ELSEVIER

Journal of Organometallic Chemistry 545–546 (1997) 225–247

Journal of Organometallic Chemistry

Stereoselective synthesis and some reactions of β-(η⁶-arene)Cr(CO)₃ complexes of podocarpic acid derivatives

George R. Clark, Bianca Kuipers, Michael R. Metzler, Manh H. Nguyen, Paul D. Woodgate *

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

Received 18 February 1997

Abstract

The stereoselective synthesis of a number of (η⁶-arene)tricarbonylchromium(0) complexes derived from podocarpic acid has been achieved in good to excellent yield. The stereochemistry of complexes **36** and **37** was established by X-ray crystallography. Reactions of some of the deprotonated complexes with electrophiles were investigated. © 1997 Elsevier Science S.A.

Keywords: Chromium; Carbonyl; Podocarpic acid derivatives,; Stereoselective synthesis; Crystal structure

1. Introduction

Earlier we reported the functionalisation of ring C of derivatives of the diterpenoid podocarpic acid (**1**) via arene complexes of some transition metals. For example, nucleophile addition to a mixture of diastereoisomeric (η⁶-arene)tricarbonylchromium(0) complexes followed by either oxidation or protonation resulted in the formation of tetracyclic steroidal compounds from the tricyclic natural product [1–5]. A diterpenoid chromium carbene complex has also been used as a key intermediate in a cyclopentaannulation sequence [6]. Functionalisation of (η⁴-diene)tricarbonyliron(0) and related cationic (η⁵-dienyl)tricarbonyliron(II) complexes of podocarpic acid derivatives was less successful [7]. Recently, the synthesis of a number of ring-C aromatic androstane analogues was achieved in high yield from reaction of either an alkene or an alkyne with a diterpenoid η²-13-acyltetracarbonylmanganese(I) complex [8,9]. The related η²-7-oxotetracarbonylmanganase(I) complexes reacted with an alkene to afford C-14 alkylated derivatives in high yields; in some cases cyclisation to C-7 also occurred, giving novel tetracyclic 4*H*-acephenanthrylene derivatives [10].

We now report the stereoselective synthesis in high yield of a number of (η⁶-arene)tricarbonylchromium(0) complexes of podocarpic acid derivatives. The generation of aryl anions from some of these complexes and their quenching with an electrophile is also reported.

2. Results and discussion

Complexation of ring-C aromatic chiral diterpenoid ligands using the method introduced by Pauson and Mahaffy [11], which involves reaction of the arene with $Cr(CO)_6$ at ca. 140°C in a solvent such as dibutyl ether containing 10–20% tetrahydrofuran, invariably gives rise to a mixture of the α and β diastereoisomers. The ratio of these facial isomers is dependent not only on the reaction time, but also on the nature and stereochemistry of substituents at C(4), a site relatively remote from the aromatic ring [12,13]. Other $Cr(CO)_3$ transfer reagents such as $Cr(CO)_3(NH_3)_3$ [14] and $Cr(CO)_3(CH_3CN)_3$ [15] have also been employed. Kundig et al. have introduced (η⁶-naphthalene)tricarbonylchromium(0) as a transfer reagent permitting the use of a lower reaction temperature [16], which has been shown to promote discrimination between the diastereotopic faces of a suitably substituted arene and lead to enhanced diastereoselection. For example, Schmalz et al. [17] have applied Kundig's method to a 1-tetralol derivative and found that the relatively mild conditions afforded the η⁶-$Cr(CO)_3$ complex in excellent yield and with high diastereoselection compared with the more vigorous thermal conditions of the Pauson–Mahaffy procedure.

* Corresponding author.

PII S0022-328X(97)00220-9

For some 12-methoxy diterpenoid substrates we have reported [3] results supporting the view that an α tricarbonylchromium(0) complex (in which one carbonyl ligand eclipses C-14 in the solid state [12], and preferentially in solution) gives predominantly or exclusively the 14-substituted product on reaction with a nucleophile [18]. Conversely, the β stereoisomer (in which C-13 is nearly eclipsed by a carbonyl ligand [12]) leads to the 13-substituted product. In these earlier studies a mixture of the α (mainly) and β complexes was used, since they are often not easy to separate chromatographically on a scale suitable for use in synthesis. A similar problem arises with separation of the decomplexed regioisomeric substituted products. It is therefore practically advantageous to develop synthetic methods that will allow the exclusive formation and then use, of only one η^6-$Cr(CO)_3$ diastereoisomer.

Substituents on the diterpenoid skeleton as far removed from ring C as C-4 (β-CO_2Me, β-Me, [12,13]; $=CH_2$ [19]) have been shown to affect the diastereoselection during arene complexation. For example, a β-CO_2Me group at C-4, as in **2**, favours the β-$Cr(CO)_3$ complex under kinetically controlled conditions and the α isomer under thermodynamic control. With the aim of influencing significantly the stereodirection of complexation by a group proximal to the aromatic ring, a number of 7β-OR (R = H, Me, CH_2OMe, OCOMe, THP, *t*-$BuMe_2Si$; **3–13**) derivatives of podocarpic acid have been synthesised in the present work. It was anticipated that use of milder $Cr(CO)_3$ transfer reagents with such substrates containing 7β-OR groups would promote complexation exclusively or primarily on the β face (the minor isomer under Pauson–Mahaffy conditions) of the diterpenoid. Further potential ligands for complexation reactions, the tetraenes **26–28** in which the effect of a C-4 β substituent was expected to be moderated due to the flattening of ring B as a consequence of introduction of the 6,7 double bond, were synthesised by acid-catalysed elimination of water from their corresponding 7β-OH precursors.

Complexation of methyl 12-methoxypodocarpa-8,11,13-trien-19-oate (**2**) using $Cr(CO)_6$/dibutyl ether-THF has been reported previously [12,13]. In the present work complexation of **2** with $Cr(CO)_3(Py)_3$ [20] in diethyl ether containing $BF_3 \cdot Et_2O$ at room temperature for 2 h afforded a mixture (1.2:1) (78%) of the β isomer **30** and the α isomer **42**. Although lowering the reaction temperature to 0°C for the same time improved the diastereoselection in favour of the β isomer (**30**:**42** = 2:1), the combined yield was decreased (40%). Extending the reaction time to 24 h at 0°C reversed the ratio in favour of the α isomer (**30**:**42** = 1:4), presumably as a consequence of the reversibility of complexation induced by the Lewis acid, but decreased the combined yield still further (23%).

Complexation of the 7-oxo diterpenoid **23** with

Table 1
Complexation of diterpenoid ligands using (η^6-naphthalene)tricarbonylchromium(0)

Ligand	Reaction conditions	β-Complex	α-Complex
3	70°C/33 h	**31** (60%)	
4	room temperature/72 h	**32** (98%)	
5	70°C/40 h	**35** (57%)	
6	70°C/50 h	**33** (60%)	
8	70°C/32 h	**36** (62%)	
9	room temperature/120 h	**37** (74%)	
10	room temperature/96 h	**38** (50%)	
11	60–65°C/20 h	**39** (34%)	**48** (16%)
12	70°C/33 h	**40** (50%)	**49** (12%)
13	room temperature/120 h then 70°C/48 h	**41** (0%)	**50** (0%)

$Cr(CO)_6/Bu_2O$–THF afforded the expected thermodynamically favoured α isomer **56** (42%). The stereochemistry of **56** was assigned on the basis of the shift downfield (~ 0.1 ppm) of the signal due to $H(20)_3$ in the ^{1}H-NMR spectrum relative to that in the free ligand **23**. Furthermore, the upfield shifts of the signals due to C-1 and C-5 in the ^{13}C-NMR spectrum of **56** relative to **23** are in agreement with the α stereochemistry of the η^6-$Cr(CO)_3$ moiety [13].

Attention was then turned to the milder and non-acidic conditions offered by Kundig's method. With tricarbonyl(η^6-naphthalene)chromium(0) as the transfer reagent, optimum complexation was achieved by reaction of a diterpenoid ligand (0.2–0.3 g) with the degassed solution in EtO_2-THF, and the progress of each reaction was monitored by TLC. Using this procedure, the 7β-OR (R = H, OMe and OCH_2OMe; **3–6, 9, 10**) diterpenoids were complexed to give exclusively the corresponding β-$Cr(CO)_3$ isomer (**31–33, 35–38**) in good to excellent yield (50–98%) (Table 1).

The stereochemistry of complexes **36** and **37** was assigned initially from NMR data [cf. Refs. [5,13]] and then confirmed as β in each case by single crystal X-ray diffraction (Figs. 1 and 2, Tables 2–6). Interestingly, the average Cr–CO bond length (1.834 Å) in the

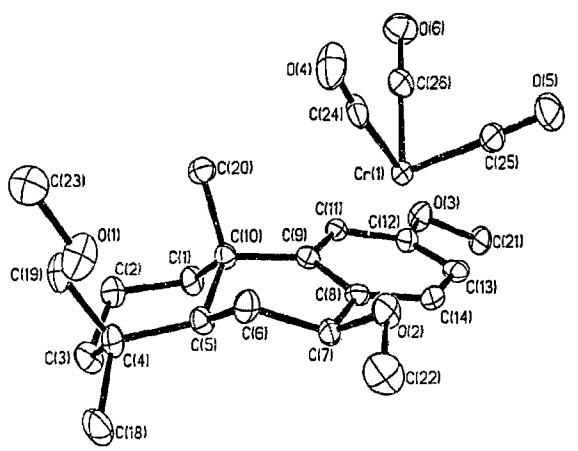


Fig. 1. The atomic arrangement in **36**.

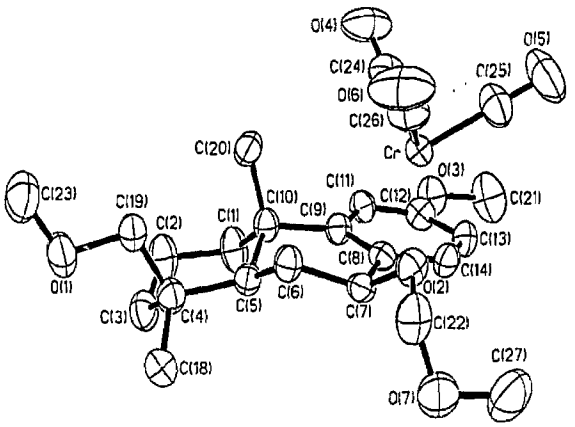


Fig. 2. The atomic arrangement in **37**.

7β-OMe compound **36** is longer than that (1.820 Å) in the 7β-OCH_2OMe analogue **37**, although the average Cr–C_{aryl} distances are the same (2.241 Å) for each. Otherwise the crystal structure data are typical of related diterpenoid η^6-$Cr(CO)_3$ complexes [5].

In contrast to the exclusive stereocontrol exhibited by the benzylic OH, OMe, or OCH_2OMe substituents, complexation of either the 7β-acetate **11** or the 7β-tetrahydropyranyl ether **12** using the Kundig procedure afforded mixtures, although the β diastereoisomer(s) still predominated [**39**/**48**, 50%, 2.1:1; **40**/**49**, 62%, 4.2:1]. The 7β-OTHP ligand **12** was itself a mixture of *four* isomers (two epimeric pairs, two conformers of each; ^{1}H-NMR) reflecting the generation of a new stereogenic centre in the ether substituent during its formation, and four diastereoisomers were formed in the complexation step. However, a pure sample of each of the two β-$Cr(CO)_3$ complexes was isolated by chromatography and then crystallisation, and their stereochemistry was confirmed by their NMR data relative to that of an inseparable mixture of the pair of α-$Cr(CO)_3$ isomers.

Table 2
Crystal data and structure refinement for **36** and **37**

	36	**37**
Empirical formula	$C_{23}H_{30}CrO_6$	$C_{24}H_{32}CrO_7$
Formula weight	454.47	484.50
Temperature (K)	193(2)	292(2)
Wavelength (Å)	0.71069	0.71069
Crystal system	Orthorhombic	Monoclinic
Space group	$P2_12_12_1$	$P2_1$
Unit cell dimensions (Å)	$a = 9.975(7)$	$a = 10.5010(10)$
	$b = 9.921(2)$	$b = 6.623(2)$
	$c = 21.593(3)$	$c = 16.986(6)$
	$\alpha = 90.00°$	$\alpha = 90.00°$
	$\beta = 90.00°$	$\beta = 92.95(2)°$
	$\gamma = 90.00°$	$\gamma = 90.00°$
Volume (Å^3)	2137(2)	1179.8(6)
Z	4	2
Density (calculated, Mg m^{-3})	1.413	1.364
Absorption coefficient (mm^{-1})	0.572	0.526
$F(000)$	960	512
Crystal size (mm)	0.27 × 0.25 × 0.25	0.33 × 0.25 × 0.25
θ range for data collection	1.89 to 26.45°	1.20 to 25.97°
Index ranges	$0 \le h \le 12$	$-12 \le h \le 12$
	$0 \le k < 12$	$0 \le k \le 8$
	$0 \le l \le 27$	$0 \le l \le 20$
Reflections collected	2471	2604
Independent reflections	2471 [R(int) = 0.0000]	2519 [R(int) = 0.0222]
Refinement method	Full-matrix least-squares on F^2	Full-matrix least-squares on F^2
Data/restraints/parameters	2470/0/380	2519/1/294
Goodness-of-fit on F^2	1.030	1.037
Final R indices [$I > 2\sigma(I)$]	$R1 = 0.0325$	$R1 = 0.0381$
	$wR2 = 0.0756$	$wR2 = 0.0876$
R indices (all data)	$R1 = 0.0532$	$R1 = 0.0652$
	$wR2 = 0.0838$	$wR2 = 0.0984$
Largest difference max. (e Å^{-3})	0.304	0.242
Largest difference min. (e Å^{-3})	−0.386	−0.256
$\omega = 1/[\sigma^2(F_o)^2 + (aP)^2 + bP]$	$a = 0.0496$	$a = 0.0543$
	$b = 0.33$	$b = 0.10$
Number of observed reflections [$> 2\sigma(I)$]	2045	1982
Absolute structure parameter	−0.06(3)	0.03(3)

Table 3
AAtomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **36**; U_{eq} is defined as one third of the trace of the orthogonalised U_{ij} tensor

Atom	X	Y	Z	U_{eq}
Cr	302(1)	9579(1)	135(1)	17(1)
O(1)	5053(3)	10154(3)	2068(2)	37(1)
O(2)	1835(3)	6897(2)	1030(1)	24(1)
O(3)	−2672(3)	11071(3)	286(1)	26(1)
O(4)	3240(3)	9631(3)	−116(1)	40(1)
O(5)	281(4)	7559(3)	−894(1)	35(1)
O(6)	106(4)	11741(3)	−823(1)	36(1)
C(1)	633(4)	12141(4)	1914(2)	22(1)
C(2)	1532(4)	12804(4)	2399(2)	24(1)
C(3)	2092(5)	11767(4)	2849(2)	27(1)
C(4)	2900(4)	10638(4)	2533(2)	23(1)
C(5)	2019(4)	10033(3)	2006(2)	19(1)
C(6)	2608(4)	8818(4)	1658(2)	21(1)
C(7)	1438(4)	7963(4)	1433(2)	19(1)
C(8)	384(4)	8799(4)	1105(2)	18(1)
C(9)	375(4)	10251(3)	1143(1)	17(1)
C(10)	1396(4)	11041(4)	1540(2)	18(1)
C(11)	−637(4)	10938(4)	827(2)	19(1)
C(12)	−1707(4)	10264(4)	526(2)	22(1)
C(13)	−1689(4)	8855(4)	483(2)	21(1)
C(14)	−644(4)	8146(4)	773(2)	20(1)
C(18)	3931(4)	9556(5)	3026(2)	33(1)
C(19)	4261(4)	11199(4)	2334(2)	26(1)
C(20)	2406(4)	11750(4)	1113(2)	23(1)
C(21)	−3931(4)	10453(5)	126(2)	27(1)
C(22)	2413(5)	5794(4)	1353(2)	33(1)
C(23)	6314(5)	10605(5)	1865(2)	33(1)
C(24)	2111(4)	9619(4)	5(1)	23(1)
C(25)	269(5)	8321(3)	−493(2)	22(1)
C(26)	185(5)	10906(4)	−455(2)	22(1)

Attempted complexation of the relatively sterically congested 7β-*t*-BuMe$_2$SiO derivative **13** with the transfer reagent at either room temperature (5 days) or 70°C (2 days) returned only naphthalene and the starting diterpenoid. Treatment of **13** with $Cr(CO)_6$ in refluxing Bu_2O–THF for 21 h was successful, but afforded a mixture (7:3) (93%) of the α and β diastereoisomeric tricarbonylchromium(0) complexes (**50**, **41**) as yellow needles, m.p. 135–137°C. The ^{1}H-NMR spectrum of the minor β complex **41** showed singlets due to $H(18)_3$ and $H(20)_3$ at δ 1.24 and 1.23 ppm, respectively. The resonances for C-1 and C-5 occurred at δ 41.5 and 50.8 ppm in the ^{13}C-NMR spectrum, both signals being downfield relative to those in the free ligand **13**. The corresponding signals for the major α isomer **50** occurred at δ 1.27 and 1.15 ppm [$H(18)_3$, $H(20)_3$], and at δ 37.2 and 47.6 ppm [C-1, C-5].

Application of the Kundig procedure to the 12-desoxy-7β-hydroxy diterpenoid **4** gave only the β isomer **32** in excellent yield (Table 1). However, treatment of **4** with $Cr(CO)_6$ in refluxing Bu_2O–THF for 24 h afforded a mixture of the α and β diastereoisomers **43** and **32** (68%), together with a mixture (24%) of the α

Table 4
Bond lengths (Å) and angles (°) for **36**

Cr–C(24)	1.826(4)	C(24)–Cr–C(12)	156.8(2)
Cr–C(26)	1.835(4)	C(26)–Cr–C(12)	89.3(2)
Cr–C(25)	1.842(4)	C(25)–Cr–C(12)	117.3(2)
Cr–C(14)	2.193(4)	C(14)–Cr–C(12)	65.29(14)
Cr–C(11)	2.221(4)	C(11)–Cr–C(12)	36.68(14)
Cr–C(8)	2.235(3)	C(8)–Cr–C(12)	77.7(2)
Cr–C(13)	2.241(4)	C(13)–Cr–C(12)	36.11(12)
Cr–C(9)	2.278(3)	C(9)–Cr–C(12)	65.55(14)
Cr–C(12)	2.279(4)	C(23)–O(1)–C(19)	113.0(3)
O(1)–C(23)	1.405(5)	C(22)–O(2)–C(7)	112.6(3)
O(1)–C(19)	1.425(5)	C(12)–O(3)–C(21)	117.4(3)
O(2)–C(22)	1.420(4)	C(2)–C(1)–C(10)	111.8(3)
O(2)–C(7)	1.427(4)	C(3)–C(2)–C(1)	111.2(3)
O(3)–C(12)	1.355(5)	C(2)–C(3)–C(4)	113.7(3)
O(3)–C(21)	1.440(4)	C(19)–C(4)–C(18)	107.2(3)
O(4)–C(24)	1.157(5)	C(19)–C(4)–C(3)	109.0(3)
O(5)–C(25)	1.150(4)	C(18)–C(4)–C(3)	107.0(3)
O(6)–C(26)	1.151(4)	C(19)–C(4)–C(5)	115.9(3)
C(1)–C(2)	1.528(5)	C(18)–C(4)–C(5)	109.5(3)
C(1)–C(10)	1.556(5)	C(3)–C(4)–C(5)	108.0(3)
C(2)–C(3)	1.521(6)	C(6)–C(5)–C(10)	110.1(3)
C(3)–C(4)	1.539(5)	C(6)–C(5)–C(4)	116.3(3)
C(4)–C(19)	1.528(6)	C(10)–C(5)–C(4)	116.9(3)
C(4)–C(18)	1.536(5)	C(7)–C(6)–C(5)	107.5(3)
C(4)–C(5)	1.558(5)	O(2)–C(7)–C(8)	108.3(3)
C(5)–C(6)	1.536(5)	O(2)–C(7)–C(6)	113.3(3)
C(5)–C(10)	1.548(5)	C(8)–C(7)–C(6)	112.1(3)
C(6)–C(7)	1.523(5)	C(14)–C(8)–C(9)	118.9(4)
C(7)–C(8)	1.514(5)	C(14)–C(8)–C(7)	119.4(3)
C(8)–C(14)	1.409(5)	C(9)–C(8)–C(7)	121.6(4)
C(8)–C(9)	1.443(4)	C(14)–C(8)–Cr(1)	69.8(2)
C(9)–C(11)	1.396(5)	C(9)–C(8)–Cr(1)	73.0(2)
C(9)–C(10)	1.545(5)	C(7)–C(8)–Cr(1)	130.7(3)
C(10)–C(20)	1.537(5)	C(11)–C(9)–C(8)	117.7(4)
C(11) C(12)	1.417(6)	C(11)–C(9)–C(10)	120.0(3)
C(12)–C(13)	1.402(5)	C(8)–C(9)–C(10)	122.2(4)
C(13)–C(14)	1.405(6)	C(11)–C(9)–Cr(1)	69.7(2)
C(24)–Cr–C(26)	86.6(2)	C(8)–C(9)–Cr(1)	69.8(2)
C(24)–Cr–C(25)	85.42	C(10)–C(9)–Cr(1)	134.4(3)
C(26)–Cr–C(25)	88.53(14)	C(20)–C(10)–C(9)	109.3(3)
C(24)–Cr–C(14)	122.4(2)	C(20)–C(10)–C(5)	115.0(3)
C(26)–Cr–C(14)	150.9(2)	C(9)–C(10)–C(5)	107.3(3)
C(25)–Cr–C(14)	90.9(2)	C(20)–C(10)–C(1)	108.1(3)
C(24)–Cr–C(11)	120.5(2)	C(9)–C(10)–C(1)	108.7(3)
C(26)–Cr–C(11)	90.3(2)	C(5)–C(10)–C(1)	108.2(3)
C(25)–Cr–C(11)	154.0(2)	C(9)–C(11)–C(12)	122.6(3)
C(14)–Cr–C(11)	77.82(12)	C(9)–C(11)–Cr	74.2(2)
C(24)–Cr–C(8)	96.6(2)	C(12)–C(11)–Cr	73.9(2)
C(26)–Cr–C(8)	154.28(14)	O(3)–C(12)–C(13)	125.0(4)
C(25)–Cr–C(8)	117.13(14)	O(3)–C(12)–C(11)	115.6(3)
C(14)–Cr–C(8)	37.09(14)	C(13)–C(12)–C(11)	119.4(4)
C(11)–Cr–C(8)	66.06(13)	O(3)–C(12)–Cr	131.2(2)
C(24)–Cr–C(13)	159.0(2)	C(13)–C(12)–Cr	70.5(3)
C(26)–Cr–C(13)	114.0(2)	C(11)–C(12)–Cr	69.4(2)
C(25)–Cr–C(13)	90.8(2)	C(12)–C(13)–C(14)	118.7(4)
C(14)–Cr–C(13)	36.92(14)	C(12)–C(13)–Cr	73.4(3)
C(11)–Cr–C(13)	66.11(14)	C(14)–C(13)–Cr	69.7(2)
C(8)–Cr–C(13)	66.9(2)	C(13)–C(14)–C(8)	122.5(3)
C(24)–Cr–C(9)	96.3(2)	C(13)–C(14)–Cr	73.4(2)
C(26)–Cr–C(9)	117.06(14)	C(8)–C(14)–Cr	73.1(2)
C(25)–Cr–C(9)	154.40(14)	O(1)–C(19)–C(4)	109.9(3)
C(14)–Cr–C(9)	66.61(13)	O(4)–C(24)–Cr	175.7(3)
C(11)–Cr–C(9)	36.12(14)	O(5)–C(25)–Cr	177.8(4)
C(8)–Cr–C(9)	37.27(10)	O(6)–C(26)–Cr	179.7(4)
C(13)–Cr–C(9)	78.55(14)		

Table 5
Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($Å^2 \times 10^3$) for **37**; U_{eq} is defined as one third of the trace of the orthogonalised U_{ij} tensor

Atom	X	Y	Z	U_{eq}
Cr	1723(1)	9992(1)	8241(1)	36(1)
O(1)	−5154(3)	11156(7)	6482(3)	66(1)
O(2)	1204(3)	11467(5)	6160(2)	40(1)
O(3)	2309(3)	12852(6)	9821(2)	53(1)
O(4)	802(5)	6913(7)	9362(2)	87(1)
O(5)	4279(4)	8048(9)	8444(3)	100(2)
O(6)	1142(6)	7143(7)	6920(3)	102(2)
O(7)	1496(4)	13983(7)	5217(2)	67(1)
C(1)	−2086(4)	13251(11)	8603(3)	56(2)
C(2)	−3533(4)	13312(12)	8433(3)	62(2)
C(3)	−3874(4)	14101(9)	7607(3)	52(1)
C(4)	−3253(4)	12935(8)	6949(3)	42(1)
C(5)	−1801(4)	12723(7)	7171(2)	35(1)
C(6)	−1026(4)	11639(7)	6560(2)	38(1)
C(7)	324(4)	12504(7)	6637(2)	33(1)
C(8)	848(4)	12477(7)	7486(2)	33(1)
C(9)	56(4)	12207(7)	8128(2)	33(1)
C(10)	−1403(4)	11904(7)	8013(2)	36(1)
C(11)	633(4)	12248(8)	8893(3)	38(1)
C(12)	1915(4)	12709(8)	9042(3)	41(1)
C(13)	2707(4)	12955(8)	8409(3)	43(1)
C(14)	2167(4)	12836(8)	7638(2)	38(1)
C(18)	−3420(5)	14198(8)	6197(3)	56(1)
C(19)	−3896(4)	10878(8)	6805(3)	46(1)
C(20)	−1726(4)	9680(8)	8162(3)	46(1)
C(21)	3623(5)	13137(13)	10000(3)	77(2)
C(22)	1100(5)	12018(10)	5352(3)	55(1)
C(23)	−5743(5)	9294(9)	6280(4)	66(2)
C(24)	1162(6)	8083(9)	8916(3)	55(2)
C(25)	3278(5)	8809(10)	8356(3)	62(2)
C(26)	1362(6)	8237(9)	7436(3)	55(1)
C(27)	2800(5)	14305(12)	5397(4)	84(2)

and β diastereoisomers **54** and **52** of the derived 7-oxo complexes. As expected from these reaction conditions, the α diastereoisomer predominated in both sets of complexes. Similarly, treatment of the 7β-hydroxy-12,19-dimethoxy diterpenoid **6** with hexacarbonylchromium(0) in Bu_2O–THF afforded, in addition to recovered starting material, the α diastereoisomers of both the 7β-hydroxy complex **44** (36%) and the 7-oxo complex **55** (14%). Complexation of the 7β-hydroxy-19-methoxycarbonyl analogue **7** with $Cr(CO)_6$ afforded mainly the α diastereoisomer **45** (75%) as a yellow oil, together with a small amount of the β complex **34** contaminated with a trace of the α diastereoisomer of the 7-oxo complex **56**. The latter orange complex was also formed directly from the 7-ketone **23** in moderate yield (42%). Under similar conditions, the 7β,12,19-trimethoxy diterpenoid **8** afforded only the α complex **46** (69%). Benzylic oxidation (CH_2 to CO) has been reported using $Cr(CO)_6$/*t*-BuOOH [21,22]. The formation of 7-oxo complexes during Pauson–Mahaffy complexation of the 7β-hydroxy diterpenoids in the present work may reflect either the occlusion of some oxygen in the

Table 6
Bond lengths (Å) and angles (°) for **37**

Cr–C(25)	1.812(5)	C(25)–Cr–C(9)	165.7(2)
Cr–C(26)	1.823(6)	C(26)–Cr–C(9)	102.6(2)
Cr–C(24)	1.824(6)	C(24)–Cr–C(9)	103.1(2)
Cr–C(14)	2.205(5)	C(14)–Cr–C(9)	65.9(2)
Cr–C(11)	2.213(5)	C(11)–Cr–C(9)	36.4(2)
Cr–C(13)	2.229(5)	C(13)–Cr–C(9)	78.1(2)
Cr–C(8)	2.253(4)	C(8)–Cr–C(9)	36.36(14)
Cr–C(12)	2.258(5)	C(12)–Cr–C(9)	65.4(2)
Cr–C(9)	2.285(4)	C(23)–O(1)–C(19)	111.6(4)
O(1)–C(23)	1.414(7)	C(22)–O(2)–C(7)	113.8(4)
O(1)–C(19)	1.416(5)	C(12)–O(3)–C(21)	117.4(4)
O(2)–C(22)	1.419(6)	C(22)–O(7)–C(27)	113.8(5)
O(2)–C(7)	1.436(5)	C(2)–C(1)–C(10)	112.4(4)
O(3)–C(12)	1.370(5)	C(3)–C(2)–C(1)	111.5(4)
O(3)–C(21)	1.410(6)	C(2)–C(3)–C(4)	114.2(4)
O(4)–C(24)	1.161(7)	C(18)–C(4)–C(3)	107.4(4)
O(5)–C(25)	1.168(6)	C(18)–C(4)–C(19)	108.8(4)
O(6)–C(26)	1.148(7)	C(3)–C(4)–C(19)	111.3(4)
O(7)–C(22)	1.389(7)	C(18)–C(4)–C(5)	108.6(4)
O(7)–C(27)	1.404(6)	C(3)–C(4)–C(5)	108.5(4)
C(1)–C(2)	1.533(6)	C(19)–C(4)–C(5)	112.1(4)
C(1)–C(10)	1.546(6)	C(6)–C(5)–C(4)	115.2(3)
C(2)–C(3)	1.522(7)	C(6)–C(5)–C(10)	109.3(3)
C(3)–C(4)	1.531(6)	C(4)–C(5)–C(10)	117.6(3)
C(4)–C(18)	1.530(6)	C(7)–C(6)–C(5)	105.8(3)
C(4)–C(19)	1.535(7)	O(2)–C(7)–C(8)	108.6(4)
C(4)–C(5)	1.558(5)	O(2)–C(7)–C(6)	113.2(4)
C(5)–C(6)	1.530(6)	C(8)–C(7)–C(6)	111.5(3)
C(5)–C(10)	1.566(6)	C(14)–C(8)–C(9)	119.2(4)
C(6)–C(7)	1.528(5)	C(14)–C(8)–C(7)	118.4(4)
C(7)–C(8)	1.518(6)	C(9)–C(8)–C(7)	122.3(3)
C(8)–C(14)	1.416(6)	C(14)–C(8)–Cr	69.7(3)
C(8)–C(9)	1.416(5)	C(9)–C(8)–Cr	73.0(2)
C(9)–C(11)	1.405(6)	C(7)–C(8)–Cr	131.8(3)
C(9)–C(10)	1.548(5)	C(11)–C(9)–C(8)	117.8(4)
C(10)–C(20)	1.536(7)	C(11)–C(9)–C(10)	119.8(4)
C(11)–C(12)	1.391(6)	C(8)–C(9)–C(10)	122.4(3)
C(12)–C(13)	1.401(6)	C(11)–C(9)–Cr	69.0(2)
C(13)–C(14)	1.403(6)	C(8)–C(9)–Cr	70.6(2)
C(25)–Cr–C(26)	87.5(3)	C(10)–C(9)–Cr	132.6(3)
C(25)–Cr–C(24)	87.2(3)	C(20)–C(10)–C(1)	109.4(4)
C(26)–Cr–C(24)	88.1(3)	C(20)–C(10)–C(9)	109.2(4)
C(25)–Cr–C(14)	102.0(2)	C(1)–C(10)–C(9)	109.4(4)
C(26)–Cr–C(14)	103.8(2)	C(20)–C(10)–C(5)	115.6(4)
C(24)–Cr–C(14)	165.1(2)	C(1)–C(10)–C(5)	106.3(4)
C(25)–Cr–C(11)	136.4(2)	C(9)–C(10)–C(5)	106.6(3)
C(26)–Cr–C(11)	135.6(2)	C(12)–C(11)–C(9)	122.6(4)
C(24)–Cr–C(11)	87.8(2)	C(12)–C(11)–Cr	73.6(3)
C(14)–Cr–C(11)	77.5(2)	C(9)–C(11)–Cr	74.6(3)
C(25)–Cr–C(13)	87.6(2)	O(3)–C(12)–C(11)	115.6(4)
C(26)–Cr–C(13)	137.4(2)	O(3)–C(12)–C(13)	124.8(4)
C(24)–Cr–C(13)	133.8(2)	C(11)–C(12)–C(13)	119.6(4)
C(14)–Cr–C(13)	36.9(2)	O(3)–C(12)–Cr	130.6(4)
C(11)–Cr–C(13)	65.8(2)	C(11)–C(12)–Cr	70.1(3)
C(25)–Cr–C(8)	135.7(2)	C(13)–C(12)–Cr	70.7(3)
C(26)–Cr–C(8)	88.7(2)	C(12)–C(13)–C(14)	118.8(4)
C(24)–Cr–C(8)	136.7(2)	C(12)–C(13)–Cr	72.9(3)
C(14)–Cr–C(8)	37.0(2)	C(14)–C(13)–Cr	70.6(3)
C(11)–Cr–C(8)	65.5(2)	C(13)–C(14)–C(8)	121.6(4)
C(13)–Cr–C(8)	66.6(2)	C(13)–C(14)–Cr	72.5(3)
C(25)–Cr–C(12)	103.2(2)	C(8)–C(14)–Cr	73.3(3)
C(26)–Cr–C(12)	166.0(2)	O(1)–C(19)–C(14)	109.9(4)
C(24)–Cr–C(12)	101.3(2)	O(7)–C(22)–O(2)	113.0(4)
C(14)–Cr–C(12)	65.5(2)	O(4)–C(24)–Cr	178.0(5)

Table 6 (continued)

C(11)–Cr–C(12)	36.2(2)	O(5)–C(25)–Cr	178.9(6)
C(13)–Cr–C(12)	36.4(2)	O(6)–C(26)–Cr	179.0(5)
C(8)–Cr–C(12)	77.4(2)		

solvents, notwithstanding the three freeze–pump–thaw degassing cycles used routinely, or the effect of some Cr(III) generated in situ.

The availability of the 7-oxo α complex **56** opened a stereoselective route to 7α-hydroxypodocarpanes. Treatment of a non-complexed 7-oxo diterpenoid with sodium borohydride leads either exclusively or mainly to a 7β-alcohol by preferential delivery of hydride to the underface of the molecule (e.g. **20** → **3**, 100%; **21** → **4**, 82%). Moreover, attempted inversion of configuration of the acetate **11** using diethyl azodicarboxylate in a Mitsunobu sequence [23] was unsuccessful, while application of a modified method to the parent alcohol **6** gave only a low yield (25%) of an inseparable mixture (1:2) of the 7β-acetate **11** and the 7α-acetate **19**. As expected, however, treatment of the 7-oxo α-Cr(CO)$_3$ complex **56** with sodium borohydride resulted in stereospecific delivery of hydride to the upper face of the molecule to afford the 7α-hydroxy α-Cr(CO)$_3$ complex **51** (80%). This complex was isolated as a yellow oil which showed the molecular ion at m/z 454 with an accurate mass measurement that was correct for $C_{22}H_{26}CrO_7$. In the ^{1}H-NMR spectrum of the α complex **51** of the axial alcohol the signal due to H-7β at δ 4.33 ppm was a multiplet of $W_{1/2}$ 16.0 Hz. In contrast, the ^{1}H-NMR spectrum of the α Cr(CO)$_3$ complex **45** of the epimeric alcohol showed H-7α (axial) as a broader multiplet ($W_{1/2}$ 26.0 Hz) at δ 4.53 ppm.

Thermally promoted complexation of the 12-methoxy $\Delta^{6,7}$ tetraene **28** by reaction with Cr(CO)$_6$ for 24 h afforded not only the $\Delta^{6,7}$ α complex **59** (66%) but also the β stereoisomer of the $\Delta^{5,6}$ alkene **58** (13%). Treatment of **28** with (η^6-naphthalene)tricarbonylchromium(0) in Et$_2$O containing THF for 60 h at room temperature also afforded both **59** (58%) and **58** (22%), together with recovered **28** (20%). The fact that only one η^6 facial isomer was isolated for each of the isomeric alkenes suggests that shift of the double bond occurs only in the β-Cr(CO)$_3$ complex, even at room temperature. Presumably this reflects a thermodynamic preference for the alkene to be non-conjugated in the β-Cr(CO)$_3$ complex. The α stereochemistry of the 6,8,11,13-tetraene complex **59** was verified by its independent synthesis. Thus, dehydration of the 7β-hydroxy α complex **45** by treatment with potassium hydrogensulfate in benzene afforded the $\Delta^{6,7}$ α complex **59** (31%) and its free ligand **28** (44%). Decomplexation (diethyl ether/light/air) of a mixture (3:2) of stereoisomers **58** and **59** followed by PLC afforded the 6,8,11,13-tetraene **28** (27%) and its non-conjugated $\Delta^{5,6}$ isomer **29** (42%). The latter alkene was isolated as white needles, m.p. 115–117°C. Accurate measurement of the molecular ion at m/z 300 in the mass spectrum was consistent with the formula $C_{19}H_{24}O_3$. In the ^{1}H-NMR spectrum of **29** signals due to H-6 at δ 5.99 ppm (dd, J 4.9, 2.9 Hz), to H-7ax at δ 3.40 (dd, J 21.5, 4.9 Hz) and to H-7eq at δ 3.49 (dd, J 21.5, 2.9 Hz) were in agreement with the proposed structure.

As mentioned in the Introduction, functionalisation of ring C in diterpenoid η^6-Cr(CO)$_3$ complexes has been achieved in previous work by nucleophile addition-oxidation or -protonation sequences, C-14 being the preferred site of nucleophile attack in an α stereoisomer. The availability in the present work of a number of stereochemically pure η^6-Cr(CO)$_3$ complexes offered the opportunity briefly to explore the regiochemistry of metallation-electrophile quenching in ring C. Thus, treatment of the 7β-hydroxy β-Cr(CO)$_3$ complex **33** with t-BuLi/TMEDA in THF at −78°C followed by trapping of the aryl anion with chlorotrimethylsilane and decomplexation afforded the 13-trimethylsilyl-7β-ol **14** (36%), and an inseparable mixture (1:1) of the 14-trimethylsilyl-7-ketone **24** and its 13-trimethylsilyl regioisomer **25** (10%). The regioselectivity is therefore ca. 8:1 in favour of functionalisation of C-13. The 13-SiMe$_3$ product **14** showed ^{1}H and ^{13}C NMR, and infrared and mass spectral data consistent with the proposed structure. In particular, the ^{1}H-NMR spectrum showed only two singlets in the aromatic region, confirming electrophile incorporation at C-13.

Conversion of the benzylic hydroxy group into an ether resulted in a cleaner reaction. Thus, treatment of the 7β-methoxy α-Cr(CO)$_3$ complex **46** in a similar manner as for **33** afforded only the 13-trimethylsilyl derivative **60** (80%). Similarly, deprotonation of the stereoisomeric 7β-methoxy β-Cr(CO)$_3$ complex **36** with t-BuLi/TMEDA/THF/−78°C followed by reaction with chlorotrimethylsilane and decomplexation also afforded only the analogous 13-trimethylsilyl derivative **15** (97%).

Allylation of the anions generated from a mixture (1:1) of the 7β-methoxy α and β diastereoisomers **46** and **36** afforded a similar mixture (~ 1:1) of the α and β 13-(3′-propenyl)tricarbonylchromium complexes **61** and **62** (87%). The presence of an uncharged chelating dioxygenated ether substituent at the benzylic site is known to deliver an alkyllithium base regioselectively to the proximal proton of some (η^6-arene)chromium complexes, resulting in lithiation at the *ortho* (in the present case, C-14) site [24]. However, deprotonation of the β diastereoisomer of the 7β-methoxymethoxy complex **37** followed by either silylation or methylation afforded only the 13-trimethylsilyl **17** and 13-methyl **63** derivatives in high yield (95 and 90%, respectively).

If a benzylic substituent has any influence on kinetically controlled deprotonation, a difference in the regioselectivity of arene lithiation between the 7β-alcohol complex **33** and the derived 7β-ether complexes **36**, **37**, and **46** may have been expected [25], because the electrostatic interaction between a 7β-alkoxy anion and an alkyllithium base (resulting in its potential delivery to H-14) is absent in the latter compounds. The results presented here, however, establish that the electron-withdrawing η^6-Cr(CO)$_3$ group coordinated to either the α face or the β face of ring C of 7β-OMe or 7β-OCH$_2$Me podocarpane derivatives always activates exclusively H-13 to deprotonation/electrophile addition under standard kinetically controlled reaction conditions. That is, in these diterpenoid complexes the substituent bound directly to the aromatic ring (i.e. the 12-OMe group) controls the regioselectivity of arene lithiation. This regioselectivity parallels that established [18] for simple achiral analogues; metallation of either the anisole, fluorobenzene, or chlorobenzene complexes always occurs *ortho* to the functional group. Moreover, the preferred conformation of a Cr(CO)$_3$ tripod appears to have no controlling effect. The X-ray structure (Fig. 1) of the β isomer of (7β,12,19-trimethoxypodocarpa-8,11,13-triene)Cr(CO)$_3$ **36** showed the tripod in a staggered conformation, suggesting that lithiation might occur at either C-13 or C-14, or both. On the other hand, eclipsing of H-14 in the solution conformation (^{1}H-NMR) of the stereoisomeric α complex **46** suggests preferential activation of H-14 towards deprotonation. In fact, the experimental results confirm that H-13 is the favoured site for metallation/electrophile incorporation, irrespective of the stereochemistry of η^6-Cr(CO)$_3$ coordination.

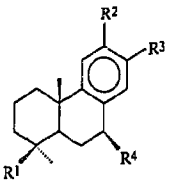
2.1. X-ray crystal structures for 36 and 37

Crystals suitable for data collection were mounted on glass fibres and positioned on a Nonius CAD-4 diffractometer. Unit cell dimensions were derived from least-squares fits to the observed setting angles of 25 reflections, using monochromated Mo-$K\alpha$ radiation. Intensity data collection employed the $2\theta/\omega$ technique with a total peak/background count time of 2:1. Reflections were counted for 60 s or until $\sigma(I)/I$ was 0.02. Crystal alignment and decomposition were monitored throughout data collection by measuring three standard reflections every 100 measurements; no statistical variation was observed. The data were corrected for Lorentz and polarisation effects and equivalent reflections averaged. Computing was carried out using the SDP suite of programs on a PDP-11 for initial data processing, SHELXS-86 [26] and SHELXL-93 [27] on an IBM 4341 or Microvax computer for structure solution and refinement. Details of crystal data and intensity data collection parameters are summarised in Table 2.

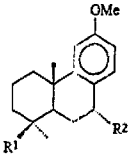
2.2. Structure solution and refinement

The structures were solved by direct methods using SHELXS-86 [26]. Refinement was by full-matrix least squares [27], minimising the function $\Sigma\omega(\|F_o\|^2 - \|F_c\|^2)^2$. Atomic scattering factors were for neutral atoms. After initial isotropic refinement, anisotropic thermal parameters were refined for all non-hydrogen atoms. Hydrogen atoms were located from difference maps and refined with a common thermal parameter. A final electron density difference map showed no feature greater than 0.5 e Å^{-3}. Weights used were $\omega = 1/[(\sigma^2(F_o)^2 + (aP)^2 + bP)]$ where $P = [(F_o)^2 + 2(F_c)^2]/3$, and the final values of a and b are given in Table 2.

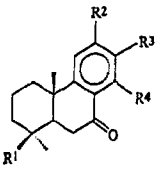
Final atomic coordinates, bond distances and bond angles are given in Tables 3–6. Lists of hydrogen coordinates, thermal parameters, bond angles and observed and calculated structure factors are available from the authors.



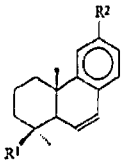
(1: R1 = CO_2H, R2 = OH, R3 = R4 = H
2: R1 = CO_2Me, R2 = OMe, R3 = R4 = H
3: R1 = CH_2OMe, R2 = R3 = H, R4 = OH
4: R1 = CO_2Me, R2 = R3 = H, R4 = OH
5: R1 = CH_2OMe, R2 = R3 = H, R4 = OMe
6: R1 = CH_2OMe, R2 = OMe, R3 = H, R4 = OH
7: R1 = CO_2Me, R2 = OMe, R3 = H, R4 = OH
8: R1 = CH_2OMe, R2 = OMe, R3 = H, R4 = OMe
9: R1 = CH_2OMe, R2 = OMe, R3 = H, R4 = OCH_2OMe
10: R1 = CO_2Me, R2 = OMe, R3 = H, R4 = OCH_2OMe
11: R1 = CH_2OMe, R2 = OMe, R3 = H, R4 = OCOMe
12: R1 = CH_2OMe, R2 = OMe, R3 = H, R4 = OTHP
13: R1 = CO_2Me, R2 = OMe, R3 = H, R4 = t-$BuMe_2SiO$
14: R1 = CH_2OMe, R2 = OMe, R3 = $SiMe_3$, R4 = OH
15: R1 = CH_2OMe, R2 = OMe, R3 = $SiMe_3$, R4 = OMe
16: R1 = CH_2OMe, R2 = OMe, R3 = $CH_2CH{=}CH_2$, R4 = OMe
17: R1 = CH_2OMe, R2 = OMe, R3 = $SiMe_3$, R4 = OCH_2OMe)



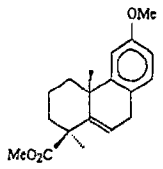
(18: R1 = CO_2Me, R2 = CH_2OMe
19: R1 = CH_2OMe, R2 = OCOMe)



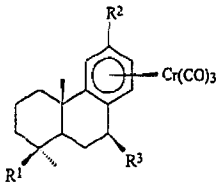
(20: R1 = CH_2OMe, R2 = R3 = R4 = H
21: R1 = CO_2Me, R2 = R3 = R4 = H
22: R1 = CH_2OMe, R2 = OMe, R3 = R4 = H
23: R1 = CO_2Me, R2 = OMe, R3 = R4 = H
24: R1 = CH_2OMe, R2 = OMe, R3 = $SiMe_3$, R4 = H
25: R1 = CH_2OMe, R2 = OMe, R3 = H, R4 = $SiMe_3$)



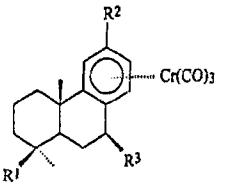
(26: R1 = CO_2Me, R2 = H
27: R1 = CH_2OMe, R2 = OMe
28: R1 = CO_2Me, R2 = OMe)



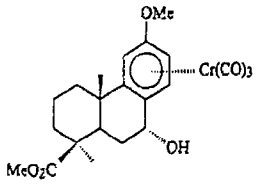
(29)



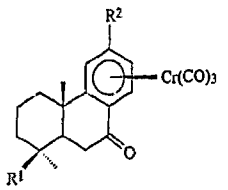
(30: R1 = CO_2Me, R2 = OMe, R3 = H
31: R1 = CH_2OMe, R2 = H, R3 = OH
32: R1 = CO_2Me, R2 = H, R3 = OH
33: R1 = CH_2OMe, R2 = OMe, R3 = OH
34: R1 = CO_2Me, R2 = OMe, R3 = OH
35: R1 = CH_2OMe, R2 = H, R3 = OMe
36: R1 = CH_2OMe, R2 = R3 = OMe
37: R1 = CH_2OMe, R2 = OMe, R3 = OCH_2OMe
38: R1 = CO_2Me, R2 = OMe, R3 = OCH_2OMe
39: R1 = CH_2OMe, R2 = OMe, R3 = OCOMe
40: R1 = CH_2OMe, R2 = OMe, R3 = OTHP
41: R1 = CO_2Me, R2 = OMe, R3 = t-$BuMe_2SiO$)



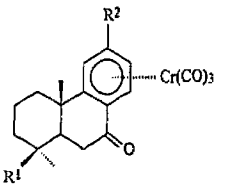
(42: R1 = CO_2Me, R2 = OMe, R3 = H
43: R1 = CO_2Me, R2 = H, R3 = OH
44: R1 = CH_2OMe, R2 = OMe, R3 = OH
45: R1 = CO_2Me, R2 = OMe, R3 = OH
46: R1 = CH_2OMe, R2 = R3 = OMe
47: R1 = CH_2OMe, R2 = OMe, R3 = OCH_2OMe
48: R1 = CH_2OMe, R2 = OMe, R3 = OCOMe
49: R1 = CH_2OMe, R2 = OMe, R3 = OTHP
50: R1 = CO_2Me, R2 = OMe, R3 = t-$BuMe_2SiO$)



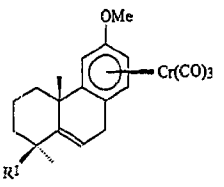
(51)



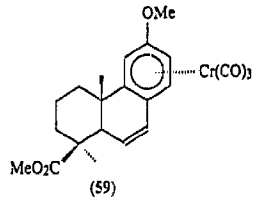
(52: R1 = CO_2Me, R2 = H
53: R1 = CH_2OMe, R2 = OMe)



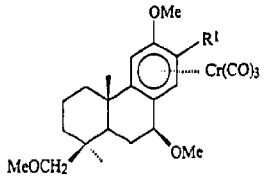
(54: R1 = CO_2Me, R2 = H
55: R1 = CH_2OMe, R2 = OMe
56: R1 = CO_2Me, R2 = OMe)



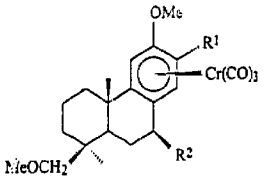
(57: R1 = CH_2OMe
58: R1 = CO_2Me)



(59)



(60: R1 = SiMe3
61: R1 = $CH_2CH{=}CH_2$)



(62: R1 = $CH_2CH{=}CH_2$, R2 = OMe
63: R1 = Me, R2 = OCH_2OMe)

3. Experimental

For general experimental details, see Refs. [1,6]. High field ^{1}H-NMR spectra were recorded at 400.13 MHz and ^{13}C-NMR at 100.62 MHz on a Bruker AM400 instrument operating at 9.2 T. Multiplicities were determined by DEPT spectra.

3.1. Ligand synthesis

3.1.1. 19-Methoxypodocarpa-8,11,13-trien-7β-ol (3)

Sodium borohydride (0.56 g, 14.7 mmol) was added in five portions over 2 h to a stirred solution of **20** (1.10 g, 4.04 mmol) in THF (7 ml) and methanol (10 ml). The mixture was then stirred overnight. Workup gave **3** (1.10 g, 100%) as a clear oil. ν_{max} 3382, (OH), 1602, 1574 (C=C), 1108 cm^{-1}. δ_H 1.03, s, 3H, $H(18)_3$; 1.27, s, 3H, $H(20)_3$; 2.37, m, 1H, H6eq; 3.32, s, 3H, 19-OMe; 3.26 and 3.47, d, *J* 9.0 Hz, 1H, $H(19)_2$; 4.76, dd, *J* 9.9, 7.6 Hz, 1H, H7; 7.17–7.25, m, 3H, H11, H12 and H13; 7.52, m, 1H, H14. δ_C 19.0, C2; 25.8, C20; 27.6, C18; 30.4, C6; 36.0, C3; 37.7, C10; 38.5, C4; 38.9, C1; 49.7, C5; 59.4, 19-OMe; 71.4, C7; 76.1, C19; 124.5, C13; 125.9, C12; 127.2, C11; 127.6, C14; 137.9, C8; 149.6, C9.

3.1.2. Methyl 7β-hydroxypodocarpa-8,11,13-trien-19-oate (4)

Sodium borohydride (0.65 g, 17.2 mmol) was added in portions over 2 h to a stirred solution of **21** (1.56 g, 5.74 mmol) in THF (30 ml) and methanol (40 ml). The mixture was stirred overnight and then worked up. Flash chromatography (hexanes:diethyl ether, 4:1) gave **4** (1.29 g, 82%) as globular crystals (hexanes/diethyl ether), m.p. 174–177°C. (Found: M$^+$, 288.1727. $C_{18}H_{24}O_3$ calc.: M, 288.1725). *m/z* 288 (6, M$^+$), 270 (32, M–H_2O), 211 (22, 270-CO_2Me), 196 (43), 195 (100). ν_{max} (CH_2Cl_2) 3591 (OH), 1722 (C=O), 1485, 1470, 1449, 1233, 1152 cm^{-1}. δ_H 1.08, s, 3H, $H(20)_3$; 1.09, td, *J* 13.7, 4.2 Hz, 1H, H3ax; 1.28, s, 3H, $H(18)_3$; 1.36, td, *J* 13.4, 4.0 Hz, H1ax; 1.58, bd, *J* 12.6 Hz, 1H, H5; 1.63, bd, *J* 14.1 Hz, 1H, H2eq; 1.86, bd, *J* 8.1 Hz, 7-OH; 1.96, td, *J* 12.8, 11.3 Hz, 1H, H6ax; 1.99, qt, *J* 13.6, 3.8 Hz, 1H, H2ax; 2.25, bd, *J* 13.9 Hz, 1H, H1eq; 2.29, bd, *J* 13.8 Hz, 1H, H3eq; 2.57, bdd, *J* 13.0, 6.3 Hz, 1H, H6eq; 3.67, s, 3H, 19-OMe; 4.75, bdt, *J* 10.7, 7.4 Hz, 1H, H7; 7.18–7.26, m, 3H, H11, H12 and H13; 7.57–7.59, m, 1H, H14. δ_C 19.7, C2; 22.9, C20; 28.3, C18; 31.8, C6; 37.4, C3; 39.0, C10; 39.2, C1; 43.6, C4; 50.0, C5; 51.3, 19-OMe; 71.3, C7; 125.3, C13; 126.0, C12; 126.6, C11; 127.5, C14; 138.4, C8; 147.6, C9; 177.6, C19.

3.1.3. 7β,19-Dimethoxypodocarpa-8,11,13-triene (5)

A solution of **3** (0.77 g, 1.89 mmol) and imidazole (18 mg, 0.26 mmol) in THF (15 ml) was added dropwise to sodium hydride (50% dispersion in oil, 0.45 g, 9.4 mmol). The mixture was heated to reflux for 3 h, stirred overnight, and then excess sodium hydride discharged with methanol. Workup and flash chromatography (hexanes:diethyl ether, 6:1) gave **5** (0.79 g, 78%) as a clear oil. ν_{max} 1598 (C=C), 1254, 1106 cm^{-1}. δ_H 1.05, s, 3H, $H(18)_3$; 1.25, s, 3H, $H(20)_3$; 2.40, dd, *J* 12.5, 7.0 Hz, 1H, H6eq; 3.30 and 3.55, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.34, s, 3H, 19-OMe; 3.47, s, 3H, 7-OMe; 4.49, dd, *J* 9.8, 7.1 Hz, 1H, H7; 7.14–7.27, m, 3H, H11, H12 and H13; 7.47, m, 1H, H14. δ_C 19.0, C2; 24.9, C20; 25.7, C6; 27.6, C18; 36.0, C3; 37.8, C10; 38.2, C4; 39.0, C1; 49.4, C5; 55.4, 7-OMe; 59.4, 19-OMe; 75.9, C19; 79.3, C7; 124.3, C13; 125.7, C12; 127.8, C11; 128.2, C14; 135.5, C8; 150.1, C9.

3.1.4. 12,19-Dimethoxypodocarpa-8,11,13-trien-7β-ol (6)

Sodium borohydride (1.89 g, 49.7 mmol) was added in portions over 3 h to a stirred solution of **22** (5.00 g, 16.6 mmol) in THF (30 ml) and methanol (40 ml). After

stirring the mixture overnight workup afforded **6** (4.95 g, 98%) as white crystals, m.p. 122–123°C. (Found: $M^{+\cdot}$, 304.2034. $C_{19}H_{28}O_3$ calc.: M, 304.2038). *m/z* 304 (58, M^+); 286 (22, M–H_2O), 273 (5, M–OMe), 150 (100). ν_{max} (CH_2Cl_2) 3585 (OH), 1609, 1574 (C=C), 1491, 1106, 1069 cm^{-1}. δ_H 1.01, td, *J* 13.7, 4.1 Hz, 1H, H3ax; 1.03, s, 3H, $H(18)_3$; 1.26, s, 3H, $H(20)_3$; 1.38, td, *J* 13.1, 3.8 Hz, 1H, H1ax; 1.44, dd, *J* 13.0, 1.2 Hz, 1H, H5; 1.60, dp, *J* 14.4, 3.5 Hz, 1H, H2eq; 1.65, td, *J* 12.9, 10.4 Hz, 1H, H6ax; 1.72, qt, *J* 13.6, 3.4 Hz, 1H, H2ax; 1.84, bd, *J* 13.7 Hz, H1eq; 1.90, bd, *J* 7.2 Hz, 1H, 7-OH; 2.24, bd, *J* 12.8 Hz, 1H, H3eq; 2.35, ddd, *J* 12.3, 7.2, 0.8 Hz, 1H, H6eq; 3.27 and 3.49, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.32, s, 3H, 19-OMe; 3.78, s, 3H 12-OMe; 4.72, dd, *J* 8.8, 7.2 Hz, 1H, H7; 6.75, dd, *J* 8.3, 2.5 Hz, H13; 6.76, bs, 1H, H11; 7.42, d, *J* 9.5 Hz, 1H, H14. δ_C 19.0, C2; 25.7, C20; 27.6, C18; 30.6, C6; 35.9, C3; 37.7, C10; 38.6, C4; 39.0, C1; 49.8, C5; 55.2, 12-OMe; 59.4, 19-OMe; 71.0, C7; 76.0, C19; 110.1, C11; 111.3, C13; 128.5, C14; 130.5, C8; 151.3, C9; 158.9, C12.

3.1.5. Methyl 7β-hydroxy-12-methoxypodocarpa-8,11,13-trien-19-oate (7)

Sodium borohydride (1.41 g, 37.2 mmol) was added in portions to a stirred solution of **23** (5.87 g, 18.6 mmol) in THF (45 ml) and methanol (85 ml). The mixture was stirred at room temperature for 18 h and then worked up. Flash chromatography (hexanes:diethyl ether, 1:1) gave **7** (5.78 g, 98%) as white needles (methanol), m.p. 111–113°C ([28] 110–112°C). ν_{max} 3589 (OH), 1720 (C=O), 1610 cm^{-1} (C=C). δ_H 1.08, s, 3H, $H(20)_3$; 1.08, td, *J* 13.5, 4.3 Hz, 1H, H3ax; 1.28, s, 3H, $H(18)_3$; 1.36, td, *J* 13.3, 4.1 Hz, 1H, H1ax; 1.56, dd, *J* 12.5, 1.0 Hz, 1H, H5; 1.62, bd, *J* 14.2 Hz, 1H, H2eq; 1.74, d, *J* 8.3 Hz, 1H, 7-OH; 1.92, td, *J* 12.9, 11.0 Hz, 1H, H6ax; 1.98, qt, *J* 13.6, 3.8 Hz, 1H, H2ax; 2.20, bd, *J* 12.9 Hz, 1H, H1eq; 2.29, bd, *J* 13.4 Hz, 1H, H3eq; 2.55, dd, *J* 13.1, 5.7 Hz, 1H, H6eq; 3.66, s, 3H, 19-OMe; 3.78, s, 3H, 12-OMe; 4.70, dt, *J* 10.8, 7.3 Hz, 1H, H7; 6.77, bs, 1H, H11; 6.78, dd, *J* 8.4, 2.6 Hz, 1 H, H13; 7.50, d, *J* 8.2 Hz:, H14. δ_C 19.7, C2; 22.8, C20; 28.3, C18; 32.0, C6; 37.3, C3; 39.2, C10; 39.3, C1; 43.6, C4; 50.1, C5; 51.3, 19-OMe; 55.1, 12-OMe; 71.0, C7; 110.8, C11; 111.5, C13; 127.9, C14; 131.0, C8; 149.3, C9; 158.9, C12; 177.6, C19. δ_H (C_6D_6) 0.83, td, *J* 13.2, 4.3 Hz, 1H, H3ax; 1.08, s, 3H, $H(20)_3$; 1.10, s, 3H, $H(18)_3$; 1.20, td, *J* 14.4, 4.1 Hz, 1H, H1ax; 1.32, dd, *J* 12.7, 1.2 Hz, 1H, H5; 1.46, bd, *J* 14.2 Hz, 1H, H2eq; 1.80–2.05, m, 2H, H1eq and 7-OH; 1.97, td, *J* 12.8, 11.0 Hz, 1H, H6ax; 2.07, qt, *J* 13.7, 3.8 Hz, 1H, H2ax; 2.31, bd, *J* 12.7 Hz, 1H, H3eq; 2.47, dd, *J* 13.0, 6.3 Hz, 1H, H6eq; 3.30, s, 3H, 19-OMe; 3.39, s, 3H, 12-OMe; 4.59, dd, *J* 10.8, 6.3 Hz, 1H, H7; 6.74, dd, *J* 8.5, 2.6 Hz, 1H, H13; 6.83, d, *J* 2.6 Hz, 1H, H11; 7.68, d, *J* 8.5 Hz, 1H, H14. δ_C (C_6D_6) 20.2, C2; 23.1, C20; 28.3, C18; 32.5, C6; 37.6, C3; 39.5, C1, C10; 43.8, C4; 50.4, C5; 50.9, 19-OMe; 54.8, 12-OMe; 71.1, C7; 111.0, C11; 111.8, C13; 128.7, C14; 132.0, C8; 149.5, C9; 159.5, C12; 177.2, C19.

3.1.6. 7β.12,19-Trimethoxypodocarpa-8,11,13-triene (8)

A solution of **6** (0.78 g, 2.59 mmol) and imidazole (18 mg, 0.26 mmol) m THF (15 ml) was added dropwise to sodium hydride (50% w/w dispersion in oil, 0.37 g, 7.7 mmol). The mixture was heated under reflux for 4 h, cooled to room temperature, treated with iodomethane (1.62 ml, 0.26 mmol) and then heated to reflux for a further 5.5 h. Workup afforded **8** (0.81 g, 98%) as a clear oil. (Found: $M^{+\cdot}$, 318.2187. $C_{20}H_{30}O_3$ calc.: M, 318.2195). *m/z* 318 (2, M^+), 303 (5, M–Me), 286 (90, M–MeOH), 241 (22), 185 (95), 174 (100), 172 (85). ν_{max} 1605, 1565 (C=C), 1243, 1110, 1074, 1038 cm^{-1}. δ_H 1.03, s, 3H, $H(18)_3$; 1.24, s, 3H, $H(20)_3$; 2.35, dd, *J* 12.6, 7.2 Hz, 1H, H6eq; 3.28 and 3.55, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.33, s, 3H, 19-OMe; 3.44, s, 3H, 7-OMe; 3.77, s, 3H, 12-OMe; 4.42, dd, *J* 9.4, 7.2 Hz, 1H, H7; 6.72, bd, *J* 8.1 Hz, 1H, H13; 6.75, bs, 1H, H11; 7.37, d, *J* 8.0 Hz, 1H, H14. δ_C 18.9, C2; 24.9, C20; 25.5, C6; 27.5, C18; 35.9, C3; 37.8, C10; 38.3, C4; 38.9, C1; 49.8, C5; 55.0, 7-OMe; 55.1, 12-OMe; 59.3, 19-OMe; 75.8, C19; 78.9, C7; 109.7, C11; 111.1, C13; 127.9, C8; 129.1, C14; 151.7, C9; 158.8, C12.

3.1.7. 12,19-Dimethoxy-7β-methoxymethoxypodocarpa-8,11,13-triene (9)

Bromomethyl methyl ether (0.52 ml, 6.30 mmol) was added dropwise to a solution of **6** (0.16 g, 0.53 mmol) in ethyldiisopropylamine (15 ml) under a nitrogen atmosphere at 0°C. The resulting white precipitate was stirred at 0°C for 1 h and then at room temperature overnight. Workup followed by flash chromatography (hexanes:diethyl ether, 2:1) gave: (i) **9** (0.15 g, 81%) as a clear oil. (Found: $M^{+\cdot}$, 348.2299. $C_{21}H_{32}O_4$ calc.: M, 348.2301). *m/z* 348 (30, M^+), 303 (2, M–CH_2OMe), 316 (18, M–MeOH), 287 (30, M–OCH_2OMe), 255 (28, 287-MeOH), 241 (18), 185 (42), 173 (20), 161 (32), 45 (100, CH_2OMe). ν_{max} 1608, 1572 (C=C), 1246, 1144, 1107, 1036 cm^{-1}. δ_H 1.03, s, 3H, $H(18)_3$; 1.27, s, 3H, $H(20)_3$; 2.42, ddd, *J* 12.7, 7.4, 1.2 Hz, 1H, H6eq; 3.28 and 3.55, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.33, s, 3H, 19-OMe; 3.51, s, 3H, 7-OCH_2OMe; 3.78, s, 3H, 12-OMe; 4.72, dd, *J* 9.6, 7.5 Hz, 1H, H7; 4.81 and 4.98, d, *J* 6.9 Hz, 1H, OCH_2OMe; 6.74, dd, *J* 8.0, 2.6 Hz, 1H, H13; 6.77, bs, 1H, H11; 7.35, bd, *J* 8.9 Hz, 1H, H14. δ_C 19.0, C2; 25.5, C20; 26.8, C6; 27.5, C18; 35.9, C3; 37.8, C10; 38.3, C4; 38.9, C1; 49.6, C5; 55.2, 12-OMe; 55.7, 7-OCH_2OMe; 59.3, 19-OMe; 75.8, C19; 76.22, C7; 95.4, 7-OCH_2OMe; 109.8, C11; 111.2, C13; 128.0,

C8; 129.1, C14; 151.8, C9; 158.9, C12; and (ii) **6** (9 mg, 6%).

3.1.8. Methyl 12-methoxy-7β-methoxymethoxypodocarpa-8,11,13-trien-19-oate (10)

Bromomethyl methyl ether (0.93 ml, 11.4 mmol) was added dropwise to a solution of **7** (0.30 g, 0.95 mmol) in ethyldiisopropylamine (15 ml) under a nitrogen atmosphere. The resulting white precipitate was stirred at room temperature overnight. Workup followed by flash chromatography (hexanes:diethyl ether, 4:1) afforded: (i) **28** (67 mg, 23%); and (ii) methyl 12-methoxy-7α-methoxymethoxypodocarpa-8,11,13-trien-19-oate (**18**) (8 mg, 2%) as a clear oil. (Found: $M^{+\cdot}$, 362.2089. $C_{21}H_{30}O_5$ calc.: M, 362.2093). *m/z* 362 (20, M^+), 330 (28, M–MeOH), 317 (2, M–CH_2OMe), 301 (77, $MOCH_2OMe$), 269 (4, 301-MeOH), 257 (8), 241(100, 301-HCO_2Me), 225 (37), 215 (5), 199 (9), 185 (67), 171 (18), 161 (17), 45 (25, $^+CH_2OMe$). ν_{max} 2948, 1726 (C=O), 1610, 1575 (C=C), 1504, 1465, 1273, 1144, 1038 cm^{-1}. δ_H 0.97, s, 3H, $H(20)_3$; 1.14, td, *J* 13.6, 4.2 Hz, 1H, H3ax; 1.27, s, 3H, $H(18)_3$; 1.47, td, *J* 13.4, 4.1 Hz, 1H, H1ax; 1.64, bd, *J* 14.3 Hz, 1H, H2eq; 1.98, qt, *J* 14.2, 3.7 Hz, 1H, H2ax; 2.03, bd, *J* 12.9 Hz, 1H, H5; 2.07, td, *J* 12.9, 3.3 Hz, 1H, H6ax; 2.21, bd, *J* 13.0 Hz, 1H, H1eq; 2.29, bd, *J* 13.5 Hz, 1H, H3eq; 2.42, dd, *J* 13.0, 2.0 Hz, 1H, H6eq; 3.48, s, 3H, 7-OCH_2OMe; 3.66, s, 3H, 19-OMe; 3.78, s, 3H, 12-OMe; 4.68, dd, *J* 3.3, 2.0 Hz, 1H, H7; 4.71 and 4.87, d, *J* 7.0 Hz, 1H, 7-OCH_2OMe; 6.77, dd, *J* 8.4, 2.6 Hz, 1H, H13; 6.81, d, *J* 2.6 Hz, 1H, H11; 7.18, d, *J* 8.5 Hz, 1H, H14. δ_C 18.9, C2; 21.9, C20; 26.4, C6; 28.2, C18; 37.4, C3; 38.7, C10; 38.8, C1; 43.6, C4; 45.6, C5; 51.3, 19-OMe; 55.2, 12-OMe; 55.7, 7-OCH_2OMe; 72.7, C7; 94.5, 7-OCH_2OMe; 110.8, C11; 111.7, C13; 126.6, C8; 132.1, C14; 150.2, C9; 159.5, C12; 178.0, C19; and (iii) **10** (0.25 g, 75%) as a clear oil. (Found: $M^{+\cdot}$, 362.2096. $C_{21}H_{30}O_5$ calc.: M, 362.2093). *m/z* 362 (35, M^+), 330 (27, M-MeOH), 317 (4, M-CH_2OMe), 301 (66, M-OCH_2OMe), 289 (3), 269 (5, 301-MeOH), 257 (8), 241 (100, 301-HCO_2Me), 225 (12), 215 (10), 185 (37), 161(21), 45 (48, $^+CH_2OMe$). ν_{max} 2948, 1725 (C=O), 1611, 1575 (C=C), 1503, 1470, 1232, 1149, 1038 cm^{-1}. δ_H 1.08, s, 3H, $H(20)_3$; 1.08, td, *J* 13.5, 4.2 Hz, 1H, H3ax; 1.28, s, 3H, $H(18)_3$, 1.36, td, *J* 13.3, 4.1 Hz, 1H, H1ax, 1.54, dd, *J* 12.8, 1.2 Hz, 1H, H5, 1.62, dp, *J* 14.3, 3.0 Hz, 1H, H2eq; 1.98, qt, *J* 13.9, 3.7 Hz, 1H, H2ax, 1.99, td, *J* 12.9, 10.9 Hz, 1H, H6ax, 2.21, bd, *J* 13.0 Hz, 1H, H1eq, 2.28, bd, *J* 13.5 Hz, 1H, H3eq, 2.61, ddd, *J* 13.1, 6.4, 1.0 Hz, 1H, H6eq, 3.54, s, 3H, 7-OCH_2OMe; 3.67, s, 3H, 19-OMe; 3.78, s, 3H, 12-OMe, 4.68, dd, *J* 10.8, 6.5 Hz, 1H, H7; 4.83 and 5.03, d, *J* 6.8 Hz, 1H, 7-OCH_2OMe; 6.76 (2), dd, *J* 9.5, 2.6 Hz, 1H, H13, 6.76 (3), d, *J* 2.6 Hz, 1H, H11, 741, dd, *J* 9.5, 0.6 Hz, 1H, H14. δ_C 19.7, C2, 22.6, C20; 28.0, C6; 28.3, C18; 37.3, C3; 38.8, C10; 39.2, C1; 43.6, C4; 49.9, C5; 51.2, 19-OMe; 55.0, 12-OMe; 55.6, 7-OCH_2OMe; 76.4, C7; 95.4, 7-OCH_2OMe; 110.5, C11; 111.4, C13; 128.3, C14; 128.5, C8; 149.6, C9; 158.8, C12; 177.4, C19.

3.1.9. 12,19-Dimethoxypodocarpa-8,11,13-trien-7β-yl acetate (11)

Acetic anhydride (22 ml, 0.23 mol) was added to a stirred solution of **6** (0.80 g, 2.60 mmol) in pyridine (23 ml). The yellow mixture was stirred at room temperature overnight and worked up. Flash chromatography (hexanes:diethyl ether, 1:1) afforded **11** (0.80 g, 90%) as a yellow oil. (Found: $M^{+\cdot}$, 346.2147. $C_{21}H_{30}O_4$ calc.: M, 346.2144). *m/z* 346 (23, M^+), 286 (66, M–OAcOH), 241 (42, 286-CH_2OMe), 185 (100), 174 (90), 172 (68). ν_{max} 1731 (C=O), 1610, 1565 (C=C), 1236, 1110, 1020 cm^{-1}. δ_H 1.03, s, 3H, $H(18)_3$; 1.28, s, 3H, $H(20)_3$; 2.12, s, 3H, OCOMe; 2.44, dd, *J* 12.0, 8.5, Hz, 1H, H6eq; 3.27 and 3.45, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.30, s, 3H, 19-OMe; 3.78, s, 3H, 12-OMe; 6.00, t, *J* 8.6 Hz, 1H, H7; 6.72, dd, *J* 8.5, 2.5 Hz, 1H, H13; 6.79, d, *J* 2.6 Hz, 1H, H11; 7.09, d, *J* 8.5 Hz, 1H, H14. δ_C 18.9, C2; 21.5, 7-OCOMe; 25.3, C20; 26.3, C6; 27.6, C18; 36.0, C3; 37.7, C10; 38.2, C4; 38.8, C1; 49.5, C5; 55.2, 12-OMe; 59.3, 19-OMe; 72.8, C7; 75.9, C19; 110.0, C11; 111.3, C13; 125.8, C8; 129.1, C14; 152.4, C9; 159.2, C12; 171.2, 7-OCOMe.

3.1.10. 12,19-Dimethoxypodocarpa-8,11,13-trien-7α-yl acetate (19)

A solution of diethyl azodicarboxylate (18.0 μl, 0.12 mmol) and acetic acid (6.0 μl, 0.10 mmol) in benzene (2 ml) was added to a stirred solution of **6** (25 mg, 80 μmol) and Ph_3P (26 mg, 0.10 mmol) in benzene (5 ml). The mixture was heated to reflux for 5 h and then stirred overnight at room temperature. Removal of the solvent followed by flash chromatography (hexanes:diethyl ether, 3:1) gave an inseparable mixture (2:1) of **11** and **19** (7 mg, 25%) as a clear oil. The 7α acetate **19**: ν_{max} 1731 cm^{-1} (C=O). δ_H 0.99, s, 3H, $H(18)_3$; 1.16, s, 3H, $H(20)_3$; 2.04, s, 3H, 7-OCOMe; 2.49, dd, *J* 12.1, 8.5 Hz, 1H, H6eq; 3.30, s, 3H, 19-OMe; 3.87, s, 3H, 12-OMe; 5.94, dd, *J* 3.7, 2.3 Hz, 1H, H7; 6.75, dd, *J* 8.5, 2.6 Hz, 1H, H13; 6.84, d, *J* 2.6 Hz, 1H, H11; 7.09, d, *J* 8.5 Hz, H14.

3.1.11. 12,19-Dimethoxy-7β-tetrahydropyranyloxypodocarpa-8,11,13-triene (12)

Pyridinium *p*-toluenesulfonate (0.14 g, 0.56 mmol) was added to a solution of **6** (2.00 g, 0.66 mmol) and 2,3-dihydropyran (1.53 ml, 16.8 mmol) in dichloromethane (11.0 ml). The mixture was stirred at room temperature for 4 h and then worked up. Flash chromatography (hexanes:diethyl ether, 8:1) afforded (i) **27** (15 mg, 9%); and (ii) an inseparable mixture of 4 isomers (2 epimeric pairs, each consisting of 2 conform-

ers) (0.3:1:1:1) of **12** (2.25 g, 91%) as a clear oil. (Found: $M^{+\cdot}$, 388.2618. $C_{24}H_{36}O_4$ calc.: M, 388.2614). *m/z* 388 (60, M^+), 375 (3, M–Me), 357 (4, M–OMe), 343 (6, M–CH_2OMe), 303 (37, M–C_5H_9O), 302 (52), 287 (80, M–OTHP), 255 (72, 277-MeOH), 185 (60), 175 (100), 161(70), 135 (40), 85 (65). ν_{max} 1609, 1576 (C=C), 1112, 1075, 1026 cm^{-1}. δ_H 7.15, d, *J* 8.5 Hz, 1H, H14 (minor isomer); 7.24, d, *J* 8.5 Hz, 1H, H14; 7.32, d, *J* 8.4 Hz, 1H, H14; and 7.52, d, *J* 9.6 Hz, 1H, H14.

3.1.12. Methyl 7β-[(1,1-dimethylethyl)dimethylsilyl]oxy-12-methoxypodocarpa-8,11,13-trien-19-oate (13)

A solution of *t*-butyldimethylchlorosilane (0.79 g, 5.22 mmol) and DBU (0.93 g, 6.09 mmol) in benzene (50 ml) was treated with **7** (1.10 g, 3.48 mmol). The mixture was heated to reflux for 24 h and then worked up. Flash chromatography (hexanes:diethyl ether, 1:1) gave **13** (1.41 g, 94%) as a clear oil which crystallised to give needles, m.p. 78–81°C. (Found: C, 69.6; H, 9.2. $C_{25}H_{40}O_4Si$ calc.: C, 69.4; H, 9.3%) (Found: $M^{+\cdot}$–H, 431.2601. $C_{25}H_{39}O_4Si$ calc.: M–H, 431.2618). *m/z* (CI) 431(3, M^+–H); 375 (98, M–CMe_3), 360 (4, 375-Me), 301 (53, 375-CO_2Me), 300 (49, 375-HCO_2Me), 241 (100), 225 (24), 185 (70), 75 (78). *m/z* (FAB) 431 (17, M^+–H), 417 (4, M–Me), 375 (58, M–CMe_3), 301 (54, 375-CO_2Me), 241 (56), 225 (11), 185 (27), 73 (100). ν_{max} 2956, 1732 (C=O), 1610, 1574 (C=C), 1083 cm^{-1}. δ_H 0.17 and 0.21, s, 3H, $SiMe_2$; 0.99, s, 9H, $SiCMe_3$; 1.06(7), 3H, $H(20)_3$; 1.07(4), td, *J* 13.6, 4.2 Hz, 1H, H3ax; 1.27, s, 3H, $H(18)_3$; 1.37, td, *J* 13.4, 4.1 Hz, 1H, H1ax; 1.56, dd, *J* 12.3, 1.2 Hz, 1H, H5; 1.62, bd, *J* 14.3 Hz, 1H, H2eq; 1.98, qt, *J* 13.9, 3.7 Hz, 1H, H2ax; 1.99, td, *J* 12.8, 11.3 Hz, 1H, H6ax, 2.19, bd, *J* 12.9 Hz, 1H, H1eq, 2.29, bd, *J* 13.5 Hz, 1H, H3eq, 2.38, bdd, *J* 12.6, 5.8 Hz, 1H, H6eq; 3.66, s, 3H, 19-OMe; 3.77, s, 3H, 12-OMe; 4.72, dd, *J* 11.0, 5.9 Hz, 1H, H7; 6.74, d, *J* 2.4 Hz, 1H, H11; 6.75, dd, *J* 8.4, 2.5 Hz, 1H, H13, 7.38, d, J 8.4 Hz, H14. δ_C −4.6 and −4.0, $SiMe_2$; 18.3, $SiCMe_3$, 19.8, C2, 22.8, C20, 26.0, 3C, $SiCMe_3$; 28.2, C18; 31.7, C6; 37.4, C3; 39.3, C1; 39.4, C10; 43.5, C4; 50.4, C5; 51.2, 19-OMe; 55.1, 12-OMe; 72.2, C7; 110.7, C11; 111.3, C13; 127.9, C14; 131.6, C8; 148.9, C9; 158.6, C12; 177.5, C19.

3.1.13. Methyl podocarpa-6,8,11,13-tetraen-19-oate (26)

Sulfuric acid (3.6 ml, 3.0 mol l^{-1}) was added to a solution of **4** (0.64 g, 2.2 mmol) in THF (13 ml) and the mixture was refluxed for 78 h. Workup afforded a white solid which was purified by flash chromatography (hexanes/diethyl ether, 4:1) to yield **26** (0.52 g, 87%) as white crystals (methanol), m.p. 93–94.5°C. (Found: $M^{+\cdot}$, 270.1619. $C_{18}H_{22}O_2$ calc.: M, 270.1620). *m/z* 270 (83, M^+), 255 (4, M–Me), 238 (9, M-MeOH), 211 (15, M–CO_2Me), 197 (70, 255-HCO_2Me), 182 (10), 168 (21), 155 (100), 141 (40), 128 (21), 115 (23), 101 (17). ν_{max} (CH_2Cl_2) 2950, 1723 (C=O), 1655, 1602 (C=C), 1484, 1464, 1378, 1332, 1225, 1146 cm^{-1}. δ_H 0.87, s, 3H, $H(20)_3$; 1.12, td, *J* 13.4, 3.9 Hz, 1H, H3ax; 1.31, s, 3H, $H(18)_3$; 1.67, td, *J* 13.2, 4.1 Hz, 1H, H1ax; 1.72, bd, *J* 14.4 Hz, 1H, H2eq; 1.95, qt, *J* 13.7, 3.5 Hz, 1H, H2ax; 2.23, bd, *J* 13.4 Hz, 1H, H1eq; 2.34, bd, *J* 13.4 Hz, 1H, H3eq; 2.37, bs, 1H, H5; 3.68, s, 3H, 19-OMe; 6.45, dd, *J* 9.8, 0.8 Hz, H6; 6.48, dd, *J* 9.8 Hz, H7; 7.04, dd, *J* 6.7, 1.9 Hz, 1H, H11; 7.15, td, *J* 6.9, 2.0 Hz, 1H, H12*; 7.17, td, *J* 7.2, 1.4 Hz, H13*; 7.20, *J* 7.8, 2.1 Hz, 1H, H14. δ_C 19.4, C20; 19.7, C2; 27.8, C18; 36.0, C3; 37.3, C1; 38.0, C10; 43.4, C4; 51.3, C5; 51.6, 19-OMe; 122.6, 125.5, 126.1 and 126.3, C11, C12, C13 and C14; 127.5, C6; 130.1, C7; 132.6, C8; 146.2, C9; 177.6, C19.

3.1.14. 12,19-Dimethoxypodocarpa-6,8,11,13-tetraene (27)

Sulfuric acid (2 ml, 5.0 mol l^{-1}) was added to a stirred solution of **6** (2.61 g, 8.57 mmol) in THF (10 ml) at room temperature. After 20 h the mixture was worked up to give **27** (2.32 g, 94%) as white crystals, m.p. 57–59°C ([29] 56–59°C). (Found: $M^{+\cdot}$, 286.1929. $C_{19}H_{26}O_2$ calc.: M, 286.1932). *m/z* 286 (95, M^+), 271(4, M–Me), 254 (7, M–MeOH), 241 (28, M–CH_2OMe), 239 (34, 271-MeOH), 225 (12), 211 (14), 198 (19), 185 (97), 174 (100), 172 (88), 128 (19), 115 (14), 45 (22). ν_{max} 2927, 1605, 1564 (C=C), 1486, 1443, 1072 cm^{-1}. δ_H 1.01, s, 3H, $H(18)_3$; 1.04(5), s, 3H, $H(20)_3$; 1.05(2), td, *J* 12.3, 4.1 Hz, 1H, H3ax, 1.60–1.72, m, 2H, H1ax and H2eq, 1.73, qt, *J* 13.6, 3.0 Hz, H2ax; 1.91, bd, *J* 13.6 Hz, 1H, H3eq, 2.16, bd, *J* 12.4 Hz, 1H, H3eq, 2.19, t, *J* 3.1 Hz, 1H, H5; 3.35, s, 3H, 19-OMe; 3.39 and 3.57, d, *J* 9.2 Hz, 1H, $H(19)_2$; 3.80, s, 3H, 12-OMe; 6.00, dd, *J* 9.7, 2.8 Hz, 1H, H(6); 6.47, dd, *J* 9.6, 3.1 Hz, 1H, H7; 6.67, dd, *J* 8.2, 2.6 Hz, 1H, H13; 6.76, d, *J* 2.6 Hz, 1H, H11; 6.99, d, *J* 8.2 Hz, 1H, H14. δ_C 18.8, C2; 20.8, C20; 26.6, C18; 35.7, C3; 35.9, C1; 37.6, C10; 37.9, C4; 51.0, C5; 55.2, 12-OMe; 59.4, 19-OMe; 76.1, C19; 108.9, C11; 109.7, C13; 126.1, C14; 126.6, C8; 127.1, C6; 127.4, C7; 149.9, C9; 159.2, C12.

3.1.15. Methyl 12-methoxypodocarpa-6,8,11,13-tetraen-19-oate (28)

Sulfuric acid (4 ml, 5.0 mol l^{-1}) was added to a stirred solution of **7** (3.70 g, 11.6 mmol) in THF (50 ml) at room temperature. The reaction mixture was stirred for 20 h and then worked up to give **28** (3.18 g 91%) as white crystals, m.p. 82–84°C ([28] 85–86°C). (Found: $M^{+\cdot}$, 300.1725. $C_{19}H_{24}O_3$ calc.: M, 300.1725). *m/z* 300 (100, M^+), 241 (10, M–CO_2Me), 225 (39, M–Me–HCO_2Me), 212 (8), 197 (8), 185 (56), 172 (18). ν_{max} 2936, 1726 (C=O), 1605, 1566 (C=C), 1489, 1463, 1307, 1220, 1144, 1074 cm^{-1}. δ_H 0.85, s, 3H,

H(20)$_3$; 1.12, td, *J* 13.5, 4.1 Hz, 1H, H3ax; 1.30, s, 3H, H(18)$_3$; 1.64, td, *J* 13.0, 4.1 Hz, H1ax; 1.72, bd, *J* 14.2 Hz, 1H, H2eq; 1.94, qt, *J* 13.9, 3.7 Hz, 1H, H2ax; 2.19, bd, *J* 12.4 Hz, 1H, H1eq; 2.30–2.37, m, 1H, H3eq; 2.33, t, *J* 2.6 Hz, 1H, H5; 3.68, s, 3H, 19-OMe; 3.82, s. 12-OMe; 6.35, dd, *J* 9.9, 2.3 Hz, 1H, H6; 6.42, dd, *J* 9.9, 3.0 Hz, 1H, H7; 6.68, dd, *J* 8.2, 2.5 Hz, 1H, H13; 6.79, d, *J* 2.5 Hz, 1H, H11; 6.99, d, *J* 8.2 Hz, 1H, H14. δ_C 19.3, C20; 19.7, C2; 27.8, C18; 36.0, C3; 37.3, C1; 38.1, C10; 43.4, C4; 51.2, C5; 51.5, 19-OMe; 55.2, 12-OMe; 109.7, C11; 110.0, C13; 124.8, C14; 126.0, C8; 127.3, C6; 127.4, C7; 148.1, C9; 159.1, C12; 177.5, C19.

3.2. Complexation reactions

3.2.1. The α and β diastereoisomers of tricarbonyl[(8,9,11,12,13,14-η)-methyl 12-methoxypodocarpa-8,11,13-trien-19-oate]chromium(0) (42, 30)

A nitrogen-degassed solution of methyl 12-methoxypodocarpa-8,11,13-trien-19-oate (**2**) (0.19 g, 0.63 mmol) and tricarbonyltrispyridinechromium(0) (0.23 g, 0.60 mmol) in diethyl ether (10 ml) and $BF_3 \cdot Et_2O$ (0.31 ml, 2.5 mmol) was stirred at room temperature under a nitrogen atmosphere for 1.5 h. The brown yellow mixture was diluted with water and extracted with diethyl ether. Removal of the solvent followed by flash chromatography (hexanes:diethyl ether, 4:1) afforded: (i) **2** (73 mg, 4%); (ii) **30** (95 mg, 35%) as a yellow tablets (hexanes/diethyl ether), m.p. 183–185°C ([12,13] m.p. 182–184°C); and (iii) **42** (0.12 g, 43%) as a yellow needles (hexanes/diethyl ether), m.p. 143–146°C ([12,13] 142–143°C).

When the reaction was conducted for 2 h at 0°C a mixture (2:1) (40%) of **30** and **42** was formed. Extending the reaction time to 24 h afforded a mixture (1:4) (23%) of **30** and **42**.

3.2.2. The α diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-methyl 12-methoxy-7-oxopodocarpa-8,11,13-trien-19-oate]chromium(0) (56)

A nitrogen-degassed solution of **23** (0.46 g, 1.44 mmol) and hexacarbonylchromium(0) (0.35 g, 1.59 mmol) in dibutyl ether (40 ml) and THF (3.3 ml) was refluxed for 48 h under positive nitrogen pressure. The cooled mixture was filtered (Celite) and the solvents removed in vacuo to give a yellow oil. Flash chromatography (hexanes:diethyl ether, 2:1) yielded, in order of increasing polarity: (i) **23** (0.16 g, 35%); and (ii) **56** (0.28 g, 42%) as orange crystals, m.p. 132–137°C. (Found: M^+, 452.0925. $C_{22}H_{24}O_7Cr$ calc.: M, 452.0927). *m/z* 452 (13, M^+), 396 (2, M–2CO), 393 (3, M–CO_2Me), 368 (100, M–3CO), 316 (12, M–Cr(CO)$_3$), 308 (18), 300 (17), 241 (20), 225 (10), 201 (8), 185 (12), 52 (30, Cr^+). ν_{max} 1974 (sharp, C≡O), 1905 (broad, C≡O), 1721 (ester, C=O), 1676 (ketone, C=O), 1534, 1459, 1382, 1275 cm^{-1}. δ_H 1.18, s, 3H, H(20)$_3$; 1.28, s, 3H, H(18)$_3$; 2.93, dd, *J* 18.9, 4.1 Hz, 1H, H6eq; 3.20, dd, *J* 18.9, 13.8 Hz, 1H, H6ax; 3.69, s, 3H, 19-OMe; 3.79, s, 3H, 12-OMe; 5.11, d, *J* 2.1 Hz, 1H, H11; 5.24, dd, *J* 7.2, 2.2 Hz, 1H, H13; 6.39, d, *J* 7.2 Hz, 1H, H14. δ_C 19.3, C2; 24.2, C20; 28.0, C18; 35.3, C6; 36.8, C3; 37.0, C1; 37.3, C10; 44.1, C4; 47.6, C5; 51.7, 19-OMe; 55.8, 12-OMe; 73.9, C11; 76.3, C13; 87.1, C12; 92.1, C14; 129.0, C8; 144.5, C9; 176.7, C19; 195.7, C7; 231.0, 3C, Cr(CO)$_3$.

3.2.3. The β diastereoisomer of tricarbonyl[(8,9,11,12,-13,14-η)-19-methoxypodocarpa-8,11,13-triene-7β-ol]chromium(0) (31)

A nitrogen-degassed solution of **3** (0.30 g, 1.10 mmol) and tricarbonyl(η^6-naphthalene)chromium(0) (0.35 g, 1.32 mmol) in diethyl ether (15 ml) and THF (0.10 ml, 1.60 mmol) was heated at 70°C for 33 h in a closed reaction vessel. The reaction mixture was filtered (Celite) and the solvents were removed in vacuo. Flash chromatography (hexanes:diethyl ether:dichloromethane, 6:1:2) gave, in order of increasing polarity: (i) tricarbonyl(η^6-naphthalene)chromium(0) (74 mg); and (ii) **31** (0.27 g, 60%) as yellow crystals, m.p. 146–149°C. (Found: C, 58.0; H, 6.4. $C_{21}H_{26}O_5Cr \cdot 0.25C_6H_{14}$ calc.: C, 61.5; H, 6.4%) (Found: M^+, 410.1185. $C_{21}H_{26}O_5Cr$ calc.: M, 410.1185). *m/z* 410 (40, M^+); 354 (4, M–2CO), 326 (100, M–3CO), 308 (67, 326-H_2O), 256 (6, M–Cr(CO)$_3$–H_2O), 224 (30), 209 (61), 181 (19), 168 (40), 155 (100), 141 (70), 131 (85), 52 (27, Cr^+). ν_{max} (nujol) 3498 (OH), 1947 (sharp, C≡O), 1879 (broad, C≡O), 1540 (C=C), 1088, 1015 cm^{-1}. δ_H 1.01, td, *J* 13.5, 4.7 Hz, 1H, H3ax; 1.03, s, 3H, H(18)$_3$; 1.23, bd, *J* 10.8 Hz, 1H, H5; 1.30, td, *J* 12.8, 3.8, Hz, 1H, H1ax; 1.38, s, 3H, H(20)$_3$; 1.58, bd, *J* 13.8 Hz, 1H, H2eq; 1.67, qt, *J* 13.3, 3.6 Hz, 1H, H2ax; 1.70–1.79, m, 1H, H6ax; 1.75, bd, *J* 12.9 Hz, 1H, H1eq; 1.85, d, *J* 10.8 Hz, 1H, 7-OH; 1.96, bd, *J* 12.4 Hz, 1H, H3eq; 2.50, dd, *J* 12.9, 6.0 Hz, 1H, H6eq; 3.28 and 3.34, d, *J* 9.1 Hz, 1H, H(19)$_2$; 3.30, s, 3H, 19-OMe; 4.52, td, *J* 10.6, 6.0 Hz, 1H, H7; 5.23, td, *J* 6.5, 1.2 Hz, 1H, H13; 5.39, dd, *J* 6.2, 1.0 Hz, 1H, H11; 5.45, td, *J* 6.3, 0.7 Hz, 1H, H12; 5.57, dd, *J* 6.6, 0.6, Hz, 1H, H14. δ_C 19.8, C2; 27.7, C20; 28.0, C18; 29.6, C6; 35.9, C3; 37.8, C10; 37.9, C4; 40.9, C1; 50.7, C5; 59.30, 19-OMe; 70.8, C7; 76.40, C19; 86.8, C13; 89.1, C12; 93.1, C11; 95.7, C14; 117.7, C8; 127.9, C9; 233.5, 3C, Cr(CO)$_3$.

3.2.4. The β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-methyl 7β-hydroxypodocarpa-8,11,13-trien-19-oate]chromium(0) (32)

A nitrogen-degassed solution of **4** (0.19 g, 0.66 mmol) and tricarbonyl(η^6-naphthalene)chromium(0) (0.23 g, 0.86 mmol) in diethyl ether (12 ml) and THF (91 μl, 0.86 mmol) was stirred at room temperature for 3 days in a closed reaction vessel. The reaction mixture

was filtered (Celite) and concentrated in vacuo. Flash chromatography (hexanes/diethyl ether) gave, in order of increasing polarity: (i) tricarbonyl(η^6-naphthalene)chromium(0) (40 mg); and (ii) **32** (0.28 g, 98%) as yellow micro rods (hexanes/diethyl ether), m.p. 165–170°C. (Found. $M^{+\cdot}$, 424.0979 $C_{21}H_{24}O_6Cr$ calc.: M, 424.0978). *m/z* 424 (18, M^+), 392 (2, M–MeOH), 368 (4, M–2CO), 340 (24, 368-CO), 338 (12, 368-CH_2O), 322 (100, 340-H_2O), 307 (10), 270 (8), 248 (11), 195 (13), 155 (14), 141 (12), 109 (5), 69 (8), 52 (17, Cr^+). ν_{max} (CH_2Cl_2) 3595 (OH), 1963 (sharp, C=O), 1887 (broad, C≡O), 1724 (C=O), 1446, 1383 (C=C), 1113 cm^{-1}. δ_H 1.04, td, *J* 13.6, 4.7 Hz, 1H, H3ax; 1.15, s, 3H, $H(20)_3$; 1.25, s, 3H, $H(18)_3$; 1.26–1.37, m, 1H, H1ax; 1.39, d, *J* 12.4 Hz, 1H, H5; 1.55–1.68, m, 1H, H2eq; 1.84–2.05, m, 3H, H1eq, H2ax and H6ax; 2.29, bd, *J* 13.7 Hz, 1H, H3eq; 2.54, dd, *J* 13.2, 5.6 Hz, 1H, H6eq; 3.65–3.69, m, 1H, 7-OH; 3.70, s, 3H, 19-OMe; 4.55, td, *J* 11.1, 5.7 Hz, 1H, H7; 5.22, td, *J* 6.5, 1.3 Hz, 1H, H13; 5.41, dd, *J* 6.1, 0.7 Hz, 1H, H11; 5.48, bt, *J* 6.2 Hz, 1H, H12; 5.55, bd, *J* 6.5 Hz, 1H, H14. δ_C 20.3, C2; 24.8, C20; 28.1, C18; 30.7, C6; 36.9, C3; 38.1, C10; 40.9, C1; 43.5, C4; 50.6, C5; 51.5, 19-OMe; 70.5, C7; 86.4, C13; 88.8, C12; 93.2, C11; 95.8, C14; 117.6, C8; 125.1, C9; 176.9, C19; 233.4, 3C, $Cr(CO)_3$. δ_H (CD_3COCD_3) 1.12, td, *J* 14.0, 4.5 Hz, 1H, H3ax; 1.17, s, 3H, $H(20)_3$; 1.24, s, 3H, $H(18)_3$; 1.38, td, *J* 13.0, 4.0 Hz, 1H, H1ax; 1.50–1.64, m, 1H, H2eq; 1.56, bd, *J* 11.9 Hz, 1H, H5; 1.90, qt, *J* 13.7, 3.8 Hz, 1H H2ax; 2.00–2.14, m, 2H, H1eq and H6ax; 2.21, bd, *J* 13.5 Hz, 1H, H3eq; 2.42, dd, *J* 13.1, 5.5 Hz, 1H, H6eq; 3.67, s, 3H, 19-OMe; 4.54, d, *J* 5.6 Hz, 1H, 7-OH; 4.69, dt, *J* 10.9, 5.5 Hz, 1H, H7; 5.37, bt, *J* 6.2 Hz, 1H, H13; 5.48, d, *J* 6.3 Hz, 1H, H11; 5.70, t, *J* 6.3 Hz, 1H, H12; 5.88, d, *J* 6.7 Hz, 1H, H14. δ_C (CD_3COCD_3) 21.1, C2; 25.5, C20; 28.3, C18; 31.2, C6; 37.5, C3; 38.9, C10; 41.2, C1; 44.1, C4; 50.9, C5; 51.7, 19-OMe; 70.2, C7; 87.9, C13; 90.0, C12; 95.1, C11; 97.4, C14; 120.4, C8; 125.9, C9; 177.5, C19; 235.0, 3C, $Cr(CO)_3$.

3.2.5. Complexation of 4 with hexacarbonylchromium(0)

A nitrogen-degassed solution of **4** (0.60 g, 2.08 mmol) and hexacarbonylchromium(0) (0.69 g, 3.12 mmol) in dibutyl ether (60 ml) and THF (6.7 ml) was heated to reflux for 24 h under positive nitrogen pressure. The reaction mixture was filtered (Celite) and concentrated in vacuo. Flash chromatography (hexanes/diethyl ether; then CH_2Cl_2) gave, in order of increasing polarity: (i) a mixture (10:3:1, 0.10 g) of (η^6-benzene)tricarbonylchromium(0), **21**, and a unidentified tricarbonylchromium complex; (ii) a mixture (2:3) (97 mg, 11%) of the α and β diastereoisomers of tricarbonyl[(8,9,11,12,13,14-η)-methyl 7-oxopodocarpa-8,11,13-trien-19-oate]chromium(0) (**54**, **52**) as orange rods (hexanes/diethyl ether), m.p. 141–149°C. (Found $M^{+\cdot}$, 422.00824. $C_{21}H_{22}O_6Cr$ calc.: M, 422.00821. *m/z* 422 (17, M^+), 366 (2, M–2CO), 338 (100, 366-CO), 336 (10, 366-CH_2O), 322 (12), 278 (14), 52 (28, Cr^+). ν_{max} (CH_2Cl_2) 1975 (sharp, C≡O), 1903 (broad, C≡O), 1724 (ester, C=O), 1696 (ketone, C=O), 1518, 1466, 1412 (C=C); 1381 cm^{-1}. The β diastereoisomer **52**: δ_H 1.09, td, *J* 13.8, 4.4 Hz, 1H, H3ax; 1.24, s, 3H, $H(20)_3$; 1.29, s, 3H, $H(18)_3$; 1.43, td, *J* 13.3, 3.4 Hz, 1H, H1ax; 1.67, dm, *J* 14.4 Hz, 1H, H2eq; 1.88, dd, *J* 14.4, 2.4 Hz, 1H, H5; 1.89–2.00, m, 1H, H2ax; 2.08, bd, *J* 13.2 Hz, 1H, H1eq; 2.32, bd, *J* 13.6 Hz, 1H, H3eq; 2.94, dd, *J* 17.1, 2.4 Hz, 1H, H6eq; 3.06, dd, *J* 17.1, 14.4 Hz, 1H, H6ax; 3.72, s, 3H, 19-OMe; 5.43, td, *J* 6.1, 1.2 Hz, 1H, H13; 5.46, td, *J* 6.1, 1.7 Hz, 1H, H12; 5.58, dd, *J* 6.1, 1.4 Hz, 1H, H11; 5.91, dd, *J* 5.9, 1.8 Hz, 1H, H14. δ_C 20.0, C2; 22.8, C20; 27.7, C18; 36.2, C3; 36.7, C6; 38.3, C10; 40.8, C1; 43.6, C4; 51.0, C5; 51.7, 19-OMe; 86.8, C11; 90.4, C13; 91.1, C14; 93.3, C12; 94.4, C8; 129.5, C9; 176.4, C19; 197.2, C7; 231.7, 3C, $Cr(CO)_3$; (iii) **54** (92 mg, 10%) as orange rods (hexanes/diethyl ether), m.p. 160–170°C (dec). (Found: $M^{+\cdot}$, 422.00818. $C_{21}H_{22}O_6Cr$ calc.: M, 422.00821). *m/z* 422 (14, M^+), 366 (4, M–2CO), 338 (100, 366-CO), 336 (14, 366-CH_2O), 323 (4, 338-Me), 286 (4), 278 (14), 211 (4), 69 (18), 52 (27, Cr^+). ν_{max} (CH_2Cl_2) 1975 (sharp, C≡O), 1910 (broad, C≡O), 1724 (ester, C=O), 1680 (ketone, C=O), 1520, 1466, 1415 (C=C), 1381 cm^{-1}. δ_H 1.16, s, 3H, $H(20)_3$; 1.23–1.31, m, 1H, H3ax; 1.29, s, 3H, $H(18)_3$; 1.76, dp, *J* 13.3, 3.0 Hz, 1H, H2eq; 1.85–1.94, m, 1H, H1ax; 1.94, qt, *J* 12.9, 3.1 Hz, 1H, H2ax; 2.01, bd, *J* 11.7 Hz, 1H, H1eq; 2.22, dd, *J* 13.8, 4.1 Hz, 1H, H5; 2.31, bd, *J* 13.8 Hz, 1H, H3eq; 2.98, dd, *J* 19.2, 3.8 Hz, 1H, H6eq; 3.27, dd, *J* 19.1, 13.9 Hz, 1H, H6ax; 3.70, s, 3H, 19-OMe; 5.28, d, *J* 6.7 Hz, 1H, H11; 5.35, td, *J* 6.4, 0.6 Hz, 1H, H13; 5.65, td, *J* 6.4, 1.2 Hz, 1H, H12; 6.17, dd, *J* 6.7, 1.1 Hz, 1H, H14. δ_C 19.3, C2; 24.2, C20; 27.9, C18; 35.4, C3; 36.7, C6; 37.0(4), C1; 37.0(5), C10; 44.1, C4; 48.0, C5; 51.7, 19-OMe; 85.9, C11; 89.5, C13; 91.1, 2C, C8 and C14; 94.8, C12; 128.5, C9; 176.7, C19; 196.4, C7; 231.1, 3C, $Cr(CO)_3$; (iv) a mixture (2.2:1.2) of **32** and **54** (94 mg, 11%); (v) **32** (22 mg, 3%); (vi) a mixture (1.2:1.0) (0.38 g, 43%) of **32** and the α diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-methyl 7β-hydroxypodocarpa-8,11,13-trien-19-oate]chromium(0) (**43**); and (vii) a mixture (1.0:3.2) (0.12 g, 14%) of **32** and **43** as yellow micro rods (hexanes/diethyl ether), m.p. 160–167°C. (Found: $M^{+\cdot}$, 424.0975. $C_{21}H_{24}O_6Cr$ calc.: M, 424.0978). *m/z* 424 (20, M^+), 406 (4, M–H_2O), 368 (2, M–2CO), 365 (2, M–CO–OMe), 340 (28, 368-CO), 338 (19, 368-CH_2O), 322 (100, 340-H_2O), 307 (10), 248 (12), 211 (9), 195 (17), 179 (5), 155 (16), 141 (14), 52 (22, Cr^+). ν_{max} (CH_2Cl_2) 3595 (OH), 1962 (sharp, C≡O), 1884 (broad, C≡O), 1724 (C=O), 1452, 1383 (C=C), 1233, 1193, 1149 cm^{-1}. The α diastereoisomer

43. δ_H 1.11, s, 3H, $H(20)_3$, 1.28 s, 3H, $H(18)_3$; 3.67, s, 3H, 19-OMe; 4.71, dt, *J* 11.0, 4.3 Hz, 1H, H7, 5.10, td, *J* 6.4, 1.4 Hz, 1H, H13; 5.42, dd, *J* 6.7, 1.0 Hz, 1H, H11; 5.56, td, *J* 6.3, 1.1 Hz, 1H, H12; 5.73, dd, *J* 6.4, 1.0 Hz, 1H, H14. δ_C 19.6, C2; 24.6, C20; 28.4, C18; 31.5, C6; 37.0, C3; 36.9, C10; 38.9, Cl; 43.7, C4; 47.8, C5; 51.5, 19-OMe; 69.5, C7; 89.8, C13; 90.0, C12; 91.3, C11; 94.4, C14. Signals due to quaternary carbons were not observed. δ_H (CD_3COCD_3) 1.15, s, 3H, $H(20)_3$; 1.25, td, *J* 13.1, 3.8 Hz, 1H, H3ax; 1.28, s, 3H, $H(18)_3$; 1.62–1.68, m, 1H, H2eq; 1.75, bd, *J* 12.8 Hz, 1H, H5; 1.91–2.08, m, 3H, H1ax, H2ax and H6ax; 2.17, bd, *J* 13.0 Hz, 1H, H1eq, 2.28, bd, *J* 13.7 Hz, 1H, H3eq; 2.49, dd, *J* 13.5, 6.5 Hz, 1H, H6eq; 3.67, s, 3H, 19-OMe; 4.63, dt, *J* 11.2, 6.7 Hz, 1H, H7; 4.91, d, *J* 7.0 Hz, 1H, 7-OH; 5.38, t, *J* 6.2 Hz, 1H, H13; 5.81, d, *J* 6.7 Hz, 1H, H11; 5.84, t, *J* 6.5 Hz, 1H, H12; 5.92, d, *J* 6.4 Hz, 1H, H14. δ_C (CD_3COCD_3) 20.4, C2; 24.7, C20; 28.7, C18; 31.8, C6; 38.1, C3; 39.0, C10; 39.6, C1; 44.3, C4; 49.0, C5; 51.7, 19-OMe; 69.7, C7; 92.0, C13; 92.1, C12; 93.8, C11; 96.6, C14; 115.9, C8; 123.5, C9; 177.4, C19; 235.4, 3C, $Cr(CO)_3$.

3.2.6. The β diastereoisomer of tricarbonyl[(8,9,-11,12,13,14-η)-12,19-dimethoxypodocarpa-8,11,13-trien-7β-ol]chromium(0) (33)

A nitrogen-degassed solution of **6** (0.30 g, 0.99 mmol) and tricarbonyl(η^6-naphthalene)chromium(0) (0.40 g, 1.50 mmol) in diethyl ether (15 ml) and THF (0.12 ml, 1.50 mmol) was heated at 70°C for 50 h in a closed reaction vessel. The reaction mixture was filtered (Celite) and the solvents were removed in vacuo. Flash chromatography (hexanes:ether:dichloromethane, 10:1:1, then 6:1:1) gave: (i) tricarbonyl(η^6-naphthalene)chromium(0) (57 mg); (ii) the *β* diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-12,19-dimethoxypodocarpa-8,11,13-trien-7-one]chromium(0) (**53**) (10 mg, 2%) as an orange-yellow solid. (Found: M^+, 438.1135. $C_{22}H_{26}O_6Cr$ calc.: M, 438.1143). *m/z* 438 (10, M^+), 382 (4, M–2CO), 354 (100, M–3CO), 339 (10, 354-Me), 322 (8, 354-MeOH), 302 (27, M–$Cr(CO)_3$), 286 (18), 255 (10), 239 (17), 215 (13), 185 (24), 175 (65), 150 (20). ν_{max} 2962, 1961 (sharp, C≡O), 1879 (broad, C≡O), 1684 (C=O), 1272 cm^{-1}. δ_H 1.01, s, 3H, $H(18)_3$, 1.55, s, 3H, $H(20)_3$, 3.30, s, 3H, 19 OMe, 3.76, s, 3H, 12-OMe, 5.10, dd, *J* 7.0, 2.0 Hz, 1H, H13; 5.38, d, *J* 2.1 Hz, 1H, H11, 6.29, d, *J* 7.0 Hz, 1H, H14, and (iii) **33** (0.25 g, 60%) as bright yellow crystals, m.p. 129–132°C. (Found: C, 60.0; H, 6.4. $C_{22}H_{28}O_6Cr$ calc.: C, 59.9; H, 6.6%) (Found: M^+, 440.1294. $C_{22}H_{28}O_6Cr$ calc.: M, 440.1291). *m/z* 440 (18, M^+), 384 (3, M–2CO), 356 (31, M–3CO), 354 (60), 339 (37), 304 (48, M $Cr(CO)_3$), 286 (60), 255 (20), 239 (47), 197 (20), 185 (100), 175 (70), 161 (40), 150 (55), 52 (40, Cr^+). ν_{max} 3483 (OH), 1954 (sharp, C≡O), 1883 (broad, C≡O), 1842 (sharp, C≡O), 1537 (C=C), 1279, 1108 cm^{-1}. δ_H 0.98–1.04, m, 1H, H3ax; 1.02, s, 3H, $H(18)_3$; 1.22, d, *J* 11.9 Hz, 1H, H5; 1.31, td, *J* 13.2, 4.2 Hz, 1H, H1ax; 1.38, bd, *J* 11.6 Hz, 1H, H6ax; 1.48, s, 3H, $H(20)_3$; 1.53–1.62, m, 1H, H2eq; 1.58, bd, *J* 11.6 Hz, 1H, 7-OH; 1.73, qt, *J* 13.8, 3.7 Hz, 1H, H2ax; 1.75, bd, *J* 12.8 Hz, 1H, H1eq; 1.94, bd, *J* 13.1 Hz, 1H, H3eq; 2.31, dd, *J* 13.0, 6.1 Hz, 1H, H6eq; 3.27 and 3.33, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.30, s, 3H, 19-OMe; 3.71, s, 3H, 12-OMe; 4.34, ddd, *J* 11.2, 11.1, 6.1 Hz, 1H, H7; 5.02, dd, *J* 6.8, 2.1 Hz, 1H, H13; 5.39, d, *J* 2.1 Hz, 1H, H11; 5.67, d, *J* 6.9 Hz, 1H, H14. δ_C 19.8, C2; 26.3, C20; 27.8, C18; 29.9, C6; 35.8, C3; 37.8, C10; 38.6, C4; 41.7, C1; 51.0, C5; 55.9, 12-OMe; 59.3, 19-OMe; 69.8, C7; 76.3, C13; 76.6, C19; 81.1, C11; 89.8, C14; 110.6, C8; 132.5, C9; 141.3, C12; 233.6, 3C, $Cr(CO)_3$.

3.2.7. Complexation of 6 with hexacarbonylchromium(0)

A nitrogen-degassed solution of **6** (60 mg, 0.20 mmol) and hexacarbonylchromium(0) (48 mg, 0.22 mmol) in dibutyl ether (5.1 ml) and THF (0.43 ml) was refluxed for 20 h, cooled, filtered (Celite), and the filtrate concentrated in vacuo. The residue was purified by PLC (hexanes:diethyl ether, 1:1) to yield, in order of decreasing polarity: (i) a mixture (1.0:1.5) (21 mg) of **6** and the *α* diastereoisomer of tricarbonyl-[(8,9,11,12,13,14-η)-12,19-dimethoxypodocarpa-8,11, 13-trien-7-one]chromium(0) (**55**). The *α* diastereoisomer **55**: δ_H 1.07, s, 3H, $H(18)_3$; 1.36, 3H, s, 3H, $H(20)_3$; 2.66–2.76, m, 2H, $H(6)_2$; 3.28, s, 3H, 19-OMe; 3.79, s, 3H, 12-OMe; 5.11, d, *J* 2.1 Hz, 1H, H11; 5.23, dd, *J* 7.2, 2.1 Hz, 1H, H13; 6.33, d, *J* 7.2 Hz, 1H, H14; and (ii) the *α* diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-12,19-dimethoxypodocarpa-8,11,13-tr ien-7β-ol]chromium(0) (**44**) (31 mg, 36%) as a yellow oil. (Found: M^+, 440.1288. $C_{22}H_{28}O_6Cr$ calc.: M, 440.1291). *m/z* 440 (9, M^+), 422 (16, M–H_2O), 384 (3, M–2CO), 366 (8, 422-2CO), 356 (17, M–3CO), 354 (32), 338 (100, 356-H_2O), 322 (8), 291(30), 239 (20), 222 (20), 185 (28), 172 (18), 52 (57, Cr^+). ν_{max} 1960 (sharp, C≡O), 1884 (broad, C≡O), 1103 cm^{-1}. δ_H 1.06, s, 3H, $H(18)_3$; 1.36, s, 3H, $H(20)_3$; 3.30, s, 3H, 19-OMe; 3.68, s, 3H, 12-OMe, 4.52, m, $W_{1/2}$ 26 Hz, 1H, H7, 5.15 5.20, m, 2H, H11 and H13, 6.01, d, *J* 6.8 Hz, 1H, H14. δ_C 18.6, C2, 27.6, C20; 27.7, C18; 30.3, C6; 35.7, C3; 36.7, C1; 37.6, 2C, C4 and C10; 46.9, C5; 55.6, 12-OMe; 59.3, 19-OMe; 68.8, C7; 76.0, C11; 76.2, C13; 76.8, C19; 94.4, C14; 103.4, C8; 128.3, C9; 142.5, C12; 234.4, 3C, $Cr(CO)_3$. δ_H (C_6D_6) 1.03, s, 3H, $H(18)_3$; 1.10, s, 3H, $H(20)_3$; 2.99, s, 3H, 19-OMe; 3.05, s, 3H, 12-OMe; 4.094.20, m, $W_{1/2}$ 26 Hz, 1H, H7; 4.47, dd, *J*7.0, 1.9 Hz, 1H, H13; 4.95, d, *J* 1.9 Hz, 1H, H11; 5.69, d, *J* 7.0 Hz, 1H, H14. δ_C (C_6D_6) 18.9, C2; 27.4, C20; 28.1, C18; 30.4, C6; 36.1, C3; 36.8, C1; 37.6, C10; 37.8, C4; 47.0, C5; 55.1, 12-OMe; 59.0, 19-OMe; 68.8, C7; 76.3,

C11; 76.4, C13; 76.7, C19; 94.7, C14; 103.2, C8; 128.3, C9; 142.4, C12, 234.3, 3C, $Cr(CO)_3$.

3.2.8. The α and β diastereoisomers of tricarbonyl[(8,9,11,12,13,14-η)-methyl 7β-hydroxy-12-methoxypodocarpa-8,11,13-trien-19-oate]chromium(0) (45, 34)

A nitrogen-degassed solution of **7** (0.15 g, 0.47 mmol) and hexacarbonylchromium(0) (0.11 g, 0.52 mmol) in dibutyl ether (12.8 ml) and THF (1.1 ml) was heated at reflux for 18 h under positive nitrogen pressure. The reaction mixture was filtered (Celite) and the solvents removed from the filtrate in vacuo to give a yellow oil. Purification by PLC. (hexanes:diethyl ether, 1:1) yielded, in order of decreasing polarity: (i) a mixture (1.0:9.4:1.2) (44 mg) of **7**, **34** and **56** as an orange oil. The β diastereoisomer **34**: δ_H 1.25, s, 6H, $H(20)_3$ and $H(18)_3$; 2.50, dd, J 13.0, 5.3 Hz, 1H, H6eq; 3.69, s, 3H, 19-OMe; 3.71, s, 3H, 12-OMe; 4.37, m, $W_{1/2}$ 26.0 Hz, 1H, H7; 5.05, d, J 5.9 Hz, 1H, H13; 5.35, s, 1H, H11; 5.70, d, J 6.7 Hz, 1H, H14. δ_C 20.3, C2; 23.0, C20; 28.0, C18; 31.1, C6; 36.8, C3; 38.8, C10; 41.8, C1; 43.4, C4; 50.9, C5; 51.5, 19-OMe; 55.9, 12-OMe; 69.6, C7; 76.9, C11; 80.6, C13; 89.5, C14; 110.3, C8; 129.8, C9; 141.2, C12; 177.6, C19; 233.5, 3C, $Cr(CO)_3$. δ_H (C_6D_6) 0.61, td, J 13.2, 3.9 Hz, 1H, H3ax; 0.92, s, 3H, $H(20)_3$; 1.19, s, 3H, $H(18)_3$; 2.28, m, 1H, H6eq; 2.98, s, 3H, 19-OMe; 3.28, s, 3H, 12-OMe; 3.94, m, $W_{1/2}$ 25 Hz, 1H, H7; 4.26, d, J 7.0 Hz, 1H, H13; 5.03, s, 1H, H11; 5.36, d, J 6.8 Hz, 1H, H14. δ_C (C_6D_6) 20.5, C2; 23.1, C20; 27.8, C18; 31.4, C6; 36.9, C3; 38.6, C10; 41.3, C1; 43.3, C4; 50.7, C5; 50.9, 19-OMe; 55.4, 12-OMe; 69.5, C7; 76.6, C11; 80.9, C13; 89.6, C14; 109.7, C8; 128.3, C9; 141.2, C12, 176.4, C19, 234.3, 3C, $Cr(CO)_3$, and (ii) **45** (0.16 g, 75%) as a yellow oil. (Found: $M^{+\cdot}$, 454.1079. $C_{22}H_{26}O_7Cr$ calc.: M, 454.1084). m/z 454 (7, M^+), 436 (7, $M-H_2O$), 395 (2, $M-CO_2Me$), 370 (9, M–3CO), 352 (100, 370 H_2O), 300 (13, 436 $Cr(CO)_3$), 276 (12), 241 (18), 225 (14), 185 (25), 52 (33, Cr^+). ν_{max} 1962 (sharp, C≡O), 1888 (broad, C≡O), 1722 cm^{-1} (C=O). δ_H 1.15, s, 3H, $H(20)_3$; 1.28, s, 3H, $H(18)_3$; 2.45, dd, J 11.5, 6.2 Hz, 1H, H6eq; 3.67, s, 6H, 19-OMe and 12-OMe; 4.53, m, $W_{1/2}$ 26 Hz, 1H, H7; 5.17–5.22, m, 2H, H11 and H13; 6.05, d, J 7.4 Hz, 1H, H14. δ_C 19.5, C2; 25.1, C20; 28.4, C18; 31.4, C6; 36.9, C3; 37.2, C1; 38.0, C10; 43.7, C4; 47.3, C5; 51.6, 19-OMe; 55.7, 12-OMe; 66.9, C7; 76.6, C11; 77.8, C13; 93.4, C14; 103.6, C8; 125.2, C9; 141.6, C12; 177.2, C19; 233.7, 3C, $Cr(CO)_3$. δ_H (C_6D_6) 0.90, s, 3H, $H(20)_3$; 1.10, s, 3H, $H(18)_3$; 2.93, s, 3H, 19-OMe; 3.21, s, 3H, 12-OMe; 4.07, m, $W_{1/2}$ 25 Hz, 1H, H7; 4.39, bd, J 7.1 Hz, 1H, H13; 4.98, s, 1H, H11; 5.72, d, J 7.2 Hz, 1H, H14. δ_C (C_6D_6) 19.9, C2; 25.0, C20; 28.4, C18; 31.6, C6; 37.3, 2C, C1 and C3; 38.1, C10; 43.8, C4; 47.6, C5; 50.9, 19-OMe; 55.1, 12-OMe; 69.0, C7; 76.1, C11; 78.5, C13; 93.6, C14; 104.0, C8; 125.3, C9; 142.0, C12; 176.6, C19; 234.4, 3C, $Cr(CO)_3$.

3.2.9. The α diastereoisomer of tricarbonyl-[(8,9,11,12,13,14-η)-methyl 12-methoxy-7α-hydroxy-podocarpa-8,11,13-trien-19-oate]chromium(0) (51)

Sodium borohydride (8 mg, 0.21 mmol) was added to a stirred solution of the α diastereoisomer **56** (0.10 g, 0.22 mmol) in THF (7 ml) and methanol (2 ml) and the mixture was stirred for 2 h at room temperature. Workup followed by flash chromatography (hexanes:diethyl ether, 2:1) afforded **51** (80 mg, 80%) as a yellow oil. (Found: $M^{+\cdot}$, 454.1083. $C_{22}H_{26}O_7Cr$ calc.: M, 454.1087). m/z 454 (17, M^+), 436 (3, $M-H_2O$), 370 (17, M–3CO), 352 (78, 370-H_2O), 318 (18, M–$Cr(CO)_3$), 300 (83, 436-$Cr(CO)_3$), 241 (62), 225 (70), 185 (100), 52 (43, Cr^+). ν_{max} 1961 (sharp, C≡O), 1885 (broad, C≡O), 1721 (C=O), 1541, 1459, 1275 cm^{-1}. δ_H 1.06, s, 3H, $H(20)_3$; 1.29, s, 3H, $H(18)_3$; 3.67, s, 3H, 19-OMe; 3.72, s, 3H, 12-OMe; 4.33, bs, 1H, $W_{1/2}$ 16.0 Hz, H7; 5.01, d, J 5.6 Hz, 1H, H13; 5.11, s, 1H, H11; 5.73, d, J 6.7 Hz, 1H, H14. δ_C 19.6, C2; 24.5, C20; 28.3, C18; 29.7, C6; 36.8, C3; 37.0, C1; 37.6, C10; 43.1, C5; 43.9, C4; 51.5, 19-OMe; 55.6, 12-OMe; 63.5, C7; 73.8, C11; 75.8, C13; 96.6, C14; 107.2, C8; 128.8, C9; 143.6, C12; 177.3, C19; 232.6, 3C, $Cr(CO)_3$. δ_H (C_6D_6) 0.81, s, 3H, $H(20)_3$; 1.18, s, 3H, $H(18)_3$; 2.94, s, 3H, 19-OMe, 3.23, s, 3H, 12 OMe, 3.98, m, $W_{1/2}$ 16 Hz, 1H, H7, 4.10, dd, J 6.8, 1.7 Hz, 1H, H13, 4.84, d, J 1.9 Hz, 1H, H11; 5.03, d, J 6.9 Hz, 1H, H14. δ_C (C_6D_6) 19.8, C2; 24.3, C20; 28.3, C18; 30.2, C6; 36.9, C3; 37.4, C1; 37.9, C10; 43.4, C5; 43.8, C4; 50.9, 19 OMe, 55.0, 12-OMe, 63.5, C7; 73.6, C11; 76.1, C13; 96.6, C14; 111.1, C8; 143.5, C12; 233.5, 3C, $Cr(CO)_3$. C_9 and C_{19} were not observed.

3.2.10. The β diastereoisomer of tricarbonyl[(8,9,11,-12,13,14-η)-12,19-dimethoxypodocarpa-5,8,11,13-tetraene]chromium(0) (57)

Treatment of a solution of **8** (0.19 g, 0.59 mmol) and tricarbonyltrispyridinechromium(0) (0.22 g, 0.59 mmol) in diethyl ether (7 ml) with $BF_3 \cdot Et_2O$ (0.22 ml, 1.76 mmol) at −78°C, and then at 0°C for 20 h, followed by flash chromatography (hexanes:diethyl ether, 4:1) afforded **57** (40 mg, 15%) as yellow micro needles (hexanes/diethyl ether), m.p. 94–95°C. (Found: $M^{+\cdot}$, 422.1188. $C_{22}H_{26}CrO_5$ calc.: M, 422.1185). m/z 422 (22, M), 366 (10, M–2CO), 338 (45, M–3CO), 322 (100), 290 (35), 274 (15), 52 (70, Cr^+). ν_{max} 1947 (sharp, C≡O), 1862 (broad, C≡O) 1465, 1387 cm^{-1}. δ_H 1.19, s, 3H, $H(18)_3$; 1.29, s, 3H, $H(20)_3$; 2.83, dd, J 20.2, 6.3 Hz, 1H H7ax; 3.12, bd, J 20.2 Hz, 1H, H7eq;

3.13 and 3.44, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.33, s, 3H, 19-OMe; 3.68, s, 3H, 12-OMe; 5.04, dd, *J* 5.9, 0.8 Hz, 1H, H13; 5.21, d, *J* 0.9 Hz, 1H, H11; 5.52, d, *J* 6.2 Hz, 1H, H14; 5.83, bd, *J* 5.9 Hz, 1H, H6.

3.2.11. Complexation of 28 with hexacarbonylchromium(0)

A nitrogen-degassed solution of **28** (0.35 g, 1.17 mmol) and hexacarbonylchromium(0) (0.39 g, 1.80 mmol) in dibutyl ether (50 ml) and THF (5.5 ml) was heated to reflux for 24 h under positive nitrogen pressure. The reaction mixture was then filtered (Celite) and the solvents removed in vacuo to give a deep yellow oil. Flash chromatography (hexanes/diethyl ether) afforded, in order of increasing polarity: (i) tricarbonyl(η^6-benzene)chromium(0) (0.12 g); (ii) the α diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-methyl 12-methoxypodocarpa-6,8,11,13-tetraen-19-oate]chromium(0) (**59**) (0.23 g, 46%) as yellow micro needles (hexanes/diethyl ether), m.p. 175–176°C. (Found: M^+, 436.0974. $C_{22}H_{24}O_6Cr$ calc.: M, 436.0978). *m/z* 436 (13, M^+), 380 (4, M–2CO), 352 (100, 380-CO), 337 (7, 352-Me), 321(3, 352-OMe), 307 (9), 278 (17), 224 (8), 185 (9), 52 (25, Cr^+). ν_{max} (CH_2Cl_2) 1957 (sharp, C≡O), 1877 (broad, C≡O), 1724 (C=O), 1541, 1464 (C=C), 1225, 1148 cm^{-1}. δ_H 0.92, s, 3H, $H(20)_3$; 1.34, s, 3H, $H(18)_3$; 2.34, bd, *J* 13.4 Hz, 1H, H3eq; 2.63, t, *J* 2.7 Hz, 1H, H5; 3.66, s, 3H, 19-OMe, 3.70, s, 3H, 12-Ome; 5.12, d, *J* 2.1 Hz, H11, 5.20, dd, *J* 7.0, 2.2 Hz, 1H, H13; 5.44, d, *J* 6.9 Hz, 1H, H14; 6.03, dd, *J* 9.9, 3.1 Hz, 1H, H6; 6.44, dd, *J* 10.0, 2.4 Hz, 1H, H7. δ_C 19.2, C2, 20.7, C20, 27.8, C18, 34.1 3 36.6, C1, 37.6, C10; 43.4, C4; 50.3, C5; 51.6, 19-OMe; 55.6, 12-OMe; 75.6, C11; 76.9, C13; 92.9, C14; 96.0, C8; 120.4, C6; 122.4, C9; 132.8, C7; 141.4, C12; 177.1, C19; 234.0, 3C, $Cr(CO)_3$; and (iii) a mixture (2:3) (0.17 g, 33%) of **59** and the β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-methyl 12-methoxypodocarpa-5,8,11,13-tetraen-19-oate]chromium(0) (**58**). The β diastereoisomer **58**: δ_H 1.21, s, 3H, $H(20)_3$; 1.43, s, 3H, $H(18)_3$; 1.45, td, *J* 13.1, 4.0 Hz, 1H, H3ax; 1.77, dm, *J* 13.8 Hz, 1H, H2eq; 1.85–1.95, m, 1H, H1eq; 1.87, qt, *J* 13.5, 3.2 Hz, 1H, H2ax; 2.01, td, *J* 13.1, 4.5 Hz, 1H, H1ax; 2.27, dm, *J* 14.8 Hz, 1H, H3eq; 2.92, dd, *J* 20.2, 6.0 Hz, 1H, H7ax; 3.27, dd, *J* 20.1, 1.9 Hz, 1H, H7eq; 3.66, s, 3H, 19-OMe; 3.69, s, 3H, 12-OMe; 5.06, dd, *J* 6.7, 2.2 Hz, H13; 5.26, d, *J* 2.2 Hz, 1H, H11; 5.49, d, *J* 6.7 Hz, 1H, H14; 5.98, dd, *J* 6.0, 2.1 Hz, 1H, H6. δ_C 19.3, C2; 27.4, C20; 28.9, C7; 29.5, C18; 35.2, C3; 36.2, C1; 37.9, C10; 46.7, C4; 52.0, 19-OMe; 55.6, 12-OMe; 75.1, C11; 77.5, C13; 93.0, C14; 100.1, C8; 122.0, C6; 123.8, C9; 140.9, C5; 142.1, C12; 177.2, C19; 233.9, 3C, $Cr(CO)_3$.

A solution of a mixture (2:3) (0.13 g, 0.30 mmol) of **59** and **58** in diethyl ether (50 ml) was exposed to bright sunlight while open to the air. After 7 h the reaction mixture was filtered (Celite) and the solvents removed in vacuo. Purification by PLC afforded, in order of increasing polarity: (i) **28** (24 mg, 27%); and (ii) methyl 12-methoxypodocarpa-5,8,11,13-tetraen-19-oate (**29**) (38 mg, 42%) as a clear oil which crystallised to give needles, m.p. 115–117°C. (Found: M^+, 300.1724. $C_{19}H_{24}O_3$ calc.: M, 300.1725). *m/z* 300 (58, M^+), 285 (7, M–Me), 268 (2, M–MeOH), 253 (2, 268-Me), 241 (10, M–CO_2Me), 225 (100, 285-HCO_2Me), 210 (5), 197 (7), 185 (35), 171(11), 165 (9), 128 (8). ν_{max} 2947, 1727 (C=O), 1656, 1610, 1504 (C=C), 1373, 1244, 1047 cm^{-1}. δ_H 1.16, td, *J* 13.3, 4.1 Hz, 1H, H3ax; 1.18, s, 3H, $H(20)_3$; 1.38, s, 3H, $H(18)_3$; 1.58, td, *J* 13.5, 4.1 Hz, H1ax; 1.66, dp, *J* 14.0, 4.0 Hz, 1H, H2eq; 2.04, qt, *J* 13.7, 3.6 Hz, 1H, H2ax; 2.22, dm, *J* 13.0 Hz, 1H, H1eq; 2.34, dm, *J* 13.2 Hz, 1H, H3eq; 3.40, dd, *J* 21.5, 4.9 Hz, 1H, H7ax; 3.49. bdd, *J* 21.6, 2.9 Hz, 1H, H7eq; 3.64, s, 3H, 19-OMe; 3.79, s, 12-OMe, 5.99, dd, *J* 4.9, 2.9 Hz, 1H, H6; 6.72, dd. *J* 8.3, 2.5 Hz, 1H, H13; 6.87, d, *J* 2.6 Hz, 1H, H11; 7.02, d, *J* 8.3 Hz, 1H, H14. δ_C 19.8, C2; 27.7, C20; 27.8, C18; 29.6, C7; 36.7, C3; 39.2, C10; 39.9, C1; 46.8, C4; 51.8, 19-OMe; 55.2, 12-OMe; 111.0, C11; 111.3, C13; 121.4, C6; 124.7, C8; 128.5, C14; 141.1, C5; 146.8, C9; 158.1, C12; 177.8, C19.

3.2.12. Complexation of 28 with tricarbonyl(η^6-naphthalene)chromium(0)

A nitrogen-degassed solution of **28** (0.41 g, 1.37 mmol) and tricarbonyl(η^6-naphthalene)chromium(0) (0.47 g, 1.78 mmol) in diethyl ether (15 ml) and THF (0.17 ml, 2.05 mmol) was stirred at room temperature for 60 h in a closed reaction vessel. The mixture was filtered (Celite) and concentrated in vacuo. The crude product was purified by flash chromatography (hexanes/diethyl ether) to give, in order of increasing polarity: (i) **28** (80 mg, 20%); (ii) tricarbonyl(η^6-naphthalene)chromium(0) (0.15 g); (iii) **59** (0.15 g, 25%); and (iv) a mixture (2:3) of **58** and **59** (0.32 g, 54%).

3.2.13. The α diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-methyl 12-methoxypodocarpa-6,8,11,13-tetraen-19-oate]chromium(0) (59)

A mixture of **45** (10 mg, 22 μmol) and potassium hydrogensulfate (3 mg, 22 μmol) was heated to reflux in benzene (1.0 ml) for 4.5 h. Workup followed by flash chromatography (hexanes:diethyl ether, 1:1) yielded (i) **28** (3 mg, 44%); and (ii) **59** (3 mg, 31%).

3.2.14. The β diastereoisomer of tricarbonyl-[(8,9,11,12,13,14-η)-7β,19-dimethoxypodocarpa-8,11,13-triene]chromium(0) (35)

A nitrogen-degassed solution of **5** (0.22 g, 0.76 mmol) and tricarbonyl(η^6-naphthalene)chromium(0)

(0.24 g, 0.92 mmol) in diethyl ether (10 ml) and THF (90 μl, 1.15 mmol) was heated at 70°C for 40 h. The reaction mixture was filtered (Celite) and the solvent was removed in vacuo. Flash chromatography (hexanes:diethyl ether, 7:1) gave, in order of increasing polarity (i) tricarbonyl(η^6-naphthalene)chromium(0) (56 mg); and (ii) **35** (0.18 g, 57%) as yellow crystals, m.p. 196–198°C. (Found: M^+, 424.1346. $C_{22}H_{28}O_5Cr$ calc.: M, 424.1342). *m/z* 424 (24, M^+), 392 (2, M–MeOH, 368 (4, M–2CO), 340 (85, M–3CO), 338 (30), 323 (18), 308 (100, 340-MeOH), 292 (18), 261 (22), 209 (20), 193 (18), 155 (30), 141 (28), 52 (75, Cr^+). ν_{max} (nujol) 1948 (sharp, C≡O), 1871 (broad, C≡O), 1540 (C=C), 1015 cm^{-1}. δ_H 1.02, s, 3H, $H(18)_3$; 1.38, s, 3H, $H(20)_3$; 2.45, dd, *J* 12.7, 6.0 Hz, 1H, H6eq; 3.30 and 3.40, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.30, s, 3H, 19-OMe, 3.55, s, 7 OMe, 4.13, dd, *J* 10.6, 5.8 Hz, 1H, H7; 5.06, td, *J* 6.4, 1.3 Hz, 1H, H13, 5.20, dd, *J* 6.4, 1.0 Hz, 1H, H11; 5.41, td, *J* 6.4, 0.9 Hz, 1H, H12, 5.56, dd, *J* 6.6, 0.6 Hz, 1H, H14. δ_C 19.8, C2; 24.0, C6; 27.8, C20; 28.0, C18; 35.9, C3; 37.7, C10; 37.9, C4; 40.7, C1; 50.2, C5; 57.1. 7-OMe; 59.3, 19-OMe; 76.3, C19; 78.9, C7; 86.2, C13; 87.4, C12; 93.1, C11; 95.5, C14; 114.9, C8; 125.7, C9; 233.5, 3C, $Cr(CO)_3$.

3.2.15. The α diastereoisomer of tricarbonyl-[(8,9,11,12,13,14-η)-7β,12,19-trimethoxypodocarpa-8, 11,13-triene]chromium(0) (46)

A nitrogen-degassed solution of **8** (0.38 g, 1.18 mmol) and hexacarbonylchromium(0) (0.33 g, 1.50 mmol) in dibutyl ether (40 ml) and THF (3.3 ml, 4.6 mmol) was heated to reflux for 24 h. The mixture was filtered (Celite) and the solvent removed in vacuo to give a yellow oil which was purified by flash chromatography (hexanes:diethyl ether, 5:1) to give **46** (0.37 g, 69%) as yellow crystals, m.p 106–108°C. (Found: C, 61.3; H, 6.9. $C_{23}H_{30}O_6Cr$ calc.: C, 60.8; H, 6.7%) (Found: M^+, 454.1449. $C_{23}H_{30}O_6Cr$ calc.: M, 454.1448). *m/z* 454, (18, M^+), 422 (2, M–MeOH), 370 (44, M–3CO), 398 (5, M–2CO), 368 (56, 398-CH_2O), 338 (100, 370-MeOH), 322 (18), 291 (17), 239 (22), 185 (20), 52 (32, Cr^+). ν_{max} 1954 (sharp, C≡O), 1876 (broad, C≡O), 1544 (C=C), 1272, 1209 cm^{-1}. δ_H 1.06, s, 3H, $H(18)_3$; 1.15–1.24, m, 1H, H3ax; 1.18, td, *J* 13.6, 4.3 Hz, 1H, H1ax; 1.33, s, 3H, $H(20)_3$; 1.56, td, *J* 13.3, 10.0 Hz, 1H, H6ax; 1.60–1.67, m, 2H, H2eq and H5; 1.80–2.00, m, 3H, H1eq, H2ax and H3eq; 2.35, ddd, *J* 13.2, 7.5, 1.5 Hz, 1H, H6eq; 3.27 and 3.43, d, *J* 9.2 Hz, 1H, $H(19)_2$; 3.32, s, 3H, 19-OMe; 3.45, s, 3H, 7-OMe; 3.67, s, 3H, 12-OMe; 4.13, dd, *J* 9.8, 7.6 Hz, 1H, H7; 5.14, d, *J* 2.1 Hz, 1H, H11; 5.16, dd, *J* 7.0, 2.1 Hz, 1H, H13; 5.95, d, *J* 7.0 Hz, 1H, H14. δ_C 19.0, C2; 25.6, C6; 27.9, C20; 28.0, 18; 36.0, C3; 37.0, C1; 37.7, C10; 38.1, C4; 47.0, C5; 56.0, 12-OMe; 56.7, 7-OMe; 59.8, 19-OMe; 76.2, C7; 76.4, C19; 77.3, C11; 77.4, C13; 95.3, C14; 101.0, C8; 128.2, C9; 142.8, C12; 234.1, 3C, $Cr(CO)_3$.

3.2.16. The β diastereoisomer of tricarbonyl-[(8,9,11,12,13,14-η)-7β,12,19-trimethoxypodocarpa-8, 11,1 3-triene]chromium(0) (36)

A nitrogen-degassed solution of **8** (0.16 g, 0.5 mmol) and tricarbonyl(η^6-naphthalene)chromium 0.20 g, 0.75 mmol) in diethyl ether (8 ml) and THF (60 μl, 0.75 mmol) was heated at 70°C for 32 h in a closed reaction vessel. The mixture was filtered (Celite) and the solvent was removed in vacuo. Flash chromatography (hexanes:diethyl ether, 6:1) gave: (i) a mixture (5.1:2.1) of (η^6-carbonyl(η^6-naphthalene)chromium(0) and **8** (0.1 g), and (ii) **36** (0.13 g, 62%) as yellow crystals, m.p. 119–120°C. (Found: M^+, 454.1444. $C_{23}H_{30}O_6Cr$ calc.: M 454.1447) (Found: C, 61.0; H, 6.7. $C_{23}H_{30}O_6Cr$ calc.: C, 60.8; H, 6.7%). *m/z* 454 (18, M^+), 422 (2, M–MeOH), 398 (5, M–2CO), 370 (44, M–3CO), 368 (56, 398-CH_2O), 353 (20), 322 (10), 318 (18), 291 (14), 255 (12), 239 (28), 185 (40), 52 (28, Cr^+). ν_{max} 1961 (broad, C≡O), 1879 (broad, C≡O), 1540, 1268, 1115, 1097, 1015 cm^{-1}. δ_H 1.00, s, 3H, $H(18)_3$; 1.49, s, 3H, $H(20)_3$; 2.37, dd, *J* 12.6, 5.8 Hz, 1H, H6eq; 3.26 and 3.39, d, *J* 9.3 Hz, 1H, $H(19)_2$; 3.31, s, 3H, 19-OMe; 3.53, s, 3H, 7-OMe; 3.69, s, 3H, 12-OMe; 3.99, dd, *J* 10.4, 5.8 Hz, 1H, H7; 5.07, dd, *J* 6.9, 2.1 Hz, 1H, H13; 5.35, d, *J* 2.1 Hz, 1H, H11; 5.47, d, *J* 6.9 Hz, 1H, H14. δ_C 19.8, C2; 24.3, C6; 26.9, C20; 27.8, C18; 35.9, C3; 37.9, C10; 38.4, C4; 41.4, C1; 50.6, C5; 55.9, 12-OMe; 56.9, 7-OMe; 59.3, 19-OMe; 76.3, C19; 78.1, C7; 78.4, C13; 80.3, C11; 89.1, C14; 107.7, C8; 129.8, C9; 139.8, C12; 234.1, 3C, $Cr(CO)_3$.

3.2.17. The β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-12,19-dimethoxy-7β-methoxymethoxypodocarpa-8,11,13-triene]chromium(0) (37)

A nitrogen-degassed solution of **9** (0.25 g, 0.72 mmol) and tricarbonyl(η^6-naphthalene)chromium(0) (0.25 g, 0.93 mmol) in diethyl ether (9 ml) and THF (90 μl, 1.08 mmol) was stirred at room temperature for 5 days in a closed reaction vessel. The mixture was filtered (Celite) and concentrated in vacuo. The crude product was purified by flash chromatography (hexanes:diethyl ether, 4:1) to give, in order of increasing polarity: (i) tricarbonyl(η^6-naphthalene)chromium(0) (49 mg); and (ii) **37** (0.26 g, 74%) as yellow crystals, m.p. 126–128°C. (Found: M^+, 484.1556. $C_{24}H_{32}O_7Cr$ calc.: M, 484.1553). *m/z* 484 (18, M^+), 400 (20, M–3CO), 369 (25, 400-OMe), 370 (5, 400-CH_2O), 338 (100, 400-$HOCH_2OMe$), 322 (10), 291 (10), 255 (8), 239 (20), 185 (35), 52 (47, Cr^+). ν_{max} (nujol) 1938 (sharp, C≡O), 1878 (broad, C≡O), 1540 (C=C), 1268, 1102, 1097, 1020 cm^{-1}. δ_H 1.00, s, 3H, $H(18)_3$, 1.49, s, $H(20)_3$; 2.30, dd, *J* 12.9, 6.0 Hz, 1H, H6eq, 3.28 and

3.33. d, *J* 9.1 Hz, 1H, H(19)$_2$; 3.30, s, 3H, 19-OMe; 3.50, s, 3H, 7 OCH$_2$OMe; 3.69, s, 3H, 12-OMe; 4.36, dd, *J* 10.6, 6.2 Hz, 1H, H7, 4.75 and 4.90, d, *J* 6.9 Hz, 1H, 7-OC*H*$_2$OMe; 5.08, dd, *J* 6.9, 2.1 Hz, 1H, H13; 5.36, d, *J* 2.1 Hz, 1H, H11, 5.47, d, *J* 6.9 Hz, 1H, H14. δ_C 19.8, C2; 26.0, C6; 26.8, C20; 27.8, C18; 35.8, C3; 37.9, C10; 38.3, C4; 41.5, C1, 50.7, C5, 56.0, 2C, 7-OCH$_2$OMe and 12 OMe; 59.3, 19-OMe; 75.6, C19, 76.2, C7, 71.9, C13, 80.2, C11, 89.3, C14, 95.7, 7 OCH$_2$OMe, 107.2, C8, 130.6, C9; 139.8, C12; 234.1, 3C, Cr(CO)$_3$.

Treatment of **9** (30 mg, 86 μmol) with tricarbonyl(η^6-naphthalene)chromium(0) (27 mg, 0.10 mmol) in diethyl ether (6 ml)/THF (20 μl, 0.25 mmol) for 22 h at 70°C gave an inseparable mixture (1:1) of **37** and the α diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-12,19-dimethoxy-7β-methoxymethoxypodocarpa-8,11,13-triene]chromium(0) **47** (14 mg, 34%) as a yellow oil. The α diastereoisomer **47**: δ_H 1.05, s, 3H, H(18)$_3$; 1.30, s, 3H, H(20)$_3$; 2.30, dd, *J* 12.9, 6.0 Hz, 1H, H6eq; 3.28 and 3.39, d, *J* 9.1 Hz, 1H each, H(19)$_2$; 3.33, s, 3H, 19-OMe; 3.47, s, 3H, 7-OCH$_2$OMe; 3.68, s, 3H, 12-OMe; 4.49, dd, *J* 10.6, 6.5 Hz, 1H, H7; 4.74 and 4.85, d, *J* 6.7 Hz, 2H, 7-OC*H*$_2$OMe; 5.13, bs, 1H, H11; 5.15, dd, *J* 6.9, 2.1 Hz, 1H, H13; 5.95, d, *J* 6.8 Hz, 1H, H14.

3.2.18. The β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-methyl 12-methoxy-7β-methoxymethoxypodocarpa-8,11,13-trien-19-oate]chromium(0) (38)

A nitrogen-degassed solution of **10** (0.18 g, 0.50 mmol) and tricarbonyl(η^6-naphthalene)chromium(0) (0.17 g, 0.65 mmol) in diethyl ether (12 ml) and THF (60 μl, 0.75 mmol) was stirred at room temperature for 4 days in a closed reaction vessel. The mixture was filtered (Celite) and concentrated in vacuo. The crude product was purified by flash chromatography (hexanes/diethyl ether) to give, in order of increasing polarity: (i) tricarbonyl(η^6-naphthalene)chromium(0) (60 mg); (ii) **10** (69 mg, 38%); and (iii) **38** (0.16 g, 50%) as yellow needles (hexanes/diethyl ether), m.p. 102–104°C. (Found: M^+, 498.1348. $C_{24}H_{30}O_8Cr$ calc.: M, 498.1346). *m/z* 498 (9, M^+), 439 (4, M–CO_2Me), 414 (11, M–3CO), 384 (18, 414-CH_2O), 382 (16, 414-MeOH), 367 (8, 382-Me), 362 (1, M–Cr(CO)$_3$), 352 (100), 337 (6), 301 (12), 278 (9), 241 (13), 225 (8), 185 (16), 171 (8), 52 (11, Cr^+). ν_{max} 1954 (sharp, C≡O), 1865 (broad, C≡O), 1725 (C=O), 1540, 1465 (C=C), 1270, 1234, 1041 cm^{-1}. δ_H 1.02, td, *J* 13.3, 3.8 Hz, 1H, H3ax; 1.24, s, 3H, H(20)$_3$; 1.27–1.39, m, 1H, H1ax; 1.28, s, 3H, H(18)$_3$; 1.31, bd, *J* 12.4 Hz, 1H, H5; 1.58–1.66, m, 1H, H2eq; 1.82–1.99, m, 3H, H1eq, H2ax and H6ax; 2.28, bd, *J* 13.5 Hz, 1H, H3eq; 2.49, dd, *J* 13.3, 5.5 Hz, 1H, H6eq; 3.53, s, 3H, 7-OCH$_2$OMe; 3.69, s, 3 H, 12-OMe; 3.70, s, 3H, 19-OMe; 4.38, dd, *J* 10.8, 5.7 Hz, 1H, H7; 4.77 and 4.95, d, *J* 7.0 Hz, 1H, 7-OCH$_2$OMe; 5.13, dd, *J* 6.9, 1.9 Hz, 1H, H13; 5.30, d, *J* 1.9 Hz, 1H, H11; 5.50, d, *J* 6.9 Hz, 1H, H14. δ_C 20.2, C2; 23.5, C20; 27.2, C6; 28.0, C18; 36.8, C3; 38.5, C10; 41.5, C1; 43.4, C4; 50.5, C5; 51.4, 19-OMe; 55.9, 2C, 7-OCH$_2$OMe and 12-OMe; 75.1, C7; 78.5, C11; 79.5, C13; 89.0, C14; 95.7, 7-OCH$_2$OMe; 107.2, C8; 127.8, C9; 139.9, C12; 176.9, C19; 233.9, 3C, Cr(CO)$_3$.

3.2.19. The α and β diastereoisomers of tricarbonyl-[(8,9,11,12,13,14-η)-12,19-dimethoxypodocarpa-8,11,13-trien-7β-yl acetate]chromium(0) (48, 39)

A nitrogen-degassed solution of **11** (0.18 g, 0.50 mmol) and tricarbonyl(η^6-naphthalene)chromium(0) (0.17 g, 0.63 mmol) in diethyl ether (10 ml) and THF (60 μl, 0.76 mmol) was heated at 60–65°C for 20 h in a closed reaction vessel. The reaction mixture was filtered (Celite) and concentrated in vacuo. Flash chromatography (hexanes:diethyl ether, 6:1) gave: (i) **11** (37 mg, 21%); (ii) tricarbonyl(η^6-naphthalene)chromium(0) (20 mg); and (iii) an inseparable mixture (2:1) of **39** and **48** (0.12 g, 50%) as a yellow oil which crystallised to give yellow rods, m.p. 111–114°C. (Found: M^+, 482.1395. $C_{24}H_{30}O_7Cr$ calc.: M, 482.1397). *m/z* 482 (5, M^+), 422 (14, M–$MeCO_2H$), 398 (4, M–3CO), 392 (5, M–2CO–CH_2O), 381 (46), 340 (45), 338 (100), 291 (40), 286 (20), 224 (21), 185 (32), 52 (39, Cr^+). The β diastereoisomer **39**: ν_{max} (nujol) 1965 (sharp, C≡O), 1874 (broad, C≡O), 1732 cm^{-1} (C=O). δ_H 1.03, td, *J* 13.3, 5.4 Hz, 1H, H3ax; 1.03, s, 3H, H(18)$_3$; 1.28, bd, *J* 11.7 Hz, 1H, H5; 1.31, td, *J* 12.7, 3.6 Hz, 1H, H1ax; 1.55, s, 3H, H(20)$_3$; 1.60, bd, *J* 14.1 Hz, 1H, H2eq; 1.67–1.75, m, 3H, H1eq, H2ax and H6ax; 1.99, bd, *J* 12.7 Hz, 1H, H3eq; 2.19, s, 3H, 7-OCOMe; 2.27, dd, *J* 12.9, 6.6 Hz, 1H, H6eq; 3.27 and 3.33, d, *J* 9.2 Hz, 1H, H(19)$_2$; 3.29, s, 3H, 19-OMe; 3.70, s, 3H, 12-OMe; 5.00, dd, *J* 6.8, 2.1 Hz, 1H, H13; 5.30, d, *J* 6.8 Hz, 1H, H14; 5.31, d, *J* 2.1 Hz, 1H, H11; 5.67, dd, *J* 10.6, 6.6 Hz, 1H, H7. δ_C 19.8, C2; 21.0, 7-OCOMe; 25.7, C6; 26.2, C20; 28.0, C18; 36.0, C3; 37.8, C10; 38.5, C4; 41.5, C1; 50.6, C5; 55.8, 12-OMe; 59.2, 19-OMe; 70.4, C7; 76.5, C19; 76.7, C13; 79.1, C11; 89.9, C14; 103.4, C8; 132.7, C9; 140.9, C12; 171.4, 7-OCOMe; 233.7, 3C, Cr(CO)$_3$. The α diastereoisomer **48**: ν_{max} ($CHCl_3$) 1962 (sharp, C≡O), 1887 (broad, C≡O), 1730 cm^{-1} (C=O). δ_H 1.04, s, 3H, H(18)$_3$; 1.06, s, 3H, H(20)$_3$; 2.13, s, 3H, 7-OCOMe; 2.43, ddd, *J* 13.5, 8.3, 2.1 Hz, 1H, H6eq; 3.32, s, 3H, 19-OMe; 3.70, s, 3H, 12-OMe, 3.41 and 3.70, d, *J* 9.2 Hz, 1H, H(19)$_2$; 5.11, dd, *J* 6.9, 2.2 Hz, 1H, H13, 5.14, d, *J* 2.2 Hz, 1H, H11; 5.62, t, *J* 8.8 Hz, 1H, H7; 5.64, d, *J* 6.9 Hz, 1H, H14. δ_C 18.5, C2; 21.3, 7-OCOMe; 26.1, C6; 27.1, C20; 27.6, C18; 35.6, C3, 36.4, C1; 36.7, C10, 36.9, C4; 46.7, C5; 55.6, 12-OMe; 59.4, 19-OMe; 70.5, C7; 75.1, C13; 75.9, C11; 76.3, C19; 94.2, C14; 110.1, C8;

127.8, C9; 142.4, C12; 170.2, 7-OCOMe; 233.3, 3C, $Cr(CO)_3$.

3.2.20. The α and β diastereoisomers of tricarbonyl-[(8,9,11,12,13,14-η)-12,19-dimethoxy-7β-tetrahydropyranyloxypodocarpa-8,11,13-triene]chromium(0) (49, 40)

A nitrogen-degassed solution of **12** (0.30 g, 0.80 mmol) and tricarbonyl(η^6-naphthalene)chromium(0) (0.32 g, 1.20 mmol) in diethyl ether (14.0 ml) and THF (1.0 ml, 12.0 mmol) was heated at 70°C for 50 h. The mixture was filtered (Celite) and the solvents were removed in vacuo. Flash chromatography (hexanes: diethyl ether, 12:1 then 3:7) gave, in order of increasing polarity: (i) tricarbonyl(η^6-naphthalene)chromium(0) (15 mg); (ii) an inseparable mixture (6:6:2:1) (0.26 g, 62%) of a pair of β diastereoisomers of **40** and a pair of α diastereoisomers of **49** as a yellow oil. (Found: M^+, 524.1867. $C_{27}H_{36}O_7Cr$ calc.: M, 524.1866). *m/z* 524 (14, M^+), 468 (2, M–2CO), 440 (100, M–3CO), 423 (30), 356 (16), 340 (55), 338 (70), 305 (20), 287 (65), 255 (30), 185 (57), 173 (20), 161 (30), 152 (50), 52 (93, Cr^+). The major β diastereoisomer of **40**: δ_H 1.01, s, 3H, $H(18)_3$; 1.51 s, 3H, $H(20)_3$; 2.26, dd, *J* 12.7, 6.0 Hz, 1H, H6eq; 3.26 and 3.30, d, *J* 9.3 Hz, 1H, $H(19)_2$; 3.30, s, 3H, 19-OMe; 3.59, m, 1H, H5′ax; 3.68, s, 3H, 12-OMe; 3.92–4.01, m, 1H, H5′eq; 4.50, dd, *J* 10.6, 6.0 Hz, 1H, H7; 4.89, t, *J* 4.1 Hz, 1H, H11; 5.09, dd, *J* 6.7, 1.9 Hz, 1H, H13; 5.31, d, *J* 1.9 Hz, 1H, H11; 5.71, d, *J* 6.9 Hz, 1H, H14. δ_C 19.6, C2; 19.8, C3′; 24.7, C4; 25.5, C6; 26.7, C20; 27.8, C18; 30.8, C2′; 35.9, C3; 37.9, C10; 38.4, C4; 41.5, C1; 50.5, C5; 55.8, 12-OMe; 59.25, 19-OMe; 63.3, C5′; 72.3, C7; 76.0, C19; 77.9, C13; 79.4, C11; 90.1, C14; 95.0, C1′; 107.6, C8; 130.0, C9; 140.0, C12; 234.1, 3C, $Cr(CO)_3$. The minor β diastereoisomer of **40**: δ_H 1.00, s, 3H, $H(18)_3$; 1.51, s, 3H, $H(20)_3$; 2.38, dd, *J* 12.9, 6.0 Hz, 1H, H6eq; 3.22 and 3.42, d, *J* 9.2 Hz, 1H, $H(19)_2$; 3.31, s, 3H, 19-OMe; 3.55–3.61, m, 1H, H5′ax; 3.69, s, 3H, 12-OMe; 4.00–4.10, m, 1H, H5′eq, 4.31, dd, *J* 10.6, 6.0 Hz, 1H, H7, 4.93, t, *J* 3.0 Hz, 1H, H1′; 5.04, dd, *J* 6.9, 2.0 Hz, 1H, H13, 5.31, bs, 1H, H11; 5.32, d, *J* 6.7 Hz, 1H, H14. δ_C 18.7, C2; 19.8, C3′; 25.6, C6; 26.9, C4′; 26.9, C20, 27.6, C18; 31.0, C2′; 35.5, C3; 37.9, C10; 38.4, C4; 41.5, C1; 51.0, C5; 55.9, 12-OMe; 59.4, 19-OMe; 61.8, C5′; 75.8, C19; 77.3, C7; 77.6, C13; 79.7, C11; 89.7, C14; 100.0, C1′; 107.6, C8; 131.0, C9; 140.0, C12; 234.1, 3C, $Cr(CO)_3$. The major α diastereoisomer of **49**: δ_H 1.00, s, 3H, $H(18)_3$, 1.25, s, 3H, $H(20)_3$; 3.25 and 3.39, d, *J* 9.2 Hz, 1H, $H(19)_2$; 3.30, s, 3H, 19-OMe; 3.54–3.62, m, 1H, H5′ax; 3.69, s, 3H, 12-OMe; 4.02–4.09, m, 1H, H5′eq; 4.29–4.36, m, 1H, H7; 4.97, bs, 1H, H1′; 5.03, dd, *J* 6.9, 2.2 Hz, 1H, H13; 5.10, d, *J* 2.2 Hz, 1H, H11; 5.64, d, *J* 6.8 Hz, 1H, H14. δ_C 18.8, 2C, C2 and C3′; 24.4, C4′; 25.6, C6; 26.4, C20; 27.4, C18; 30.7, C2′; 35.8, C3; 37.1, C10; 37.3, C4; 37.2, C1; 42.8, C5; 55.5, 12-OMe; 59.4, 19-OMe; 62.3, C5′; 66.5, C7; 74.3, C19; 75.7, C13; 76.5, C11; 95.0, C1′; 96.4, C14; 110.6, C8; 131.0, C9; 140.0, C12; 234.1, 3C, $Cr(CO)_3$. The minor α diastereoisomer of **49**: δ_H 1.09, s, 3H, $H(18)_3$; 1.23, s, 3H, $H(20)_3$; 3.25 and 3.42, d, *J* 9.2 Hz, $H(19)_2$; 3.30, s, 3H, 19-OMe; 3.51–3.58, m, 1H, H5′ax; 3.69, s, 3H, 12-OMe; 3.96, bt, *J* 10.1 Hz, 1H, H5′eq; 4.29, d, *J* 3.9 Hz, 1H, H7; 4.94, bs, 1H, H1′; 4.99, bd, *J* 6.8 Hz, 1H, H13; 5.10., bs. 1H, H11; 5.46, d, *J* 6.8 Hz, 1H, H14.

3.2.21. The α and β diastereoisomers of tricarbonyl[(8,9,11,12,13,14-η)-methyl 7β-[(1,1-dimethylethyl)dimethylsilyl]oxy-12-methoxypodocarpa-8,11,13-trien-19- oate]chromium(0) (50, 41)

A nitrogen-degassed solution of **13** (0.45 g, 1.04 mmol) and hexacarbonylchromium(0) (0.34 g, 1.56 mmol) in dibutyl ether (40 ml) and THF (4.4 ml) was heated to reflux for 21 h under positive nitrogen pressure. The reaction mixture was then filtered (Celite) and the solvents removed in vacuo to give a bright yellow oil. Flash chromatography (hexanes/diethyl ether) gave, in order of increasing polarity: (i) a mixture (3 : 7) (0.55 g, 93%) of **41** and **50** as yellow micro needles (hexanes/diethyl ether). m.p. 135–137°C. (Found: M^+, 568.1955. $C_{28}H_{40}O_7CrSi$ calc.: M, 568.1948). *m/z* 568 (10, M^+), 553 (2, M–Me), 509 (2, M–CO_2Me), 484 (12, M–3CO), 482 (10, M–2CO–CH_2O). 467 (10, 482-Me), 425 (5), 411 (5), 375 (9), 352 (100), 278 (8), 241 (14), 185 (14), 126 (8), 52 (13, Cr^+). ν_{max} (CH_2Cl_2) 1957 (sharp, C≡O), 1880 (broad, C≡O), 1723 (C=O), 1605, 1542, 1464 (C=C), 1236, 1150 cm^{-1}. The β diastereoisomer **41**: δ_H 0.18 and 0.19, s, 3H, $SiMe_2$; 0.99, s, 9H, $SiCMe_3$; 1.23, 3H, $H(20)_3$; 1.24, s, 3H, $H(18)_3$; 3.66, s, 3H, 19-OMe; 3.69, s, 3H, 12-OMe; 4.45–4.51, m, 1H, H7; 5.14, dd, *J* 7.0, 2.2 Hz, 1H, H13; 5.21, d, *J* 2.2 Hz, 1H, H11; 5.33, d, *J* 6.8 Hz, H14. δ_C −5.1 and −4.2, $SiMe_2$; 18.0, $SiCMe_3$; 20.3, C2, 23.7, C20, 25.7, 3C, $SiCMe_3$; 27.9, C18; 30.6, C6; 36.8. C3; 38.5, C10; 41.5, C1; 43.2, C4, 50.8, C5, 51.4, 19-OMe; 56.0, 12-OMe, 70.7, C7; 78.8, C11, 81.0, C13, 87.2, C14, 111.7, C8, 126.5, C9; 139.0, C12; 176.9, C19; 233.9. C, $Cr(CO)_3$. The α diastereoisomer **50**: δ_H 0.16 and 0.21, s, 3H, $SiMe_2$; 0.97, s, 9H, $SiCMe_3$; 1.15, 3H, $H(20)_3$; 1.27, s, 3H, $H(18)_3$; 3.66, s, 3H, 19-OMe; 3.67, s, 3H, 12-OMe; 4.49, dd. *J* 10.7, 6.4 Hz, 1H. H7; 5.17, bs, 1H, H11; 5.19, dd, *J* 6.9, 2.2 Hz, 1H, H13; 5.88, d, *J* 6.8 Hz, H14. δ_C −5.0 and −4.4, $SiMe_2$; 18.0, $SiCMe_3$; 19.5, C2; 25.2, C20; 25.8, 3C, $SiCMe_3$; 28.2, C18; 31.4, C6; 36.9, C3; 37.2, C1; 38.2, C10; 43.6, C4; 47.6, C5; 51.4, 19-OMe; 55.6, 12-OMe; 70.4, C7; 76.8, C11; 77.8, C13; 93.7, C14; 104.4, C8; 125.2, C9; 141.8, C12; 177.0, C19; 233.8, 3C, $Cr(CO)_3$; and (ii) **59** (18 mg, 4%).

Treatment of **13** with tricarbonyl(η^6-naphthalene)chromium(0) in diethyl ether/THF for 5 days at room temperature and then for 2 days at 70°C

afforded only naphthalene and recovered starting material.

3.3. Lithiation / electrophile addition reactions

3.3.1. Silylation of the β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-1 2,19-dimethoxypodocarpa-8,11,13-trien-7β-ol]chromium(0) (33)

t-Butyllithium (1.31 mol l^{-1}, 0.19 ml, 0.25 mmol) was added dropwise to a solution of **33** (42 mg, 95 μmol) and TMEDA (65 μl, 0.45 mmol) in THF (2.5 ml) at −78°C. After 25 min chlorotrimethylsilane (96 μl, 0.76 mmol) was added and the mixture was stirred for 4 h. Workup followed by decomplexation (dichloromethane/air/sunlight) and purification by PLC (hexanes:diethyl ether, 4:1) afforded: (i) an inseparable mixture (1:1) (5 mg, 10%) of 12,19-dimethoxy-13-trimethylsilylpodocarpa-8,11,13-trien-7-one (**24**) and 12,19-dimethoxy-14-trimethylsilylpodocarpa-8,11,13-trien-7-one (**25**). The 13 trimethylsilyl isomer **24**: δ_H 0.28, s, 9H, $SiMe_3$; 1.04, s, 3H, $H(18)_3$; 1.32, s, 3H, $H(20)_3$; 2.75, m, 2H, $H(6)_2$; 3.33, s, 3H, 19-OMe; 3.79 s, 3H, 12-OMe; 6.73, s, 1H, H11; 8.06, s, 1H, H14. The 14-trimethylsilyl isomer **25**: δ_H 0.33, s, 9H, $SiMe_3$; 1.02, s, 3H, $H(18)_3$; 1.27, s, 3H, $H(20)_3$; 2.75, m, 2H, $H(6)_2$; 3.30, s, 3H, 19-OMe; 3.79, s, 3H, 12-OMe; 6.90, bs, 1H, H11; 7.04, bs, 1 H, H13; and (ii) 12,19-dimethoxy-13-trimethylsilylpodocarpa-8,11,13-trien-7β-ol (**14**) (13 mg, 36%) as a clear oil. (Found: M^+, 376.2417. $C_{22}H_{36}O_3Si$ calc.: M, 376.2434). *m/z* 376 (85, M^+), 361 (30, M-Me), 359 (22, M−OH), 348 (10), 331 (37, M−CH_2OMe), 311 (20), 303 (20, M−Me_3Si), 222 (58), 207 (20), 175 (18), 161(15), 45 (85), 73 (100). ν_{max} 3416 (OH), 1597 (C=C), 1242, 1109, 1039 cm^{-1}. δ_H 0.25, s, 9H, $SiMe_3$; 1.03, s, 3H, $H(18)_3$; 1.29, s, 3H, $H(20)_3$; 2.39 dd, *J* 12.3, 6.5, Hz, 1H, H6eq; 3.28 and 3.46, d, *J* 9.2 Hz, 1H, $H(19)_2$; 3.33, s, 3H, 19-OMe; 3.78, s, 3H, 12-OMe; 4.69–4.75, m, 1H, H7; 6.66, s, 1H, H11; 7.49, s, 1H, H14.

3.3.2. Silylation of the α diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-7β,12,19-trimethoxypodocarpa-8,11,13-triene]chromium(0) (46)

t-Butyllithium (1.31 mol l^{-1}, 0.19 ml, 0.25 mmol) was added dropwise to a solution of **46** (40 mg, 89 μmol) in THF (2.5 ml) at −78°C. After 10 min TMEDA (40 μl, 0.25 mmol) was injected and the mixture was stirred at −78°C for 1 h. Chlorotrimethylsilane (90 μl, 0.71 mmol) was added and the mixture was stirred at −78°C for 3 h and then allowed to warm to room temperature overnight. Workup and purification by flash chromatography afforded the α diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-7β,12,19-trimethoxy-13-trimethylsilylpodocarpa-8,11,13-triene]chromium(0) (**60**) (42 mg, 90%) as yellow crystals (hexanes/diethyl ether), m.p. 230–232°C. (Found: M^+, 526.1844. $C_{26}H_{38}O_6CrSi$ calc.: M, 526.1843). *m/z* 526 (15, M^+), 442 (10, M−3CO), 410 (100, 442-MeOH), 169 (10), 73 (38), 52 (12, Cr^+). ν_{max} (nujol) 1950 (sharp, C≡O), 1867 (broad, C≡O), 1526 (C=C), 1247, 1113, 1028 cm^{-1}. δ_H 0.32, s, 9H, $SiMe_3$; 1.07, s, 3H, $H(18)_3$; 1.36, s, 3H, $H(20)_3$; 2.32, ddd, *J* 13.1, 7.6, 1.5 Hz, 1H, H6eq; 3.27 and 3.49, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.32, s, 3H, 19-OMe; 3.45, s, 3H, 7-OMe; 3.69, s, 3H, 12-OMe; 4.09, dd, *J* 9.6, 7.7 Hz, 1H, H7; 4.93, s, 1H, H11; 5.97, s, 1H, H14. δ_C −0.64, 3C, $SiMe_3$; 18.6, C2; 25.4, C6; 27.5, C20; 27.7, C18; 35.4, C3; 36.3, C1; 37.2, C10; 37.8, C4; 46.5, C5; 55.2, 12-OMe; 56.4, 7-OMe; 59.4, 19-OMe; 69.7, C7; 75.8, C19; 76.8, C11; 87.8, C13; 99.4, C8; 102.3, C14; 128.6, C9; 147.1, C12; 233.9, 3C, $Cr(CO)_3$.

3.3.3. Silylation of the β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-7β,12,19-trimethoxypodocarpa-8,11,13-triene]chromium(0) (36)

t-Butyllithium (1.31 mol l^{-1} in hexanes, 0.11 ml, 0.13 mmol) was added dropwise to a solution of **36** (21 mg, 46 μmol) and TMEDA (24.0 μl, 0.16 mmol) in THF (1.0 ml) at −78°C. After 5 min chlorotrimethylsilane (50 μl, 0.37 mmol) was added and the mixture was stirred for 3 h. Workup followed by decomplexation (diethyl ether/air/sunlight) afforded 7β,12,19-trimethoxy-13-trimethylsilylpodocarpa-8,11,13-triene (**15**) (18 mg, 97%) as a clear oil. (Found: M^+, 390.2588. $C_{23}H_{38}O_3Si$ calc.: M 390.2590). *m/z* 390 (70, M^+), 375 (34, M−Me), 359 (57, M−CH_2OH), 345 (14), 329 (28), 317 (30, M−Me_3Si), 236 (40), 73 (100). ν_{max} 1599, 1552, (C=C), 1237, 1109, 1037 cm^{-1}. δ_H 0.24, s, 9H, $SiMe_3$; 1.03, s, 3H, $H(18)_3$; 1.26, s, 3H, $H(20)_3$; 2.38, dd, *J* 12.5, 7.3 Hz, 1H, H6eq; 3.27 and 3.55, d, *J* 9.1 Hz, 1H, $H(19)_2$; 3.34, s, 3H, 19-OMe; 3.46, s, 3H, 7-OMe; 3.77, s, 3H, 12-OMe; 4.44, dd, *J* 9.2, 7.2 Hz, 1H, H7; 6.65, s, 1H, H11; 7.42, s, 1H, H14.

3.3.4. Allylation of a mixture (1:1) of the α and β diastereoisomers of tricarbonyl[(8,9,11,12,13,14-η)-7β,12,19-trimethoxypodocarpa-8,11,13-trienechromium-(0) (46, 36)

t-Butyllithium (1.31 mol l^{-1}, 0.18 ml, 0.24 mmol) was added dropwise to a solution of a mixture (1:1) of **36** and **46** (50 mg, 0.11 mmol) in THF (1.5 ml) at −78°C. After 12 min $CuBr \cdot SMe_2$ (50 mg, 0.24 mmol) was added and the mixture was stirred for 45 min before being treated with 3-bromopropene (60 μl, 0.66 mmol). The mixture was stirred for 1.5 h at −78°C and then at room temperature overnight. Workup followed by flash chromatography (hexanes:diethyl ether, 6:1) afforded: (i) the β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-7β,12,19-trimethoxy-13-(3′-propenyl) podocarpa-8,11,13-triene]chromium(0) (**62**) (25 mg, 46%) as a yellow oil. (Found: M^+, 494.1764. $C_{26}H_{34}O_6Cr$ calc.: M, 494.1761). *m/z* 494

(30, M^+), 438 (5, M–2CO), 410 (87, M–3CO), 408 (74, 438-CH_2O), 393 (63, 408-CH_2OMe), 382 (50), 378 (100, 410-MeOH), 338 (30), 352 (20), 326 (25), 279 (25), 225 (38), 214 (20), 204 (25), 52 (55, Cr^+). ν_{max} ($CHCl_3$) 1957 (sharp, C≡O), 1882 cm^{-1} (broad, C≡O). δ_H 1.01, s, 3H, $H(18)_3$; 1.48, s, 3H, $H(20)_3$; 2.35, dd, J 12.6, 5.8 Hz, 1H, H6eq; 3.01 and 3.08, bd, J 7.1 Hz, 1H, 13-CH_2CH=CH_2; 3.30, s, 3H, 19-OMe; 3.30–3.45, m, 2H, $H(19)_2$; 3.53, s, 3H, 7-OMe; 3.74 s, 3H, 12-OMe; 4.04, dd, J 10.5, 5.8 Hz, 1H, H7; 5.09, bs, 1H, 13-CH_2CH=CH_2 (*cis*); 5.13–5.18, m, 1H, 13-CH_2CH=CH_2 (*trans*); 5.33, s, 1H, H11; 5.34, s, 1H, H14; 5.85, ddt, J 17.4, 9.5, 6.7 Hz, 1H, 13-CH_2CH=CH_2. δ_C 19.8, C2; 24.2, C6; 27.5, C20; 27.9, C18; 33.6, 13-CH_2CH=CH_2; 35.9, C3; 37.9, C10; 38.3, C4, 41.1, C1; 50.6, C5; 56.5, 12-OMe; 56.9, 7-OMe; 59.3, 19-OMe; 75.8, C19; 76.4, C11, 78.5, C7; 89.9, C14; 109.2; C8; 117.3, 13-CH_2CH=CH_2, 126.2, C9; 135.1, 13-CH_2CH=CH_2; 234.2, 3C, $Cr(CO)_3$. C12 anti C13 were not observed; and (ii) the α diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-7β,12,19-trimethoxy-13-(3′-propenyl)podocarpa-8,11,13-triene]chromium(0) (**61**) (22 mg, 41%) as a yellow oil. (Found: M^+, 494.1764. $C_{26}H_{34}O_6Cr$ calc.: M, 494.1761). m/z 494 (40, M^+), 463 (3, M–OMe), 448 (3, 463-Me), 422 (3, 463-CH_2CH=CH_2), 410 (90, M–3CO), 378 (100, 410-MeOH), 362 (18), 352 (17), 225 (19), 52 (60, Cr^+). ν_{max} ($CHCl_3$) 1956 (sharp, C≡O), 1879 cm^{-1} (broad, C≡O). δ_H 1.06, s, 3H, $H(18)_3$; 1.31, s, 3H, $H(20)_3$; 2.34, dd, J 12.4, 7.8 Hz, 1H, H6eq; 3.11–3.43, m, 4H, 13-CH_2CH=CH_2 and $(H19)_2$; 3.31, s, 3H, 19-OMe; 3.45, s, 3H, 7-OMe; 3.69, s, 3H, 12-OMe; 4.18, dd, J 9.0, 7.8 Hz, 1H, H7; 5.06, s, 1H, H11; 5.13, bs, 1H, 13-CH_2CH=CH_2 (*cis*); 5.20, bd, J 5.4 Hz, 1H, 13-CH_2CH=CH_2 (*trans*); 5.81, s, 1H, H14; 5.84–6.01, m, 1H, 13-CH_2CH=CH_2. δ_C 18.6, C2; 25.3, C6; 27.3, C20; 27.5, C18; 33.0, 13-CH_2CH=CH_2; 35.5, C3; 36.6, C10; 37.1, C4; 37.7, C1; 47.3, C5; 55.9, 12-OMe; 56.4, 7-OMe; 59.4, 19-OMe; 71.2, C7; 75.8, C19; 76.7, C11; 96.1, C14; 109.7; C8; 117.7, 13-CH_2CH=CH_2; 130.0, C9; 134.7, 13-CH_2CH=CH_2; 233.8, 3C, $Cr(CO)_3$. C12 and C13 were not observed.

A solution of **61** in diethyl ether was exposed to sunlight for 2 h and then purified by PLC to give 7β,12,19-trimethoxy-13-(3′-propenyl)podocarpa-8,11,13-triene (**16**) as a clear oil. δ_H 1.03, s, 3H, $H(18)_3$; 1.26, s, 3H, $H(20)_3$; 2.30, bd, J 13.8 Hz, 1H, H3eq; 2.36, ddd, J 12.7, 7.3, 1.3 Hz, 1H, H6eq; 3.28 and 3.57, d, J 9.1 Hz, 1H, $H(19)_2$; 3.30–3.36, m, 2H, 13-CH_2CH=CH_2; 3.34, s, 3H, 19-OMe; 3.44, s, 3H, 7-OMe; 3.79 s, 3H, 12-OMe; 4.23, dd, J 9.5, 7.1 Hz, 1H, H7; 4.93, bdd, J 10.0, 1.6 Hz, 1H, 13-CH_2CH=CH_2 (*cis*); 5.09, bdd, J 17.2, 1.6 Hz, 1H, 13-CH_2CH=CH_2 (*trans*); 6.00, ddt, J 17.0, 10.0, 6.6 Hz, 1H; 13-CH_2CH=CH_2; 6.08, s, 1H, H11; 7.18, s, 1H, H14.

3.3.5. Silylation of the β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-12,19-dimethoxy-7β-methoxymethoxypodocarpa-8,11,13-triene]chromium(0) (37)

t-Butyllithium (1.31 mol l^{-1}, 0.15 ml, 0.20 mmol) was added dropwise to a solution of **37** (40 m g, 83 μmol) in THF (2.5 ml) at −78°C, followed by TMEDA (40 μl, 0.25 mmol). After 45 min chlorotrimethylsilane (80 μl, 0.66 mmol) was added and the mixture was stirred for 3 h at −78°C and then at room temperature overnight. Workup afforded a bright yellow oil which was decomplexed (diethyl/air/sunlight) and then purified by PLC (hexanes:diethyl ether, 4:1) to give 12,19-dimethoxy-7β-methoxymethoxy-13-trimethylsilylpodocarpa-8,11,13-triene (**17**) (19 mg, 95%) as a clear oil. (Found: M^+, 420.2694. $C_{24}H_{40}O_4Si$ calc.: M, 420.2696). m/z 420 (30, M^+), 405 (9, M–Me), 375 (8, M–CH_2OMe), 359 (40, M–OCH_2OMe), 348 (30, M–CH_2SiMe_2), 327 (15), 315 (20), 287 (15), 255 (20), 233 (20), 185 (17), 73 (100), 45 (98). ν_{max} 1598 (C=C), 1241, 1108, 1040 cm^{-1}. δ_H 0.24, s, 9H, $SiMe_3$; 1.03, s, 3H, $H(18)_3$; 1.28, s, 3H, $H(20)_3$; 2.40, dd, J 12.7, 7.3 Hz, 1H, H6eq; 3.28 and 3.49, d, J 9.1 Hz, 1H, $H(19)_2$; 3.34, s, 3H, 19-OMe; 3.53, s, 3H, 7-OCH_2OMe; 3.79, s, 3H, 12-OMe; 4.65–4.73, m, 1H, H7; 4.78 and 4.98, J 7.0 Hz, 1H, 7-OCH_2OMe; 6.66, s, 1H, H11; 7.44, s, 1H, H14. δ_C −0.99, $SiMe_3$; 19.0, C2; 25.5, C20; 26.7, C6; 27.6, C18; 35.9, C3; 37.8, C10; 38.5, C4; 38.9, C1; 49.6, C5; 55.1, 12-OMe; 55.8, 7-OCH_2OMe; 59.4, 19-OMe; 75.8, C19; 76.0, C7; 95.2, 7-OCH_2OMe; 104.9, C11; 127.1, C8; 135.0, C14; 153.1, C9; 163.9, C12.

3.3.6. Methylation of the β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-12,19-dimethoxy-7β-methoxymethox ypodocarpa-8,11,13-triene]chromium(0) (37)

t-Butyllithium (1.31 mol l^{-1}, 0.15 ml, 0.20 mmol) was added to a solution of **37** (30 mg, 60 μmol) and TMEDA (40 μl, 0.24 mmol) in THF (1.5 ml) at −78°C. After 7 min iodomethane (40 μl, 0.62 mmol) was added and the mixture was stirred for 2.5 h at −78°C and then for 2.0 h at room temperature. Workup followed by crystallisation of the crude product from hexanes/diethyl ether afforded the β diastereoisomer of tricarbonyl[(8,9,11,12,13,14-η)-12,19-dimethoxy-7β-methoxymethoxy-13-methyl-podocarpa-8,11,13-triene]chromium(0) (**63**) (27 mg, 90%) as yellow crystals, m.p. 140–143°C. (Found: M^+, 498.1719. $C_{25}H_{34}O_7Cr$ calc.: M, 498.1709). m/z 498 (20, M^+), 414 (22, M–3CO), 437 (5, M–OCH_2OMe), 382 (72, M–3CO–MeOH), 352 (100, 414-$HOCH_2OMe$), 305 (13), 269 (11), 253 (14), 199 (27), 113 (18), 52 (38, Cr^+). ν_{max} (nujol) 1933 (sharp, C≡O), 1864 (sharp, C≡O), 1842 (sharp, C≡O), 1548 (C=C), 1464, 1051 cm^{-1}. δ_H 1.00, s, 3H, $H(18)_3$; 1.47, s, 3H, $H(20)_3$, 2.14, s, 1H, 13-Me; 2.30, dd, J 12.7, 6.1 Hz, 1H, H6eq; 3.27 and 3.49, d, J 9.4 Hz, 1H, $H(19)_2$, 3.30, s, 3H, 19-OMe,

3.52, s, 3H, 7-OCH$_2$OMe; 3.76, s, 3H, 12-OMe, 4.36, dd, J 10.6, 6.1 Hz, 1H, H7, 4.77 and 4.93, d, J 7.0 Hz, 1H, 7-OCH_2OMe, 5.30, s, 1H, H11; 5.38, s, 1H, H14.

References

[1] R.C. Cambie, G.R. Clark, S.R. Gallagher, P.S. Rutledge, M.J. Stone, P.D. Woodgate, J. Organomet. Chem. 342 (1988) 315.
[2] R.C. Cambie, P.S. Rutledge, R.J. Stevenson, P.D. Woodgate, J. Organomet. Chem. 471 (1994) 133.
[3] R.C. Cambie, P.S. Rutledge, R.J. Stevenson, P.D. Woodgate, J. Organomet. Chem. 471 (1994) 149.
[4] R.C. Cambie, P.S. Rutledge, R.J. Stevenson, P.D. Woodgate, J. Organomet. Chem. 486 (1995) 199.
[5] R.C. Cambie, A.D. Erson, A.C. Gourdie, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 348 (1988) 317.
[6] R.C. Cambie, P.S. Rutledge, M. Tercel, P.D. Woodgate, J. Organomet. Chem. 315 (1986) 171.
[7] R.C. Cambie, M.R. Metzler, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 398 (1990) 117.
[8] R.C. Cambie, M.R. Metzler, C.E.F. Rickard, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 426 (1992) 213.
[9] R.C. Cambie, M.R. Metzler, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 429 (1992) 41.
[10] R.C. Cambie, M.R. Metzler, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 429 (1992) 59.
[11] C.A.L. Mahaffy, P.L. Pauson, Inorg. Synth. 19 (1979) 154.
[12] R.C. Cambie, G.R. Clark, A.C. Gourdie, P.S. Rutledge, P.D. Woodgate, J. Organomet. Chem. 297 (1985) 177.
[13] B. Mailvaganam, R.E. Perrier, B.G. Sayer, B.E. McCarry, R.A. Bell, M.J. McGlinchey, J. Organomet. Chem. 354 (1988) 325.
[14] M.D. Rausch, G.A. Moser, E.J. Zaiko, A.L. Lipman, J. Organomet. Chem. 23 (1970) 185.
[15] H. Werner, K. Deckelmann, U. Schönenberger, Helv. Chim. Acta 53 (1970) 2002.
[16] E.P. Kundig, D. Amurrio, R. Liu, A. Ripa, Synlett. (1991) 657.
[17] H.G. Schmalz, B. Miles, J.W. Bat, G. Durner, Angew. Chem. In. Ed. Engl. 31 (1992) 5.
[18] M.F. Semmelhack, in: B.M. Trost, I. Fleming (Eds.), Comprehensive Organic Synthesis, Vol. 4, Pergamon, Oxford, 1991, p. 517.
[19] J.G. Bendall, Ph.D. Thesis, University of Auckland, 1993.
[20] P.L. Pauson, G.H. Smith, J. Chem. Soc. (1967) 1061.
[21] A.J. Pearson, G.R. Han, J. Org. Chem. 50 (1985) 2791.
[22] A.J. Pearson, Y.S. Chen, G.R. Han, S.Y. Hsu, T. Ray, J. Chem. Soc. Perkin Trans I (1985) 267.
[23] O. Mitsunobu, Synthesis (1981) 1.
[24] J.A. Heppert, J. Aube, M.A. Thomas-Miller, M.L. Milligan, F. Takusagawa, Organometallics 9 (1990) 727.
[25] M. Uemura, N. Nishikawa, K. Take, M. Ohnishi, K. Hirotsu, T. Higuchi, Y. Hayashi, J. Org. Chem. 48 (1983) 2349.
[26] G.M. Sheldrick, SHELXS-86, Institut für Anorganische Chemie, Universität Göttingen, Germany, 1986.
[27] G.M. Sheldrick, SHELXL-93, Institut für Anorganische Chemie, Universität Göttingen, Germany, 1993.
[28] C.R. Bennett, R.C. Cambie, W.A. Denny, Aust. J. Chem. 22 (1969) 1699.
[29] R.C. Cambie, J.D. Robertson, P.S. Rutledge, P.D. Woodgate, Aust. J. Chem. 34 (1981) 2687.