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CHEMISTRY OF THE PODOCARPACEAE

LXX. SYNTHESIS AND CYCLOPENTAANNULATION OF A DITERPENOID CHROMIUM CARBENE COMPLEX

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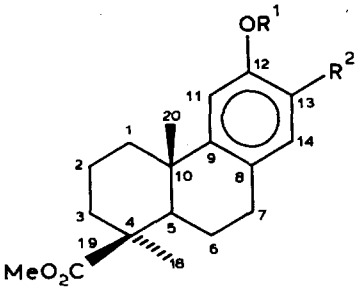
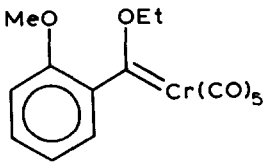
Summary

A pentacarbonylcarbene chromium complex of the diterpenoid methyl *O*-methylpodocarpate has been prepared and its reactions with some alkynes have been studied with the aim of synthesising ring-C aromatic steroids. The use of diphenylacetylene resulted in cyclisation to give steroidal derivatives in moderate yield.

Introduction

12-Hydroxypodocarpa-8,11,13-trien-19-oic acid (podocarpic acid) (**1**), a diterpenoid resin acid which is readily available from the New Zealand species





(6)

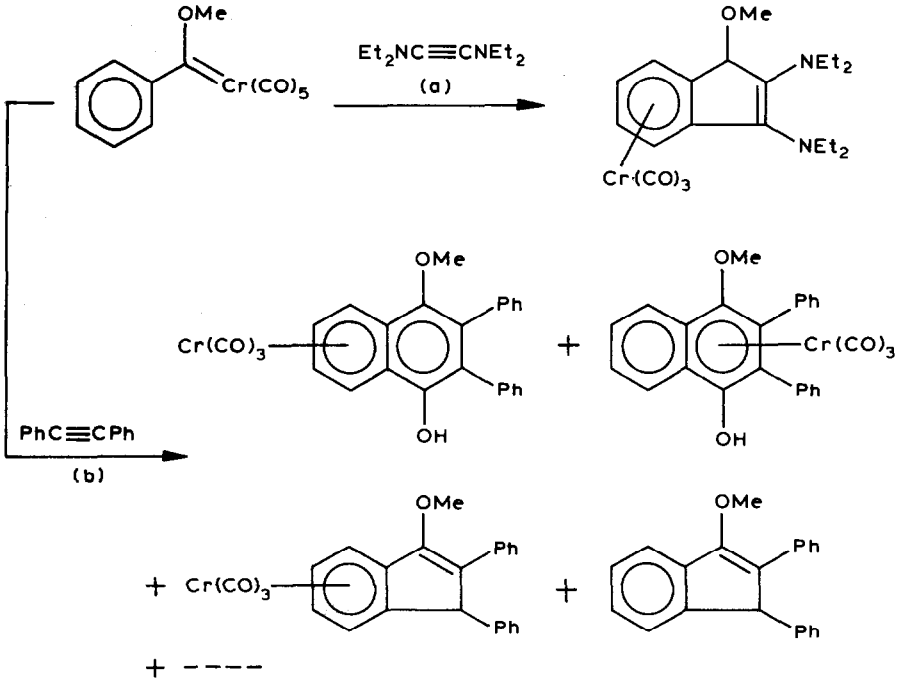
(**1** : $R^1 = R^2 = H$;
2 : $R^1 = Me, R^2 = H$;
3 : $R^1 = Me, R^2 = Br$;
4 : $R^1 = Me, R^2 = Li$;
5 : $R^1 = Me, R^2 = SiMe_3$)

0022-328X/86/$03.50

Dacrydium cupressinum, has potential as a precursor for the synthesis of other chiral terpenoid compounds e.g. ring-C aromatic steroids. Attempts by Davis and Watkins [1] to effect cyclopentaannulation of methyl *O*-methylpodocarpate (**2**) via an initial Friedel–Crafts reaction at C(13) followed by electrophilic substitution at C(14) to complete the cycloalkylation were largely unsuccessful. However, an alternative strategy involves a transition metal mediated process which does not rely on the susceptibility of the aromatic ring to electrophilic attack. This paper reports attempts to achieve the desired cyclopentaannulation via a Fischer-type carbene complex of chromium(0) [2].

Results and discussion

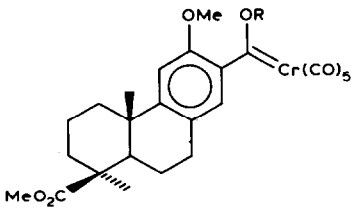
Highly nucleophilic alkynes such as yndiamines can attack the electrophilic carbene carbon atom of a Fischer-type complex, resulting in an insertion reaction [3,4]. When the carbene carbon atom also bears an aryl substituent the insertion product can cyclise onto the aromatic ring, yielding indene derivatives in a net cyclopentaannulation process (Scheme 1, a) [5]. In contrast, alkynes of low nucleophilicity react in a donor solvent via initial coordination to the metal, leading to products of benzannulation. With a moderately nucleophilic alkyne such as diphenylacetylene in a non-polar solvent these pathways become competitive and mixtures of products result (Scheme 1, b) [6,7]. However, most attempts to utilise transition metal complexes of carbenes for synthetic purposes have used relatively simple aromatic substrates e.g. **6** [4]. In the present case methyl *O*-methyl podocar-



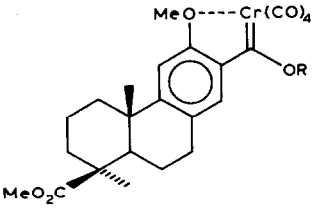
SCHEME 1

pate represents a chiral, optically active, polyfunctional compound in which the aryl ring corresponds to a disubstituted derivative of anisole.

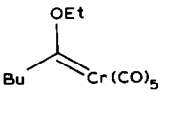
In order to form a suitable carbene complex **7**, the 13-bromo derivative **3** [8] was treated with butyllithium and then hexacarbonylchromium(0) using reaction conditions which were satisfactory for the formation of the carbene complex **6** derived from anisole [9]. However, while generation of the aryllithium species **4** from the bromide occurred at room temperature, nucleophilic attack of butyl carbanion at the C(19) ester group occurred also. Generation of the aryllithium **4** using butyllithium at −78°C in tetrahydrofuran followed by brief treatment with chlorotrimethylsilane indicated that the aryllithium **4** had limited stability relative to that derived from 2-bromoanisole, since the yield of the silylated diterpenoid **5** fell from 93 to 70% as the reaction time was increased from 3 to 60 min. Most of the remainder of the product consisted of the product **2** of protonation of the aryllithium. Use of diethyl ether as solvent at −78°C resulted in a lower yield of the silane **5**. Treatment of the aryllithium **4** in tetrahydrofuran with hexacarbonylchromium at −78°C for 60 min, followed by warming the mixture to room temperature and then alkylation of the lithium acyl metallate with triethyloxonium tetrafluoroborate [10] afforded the desired pentacarbonylcarbene complex **7** (47%) as a dark red oil, together with the tetracarbonyl methoxy-ligated carbene complex **9** (3%), the product **2** (43%) of reductive debromination of **3**, and an unstable yellow oil (variable yield) identified tentatively as pentacarbonyl[ethoxy(butyl)carbene]chromium(0) (**11**) [11]. The pentacarbonylchromium group of **7** was evident from the IR spectrum which showed three intense absorptions, at 2070, 1988, and 1948 cm^{-1}. The spectrum also showed a carbonyl band due to an ester (1718 cm^{-1}), while the ^1H NMR spectrum exhibited a triplet and quartet at δ 1.50 and 4.36 ppm, respectively, due to the carbene ethoxy substituent. Two singlets in the aromatic region at δ 6.35 and 6.64 ppm were assigned to the C(14) and C(11) protons respectively, since the upfield singlet was broadened slightly as a result of weak coupling to the benzylic C(7) proton(s). The remainder of the spectrum was consistent with a podocarpa-8,11,13-triene skeleton. The ^{13}C NMR spectrum of **7** showed the carbene carbon signal at characteristically low field (δ 353 ppm), and the signals due to the *cis*- and *trans*-carbonyl ligands at 216 and 225 ppm (ratio 4/1), respectively. These chemical shifts are in accord with those (δ 354, 217, and 225 ppm) previously assigned to analogous carbon atoms in the anisole-derived complex **6** [9]. As is not uncommon with transition metal carbene complexes [12] the



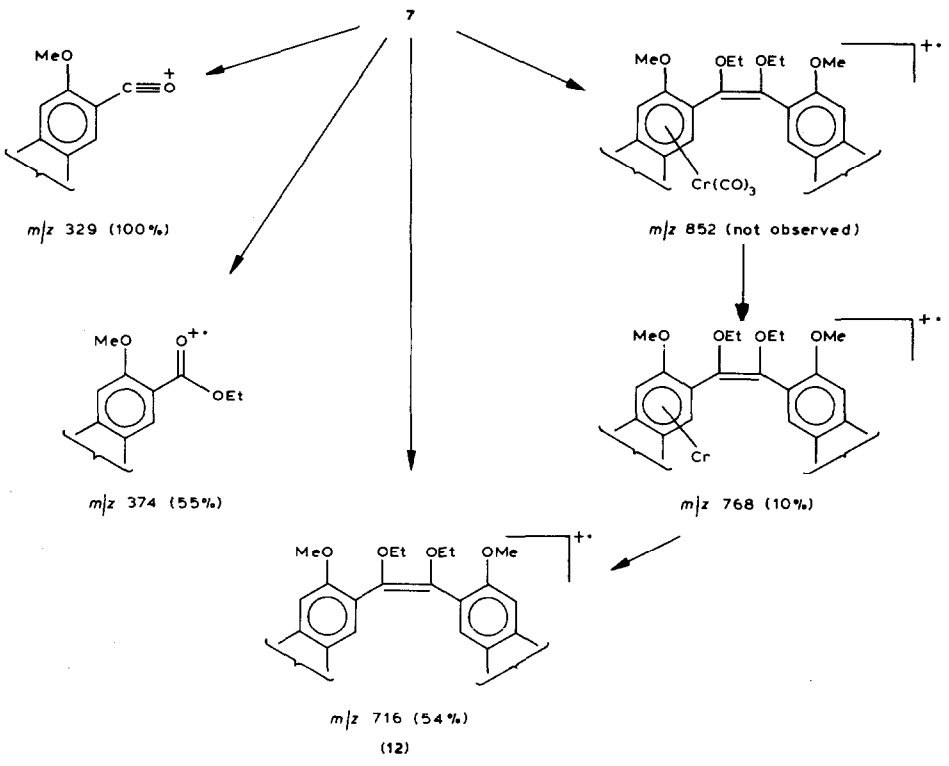
(7: R = Et;
8: R = Me)



(9: R = Et;
10: R = Me)



(11)



SCHEME 2

molecular ion (m/z 550) was not detected in the electron-impact induced mass spectrum of the diterpenoid chromium carbene complex **7** at any probe temperature. Instead, a peak which appeared at m/z 716 (54%) on heating the probe to 150°C was indicative of formation of the metal-free dimer **12**. A plausible fragmentation pattern incorporating this peak as well as others detected at m/z 768, 374, and 329 is presented in Scheme 2.

Like the analogous complex from anisole, the diterpenoid carbene complex **7** was unstable with regard to loss of a *cis*-carbonyl ligand and coordination of the *ortho*-methoxy group to chromium, the methoxy-ligated tetracarbonyl carbene complex **9** being formed in 60% yield simply by heating the pentacarbonyl precursor **7** at 100°C/10 mmHg for 15 min. Loss of a carbonyl ligand also occurred when a concentrated solution of **7** in pentane was allowed to stand at 4°C under nitrogen for several days. The new carbene complex **9** was characterised from its IR (2020, 1927, 1844 cm^{-1}), ^1H NMR (δ 4.20, OMe; 1.65, CH_3CH_2; 5.17 ppm, CH_3CH_2O), and mass spectra (m/z 716, 78%, cf. above).

The persistent appearance of compound **2** as a major by-product during formation of the carbene complex **7** could not be avoided, even after use of a variety of reaction conditions (Table 1). Since care was taken not to add an excess of the oxonium salt when alkylating the acyl metallate [13–15], compound **2** is thought to arise by deprotonation of the solvent by the aryllithium (**4**). The relatively slow reaction of this latter species with hexacarbonylchromium requires a temperature

TABLE 1

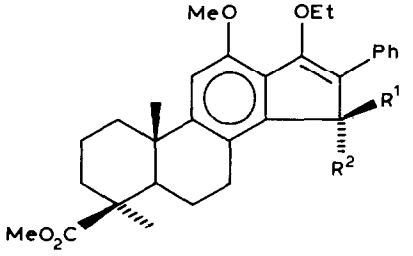
PREPARATION OF PENTACARBONYL[ETHOXY(METHYL 12-METHOXY-13-PODOCARPA-8,11,13-TRIEN-19-OATE)CARBENE]CHROMIUM(0) (7)

Reaction conditions							Products and yields (%) [a]		
Solvent	Alkyllithium	Temp./time (°C/min)	$Cr(CO)_6$	Temp./time (°C/h)	Alkylating agent	Time (h)	**7**	**9**	**2**
Et_2O	BuLi	r.t./90		r.t./3	Et_3OBF_4		17[b]	–	–
Et_2O	BuLi	−78/10		−78–r.t./2	Et_3OBF_4		40	5	50
Et_2O	BuLi	−78/10		−78–r.t./3	Et_3OBF_4		42	–	38
Et_2O	BuLi	−100/10		−100–r.t./6	Et_3OBF_4		28	–	33
THF	BuLi	−78/3		−78–r.t./1	Et_3OBF_4		47	3	43
THF	BuLi	−78/3	1.8 equiv.	−78/1.5 –r.t./2	Et_3OBF_4		39	–	43
THF	BuLi	−78/3		−78/0.5 –r.t./1	$MeOSO_2CF_3$	1.5	25[b]	3[c]	36
THF	t-BuLi (2 equiv.)	−78/70		−78/0.5 –r.t./3	$MeOSO_2CF_3$	3	0[d]		

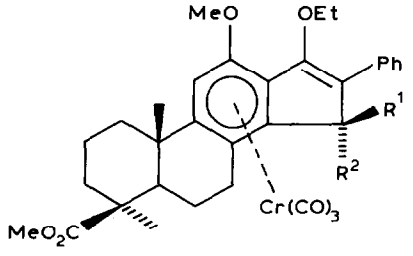
[a] Isolated yield from flash chromatography. [b] Structure of product **8**. [c] Structure of product **10**. [d] Products not separated after addition of alkylating agent failed to produce red colour of carbene complex.

higher than −78°C, which coincidentally allows the unwanted acid–base reaction to be competitive [cf. 16]. The use of methyl trifluoromethanesulfonate as alkylating agent [17] was only moderately successful, affording again the product **2** of reductive debromination (36%), the tetracarbonyl carbene complex **10** (2%), and the pentacarbonyl methoxycarbene complex **8** (25%), which was characterised from its ^{1}H and ^{13}C NMR, and mass spectra.

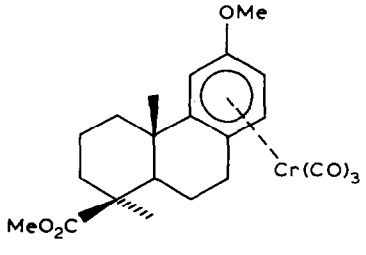
Reaction of the pentacarbonyl ethoxy carbene complex **7** with diphenylacetylene following the procedure of Dötz [6] gave a mixture of compounds including starting material (14%), its methoxy-ligated analogue **9** (11%), and four distinctly yellow oils; the IR spectra of each of these oils (1964–1950, 1882–1875 cm^{-1}) indicated an (η^6-arene)tricarbonylchromium structure. In order to assist their characterisation the aryl–chromium bond was cleaved in each of these products by photolysis in the presence of air. This resulted in the formation of sufficient material for the identification of two of the metal-free products as the ring-C aromatic compounds **12** (11%) and **13** (21%). Each of these tetracyclic products was characterised by accurate mass measurement of its molecular ion (*m/z* 536, 100%), and in the case of **13** by elemental analysis. Assignment of the position of the double bond in ring D was made by analogy with related work [6,18] in which the formation of derivatives of 3-alkoxy-1,2-diphenylindene has been determined by X-ray crystallography. The stereochemistry of the steroidal analogues **12** and **13**, and of their precursor $Cr(CO)_3$ complexes **14** and **15**, was assigned by comparison of their ^{1}H NMR chemical shift data (Table 2) with the spectra of the η^6-arene complexes **16** and **17**



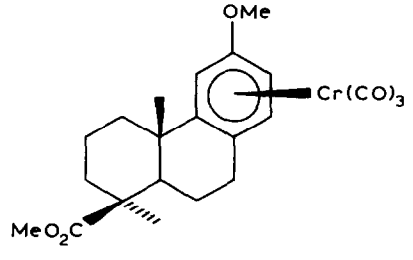
(**12**: R^1 = H, R^2 = Ph;
13: R^1 = Ph, R^2 = H)



(**14**: R^1 = H, R^2 = Ph;
15: R^1 = Ph, R^2 = H)



(**16**)



(**17**)

TABLE 2

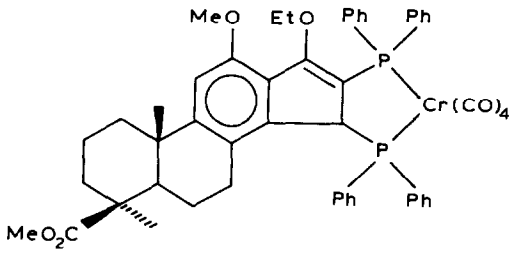
^{1}H NMR DATA ($\delta CDCl_3$) OF STEROID ANALOGUES **12** AND **13** AND RELATED COMPOUNDS

Compound	10-Me	H(11)	H(15)
2	1.27		
16	1.11	5.35	
17	1.25	5.65	
14	1.05	5.68	4.81
15	1.09	5.57	4.88
12	1.19	6.70	4.53
13	1.15	6.59	4.61

of established stereochemistry [19]. For the diastereoisomer **16** in which the $Cr(CO)_3$ group is α, the singlet due to the C(10) methyl group showed a significant shift upfield ($\Delta\delta$ 0.16 ppm) compared with the analogous resonance of methyl *O*-methylpodocarpate (2). In the β-diastereomer **17**, however, this signal was essentially unshifted ($\Delta\delta$ 0.02 ppm). The $Cr(CO)_3$-complexed steroidal products **14** and **15** displayed upfield shifts relative to that of the C(10) methyl resonance of **2** of $\Delta\delta$ 0.22 and 0.18 ppm, respectively. Hence, each product complex was an α-diastereomer. Moreover, the $\Delta\delta$ values for the resonances of H(11) (i.e. **12** vs. **14** and **13** vs. **15**) were identical (δ 1.02 ppm), indicating that the conformation of the $Cr(CO)_3$ tripod was the same in both **14** and **15**. With the bulky tricarbonylchromium group in the thermodynamically favoured α configuration it is probable that the major stereoisomer **13** is that with the C(15) phenyl group *trans* (i.e. β).

The formation of the steroid derivatives **12** and **13** in an overall cyclopentaannulation was an encouraging result. A potentially more useful steroid, however, would be one in which the phenyl substituents at C(15) and C(16) were absent. Formally, acetylene itself could lead to a steroidal ring-D, but the lack of a donor substituent on this alkyne tends to promote benzannulation at the expense of cyclopentaannulation. Accordingly, the diterpenoid carbene complex **7** was treated with ethoxyacetylene. With an excess of this alkyne [20] at room temperature, however, only starting carbene complex (33%) and polymerised ethoxyacetylene were recovered, while no reaction was observed at $-78°C$ with an equimolar amount of ethoxyacetylene. Warming this latter mixture and then refluxing in dichloromethane/heptane produced mainly the methoxy-ligated tetracarbonyl complex **9** (ca. 50%), and three minor unidentified fractions. Recent work [21,22] indicates that ethoxyacetylene reacts with carbene complexes derived from heterocycles to give moderate yields of benzannulation products.

The carbene complex **7** was treated also with bis(diphenylphosphino)acetylene, prepared by a modification of the method of Charrier et al. [23] (see Experimental), since this highly nucleophilic alkyne gives good yields (75–85%) of indene products on reaction with chromium carbene complexes derived from benzene [24]. However, both **7** and the simple analogue **6** gave mixtures containing many products. One product from the complex **7** was methyl *O*-methylpodocarpate (**2**) (30%), while another (7%) was provisionally assigned the structure **18** from its spectral characteristics. The IR spectrum showed bands at 2010, 1904, and 1888 cm^{-1}, and resembled



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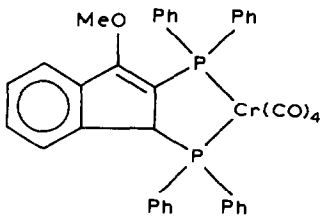


(19)

that of the chromacycle **19** (2014, 1930, and 1903 cm^{-1}). In the ^1H NMR spectrum a doublet (J 13 Hz) centred at δ 4.55 ppm was assigned to the ^{31}P-coupled proton at C(15) (cf. δ 4.64 ppm, J 13.7 Hz for the corresponding proton in **19**). Moreover, the aromatic region of the spectrum of **18** showed a singlet at δ 6.62 ppm, similar to that of H(11) (ca. 6.65 ppm) in the spectra of **12** and **13**. The mass spectrum of **18** did not show the required molecular ion, but did show a peak at m/z 804 corresponding to the loss of four carbonyl ligands from the molecular ion (m/z 916), and also confirmed the incorporation of the phosphine groups. A fragmentation pattern which accounts for the major peaks of the mass spectrum based on structure **18** is given in Scheme 3.

Experimental

IR spectra were recorded in $CDCl_3$ using a Perkin–Elmer 397 spectrophotometer, ^1H NMR spectra were recorded in $CDCl_3$ on a Varian T60 spectrometer, and low resolution mass spectra were determined on a Varian-MAT CH7 mass spectrometer operating at nominal 70 eV. High resolution mass spectra were recorded on an A.E.I. MS-30 spectrometer at a resolution of 3000. Noise-decoupled ^{13}C NMR spectra were measured in $CDCl_3$ at 15 MHz on a JEOL JNM-FX60 Fourier Transform NMR spectrometer.

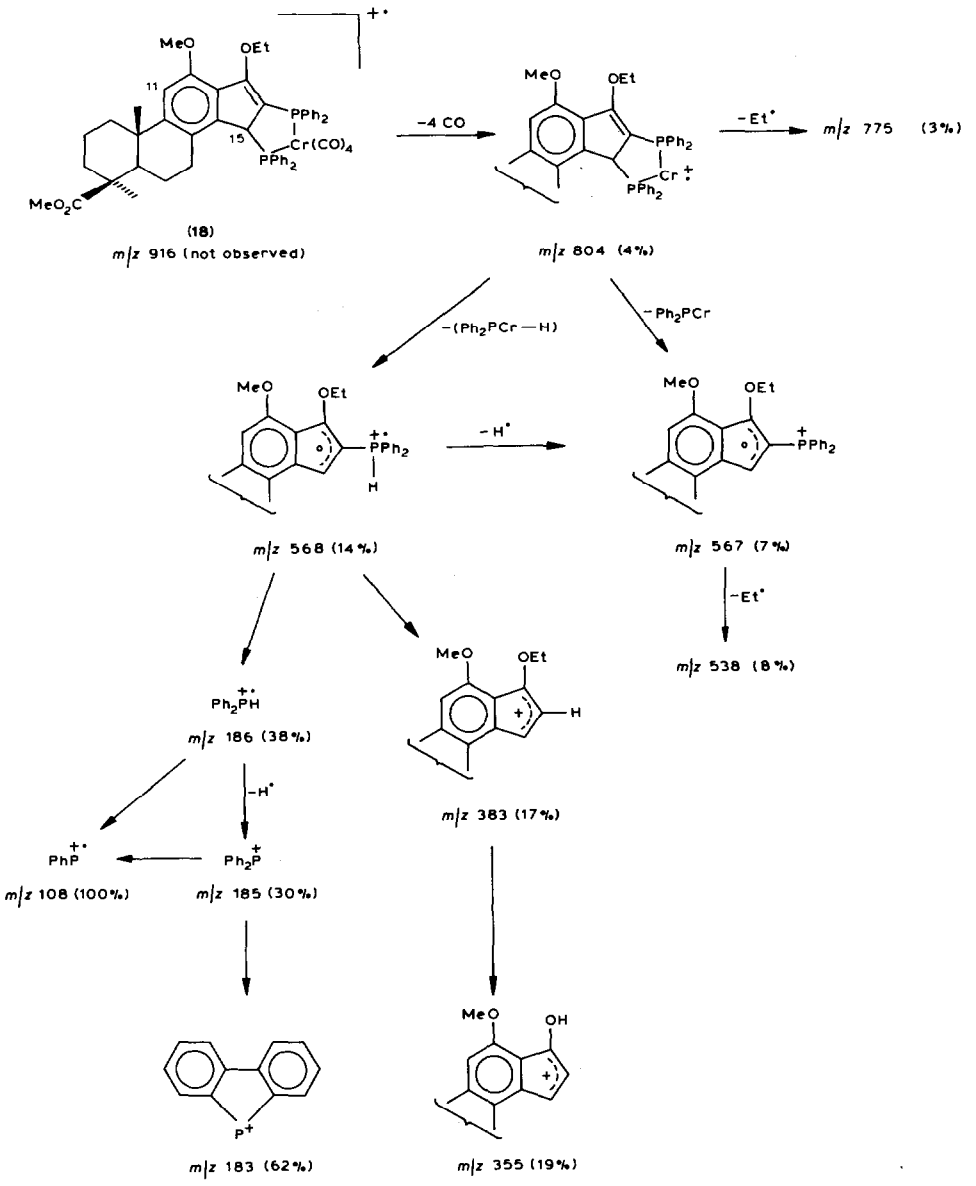
Dry ether and tetrahydrofuran (THF) were obtained by refluxing over and fractional distillation from sodium benzophenone ketyl under nitrogen. Dichloromethane and pentane were dried and purified by distillation from phosphorus pentoxide and stored over molecular sieves.

Reactions involving air- and moisture-sensitive reagents were carried out under an inert atmosphere (nitrogen or argon) in glassware dried overnight in an oven at 110°C. Solvents and solutions were added with a nitrogen-flushed syringe.

"Work-up" refers to the following generalised procedure. The reaction mixture was quenched with water, filtered if necessary, and extracted with water and brine, dried over magnesium sulphate or sodium sulphate, and the solvent removed by rotary evaporation.

Methyl 13-trimethylsilyl-12-methoxypodocarpa-8,11,13-trien-19-oate (5)

(a) Tetrahydrofuran as solvent. A solution of methyl 13-bromo-12-methoxypodocarpa-8,11,13-trien-19-oate (**3**) (0.50 g, 1.31 mmol) in THF (24 ml) under



SCHEME 3

nitrogen was cooled in an acetone/dry ice bath for 10 min, butyllithium (1.65 mol l^{-1} solution in hexanes, 1.0 ml, 1.65 mmol) was added dropwise over 1.5 min, and after 3 min an aliquot (6 ml) of the solution was transferred by syringe into a septum-capped nitrogen flushed flask precooled in an acetone/dry ice bath. Chlorotrimethylsilane (52 μl, 0.41 mmol) was added rapidly, the mixture stirred at $-78°C$ for 3 min, and the solution was warmed to room temperature over 1.5 h. Removal of the solvent yielded methyl 13-trimethylsilyl-12-methoxypodocarpa-8,11,13-trien-19-

oate which after PLC (pentane/dichloromethane, 1/1) gave a pure sample, m.p. 164–169°C (Found (Kugelrohr, b.p. 120–140°C, 0.1 mmHg): C, 70.8; H, 9.5. $C_{22}H_{34}O_3Si$ calcd.: C, 70.5; H, 9.15%). ν_{max} 1750 cm^{-1} (CO). δ(H) (ppm) 0.28, s, $SiMe_3$; 1.07, s, 3H(18); 1.29, s, 3H(20); 1.54–1.28, m, CH_2 and CH; 2.64–2.96, m, $H(7)_2$; 3.67, s, CO_2CH_3; 3.78, s, $ArOCH_3$; 6.72, s, H(11); 7.05, s, H(14). *m/z* 374(100, M^+), 329(44, $M^+ - 3^{\cdot}CH_3$), 73(54, $^+SiMe_3$), 59(23, CH_3OCO^+). Further aliquots (6 ml) were quenched after treatment of **3** with butyllithium for 10, 30, and 60 min. ^{1}H NMR spectral analyses showed that 76, 73, and 70% respectively of the isolated product was **5**.

(b) Diethyl ether as solvent. A solution of **3** (0.40 g, 1.05 mmol) in ether (18 ml) under nitrogen was cooled in an acetone/dry ice bath for 10 min, butyllithium (1.59 mol l^{-1} solution in hexane, 0.83 ml, 1.32 mmol) was added dropwise over 1.5 min, and after 10, 30, and 60 min aliquots (6 ml) were quenched with chlorotrimethylsilane (56 μl, 0.33 mmol) as above. The first sample was worked up and separated by PLC to yield (i) **5** (19 mg, 33%); (ii) **2** (13 mg, 22%); (iii) a mixture of colourless oils (13 mg, 22%); δ(H) (ppm) 0.24, s, $SiMe_3$; 1.04, s; 1.27, s; 1.38, s; 0.74–2.46, m; 2.67–2.94, m, benzylic CH_2; 3.66, s; 3.74, s; 6.67–7.14, m, ArH; (iv) a mixture of colourless oils (13 mg, 22%); δ(H) (ppm) 0.22, s, $SiMe_3$; 1.04 , s; 1.26, s; 1.38, s; 0.87–3.07, m, CH_2 and CH; 3.63, s; 3.74, s, $ArOCH_3$; 6.48–6.94, m, ArH.

Pentacarbonyl[ethoxy(methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate)carbene]chromium(0) (7)

A 3-necked flask containing the bromide **3** (0.40 g, 1.05 mmol) and fitted with a solid-addition side arm containing hexacarbonylchromium (0.29 g, 1.32 mmol) was evacuated and flushed 3 times with dry nitrogen, THF (15 ml) was added, and the solution was cooled in an acetone/dry ice bath. After 10 min, butyllithium (1.57 mol l^{-1} solution in hexane, 0.84 ml, 1.32 mmol) was added dropwise over 1.5 min to the stirred solution, and after a further 3 min the hexacarbonylchromium was transferred into the solution. After 1 h at −78°C the yellow solution was warmed to room temperature over 15 min, the solvent was removed under reduced pressure, and the yellow-brown residue was alkylated with triethyloxonium tetrafluoroborate (0.38 g, 1.5 mmol) in a mixture of degassed pentane (25 ml) and degassed water (5 ml). The pentane layer was combined with a pentane extract of the aqueous layer and passed quickly (vacuum) through a short column of Celite and magnesium sulphate. Removal of the solvent from the filtrate left a red oil which was separated by flash chromatography (hexane/dichloromethane, 3/1), yielding (i) pentacarbonyl[ethoxy(butyl)carbene]chromium(0) (**11**) (0.21 g) which rapidly decomposed to green chromium(III) by-products on exposure to air or in deuterochloroform solution; ν_{max} 2050(CO), 1985(CO), 1945 cm^{-1} (CO). δ(H) (ppm) 0.65–1.5, br, m; 1.65, t, *J* 7 Hz, OCH_2CH_3; 3.02–3.45, m, $W_{\frac{1}{2}}$ 18 Hz; 3.45–3.74, m, $W_{\frac{1}{2}}$ 12 Hz; 5.08, q, *J* 7 Hz, OCH_2CH_3; (ii) pentacarbonyl[ethoxy(methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate)carbene]chromium(0) (0.27 g, 47%) as a dark red oil; ν_{max} 2070 (CO), 1988(CO), 1948(CO), 1718 cm^{-1} (CO, methoxycarbonyl); δ(H) (ppm) 1.03, s, 3H(18); 1.28, s, 3H(20); 1.50, t, *J* 7 Hz, OCH_2CH_3; 1.3–2.47, m, CH_2 and CH; 2.58–3.00, m, 2H(7); 3.64, s, $COCH_3$; 3.71, s, $ArOCH_3$; 4.36, q, *J* 7Hz, OCH_2CH_3; 6.35, s, H(14); 6.64, s, H(11). δ(C) (ppm) 14.8, OCH_2CH_3; 20.0, C(2); 21.0, C(6); 22.9, C(20); 28.5, C(18); 31.3, C(7), 37.6, C(3); 38.9, C(10); 39.5, C(1); 44.0, C(4); 51.3, CO_2CH_3; 52.5, C(5); 55.2, $ArOCH_3$; 75.0, OCH_2CH_3; 107.5, C(11); 121.3,

C(14); 127.3, C(8); 139.4, C(13); 147.0, C(12); 149.4, C(9); 177.7, C(19); 216.2, (*cis*-CO); 225.3, (*trans*-CO); 353.0, carbene C; *m/z* at 150°C, $M^{+\cdot}$ not observed, 768(10,(dimer-**12** + Cr)$^+$), 716(54, $^+$dimer-**12**), 687(74, $^+$dimer-**12** − ·OMe), 329(100, $M^+ - (\cdot Cr(CO)_5 + \cdot Et)$); at 50°C, 374(55), 299(80), 52(100, Cr^+); (iii) a mixture, separated by PLC (pentane/dichloromethane, 3/1) into **2** (0.17 g, 43%) and *cis*-tetracarbonyl[ethoxy(methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate)carbene]chromium(0) (**9**) (19 mg, 3%) as an oil which slowly crystallised as violet flakes, dec. 145–150°C. ν_{max} 2020(CO), 1927(CO), 1844(CO), 1714 cm^{-1} (CO, methoxycarbonyl); δ(H) 1.02, s, 3H(18); 1.28, s, 3H(20); 1.65, t, *J* 7 Hz, OCH_2CH_3; 1.3–2.47, m, CH_2 and CH; 2.62–3.01, m, 2H(7); 3.68, s, CO_2CH_3; 4.20, s, $ArOCH_3$; 5.17, q, *J* 7 Hz, OCH_2CH_3; 6.79, s, H(11) and H(14); *m/z* at 200°C, no M^+, 716 (78, $^+$dimer-**12**), 687(40, $^+$dimer-**12** − ·OMe), 329(100, $M^+ - (\cdot Cr(CO)_5 + \cdot Et)$), 45(50, $^+$OEt).

*Pentacarbonyl[methoxy(methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate)carbene]chromium(0) (**8**)*

The bromide **3** (0.20 g, 0.52 mmol) was treated with butyllithium (1.85 mol l^{-1} solution in hexane, 0.28 ml, 0.52 mmol) and hexacarbonylchromium (0.17 g, 0.52 mmol) in THF (10 ml) as above. After 30 min at −78°C the solution was warmed to room temperature, and after 50 min methyl trifluoromethanesulfonate (65 μl, 0.58 mmol) was added dropwise. After 1.5 h the solvent was removed under reduced pressure and the resulting red oil separated by PLC (pentane/dichloromethane, 2/1) yielding (i) pentacarbonyl[methoxy(methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate)carbene]chromium(0) (R_f 0.73–0.63, 69 mg, 25%) as a red oil; δ(H) (ppm) 1.05, s, 3H(18); 1.27, s, 3H(20); 1.5–2.47, m, CH_2 and CH; 2.61–2.99, m, 2H(7); 3.68, s, CO_2CH_3; 3.75, s, $ArOCH_3$; 4.19, s, OCH_3; 6.45, s, H(14); 6.74, s, H(11). δ(C) (ppm) 19.9 C(2); 21.0, C(6); 22.8 C(20); 28.5, C(18); 31.0, C(7); 37.5, C(3); 38.9, C(10); 39.5, C(1); 44.1, C(4); 51.3, CO_2CH_3; 52.5, C(5); 55.3, $ArOCH_3$; 107.5, C(11); 121.7, C(14); 127.6, C(8); 147.0, C(12); 149.4, C(9); 177.5, C(19); 216.1, (*cis*-CO); 349.9, carbene C; OCH_3, C(13), *trans*-CO) not detected; *m/z* at 170°C, no M^+, 688 (100, $^+$dimer), 673(54, $^+$dimer − ·Me), 329(11, $M^+ - (\cdot Cr(CO)_5 + \cdot Me)$); at 50°C, 360 (70), 286(100), 52(85, Cr^+). This fraction contained a trace of *cis*-tetracarbonyl[methoxy(methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate)-carbene]chromium(0) (**10**) (2%); δ(H) (ppm) 4.85, s, $ArOCH_3$; (ii) methyl 12-methoxypodocarpa-8,11,13-trien-19-oate (**2**) (56 mg, 36%).

The ^{13}C NMR spectrum of the complex **8** changed on standing in $CDCl_3$ solution at 27°C. After 23 h δ(C) 19.9, C(2); 21.1, C(6); 22.9, C(20); 28.5, C(18); 31.3, C(7); 37.5, C(3); 38.8, C(10); 39.5, C(1); 51.3, CCO_2CH_3; 52.5, C(5); 53.9, $ArOCH_3$; 65.4, OCH_3; 107.8, C(11); 127.5, C(8); 132.3; 211.4; 216.0, (*cis*-CO). TLC analysis indicated the presence of the methoxy-ligated carbene complex **10** and two fractions of lower R_f, which on PLC (pentane/dichloromethane, 1/1) yielded unidentified colourless oils (7 and 8 mg).

*[4S-(4α,5β,10α,15ξ)]-1,2,3,4,5,6,7,10,15-Octahydro-17-ethoxy-4,10-dimethyl-4-methoxycarbonyl-15,16-diphenyl-1H-cyclopenta[a]phenanthrene (**12** and **13**)*

A mixture of the complex **7** (0.14 g, 0.25 mmol) and diphenylacetylene (52 mg, 0.29 mmol) in degassed heptane (3 ml) was heated under nitrogen at 76–80°C for 1 h; a yellow-brown oil separated after 15 min. Solvent was removed under reduced

pressure and the resulting solid (0.30 g) was separated by PLC (hexane/ethyl acetate, 5/1) to yield (i) diphenylacetylene (R_f 0.98–0.93, 20 mg, 0.11 mmol, 22% in addition to the excess); (ii) a red-yellow oil (R_f 0.68–0.64, 21 mg) containing the carbene complex **7** (10 mg, 7%); ν_{max} 2060(CO), 1988(CO), 1948(CO), 1718 cm^{-1} (CO, methoxycarbonyl); (iii) methoxy-ligated carbene complex **9** (R_f 0.59–0.48, 14 mg, 11%) as a yellow-brown oil; (iv) a yellow-orange oil (R_f 0.44–0.36, 14 mg); ν_{max} 1964(CO, $ArCr(CO)_3$), 1882(CO, $ArCr(CO)_3$), 1716 cm^{-1} (CO, methoxycarbonyl); (v) complex **14** as a yellow-orange oil (R_f 0.36–0.32, 21 mg); ν_{max} 1950(CO, $ArCr(CO)_3$), 1875(CO, $ArCr(CO)_3$), 1715 cm^{-1} (CO, methoxycarbonyl); δ(H) (ppm) 4.81, s; 5.68, s; (vi) complex **15** as a red-orange oil (R_f 0.31–0.26, 41 mg); ν_{max} 1950 (CO, $ArCr(CO)_3$), 1875(CO, $ArCr(CO)_3$), 1715 cm^{-1} (CO, methoxycarbonyl); δ(H) (ppm) 1.06, s, $H(4\beta)_3$; 1.27, s, $H(10\alpha)_3$; 1.36, t, J 7Hz, OCH_2CH_3; 1.1–2.8, CH_2, CH, and benzylic CH_2; 3.63, s, CO_2CH_3; 3.81, s, $ArOCH_3$; 4.09, q, J 7 Hz, OCH_2CH_3; 4.88, s, H(15); 5.57, s, H(11); 6.98–7.52, m, ArH; (vii) a yellow-orange oil (R_f 0.26–0.22, 25 mg); ν_{max} 1950(CO, $ArCr(CO)_3$), 1879(CO, $ArCr(CO)_3$), 1715(CO, methoxycarbonyl), 1697 cm^{-1} (CO).

Each of the four fractions containing an $ArCr(CO)_3$ group was separately dissolved in dichloromethane (5 ml) and exposed to bright sunlight or irradiated with a standard 60 W light bulb for 40 h while a stream of air was occasionally bubbled through the solutions. Separation of the main, highly fluorescent fraction from each of two colourless products by PLC (hexane/ethyl acetate, 5/1) yielded (i) from fraction (vi) [4*S*-(4α,5β,10α,15α)]-1,2,3,4,5,6,7,10,15-octahydro-17-ethoxy-4,10-dimethyl-4-methoxycarbonyl-15,16-diphenyl-1*H*-cyclopenta[*a*]phenanthrene (**13**) (R_f 0.72–0.64, 15 mg, 21% as tricarbonylchromium complex) as a pale yellow oil (Found: C, 80.3; H, 7.7; M^+ 536.2931. $C_{36}H_{40}O_4$ calcd.: C, 80.6; H, 7.5%; M, 536.2927). ν_{max} 1715 cm^{-1} (CO, methoxycarbonyl); δ(H) (ppm) 0.97, s, $H(4\beta)_3$; 1.15, s, $H(10\alpha)_3$; 1.30, t, J 7Hz, OCH_2CH_3; 1.2–2.8, m, CH_2, CH, and benzylic CH_2; 3.57, s, CO_2CH_3; 3.86, s, $ArOCH_3$; 4.13, m, $W_{\frac{1}{2}}$ 15 Hz, OCH_2CH_3 4.61, s, H(15); 6.59, s, H(11); 6.98, s, ArH; 7.28–7.51, m, $W_{\frac{1}{2}}$ 12 Hz, ArH; m/z 536(100, M^+), 507(26, $M^+ - {}^{\cdot}Et$), 325(10, $M^+ - PhCH{=}CHPh$); (ii) from fraction (v) [4*S*-(4α,5β,10α,15β)]-1,2,3,4,5,6,7,10,15-octahydro-17-ethoxy-4,10-dimethyl-4-methoxycarbonyl-15,16-diphenyl-1*H*-cyclopenta[*a*]phenanthrene (**12**) (R_f 0.72–0.64, 8 mg, 11% as tricarbonylchromium complex) as a pale yellow oil (Found: M^+ 536.2942. $C_{36}H_{40}O_4$ calcd.: M 536.2927); δ(H) (ppm) 0.99, s, $H(4\beta)_3$; 1.19, s, $H(10\alpha)_3$; 1.31, t, J 7 Hz, OCH_2CH_3; 1.2–2.8, m, CH_2, CH, and benzylic CH_2; 3.56, s, CO_2CH_3; 3.88, s, $ArOCH_3$; 4.1, m, $W_{\frac{1}{2}}$ 18 Hz, OCH_2CH_3; 4.53, s, H(15); 6.70, s, H(11); 7.03, s, ArH; 7.38–7.60, m, $W_{\frac{1}{2}}$ 12 Hz, ArH; m/z 536(100, M^+), 507(29, $M^+ - {}^{\cdot}Et$), 325(11, $M^+ - PhCH{=}CHPh$).

Reactions of pentacarbonyl[ethoxy(methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate)carbene]chromium(0) (7) with ethoxyacetylene

(a) With a twenty-fold excess of ethoxyacetylene. Ethoxyacetylene (0.52 ml, 5.9 mmol) was added dropwise over 1 min to a stirred solution of complex **7** (0.16 g, 0.30 mmol) in dichloromethane (2.5 ml) under nitrogen at room temperature. After 2 h further dichloromethane (5 ml) was added, a black solid (0.15 g) was filtered off, and the solvent was removed from the filtrate under reduced pressure leaving a red-brown oil. PLC (pentane/dichloromethane, 1/1) yielded (i) the complex **7** (R_f 0.93–0.79, 53 mg, 33%) as a red oil, identical ^1H NMR spectrum; (ii) a yellow oil

(R_f 0.68–0.57, 7 mg); (iii) a red-brown oil (extracted from baseline, 7 mg), ν_{max} 3005, 2960, 1718, 1605, and 1170 cm^{-1}.

(b) With equimolar portions of ethoxyacetylene. Ethoxyacetylene (9 μl, 0.10 mmol) was added to a stirred solution of the complex **7** (28 mg, 0.05 mmol) and the complex **9** (27 mg, 0.05 mmol) in heptane (5 ml) and dichloromethane (5 ml) at −78°C under nitrogen. After 10 min the solution warmed to room temperature over 0.5 h but spectral analysis (IR and ^1H NMR) showed only starting material was present. Further ethoxyacetylene (9 μl, 0.10 mmol) was added, and the solution was heated to reflux under argon. After 9 h the solvent was removed and the red-brown residue separated by PLC (pentane/dichloromethane, 1/2) to yield (i) the complex **9** (R_f 0.92–0.80, 33 mg, 60%) as a yellow-brown oil, identical ^1H NMR spectrum; (ii) three unidentified minor coloured fractions: a red-brown oil (R_f 0.80–0.76, 8 mg), a red-brown oil (R_f 0.76–0.68, 3 mg), and a red oil (R_f 0.68–0.56, 4 mg).

Bis(diphenylphosphino)acetylene

An oven-dried 3-necked flask fitted with a sintered glass gas inlet, a condenser and gas outlet, and a septum cap, and containing triphenylmethane (ca. 5 mg) as an anion indicator, was flushed with nitrogen; a slow flow of nitrogen was maintained throughout the reaction. THF (20 ml) was added and stirred to dissolve the triphenylmethane, and the colourless solution was cooled in an acetone/dry ice bath for 5 min. Addition of butyllithium (1.57 mol l^{-1} solution in hexanes, 6.4 ml, 10.1 mmol) failed to generate the red triphenylmethane anion colour. After 1 min acetylene (5.1 mmol required) was bubbled into the pale yellow solution, which faded to a slightly cloudy colourless solution over 5 min. Chlorodiphenylphosphine (1.88 ml, 10.1 mmol) was added dropwise and the mixture was warmed to room temperature. After 1.5 h the mixture was heated under reflux for 25 min. Work-up yielded a brown oil which was separated by column chromatography (hexane/ether, 100/1) yielding bis(diphenylphosphino)acetylene (0.59 g, 30%) as needles from ethanol, m.p. 85.5–86°C (lit. [22] m.p. 86°C); *m/z* 394(69, M^+), 209(100, $M^+ - {}^{\cdot}PPh_2$), 185(60, $^+PPh_2$), 77(18, ^+Ph).

Reactions of pentacarbonyl[ethoxy(methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate)carbene]chromium(0) (7) with bis(diphenylphosphino)acetylene

(a) In refluxing heptane. A solution of the complex **7** (0.15 g, 0.27 mmol) in degassed heptane (8 ml) was added to bis(diphenylphosphino)acetylene (0.13 g, 0.33 mmol) and the mixture was heated to reflux under nitrogen. After 4 h the solvent was removed under reduced pressure leaving a mixture of yellow and brown solids (0.31 g) which was separated by PLC (pentane/dichloromethane, 1/1) into (i) bis(diphenylphosphino)acetylene (R_f 0.97–0.90, 18 mg, 0.04 mmol, recovered excess); (ii) methyl 12-methoxy-13-podocarpa-8,11,13-trien-19-oate (**2**) (R_f 0.58–0.48, 25 mg, 30%), identical IR and ^1H NMR spectra; (iii) the chromacycle **18** as a yellow oil (R_f 0.42–0.36, 19 mg); ν_{max} 2010(CO), 1904(CO), 1880(CO), 1708 cm^{-1} (CO, methoxycarbonyl); δ(H) (ppm) 3.58, s, CO_2CH_3; 3.62, s, CO_2CH_3; 3.68, s, $ArOCH_3$; 3.72, s, $ArOCH_3$; 4.55, d, *J* 13 Hz; 6.62, s; 6.95–7.80, m, $W_{\frac{1}{2}}$ 32 Hz, ArH; *m/z* no M^+, 804(4, $M^+ - 4CO$), 775(3, $M^+ - (4CO + {}^{\cdot}Et)$), 568(14, $M^+ - 4CO - (Ph_2PCr-H)$), 567(7, $M^+ - (4CO + Ph_2PCr)$), 383(17, (142)–Ph_2P.), 186(38, Ph_2PH^+), 185(30, Ph_2P^+), 183(62), 108(100, PhP^+); (iv) a yellow oil (R_f 0.36–0.30, 16 mg); ν_{max}

2010(CO), 1915(CO), 1895(CO), 1713 cm^{-1} (CO, methoxycarbonyl); (v) a yellow oil (R_f 0.30–0.15, 76 mg); ν_{max} 2010(CO), 1960(CO), 1868(CO), 1710 cm^{-1} (CO, methoxycarbonyl); further purified by PLC (pentane/dichloromethane, 3/7) yielding (as 1 of 9 fractions) a yellow oil (R_f 0.70–0.45, 41 mg); δ(H) (ppm) 5.55, d, J 7Hz; (vi) a yellow oil (R_f 0.06–0.03, 41 mg); ν_{max} 2020(CO), 1960(CO), 1895(CO), 1715 cm^{-1} (CO), methoxycarbonyl); separated by PLC (pentane/dichloromethane, 3/7) yielding 9 fractions, not further investigated.

(b) In refluxing pentane. A solution of the complex **7** (0.12 g, 0.22 mmol) in pentane (6 ml) was added to bis(diphenylphosphino)acetylene (86 mg, 0.22 mmol) and the mixture heated to reflux under nitrogen. After 7.5 h the solvent was removed leaving a mixture of yellow and brown oils that was separated by PLC (pentane/dichloromethane, 1/1) yielding (i) bis(diphenylphosphino)acetylene (R_f 0.96–0.88, 39 mg, 45%); (ii) a mixture of at least 25 fractions (R_f 0.77–0.05), some of which were unstable to oxidation, yielding green and yellow by-products after several hours exposure to air.

Reaction of pentacarbonyl[ethoxy(2-methoxyphenyl)carbene]chromium(0) (6) with bis(diphenylphosphino)acetylene

A solution of the complex **6** (0.14 g, 0.40 mmol) in pentane (5 ml) was added to bis(diphenylphosphino)acetylene (0.16 g, 0.40 mmol) under nitrogen, the mixture was heated to reflux for 4 h, and the solvent was removed under reduced pressure leaving a brown oil. PLC (pentane/dichloromethane, 4/1) yielded (i) a colourless oil (R_f 0.89–0.81, 13 mg); (ii) complex **6** (R_f 0.73–0.61, 55 mg, 39%) as a red oil; (iii) bis(diphenylphosphino)acetylene (R_f 0.61–0.44, 70 mg, 45%); (iv) a red oil (R_f 0.35–0.10, 0.13 g); ν_{max} 2020(CO), 1909(CO), 1845 cm^{-1} (CO); further separated by PLC (pentane/dichloromethane, 3/2), yielding (as 1 of 7 fractions) a red oil (R_f 0.86–0.63, 43 mg); ν_{max} 2020(CO), 1915(CO), 1844 cm^{-1} (CO); (v) an orange-brown oil (R_f 0.09–0.03, 0.11 g); ν_{max} 2015(CO), 1940(CO), 1902(CO), 1804 cm^{-1} (CO); further separated by PLC (pentane/dichloromethane, 3/2), yielding (as 1 of 10 fractions) an orange-brown oil (R_f 0.67–0.85, 5 mg); ν_{max} 1941(CO), 1877(CO), 1808 cm^{-1} (CO).

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