Journal of Organometallic Chemistry 626 (2001) 199–220

Journal of Organometallic Chemistry

www.elsevier.nl/locate/jorganchem

Synthesis of chromium aminocarbene complexes of diterpenoids

Paul D. Woodgate *, Hamish S. Sutherland, Clifton E.F. Rickard

Department of Chemistry, The University of Auckland, Private Bag 92019, Auckland, New Zealand

Received 4 January 2001; received in revised form 19 January 2001

Abstract

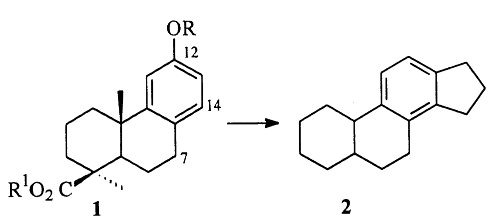
Chromium aminocarbene complexes of podocarpane diterpenoids have been synthesised in good to excellent yields, either by aminolysis of the corresponding alkoxycarbene, or by treatment of the morpholino amide with disodium pentacarbonylchromium and subsequent elimination of silyloxide.

Keywords: Chromium; Aminocarbene; Diterpenoid

1. Introduction

The use of organotransition metal mediated chemistry in the transformation of podocarpic acid (**1**; $R^1 = R^2 = H$) derivatives in earlier work by us has been directed generally towards the modification of the aromatic ring-C by the construction of a fused pentacyclic ring (D ring), leading to molecules possessing a steroidal skeleton **2** (Scheme 1).

During the course of this work we have investigated nucleophile addition to (η^6-diterpenoidarene)-tricarbonylchromium complexes [1–5] (generally limited to carbanions derived from carbon acids with a $pK_a > 22$). Sweigart et al. [6] have prepared the analogous cationic (η^6-arene)tricarbonylmanganese diterpenoid complexes as a 1.1:1 mixture of α and β diastereoisomers. Reaction of these complexes with phenylmagnesium bromide gave an inseparable mixture of 13- and 14-phenyldienyl products in 90% yield. With the aim of minimising the number of products [7] we attempted to complex a 7β-OR diterpenoid (R = H, TBDMS) using the Sweigart procedure, the expectation being that a benzylic hydroxy or alkoxy group would direct the $Mn(CO)_3$ moiety to the β face of the arene, by analogy with the $Cr(CO)_3$ work. In the event, the only identifiable product was the non-complexed styrene analogue resulting from elimination promoted by either $AgBF_4$ or a cationic manganese species. The use of $Mn(CO)_3(\eta^6\text{-naphthalene})^+$ in an attempt to transfer the $Mn(CO)_3^+$ moiety to a 7β-OCH_2OMe podocarpic acid derivative gave only a trace of the desired (η^6-diterpenoidarene)tricarbonylmanganese complex. We have synthesised the analogous cationic (η^6-diterpenoidarene)(cyclopentadienyl)ruthenium complexes (α/β, 5:1) in good yield using the transfer reagent $(MeCN)_3RuCp^+$ [8]. However, nucleophile addition to simple (η^6-arene)$RuCp^+$ complexes is limited [9] to either hydride or phenyllithium, although the related η^6-arene (pyrazolylborate)ruthenium [10] complexes will also react with hydroxide and cyanide to give η^5-cyclopentadienyl complexes [11]. Since a much wider range of nucleophiles [12–17] undergo addition to cationic tricarbonyl(η^5-pentadienyl)iron complexes, preparation of some diterpenoid congeners was also studied [18]. The yields of the β 8(9),10(11) and α 8(14),12(13) η^4-dienyliron intermediates, and of the derived cationic η^5-cyclopentadienyl complex(es), were too low, however, to warrant investigation of reactions of the latter.

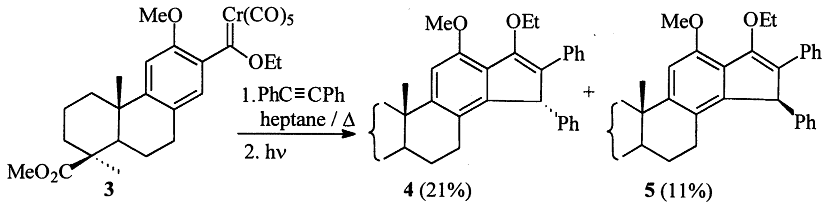


Scheme 1.

* Corresponding author. Tel.: + 64-9-3737599 ext. 8262; fax: + 64-9-3737422.

E-mail address: p.woodgate@auckland.ac.nz (P.D. Woodgate).

0022-328X/01/$ - see front matter
PII: S0022-328X(01)00700-8

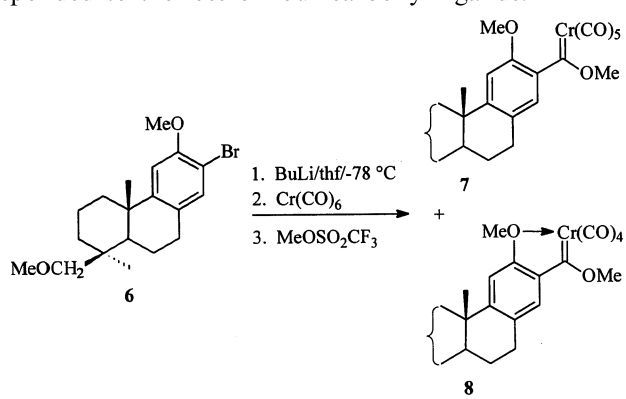


Scheme 2.

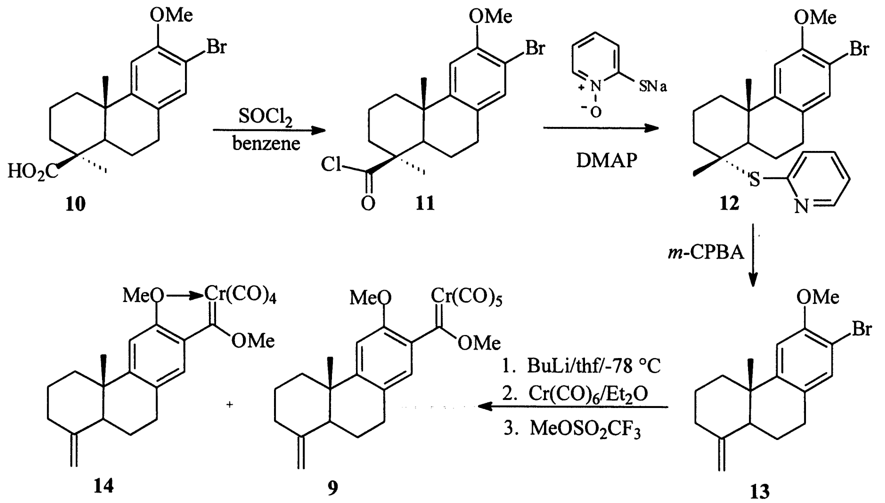
In contrast to exploration of the above options for attaching carbon nucleophiles to η[6]-arene transition metal complexes, chromium alkoxycarbenes offer a different mode of preparation and reaction. Initial investigations showed that reaction of phenylacetylene with the pentacarbonylchromium ethoxycarbene complex of the diterpenoid **3** led to the ring-C aromatic steroidal analogues **4/5** (Scheme 2) [19]. Since our initial study, greater understanding has been accumulated with regard to potential control of the benzannulation versus cyclopentaannulation pathways [20] during reaction of an alkyne with a chromium carbene complex. In particular, chromium aminocarbenes offer the opportunity for the cyclopentaannulation route to dominate. These findings provided the impetus to extend our earlier work by investigating the preparation of chromium aminocarbenes derived from podocarpic acid, and their reactions with alkenes and alkynes, as a route to ring-C aromatic steroidal analogues.

2. Discussion

Preparation of the diterpenoid aminocarbenes required the synthesis of the corresponding precursor alkoxycarbenes. In order to avoid reaction of a 19-carbonyl group with BuLi, the diterpenoid alkoxycarbene chosen as the synthesis target was the 19-ether, pentacarbonyl[methoxy(13 - (12,19 - dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**7**) (Scheme 3). The aryl bromide **6** [21] underwent metal–halogen exchange with BuLi in THF at −78°C; after 3 min the solution of the 13-lithioarene was transferred into a slurry of $Cr(CO)_6$ (1.05 equivalents) in diethyl ether at 0°C. After 3 h at room temperature the resulting lithio acylate was treated at 0°C with methyl triflate. This sequence gave **7** (76%) and tetracarbonyl [(methoxy)(13-(12,19-dimethoxypodocarpa-8,11,13-triene-C^{13},O^{12}))carbene]-chromium (**8**) (2%; a higher percentage was isolated from some runs due to the variable length of time needed for removal of solvent under vacuum). The pentacarbonyl carbene complex **7** showed a weak molecular ion in the mass spectrum at m/z 522.1349 ($C_{26}H_{30}CrO_8$), and the base peak at m/z 382 corresponded to expulsion of all five carbonyl ligands. Peaks due to carbonyl ligands occurred at 2063, 1989 and 1954 cm^{-1} in the IR spectrum (hexanes). A broad singlet at 4.16 ppm in the ^{1}H-NMR spectrum was assigned to the carbene methoxy group, and the singlets at 6.42 and 6.74 ppm were assigned to H(14) and H(11), respectively [19]. Resonances at 216.1 and 225.3 ppm in the ^{13}C-NMR spectrum were characteristic of the *cis*- and *trans*-carbonyl ligands, respectively, and the signal due to the carbene carbon was observed at 355.4 ppm. The NMR spectra of the minor product **8** confirmed the presence of the ligated 12-methoxy group ($\delta_{H(OMe)}$ 4.85, $\delta_{C(OMe)}$ 64.5 ppm: δ_{CCr} 333.8; δ_{CO} 232.0, 231.3 and 213.9 ppm). For a related series of compounds, it has been shown that the lower the carbonyl force constant, the longer the C≡O bond and the higher the δ_{CO} [22]. The X-ray structural data [23] for the benzenoid analogue, pentacarbonyl[(methoxy)(η-2-methoxyphenyl)carbene]chromium, indicates that the CO ligand which is *trans* to the 2-methoxy group has the longest C≡O bond. Consequently, it has the carbonyl signal at lowest field in the ^{13}C-NMR spectrum, followed (decreasing δ) by the CO ligand which is *trans* to the carbene carbon and then the carbonyls which are *trans* to each other. Therefore, the signal at 232.0 ppm in the ^{13}C-NMR spectrum of the diterpenoid carbene **8** was assigned to the carbonyl ligand *trans* to the O-donor, the signal at 231.3 ppm was assigned to the carbonyl ligand *trans* to the carbene, and the signal at 213.9 ppm was assigned to the carbonyl ligands which are *trans* to each other. High-resolution mass spectroscopy gave the molecular ion at 494.1408 ($C_{25}H_{30}CrO_7$), and the base peak at m/z 382 corresponded to the loss of four carbonyl ligands.



Scheme 3.



Scheme 4.

Small amounts (< 5%) of 12,19-dimethoxypodocarpa-8,11,13-triene were also isolated, due to deprotonation of the solvent (THF [24] or diethyl ether) by the intermediate 13-lithio diterpenoid. The use of THF as the solvent in the metal–halogen exchange, and of diethyl ether for reaction of the ensuing aryllithium with $Cr(CO)_6$, was crucial to the success of the diterpenoid alkoxycarbene synthesis. The insolubility of the 13-bromo diterpenoid **6** in diethyl ether at −78°C precluded use of the latter as the solvent for the metal–halogen exchange reaction. When THF was used as the solvent for both the metal–bromide exchange and the subsequent reactions with $Cr(CO)_6$ and methyl triflate, a polymer ($[CH_2(CH_2)_2CH_2O]_n$; δ_H 1.62, 3.41 ppm) formed which was impossible to separate from the desired carbene complex.

In order to convert the diterpenoid derivatives eventually into the more common (e.g. 3-oxo) steroidal analogues, modification of the diterpenoid A-ring into an exocyclic 4(18)-alkene was desirable, since further functionalisation could be achieved using the *exo* methylene group as a handle. The alkoxycarbene **9** was synthesised (Scheme 4) in four steps from 13-bromo-12-methoxypodocarpa-8,11,13-trien-19-oate (**10**). Treatment of the acid chloride **11** with the sodium salt of 1-hydroxy-2-pyridinethione gave the sulfide **12** in quantitative yield; an X-ray crystallographic analysis (Fig. 1) showed that inversion had occurred at C(4) [25]. Since formation of **12** was 100% stereoselective it is suggested that the pyridyl ester derived from **11** reacts via a near-concerted pathway, involving attack of thione sulfur at the least hindered α face of the diterpenoid concomitant with decarboxylation. The sulfide was oxidised to the sulfoxide with *m*-CPBA, and subsequent thermally promoted cycloelimination gave the desired 4(18)-alkene **13**. Formation of the carbene complex **9** was achieved (72%) using the methodology developed for **7**; small amounts of the tetracarbonyl carbene complex **14** were also isolated.

Four routes have been devised for the synthesis of chromium aminocarbenes [26,27]. Aminolysis of the corresponding alkoxycarbene is restricted to primary amines or non-hindered secondary amines. Sterically demanding amine groups can be introduced by aminolysis of acyloxycarbenes, which are highly reactive species available from the corresponding tetraalkylammonium acylate and acetyl bromide [28]. Aminocarbene complexes having hydrogen on the carbene carbon cannot be prepared by aminolysis of either an alkoxycarbene or an acyloxycarbene, since the corresponding formyl complexes are strong hydride donors which cannot be O-alkylated or O-acylated. Such aminocarbene complexes can, however, be synthesised by reacting $Na_2Cr(CO)_5$ with (chloromethylene)-dialkylammonium chlorides [29,30]. A better route involves reaction of alkyl and aryl *N*,*N*-dialkylamides,

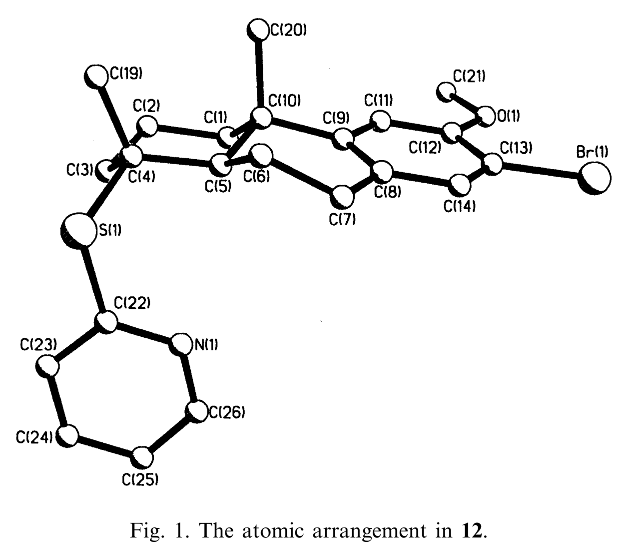
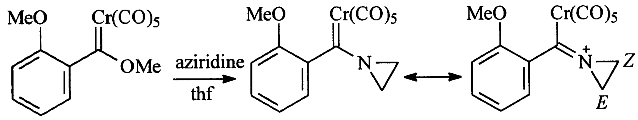


Fig. 1. The atomic arrangement in **12**.

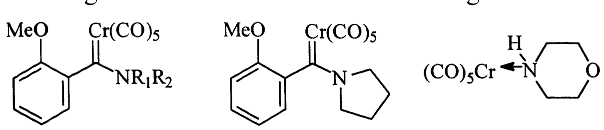


15 16

Scheme 5.

lactams or tertiary formamides with $Na_2Cr(CO)_5$ [31,32] or $K_2Cr(CO)_5$ [33] to give a dianionic intermediate which undergoes O-silylation with chlorotrimethylsilane to give the monoanionic intermediate. Alumina-promoted elimination of trimethylsilyloxide then affords the aminocarbene in good to excellent yields.

In the present work, a number of benzenoid aminocarbene model compounds were synthesised in order to allow assignments derived from the spectroscopic data of the simple compounds to be applied to the diterpenoid aminocarbenes. Aminolysis of pentacarbonyl-[(methoxy)(2-methoxyphenyl)carbene]chromium (**15**) with aziridine gave pentacarbonyl[(aziridinyl)(2-methoxyphenyl)carbene]chromium (**16**) (86%) (Scheme 5). The molecular ion at m/z 352.9968 ($C_{15}H_{11}CrNO_6$) in the mass spectrum underwent sequential loss of five carbonyl ligands and then of ethene from the aziridine group to give an odd electron fragment ion at m/z 185. A NOESY spectrum of the aziridinyl carbene showed a weak nOe between a doublet at 6.91 ppm ($J = 8.3$ Hz) and the methoxy group (3.78 ppm), and therefore the signal at 6.91 ppm was assigned to H(3). A ddd splitting pattern at 7.24 ppm ($J = 8.3$, 7.5, 1.6 Hz) was assigned to H(4), a triplet at 6.99 ppm ($J = 7.5$ Hz) to H(5) and the doublet of doublets at 6.83 ppm ($J = 7.5$, 1.6 Hz) to H(6). Strong overlap of the nitrogen π-orbital with the metal π-orbitals results in significant carbene carbon–nitrogen double bond character. That is, restricted rotation around the C=N bond results in *E* and *Z* aziridinyl methylene groups. For an *N*,*N*-diethylaminocarbene derivative the solvent induced chemical shift difference [$\Delta\delta(CHCl_3\text{-}d\text{–}C_6H_6\text{-}d_6)$ 1.00] for an *E*-CH_2 group is larger than for a *Z*-CH_2 group ($\Delta\delta$ 0.54) [34]. The triplet at δ_H 2.58 in the spectrum of the aziridinyl complex **16** in C_6H_6-d_6 was therefore assigned to $NCH_2(E)$ [$\Delta\delta(CHCl_3\text{-}d\text{–}C_6H_6\text{-}d_6) = 1.20$] while that at 3.24 ppm was assigned to $NCH_2(Z)$ ($\Delta\delta$ 1.04). A ^{13}C–^1H correlation spectrum then showed that the signal at δ_C 27.6 represented $CH_2(Z)$, while that at 28.4 ppm represented $CH_2(E)$. The ^{13}C-NMR spectrum included signals for the *cis* CO ligands at 217.5 and the *trans* CO ligand at 224.0,



17: $R_1 = R_2 = H$
18: $R_1 = Me, R_2 = H$
19: $R_1 = R_2 = Me$

20

21

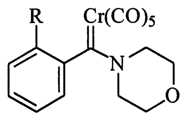
while the signal due to the carbene carbon occurred at 270.2 ppm.

Reaction of pentacarbonyl[(methoxy)(2-methoxyphenyl)carbene]chromium (**15**) with ammonia in THF at room temperature gave pentacarbonyl[(dihydroamino)-(2-methoxyphenyl)carbene]chromium (**17**) (99%). Assignment of the signals due to the NH hydrogens in the ^1H-NMR spectrum of **17** (*Z*-NH, 8.46; *E*-NH, 9.01 ppm) was based upon the positions of the signals due to the *E* and *Z* NH protons in the NMR spectrum of the aminocarbene (**18**) (92%; *E*/*Z*, 2:1), prepared similarly from reaction of the methoxycarbene **15** with methylamine. In the ^1H-NMR spectrum of **18**, the methyl groups appeared as doublets at 2.94 ($J = 4.8$ Hz) and 3.73 ppm ($J = 5$ Hz) and were assigned to $NCH_3(E)$ and $NCH_3(Z)$ on the basis of their respective $\Delta\delta$ values. The *E*-NH signal at 9.12 was broad, as was the *Z*-NH signal at 8.78 ppm [35]. The *E* and *Z* isomers also showed different chemical shifts for the aromatic protons, the relative intensity of each signal being used to aid assignments. Different chemical shifts [except for C(2)] were also observed for each isomer in the ^{13}C-NMR spectrum.

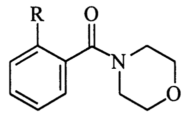
Aminolysis of **15** with dimethylamine gave the (dimethylamino)carbene **19** (92%) [31]. The singlets at 3.06 and 3.97 ppm were assigned to $NCH_3(E)$ and $NCH_3(Z)$, respectively, by comparison with those from the carbene **18**, as were the *N*-methyl groups in the ^{13}C-NMR spectrum [$NCH_3(E)$, 45.3; $CH_3(Z)$, 50.9 ppm].

Reaction of pyrrolidine with **15** gave pentacarbonyl[(2-methoxyphenyl)(pyrrolidinyl)carbene]chromium (**20**) (96%). The COSY NMR spectrum showed that the signals due to CH_2CH_2N at 1.98 ppm correlated with those due to NCH_2 at 3.19 and 3.35 ppm, while those due to CH_2CH_2N at 2.19 ppm correlated with those due to NCH_2 at 4.24 and 4.30 ppm. Signals in the ^1H-NMR spectrum were assigned to either the *E* or *Z* isomer on the basis of $\Delta\delta$ values, and assignments of signals to either axial or equatorial hydrogens were made by comparison with those in the morpholino aminocarbene complex (see later). The ^{13}C-NMR data was assigned from ^{13}C–^1H correlation spectra.

Reaction of morpholine with the methoxycarbene **15** did not afford the expected aminocarbene, but gave (morpholino)pentacarbonylchromium (**21**) (37%) [36]. Repeating the reaction using 20 molar equivalents of morpholine again gave (**21**) (28%). Although the parent pentacarbonyl[(morpholino)(phenylcarbene]chromium (**22**) has been synthesised (76%) from treatment of the corresponding phenylmethoxy carbene with an excess of morpholine [37], the increase in steric hindrance due to the presence of an *ortho* methoxy group in (**15**) is apparently enough to inhibit the desired substitution. The failure of morpholine to give an aminocarbene complex contrasts with the successful reaction with pyrrolidine, and emphasizes that aminolysis of the methoxycarbene **15** is highly dependent on the steric bulk of the amine.



22: R = H
25: R = OMe



23: R = H
24: R = OMe

The non-aromatic carbene, pentacarbonyl-[(methyl)(morpholino)carbene]chromium has been synthesised (78%) by treatment of *N*-acetylmorpholine with $Na_2Cr(CO)_5$, followed by O-silylation then elimination of trimethylsiloxide [33]. In the present work, pentacarbonyl[(morpholino)(phenyl)carbene]chromium (**22**) was chosen as a model system to explore this route. Treatment of *N*-(morpholino)phenylamide [38] (**23**) in THF with $Na_2Cr(CO)_5$ freshly prepared from sodium naphthalenide and $Cr(CO)_6$ [32,39], followed by O-silylation with chlorotrimethylsilane and then alumina-mediated elimination, gave **22** (48%). Mass spectroscopy (DEI) gave the molecular ion at m/z 367.0148 ($C_{16}H_{13}CrNO_6$) and the base peak at m/z 227, corresponding to the sequential loss of five carbon monoxide ligands. A weak peak at m/z 350 analysed correctly for $C_{22}H_{26}N_2O_2$ and is due to the dimerisation of two metal-free carbene units. Pleasingly, reaction of (*N*-morpholino)2-methoxyphenylamide (**24**) (from 2-methoxybenzoyl chloride and $SOCl_2$, then morpholine) with $Na_2Cr(CO)_5$, followed by O-silylation and silyloxide elimination, gave pentacarbonyl[(morpholino)(2-methoxyphenyl)carbene]chromium (**25**) (79%). The molecular ion occurred at m/z 397.0240 ($C_{17}H_{15}CrNO_7$) in the mass spectrum, and the carbene "dimer" was detected as a weak peak at m/z 410.2198 ($C_{24}H_{30}N_2O_4$). The COSY and $^{13}C-^{1}H$-NMR spectra of **25** in $CHCl_3$-*d* led to the assignments in Table 1. Solvent induced chemical shifts were studied in an attempt to determine the E/Z assignments for **25**, but no reliable information could be obtained as the signals due to the axial and equatorial hydrogens on a particular carbon did not show the same chemical shift differences on changing the solvent from $CHCl_3$-*d* to C_6H_6-d_6. However, $\Delta\delta$ values could be determined for the phenyl complex **22** (Table 2; assignments were confirmed by selective decoupling experiments), and this information was then applied to the chemical shifts for the 2-methoxyphenyl derivative **25**. Since the distinction between the CH_2 signals as either axial or equatorial for the aminocarbene derivative **25** could not be made from the NMR spectra, tentative assignments were made by comparison with those for a related *trans*-2,6-dimethylmorpholino aminocarbene [40].

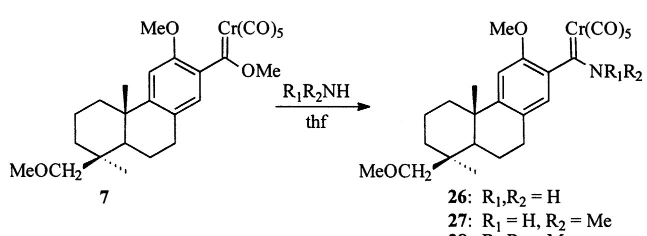
Table 1
C–H correlations for (morpholino)(2-methoxyphenyl)carbene) **25**

δ_H ($CHCl_3$-*d*, ppm)	δ_C ($CHCl_3$-*d*, ppm)	Assignment
3.42–3.57	55.1	$NCH_{2(E)}$
3.57–3.68	67.2	$OCH_{2(E)}$
4.02	67.9	$OCH_{(Z)axial}$
4.09	67.9	$OCH_{(Z)equatorial}$
4.43	60.1	$NCH_{(Z)axial}$
4.71	60.1	$NCH_{(Z)equatorial}$

Table 2
Solvent induced shifts for (morpholino)(phenyl)carbene **22**

δ ($CHCl_3$-*d*, ppm)	δ ($CHCl_3$-*d*, ppm)	$\Delta\delta$ ($CHCl_3$-*d*–C_6H_6-d_6)	Assignment
4.58	3.93	0.65	$NCH_2(Z)$
4.08	3.40	0.68	$OCH_2(Z)$
3.62	2.72	0.90	$OCH_2(E)$
3.50	2.56	0.94	$NCH_2(E)$

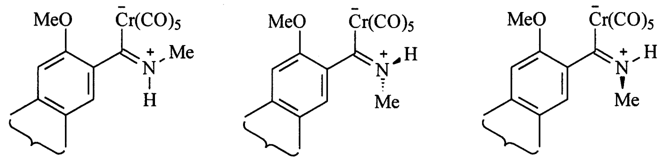
With the practical experience and spectroscopic information garnered from the model aminocarbenes in hand, syntheses of the diterpenoid analogues were investigated, following the particular method developed for the corresponding benzenoid aminocarbene. Thus, treatment of the methoxy carbene **7** with ammonia in THF gave pentacarbonyl[(dihydroamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene)carbene]chromium (**26**) (89%) (Scheme 6). Broad signals in the ^1H-NMR spectrum at 8.65 and 8.94 ppm were assigned to NH(Z) and NH(E), respectively. Two singlets at 6.74 [H(14)] and 7.77 ppm [H(11)] were observed in the aromatic region. Reaction of methylamine with **7** gave pentacarbonyl[(methylamino)(13 - (12,19 - dimethoxypodocarpa-8,11,13-triene) carbenechromium (**27**) (82%). In the ^1H-NMR spectrum ($CHCl_3$-*d*, 298 K, 400 MHz) the pairs of doublets ($J = 4.6$ Hz; two rotamers) at 2.93 and 2.94 were assigned to *N*-methyl (E) and the doublet at 3.69 ppm ($J = 5.0$ Hz) was assigned to *N*-methyl (Z) ($E/Z = 3{:}2$). There were three singlets for H(14), each isomer as well as each rotamer of the E isomer (Scheme



7

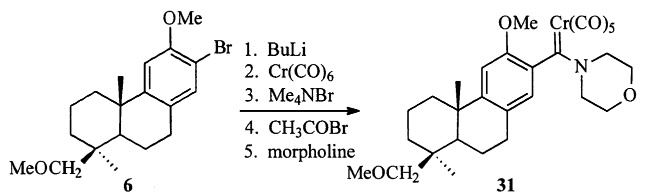
26: $R_1,R_2 = H$
27: $R_1 = H, R_2 = Me$
28: $R_1,R_2 = Me$
29: $R_1,R_2 = (CH_2)_2$
30: $R_1,R_2 = (CH_2)_4$

Scheme 6.



27 (*Z*) **27** (*E*) **27** (*E*)

Scheme 7.



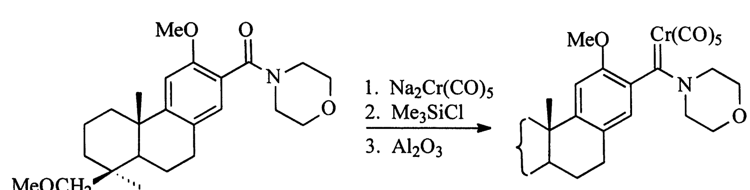
6 **31**

Scheme 8.

7) (atropisomers are also possible) having a distinct chemical shift; the *E*/*Z* assignments for H(14) were made by comparison with the integral areas of the signals due to NH(*E*) and NH(*Z*) (9.08 and 8.75 ppm, respectively). The isomer/rotamer mixture was also indicated by the ^{13}C-NMR spectrum, in which there were three signals due to a carbene carbon (268.6, 280.7 and 281.4) and two [223.6, ($C{\equiv}O_{(E)}$); 224.2 ppm, ($C{\equiv}O_{(Z)}$)] for a *trans* carbonyl ligand.

Reaction of dimethylamine with **7** in THF at room temperature gave pentacarbonyl[(dimethylamino)(13-(12,19 - dimethoxypodocarpa - 8,11,13 - triene)carbene]-chromium (**28**) (89%). The carbene moiety was evident by ^{1}H-NMR signals due to the *N*-methyl protons as singlets at 3.06 [NCH_3(*E*)] and 3.94 ppm [NCH_3(*Z*)]. Pentacarbonyl[(aziridinyl)(13 - (12,19 - dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**29**) (81%) ($M^{+\bullet}$ 533.1500, $C_{27}H_{31}CrNO_7$) was synthesised by aminolysis of the alkoxycarbene **10** with aziridine. The presence of an aziridinyl group was confirmed by the doublets ($J = 5.5$ Hz) at 2.59 [NCH_2(*E*)] and 3.20 ppm [NCH_2(*Z*)] in the ^{1}H-NMR spectrum, a COSY spectrum showing that these doublets were coupled only with each other. Pentacarbonyl[(pyrrolidinyl)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**30**) ($M^{+\bullet}$ 561.1833, $C_{29}H_{35}CrNO_7$) was prepared (91%) similarly. The pyrrolidinyl *N*-methylene protons were observed as doublets of doublets of doublets at 3.21 [$CH_{ax(E)}$], 3.37 [$CH_{eq(E)}$], 4.20 [$CH_{ax(Z)}$], and 4.26 ppm [$CH_{eq(Z)}$]. COSY, ^{13}C–^{1}H and long range ^{13}C–^{1}H-NMR spectra confirmed that the relative assignments for H(11) and H(14) in the diterpenoid alkoxycarbene **3** [19] are also applicable to the aminocarbenes.

In contrast to the successful aminolyses describe above, the morpholino carbene **31** could not be synthesised from the methoxy carbene, but was available from an acyloxycarbene (Scheme 8). Thus, lithium–halogen exchange (*t*-BuLi, −100°C) of the 13-bromoarene **6** followed by reaction of the aryl carbanion with $Cr(CO)_6$ gave a lithium acylate which was converted into the tetramethylammonium acylate. Reaction of this salt with acetyl bromide gave the acetyloxycarbene, treatment of which with morpholine afforded the morpholino carbene **31** (37%). A better route to **31** proceeded via *N*-morpholino-12,19-dimethoxypodocarpa-8,11,13-triene-13-carboxamide (**32**), prepared (90%) from the 13-lithio diterpenoid and 4-morpholinocarbamoyl chloride (Scheme 9). Addition of the amide **32** to a solution of disodium pentacarbonylchromium, followed by O-silylation and alumina-mediated silyloxide elimination gave pentacarbonyl[(morpholino)(13-(12,19 - dimethoxypodocarpa - 8,11,13 - triene)carbene]-chromium (**31**) (76%) ($M^{+\bullet}$ 577.1803, $C_{29}H_{35}CrNO_8$). The ^{13}C-NMR spectrum showed peaks at 217.3 ($C{\equiv}O_{cis}$), 224.0 ($C{\equiv}O_{trans}$) and 271.6 ppm ($C_{carbene}$) while the infrared spectrum showed absorptions due to carbonyl ligands at 2052, 1971 and 1926 cm^{-1}. As with the pyrrolidino carbene, high concentrations of the morpholino carbene in $CHCl_3$-*d* caused the signal due to H(14) to double, due to the detection of rotamers. Increasing the temperature ($CHCl_3$-*d* or C_6H_6-d_6) resulted in broadening of the NMR signals due to partial decomposition of the carbene, and therefore the rotational energy barriers could not be measured. A single crystal of the aminocarbene **31** suitable for X-ray diffraction analysis (Fig. 2) was grown from a solution in hexanes at 0°C. The morpholino substituent is a good π-donor, and therefore the N–$C_{carbene}$ bond [1.315(4) Å] shows significant double bond character. Increasing the π-donor capacity of the carbene heteroatom decreases the amount of back-bonding, and consequently the Cr–$C_{aminocarbene}$ bond [2.111(3) Å] is longer than the Cr–$C_{alkoxycarbene}$ bond (1.97–2.05 Å) [23]. The *cis* CO bonds are longer Cr–C [1.884(5)–1.891(5) Å] than the *trans* CO bond [1.857(4) Å]; the carbene is a poorer π-acceptor than a carbonyl ligand, and therefore the



32 **31**

Scheme 9.

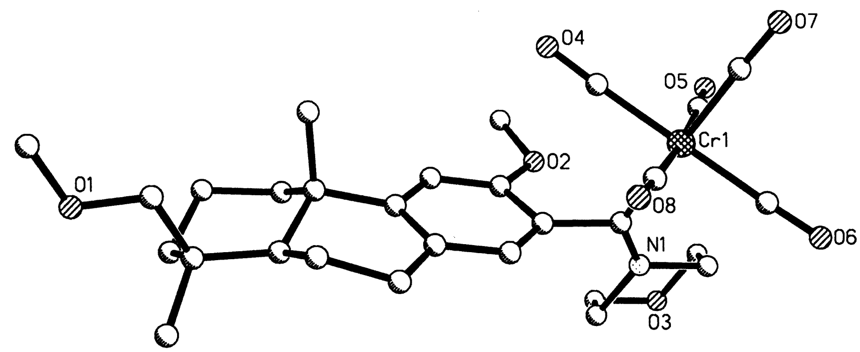


Fig. 2. The atomic arrangement in **31**.

trans CO can accept more of the π-electron density from the chromium relative to the *cis* CO ligands, which have to compete with each other.

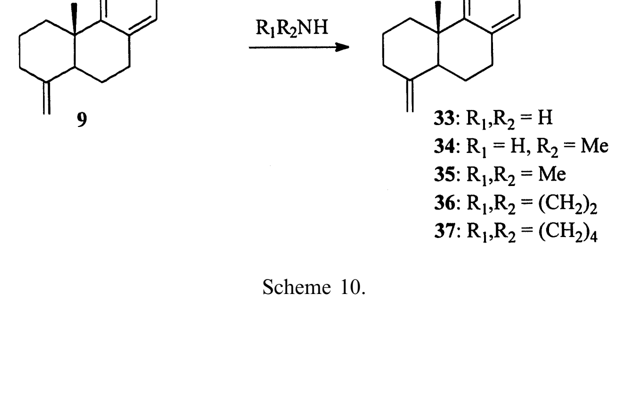
Condensation of ammonia gas into a solution of the alkoxycarbene **9** gave pentacarbonyl[(dihydroamino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**33**) (Scheme 10). Recrystallisation of **33** from hexanes gave yellow flaky crystals suitable for X-ray crystallographic analysis (Fig. 3). The Cr–$C_{carbene}$ [2.105(4) Å] and N–$C_{carbene}$ [1.302(5) Å] bond lengths were similar to those of the morpholino analogue **31**.

Similar reaction of **9** with methylamine gave pentacarbonyl[(methylamino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene)carbene]chromium (**34**) (92%), as a mixture (5:1) of *E* and *Z* isomers (cf. Scheme 7). The *E* isomer existed as a pair of rotamers at 298 K (^{1}H-NMR, 400 MHz). Both *E* and *Z* isomers had different chemical shifts for a particular hydrogen or carbon. For example, signals due to the carbene carbon were observed at 280.7 ($C_{carbene(Z)}$) and 281.3 ppm ($C_{carbene(E)}$). The signals due to the *N*-methyl hydrogens were observed as doublets at 2.95 (*E* isomer, $J = 4.9$ Hz) and 3.70 ppm (*Z* isomer, $J = 5.1$ Hz), and broad signals at 8.77 and 9.10 ppm were assigned to $NH_{(Z)}$ and $NH_{(E)}$, respectively. Surprisingly, the analogous dimethylaminocarbene **35** was relatively unstable. Signals in the ^{13}C-NMR spectrum at 45.2(5) and 45.3 ppm were assigned to $NCH_{3(Z)}$ and that at 50.8 ppm was assigned to $NCH_{3(E)}$. Reaction of aziridine with the alkoxycarbene **9** gave pentacarbonyl-[(aziridinyl)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]-chromium (**36**). Signals due to the aziridinyl group appeared at 28.7 ($NCH_{2(Z)}$) and 29.1(5) ppm ($NCH_{2(E)}$) in the ^{13}C-NMR spectrum. Pentacarbonyl[(pyrrolidinyl)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (37) (89%) was shown to be a mixture (7:3) of rotamers by ^{1}H-NMR analysis (298 K, 400 MHz). Singlets due to H(14) at 6.33 and 6.37 ppm were assigned to the major and minor rotamers, respectively.

Although pentacarbonyl[(morpholino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]-chromium (**38**) could not be synthesised from treatment of **9** with morpholine, it was available in good yield (77%) by adding the amide **39** to a solution of $Na_2Cr(CO)_5$ at −78°C, followed by O-silylation of the dianion and then alumina-mediated elimination of trimethylsilyloxide (Scheme 11). ^{1}H-NMR spectra showed that **38** existed as a mixture (1:1) of rotamers (298 K, 400 MHz), signals due to H(14) being observed at 6.35 and 6.40 ppm.

In order to ascertain whether steric or electronic effects were responsible for the variation in yields of insertion products (to be published), *trans*-2,6-dimethylmorpholino carbene complexes (Scheme 12) were synthesised to compare with the yields from the morpholino complexes. 12-Methoxy-19-norpodocarpa-4(18),8,11,13-tetraen-13-oic acid (**41**) was prepared by metal–halogen exchange on the 13-bromo diterpenoid **13** followed by quenching of the lithioarene with solid carbon dioxide. Reaction of racemic *trans*-2,6-dimethylmorpholine [40] with the derived acid chloride **41** gave 12-methoxy-*N*-(*trans*-2,6-dimethylmorpholino)-19-norpodocarpa-4(18),8,11,13-tetraene-13-carboxamide (**43**). Signals in the ^{1}H-NMR spectrum (400 MHz) at 6.72, 6.79, 6.80 and 6.84 ppm were assigned to H(11), indicating that the amide was a mixture of four rotamers (two from each diastereoisomer) at 298 K.

Addition of the amide **43** to $Na_2Cr(CO)_5$ in THF at −78°C followed by quenching with chlorotrimethylsi-



Scheme 10.

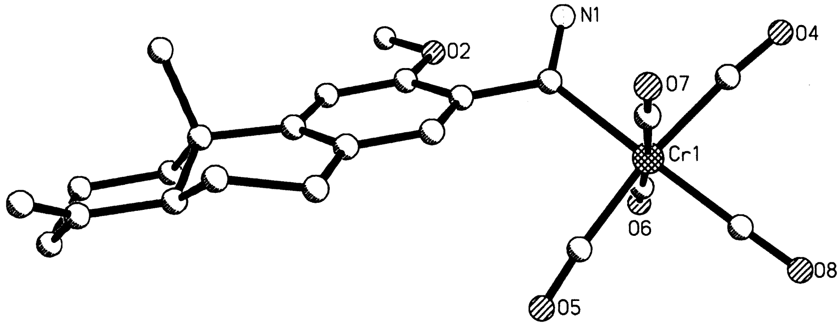
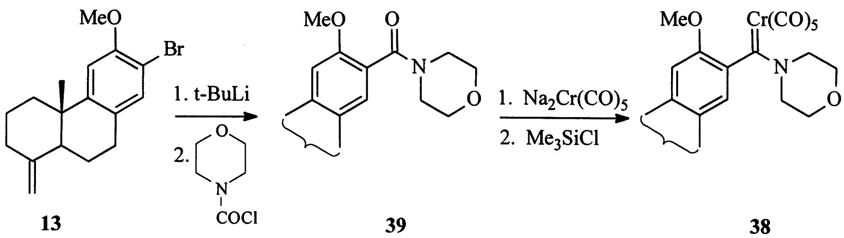
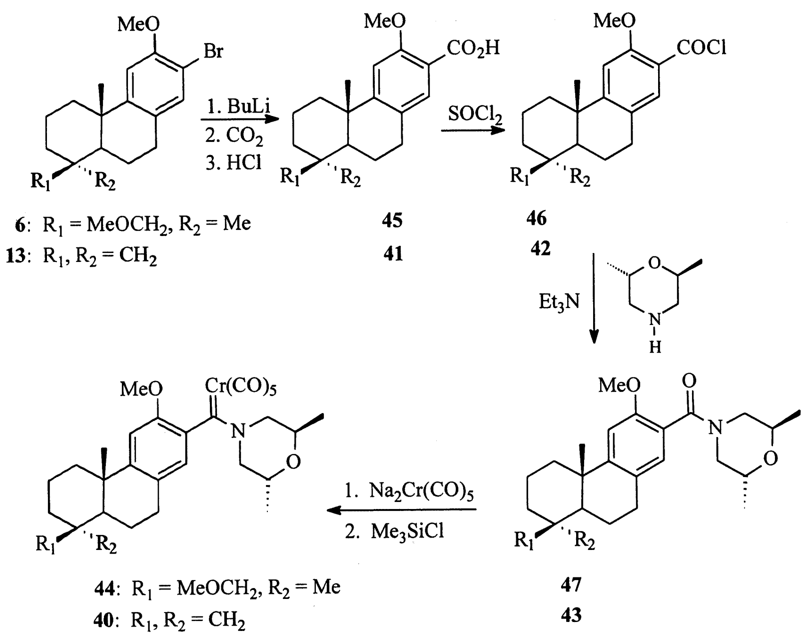


Fig. 3. The atomic arrangement in **33**.



Scheme 11.



Scheme 12.

lane and alumina-mediated silyloxide elimination gave pentacarbonyl[(*trans*-2,6-dimethylmorpholino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene)-carbene] chromium (**40**) (57%) (Scheme 12). The NMR spectra of **40** were complicated, three carbene carbon signals being observed in the ^{13}C spectrum, at 272.1, 272.2 and 272.3 ppm. The molecular ion was observed at m/z 559.1668 ($C_{29}H_{33}CrNO_7$) in the mass spectrum, the base peak at m/z 419 corresponding to the loss of five carbonyl ligands from the molecular ion. The 19-methyl ether analogue, pentacarbonyl[(*trans*-2,6-dimethylmorpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**44**), was synthesised (**6** → **45** → **46** → **47** → **44**) by the route developed for the 4(18)-alkene aminocarbene (**40**). Again, the NMR spectra were complicated by the presence of rotamers. Thus, four signals due to the carbene carbon were observed in the ^{13}C-NMR spectrum (272.0, 272.2, 273.9

and 274.1 ppm), and four singlets assigned to H(14) were observed in the ^{1}H-NMR spectrum (6.22, 6.25, 6.32 and 6.35 ppm).

2.1. X-ray crystal structures of **12**, **31**, and **33**

Data were collected on a Siemens SMART area detector diffractometer using 0.3° frames and profile fitting. Lorentz, polarisation and absorption corrections [41] were applied and equivalent reflections averaged to give 4554 unique data for **12**, 5078 unique data for **31**, and 4631 unique data for **33**. Unit cell parameters were obtained by least-squares fit to all data with $I > 10\sigma(I)$. The structures were solved by direct methods [42] and refined by full-matrix least-squares on F^2 [43]. 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) 0.0204 for **12**, 0.0467 for **31**, and 0.0514 for **33**. Crystal data and refinement parameters are given in Table 3 and the structures, including the absolute configuration, are shown in Figs. 1–3.

2.2. Summary

We have shown that aminocarbene complexes of diterpenoids can be synthesised in excellent yield either by the aminolysis of the corresponding alkoxycarbene or by treatment of the morpholino amide with disodium pentacarbonylchromium and subsequent elimination of silyloxide. Reactions of these complexes with alkenes and alkynes will be reported in due course.

3. Experimental

3.1. Pentacarbonyl[(methoxy)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]-chromium (7)

Butyllithium (1.30 ml, 2.09 mol l^{-1}) was added to a solution of 13-bromo-12,19-dimethoxypodocarpa-8,11,13-triene (**6**) (0.996 g, 2.71 mmol) [21] in THF (7 ml) at −78°C. The solution was stirred at −78°C for 4 min and then, transferred into a slurry of $Cr(CO)_6$ (0.73 g, 3.31 mmol) in ether (10 ml) at 0°C. The solution was warmed to room temperature and stirred for 3 h. Methyl triflate (0.45 ml, 3.97 mmol) was added,

Table 3
X-ray data collection and processing parameters

	12	**31**	**33**
Formula	$C_{22}H_{26}BrNOS$	$C_{29}H_{35}CrNO_8$	$C_{23}H_{23}CrNO_6$
Molecular weight	432.41	577.58	461.42
Temperature (K)	203	293	293
Wavelength (Å)	0.71073	0.71073	0.71073
Crystal system	Orthorhombic	Monoclinic	Orthorhombic
Space group	$P2_12_12_1$	$C2$	$P2_12_12_1$
a (Å)	7.3691(1)	24.6901(8)	7.1376(1)
b (Å)	12.3346(2)	7.6247(2)	8.8489(2)
c (Å)	22.0360(1)	15.6622(5)	36.3063(3)
β (°)		97.257(1)	
V (Å^3)	2002.96(5)	2924.86(15)	2293.10(6)
Z	4	4	4
D_{calc} (g cm^{-3})	1.434	1.312	1.337
$F(000)$	896	1216	960
μ (mm^{-1})	2.17	0.44	0.54
Crystal size (mm)	0.40 × 0.38 × 0.36	0.25 × 0.20 × 0.06	0.43 × 0.22 × 0.04
2θ Range (°)	1.8–28.3	1.3–26.0	1.2–26.4
Reflections collected	12481	17241	13353
Independent reflections	4554 [R_{int} 0.0185]	5078 [R_{int} 0.0298]	4631 [R_{int} 0.0416]
Observed data	4325	3896	3486
A (min/max)	0.478, 0.509	0.898, 0.974	0.802, 0.978
Function minimised	$\Sigma w(F_o^2–F_c^2)^2$	$\Sigma w(F_o^2–F_c^2)^2$	$\Sigma w(F_o^2–F_c^2)^2$
Absolute structure parameter	0.017(5)	0.02(2)	0.04(3)
Goodness-of-fit on F^2	1.011	1.101	1.110
R_1 (observed data)	0.0204	0.0467	0.0514
wR_2 (all data)	0.0.0536	0.0929	0.1067
Difference map (min/max) (e Å^{-3})	+0.21, −0.42	+0.19, −0.27	+0.21, −0.27
$R_1 = \Sigma\|\|F_o\|-\|F_c\|\|/\Sigma\|F_o\|$		$wR_2 = \{\Sigma[w(F_o^2-F_c^2)^2]/\Sigma[w(F_o^2)^2]\}^{1/2}$	
Weight $= 1.0/[\sigma^2(F_o^2)+a*P^2+b*P]$		$P = (F_o^2+2F_c^2)/3$	

producing a red solution which was stirred for 1 h. The solution was diluted with ether (50 ml), washed with water, and dried. Column chromatography (hexanes/ether, 9:1) gave: (i) pentacarbonyl[(methoxy)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**7**) (1.08 g, 76%) as a red solid, m.p. 94–96°C. Found: $M^{+\bullet}$ 522.1349. Calc. for $C_{26}H_{30}CrO_8$: 522.1346. λ_{max} ($\log_{10}\varepsilon$): 402 nm (3.94). ν_{max} (cm^{-1}): 2060 (s, C≡O), 2015 (sh, C≡O), 1943, (br, C≡O), 1849 (s, C≡O). ^{1}H-NMR (δ ppm): 1.03 (b, H(3ax)); 1.05 (s, H(18)); 1.20 (s, H(20)); 1.42 (dd, $J = 12.8$, 1.6 Hz, H(5)); 1.44 (ddd, $J = 13.0$, 3.6 Hz, H(1ax)); 1.60–1.80 (m, H(2ax), H(2eq), H(6ax)); 1.88 (bd, $J = 13.5$ Hz, H(3eq)); 1.99 (bdd, $J = 13.4$, 6.8 Hz, H(6eq)); 2.26 (bd, $J = 12.7$ Hz, H(1eq)); 2.77 (m, H(7ax)); 2.85 (bdd, $J = 16.9$, 6.3 Hz, H(7eq)); 3.25 (d, $J = 9.1$ Hz, H(19)); 3.33 (s, 19-OMe); 3.52 (d, $J = 9.1$ Hz, H(19)); 3.76 (s, 12-OMe); 4.16 (bs, $OMe_{(carbene)}$); 6.42 (s, H(14)); 6.74 (s, H(11)). ^{13}C-NMR (δ ppm): 19.1, C(2); 19.2, C(6); 25.6, C(20); 27.6, C(18); 30.3, C(7); 35.9, C(3); 38.0, C(10); 38.2, C(4); 39.0, C(1); 51.1, C(5); 55.2, 12-OMe; 59.4, 19-OMe; 67.3, $OMe_{(carbene)}$; 75.9, C(19); 106.7, C(11); 121.7, C(14); 127.1, C(13), 139.0, C(8); 146.9, C(12); 151.6, C(9); 216.0, $C{\equiv}O_{cis}$; 225.3, $C{\equiv}O_{trans}$; 355.4, $C_{carbene}$. Mass spectroscopy: m/z 522 [M^+, 2], 494 (3, M − CO), 466 (2, M − 2CO), 438 (2, M − 3CO), 410 (21, M − 4CO), 382 (100, M − 5CO); and (ii) tetracarbonyl-[(methoxy)(13 - (12,19 - dimethoxypodocarpa - 8,11,13-triene-C^{13},O^{12}))carbene]chromium (**8**) (0.05 g, 3%) as a black oil. Found: $M^{+\bullet}$, 494.1408. Calc. for $C_{25}H_{30}CrO_7$: 494.1397. ν_{max} (cm^{-1}): 2015 (s, C≡O), 1911 (br, C≡O), 1843 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (ddd, $J = 13.5$, 4.2 Hz, H(3ax)); 1.04 (s, H(18)); 1.18 (s, H(20)); 1.39 (dd, $J = 12.8$, 2.0 Hz, H(5)); 1.43 (ddd, $J = 12.8$, 3.8 Hz, H(1ax)); 1.60–1.80 (m, H(2ax), H(2eq), H(6eq)); 1.87 (bd, $J = 13.6$ Hz, H(3eq)); 2.01 (ddt, $J = 13.5$, 7.4, 1.7 Hz, H(6eq)); 2.23 (bd, $J = 12.4$ Hz, H(1eq)); 2.78 (ddd, $J = 17.1$, 11.3, 7.2 Hz, H(7ax)); 2.91 (bdd, $J = 17.0$, 6.0 Hz, H(7eq)); 3.25 (d, $J = 9.1$ Hz, H(19)); 3.33 (s, 19-OMe); 3.48 (d, $J = 9.1$ Hz, H(19)); 4.19 (s, $OMe_{carbene}$); 4.85 (s, 12-OMe); 6.85 (s, H(14)); 7.22 (s, H(11)). ^{13}C-NMR (δ ppm): 19.0, C(2); 19.1, C(6); 25.3, C(20); 27.7, C(18); 30.1, C(7); 35.8, C(3); 38.0(5), C(10); 38.7, C(4); 38.9, C(1); 50.8, C(5); 59.4, 19-OMe; 64.5, 12-OMe; 67.8; $OMe_{carbene}$; 75.9, C(19); 106.6, C(11); 118.0, C(14); 128.9, C(13); 130.3, C(8); 156.8, C(12); 163.8; C(9); 213.9, $C{\equiv}O_{(trans\ \mathrm{to\ carbonyl})}$; 231.2, $C{\equiv}O_{(trans\ \mathrm{to\ carbene})}$; 232.1, $C{\equiv}O_{(trans\ \mathrm{to\ OMe})}$; 333.9, $C_{carbene}$. Mass spectroscopy: m/z 494 [M^+, 2], 466 (2, M − CO), 410 (17, M − 3CO), 382, (100, M − 4CO), 367, (10, 382 − $Me^\bullet$).

When this reaction was performed using a slurry of $Cr(CO)_6$ in THF instead of ether, a polymeric product formed upon methylation with methyl triflate. ^{1}H-NMR (δ ppm): 1.62 (b, $[CH_2(CH_2)_2CH_2O]_n$), 3.41 (b, $[CH_2(CH_2)_2CH_2O]_n$).

3.2. 13-Bromo-12-methoxypodocarpa-8,11,13-triene-19-carboxylic acid (10)

A solution of bromine (3.48 g, 21.8 mmol) in CH_2Cl_2 (10 ml) was added dropwise to a solution of 12-methoxypodocarpa-8,11,13-triene-19-carboxylic acid [44] (6.120 g, 21.1 mmol) in dichloromethane (75 ml) at 0 °C. The solution was stirred at 0°C for 2 h, washed with aqueous sodium dithionite, and brine, and dried. Removal of solvent gave 13-bromo-12-methoxypodocarpa-8,11,13-triene-carboxylic acid (**10**) (7.53 g, 97%) as flaky white crystals, m.p. 227–228°C (MeOH). ν_{max} (cm^{-1}): 3300–2600 (v. br, OH), 1690 (C=O). ^{1}H-NMR (δ ppm): 1.10 (ddd, $J = 13.6$, 13.6, 4.2 Hz, H(3ax)); 1.12 (s, H(20)); 1.34 (s, H(18)); 1.40 (ddd, $J = 13.2$, 13.2, 3.8 Hz, H(1ax)); 1.53 (dd, $J = 12.0$, 1.4 Hz, H(5)); 1.63 (bd, $J = 14.2$ Hz, H(2eq)); 1.95–2.07 (m, H(2ax), H(6ax)); 2.14–2.27 (m, H(1eq), H(3eq), H(6eq)); 2.70 (ddd, $J =$ 16.5, 12.4, 6.0 Hz, H(7ax)); 2.81 (bdd, $J = 16.5$, 5.4 Hz, H(7eq)); 6.76 (s, H(11)); 7.20 (s, H(14)); 11.54 (b, COO*H*). ^{13}C-NMR (δ ppm): 19.8, C(2); 20.7, C(6); 23.0, C(20); 28.6, C(18); 30.8, C(7); 37.1, C(3); 38.9, C(10); 39.3, C(1); 43.8(5), C(4); 52.5, C(5); 56.2, 12-OMe; 108.9, C(13); 109.2, C(11); 129.4, C(8); 133.2, C(14); 148.4, C(9); 153.9, C(12); 184.2, C(19).

3.3. 13-Bromo-12-methoxypodocarpa-8,11,13-trien-19-oyl chloride (11)

Thionyl chloride and **10** (0.999 g, 2.72 mmol) (0.60 ml, 8.2 mmol) were refluxed in benzene (10 ml) for 18.5 h. Removal of excess thionyl chloride gave 13-bromo-12-methoxypodocarpa-8,11,13-trien-19-oyl chloride (**11**) (1.040, 99%) as a white solid. ν_{max} (cm^{-1}): 1814 (C=O). Mass spectroscopy: m/z 388 [M^+, 27], 386 (100, M^+), 384 (76, M^+).

3.4. 13-Bromo-12-methoxy-4α-(2′-pyridylthio)-18-norpodocarpa-8,11,13-triene (12)

13-Bromo-12-methoxypodocarpa-8,11,13-trien-19-oyl chloride (**11**) (7.791 g, 20.2 mmol) in benzene (80 ml) was added to the sodium salt of 1-hydroxy-2-pyridinethione (3.282 g, 22.0 mmol) and 4-*N*,*N*-dimethylaminopyridine (0.259 g, 2.12 mmol) and the mixture was refluxed for 1.75 h under a nitrogen atmosphere. The lemon coloured mixture was filtered through Celite. Column chromatography (hexanes/ether, 8:2) gave 13-bromo-12-methoxy-4α-(2′-pyridylthio)-18-norpodocarpa-8,11,13-triene (**12**) (8.705 g, 100%) as colourless crystals, m.p. 145–146.5°C. Found: M^+ 433.0894. Calc. for $C_{22}H_{26}^{81}BrNOS$: 433.0898. Found: M^+ 431.0913. Calc. for $C_{22}H_{26}^{79}BrNOS$: 431.0918. ν_{max} (cm^{-1}): 1592 (C=C), 1569 (C=C), 1251 (C–O–C_{anti}), 774, 731, 722 (CH). ^{1}H-NMR (δ ppm): 1.23 (s, H(20)); 1.40 (ddd, $J = 12.8$, 4.0 Hz, H(1ax)); 1.45 (s, H(19)); 1.71–1.85 (m, H(2ax), H(2eq), H(6ax)); 1.97 (bd, $J = 12.1$ Hz, H(5)); 2.09 (bd, $J = 13.2$ Hz, H(3eq)); 2.20 (bd, $J = 12.0$ Hz, H(1eq)); 2.24 (ddd, $J = 13.2$, 4.7 Hz, H(3ax)); 2.54 (dd, $J = 13.0$, 7.0 Hz, H(6eq)); 2.72 (ddd, $J = 16.8$, 11.6, 7.2 Hz, H(7ax)); 2.83 (bdd, $J = 16.8$, 6.2 Hz, H(7eq)); 3.86 (s, 12-OMe); 6.73 (s, H(11)); 7.09 (dd, $J = 7.4$, 4.9 Hz, H(4′)); 7.18 (s, H(14)); 7.40 (d, $J = 7.8$ Hz, H(6′)); 7.52 (td, $J = 7.7$, 1.6 Hz, H(5′)); 8.50 (dd, $J = 4.8$, 0.8 Hz, H(3′)). ^{13}C-NMR (δ ppm): 20.3, C(2); 20.4, C(6); 22.1, C(20); 25.8, C(19); 29.6, C(7); 38.4, C(3); 40.2, C(10); 40.7, C(1); 47.7(5), C(5); 56.7, 12-OMe; 58.1, C(4); 108.7, C(11); 109.1, C(13); 122.2, C(4′); 129.7, C(8); 130.2, C(6′); 133.7, C(14); 136.6, C(5′); 150.2(3), C(3′); 150.2(9), C(9); 154.2, C(1′); 157.4, C(12). Mass spectroscopy: m/z 433 [M$^+$, 2], 431 (2, M$^+$), 322 (10, 433 − $C_5H_5NS^\bullet$), 320 (10, 431 − $C_5H_5NS^\bullet$), 307 (18, 322 − Me$^\bullet$), 305 (18, 320 − Me$^\bullet$), 112 (100, $C_5H_6NS^+$).

3.5. *13-Bromo-12-methoxypodocarpa-4(18),8,11,13-tetraene (**13**)*

A solution of *m*-chloroperoxybenzoic acid (0.542 g, 2.67 mmol) in dichloromethane (15 ml) was added to a stirred solution of 12 (1.076 g, 2.67 mmol) in dichloromethane (10 ml) at −78 °C under a nitrogen atmosphere. After 1 h the solution was allowed to warm to room temperature and added to sodium-dried benzene (100 ml) at reflux. After 3 h the solution was cooled to room temperature. Flash chromatography (hexanes/ether, 9:1) gave 13-bromo-12-methoxy-19-nor-podocarpa-4(18),8,11,13-tetraene (**13**) (0.697 g, 87%) as colourless needles, m.p. 120–122°C. Found: M$^{+\bullet}$, 322.0754. Calc. for $C_{17}H_{21}^{81}BrO$: 322.0755. Found: M$^{+\bullet}$, 320.0771. Calc. for $C_{17}H_{22}^{79}BrO$: 320.776. ν_{max} (cm^{-1}): 1647 (C=C$_{alkene}$), 1595 (C=C), 1257 (C–O–C$_{assym}$), 882 (CH). ^{1}H-NMR (δ ppm): 1.01 (s, H(20)); 1.57 (ddd, $J = 12.9$, 4.7 Hz, H(1ax)); 1.67–1.87 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 2.06 (ddd, $J = 13.1$, 4.5 Hz, H(3ax)); 2.17 (bd, $J = 12.1$ Hz, H(5)); 2.23 (bd, $J = 12.7$ Hz, H(1eq)); 2.38 (ddd, $J = 13.0$, 4.3, 2.2 Hz, H(3eq)); 2.81 (4 lines, H(7ax), H(7eq)); 4.60 (d, $J = 1.5$ Hz, H(18)); 4.86 (d, $J = 1.5$ Hz, H(18)); 3.86 (s, 12-OMe); 6.82 (s, H(11)); 7.24 (s, H(14)). ^{13}C-NMR (δ ppm): 21.2, C(6); 22.7, C(20); 23.6, C(2); 28.8, C(7); 36.2, C(3); 38.4, C(1); 39.6, C(10); 47.6, C(5); 56.3, 12-OMe; 106.8, C(18); 108.8, C(13); 109.3, C(11); 129.1, C(8); 133.4, C(14); 147.7, C(4); 150.0, C(9); 153.8, C(12). Mass spectroscopy: m/z 322 [M$^+$, 45], 320 (45, M$^+$), 305 (11, 322 − Me·), 303 (11, 320 − Me$^\bullet$), 226 (100, M − Me$^\bullet$ − Br$^\bullet$).

3.6. *Pentacarbonyl[(methoxy)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]-chromium (**9**)*

Butyllithium (1.49 ml, 2.09 mol l^{-1}, 3.11 mmol) was added to a solution of 13 (0.999 g, 3.11 mmol) in THF (6 ml) cooled to −78°C. After 4 min the solution was added to $Cr(CO)_6$ (3.69 mmol) in ether (10 ml) at 0°C. After 40 min methyl triflate (0.6 ml, 5.3 mmol) was added, producing a deep red solution which was stirred at room temperature for 40 min. The solution was diluted with ether, washed with aqueous sodium hydrogencarbonate and dried. Radial chromatography (hexanes/ether, 9:1) gave: (i) pentacarbonyl[(methoxy)-(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene)carbene]chromium (**9**) (1.068 g, 72%) as a red solid, m.p. 79–81°C. Found: M$^{+\bullet}$ 476.0942. Calc. for $C_{24}H_{24}CrO_7$: 476.0327. ν_{max} (cm^{-1}): 2060 (C≡O), 2015 (C≡O), 1943 (C≡O). λ_{max} ($\log_{10} \varepsilon$): 403 nm (3.94). ^{1}H-NMR (δ ppm): 1.02 (s, H(20)); 1.60 (ddd, $J = 12.8$, 12.8, 4.3 Hz, H(1ax)); 1.68 − 1.89 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 2.08 (ddd, $J = 12.9$, 12.9, 5.4 Hz, H(3ax)); 2.21 (bd, $J = 10.6$ Hz, H(5)); 2.23 (bd, $J = 12.3$ Hz, H(1eq)); 2.39 (ddd, $J = 13.1$, 3.8, 2.2 Hz, H(3eq)); 2.83–2.85 (m, H(7ax), H(7eq)); 3.78 (s, 12-OMe); 4.18 (bs, OMe$_{carbene}$); 4.62 (d, $J = 1.2$ Hz, H(18)); 4.87 (d, $J = 1.2$ Hz, H(18)); 6.49 (s, H(14)); 6.78 (s, H(11)). ^{13}C-NMR (δ ppm): 21.2, C(6); 22.8, C(20); 23.6, C(2); 29.2, C(7); 36.2, C(3); 38.4, C(1); 39.8, C(10); 47.5(5), C(5); 55.2, 12-OMe; 65.4, OMe$_{carbene}$; 106.8, C(18); 107.5, C(11); 122.0, C(14); 127.2, C(13); 148.9, C(9), C(12); 150.1, C(4); 216.1, C≡O$_{cis}$; 225.3, C≡O$_{trans}$; 355.4, C$_{carbene}$; (C(8) not observed). Mass spectroscopy: m/z 446 [M$^+$, 10], 431 (10, M − Me$^\bullet$), 418 (4, M − CO), 390 (5, M − 2CO), 362 (3, M − 3CO), 334 (20, M − 4CO), 306 (100, M − 5CO), 263 (34), 52 (56, Cr); and (ii) [(methoxy)(13-(η-12-methoxy-19-norpodocarpa4(18),8,11,13-tetraene))carbene-C^{13},O^{12}]chromium (**14**) (65 mg, 5%) as a black solid, m.p. 155°C (dec.). Found: M$^{+\cdot}$ 448.0991. Calc. for $C_{23}H_{24}CrO_6$: 448.0978. ν_{max} (cm^{-1}): 2015 (s, C≡O), 1909 (sh, C≡O), 1845 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (s, H(20)); 1.57 (ddd, $J = 12.8$, 12.8, 4.3 Hz, H(1ax)); 1.67–1.90 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 2.05 (ddd, $J = 13.1$, 13.1, 5.1 Hz, H(3ax)); 2.15–2.21 (m, H(5), H(1ax)); 2.39 (ddd, $J =$ 13.1, 4.1, 2.2 Hz, H(3eq)); 2.85 (ddd, $J = 16.7$, 11.6, 5.4 Hz, H(7ax)); 2.92 (ddd, $J = 16.7$, 6.5, 1.8 Hz, H(7eq)); 4.20 (s, 12-OMe); 4.62 (d, $J = 1.1$ Hz, H(18)); 4.86 (s, OMe$_{carbene}$); 4.89 (d, $J = 1.2$ Hz, H(18)); 6.88 (s, H(14)); 7.27 (s, H(11)). ^{13}C-NMR (δ ppm): 21.1, C(6); 22.6, C(20); 23.4, C(2); 29.1, C(7); 36.0, C(3); 38.2, C(1); 40.4, C(10); 47.3, C(5); 64.5, 12-OMe; 67.8, OMe$_{carbene}$; 107.3, C(18), 107.4, C(11); 118.2, C(14); 129.0, C(13); 130.5, C(8); 149.4, C(4); 154.1(5), C(9); 163.6, C(12); 213.9, C≡O$_{(trans\ to\ CO)}$; 231.2(5), C≡O$_{(trans\ to\ carbene)}$; 232.1, C≡O$_{(trans\ to\ OMe)}$; 333.9, C$_{carbene}$. Mass spectroscopy: m/z 448 [M$^+$, 5], 420 (5, M − CO), 392 (1, M − 2CO), 364 (20, M − 3CO), 336 (100, M − 4CO), 52 (35, Cr).

3.7. Pentacarbonyl[(aziridinyl)(2-methoxyphenyl)-carbene]chromium (16)

Aziridine (0.50 ml, 9.65 mmol) was added to a solution of **15** [45] (0.39 g, 1.15 mmol) in THF (8 ml). The solution was stirred for 17.5 h under nitrogen, the colour changing from red to yellow-orange. The solvent was removed and column chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(aziridinyl)(2-methoxyphenyl)carbene]chromium (**16**) (0.35 g, 86%) as bright yellow crystals, m.p. 132–133°C. Found: M^+ 352.9968. Calc. for $C_{15}H_{11}Cr NO_6$: 352.9991. ν_{max} ($CHCl_3$, cm^{-1}): 2055 (s, C≡O), 1975 (sh, C≡O), 1930 (br, C≡O). ^{1}H-NMR ($CHCl_3$-*d*, δ ppm): 2.58 (dd, J=5.6 Hz, $CH_{2(E)}$); 3.24 (dd, $J=5.6$ Hz, $CH_{2(Z)}$); 3.78 (s, OMe); 6.83 (dd, $J=7.5$, 1.5 Hz, H(6)); 6.91 (d, $J=8.3$ Hz, H(3)); 6.99 (t, $J=7.5$ Hz, H(5)); 7.24 (ddd, $J=8.3$, 7.5, 1.6 Hz, H(4)). ^{1}H-NMR (C_6H_6-d_6, δ ppm): 1.38 (dd, $J=5.3$ Hz, $CH_{2(E)}$); 2.20 (dd, $J=5.3$ Hz, $CH_{2(Z)}$); 3.26 (s, OMe); 6.46 (d, $J=8.0$ Hz, H(3)); 6.74 (dd, $J=7.5$, 2.1 Hz, H(6)); 6.79 (t, $J=7.5$ Hz, H(5)); 6.95 (ddd, $J=8.0$, 7.5, 2.1 Hz, H(4)). ^{13}C-NMR ($CHCl_3$-*d*, δ ppm): 27.6, $CH_{2(Z)}$; 28.4, $CH_{2(E)}$; 55.4, OMe; 111.1, C(3); 120.5, C(5); 122.3, C(6); 128.5, C(4); 140.8, C(1); 150.1, C(2); 217.5, C≡O_{cis}; 224.1, C≡O_{trans}; 270.2, $C_{carbene}$. Mass spectroscopy: m/z 353 [M^+, 7], 325 (10, M − CO), 297 (9, M − 2CO), 269 (12, M − 3CO), 241 (29, M − 4CO), 213 (31, M − 5CO), 185 (83, 213 − CH_2CH_2), 170 (40), 133 (35,185 − Cr), 52 (100, Cr).

3.8. Pentacarbonyl[(dihydroamino)(2-methoxyphenyl)-carbene]chromium (17)

Liquid ammonia was condensed into a solution of **15** (0.22 g, 6.45 mmol) in THF (10 ml) at 0°C until the solution colour changed from red to yellow. Column chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(dihydroamino)(methoxyphenyl)carbene]chromium (**17**) (0.21 g, 99%) as yellow crystals, m.p. 73–75°C. Found: $M^{+\bullet}$ 326.9835. Calc. for $C_{13}H_9O_6CrN$: M 326.9835. ν_{max} (cm^{-1}): 2058 (s, C≡O), 1979 (sh, C≡O), 1934 (br, C≡O). ^{1}H-NMR (δ ppm): 3.82 (s, OCH_3); 6.90–6.93 (m, H(3), H(6)); 7.00 (td, $J=7.5$, 1.0 Hz, H(5)); 7.27 (ddd, $J=8.7$, 7.1, 1.7 Hz, H(4)); 8.46 (bs, NH_Z); 9.01 (bs, NH_E). ^{13}C-NMR (δ ppm): 55.2, OMe; 111.1, C(3); 120.5(5), C(5); 122.4(5), C(6); 129.6, C(4); 141.1(5), C(1); 150.8, C(2); 217.1, C≡O_{cis}; 223.5, C≡O_{trans}; 290.9, $C_{carbene}$. Mass spectroscopy: m/z 327 [M^+, 8], 299 (13, M − CO), 271 (10, M − 2CO), 243 (13, M − 3CO), 215, (23, M − 4CO), 187 (100, M − 5CO), 172 (187 − $Me^\bullet$), 52 (58, Cr).

3.9. Pentacarbonyl[(methylamino)(2-methoxyphenyl)-carbene]chromium (18)

Methylamine gas (from KOH, 8 g, and methylamine hydrochloride, 10 g) was added to a solution of **15** (0.53 g, 1.55 mmol) in THF (15 ml) at −78°C, causing a colour change from red to yellow. Column chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(methylamino)-(methoxyphenyl)carbene]chromium (**18**) (0.493 g, 94%) as a yellow oil. Found: $M^{+\bullet}$ 340.9984. Calc. for $C_{14}H_{11}CrNO_6$: 340.9991. ν_{max} ($CHCl_3$, cm^{-1}): 2056 (s, C≡O), 1976 (sh, C≡O), 1929 (br, C≡O). ^{1}H-NMR ($CHCl_3$-*d*, δ ppm): 2.94 (d, $J=4.8$ Hz, $NCH_{3(E)}$); 3.73 (d, $J=5.0$ Hz, $NCH_{3(Z)}$); 3.78 (s, $OCH_{3(Z)}$); 3.82 (s, $OCH_{3(E)}$); 6.73 (dd, $J=7.5$, 1.6 Hz, $H(6)_{(E)}$); 6.77 (dd, $J=7.5$, 1.7 Hz, $H(6)_{(Z)}$); 6.88 (d, $J=8.3$ Hz, $H(3)_{(Z)}$); 6.92 (d, $J=8.3$ Hz, $H(3)_{(E)}$); 6.96 (td, $J=7.5$, 0.8 Hz, $H(5)_{(Z)}$); 7.02 (td, $J=7.5$, 0.9 Hz, $H(5)_{(E)}$); 7.20–7.25 (m, H(4)); 8.78 (bs, $NH_{(Z)}$); 9.12 (bs, $NH_{(E)}$). ^{1}H-NMR (C_6H_6-d_6, δ ppm): 1.83 (d, $J=4.9$ Hz, $NCH_{3(E)}$); 2.77 (d, $J=5.0$ Hz, $NCH_{3(Z)}$); 3.06 (s, OCH_3); 3.27 (s, OCH_3); 6.38 (bd, $J=8.3$ Hz, H(3)); 6.53 (bd, $J=7.2$ Hz, H(6)); 6.75 (bt, $J=7.2$ Hz, H(5)); 6.90 (bt, $J=7.5$ Hz, H(4)); 7.43 (bs, $NH_{(Z)}$); 8.39 (bs, $NH_{(E)}$). ^{13}C-NMR ($CHCl_3$-*d*, δ ppm): 37.4, $NCH_{3(E)}$; 39.8, $NCH_{3(Z)}$; 55.1, $OCH_{3(Z)}$; 55.3, $OCH_{3(E)}$; 110.8,$C(3)_{(E)}$; 110.9, $C(3)_{(Z)}$; 120.3, $C(5)_{(Z)}$; 120.7, $C(5)_{(E)}$; 120.9, $C(6)_{(E)}$; 121.6, $C(6)_{(Z)}$; 128.3, $C(4)_{(E)}$; 128.5, $C(4)_{(Z)}$; 137.7, C(1); 148.7, $C(2)_{(E)}$; 150.3, $C(2)_{(Z)}$; 217.3, C≡O_{cis}; 223.4, C≡$O_{trans(E)}$; 224.0, C≡$O_{trans(Z)}$; 280.8, $C_{carbene(Z)}$; 281.3, $C_{carbene(E)}$. Mass spectroscopy: m/z 341 [$M^{+\bullet}$, 3], 313 (14, M − CO), 285 (7, M − 2CO), 257 (10, M − 3CO), 229 (20, M − 4CO), 201 (100, M − 5CO), 186 (53, 201 − Me·), 52 (47, Cr).

3.10. Pentacarbonyl[(dimethylamino)(2-methoxyphenyl)-carbene]chromium (19)

Dimethylamine (0.90 ml, 13.6 mmol) was added to a solution of **15** (0.59 g, 1.73 mmol). The solution was stirred for 16.5 h under nitrogen. Column chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(dimethylamino)(2 - methoxyphenyl)carbene]-chromium (19) (0.57 g, 92%) [32] as a yellow solid, m.p. 70.5–71°C. Found: $M^{+\bullet}$ 355.0138. Calc. for $C_{15}H_{13}CrNO_6$: 355.0148. ν_{max} (cm^{-1}): 2054 (s, C≡O), 1973 (sh, C≡O), 1926 (br, C≡O). ^{1}H-NMR (δ ppm): 3.06 (s, $NCH_{3(E)}$); 3.79 (s, OMe); 3.97 (s, $NCH_{3(Z)}$); 6.67 (dd, $J=7.5$ (1.6 Hz, H(6)); 6.87 (d, $J=8.2$ Hz, H(3)); 6.99 (t, $J=7.5$ Hz, H(5)); 7.16 (td, $J=8.3$, 7.5, 1.6 Hz, H(4)). ^{13}C-NMR (δ ppm): 45.3, $CH_{3(Z)}$; 50.9, $CH_{3(E)}$; 55.1, OCH_3; 110.8, C(3); 120.4, C(5); 120.7, C(6); 127.4, C(4); 141.1, C(1); 148.1, C(2); 217.4, C≡O_{cis}; 224.0, C≡O_{trans}; 272.6, $C_{carbene}$. Mass spectroscopy: m/z 355 [M^+, 2], 327 (7, M − CO), 299 (12, M − 2CO), 271 (8, M − 3CO), 243 (25, M − 4CO), 215 (100, M − 5CO), 200 (48, 215 − Me), 52 (45, Cr).

3.11. Pentacarbonyl[(pyrrolidinyl)(2-methoxyphenyl)-carbene]chromium (20)

Pyrrolidine (1.0 ml, 12 mmol) was added to a solution of **15** in THF (10 ml). The solution was stirred for 19 h under nitrogen, the colour changing from red to yellow. Column chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(pyrrolidinyl)(2-methoxyphenyl)carbene]-chromium (**20**) (0.67 g, 96%) as pale yellow crystals, m.p. 111–112.5°C. Found: M^+ 381.0298. Calc. for $C_{17}H_{15}CrNO_6$: M, 381.0304. ν_{max} ($CHCl_3$, cm^{-1}): 2052 (s, C≡O), 1971 (sh, C≡O), 1932 (br, C≡O). ^{1}H-NMR ($CHCl_3$-*d*, δ ppm): 1.98 (m, $CH_2CH_2N_{(E)}$); 2.19 (5 lines, $J = 13.8$, 7.1, 7.0 Hz, $CH_2CH_2N_{(Z)}$); 3.19 (ddd, $J = 13.3$, 7.5, 6.9 Hz, $CH_{ax}N_{(E)}$); 3.35 (ddd, $CH_{eq}N_{(E)}$); 3.80 (s, OCH_3); 4.24 (5 lines, $J = 13.3$, 7.3, 6.8 Hz, $CH_{ax}N_{(Z)}$); 4.30 (5 lines, $J = 13.3$, 7.0, 6.6 Hz, $CH_{eq}N_{(Z)}$); 6.68 (dd, $J = 7.5$, 1.6 Hz, H(6)); 6.88 (d, $J = 8.3$ Hz, H(3)); 6.99 (td, $J = 7.4$, 0.7 Hz, H(5)); 7.16 (td, $J = 8.3$, 1.6 Hz, H(4)). ^{1}H-NMR (C_6H_6-d_6, δ ppm): 1.00, m, CH_2CH_2N); 1.16 (5 lines, $J = 13.8$, 6.8, 6.7 Hz, CH_2CH_2N); 2.64 (m, $CH_2N_{(E)}$); 3.33 (s, OCH_3); 3.77 (5 lines, $J = 13.1$, 7.5, 6.9 Hz, $CH_{ax}N_{(Z)}$); 3.91 (5 lines, $J = 13.2$, 6.9, 6.7 Hz, $CH_{eq}N_{(Z)}$); 6.50 (d, $J = 8.2$ Hz, H(3)); 6.56 (dd, $J = 7.4$, 1.3 Hz, H(6)); 6.84 (t, $J = 7.4$ Hz, H(5)); 6.93 (ddd, $J = 8.2$, 7.4, 1.2 Hz, H(4)). ^{13}C-NMR ($CHCl_3$-*d*, δ ppm): 25.3(0), $CH_2CH_2N_{(E)}$; 25.3(3), $CH_2CH_2N_{(Z)}$; 55.16, OCH_3; 55.19, $CH_2N_{(E)}$; 59.0, $CH_2N_{(Z)}$; 110.9(5), C(3); 119.9(5), C(5); 120.8(5), C(6); 127.2, C(4); 142.2, C(1); 147.9, C(2); 217.7, $C≡O_{cis}$; 224.0, $C≡O_{trans}$; 266.9, $C_{carbene}$. Mass spectroscopy: *m*/*z* 381 [$M^{+\bullet}$, 2], 353 (10, M − CO), 325 (8, M − 2CO), 297 (8, M − 3CO), 267 (18, M − 4CO), 241 (100, M − 5CO), 226 (38, 241 − Me•), 121 (45), 91 (45), 52 (42, Cr).

3.12. Pentacarbonyl[(morpholino)(2-methoxyphenyl)-carbene]chromium: attempted synthesis

(i) Morpholine (0.40 ml, 4.6 mmol) was added to a solution of **15** (0.20 g, 5.75 mmol) in THF (10 ml) at room temperature. The solution was stirred under nitrogen for 25 h. Column chromatography gave: (i) a mixture of **15** and tetracarbonyl[(methoxy)(2-methoxyphenyl)carbene-C*¹*,O²]chromium (27 mg); and (ii) (morpholine)pentacarbonylchromium (**21**) (59 mg, 37%) as yellow crystals, m.p. 111–112°C (lit. [36] m.p. 112°C). Found: $M^{+\bullet}$, 278.9841. Calc. for $C_9H_9CrNO_6$: M, 278.9835. ν_{max} (cm^{-1}): 2067 (s, C≡O), 1980 (sh, C≡O), 1932 (br, C≡O). ^{1}H-NMR (δ ppm): 2.22, bs, NH); 2.87–2.99 (m, CH_2N (4H)); 3.43 (ddd, $J = 12.0$, 11.6, 3.3 Hz); CHO (2H)); 3.80 (bd, $J = 12.7$ Hz, CHO (2H)). ^{13}C-NMR (δ ppm): 56.6, CH_2N; 68.3, CH_2O; 213.7, $C≡O_{cis}$; 219.6, $C≡O_{trans}$. Mass spectroscopy: *m*/*z* 279 [M^+, 7], 251 (2, M − CO), 223 (4, M − 2CO), 195 (1, M − 3CO), 167 (10, M − 4CO), 139 (40, M − 5CO), 87 (73, $C_4H_9NO^+$), 57 (100, $C_3H_7N^+$), 52 (43, Cr).

(ii) Morpholine (2.4 ml, 28 mmol) was added to a solution of **15** (0.48 g, 1.39 mmol) in THF (12 ml) at room temperature in a foil-covered flask. The solution was stirred under nitrogen for 20 h. Workup gave morpholine(pentacarbonyl)chromium (**21**) (0.11 g, 28%).

3.13. Pentacarbonyl[(morpholino)phenylcarbene]-chromium (22)

Sodium naphthalenide (from sodium, 70 mg, and naphthalene, 0.29 g) was added to $Cr(CO)_6$ (0.23 g, 1.05 mmol) in THF (6 ml) at −78°C; the mixture was warmed slowly to 0°C and stirred for 20 min. The reddish-yellow solution of $Na_2Cr(CO)_5$ was cooled to −78°C, and a solution of **23** [38] (0.10 g, 0.533 mmol) in THF (2 ml) was added rapidly. After 40 min the solution was warmed to 0°C for 45 min and then cooled to −78 °C. Me_3SiCl (0.20 ml, 1.58 mmol) was added rapidly and the solution was stirred for 1.5 h. Alumina (2 g) was added and the brownish yellow slurry was warmed to room temperature. Column chromatography (1:1, hexanes/ether eluted pentacarbonyl[(morpholino)phenylcarbene]chromium (**22**) (94 mg, 48%) as yellow crystals, m.p. 98–101°C. Found $M^{+\bullet}$ 367.0145. Calc. for $C_{16}H_{13}CrNO_6$: 367.0148. ν_{max} (cm^{-1}): 2055 (s, C≡O), 1973 (sh, C≡O), 1928 (br, C≡O). ^{1}H-NMR ($CHCl_3$-*d*, δ ppm): 3.50 (3 lines, $J = 5.2$, 4.4 Hz, $NCH_{2(E)}$); 3.62 (3 lines, $J = 5.2$, 4.5 Hz, $OCH_{2(E)}$); 4.08, 3 lines, $J = 4.9$ Hz, $OCH_{2(Z)}$); 4.58 (3 lines, $J = 4.9$ Hz, $NCH_{2(Z)}$); 6.71 (dd, $J = 8.3$, 1.2 Hz, H_{ortho}); 7.18 (tt, $J = 7.5$, 1.2 Hz, H_{para}); 7.02 (tt, $J = 8.3$, 7.5, 1.7 Hz, H_{meta}). ^{1}H-NMR (C_6H_6-d_6, δ ppm): 2.56, (3 lines, $J = 4.9$ Hz, $NCH_{2(E)}$); 2.72 (3 lines, $J = 5.1$, 4.0 Hz, $OCH_{2(E)}$); 3.40 (3 lines, $J = 4.9$ Hz, $OCH_{2(Z)}$); 3.93 (3 lines, $J = 4.9$ Hz, $NCH_{2(Z)}$); 6.31 (dd, $J = 7.8$, 1.4 Hz, H_{ortho}); 6.82 (tt, $J = 7.4$, 1.2 Hz, H_{para}); 7.02 (bt, $J = 7.8$, 7.4 Hz, H_{meta}). ^{13}C-NMR ($CHCl_3$-*d*, δ ppm): 55.3, $NCH_{2(Z)}$; 60.4, $NCH_{2(E)}$; 67.8, $OCH_{2(E)}$; 68.1, $OCH_{2(Z)}$; 119.1, C_{ortho}; 126.1, C_{para}; 128.6, C_{meta}; 151.2, C_{ipso}; 217.0, $C≡O_{cis}$; 223.6, $C≡O_{trans}$; 274.6, $C_{carbene}$. Mass spectroscopy: *m*/*z* 367 [M^+, 1], 350 [5, ((morpholine)PhC)$_2$ Found: $M^{+\bullet}$ 350.1990. Calc. for $C_{22}H_{26}N_2O_2$: 350.1994)], 339 (8, M − CO), 311 (7, M − 2CO), 283 (5, M − 3CO), 264 (10, 350 − C_4 $H_8NO^\bullet$), 255 (8, M − 4CO), 227 (100, M − 5CO) 105 (50), 91 (68), 77 (29, Ph^+), 52 (45, Cr).

3.14. (N-Morpholino)-2-methoxyphenylamide (24)

A solution of 2-methoxybenzoic acid (2.09 g, 13.7 mmol) in thionyl chloride (4.0 g, 34 mmol) was heated to 50°C for 30 min. The excess thionyl chloride was removed in vacuo, and the residue was dissolved in CH_2Cl_2 (10 ml). Morpholine (5.0 ml, 57 mmol) was added dropwise to the solution at 0°C and the white slurry was stirred for 1 h. The suspension was diluted with CH_2Cl_2 (50 ml). Workup gave (*N*-morpholino)-2-methoxyphenylamide (**24**) (2.75 g, 91%) as a waxy, white solid, m.p. 50–52°C. Found: $M^{+\bullet}$ 221.1047. Calc. for $C_{12}H_{15}NO_3$: 221.1052. ν_{max} (cm^{-1}): 1634 (C=O). ^{1}H-NMR (δ ppm): 3.26 (dt, $J = 16.9$, 4.4 Hz, $NCH_{2(E)}$); 3.60 (dq, $J = 16.6$, 3.7 Hz, $OCH_{2(E)}$); 3.74–3.88 (m, $NCH_{2(Z)}$, $OCH_{2(Z)}$); 3.84 (s, OMe); 6.91 (d, $J = 8.3$ Hz, H(3)); 7.00 (td, $J = 7.4$, 0.7 Hz, H(5)); 7.25 (dd, $J = 7.5$, 1.7 Hz, H(6)); 7.36 (ddd, $J = 8.3$, 7.4, 1.7 Hz, H(4)). ^{13}C-NMR (δ ppm): 42.0(5), $NCH_{2(Z)}$; 47.2, $NCH_{2(E)}$; 55.5, OCH_3; 66.8, $OCH_{2(E)}$; 66.9, $OCH_{2(Z)}$; 110.8, C(3); 120.9(5), C(5); 125.2, C(1); 128.0, C(6); 130.5, C(4); 155.2, C(2); 167.8, C=O. Mass spectroscopy: m/z 221 [M^+, 11], 220 (13, M − H), 135 (100, $M - C_4H_8NO^\bullet$), 77 (18, Ph).

*3.15. Pentacarbonyl[(morpholino)(2-methoxyphenyl)-carbene]chromium (**25**)*

Sodium naphthalenide (from sodium, 0.29 g, and naphthalene, 1.557 g) was added to $Cr(CO)_6$ (1.25 g, 5.56 mmol) in THF (15 ml) at −78°C, and the mixture was slowly warmed to 0°C, and stirred for 10 min. The red-orange solution of $Na_2Cr(CO)_5$ was cooled to −78°C, and a solution of **24** (0.79 g, 3.59 mmol) in THF (5 ml) was added rapidly. After 30 min the solution was then warmed to 0°C for 1 h then cooled to −78°C, followed by the addition of Me_3SiCl (1.60 ml, 12.6 mmol). The mixture was stirred at −78°C for 1 h, oven-dried alumina (10 g) was added, and the yellow slurry was warmed to room temperature. Column chromatography (hexanes/ether, 1:1) gave pentacarbonyl-[(morpholino)(2-methoxyphenyl)carbene]chromium (**25**) (1.13 g, 79%) as a yellow crystalline solid, m.p. 94–96°C. Found: $M^{+\bullet}$ 397.0240. Calc. for $C_{17}H_{15}CrNO_7$: 397.0254. ν_{max} (cm^{-1}): 2055 (s, C≡O), 1973 (sh, C≡O), 1928 (br, C≡O). ^{1}H-NMR ($CHCl_3$-*d*, δ ppm): 3.42–3.57 (m, $NCH_{2(E)}$); 3.57–3.68 (m, $OCH_{2(E)}$); 3.80 (s, OMe); 4.02 (7 lines, $J = 12.0$, 8.4, 3.0 Hz, $CH_{ax}O_{(Z)}$); 4.09 (8 lines, $J = 12.0$, 8.6, 3.0 Hz, $CH_{eq}O_{(Z)}$); 4.43 (8 lines, $J = 13.1$, 7.8, 3.2 Hz, $CH_{ax}N_{(Z)}$); 4.71 (10 lines, $J =$ 13.0, 7.8, 3.2 Hz, $CH_{eq}N_{(Z)}$); 6.69 (dd, $J = 7.5$, 1.5 Hz, H(6)); 6.88 (d, $J = 8.2$ Hz, H(3)); 7.00 (td, $J = 7.6$, 0.5 Hz, H(5)); 7.18 (ddd, $J = 8.2$, 7.6, 1.5 Hz, H(4)). ^{1}H-NMR (C_6H_6-d_6, δ ppm): 2.65 (b, $NCH_{(E)}$); 2.82 (b, $NCH_{(E)}$); 2.85 (b, $OCH_{(E)}$); 2.99 (b, $OCH_{(E)}$); 3.22 (s, OMe); 3.44 (b, $OCH_{ax(Z)}$); 3.48 (2 lines, $J = 5.7$ Hz, $OCH_{eq(Z)}$); 3.85 (b, $NCH_{ax(Z)}$); 4.17 (2 lines, $J = 9.3$ Hz, $NCH_{eq(Z)}$); 6.40 (bd, $J = 7.8$ Hz, H(3)); 6.46 (bd, $J = 6.8$ Hz, H(6)); 6.79 (bt, $J = 6.8$ Hz, H(5)); 6.87 (bt, $J = 7.0$ Hz, H(4)). ^{13}C-NMR ($CHCl_3$-*d*, δ ppm): 55.0, OCH_3; 55.1, $NCH_{2(E)}$; 60.0(5), $NCH_{2(Z)}$; 67.2, $OCH_{2(E)}$; 67.9, $OCH_{2(Z)}$; 110.7, C(3); 120.6(7), C(5); 120.7(2), C(6); 127.6, C(4); 139.6, C(1); 148.2, C(2); 217.2, C≡O_{cis}; 223.8, C=O_{trans}; 270.9(5), $C_{carbene}$. Mass spectroscopy: m/z 410 (1,(MeOPh(morpholino)C)$_2$), 397 [$M^{+\bullet}$, 2], 369 (9, M − CO), 341 (8, 369 − CO), 313 (8, 341 − CO), 285 (22, 313 − CO), 257 (100, 285 − CO), 242 (23, 257 − Me), 52 (46, Cr).

*3.16. Pentacarbonyl[(dihydroamino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene)) carbene]chromium (**26**)*

Ammonia gas was condensed into a solution of **7** (0.42 g, 0.80 mmol) in THF (10 ml) until the solution colour changed from red to orange-yellow. Radial chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(dihydroamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**26**) (0.36 g, 89%) as yellow crystals, m.p. 133–136°C. Found: C, 59.23; H, 5.81; N, 2.79.Calc. for $C_{25}H_{29}CrNO_7$: C, 59.17; H, 5.76; N, 2.76%. Found: $M^{+\bullet}$ 507.1382. Calc. for $C_{25}H_{29}CrNO_7$: 507.1349%. ν_{max} (cm^{-1}): 2052 (s, C≡O), 1971 (sh, C≡O), 1926 (br, C≡O). ^{1}H-NMR (δ ppm): 1.02 (ddd, $J = 13.5$, 4.1 Hz, H(3ax)); 1.05 (s, H(18)); 1.21 (s, H(20)); 1.42 (dd, $J = 12.7$, 1.8 Hz, H(5)); 1.43 (ddd, $J = 13.0$, 3.8 Hz, H(1ax)); 1.61–1.80 (m, H(2ax), H(2eq), H(6ax)); 1.88 (bd, $J = 13.5$ Hz, H(3eq)); 1.99 (bdd, $J = 13.4$, 7.2 Hz, H(6eq)); 2.27 (bd, $J = 12.4$ Hz, H(1eq)); 2.77 (ddd, $J = 16.9$, 11.3, 7.2 Hz, H(7ax)); 2.87 (bdd, $J = 16.9$, 5.6 Hz, H(7eq)); 3.25 (d, $J = 9.1$, H(19)); 3.33 (s, 19-OMe); 3.52 (d, $J = 9.1$ Hz, H(19)); 3.80 (s, 12-OMe); 6.74 (s, H(14)); 6.77 (s, H(11)); 8.65 (bs, $NH_{(Z)}$); 8.94 (bs, $NH_{(E)}$). ^{13}C-NMR (δ ppm): 19.1, C(2); 19.2, C(6); 25.5, C(20); 27.6, C(18); 30.1, C(7); 35.9, C(3); 38.0, C(10); 38.2, C(4); 39.0, C(1); 51.1, C(5); 55.3, 12-OMe; 59.4, 19-OMe; 75.9, C(19); 107.1, C(11); 125.5, C(14); 127.2, C(13); 137.7, C(8); 149.8, C(12); 155.2, C(9); 217.4, C≡O_{cis}; 223.6, C≡O_{trans}; 288.1, $C_{carbene}$. Mass spectroscopy: m/z 507 [$M^{+\bullet}$, 1], 479 (3. M − CO), 451 (2, M − 2CO), 423 (1, M − 3CO), 395 (18, M − 4CO), 367 (100, M − 5CO), 352 (24, 367 − Me·), 186 (93), 52 (53, Cr).

*3.17. Pentacarbonyl[(methylamino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (**27**)*

Methylamine gas (from KOH, 22 g, and methylamine hydrochloride, 19 g) was added to a solution of **7** (0.42 g, 0.79 mmol) until the colour changed from red to yellow. Radial chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(methylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene)carbene]chromium (**27**) (0.34 g, 82%) as a pale yellow solid, m.p. 117–119°C (hexanes). The *E*/*Z* isomer ratio is 3:2, the *E* isomer being a mixture (1:1) of rotamers. Found: C,59.82; H, 6.00; N, 2.59. Calc. for $C_{26}H_{31}CrNO_7$: C, 59.92; H, 6.00; N, 2.69%. Found: $M^{+\cdot}$ 521.1507. Calc. for $C_{26}H_{31}CrNO_7$: 521.1506%. ν_{max} (CH_2Cl_2, cm^{-1}):

2052 (s, C≡O), 1971 (sh, C≡O), 1926 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (b, H(3ax)); 1.04 (s, H(18)$_{(E)}$); 1.05 (s, H(18)$_{(Z)}$); 1.19 (s, H(20)$_{(E)}$); 1.20 (s, H(20)$_{(Z)}$); 1.21 (s, H(20)$_{(E)}$); 1.40–1.47 (m, H(1ax), H(5)); 1.60–1.80 (H(2ax), H(2eq), H(6ax)); 1.87 (bd, $J=10.9$ Hz, H(3eq)); 1.97 (bdd, $J=13.1$, 7.5 Hz, H(6eq)); 2.26 (bd, $J=11.5$ Hz, H(1eq)); 2.66–2.80 (m, H(7ax)); 2.89 (bdd, $J=11.5$, 6.4 Hz, H(7eq)); 2.93 (d, $J=4.7$ Hz, NCH$_{3(E)}$); 2.94 (d, $J=4.6$ Hz, NCH$_{3(E)}$); 3.24 (d, $J=9.0$ Hz, H(19)); 3.34 (s, 19-OMe); 3.52 (d, $J=9.0$ Hz, H(19)$_{(E)}$); 3.54 (d, $J=9.0$ Hz, H(19)$_{(Z)}$); 3.69 (d, $J=5.0$ Hz, NCH$_{3(Z)}$); 3.73 (s, 12-OMe$_{(Z)}$); 3.76 (s, 12-OMe$_{(E)}$); 6.33 (s, H(14)$_{(E)}$); 6.36 (s, H(14)$_{(E)}$); 6.42 (s, H(14)$_{(Z)}$); 6.72 (s, H(11)$_{(Z)}$); 6.74 (s, H(11)$_{(E)}$); 8.75 (bs, NH$_{(Z)}$); 9.08 (bs, NH$_{(E)}$). ^{13}C-NMR (δ ppm): 19.2, C(2); 19.3, C(6); 25.6, C(20)$_{(E)}$; 25.7, C(20)$_{(Z)}$; 27.6, C(18); 30.2, C(7)$_{(E)}$; 30.4, C(7)$_{(Z)}$; 35.9, C(3); 37.5, NCH$_{3(E)}$; 38.0, C(10), C(4); 39.1, C(1); 39.8, NCH$_{3(Z)}$; 51.0, C(5)$_{(E)}$; 51.2, C(5)$_{(Z)}$; 51.4, C(5)$_{(E)}$; 55.0(5), 12-OMe$_{(Z)}$; 55.2, 12-OMe$_{(E)}$; 59.4, 19-OMe; 75.8, C(19)$_{(E)}$; 75.9, C(19)$_{(Z)}$; 76.0, C(19)$_{(E)}$; 106.5, C(11); 106.6(8), C(11); 106.7(4), C(11); 121.0, C(14); 121.1, C(14); 122.1, C(14); 126.6, C(13); 127.1(5), C(13); 127.2(2), C(13); 135.3, C(8)$_{(Z)}$; 135.5, C(8)$_{(E)}$; 147.9(7), C(12)$_{(E)}$; 147.0(5), C(12)$_{(Z)}$; 148.7, C(9); 149.9, C(9); 217.4(5), C≡O$_{cis}$; 223.6, C≡O$_{trans(E)}$; 224.2, C≡O$_{trans(Z)}$; 268.6, C$_{carbene}$; 280.7, C$_{carbene}$; 281.4, C$_{carbene}$. Mass spectroscopy: m/z 521 [M^{+}, 2], 493 (4, M − CO), 465 (M − 2CO), 437 (2, M − 3CO), 409 (20, M − 4CO), 381 (100, M − 5CO), 366 (381 − Me$^{\bullet}$), 52 (14, Cr).

3.18. *Pentacarbonyl[(dimethylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene)-carbene]chromium (**28**)*

Dimethylamine (1.0 ml, 15 mmol) was added to a solution of **7** (0.30 g, 0.574 mmol) in THF (10 ml). The solution was stirred for 2 h at room temperature. Radial chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(dimethylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene (**28**) (0.27 g, 89%) as a yellow solid, m.p. 115 °C (decomp.). Found: M$^{+\bullet}$ 535.1677. Calc. for $C_{27}H_{33}CrNO_7$: 535.1662. ν_{max} (CH_2Cl_2, cm^{-1}): 2053 (s, C≡O), 1973 (sh, C≡O), 1928 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (ddd, $J=13.3$, 3.9 Hz, H(3ax)); 1.04 (s, H(18)); 1.20 (s, H(20)); 1.40 (ddd, $J=13.0$, 3.8 Hz, H(1ax)); 1.41 (bd, $J=12.3$ Hz, H(5)); 1.55–1.75 (m, H(2ax), H(2eq), H(6ax)); 1.89 (bd, $J=13.8$ Hz, H(3eq)); 1.96 (bdd, $J=13.5$, 6.9 Hz, H(6eq)); 2.27 (bd, $J=12.0$ Hz, H(1eq)); 2.68 (ddd, $J=16.5$, 11.8, 7.3 Hz, H(7ax)); 2.87 (bdd, $J=16.5$, 5.6 Hz, H(7eq)); 3.06 (s, NCH$_{3(E)}$); 3.24 (d, $J=9.0$ Hz, H(19)); 3.34 (s, 19-OMe); 3.55 (d, $J=9.0$ Hz, H(19)); 3.73 (s, 12-OMe); 3.94 (s, NCH$_{3(Z)}$); 6.31 (s, H(14)); 6.69 (H(11)). ^{13}C-NMR (δ ppm): 19.2, C(2); 19.3, C(6); 25.7, C(20); 27.6, C(18); 30.4, C(7); 35.9(5), C(3); 38.0(1), C(10); 38.0(6), C(4); 39.1, C(1); 45.3, NCH$_{3(Z)}$; 50.8, NCH$_{3(E)}$; 51.5, C(5); 55.0, 12-OMe; 59.4, 19-OMe; 75.7, C(19); 106.3, C(11); 120.7, C(14); 126.9, C(13); 139.12, C(8); 146.4, C(12); 148.9(5), C(9); 217.5, C≡O$_{cis}$; 224.2, C≡O$_{trans}$; 272.8, C$_{carbene}$. Mass spectroscopy: m/z 535 [M$^{+\bullet}$, 1], 507 (5, M − CO), 479 (4, M − 2CO), 451 (1,M − 3CO), 423 (78, M − 4CO), 395 (100, M − 5CO), 380 (395 − Me$^{\bullet}$).

3.19. *Pentacarbonyl[(aziridinyl)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**29**)*

Aziridine (0.40 ml, 7.7 mmol) was added to a solution of (**7**) (0.451 g, 0.863 mmol) in THF (8 ml). The solution was stirred at room temperature for 3.5 h. Radial chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(aziridinyl)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**29**) (0.37 g, 81%) as yellow crystals, m.p. 108–109°C (decomp.). Anal. Found: C, 61.28; H, 5.93; N, 2.57. Calc. for $C_{27}H_{31}CrNO_7$: C, 60.78; H, 5.86; N, 2.63%. Found M$^{+\bullet}$ 533.1500. Calc. for $C_{27}H_{31}CrNO_7$: 533.1506. ν_{max} (CH_2Cl_2, cm^{-1}): 2054 (s,C≡O), 1973 (sh, C≡O), 1929 (br, C≡O). ^{1}H-NMR (δ ppm): 1.03 (ddd, $J=13.6$, 4.1 Hz, H(3ax)); 1.05 (s, H(18)); 1.21 (s, H(20)); 1.44 (dd, $J=12.7$, 2.0 Hz, H(5)); 1.46 (ddd, $J=13.0$, 3.8 Hz, H(1ax)); 1.59–1.80 (m, H(2ax), H(2eq), H(6ax)); 1.88 (bdd, $J=13.4$, 1.1 Hz, H(3eq)); 1.96 (ddt, $J=13.5$, 7.0, 2.1 Hz, H(6eq)); 2.27 (bd, $J=12.2$ Hz, H(1eq)); 2.59 (dd, $J=5.5$, 5.5 Hz, NCH$_{2(E)}$); 2.74 (ddd, $J=16.8$, 11.3, 7.3 Hz, H(7ax)); 2.84 (bdd, $J=16.8$, 5.6 Hz, H(7eq)); 3.20 (dd, $J=5.2$, 5.2 Hz, NCH$_{(Z)}$); 3.21 (dd, $J=5.2$, 5.2 Hz, NCH$_{(Z)}$); 3.25 (d, $J=9.1$ Hz, H(19)); 3.34 (s, 19-OMe); 3.54 (d, $J=9.1$ Hz, H(19)); 3.73 (s, 12-OMe); 6.48 (s, H(14)); 6.74 (s, H(11)). ^{13}C-NMR (δ ppm): 19.1(5), C(2); 19.3, C(6); 25.6, C(20); 26.6, C(18), CH$_{2(Z)}$; 28.7, CH$_{2(E)}$; 30.3, C(7); 35.9, C(3); 38.0(5), C(4), C(10); 39.0, C(1); 51.1(5), C(5); 55.4, 12-OMe; 59.4, 19-OMe; 75.9, C(19); 106.98, C(11); 122.8(5), C(14); 126.8, C(13); 138.5, C(8); 148.6, C(12); 150.1(5); C(9); 217.6, C≡O$_{cis}$; 224.2, C≡O$_{trans}$; 270.6, C$_{carbene}$. Mass spectroscopy: m/z 533 [M^{+}, 1], 505, (5, M − CO), 477 (1, M − 2CO), 449 (1, M − 3CO), 421 (25, M − 4CO), 393 (25, M − 5CO), 365 (100, 393 − C_2H_4), 313 (20, 365 − Cr), 180 (53), 52 (42, Cr).

3.20. *Pentacarbonyl[(pyrrolidinyl)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**30**)*

A solution of pyrrolidine (0.40 ml, 4.8 mmol) and 7 (0.50 g, 0.951 mmol) was stirred at room temperature for 4 h. Radial chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(pyrrolidinyl)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**30**) (0.48

g, 91%) as a pale yellow solid, m.p. 120°C (decomp.) (hexanes). Anal. Found: C, 62.51; H, 6.65; N, 2.52. Calc. for $C_{29}H_{35}CrNO_7$: C, 62.07; H, 6.29; N, 2.50%. Found: $M^{+\bullet}$ 561.1833. Calc. for $C_{29}H_{35}CrNO_7$: 561.1819. ν_{max} (CH_2Cl_2, cm^{-1}): 2052 (s, C≡O), 1971 (sh, C≡O), 1925 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (ddd, J = 13.5, 4.3 Hz, H(3ax)); 1.04 (s, H(18)); 1.20 (s, H(20)); 1.40 (ddd, J = 12.8, 3.9 Hz, H(1ax)); 1.41 (bd, J = 12.6 Hz, H(5)); 1.60–1.78 (m, H(2ax), H(2eq), H(6eq)); 1.89 (bd, J = 12.6 Hz, H(3eq)); 1.89–2.00 (m, H(6eq), $CH_{2(E)}CH_2N$); 2.17 (ddd, J = 13.9, 7.0 Hz, $CH_{2(Z)}CH_2N$); 2.27 (bd, J = 12.4 Hz, H(1eq)); 2.68 (ddd, J = 16.7, 11.6, 7.1 Hz, H(7ax)); 2.86 (bdd, J = 16.7, 5.9 Hz, H(7eq)); 3.21 (ddd, $CH_{ax(E)}$); 3.23 (d, J = 9.1 Hz, H(19)); 3.34 (s, 19-OMe); 3.37 (ddd, J = 13.4, 7.7, 6.8 Hz, $CH_{eq(E)}$); 3.55 (d, J = 9.1 Hz, H(19)); 3.74 (s, 12-OMe); 4.20 (ddd, J = 13.2, 7.4, 6.7 Hz, $CH_{ax(Z)}$); 4.26 (ddd, J = 13.2, 7.0, 6.7 Hz, $CH_{eq(Z)}$); 6.31 (H(14)); 6.70 (H(11)). ^{13}C-NMR (δ ppm): 19.2, C(2); 19.3, C(6); 25.3, $CH_{2(E)}CH_2N$; 25.4, $CH_{2(Z)}CH_2N$; 25.7, C(20); 27.6, C(18); 30.5, C(7); 35.9, C(3); 37.9(8), C(10); 38.0(6), C(4), 39.1, C(1); 51.5, C(5); 55.0(6), 12-OMe; 55.1(2), $CH_{2(E)}N$; 58.9, 19-OMe; 59.4, $CH_{2(Z)}N$; 75.7, C(19); 106.5, C(11); 120.1, C(14); 127.0, C(13); 140.2, C(8); 146.2, C(12); 148.7(5), C(9); 217.8, $C{\equiv}O_{cis}$; 224.2, $C{\equiv}O_{trans}$; 267.3, $C_{carbene}$. Mass spectroscopy: m/z 561 [M^+, 8], 533 (14, M − CO), 505 (5, M − 2CO), 449 (100, M − 4CO), 421 (100, M − 5CO), 370 (20, 421 − Cr − $H^\bullet$).

3.21. *N-Morpholino-12,19-dimethoxypodocarpa-8,11,13-triene-13-carboxamide (**32**)*

Butyllithium (4.10 ml, 2.0 mol l^{-1}) was added dropwise to a solution of **6** (1.50 g, 4.07 mmol) in THF (40 ml) cooled to −100°C. After 3 min, 4-morpholinocarbamoyl chloride (1.42 ml, 12.2 mmol) was added to the golden-brown solution and the mixture was allowed to warm to room temperature over 1 h. Workup followed by column chromatography gave *N*-morpholino-12,19-dimethoxypodocarpa-8,11,13-triene (**32**) (1.41 g, 90%) as a colourless solid, m.p. 123–124°C. Found: $M^{+\bullet}$ 401.2565. Calc. for $C_{24}H_{35}NO_4$: 401.2566. ν_{max} (cm^{-1}): 1635 (C = O). ^{1}H-NMR (δ ppm): 1.01 (ddd, J = 13.7, 4.0 Hz, H(3ax)); 1.04 (s, H(18)); 1.17 (s, H(20)); 1.20 (s, H(20)); 1.35–1.50 (m, H(5), H(1ax)); 1.60–1.75 (m, H(2ax), H(2eq), H(6ax)); 1.88 (bd, J = 11.7 Hz, H(3eq)); 1.97 (bdd, J = 13.4, 7.0 Hz, H(6eq)); 2.27 (bd, J = 10.3 Hz, H(1eq)); 2.68–2.90 (m, H(7ax), H(7eq)); 3.24 (d, J = 9.1 Hz, H(19)); 3.33 (s, 19-OMe); 3.52 (d, J = 9.1 Hz, H(19)); 3.54–3.70 (m, $OCH_{2(E)}$); 3.70–3.86 (m, $NCH_{2(Z)}$, $OCH_{2(Z)}$); 3.79 (s, 12-OMe); 3.20–3.34 (b, $NCH_{2(E)}$); 6.76 (s, H(11)); 6.90 (s, H(14). ^{13}C-NMR (δ ppm): 18.8(2), C(2); 18.8(9), C(6); 25.2, C(20); 27.4, C(18); 29.7, C(7); 35.6(5), C(3); 37.7, C(4); 37.9, C(10); 38.7, C(1); 41.8, $NCH_{2(Z)}$; 47.0, $NCH_{2(E)}$; 50.9, C(5); 55.3, 12-OMe; 59.0(5), 19-OMe; 66.6, $OCH_{2(E)}$; 66.7, $OCH_{2(Z)}$; 75.5, C(19); 106.7, C(11); 122.4, C(14); 127.4, C(13); 128.2, C(8); 152.0(5), C(9); 153.0, C(12); 167.8, C=O. Mass spectroscopy: m/z 355 [M^+, 22], 340 (2, M − $Me^\bullet$), 269 (100, M − C_4H_8NO).

3.22. *Pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**31**)*

Sodium naphthalenide (from sodium, 0.28 g, and naphthalene, 1.17 g) was added to $Cr(CO)_6$ (0.23 g, 1.05 mmol) in THF (8 ml) at −78°C. The yellow red solution of $Na_2Cr(CO)_5$ was cooled to −78°C and a solution of **32** (0.80 g, 2.07 mmol) in THF (6 ml) was added rapidly. After 1 h the solution was warmed to 0°C for 1 h, followed by cooling to −78°C. Me_3SiCl (1.0 ml, 7.9 mmol) was added and the solution was stirred for 30 min. Alumina (9.5 g) was added and the yellow-orange slurry was warmed to room temperature. Column chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(morpholino)(13 - (12,19 - dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**31**) (0.91 g, 76%) as fine yellow plates, m.p. 115–116°C (hexanes). Anal. Found: C, 60.50; H, 6.05; N, 2.33. Calc. for $C_{29}H_{35}CrNO_8$: C, 60.35; H, 6.11; N, 2.43%. Found: $M^{+\bullet}$ 577.1803. Calc. for $C_{29}H_{35}CrNO_8$: 577.1768. ν_{max} (cm^{-1}): 2052 (s, C≡O), 1971 (sh, C≡O), 1926 (br, C≡O). ^{1}H-NMR (δ ppm): 0.99 (ddd, J = 13.1, 3.2 Hz, H(3ax)); 1.04 (s, H(18)); 1.21 (s, H(20), 1.39 (ddd, J = 13.0, 3.7 Hz, H(1ax)); 1.40 (dd, J = 12.6, 1.8 Hz, H(5)); 1.60–1.80 (m, H(2ax), H(2eq), H(6ax)); 1.89 (bd, J = 13.5 Hz, H(3eq)); 1.96 (bdd, J = 13.4, 7.4 Hz, H(6eq)); 2.26 (bd, J = 12.4 Hz, H(1eq)); 2.67 (ddd, J = 16.8, 11.5, 7.2 Hz, H(7ax)); 2.86 (bdd, J = 16.8, 5.9 Hz, H(7eq)); 3.24 (d, J = 9.1 Hz, H(19)); 3.34 (s, 19-OMe); 3.40–3.50 (m, $NCH_{2(E)}$); 3.54 (d, J = 9.1 Hz, H(19)); 3.63 (m, $OCH_{2(E)}$); 3.74 (s, 12-OMe); 4.00 (ddd, J = 12.0, 8.3, 3.0 Hz, $OCH_{ax(Z)}$); 4.07 (ddd, J = 12.0, 8.6, 3.4 Hz, $OCH_{eq(Z)}$); 4.39 (ddd, J = 13.1, 7.6, 3.3 Hz, $NCH_{ax(Z)}$); 4.68 (ddd, J = 13.0, 7.8, 3.2 Hz, $NCH_{eq(Z)}$); 6.34 (s, H(11), 6.69 (s, H(14)). ^{13}C-NMR (δ ppm): 19.1(5), C(2); 19.3, C(6); 25.7, C(20); 27.5, C(18); 27.6, C(18); 30.4, C(7); 35.8(7), C(3); 35.9(5), C(3); 37.9, C(10); 38.0, C(4); 39.1, C(1); 51.0, C(5); 51.4, C(5); 54.9, 12-OMe, $NCH_{2(E)}$; 59.4, 19-OMe; 60.0, $NCH_{2(Z)}$; 67.3, $OCH_{2(E)}$; 67.4, $OCH_{2(E)}$; 67.9, $OCH_{2(Z)}$; 75.7, C(19); 76.0, C(19); 106.2, C(11); 106.4, C(11); 120.9(5), C(14); 121.1, C(14); 126.9, C(13); 127.0, C(13); 137.2, C(8); 137.5, C(8); 146.4, C(9); 149.3, C(12); 217.3, $C{\equiv}O_{cis}$; 224.0, $C{\equiv}O_{trans}$; 271.6, $C_{carbene}$. Mass spectroscopy: m/z 577 [M^+, 3], 549 (7, M − CO), 521 (7, M − 2CO), 465 (75, M − 4CO), 437 (100, M − 5CO).

3.23. Pentacarbonyl[(morpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**31**): mixed "anhydride method"

Butyllithium (0.50 ml, 1.80 mol l^{-1}) was added to a solution of **6** (0.33 g, 0.906 mmol) in THF (12 ml) at −78°C. The solution was stirred for 6 min followed by the addition of hexacarbonylchromium (0.21 g, 0.954 mmol) and the yellow solution was allowed to warm to room temperature. Tetramethylammonium bromide (0.147 g, 0.954 mmol) was added, the solvent was removed in vacuo, and the yellow residue was dissolved in CH_2Cl_2 (12 ml). The flask was covered in foil and the solution was cooled to −42°C, followed by the addition of acetyl bromide (70 μl, 0.947 mmol). The burgundy solution was stirred at −42°C for 1 h, then morpholine (180 μl, 2.06 mmol) was added. The solution was warmed to room temperature, then refluxed for 19.5 h. Column chromatography gave pentacarbonyl[(morpholino)(13 - (12,19 - dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**31**) (0.19 g, 37%) as a yellow solid.

3.24. Pentacarbonyl[(dihydroamino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))-carbene]chromium (**33**)

Ammonia gas was condensed into a solution of **9** (0.444 g, 0.932 mmol) in THF (10 ml) until the colour changed from red to yellow. Radial chromatography gave pentacarbonyl[(dihydroamino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))-carbene]chromium (**33**) (0.390 g, 91%) as a yellow flaky crystals, m.p. 122–123°C (dec.) (hexanes). Anal. Found: C, 59.97; H, 5.25; N, 2.92. Calc. for $C_{23}H_{23}CrNO_6$: C, 59.87; H, 5.02; N, 3.04%. Found: $M^{+\bullet}$, 461.0934. Calc. for $C_{23}H_{23}CrNO_6$: 461.0930. ν_{max} (cm^{-1}): 2054 (s, C≡O), 1974 (sh, C≡O), 1926 (br, C≡O). ^{1}H-NMR (δ ppm): 1.02 (s, H(20)); 1.62 (ddd, $J = 12.7$, 4.4 Hz, H(1ax)); 1.68–1.90 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 2.07 (ddd, $J = 13.0$, 5.4 Hz, H(3ax)); 2.19–2.25 (3 lines, H(5), H(1eq)); 2.39 (ddd, $J = 13.0$, 4.1, 2.4 Hz, H(3eq)); 2.83–2.89 (4 lines, H(7ax), H(7eq)); 3.81 (s, 12-OMe); 4.62 (d, $J = 1.4$ Hz, H(18)); 4.87 (d, $J = 1.4$ Hz, H(18)); 6.78 (s, H(14)); 6.81 (s, H(11)); 8.64 (bs, $NH_{(Z)}$); 8.94 (bs, $NH_{(E)}$). ^{13}C-NMR (δ ppm): 21.2, C(6); 22.6, C(20); 23.6, C(2); 29.0, C(7); 36.2, C(3); 38.4, C(1); 39.8, C(10); 47.5, C(5); 55.3, 12-OMe; 106.8, C(18); 107.9, C(11); 125.5(5), C(14); 127.2, C(13); 138.0, C(8); 149.6, C(9); 149.7(5), C(12); 150.01, C(4); 217.4, $C≡O_{cis}$; 233.6, $C≡O_{trans}$; 288.4, $C_{carbene}$. Mass spectroscopy: m/z (FAB) 461 [M^+, 8], 433 (17, M − CO), 405 (8, M − 2CO), 377 (12, M − 3CO), 349 (M − 4CO), 321 (M − 5CO).

3.25. Pentacarbonyl[(methylamino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))-carbene]chromium (**34**)

Methylamine gas (from KOH, 13.1 g, and methylamine hydrochloride, 13.9 g) was condensed into a solution of **9** (0.623 g, 1.31 mmol) in THF (15 ml) until the colour changed from red to yellow. Radial chromatography (hexanes/ether, 1:1) gave pentacarbonyl-[(methylamino)(13 - (12 - methoxy - 19 - norpodocarpa - 4 (18),8,11,13-tetraene))-carbene]chromium (**34**) (0.575 g, 92%) as a yellow oil [$E/Z = 5$:1; the E isomer is a mixture (1:1) of two rotamers]. Found: $M^{+\bullet}$ 475.1080. Calc. for $C_{24}H_{25}CrNO_6$: 475.1087. ν_{max} (cm^{-1}): 2054 (s, C≡O), 1974 (sh, C≡O), 1926 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (s, $H(20)_{(E)}$); 1.01 (s, $H(20)_{(Z)}$); 1.03 (s, $H(20)_{(E)}$); 1.59 (ddd, $J = 12.4$, 12.4, 4.4 Hz, $H(1ax)_{(E)}$); 1.69 (ddd, $J = 12.0$, 12.0, 4.4 Hz, $H(1ax)_{(Z)}$); 1.70–1.89 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 2.06 (ddd, $J =$ 12.3, 12.3, 4.4 Hz, $H(3ax)_{(E)}$); 2.08 (ddd, $J = 12.3$, 12.3, 4.4 Hz, $H(3ax)_{(Z)}$); 2.22 (3 lines, H(5), H(1eq)); 2.39, bd, $J = 12.0$ Hz, H(3eq)); 2.73–2.99 (m, H(7ax), H(7eq)); 2.95 (d, $J = 4.9$ Hz, $CH_{3(E)}$); 3.70 (d, $J = 5.1$ Hz, $CH_{3(Z)}$); 3.74 (s, 12-$OMe_{(Z)}$); 3.78 (s, 12-$OMe_{(E)}$); 4.60 (s, $H(18)_{(E,\ Z)}$); 4.62 (d, $J = 1.1$ Hz, $H(18)_{(E)}$); 4.86 (s, H(18)); 6.38 (s, $H(14)_{(E)}$); 6.42 (s, $H(14)_{(E)}$); 6.47 (s, $H(14)_{(Z)}$); 6.76 (s, $H(11)_{(Z)}$); 6.78 (s, $H(11)_{(E)}$); 8.77 (bs, $NH_{(Z)}$); 9.10 (bs, $NH_{(E)}$). ^{13}C-NMR (δ ppm): 21.2(7), $C(6)_{(E)}$; 21.3(3), $C(6)_{(Z)}$; 22.7, $C(20)_{(E)}$; 22.8(5), $C(20)_{(Z)}$; 23.6(5), C(2); 29.1, $C(7)_{(E)}$; 29.3, $C(7)_{(Z)}$; 36.2(1), $C(3)_{(E)}$; 36.2(8), $C(3)_{(Z)}$; 37.5, $NCH_{3(E)}$; 38.4(5), $C(1)_{(E)}$; 38.4(8), $C(1)_{(Z)}$; 39.6(1), $C(10)_{(E)}$; 39.6(2), $C(10)_{(Z)}$; 39.7, $NCH_{3(Z)}$; 47.5(6), $C(5)_{(E)}$; 47.6(5), $C(5)_{(Z)}$; 47.8, $C(5)_{(E)}$; 55.1, 12-$OMe_{(Z)}$; 55.2, 12-$OMe_{(E)}$; 106.5, $C(18)_{(E)}$; 106.6(7), $C(18)_{(Z)}$; 106.7(4), $C(18)_{(E)}$; 107.3(5), $C(11)_{(E)}$; 107.5, $C(11)_{(E)}$; 107.6, $C(11)_{(Z)}$; 121.1, $C(14)_{(E)}$; 121.4, $C(14)_{(E)}$; 122.3, $C(14)_{(Z)}$; 126.7, $C(13)_{(Z)}$; 127.2(1), $C(13)_{(E)}$; 127.2(9), $C(13)_{(E)}$; 135.4(5), $C(8)_{(E)}$; 135.6, $C(8)_{(Z)}$; 146.9(5), $C(9)_{(Z)}$; 147.0, $C(9)_{(E)}$; 147.2(6), $C(12)_{(E)}$; 147.3(1), $C(12)_{(E)}$; 147.4, $C(12)_{(Z)}$; 150.2, $C(4)_{(E)}$; 150.4, $C(4)_{(Z)}$; 217.4, $C≡O_{cis}$; 223.6, $C≡O_{trans(E)}$; 224.2, $C≡O_{trans(Z)}$; 280.7, $C_{carbene(Z)}$; 281.3, $C_{carbene(E)}$. Mass spectroscopy: m/z (FAB) 475 [M^+, 3], 447 (24, M − CO), 419 (5, M − 2CO), 391 (15, M − 3CO), 363 (100, M − 4CO), 335 (78, M − 5CO), 282 (70, 335 − $H^\bullet$ − Cr).

3.26. Pentacarbonyl[(dimethylamino)(13-(12-methoxy-19-podocarpa-4(18),8,11,13-tetraene))carbene]-chromium (**35**)

Dimethylamine (2.0 ml, 38 mmol) and **9** (0.485 g, 1.02 mmol) in THF (15 ml) were stirred for 1.5 h. Radial chromatography gave pentacarbonyl[(dimethylamino) (13-(12-methoxy-19-podocarpa-4(18),8,11,13-tetraene))carbene]chromium (**35**) (0.429 g, 86%) as a yellow oil. ν_{max} (cm^{-1}): 2054 (s, C≡O), 1976 (sh, C≡O), 1929 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (s, H(20)); 1.02 (s, H(20)); 1.50–1.90 (m, H(1ax), H(2ax), H(2eq), H(6ax), H(6eq)); 2.07 (bdd, J = 13.9, 5.3 Hz, H(3ax)); 2.17–2.27 (m, H(5), H(1eq)); 2.39 (bd, J = 12.4 Hz, H(3eq)); 2.76–2.88 (m, H(7ax), H(7eq)); 3.08 (s, $NMe_{(Z)}$); 3.74 (s, 12-OMe); 3.95 (s, $NMe_{(E)}$); 3.95(5) (s, $NMe_{(E)}$); 4.60 (bs, H(18)); 4.62 (bs, H(18)); 4.86 (bs, H(18)); 6.33 (s, H(14)); 6.37 (s, H(14)); 6.73 (s, H(11)). ^{13}C-NMR (δ ppm): 21.3, C(6); 22.8, C(20); 23.7, C(2); 29.3, C(7); 36.2, C(3); 38.5, C(1); 39.6, C(10); 47.6, C(5); 47.8, C(5); 45.2(5), $NCH_{3(Z)}$; 45.3, $NCH_{3(Z)}$; 50.8, $NCH_{(E)}$; 55.0, 12-OMe; 106.4, C(18); 106.6(5), C(18); 107.3, C(11); 107.6, C(11); 120.7(5), C(14); 121.0, C(14); 126.9, C(13); 139.3, C(8); 146.4, C(9); 150.3, C(12); 150.5, C(4); 217.5, $C≡O_{cis}$; 223.6, $C≡O_{trans}$; 224.2, $C≡O_{trans}$; 272.7, $C_{carbene}$.

3.27. *Pentacarbonyl[(aziridinyl)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))-carbene]chromium (**36**)*

Aziridine (0.50 ml, 9.7 mmol) and 9 (0.492 g, 1.03 mmol) were stirred in THF (8 ml) at room temperature for 3.5 h. Radial chromatography (hexanes/ether, 1:1), gave pentacarbonyl[(aziridinyl)(13 - (12 - methoxy - 19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**36**) (0.450 g, 89%) as a yellow orange solid, m.p. 120°C (decomp). Found: $M^{+\bullet}$, 487.1110. Calc. for $C_{25}H_{25}CrNO_6$: 487.1087. ν_{max} (cm^{-1}): 2054 (s, C≡O), 1974 (sh, C≡O), 1926 (br, C≡O). ^{1}H-NMR (δ ppm): 1.03 (s, H(20)); 1.60 (ddd, J = 12.8, 4.6 Hz, H(1ax)); 1.68–1.88 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 2.07 (ddd, J = 12.9, 5.4 Hz, H(3ax)); 2.22 (dd, J = 12.0, 1.0 Hz, H(5)); 2.24 (bd, J = 12.8 Hz, H(1eq)); 2.39 (ddd, J = 13.0, 4.0, 2.2 Hz, H(3eq)); 2.58–2.62 (m, $NCH_{2(E)}$); 2.81–2.84 (4 lines, H(7ax), H(7eq)); 3.21 (dd, J = 5.2 Hz, $NCH_{2(Z)}$); 3.74 (s, 12-OMe); 4.61 (d, J = 1.4 Hz, H(18)); 4.86 (d, J = 1.4 Hz, H(18)); 6.53 (s, H(14)); 6.78 (s, H(11)). ^{13}C-NMR (δ ppm): 21.1, C(6); 22.7, C(20); 23.6, C(2); 27.5, $NCH_{2(Z)}$; 28.7, C(7); 29.1(5); $NCH_{2(E)}$; 36.2, C(3); 38.4, C(1); 39.7, C(10); 47.6, C(5); 55.3, 12-OMe; 106.6, C(18); 107.8, C(11); 123.0(5), C(14); 126.9, C(13); 138.6, C(8); 147.5, C(9); 148.5, C(12); 150.3, C(4); 217.6, $C≡O_{cis}$; 224.2, $C≡O_{trans}$; 270.4, $C_{carbene}$. Mass spectroscopy: m/z 487 [M^+, 11], 459 (12, M − CO), 431 (5, M − 2CO), 403 (9, M − 4CO), 375 (100, M − 5CO), 347 (35, 375 − CH_2CH_2), 319 (37).

3.28. *Pentacarbonyl[(pyrrolidinyl)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))-carbene]chromium (**37**)*

A solution of **9** (0.474 g, 0.995 mmol) and pyrrolidine (0.30 ml, 3.6 mmol) in THF (8 ml) was stirred at room temperature for 3.5 h. Pyrrolidine (0.3 ml, 3.6 mmol) was added and the solution was stirred for a further 19.5 h. Radial chromatography gave pentacarbonyl[(pyrrolidinyl)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))-carbene]chromium (**37**) (0.455 g, 89%) (7:3 mixture of rotamers) as a pale yellow solid, m.p. 122–124°C (hexanes). Found: $M^{+\bullet}$, 515.1427. Calc. for $C_{27}H_{29}CrNO_6$: 515.1400. ν_{max} (cm^{-1}): 2053 (C≡O), 1974 (C≡O), 1926 (C≡O). ^{1}H-NMR (δ ppm): 0.99 (s, $H(20)_{maj}$); 1.02 (s, $H(20)_{min}$); 1.64 (ddd, J = 12.0, 12.0, 3.8 Hz, H(1ax)); 1.68–1.88 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 1.95–2.01 (m, $CH_{2(E)}CH_2N$); 2.08 (ddd, J = 13.1, 13.1, 4.8 Hz, H(3ax)); 2.14–2.25 (m, H(5), H(1eq), $CH_{2(Z)}CH_2N$); 2.38 (bd, J = 11.9 Hz, H(3eq)); 2.75 (bdd, J = 16.6, 5.4 Hz, H(7eq)); 2.83 (m, H(7ax)); 3.22 (ddd, J = 13.1, 7.2, 6.7 Hz, $CH_{ax(E)}N$); 3.41 (ddd, J = 13.1, 6.6, 6.5 Hz, $CH_{eq(E)}N$); 3.75 (s, 12-OMe); 4.26 (m, $CH_{2(Z)}N$); 4.59 (s, $H(18)_{maj}$); 4.61 (s, $H(18)_{min}$); 4.85 (s, H(18)); 6.33 (s, $H(14)_{maj}$); 6.37 (s, $H(14)_{min}$); 6.73 (s, H(11)). ^{13}C-NMR (δ ppm): 21.3(5), $C(6)_{maj}$; 21.3(9), $C(6)_{min}$; 22.8(1), $C(20)_{maj}$; 22.8(6), $C(20)_{min}$; 23.7, C(2); 25.3(1), $CH_{2(E)}CH_2N$; 25.3(6), $CH_{2(Z)}CH_2N$; 29.2, $C(7)_{maj}$; 29.4, $C(7)_{min}$; 36.2(5), $C(3)_{maj}$; 36.3(2), $C(3)_{min}$; 38.5, C(1); 39.5, $C(10)_{maj}$; 39.7, $C(10)_{min}$; 47.6, $C(5)_{maj}$; 47.9, $C(5)_{min}$; 55.1, $NCH_{2(E)maj}$, 12-OMe; 55.2, $NCH_{2(E)min}$; 58.9, $NCH_{2(Z)}$; 106.4, $C(18)_{maj}$; 106.7, $C(18)_{min}$; 107.4, $C(11)_{min}$; 107.5, $C(11)_{maj}$; 120.2, $C(14)_{maj}$; 120.4, $C(14)_{min}$; 127.0(5), C(13); 140.1, C(8); 146.0(7), C(9); 146.1(2), $C(12)_{min}$; 146.2, $C(12)_{maj}$; 150.3(5), $C(4)_{min}$; 150.6, $C(4)_{maj}$; 217.8, $C≡O_{cis}$; 224.2, $C≡O_{trans}$; 267.3, $C_{carbene}$. Mass spectroscopy: m/z 515 [M^+, 4], 487 (10, M − CO), 459 (5, M − 2CO), 431 (3, M − 3CO), 403 (43, M − 4CO), 375 (38, M − 5CO).

3.29. *12-Methoxy-N-morpholino-19-norpodocarpa-4(18),8,11,13-tetraene-13-carboxamide (**39**)*

t-Butyllithium (6.6 ml, 1.45 mol l^{-1}, 9.6 mmol) was added dropwise to a solution of **13** (1.511 g, 4.70 mmol) in THF (60 ml) cooled to −100°C. After 5 min, 4-morpholinocarbamoyl chloride (1.65 ml, 14.1 mmol) was added and the mixture was allowed to warm to room temperature over 1 h. Workup and flash chromatography gave 12-methoxy-N-morpholino-19-norpodocarpa-4(18),8,11,13-tetraene-13-carboxamide (**39**) (1.450 g, 87%) as a white foam. Found: $M^{+\bullet}$ 355.2135. Calc. for $C_{22}H_{29}NO_3$: 355.2147. ν_{max} (cm^{-1}): 1635 (C=O). ^{1}H-NMR (δ ppm): 1.28 (s, H(20)); 1.50–1.87 (m, H(1ax), H(2ax), H(2eq), H(6ax), H(6eq)); 2.06 (ddd, J = 13.1, 13.1, 5.5 Hz, H(3ax)); 2.16 (bd, J = 12.6 Hz, H(5)); 2.24 (bd, J = 14.0 Hz, H(1eq)); 2.39 (bd, J = 12.8 Hz, H(3eq)); 2.78–2.84 (H(7ax), H(7eq)); 3.27 (b, $NCH_{(E)}$); 3.33 (b, NCH $_{(E)}$); 3.55–3.70 (m, $OCH_{2(E)}$); 3.70–3.88 (m, $OCH_{2(Z)}$; $NCH_{2(Z)}$); 4.61 (d, J = 1.2 Hz, H(18)); 4.87 (d, J = 1.2 Hz, H(18)); 6.80 (s, H(11)); 6.96 (s, H(14)). ^{13}C-NMR (δ ppm): 21.1, C(6);

22.6, C(20); 23.5, C(2); 28.9, C(7); 36.1, C(3); 38.3, C(1), 39.7(5), C(10); 42.1, $NCH_{2(Z)}$; 47.3, $NCH_{2(E)}$; 47.6, C(5); 55.5, 12-OMe; 66.8, $OCH_{2(E)}$; 69.0, $OCH_{2(Z)}$; 106.7, C(18); 107.8, C(11); 122.8, C(14); 127.8, C(13); 128.7, C(8); 149.7, C(9); 150.0, C(12); 153.2, C(4), 168.1, C=O. Mass spectroscopy: m/z 355 [M^+, 22], 340 (2, M − Me$^•$), 269 (100, M − $C_4H_8NO^•$).

3.30. *Pentacarbonyl[(morpholino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))-carbene]chromium* (**38**)

A solution of sodium naphthalenide (from sodium, 0.401 g, and naphthalene, 1.388 g) in THF (10 ml) was added to $Cr(CO)_6$ (1.092 g, 4.96 mmol) in THF (10 ml) at −78°C; the mixture was warmed to 0°C, and stirred for 30 min. The red-orange solution of $Na_2Cr(CO)_5$ was cooled to −78°C and **39** (1.076 g, 3.03 mmol) in THF (8 ml) was added rapidly. After 40 min the solution was warmed to 0°C for 30 min, then cooled to −78°C, followed by the addition of Me_3SiCl (1.3 ml, 10.3 mmol). After 1 h, alumina (14 g) was added and the yellow slurry was warmed to room temperature. Flash chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(morpholino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**38**) (1.244 g, 77%) as a yellow foam. Found: $M^{+•}$ 531.1371. Calc. for $C_{27}H_{29}CrNO_7$: 531.1349. ν_{max} (cm^{-1}): 2052 (s, C≡O), 1972 (sh, C≡O), 1916 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (s, H(20)); 1.03 (s, H(20)); 1.50–1.90 (m, H(1ax), H(2ax), H(2eq), H(6ax), H(6eq)); 2.06 (ddd, J = 13.0, 13.0, 5.3 Hz, H(3ax)); 2.10 (ddd, J = 12.9, 12.9, 5.1 Hz, H(3ax)); 2.18 (dd, J = 11.9, 3.1 Hz, H(5)); 2.18–2.28 (m, H(1eq), H(5)); 2.39 (bd, J = 12.6 Hz, H(3eq)); 2.70–2.91 (m, H(7ax), H(7eq)); 3.44–3.58 (m, $NCH_{(E)}$); 3.57–3.67 (m, $NCH_{(E)}$, $OCH_{2(E)}$); 3.75 (s, 12-OMe); 3.98–4.04 (m, $OCH_{ax(Z)}$); 4.06–4.11 (m, $OCH_{eq(Z)}$); 4.37–4.44 (m, $NCH_{ax(Z)}$); 4.60 (d, J = 1.2 Hz, H(18)); 4.62 (d, J = 1.2 Hz, H(18)); 4.67–4.72 (m, $NCH_{eq(Z)}$); 4.86 (d, J = 1.5 Hz, H(18)); 6.35 (s, H(14)); 6.40 (s, H(14)); 6.72(5) (s, H(11)); 6.73(3) (H(11)). ^{13}C-NMR (δ ppm): 21.2(6), C(6); 21.3(2), C(6); 22.8, C(20); 23.6(5), C(2); 29.1, C(7); 29.3, C(7); 36.2, C(3); 36.3, C(3); 38.4(6), C(1); 38.5(3), C(1); 39.5, C(10); 39.7, C(10); 47.5, C(5); 47.8, C(5); 55.0, 12-OMe, $NCH_{2(E)}$; 60.0, $NCH_{2(Z)}$; 67.3(3), $OCH_{2(E)}$; 67.3(9), $OCH_{2(E)}$; 67.9, $OCH_{2(Z)}$; 106.5, C(11); 106.8, C(11); 107.1, C(18); 107.3, C(18); 121.1, C(14); 121.4, C(14); 127.0(1), C(13); 127.0(8), C(13); 137.4, C(8); 137.8, C(8); 146.4, C(9); 146.5(8), C(12); 146.6(3), C(12); 150.2, C(4); 150.4, C(4); 217.3(0), $C{\equiv}O_{cis}$; 217.3(3), $C{\equiv}O_{cis}$; 223.9(6), $C{\equiv}O_{trans}$; 223.9(9), $C{\equiv}O_{trans}$; 271.6, $C_{carbene}$. Mass spectroscopy: m/z 531 [M^+, 4], 503 (13, M − CO), 475 (12, M − 2CO), 447 (4, M − 3CO), 419 (98, M − 4CO), 391 (100, M − 5CO), 376 (8, 391 − Me$^•$), 356 (37), 340 (21), 269 (30).

3.31. *12-Methoxy-19-norpodocarpa-4(18),8,11,13-tetraen-13-oic acid* (**41**)

Butyllithium (1.4 ml, 2.5 mol l^{-1}) was added to a solution of **13** (1.125 g, 3.93 mmol) in THF (15 ml) cooled to −78°C. After 3 min solid carbon dioxide (~3 g) was added. Workup and flash chromatography (Et_2O) gave 12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraen-13-oic acid (**41**) (0.734 g, 73%) as a white foam. Found: $M^{+•}$ 286.1572. Calc. for $C_{18}H_{22}O_3$: 286.1569. ν_{max} (cm^{-1}): 3284 (br, OH), 1734 (s, C=O), 1645 (s, $C{=}C_{alkene}$), 1612 (s, $C{=}C_{aromatic}$). ^{1}H-NMR (δ ppm): 1.03 (s, H(20)); 1.61 (ddd, J = 12.9, 12.9, 4.5 Hz, H(1ax)); 1.69–1.91 (m, H(2ax), H(2eq), H(6ax), H(6eq)); 2.07 (ddd, J = 13.1, 13.1, 5.5 Hz, H(3ax)); 2.20 (bd, J = 12.1 Hz, H(5)); 2.25 (bd, J = 12.7 Hz, H(1eq)); 2.40 (ddd, J = 13.1, 4.2, 2.3 Hz, H(3eq)); 2.85 (ddd, J = 17.1, 11.3, 7.0 Hz, H(7ax)); 2.93 (ddd, J = 17.1, 6.3, 1.5 Hz, H(7eq)); 4.03 (s, 12-OMe); 4.63 (d, J = 1.5 Hz, H(18)); 4.89 (d, J = 1.5 Hz, H(18)); 6.95 (s, H(11)); 7.90 (s, H(14)); 10.80 (b, COOH). ^{13}C-NMR (δ ppm): 20.9(5), C(6); 22.6, C(20); 23.4, C(2); 28.7, C(7); 36.0, C(3); 38.2, C(1); 40.2, C(10); 47.2, C(5); 56.5, 12-OMe; 107.2, C(18); 108.4, C(11); 114.9, C(13); 129.4, C(8); 134.4, C(14); 149.4, C(9); 155.1, C(12); 156.0, C(4); 165.5, COOH. Mass spectroscopy: m/z 286 [M^+, 100], 271 (19, M − Me$^•$), 227 (27, 271 − CO_2), 212 (24, 227 − Me$^•$), 195 (22, M − MeO$^•$ − Me$^•$ − $CO_2H^•$).

3.32. *12-Methoxy-19-norpodocarpa-4(18),8,11,13-tetraen-13-oyl chloride* (**42**)

A solution of thionyl chloride (10 ml, 0.14 mol) and **41** (0.662 g, 2.31 mmol) was stirred at room temperature for 2 h. Removal of excess thionyl chloride gave 12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraen-13-oyl chloride (**42**) (0.701 g, 100%) as a pale brown foam. ν_{max} (cm^{-1}): 1769 (C=O).

3.33. *12-Methoxy-N-(trans-2,6-dimethylmorpholino)-19-norpodocarpa-4(18),8,11,13-tetraen-13-carboxamide* (**43**)

trans-2,6-Dimethylmorpholine [40] (0.270 g, 2.34 mmol) was added to a solution of **42** (0.701 g, 2.31 mmol), triethylamine (0.40 ml, 2.9 mmol), and *N*,*N*-dimethylaminopyridine (17 mg, 0.14 mmol) in dichloromethane (20 ml). The solution was stirred at room temperature for 16.5 h, then washed with water, and dried ($MgSO_4$). Column chromatography (Et_2O) gave 12-methoxy-*N*-(*trans*-2,6-dimethylmorpholino)-19-norpodocarpa-4(18),8,11,13-tetraene-13-carboxamide (**43**) (0.439 g, 49%) as a colourless oil. Found $M^{+•}$ 383.2449. Calc. for $C_{24}H_{33}NO_3$: 383.2460. ν_{max} (cm^{-1}): 1636 (C=O). ^{1}H-NMR (δ ppm): 1.02 (bs, H(20)); 1.10 (b, O_ECHCH_3); 1.11 (b, O_ECHCH_3); 1.28 (b,

O_ZCHCH_3); 1.60–1.90 (m, H(1eq), H(2ax), H(2eq), H(6ax), H(6eq)); 2.03–2.40 (m, H(1eq), H(3ax), H(3eq), H(5)); 2.73–3.00 (m, H(7ax), H(7eq)); 3.30–3.40 (m, N_ECH_{ax})); 3.50–3.61 (m, N_ZCH_{ax})); 3.78 (s, 12-OMe); 3.79 (s, 12-OMe); 3.71–4.00 (m, OC*H*CH_3, N_ECH_{eq})); 4.05–4.17 (b, N_ZCH_{eq}); 4.61 (d, H(18)); 4.86 (H(18)); 6.72 (s, H(11)); 6.79 (s, H(11)); 6.80 (s, H(11)); 6.84 (s, H(11)); 6.90 (b, H(14)); 6.93 (b, H(14)). ^{13}C-NMR (δ ppm): 17.3, O_ECHCH_3; 17.5, O_ZCHCH_3; 20.8, C(6); 21.2, C(6); 22.7, C(20); 23.6, C(2); 29.1, C(7); 36.2, C(3); 37.8, C(1); 38.4, C(1); 40.3, C(10); 46.3, C(5); 47.6, C(5); 51.6, N_ECH_2;52.0, N_ECH_2; 52.9, N_ZCH; 55.6, 12-OMe; 65.8, OCH; 66.4, OCH; 106.8, C(18); 106.9, C(18); 107.9, C(11); 123.0, C(14); 127.8, C(13); 128.7, C(8); 149.7, C(9); 150.8, C(12); 153.3, C(4); 169.0, C=O. Mass spectroscopy: m/z 383 [M^+, 22], 368 (30, M − Me$^\bullet$), 283 (20), 270 (18), 269 (100, M − $C_5H_8NO_2^\bullet$).

3.34. Pentacarbonyl[(trans-2,6-dimethylmorpolino)-(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene)carbene]chromium (40)

A solution of sodium naphthalenide (from sodium, 0.334 g, and naphthalene, 0.544 g) was added to $Cr(CO)_6$ (0.428 g, 1.94 mmol) in THF (10 ml) at −78°C, then warmed to room temperature. The solution of $Na_2Cr(CO)_5$ was cooled to −78°C and a solution of **43** (0.493 g, 1.29 mmol) in THF (10 ml) was added. After 30 min the solution was warmed to 0°C for 45 min, then cooled to −78°C and chlorotrimethylsilane (0.50 ml, 3.95 mmol) was added. After 75 min, alumina (1 g) was added and alumina and the suspension was warmed to room temperature. Column chromatography (hexanes/ether, 1:1) gave pentacarbonyl-[(*trans*-2,6-dimethylmorpholino)(13-(12-methoxy-19-norpodocarpa-4(18),8,11,13-tetraene))carbene]chromium (**40**) (0.394 g, 57%) as a yellow foam. Found: $M^{+\cdot}$ 559.1668. Calc. for $C_{29}H_{33}CrNO_7$: 559.1662. ν_{max} (cm^{-1}): 2052 (s, C≡O), 1971 (sh, C≡O), 1916 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (s, H(20)); 1.02 (s, H(20)); 1.04 (s, H(20)); 1.09(6) (d, J = 5.4 Hz, O_ECHCH_3); 1.09(9) (d, J = 5.8 Hz, O_ECHCH_3); 1.10(4) (d, J = 5.8 Hz, O_ECHCH_3); 1.38 (d, J = 6.2 Hz, O_ZCHCH_3); 1.39 (d, J = 6.4 Hz, O_ZCHCH_3); 1.50–1.85 (m, H(1eq), H(2ax), H(2eq), H(6ax), H(6eq)); 1.94–2.28 (m, H(1eq), H(3ax), H(5)); 2.39 (d, J = 12.9 Hz, H(3eq)); 2.68–2.92 (m, H(7ax), H(7eq)); 3.18–3.36 (m, N_ECH_{ax})); 3.48–3.60 (m, N_ZCH_{ax})); 3.74(0) (12-OMe); 3.74(5) (12-OMe); 3.74(8) (12-OMe); 3.89–3.99 (m, N_ZCH_{ax}); 4.03–4.08 (m, N_ECH_{eq}); 4.15–4.22 (m, $OCHCH_3$); 4.28–4.36 (m, $OCHCH_3$); 4.56–4.62 (bd, J = 10.4 Hz, N_ZCH_{eq}); 4.66 (bs, H(18)); 4.69 (bs, H(18)); 4.86 (d, J = 1.6 Hz, H(18)); 6.23 (s, H(14)); 6.26 (s, H(14)); 6.28 (s, H(14)); 6.30 (s, H(14)); 6.34 (s, H(14)); 6.37 (s, H(14)); 6.38 (s, H(14)); 6.41 (s, H(14)); 6.42 (s, H(14)); 6.70 (s, H(11)); 6.72 (s, H(11)); 6.73 (s, H(11)); 6.76 (s, H(11)). ^{13}C-NMR (δ ppm): 17.1, O_ECHCH_3; 17.4, O_ZCHCH_3; 17.5, O_ZCHCH_3; 21.2(6), C(6); 21.3(4), C(6); 21.4(9), C(6); 22.7(5), C(20); 22.9, C(20); 23.2, C(20); 23.7, C(2); 24.2, C(2); 29.1, C(7); 29.3, C(7); 30.8, C(7); 36.2, C(3); 36.3, C(3); 38.0, C(1); 38.4(6), C(1); 38.5, C(1); 39.5, C(10); 39.7, C(10); 47.5, C(5); 47.8, C(5); 54.6, 12-OMe; 55.0, 12-OMe; 58.3, N_ECH_2; 58.3(6), N_ECH_2; 63.3(7), N_ZCH_2; 63.4(5), N_ZCH_2; 64.0(8), N_ZCH_2; 66.7(5), $OCHCH_3$; 67.0, $OCHCH_3$; 67.2, $OCHCH_3$; 106.0, C(18); 106.5, C(18); 106.7, C(18); 107.1, C(11); 107.2, C(11); 107.3, C(11); 107.9, C(11); 120.5, C(14); 120.8, C(14); 121.0, C(14); 121.1, C(14); 121.2, C(14); 121.4, C(14); 121.8, C(14); 122.0, C(14); 125.0, C(13); 125.1, C(13); 126.9, C(8); 127.0, C(8); 146.2, C(12); 146.5, C(12); 147.1, C(12); 150.2, C(4); 150.4, C(4); 217.3(0), C≡O_{cis}; 217.3(2), C≡O_{cis}; 217.4(1), C≡O_{cis}; 217.5, C≡O_{cis}; 223.8, C≡O_{trans}; 223.9, C≡O_{trans}; 272.1, $C_{carbene}$; 272.2, $C_{carbene}$; 272.3, $C_{carbene}$. Mass spectroscopy: m/z 559 [M^+, 4], 531 (12, M − CO), 503 (10, M − 2CO), 447 (92, M − 4CO), 419 (100, M − 5CO).

3.35. 12,19-Dimethoxypodocarpa-8,11,13-trien-13-oic acid (45)

Butyllithium (0.94 ml, 2.5 mol l^{-1}) was added to a solution of 13-bromo-12,19-dimethoxypodocarpa-8,11,13-triene (**6**) (0.856 g, 2.33 mmol) in THF (10 ml) at −78°C. After 5 min. solid carbon dioxide (~5 g) was added. Workup and column chromatography gave 12,19-dimethoxypodocarpa-8,11,13-trien-13-oic acid (**45**) (0.584 g, 75%) as a white foam. Found: $M^{+\bullet}$ 332.1986. Calc. for $C_{20}H_{28}O_4$: 332.1988. ν_{max} (cm^{-1}): 3292 (br, OH), 1735 (s, C=O), 1107 (C–O–C). ^{1}H-NMR (δ ppm): 1.03 (ddd, J = 13.6, 4.2 Hz, H(3ax)); 1.05 (s, H(18)); 1.21 (s, H(20)); 1.40 (dd, J = 12.8, 2.0 Hz, H(5)); 1.46 (ddd, J = 12.9, 3.8 Hz, H(1ax)); 1.61 − 1.81 (m, H(2ax), H(2eq), H(6ax)); 1.89 (bdd, J = 13.5, 1.1 Hz, H(3eq)); 2.01 (ddt, J = 13.5, 7.4, 1.8 Hz, H(6eq)); 2.28 (bd, J = 13.0 Hz, H(1eq)); 2.79 (ddd, J = 16.9, 11.5, 7.2 Hz, H(7ax)); 2.93 (bdd, J = 16.9, 6.1 Hz, H(7eq)); 3.26 (d, J = 9.1 Hz, H(19)); 3.33 (s, 19-OMe); 3.51 (d, J = 9.1 Hz, H(19)); 4.03 (s, 12-OMe); 6.91 (s, H(11)); 7.84 (s, H(14)); 10.82 (bs, COOH). ^{13}C-NMR (δ ppm): 19.0, C(2); 19.1, C(6); 25.4, C(20); 27.6, C(18); 29.7, C(7); 35.8, C(3); 38.0, C(10); 38.6, C(4); 38.9, C(1); 50.7, C(5); 56.5, 12-OMe; 59.4, 19-OMe; 75.8, C(19); 107.6, C(11); 114.7, C(13); 129.3, C(8); 134.2, C(14); 155.0, C(9); 157.6, C(12); 165.5, COOH. Mass spectroscopy: m/z 332 [M^+, 95], 205 (100).

3.36. 12,19-Dimethoxypodocarpa-8,11,13-triene-13-oyl chloride (46)

A solution of **45** (0.312 g, 0.939 mmol) and thionyl chloride (2 ml) was heated to 50°C for 30 min. Removal of excess thionyl chloride gave 12,19-dimethoxypodocarpa-8,11,13-trien-13-oyl chloride (**46**) as a white foam (0.319 g, 100%). ν_{max} (cm^{-1}) 1770 (C=O).

*3.37. 12,19-Dimethoxy-N-(trans-2,6-dimethylmorpholino)podocarpa-8,11,13-triene-13-carboxamide (**47**)*

trans-2,6-Dimethylmorpholine (0.115 g, 0.998 mmol) was added to a solution of **46** (0.319 g, 0.939 mmol) and triethylamine (0.15 ml, 1.08 mmol) in dichloromethane (10 ml). After 14 h at room temperature, workup and column chromatography (Et_2O) gave 12,19-dimethoxy-*N*-(*trans*-2,6-dimethylmorpholino)-podocarpa-8,11,13-triene-13-carboxamide (**47**) (0.384 g, 95%). Found $M^{+\bullet}$ 429.2874. Calc. for $C_{26}H_{39}NO_4$: 429.2879. ν_{max} (cm^{-1}): 1635 (C=O). ^{1}H-NMR (δ ppm): 1.01 (ddd, $J=13.8$, 13.8, 4.2 Hz, H(3ax)); 1.04 (s, H(18)); 1.10 (b, O_ECHCH_3); 1.11 (b, O_ECHCH_3); 1.17 (bs, H(20)); 1.25–1.33 (m, O_ZCHCH_3); 1.39–1.45 (m, H(1ax), H(5)); 1.60–1.80 (m, H(2ax), H(2eq), H(6eq)); 1.88 (bd, $J=12.0$ Hz, H(3eq)); 1.96 (d, $J=13.3$ Hz, H(6eq)); 1.98 (d, $J=13.3$ Hz, H(6eq)); 2.27 (bd, $J=11.0$ Hz, H(1eq)); 2.68–2.97 (m, H(7ax), H(7eq)); 3.24 (d, $J=9.1$ Hz, H(19)); 3.33 (s, 19-OMe); 3.52 (d, $J=9.1$ Hz, H(19)); 3.50–3.63 (m, N_ECH_{ax}); 3.78 (s, 12-OMe); 3.67–4.10 (m, N_ZCH_{ax}, N_ZCH_{eq}, $OCHCH_3$, N_ECH_{eq}); 6.76 (s, H(11)); 6.87 (bs, H(14)). ^{13}C-NMR (δ ppm): 17.2, O_ECHCH_3; 17.5, O_ZCHCH_3; 19.1, C(2); 19.2, C(6); 25.5, C(20); 27.6, C(18); 30.1, C(7); 30.9, C(7); 35.9, C(3); 38.0, C(10); 38.2, C(4); 39.0, C(1); 46.3, C(5); 51.2, N_ECH_2; 55.5, 12-OMe; 59.4, 19-OMe; 65.8, N_ZCH_2; 66.5, $OCHCH_3$; 75.9, C(19); 76.0, C(19); 107.1, C(11); 122.7, C(14); 123.0, C(14); 127.8, C(13); 128.5, C(13); 137.4, C(8); 152.3, C(9); 153.3, C(12); C=O not observed, very broad. Mass spectroscopy: *m*/*z* 429 [M$^+$, 30], 315 (100, M $-$ $C_5H_8NO_3$).

*3.38. Pentacarbonyl[(trans-2,6-dimethylmorpholino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]-chromium (**44**)*

A solution of sodium naphthalenide (from sodium, 0.2 g, and naphthalene, 0.2 g) in THF (5 ml) was added to $Cr(CO)_6$ (0.154 g, 0.700 mmol) in THF (5 ml) at -78°C; the mixture was then warmed to 0°C. The solution of $Na_2Cr(CO)_5$ was cooled to -78°C and **47** (0.200 g) in THF (7 ml) was added. After 30 min, the solution was warmed to 0°C for 30 min, then cooled to -78°C and chlorotrimethylsilane (0.2 ml, 1.58 mmol) was added. After 1.5 h alumina (8 g) was added, and the yellow-orange slurry was warmed to room temperature. Chromatography (hexanes/ether, 1:1) gave pentacarbonyl[(*trans*-2,6-dimethylmorpholino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**44**) (0.147 g, 52%) as a yellow foam. Found: $M^{+\cdot}$ 605.2086. Calc. for $C_{31}H_{39}CrNO_8$: 605.2081. ν_{max} (cm^{-1}): 2051 (s, C≡O), 1971 (sh, C≡O), 1916 (br, C≡O). ^{1}H-NMR (δ ppm): 1.00 (m, H(3ax)); 1.04 (s, H(18)); 1.05 (s, H(18)); 1.07 (d, $J=4.7$ Hz, O_ECHCH_3); 1.09 (d, $J=5.0$ Hz, O_ECHCH_3); 1.18 (s, H(20)); 1.20 (s, H(20)); 1.38 (d, $J=6.4$ Hz, O_ZCHCH_3); 1.39 (d, $J=6.4$ Hz, O_ZCHCH_3); 1.41–1.49 (m, H(1ax), H(5)); 1.60–1.80 (m, H(2ax), H(2eq), H(6ax)); 1.86 (bd, $J=12.3$ Hz, H(3eq)); 1.89 (d, $J=12.3$ Hz, H(3eq)); 1.93–2.02 (m, H(6eq)); 2.24 (bd, $J=12.0$ Hz, H(1eq)); 2.27 (bd, $J=12.0$ Hz, H(1eq)); 2.60–2.91 (m, H(7ax), H(7eq)); 3.21–3.27 (m, H(19)); 3.33 (s, 19-OMe); 3.34 (s, 19-OMe); 3.49–3.57 (m, H(19), N_ECH_{ax})); 3.71 (s, 12-OMe); 3.73 (s, 12-OMe); 3.89–4.01 (m, N_ZCH_{ax})); 4.01–4.10 (bdd, $J=13.0$, 6.9 Hz, N_ECH_{eq})); 4.27–4.36 (m, $OCHCH_3$)); 4.57–4.69 (m, N_ZCH_{eq})); 6.22 (s, H(14)); 6.25 (s, H(14)); 6.32 (s, H(14)); 6.35 (s, H(14)); 6.69 (bs, H(11)). ^{13}C-NMR (δ ppm): 17.0(5), O_ECHCH_3; 17.1, O_ECHCH_3; 17.2, O_ECHCH_3; 17.4, O_ZCHCH_3; 17.5, O_ZCHCH_3; 19.1, C(2); 19.3, C(6); 25.6, C(20); 25.7, C(20); 27.5, C(18); 27.6, C(18); 30.3, C(7); 30.4, C(7); 35.8(7), C(3); 35.9(3), C(3); 37.9, C(10); 38.0, C(10), C(4); 38.2, C(4); 39.0, C(1); 51.0, C(5); 51.1, C(5); 51.3, C(5); 54.5, 12-OMe; 55.0, 12-OMe; 58.2, N_ECH_2; 58.3, N_ECH_2; 58.4, N_ECH_2; 59.4, 19-OMe; 63.3, N_ZCH_2; 63.4, N_ZCH_2; 64.0, N_ZCH_2; 64.1, N_ZCH_2; 66.7, O_ECHCH_3; 66.9, O_ECHCH_3; 67.1, O_ZCHCH_3; 75.6, C(19); 75.9, C(19); 106.2, C(11); 106.3, C(11); 106.4, C(11); 120.3, C(14); 120.4, C(14); 121.6, C(14); 121.7, C(14); 126.7(5), C(13); 126.8(4), C(13); 137.4, C(8); 137.6, C(8); 137.9, C(8); 146.1(9), C(9); 146.2(3), C(9); 146.7, C(9); 149.1(5); 149.1(8), C(12); 217.2(7), $C{\equiv}O_{cis}$; 217.2(9), $C{\equiv}O_{cis}$; 217.3(9), $C{\equiv}O_{cis}$; 217.4(2), $C{\equiv}O_{cis}$; 223.8(7), $C{\equiv}O_{trans}$; 223.9(3), $C{\equiv}O_{trans}$; 224.0, $C{\equiv}O_{trans}$; 224.1, $C{\equiv}O_{trans}$; 272.0, $C_{carbene}$; 272.2, $C_{carbene}$; 273.9(5), $C_{carbene}$; 274.1, $C_{carbene}$. Mass spectroscopy: *m*/*z* 605 [M$^+$, 5], 577 (10, M $-$ CO), 549 (7, M $-$ 2CO), 493 (75, M $-$ 4CO), 465 (100, M $-$ 5CO); 450 (8, 465 $-$ Me$^\cdot$), 414 (20, 465 + H$^\bullet$ $-$ Cr).

4. Supplementary material

Crystallographic data for the structural analysis have been deposited with the Cambridge Crystallographic Data Centre, CCDC nos. 154562 for **12**, 154563 for **31**, and 154564 for **33**. 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 http://www.ccdc.cam.ac.uk).

References

[1] R.C. Cambie, P.S. Rutledge, R.J. Stevenson, P.D. Woodgate, J. Organomet. Chem. 471 (1994) 133.
[2] G.R. Clark, B. Kuipers, M.R. Metzler, M.H. Nguyen, P.D. Woodgate, J. Organomet. Chem. 545 (1997) 225.
[3] R.C. Cambie, P.S. Rutledge, R.J. Stevenson, P.D. Woodgate, J. Organomet. Chem. 471 (1994) 149.
[4] R.C. Cambie, P.I. Higgs, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 384 (1990) C6.
[5] R.C. Cambie, A.D. Erson, A.C. Gourdie, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 348 (1988) 317.
[6] K. Woo, P.G. Williard, D.A. Sweigart, N.W. Duffy, B.H. Robinson, J. Simpson, J. Organomet. Chem. 487 (1995) 111.
[7] M.R. Metzler, P.D. Woodgate, private communication.
[8] R.C. Cambie, L.G. MacKay, P.S. Rutledge, M. Tercel, P.D. Woodgate, J. Organomet. Chem. 409 (1991) 263.
[9] N.A. Vol'kenau, I.N. Bolesova, L.S. Shul'pina, A.N. Kitaigorodskii, J. Organomet. Chem. 267 (1984) 313.
[10] S. Bhambri, D.A. Tocher, J. Chem. Soc. Dalton Trans. 18 (1997) 3367.
[11] S. Bhambri, D.A. Tocher, J. Organomet. Chem. 507 (1996) 291.
[12] R.E. Ireland, G.G. Brown Jr., R.H. Stanford Jr., T.C. McKenzie, J. Org. Chem. 39 (1974) 51.
[13] J.A.S. Howell, M.J. Thomas, J. Chem. Soc. Dalton Trans. (1983) 1401.
[14] A.J. Pearson, J. Yoon, Tetrahedron Lett. 26 (1985) 2399.
[15] A.J. Pearson, T.R. Perrior, D.C. Rees, J. Organomet. Chem. 226 (1982) C39.
[16] A.J. Pearson, P. Ham, D.C. Rees, Tetrahedron Lett. 21 (1980) 4637.
[17] H.-J. Knölker, Synlett (1992) 371.
[18] R.C. Cambie, M.R. Metzler, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 398 (1990) 117.
[19] R.C. Cambie, P.S. Rutledge, M. Tercel, P.D. Woodgate, J. Organomet. Chem. 315 (1986) 171.
[20] K.H. Dötz, P. Tomuschat, Chem. Soc. Rev. 28 (1999) 187.
[21] R.C. Cambie, P.I. Higgs, K.C. Lee, M.R. Metzler, P.S. Rutledge, R.J. Stevenson, P.D. Woodgate, Aust. J. Chem. 44 (1991) 1465.
[22] B.E. Mann, B.F. Taylor, ^{13}C-NMR Data for Organometallic Compounds, Academic Press, New York, 1981 (p. 15).
[23] K.H. Dötz, M. Popall, G. Müller, J. Organomet. Chem. 334 (1987) 57.
[24] W.E. Parham, Y.A. Sayed, J. Organomet. Chem. 39 (1974) 2051.
[25] R.C. Cambie, P.K. Davy, L.H. Mitchell, C.E.F. Rickard, P.S. Rutledge, Aust. J. Chem. 51 (1998) 653.
[26] M.A. Schwindt, J.R. Miller, L.S. Hegedus, J. Organomet. Chem. 413 (1991) 143.
[27] D.B. Grotjahn, K.H. Dötz, Synlett. (1991) 381.
[28] L.S. Hegedus, M.A. Schwindt, S. de Lombaert, R. Imwinkelried, J. Am. Chem. Soc. 112 (1990) 2264.
[29] C. Borel, L.S. Hegedus, J. Krebs, J. Satoh, J. Am. Chem. Soc. 109 (1987) 1101.
[30] A.J. Hartshorn, M.F. Lappert, K. Turner, J. Chem. Soc. Dalton Trans. (1978) 348.
[31] A. Haffner, L.S. Hegedus, G. de Weck, B. Hawkins, K.H. Dötz, J. Am. Chem. Soc. 110 (1988) 8413.
[32] R. Imwinkelried, L.S. Hegedus, Organometallics 7 (1988) 702.
[33] M.A. Schwindt, T. Lejon, L.S. Hegedus, Organometallics 9 (1990) 2814.
[34] E.O. Fischer, J.A. Conner, J. Chem. Soc. (A) (1969) 578.
[35] K.H. Dötz, T. Leese, Chem. Ber. 129 (1996) 623.
[36] W.D. Wulff, A.M. Gilbert, R.P. Hsung, A. Rahm, J. Org. Chem. 60 (1995) 4566.
[37] A. Yamishita, Tetrahedron Lett. 27 (1986) 5915.
[38] W.A. Szarek, B.M. Pinko, D.M. Vyas, Can. J. Chem. 55 (1977) 937.
[39] J.M. Maher, R.P. Beatty, G.R. Lee, N.J. Cooper, Organomet. Synth. 3 (1986) 35.
[40] C. Baldoli, P. Del Buttero, E. Licandro, S. Maiorana, A. Papagni, A. Zanotti-Gerosa, J. Organomet. Chem. 486 (1995) 279.
[41] R.H. Blessing, Acta Crystallogr. A 51 (1995) 33.
[42] G.M. Sheldrick, Acta Crystallogr. A 46 (1990) 467.
[43] G.M. Sheldrick, SHELXL97, Program for the refinement of crystal structures, University of Göttingen, Germany, 1997.
[44] C.R. Bennett, R.C. Cambie, Tetrahedron 23 (1967) 927.
[45] E.O. Fischer, C.G. Kreiter, H.J. Kollmeier, J. Müller, R.D. Fischer, J. Organomet. Chem. 28 (1971) 237.