) with phenylethene*

A solution of pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**12**) (95 mg, 0.16 mmol) and phenylethene (40 μl, 0.35 mmol) in $C_6H_5CH_3$ (2 ml) was refluxed in a sealed pressure vessel under nitrogen for 4 h. Removal of the solvent followed by p.l.c. (hexanes–Et_2O, 2:1) returned **12** (46%).

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