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Synthesis of diterpenoid indole derivatives via tethered chromium alkynylaminocarbenes

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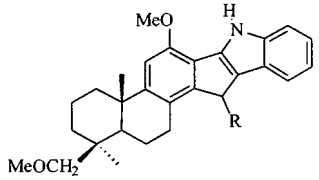
Abstract

Thermolysis of podocarpane-tethered chromiumalkynylaminocarbenes gives indole derivatives in moderate yields. (Arylalkynyl)aminocarbenes could not be isolated. Ester derivatives were formed due to trapping of the intermediate ketene in situ with butan-1-ol.

Keywords: Chromium; Alkynylaminocarbenes; Diterpenoid; Indole

1. Introduction

A variety of fused nitrogen heterocycles have been synthesised from tethered alkynyl aminocarbenes by insertion of an alkyne intramolecularly [1–9]. For example, thermolysis of a wide range of vinyl and aryl 2-alkynylanilinocarbene chromium complexes gives 9*H*-carbazoles and 11*H*-benzo[*a*]carbazoles [3–5]. The presence of the indole ring system in a wide variety of biologically active molecules led us to investigate the synthesis and reactions of some diterpenoid alkynylanilinocarbene chromium complexes, as a potential route to indenoindole **1** and naphthoindole **2** derivatives containing six fused rings.



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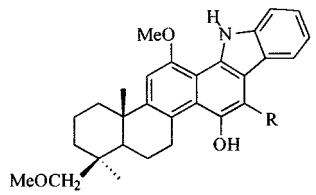
2. Results and discussion

The aminocarbene complexes were synthesised by reaction of a podocarpane acyloxycarbene with a range of functionalised 2-alkynylaniline derivatives, themselves prepared by the palladium-catalysed coupling of a terminal alkyne (RC≡CH; R = H, $SiMe_3$, phenyl, *t*-butyl, pentyl, pyridinyl, ferrocenyl) with 2-iodoaniline. Although most Sonogashira reactions [10–12] involving aryl iodides can be carried out at room temperature, substrates possessing an electron donating group *ortho* to the halide undergo oxidative addition more slowly and consequently benefit from a slightly elevated reaction temperature [13]. The coupling reactions were therefore performed by reacting 2-iodoaniline with the alkyne in the presence of $Pd(PPh_3)_2Cl_2$ and CuI, in either diethylamine or triethylamine at ca. 40°C. 2-Ethynylaniline (**3**) was synthesised by desilylation (KOH–MeOH/H_2O, 72%) [14] of 2-(trimethylsilylethynyl)aniline (**4**) (from 2-iodoaniline and trimethylsilylethyne, diethylamine, 30°C, 76%) [15]). Reaction of 2-iodoaniline with phenylethyne in triethylamine at 40°C gave 2-(phenylethynyl)aniline (**5**) (94%) [16]. The coupling of 3,3-dimethylbutyne with 2-iodoaniline using CuI (1 mol%) and $Pd(PPh_3)_2Cl_2$ (2 mol%) was performed at room temperature due to the low



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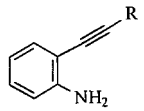
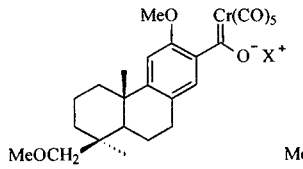
boiling point (37–38°C) of this alkyne. Although this reaction required 48 h, as well as the addition of further CuI (11 mol%) after 24 h, it afforded 2-(3′,3′-dimethylbutynyl)aniline (**6**) in high yield (95%). 2-(Hept-1-yl)aniline (**7**) was synthesised (98%) by the Pd–Cu(I) mediated coupling of 2-iodoaniline with hept-1-yne in diethylamine at 30°C. Treatment of ethynylferrocene [17] with 2-iodoaniline using standard Sonogashira conditions in diethylamine at 30°C for 18.5 h afforded only starting material. However, the use of a higher molar ratio of CuI (23 mol%) and increasing the reaction temperature to 60°C gave 2-(ferrocenyl)ethynylaniline (**8**) (99%) after 24 h. In contrast, coupling of 2-ethynylpyridine (from 2-bromopyridine and trimethylsilylethyne, 91% [18]) with 2-iodoaniline using Sonogashira conditions to give 2-(2′-pyridyl)-ethynylaniline (**9**) was more efficient at room temperature (45 h; 65%) than at 40°C (34%).



3: R = H **7**: R = pentyl
4: R = $SiMe_3$ **8**: R = ferrocenyl
5: R = Ph **9**: R = 2-pyridinyl
6: R = tBu

The 2-alkynylaniline derivatives were then reacted with a podocarpane chromium acetyloxycarbene to give the anilinocarbene complexes. The diterpenoid acetyloxycarbenes were synthesised by in situ acetylation of the corresponding tetraalkylammonium complex. The procedure used for synthesis of the acylate complex was based on literature methods [19,20], although some modifications were introduced. Thus, addition of 13-lithio-12,19-dimethoxypodocarpa-8,11,13-triene to $Cr(CO)_6$ gave the lithium acylate **10**. An aqueous solution of benzyltriethylammonium chloride was added to an aqueous solution of **10** to give water-insoluble benzyltriethylammonium pentacarbonyl[(oxo)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**11**) (78%). Tetraalkylammonium salts exhibit a strong β-shielding effect [21]; the ^{13}C-NMR spectrum of **11** showed the signal due to the triethylammonium methyl group (β to nitrogen) at 8.1 ppm, and the benzyl methylene signal was broad due to coupling with the ^{14}N nucleus.

Addition of a solution of acetyl bromide (1.05 molar equivalents) to a solution of the salt **11** gave the red–purple acetyloxycarbene complex **12**. Since acyloxycarbenes are sensitive to heat, moisture, air, and light, the acetylation was performed at −20°C in flame-dried, foil-covered flasks. The anilinocarbenes were then synthesised by adding a solution of a 2-(alkynyl)aniline and triethylamine directly to a solution of the acetyloxycarbene at −78°C. Thus, addition of 2-(trimethylsilylethynyl)aniline (**4**) (1.07 molar equivalents) and Et_3N (1.14 molar equivalents) to a solution of the acetyloxycarbene **12** followed by chromatography on silica gel gave pentacarbonyl[(2-(trimethylsilyl)ethynyl)-(13 - (12,19 - dimethoxypodocarpa - 8,11,13 - triene))-carbene]chromium (**13**) (84%) as a stable yellow–orange foam. ^{1}H-NMR analysis indicated that **13** was a mixture (1.75:1) of *E* and *Z* isomers (NH_E, 10.89 ppm; NH_Z, 10.06 ppm) [4]. In the ^{13}C-NMR spectrum, signals due to alkynyl carbons were observed at 98.8 (C≡*C*$SiMe_3$) and 103.8 ppm (*C*≡C$SiMe_3$), and those due to the carbene carbon at 289.0 and 289.1 ppm. Similarly, pentacarbonyl[(2-(ethynyl)aniline)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**14**) was synthesised (67%) by aminolysis of **12** with 2-ethynylaniline (**3**) (1.03 molar equivalents). Anilinocarbene **14** existed as a mixture (1.9:1) of *E* and *Z* isomers (NH_E, 10.89 ppm; NH_Z, 10.06 ppm).



10: X = Li **12**
11: X = $BzEt_3N$

Addition of 2-(1,1-dimethylbutynyl)aniline (**6**) (1.02 molar equivalents) to **12** in the presence of Et_3N (1.11 molar equivalents) gave pentacarbonyl[(2-(1,1-dimethylbutynyl)aniline))(13 - (12,19 - dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**15**) (77%) as a mixture (5:1) of *E* and *Z* isomers (NH_E, 10.81 ppm; NH_Z, 10.01 ppm). In the ^{13}C-NMR spectrum signals due to alkynyl carbons were observed at 73.8 (C≡*C*t-Bu), and 93.9 ppm (*C*≡Ct-Bu) while a signal at 287.4 ppm was characteristic of a carbene carbon.

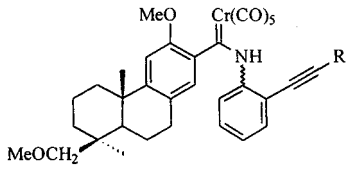
Reaction of 2-(heptyn-1-yl)aniline (**7**) (1.00 molar equivalent) with **12** in the presence of Et_3N (1.13 molar equivalents) gave pentacarbonyl[(2-(heptyn-1-yl)aniline)(13 - (12,19 - dimethoxypodocarpa - 8,11,13 - triene))-carbene]chromium (**16**) (64%) as a relatively unstable orange oil. The infrared spectrum showed absorptions characteristic of carbonyl ligands at 2054, 1977 and 1931 cm^{-1}, but attempts to obtain NMR spectra in either $CDCl_3$ or C_6D_6 led to rapid decomposition of this (2-alkylethynyl)anilinocarbene complex. Furthermore, all attempts to isolate the analogous (2-arylethynyl)aminocarbenes **17**–**19** were unsuccessful, and decomposition of these anilinocarbenes either in

Table 1
Indole ^{1}H-NMR signals for the silyl derivative **20**

Hydrogen	Signal (δ ppm; coupling constant Hz)
H(4)	7.66 (bd, $J = 7.7$ Hz); 7.80 (bd, $J = 8.0$ Hz)
H(5)	7.06 (td, $J = 8.1$, 1.1 Hz); 7.11 (td, $J = 8.1$ Hz)
H(6)	7.13 (td, $J = 8.2$, 1.2 Hz); 7.18 (td, $J = 8.1$, 1.2 Hz)
H(7)	7.29 (bd, $J = 8.0$ Hz); 7.35 (bd, $J = 7.7$ Hz)

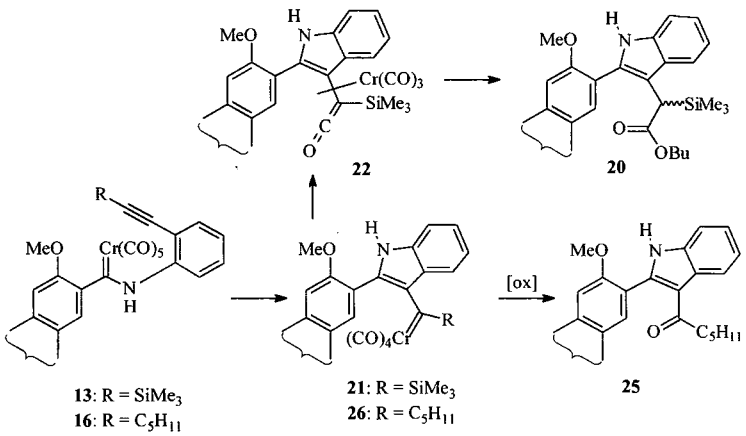
solution or during chromatography meant that they had to be thermolysed (see below) without prior isolation. There are reported examples of stable tethered (arylalkynyl)aminocarbenes [4,5,8,9]. A (phenylalkynyl)aminocarbene having a propyl spacer between the aminocarbene nitrogen and the alkyne is stable while the corresponding compound with an ethyl spacer is not; interestingly, both of the related (trimethylsilyl)-alkynyl derivatives are stable [6]. Phenylethyne polymerises more readily than trimethylsilylethyne, and so polymerisation of the phenylethynyl group in the anilinocarbene may cause gross decomposition of the carbene. However, this does not explain why one of the phenylalkynyl aminocarbenes synthesised by Wulff [6] is unstable while the other one is stable. The reason for the instability of the (arylalkynyl)aminocarbenes in the present work remains unknown.

Although tetrahydrofuran, acetonitrile, *t*-butyl methyl ether or hexane have been used as the solvent in thermolysis studies of aminocarbenes [3], dibutyl ether or toluene are most commonly employed. However, the yields of indole derivatives are generally higher when dibutyl ether is used instead of toluene as the solvent for thermolysis of (alkynyl)aminocarbenes, the superiority of dibutyl ether being significant when the products are indolylketenes [4]. Heating the diterpenoid trimethylsilyl anilinocarbene derivative **13** in dibutyl ether at 85°C for 1.5 h under a stream of nitrogen followed by aerial oxidation of the chromium-containing products gave butyl 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene]-α-(trimethylsilyl)-1*H*-indole-3-acetate (**20**) (14%). Accurate measurement of the molecular ion ($M^{+\bullet}$ 589.3580) in the mass spectrum supported the molecular formula $C_{36}H_{51}NO_4Si$. A broad absorption centred at 3369 cm^{-1} corresponding to the indole N–H stretching vibration, and an intense peak at 1730 cm^{-1} indicative of an ester carbonyl group, were observed in the infrared spectrum. The ester was a mixture (1:1) of epimers; atoms which are close to the new stereogenic centre showed different NMR chemical shifts for each epimer ($\delta_{C=O}$ 172.4, 173.9 ppm; δ_{CH} 36.5(8), 36.6(4); δ_{CH} 3.79(6), 3.80(4) ppm). Each of the indolyl aromatic protons also showed a different chemical shift for each epimer in the ^{1}H-NMR spectrum (Table 1).



13: R = $SiMe_3$
14: R = H
15: R = tBu
16: R = pentyl
17: R = Ph
18: R = ferrocenyl
19: R = 2-pyridinyl

Formation of the butyl ester **20** instead of its parent carboxylic acid was unexpected. Although the dibutyl ether had been distilled from calcium hydride under nitrogen immediately before use, GLC analysis of the distillate indicated that some butan-1-ol was present; although only in trace amount, it corresponded to 10 molar equivalents relative to the diterpenoid anilinocarbene. A route to the ester is included in Scheme 1. Insertion of the alkyne into the carbene gives the indenoyl carbene **21**, which undergoes insertion of car-

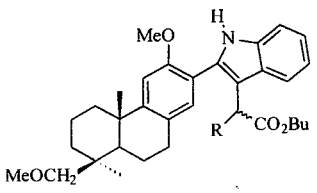


13: R = $SiMe_3$
16: R = C_5H_{11}
21: R = $SiMe_3$
26: R = C_5H_{11}

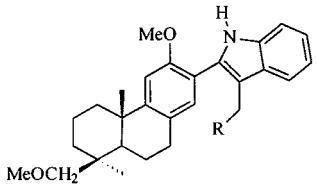
Scheme 1.

bon monoxide to afford ketene **22**; nucleophilic attack by butan-1-ol then gives **20**. Interestingly, this reaction showed no stereofacial selectivity, both epimers of the product being isolated in equal amounts.

Heating a solution of the *t*-butylethynyl anilinocarbene **15** in dibutyl ether at 85°C gave a low yield of a product assigned as butyl 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(1,1-dimethylethyl]-1*H*-indole-3-acetate (**23**) by high resolution mass spectroscopy ($M^{+\bullet}$ 573.3813, $C_{37}H_{51}NO_4$), the base peak at m/z 516 being consistent with loss of $C_4H_9^{\bullet}$ from the molecular ion. Repeated attempts to purify this compound, either by PLC (silica gel; hexanes–ether, 1:1) or by using analytical TLC plates (hexanes–ether, 2:1) failed to give material which was sufficiently pure for NMR analysis. It is suspected that hydrolysis of the butyl ester **23** led to the carboxylic acid and then to other decarboxylation-derived products. Thermolysis of **15** in toluene at 85°C for 2 h was a cleaner but still low yielding reaction, affording 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(1,1-dimethylethyl)-1*H*-indole-3-acetic acid (**24**) (17%), also as a mixture (1:1) of epimers. The elemental composition ($C_{33}H_{43}NO_4$) of the molecular ion was confirmed by mass spectroscopy ($M^{+\bullet}$ 517.3191), the base peak at m/z 460 resulting from the loss of a *t*-butyl radical from the molecular ion. Signals at 175.0 and 175.2 ppm in the ^{13}C-NMR spectrum confirmed the presence of a carboxylic acid.



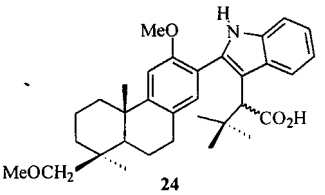
20: R = $SiMe_3$
23: R = tBu
31: R = Ph
33: R = ferrocenyl
35: R = 2-pyridinyl



30: R = Ph
32: R = ferrocenyl
34: R = 2-pyridinyl

Thermolysis of the (pentylethynyl)anilinocarbene **16** in dibutyl ether gave 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-3-(hexan-1-one)-1*H*-indole (**25**) (44%); products derived from addition of either butan-1-ol (to give an ester) or water (to give an acid) to an intermediate ketene were not detected. High resolution mass spectroscopy gave the molecular ion at m/z 501.3256 ($C_{33}H_{43}NO_3$), loss of a pentyl radical from the molecular ion yielding a resonance-stabilised indoloyl cation (m/z 430, 62%). A signal at 210.3 ppm in the ^{13}C-NMR spectrum and an intense absorption at 1667 cm^{-1} in the infrared spectrum confirmed the presence of an arylalkyl ketone. The signal due to the indolyl proton H(4) was shifted downfield (8.35 ppm) in the ^{1}H-NMR spectrum due to deshielding by the proximal carbonyl group. Assignment of the carbon signals due to the indolyl group was made using the ^{13}C–^{1}H correlation spectrum. A plausible mechanism for the formation of the pentyl ketone **25** is included in Scheme 1. Insertion of the alkyne into the chromium–carbene bond gives the indolyl carbene **26**, oxidation of which gives **25**.

Thermolysis of the (ethynyl)anilinocarbene **14** gave 2-(13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene))-3-(pentan-2-one)-1*H*-indole (**27**) (7%). The structure of **27** was indicated in the mass spectrum by the molecular ion ($M^{+\bullet}$ 487.3083, $C_{32}H_{41}NO_3$) and by the base peak at m/z 416, which arose from loss of $CH_3CH_2CH_2CO^{\bullet}$. Although an indolylcarbonyl structure was considered, the spectral data were significantly different from that of the 3-(hexan-1-one)-1*H*-indole derivative **25**. For example, while H(4) was deshielded significantly in **25** (8.35 ppm), the signal at 7.50 ppm due to H(4) in the ^{1}H-NMR spectrum of the 3-(pentan-2-one) derivative indicated that the carbonyl group in **27** was not close spatially to H(4). The singlet at 3.83 ppm was assigned to the methylene group bonded to the carbonyl group and the C(3) indolyl carbon. ^{13}C-NMR spectral data ($\delta_{CO} = 210$ ppm) also indicated that **27** was a dialkyl ketone rather than an alkylaryl ketone ($\delta \approx 199$ ppm).



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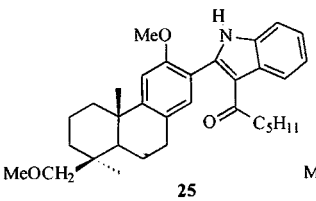

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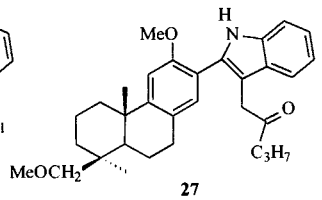
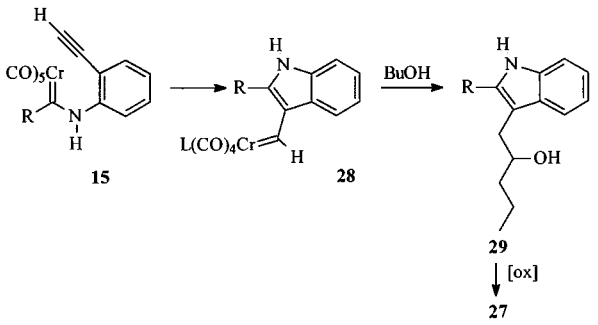


27

The intermediate in the formation of **27** is presumed to be a 3-indolyl chromium hydridocarbene. Analogous tungsten hydridocarbenes are known to react with either tetrahydrofuran or diethyl ether to give products corresponding to the insertion of the arylidene ligand into the α-CH bond of these ethereal solvents [22]. By analogy, a feasible pathway (Scheme 2) for formation of the 3-(pentan-2-one)-1*H*-indole **27** involves insertion of the alkyne into the chromium–carbene bond to give an indolyl chromium hydridocarbene **28** which inserts into the α-CH bond of butan-1-ol to give the secondary alcohol **29**, oxidation of which affords ketone **27**.

As mentioned above, the anilinocarbenes **17**, **18**, and **19** having, respectively, a phenyl, ferrocenyl, or pyridyl



Scheme 2.

substituent on the alkyne terminus had to be synthesised and thermolysed without isolation. Reaction of the acetyloxycarbene **12** with the appropriate 2-alkynylaniline and triethylamine gave the corresponding anilinocarbene. The solvent was removed in vacuo and replaced with dibutyl ether; heating at 85°C then gave the indole derivatives. Thus, thermolysis of the phenyl anilinocarbene **17** gave 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-3-benzyl-1*H*-indole (**30**) (7%) and butyl 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-phenyl-1*H*-indole-3-acetate (**31**) (7.5%). The ^{1}H-NMR spectrum of the benzyl derivative **30** included an AB coupled system, doublets at 4.20 and 4.25 ppm ($J = 16.7$ Hz) being consistent with the presence of the diastereotopic benzylic methylene hydrogens. The two outer wings of this pair of doublets had almost zero intensity, reflecting the low ratio for the difference in chemical shifts to the coupling constant ($\Delta\nu/J = 1.20$). These doublets correlated with the signal due to a CH_2 group at 31.0 ppm in the ^{13}C-NMR spectrum. Full structural assignment was made using COSY, ^{13}C–^{1}H and long-range ^{13}C–^{1}H spectra. Loss of a phenyl radical from the molecular ion ($M^{+\bullet}$ 493.2987) gave a weak fragment peak at m/z 416 in the mass spectrum. The butyl ester **31** was isolated as a mixture (4:5) of epimers, the methine α hydrogens giving rise to singlets at 5.33(0) and 5.33(5) ppm in the ^{1}H-NMR spectrum. Separate signals (8.52, 8.54 ppm) were also observed for NH, while two of the signals of the butyl group showed small differences in chemical shift for each epimer. A resonance at 173.3 ppm in the ^{13}C-NMR spectrum and a strong absorption at 1729 cm^{-1} in the infrared spectrum confirmed the presence of the ester carbonyl group. Mass spectroscopy showed the molecular formula to be $C_{39}H_{47}NO_4$ ($M^{+\bullet}$ 593.3501), the base peak at m/z 493 corresponding to the loss of $BuOCO^{\bullet}$ from the molecular ion.

The ferrocenylalkynyl anilinocarbene **18** was synthesised by the aminolysis of the acetyloxycarbene **12** with 2-(ferrocenylethynyl)aniline (**8**). Thermolysis of **18** in dibutyl ether at 85°C gave 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(ferrocenylmethyl)-1*H*-indole (**32**) (8%) and butyl 2-[13′-(12′,19′-dimethoxypodocarpa - 8′,11′,13′ - triene)] - α - (ferrocenyl) - 1*H*-indole-3-acetate (**33**) (16%), whose structures followed from their spectroscopic data.

The pyridinylalkynyl anilinocarbene **19** was synthesised by aminolysis of **12** with 2-(2′-pyridyl)ethynylaniline (**9**). TLC analysis indicated that **19** was highly unstable, some decomposition being detected in situ. Not unexpectedly, therefore, low yields resulted from thermolysis of this anilinocarbene in dibutyl ether at 85°C; 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(2-pyridylmethyl)-1H-indole (**34**) (3%) and butyl 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(2-pyridyl)-1H-indole-3-acetate (**35**) (3%) were recovered as an inseparable mixture.

Indenoindole **1** and carbazole **2** products were not isolated from the present reactions. The electrocyclic ring closure leading to these hexacyclic compounds requires a transition state in which the ketene and indole groups are essentially coplanar [4,5], a conformation which is apparently unable to be attained in the podocarpane derivatives due to steric encumbrance. Thermolysis of the isolated diterpenoid-tethered alkynylaminocarbenes gave indole derivatives in low yields, while direct thermolysis of the (arylalkynyl)aminocarbenes without isolation was characterised by the formation of more than one heterocyclic product. The low yield of indoles is attributed to the steric bulk around the carbene moiety, precluding efficient insertion of an alkyne [5]. Nevertheless, the large number of carbon–carbon bonds formed combined with the increase in synthetic complexity offsets the low yields of the indole products obtained.

3. Experimental

3.1. 2-(Trimethylsilylethynyl)aniline (4)

A mixture of 2-iodoaniline (3.303 g, 15.08 mmol), trimethylsilylethyne (2.60 ml, 18.40 mmol), CuI (15 mg, 0.079 mmol) and $PdCl_2(PPh_3)_2$ (0.216 g, 0.308 mmol) in Et_2NH (40 ml) was heated to 30°C under nitrogen in a sealed pressure vessel for 41 h. The solvent was removed in vacuo, the residue was extracted into Et_2O, and the organic layer was washed with water and dried ($MgSO_4$). Column chromatography (hexanes–Et_2O, 9:1) gave 2-(trimethylsilylethynyl)aniline (**4**) (2.156 g, 76%) [15] as a pale yellow oil. IR (cm^{-1}): ν_{max} 3479 (NH), 3384 (NH), 2959 ($CH_{aliphatic}$), 2147 (C≡C), 1614 (C=C), 1250 (C–Si), 843 (C–Si). ^{1}H-NMR: δ 0.26 (s, $Si(CH_3)_3$), 4.20 (bs, NH_2), 6.69 (td, $J = 7.8$, 1.1 Hz, H(4)), 6.72, (d, $J = 7.8$ Hz, H(6)), 7.15 (td, $J = 7.8$, 1.6 Hz, H(5)), 7.31 (dd, $J = 7.8$, 1.7 Hz, H(3)). ^{13}C-NMR: δ

0.11 ($Si(CH_3)_3$), 99.7 ($C{\equiv}CSiMe_3$), 101.8 ($C{\equiv}CSiMe_3$), 107.7 (C(2)), 114.1 (C(6)), 117.7 (C(4)), 129.8 (C(5)), 132.2 (C(3)), 148.2 (C(1)).

3.2. 2-(Ethynyl)aniline (3)

A solution of KOH (0.403 g, 7.18 mmol) in water (5 ml) was added to a solution of 2-(trimethylsilylethynyl)aniline (**4**) (0.835 g, 4.41 mmol) in MeOH (10 ml) and then stirred at room temperature (r.t.) for 3 h. The solvent was removed in vacuo and the residue was extracted into CH_2Cl_2, washed with water and dried ($MgSO_4$). The crude product was distilled, b.p. 90°C/10 mmHg (Kugelrohr) (lit. b.p. [23] 98–100°C/12 mmHg), to give 2-(ethynyl)aniline (**3**) (0.372 g, 72%) as a colourless oil. IR (cm^{-1}): ν_{max} 3471 (NH), 3387 (NH), 3279 ($CH_{alkynyl}$), 3075 (CH_{aryl}), 3030 (CH_{aryl}), 2096 (C≡C), 1614 (C=C), 751 (CH). ^{1}H-NMR: δ 3.38 (s, C≡CH), 4.23 (bs, NH_2), 6.67 (t, $J = 7.8$ Hz, H(4)), 6.69 (d, $J = 7.8$ Hz, H(6)), 7.14 (td, $J = 7.8$, 1.5 Hz, H(5)), 7.30 (dd, $J = 7.8$, 1.5 Hz, H(3)). ^{13}C-NMR: δ 80.6 (*C*≡CH), 82.4 (C≡*C*H), 106.5 (C(2)), 114.2 (C(6)), 117.7 (C(4)), 130.1 (C(5)), 132.5 (C(3)), 148.5 (C(1)).

3.3. 2-(Phenylethynyl)aniline (5)

A mixture of 2-iodoaniline (1.97 g, 8.99 mmol), phenylethyne (1.20 ml, 10.93 mmol), CuI (40 mg, 0.21 mmol) and $PdCl_2(PPh_3)_2$ (0.130 g, 0.19 mmol) in Et_3N (40 ml) was heated to 40°C under a nitrogen atmosphere in a sealed pressure vessel for 19 h. The solvent was removed in vacuo, the residue was partitioned between Et_2O and water, and the organic layer was washed with water and dried ($MgSO_4$). Chromatography on silica gel using hexanes eluted phenylethyne, while hexanes–Et_2O (9:1) gave 2-(phenylethynyl)aniline (**5**) (1.638 g, 94%) as colourless needles, m.p. 90–91°C (lit. m.p. [16] 90.5–91.5°C). IR (cm^{-1}): ν_{max} 3465 (NH), 3368 (NH), 2205 (C≡C), 1612 (C=C), 747 (CH), 691 (CH). ^{1}H-NMR: δ 4.27 (bs, NH_2), 6.67–6.76 (m, H(4), H(6)), 7.14 (td, $J = 7.7$, 1.6 Hz, H(5)), 7.31–7.39 (m, H(3), H(2′), H(4′)), 7.50–7.55 (m, H(3′)). ^{13}C-NMR: δ 85.9 (*C*≡CPh), 94.6 (C≡*C*Ph), 107.8 (C(2)), 114.3 (C(6)), 117.0 (C(4)), 123.24 (C(1′)), 128.2 (C(4′)), 128.3 (C(3′)), 129.6 (C(5)), 131.4 (C(2′)), 132.1 (C(3)), 147.7 (C(1)).

3.4. 2-(3′,3′-Dimethylbutynyl)aniline (6)

A mixture of 3,3-dimethylbutyne (0.90 ml, 6.58 mmol), 2-iodoaniline (1.125 g, 5.14 mmol), CuI (10 mg, 0.053 mmol) and $PdCl_2(PPh_3)_2$ (72 mg, 0.10 mmol) in Et_3N (15 ml) was stirred at r.t. under a nitrogen atmosphere in a sealed pressure vessel. CuI (110 mg, 0.58 mmol) was added after 25 h as the reaction had not gone to completion, and stirring was continued at r.t. for a further 23 h. Workup and chromatography (hexanes–Et_2O, 9:1) gave 2-(3′,3′-dimethylbutynyl)aniline (**6**) (0.841 g, 95%) as tan crystals, m.p. 42–43°C. Found: $M^{+\bullet}$ 173.1207. Calc. for $C_{12}H_{15}N$: 173.1204. IR (cm^{-1}): ν_{max} 3478 (NH), 3383 (NH), 3056 ($CH_{aromatic}$), 2966 (CH_{alkyl}), 1613 (C=C), 784, 749, 693 (CH). ^{1}H-NMR: δ 1.34 (s, CH_3), 4.11 (bs, NH_2), 6.65 (td, $J = 7.8$, 1.1 Hz, H(4)), 6.67 (d, $J = 7.7$ Hz, H(6)), 7.06 (td, $J = 7.8$, 1.5 Hz, H(5)), 7.23 (dd, $J = 7.8$, 1.5 Hz, H(3)). ^{13}C-NMR: δ 28.2 ($C(CH_3)_3$), 31.2 ($C(CH_3)_3$), 75.4 (*C*≡C*t*Bu), 104.09 (C≡*C**t*Bu), 108.8 (C(2)), 114.0 (C(6)), 117.8 (C(4)), 128.7 (C(5)), 131.8 (C(3)), 147.4 (C(1)). MS; m/z: 173 [80, M^+], 158 [100, $M - Me^{\bullet}$], 143 [42, $158 - Me^{\bullet}$], 118 (31), 57 [25, $(CH_3)_3C^+$], 41 (22).

3.5. 2-(Heptyn-1-yl)aniline (7)

A mixture of 2-iodoaniline (1.099 g, 5.02 mmol), 1-heptyne (0.78 ml, 5.95 mmol), CuI (11 mg, 0.06 mmol) and $PdCl_2(PPh_3)_2$ (72 mg, 0.10 mmol) in Et_2NH (15 ml) was heated to 30°C under nitrogen in a sealed pressure vessel for 24 h. Workup and chromatography (hexanes–Et_2O, 9:1) gave 2-(heptyn-1-yl)aniline (**7**) (0.921 g, 98%) as a pale brown oil. Found: $M^{+\bullet}$, 187.1354. Calc. for $C_{13}H_{17}N$: 187.1361. IR (cm^{-1}): ν_{max} 3476 (NH), 3380 (NH), 3028 ($CH_{aromatic}$), 2930 (CH_{alkyl}), 2859 (CH_{alkyl}), 2221 (C≡C), 1613 (C=C), 747 (CH). ^{1}H-NMR: δ 0.92 (t, $J = 7.2$ Hz, H(7′)), 1.37 (sextet, $J = 7.4$, 1.1 Hz, H(6′)), 1.44 (m, H(5′)), 1.63 (p, $J = 7.2$ Hz, H(4′)), 2.46 (t, $J = 7.1$ Hz, H(3′)), 4.15 (bs, NH_2), 6.66–6.67 (m, H(4), H(6)), 7.07 (td, $J = 7.6$, 1.5 Hz, H(5)), 7.24 (dd, $J = 7.5$, 1.5 Hz, H(6)). ^{13}C-NMR: δ 13.9(5) (C(7′)), 19.6 (C(6′)), 22.2 (C(5′)), 28.6 (C(4′)), 31.1 (C(3′)), 76.9 (*C*≡CPent), 95.7 (C≡*C*Pent), 108.92 (C(2)), 114.1 (C(6)), 117.8 (C(4)), 128.7 (C(5)), 131.9(5) (C(3)), 147.6 (C(1)). MS; m/z: 187 [85, $M^{+\bullet}$], 172 [25, $M - Me^{\bullet}$], 158 [33, $M - Et^{\bullet}$], 144 [52, $M - Pr^{\bullet}$], 132 (50), 130 [100, $M - Bu^{\bullet}$], 77 (Ph^+).

3.6. 2-(Trimethylsilylethynyl)pyridine

A mixture of 2-bromopyridine (3.165 g, 20.03 mmol), trimethylsilylethyne (4.2 ml, 30 mmol), CuI (0.214 g, 1.12 mmol) and $PdCl_2(PPh_3)_2$ (0.400 g, 0.57 mmol) in Et_3N (40 ml) was heated to 40°C under nitrogen in a sealed pressure vessel for 43.5 h. Workup and chromatography (hexanes–Et_2O, 3:1) gave 2-(trimethylsilylethynyl)pyridine (3.205 g, 91%) [18] as a pale yellow oil. IR (cm^{-1}): ν_{max} 3303 ($CH_{alkynyl}$), 3053 (CH_{aryl}), 2959 (CH_{alkyl}), 2167 (C≡C), 1582, 1562 (C=C), 1250 (C–Si), 845 (C–Si). ^{1}H-NMR: δ 0.26 (s, $Si(CH_3)_3$), 7.20 (ddd, $J = 7.8$, 4.9, 1.1 Hz, H(5)), 7.44 (dt, $J = 7.8$, 0.9 Hz, H(3)), 7.62 (td, $J = 7.8$, 1.8 Hz, H(4)), 8.56 (ddd, $J =$ 4.9, 1.6, 0.8 Hz, H(6)). ^{13}C-NMR: δ −0.3 ($Si(CH_3)_3$), 94.7 ($C{\equiv}CSiMe_3$), 103.6 ($C{\equiv}CSiMe_3$), 123.0 (C(6)), 127.2 (C(4)), 136.0 (C(5)), 143.0(5) (C(2)), 149.9 (C(3)).

3.7. 2-Ethynylpyridine

A solution of potassium hydroxide (0.663 g, 11.8 mmol) in water (10 ml) was added to a solution of 2-(trimethylsilylethynyl)pyridine (401) (1.500 g, 8.56 mmol) in MeOH (12 ml) at r.t. After 3.5 h the solution was extracted with Et_2O, washed twice with water, and dried ($MgSO_4$). Removal of the solvent in vacuo gave a pale yellow oil. Kugelrohr distillation (35°C, 2 mmHg) gave 2-ethynylpyridine (0.714 g, 81%) [18] as a colourless oil. IR (cm^{-1}): ν_{max} 3293 ($CH_{alkynyl}$), 3053 ($CH_{aromatic}$), 2109 (C≡C), 780. ^{1}H-NMR: δ 3.15 (s, $H_{(alkynyl)}$), 7.26 (td, $J = 7.7$, 4.9, 1.3 Hz, H(5)), 7.48 (dt, $J = 7.8$, 1.0 Hz, H(3)), 7.66 (td, $J = 7.7$, 1.8 Hz, H(4)), 8.59 (ddd, $J = 4.9$, 1.6, 0.9 Hz, H(6)). ^{13}C-NMR: δ 76.9 (C≡*C*H), 82.4 (*C*≡CH), 123.1 (C(6)), 127.1 (C(4)), 135.9 (C(5)), 141.9 (C(2)), 149.6 (C(3)).

3.8. 2-(2′-Pyridyl)ethynylaniline (9)

(A) A mixture of 2-ethynylpyridine (0.477 g, 4.63 mmol), 2-iodoaniline (0.833 g, 3.80 mmol), CuI (60 mg, 0.32 mmol) and $PdCl_2(PPh_3)_2$ (50 mg, 0.071 mmol) in Et_3N (10 ml) was heated at 40°C under nitrogen in a sealed pressure vessel for 22 h. Workup and chromatography (hexanes–Et_2O, 1:1) gave 2-(2′-pyridyl)ethynylaniline (**9**) (0.254 g, 34%) as fine tan needles, m.p. 104–106°C. Found: $M^{+\bullet}$ 194.0840. Calc. for $C_{13}H_{10}N$: M, 194.0844. IR (Nujol, cm^{-1}): ν_{max} 3376 (NH), 3306 (NH), 3192 (CH_{aryl}), 2208 (C≡C), 1639 (C = C), 773, 743, 736 (CH_{aryl}). ^{1}H-NMR: δ 4.39 (bs, NH_2), 6.70 (td, $J = 7.8$, 1.1 Hz, H(4)), 6.72 (d, $J = 7.8$ Hz, H(6)), 7.17 (td, $J = 7.8$, 1.6 Hz, H(5)), 7.24 (ddd, $J = 7.8$, 4.8, 1.2 Hz, H(5′)), 7.42 (dd, $J = 7.8$, 1.6 Hz, H(3)), 7.52 (dd, $J = 7.8$, 1.1 Hz, H(3′)), 7.68 (td, $J = 7.8$, 1.8 Hz, H(4′)), 8.61 (ddd, $J = 4.9$, 1.6, 0.8 Hz, H(6′)). ^{13}C-NMR: δ 86.2 (C≡*C*Py), 94.0(5) (*C*≡CPy), 106.6 (C(2)), 114.4 (C(6)), 117.8 (C(4)), 122.6 (C(6′)), 127.0 (C(4′)), 130.5 (C(5)), 132.6 (C(3)), 136.2 (C(5′)), 143.6 (C(2′)), 148.5 (C(1)), 150.0 (C(3′). MS; m/z: 194 [100, M^+], 193 [35, M − H].

(B) A solution of 2-iodoaniline (0.855 g, 3.90 mmol), 2-ethynylpyridine (0.444 g, 4.31 mmol), CuI (69 mg, 0.36 mmol) and $PdCl_2(PPh_3)_2$ (53 mg, 0.076 mmol) in Et_3N (40 ml) was stirred under nitrogen in a sealed pressure vessel at r.t. in a foil-covered flask for 45 h. Workup followed by chromatography gave (i) 2-iodoaniline (51 mg, 6%) and (ii) 2-(2′-pyridyl)ethynylaniline (**9**) (0.489 g, 65%).

3.9. 2-(Ferrocenyl)ethynylaniline (8)

A mixture of 2-iodoaniline (1.108 g, 5.06 mmol), ethynylferrocene (1.160 g, 5.52 mmol) [17], CuI (11 mg, 0.058 mmol) and $PdCl_2(PPh_3)_2$ (70 mg, 0.10 mmol) in Et_2NH (15 ml) was heated to 30°C under nitrogen in a sealed pressure vessel for 18.5 h; no reaction occurred. CuI (220 mg, 1.16 mmol) was added and the solution was heated to 60°C for 24 h. The reaction mixture was adsorbed onto silica gel and the solvent was removed in vacuo. Column chromatography followed by radial chromatography (CH_2Cl_2) gave 2-(ferrocenyl)ethynylaniline (**8**) (1.500 g, 99%) as a red solid. Recrystallisation of a small portion of the product from hexanes–CH_2Cl_2 gave small red needles, m.p. (dec., darkens at 80°C), 120°C. Found: $M^{+\bullet}$ 301.0547. Calc. for $C_{18}H_{15}FeN$: 301.0554. IR (cm^{-1}): ν_{max} 3432 (NH), 3378 (NH), 2199 (C≡C), 1612 cm^{-1} (C=C). ^{1}H-NMR: δ (C_6D_6) 3.78 (bs, NH_2), 3.88 (s, Cp (minor rotamer)), 3.93 (t, $J = 1.8$ Hz, H(2′)), 4.06 (s, Cp (major)), 4.34 (t, $J = 1.9$ Hz, H(3′) (minor)), 4.40 (t, $J = 1.8$ Hz, H(3′) (major)), 6.33 (dd, $J = 8.4$, 0.7 Hz, H(6)), 6.56 (td, $J = 7.5$, 1.1 Hz, H(4)), 6.96 (ddd, $J = 8.4$, 7.5, 1.5 Hz, H(5) (major)), 7.23 (m, H(5) (minor)), 7.45 (dd, $J = 7.8$, 1.5 Hz, H(3) (minor)), 7.65 (bdd, $J = 6.4$, 2.6, H(3) (major)). ^{13}C-NMR: δ 65.3 (C(1′)), 65.9 (C(1′)), 68.8 (C(2′)), 69.5 (Cp), 70.0 (Cp), 71.4 (C(3′)), 82.0 (*C*≡CFc), 93.5 (C≡*C*Fc), 98.8 (CH_{minor}), 108.7 (C(2)), 110.3 (CH_{minor}), 114.2 (C(6)), 117.9 (C(4)), 119.8 (CH_{minor}), 120.0 (CH_{minor}), 121.4 (CH_{minor}), 129.1 (C(5)), 131.9 (C(3)), 147.5 (C(1)). MS; m/z: 301 [100, M^+].

3.10. Benzyltriethylammonium pentacarbonyl[(oxo)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (11)

Butyllithium (1.63 ml, 2.5 mol l^{-1}) was added to a solution of 13-bromo-12,19-dimethoxypodocarpa-8,11,13-triene [24] (1.5 g, 4.08 mmol) in THF (12 ml) at − 78°C under nitrogen. The solution was transferred via cannula to a slurry of $Cr(CO)_6$ in Et_2O (20 ml) at 0°C under nitrogen. The mixture was stirred at 0°C for 1.25 h, then the solvent was removed in vacuo to give crude lithium pentacarbonyl[(oxo)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**10**). The salt **10** was dissolved in nitrogen-degassed water (30 ml) and a solution of benzyltriethylammonium chloride in nitrogen-degassed water (10 ml) was added, producing a yellow precipitate. The suspension was stirred for 1 h, followed by extraction into CH_2Cl_2. Workup gave benzyltriethylammonium pentacarbonyl[(oxo)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (**11**) (2.099 g, 78%) as a yellow foam. IR (cm^{-1}): ν_{max} 2031 (s, C≡O), 1943 (sh, C≡O), 1897 (br, C≡O). ^{1}H-NMR: δ 1.01 (s, H(18)), 1.13 (s, H(20)), 0.90–1.85 (m, H(1ax), H(2ax), H(2eq), H(3ax), H(6ax), CH_3CH_2N)), 1.80–2.00 (m, H(3eq),H(6eq)), 2.21 (bd, $J = 9.9$ Hz, H(1eq)), 2.60–2.90 (m, H(7ax),

H(7eq)), 3.10–3.40 (b, CH_3CH_2N), 3.20 (d, $J = 9.0$ Hz, H(19)), 3.32 (s, 19-OMe), 3.53 (d, $J = 9.0$ Hz, H(19)), 3.66 (s, 12-Ome), 4.30 (bs, CH_2Ph), 6.29 (s, H(11)), 6.58 (s, H(14)), 7.10–7.60 (b, Ph). ^{13}C-NMR: δ 8.1 (CH_3CH_2N), 19.2 (C(2)), 19.4 (C(6)), 25.6 (C(20)), 27.6 (C(18)), 30.5 (C(7)), 35.9 (C(3)), 37.7(5) (C(4)), 38.0 (C(10)), 39.1 (C(1)), 51.5 (C(5)), 52.8(5) (CH_3CH_2N), 55.0 (12-OMe), 59.4 (19-OMe), 61.1 (CH_2Ph), 75.9 (C(19)), 108.6 (C(11)), 120.8 (C(14)), 126.0 (C(13)), 126.5 (C_{para}), 129.5 (C_{ortho}), 131.0 (C(8)), 132.2 (C_{meta}), 147.2 (C_{ipso}), 148.3 (C(9)), 150.0 (C(12)), 222.2 ($C{\equiv}O_{cis}$), 228.6 ($C{\equiv}O_{trans}$), 300.3 ($C_{carbene}$).

3.11. Pentacarbonyl[(2-(trimethylsilylethynyl)-phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**13**)

Acetyl bromide in CH_2Cl_2 (0.96 ml, 0.152 g CH_3COBr per ml) was added to a solution of the benzyltriethylammonium acylate **12** (0.783 g, 1.19 mmol) in CH_2Cl_2 (15 ml) at -30°C in a foil-covered flask under nitrogen. The solution was stirred at -30°C for 1 h and then cooled to -78°C. A solution of 2-(trimethylsilylethynyl)aniline (**4**) (0.222 g, 1.27 mmol) and Et_3N (190 μl, 1.36 mmol) in CH_2Cl_2 (10 ml) was added to the acetyloxycarbene and the mixture was held at -78°C for 2.5 h, then warmed slowly to r.t. The mixture was filtered, the solvent was removed from the filtrate, and the residue was adsorbed onto silica gel. Flash chromatography (hexanes–Et_2O, 2:1) gave pentacarbonyl[(2 - (trimethylsilylethynyl)phenylamino)-(13 - (12,19 - dimethoxypodocarpa - 8,11,13 - triene))-carbene]chromium (**13**) (0.680 g, 84%) (E/Z ratio 1.75:1) as a yellow–orange foam. Found: $M^{+\bullet}$ 679.2095. Calc. for $C_{36}H_{41}CrNO_7Si$: 679.2057. IR (cm^{-1}): ν_{max} 2158 (br, C≡C), 2053 (s, C≡O), 1976 (sh, C≡O), 1926 (br, C≡O), 1251 (s, C–Si), 1110 (s, C–O–C), 845 (s, C–Si). ^{1}H-NMR: δ 0.28 (s, $SiMe_{3(Z)}$), 0.33 (s, $SiMe_{3(E)}$), 1.01 (m, H(3ax)), 1.02 (s, $H(18)_{(E)}$), 1.03 (s, $H(18)_{(E)}$), 1.06 ($H(18)_{(Z)}$), 1.09 (s, $H(18)_{(E)}$), 1.15 (s, $H(20)_{(E)}$), 1.23 (s, $H(20)_{(Z)}$), 1.42 (dd, $J = 12.9$, 1.8 Hz, H(5)), 1.43 (ddd, $J = 13.2$, 13.2, 4.0 Hz, H(1ax)), 1.54–1.73 (m, H(2ax), H(2eq), H(6ax)), 1.83–1.94 (m, H(3eq), H(6eq)), 2.19 (dd, $J = 12.7$, 2.7 Hz, $H(1eq)_{(E)}$), 2.29 (bd, $J = 13.0$ Hz, $H(1eq)_{(Z)}$), 2.53–2.75 (m, H(7ax)), 2.80 (bdd, $J = 16.6$, 5.7 Hz, $H(7eq)_{(E)}$), 2.84 (bdd, $J = 16.6$, 6.0 Hz, $H(7eq)_{(Z)}$), 3.21 (d, $J = 9.0$ Hz, H(19)), 3.23 (d, $J = 9.0$ Hz, H(19)), 3.31(7) (s, 19-$OMe_{(E)}$), 3.32(2) (s, 19-$OMe_{(E)}$), 3.34 (s, 19-$OMe_{(Z)}$), 3.48 (d, $J = 9.0$ Hz, H(19)), 3.51 (d, $J = 9.0$ Hz, H(19)), 3.67(3) (s, 12-$OMe_{(E)}$), 3.69(4) (s, 12-$OMe_{(E)}$), 3.77 (s, 12-$OMe_{(Z)}$), 3.84 (s, 12-$OMe_{(Z)}$), 6.36 (d, $J = 8.2$ Hz, H(6′)), 6.55 (bd, $J = 8.2$ Hz, H(6′)), 6.58 (bs, H(11), H(14)), 6.61 (bd, $J = 8.2$ Hz, H(6′)), 6.68 (bd, $J = 8.2$ Hz, H(6′)), 6.91 (td, $J = 7.7$, 1.2 Hz, H(4′)), 6.99 (td, $J = 7.7$, 1.2 Hz, H(4′)), 7.07 (bt, $J = 7.4$ Hz, H(5′)), 7.09 (bt, $J = 7.4$ Hz, H(5′)), 7.45 (bd, $J = 7.7$ Hz, H(3′)), 10.06 (bs, $NH_{(Z)}$), 10.89 (bs, $NH_{(E)}$). ^{13}C-NMR: δ 0.27 ($SiMe_3$), 19.1(5) (C(2)), 19.3 (C(6)), 25.6 (C(20)), 25.7 (C(20)), 27.6 (C(18)), 30.2 (C(7)), 30.4 (C(7)), 35.9 (C(3)), 37.9(5) (C(10)), 38.0(3) (C(4)), 38.9 (C(1)), 39.1 (C(1)), 50.9 (C(5)), 51.3 (C(5)), 54.9 (12-OMe), 59.4 (19-OMe), 75.8 (C(19)), 98.8 ($C{\equiv}CSiMe_3$), 103.8 ($C{\equiv}CSiMe_3$), 106.4 (C(11)), 117.5 (C(6′)), 117.6 (C(6′)), 117.7 (C(2′)), 121.3(8) (C(14)), 121.4(2) (C(14)), 123.2(7) (C(4′)), 123.3(4) (C(4′)), 126.8 (C(13)), 126.9 (C(13)), 126.9(6) (C(13)), 127.0 (C(13)), 128.3 (C(5′)), 128.6 (C(5′)), 129.9 (C(5′)), 132.2 (C(3′)), 132.6 (C(3′)), 136.8 (C(8)), 137.0 (C(8)), 140.5 (C(1′)), 147.7 (C(9)), 150.5 (C(12)), 150.6 (C(12)), 217.1 ($C{\equiv}O_{cis}$), 224.1 ($C{\equiv}O_{trans}$), 289.0 ($C_{carbene}$), 289.1 ($C_{carbene}$). FABMS; m/z: 679 [4, M^+], 651 [3, M − CO], 609 (8), 539 [100, M − 5CO], 523 [539 − $Me^{\bullet}$ − $H^{\bullet}$], 504 (24), 486 [18, M − $Cr(CO)_5$ − $H^{\bullet}$].

3.12. Pentacarbonyl[(2-(ethynyl)phenylamino)-(13-(12,19-dimethoxypodocarpa-8,11,13-triene))-carbene]chromium (**14**)

Acetyl bromide in CH_2Cl_2 (0.95 ml, 0.152 g of CH_3COBr per millilitre, 1.17 mmol) was added to a solution of the benzyltriethylammonium acylate **12** (0.769 g, 1.17 mmol) in CH_2Cl_2 (15 ml) cooled to -30°C in a foil-covered flask under nitrogen. The solution was stirred at -30°C for 1 h then cooled to -78°C. A solution of 2-ethynylaniline (**3**) (0.140 g, 1.20 mmol) and Et_3N (170 μl, 1.22 mmol) in CH_2Cl_2 (10 ml) was added to the acetyloxycarbene solution and the mixture was held at -78°C for 2.5 h then warmed slowly to r.t. Removal of solvent followed by flash chromatography (hexanes–Et_2O, 2:1) gave pentacarbonyl[(2 - (ethynyl)phenylamino)(13 - (12,19 - dimethoxypodocarpa - 8,11,13 - triene))carbene]chromium (**14**) (0.477 g, 67%) (E/Z ratio 1.9:1) as a yellow foam. Found: $M^{+\bullet}$, 607.1678. Calc. for $C_{33}H_{33}CrNO_7$: 607.1662. IR (cm^{-1}): ν_{max} 2054 (s, C≡O), 1976 (sh, C≡O), 1925 (br, C≡O). ^{1}H-NMR: δ 1.01 (m, H(3ax)), 1.02 (s, H(18)), 1.03 (s, H(18)), 1.06 (s, H(18)), 1.08 (s, H(18)), 1.16 (H(20)), 1.19 (s, H(20)), 1.23 (s, H(20)), 1.40–1.48 (m, H(5), H(1ax)), 1.52–1.80 (m, H(2ax), H(2eq), H(6ax)), 1.85–2.03 (m, H(3eq), H(6eq)), 2.13–2.25 (m, H(1eq)), 2.51–2.91 (m, H(7ax), H(7eq)), 3.21–3.28 (m, H(19)), 3.31(7) (19-$OMe_{(Z)}$), 3.32(3) (s, 19-$OMe_{(Z)}$), 3.34 (s, 19-$OMe_{(E)}$), 3.35 (s, 19-$OMe_{(E)}$), 3.56 (d, $J = 9.2$ Hz (H(19)), 3.59 (s, 12-OMe), 3.60 (s, 12-OMe), 3.77 (s, 12-OMe), 3.84 (C≡CH), 6.41 (d, $J = 8.6$ Hz, H(6′)), 6.57 (bd, $J = 7.6$ Hz, H(6′)), 6.57 (s,

H(14)), 6.63 (bd, $J = 7.7$ Hz, H(6′)), 6.65 (s, H(14)), 6.65 (d, $J = 8.4$ Hz, H(6′)), 6.66 (d, $J = 8.4$ Hz, H(6′)), 6.80(1) (s, H(11)), 6.80(6) (s, H(11)), 6.81(3) (s, H(11)), 6.96 (t, $J = 8.2$ Hz, H(4′)), 7.02 (td, $J = 8.2$, 1.5 Hz, H(4′)), 7.09 (td, $J = 7.8$, 1.1 Hz, H(5′)), 7.12 (td, $J = 7.9$, 1.1 Hz, H(5′)), 7.48 (dd, $J = 8.0$, 2.1 Hz, H(3′)), 7.57 (dd, $J = 7.9$, 1.4 Hz, H(3′)), 7.66 (bd, $J = 7.9$ Hz, H(3′)), 10.06 (b, $NH_{(Z)}$), 10.89 (b, $NH_{(E)}$). ^{13}C-NMR: δ 19.1(5) (C(2)), 19.3 (C(6)), 25.5(5) (C(20)), 25.7 (C(20)), 27.6 (C(18)), 30.1 (C(7)), 30.4 (C(7)), 35.9 (C(3)), 38.1 (C(10)), 38.8 (C(4)), 38.9(5) (C(1)), 39.1 (C(1)), 50.9 (C(5)), 51.3 (C(5)), 54.8 (12-OMe), 55.1 (12-OMe), 59.4 (19-OMe), 75.8 (C(19)), 75.9 (C(19)), 78.0 (C≡*C*H), 75.9 (C≡*C*H), 84.1(5) (*C*≡CH), 85.9 (*C*≡CH), 106.4 (C(11)), 106.9 (C(11)), 110.3 (C(6′)), 110.9 (C(6′)), 120.0 (C(2′)), 121.3 (C(14)), 121.6 (C(14)), 123.3 (C(4′)), 123.4 (C(4′)), 126.8 (C(13)), 127.1 (C(13)), 127.1(3) (C(13)), 128.7 (C(5′)), 129.5 (C(5′)), 129.8 (C(5′)), 132.3 (C(3′)), 132.7 (C(3′)), 136.5 (C(8)), 141.7 (C(1′)), 143.5 (C(9)), 150.8 (C(12)), 150.9 (C(12)), 216.8 ($C{\equiv}O_{cis}$), 217.0 ($C{\equiv}O_{cis}$), 224.0 ($C{\equiv}O_{trans}$), 224.9 ($C{\equiv}O_{trans}$), 289.3 ($C_{carbene}$). FABMS; m/z: 607 [2, M^+], 579 [4, M − CO], 495 [9, M − 4CO], 467 [100, M − 5CO], 452 [5, 467 − Me$^\bullet$], 414 [10, 467 − Cr − H$^\bullet$].

3.13. Pentacarbonyl[(2-(3,3-dimethylbutynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**15**)

Acetyl bromide in CH_2Cl_2 (0.92 ml, 0.152 g of CH_3COBr per millilitre, 1.14 mmol) was added to a solution of the benzyltriethylammonium acylate **12** (0.745 g, 1.13 mmol) in CH_2Cl_2 (15 ml) cooled to −30°C in a foil-covered flask under nitrogen. The solution was stirred at −30°C for 1 h then cooled to −78°C. A solution of 2-(3,3-dimethylbutynyl)aniline (**6**) (0.200 g, 1.15 mmol) and Et_3N (174 μl, 1.25 mmol) in CH_2Cl_2 (10 ml) was added to the acetyloxycarbene solution. The mixture was held at −78°C for 2 h then warmed slowly to r.t. Removal of the solvent and adsorption of the residue onto silica gel followed by flash chromatography (hexanes–Et_2O, 1:1) gave pentacarbonyl[(2 - (3,3 - dimethylbutynyl)phenylamino)(13-(12,19 - dimethoxypodocarpa - 8,11,13 - triene))carbene]-chromium (**15**) (0.582 g, 77%) (*E*/*Z* ratio 5:1) as an orange–yellow foam. Found: $M^{+\bullet}$ 663.2319. Calc. for $C_{37}H_{41}CrNO_7$: 663.2288. IR (cm^{-1}): ν_{max} 2054 (s, C≡O), 1976 (sh, C≡O), 1925 (br, C≡O). ^{1}H-NMR: δ 1.01 (m, H(3ax)), 1.01 (s, H(18)), 1.02 (s, H(18)), 1.03 (s, H(18)), 1.20 (s, H(20)), 1.39 (s, $(CH_3)_3C$), 1.42(0) (s, $(CH_3)_3C$), 1.42(4) (dd, $J = 12.4$, 1.8 Hz, H(5)), 1.45 (ddd, $J = 13.0$, 13.0, 3.8 Hz, H(1ax)), 1.55–1.74 (m, H(2ax), H(6ax), H(2eq)), 1.82–1.92 (m, H(3eq)), 1.96 (ddt, $J = 13.4$, 7.2, 1.9 Hz, H (6eq)), 2.18 (bd, $J = 12.6$ Hz, H(1eq)), 2.27 (bd, $J = 12.8$ Hz, H(1eq)), 2.53–2.82 (m, H(7ax), H(7eq)), 2.87 (bdd, $J = 17.1$, 6.8 Hz, H(7eq)), 3.20–3.26 (m, H(19)), 3.31(5) (s, 19-OMe), 3.32(3) (s, 19-OMe), 3.33(1) (s, 19-OMe), 3.34 (s, 19-OMe), 3.48 (d, $J = 9.1$ Hz, H(19)), 3.54 (d, $J = 9.1$ Hz, H(19)), 3.62 (s, 12-OMe), 3.63 (s, 12-OMe), 3.77 (s, 12-OMe), 6.25(0) (s, H(14)), 6.25(4) (s, H(14)), 6.25(7) (s, H(14)), 6.26 (s, H(14)), 6.35 (d, $J = 7.6$ Hz, H(6′)), 6.54 (d, $J = 8.0$ Hz, H(6′)), 6.57(5) (s, H(11)), 6.58 (s, H(11)), 6.61 (d, $J = 8.2$ Hz, H(6′)), 6.65(7) ($J = 8.4$ Hz, H(6′)), 6.66 (d, $J = 8.4$ Hz, H(6′)), 6.80 (m, H(4′)), 6.85 (td, $J = 8.2$, 1.4 Hz, H(4′)), 6.93 (d, $J = 8.4$ Hz, H(4′)), 7.06 (td, $J = 7.3$, 1.3 Hz, H(5′)), 7.11 (td, $J = 7.2$, 1.1 Hz, H(5′)), 7.31 (dd, $J = 7.9$, 0.7 Hz, H(3′)), 7.38 (dd, $J = 7.7$, 1.7 Hz, H(3′)), 7.53 (d, $J = 7.8$, 0.7 Hz, H(3′)), 10.05 (b, $NH_{(E)}$), 10.81 (b, $NH_{(Z)}$). ^{13}C-NMR: δ 19.2 (C(2)), 19.2(8) (C(6)), 19.3(4) (C(6)), 25.6 (C(20)), 25.7 (C(20)), 27.5(6) ($C(CH_3)_3$), 27.6(3) (C(18)), 30.1(3) (C(7)), 30.3 (C(7), $C(CH_3)_3$), 30.8(5) ($C(CH_3)_3$), 30.9(5) ($C(CH_3)_3$), 35.9 (C(3)), 36.0 (C(3)), 38.0 (C(10)), 38.0(5) (C(10)), 38.9 (C(4)), 39.0 (C(1)), 39.1 (C(1)), 50.9 (C(5)), 51.2(6) (C(5)), 51.3 (C(5)), 54.9 (12-OMe), 55.2(5) (12-OMe), 59.4 (19-OMe), 73.8 (C≡*C*t Bu), 75.9 (C(19)), 76.0 (C(19)), 93.9 (*C*≡C*t*Bu), 110.3 (C(11)), 110.9 (C(11)), 118.3 (C(2′)), 119.6 (C(6′)), 119.9 (C(6′)), 121.0 (C(14)), 121.3 (C(14)), 121.4 (C(14)), 123.3 (C(4′)), 126.7(8) (C(13)), 126.8(5) (C(13)), 127.0 (C(13)), 127.3 (C(5′)), 128.6 (C(5′)), 129.8 (C(5′)), 132.4(0) (C(3′)), 132.4(3) (C(3′)), 135.7 (C(8)), 140.2 (C(1′)), 147.8 (C(9)), 148.7 (C(9)), 150.4 (C(12)), 150.6 (C(12)), 217.2 ($C{\equiv}O_{cis}$), 223.9 ($C{\equiv}O_{trans}$), 287.4 ($C_{carbene}$). FABMS; m/z: 663 [5, M^+], 635 [9, M − CO], 593 (14), 551 [16, M − 4CO], 523 [100, M − 5CO], 507 (56), 488 (34), 472 [23, M − $Cr(CO)_5$ + H$^\bullet$].

3.14. Pentacarbonyl[(2-(heptyn-1-yl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**16**)

Acetyl bromide in CH_2Cl_2 (0.87 ml, 0.152 g of CH_3COBr per millilitre) was added to a solution of the benzyltriethylammonium acylate **12** (0.703 g, 1.07 mmol) in CH_2Cl_2 (15 ml) cooled to −30°C in a foil-covered flask under nitrogen. The solution was stirred at −30°C for 1 h then cooled to −78°C. A solution of 2-(1′-heptynyl)aniline (**7**) (0.202 g, 1.08 mmol) and Et_3N (170 μl, 1.22 mmol) in CH_2Cl_2 (10 ml) was added to the acetyloxycarbene solution and the mixture was held at −78°C for 2 h, then warmed slowly to r.t. Removal of solvent followed by flash chromatography (hexanes–

Et_2O, 1:1) gave pentacarbonyl[(2-(heptyn-1-yl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**16**) (0.466 g, 64%) as an unstable yellow–orange oil. IR (cm^{-1}): ν_{max} 2054 (s, C≡O), 1977 (sh, C≡O), 1931 (br, C≡O). Attempts to obtain NMR spectra in either $CDCl_3$ or C_6D_6 failed due to decomposition of the product.

3.15. Thermolysis of pentacarbonyl[(2-(trimethylsilylethynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**13**)

A solution of pentacarbonyl[(2-(trimethylsilylethynyl)phenylamino)(13-(12,19-dimethoxy-podocarpa-8,11,13-triene))carbene]chromium (**13**) (0.248 g, 0.364 mmol) in dibutyl ether (7 ml) was freeze–pump–thaw cycled three times and then heated to 85°C under a continuous stream of nitrogen for 1.5 h. The solvent was removed in vacuo and the residue was dissolved in Me_2CO–H_2O (2:1 v/v, 15 ml) and stirred at r.t. for 24 h. The product was extracted with Et_2O (3 × 50 ml) and dried. PLC (hexanes–Et_2O, 2:1) then analytical TLC (hexanes–Et_2O, 2:1) gave butyl 2-[13′-(12′,19′-dimethoxy podocarpa-8′,11′,13′-triene)]-α-(trimethylsilyl)-1*H*-indole-3-acetate (**20**) (29.2 mg, 14%) as a colourless oil. Found: $M^{+\bullet}$, 589.3580. Calc. for $C_{36}H_{51}NO_4Si$: 589.3587. IR (cm^{-1}): ν_{max} 3369 (br, NH), 1730 (C=O), 1254 (C–Si), 850 (C–Si). ^{1}H-NMR: δ 0.05, s, Me_3Si), 0.06 (s, Me_3Si), 0.89 (t, $J = 7.4$ Hz, CH_3CH_2), 0.93 (t, $J = 7.4$ Hz, CH_3CH_2), 1.04 (m, H(3′ax)), 1.06(5) (s, H(18′)), 1.07(2) (s, H(18′)), 1.26(4) (s, H(20′)), 1.26(9) (s, H(20′)), 1.35 (sextet, $J = 7.3$ Hz, $CH_3CH_2CH_2$), 1.38 (sextet, $J = 7.4$ Hz, $CH_3CH_2CH_2$), 1.49 (dd, $J = 10.9$, 2.0 Hz, H(5′)), 1.51 (dd, $J = 10.9$, 1.8 Hz, H(5′)), 1.60–1.80 (m, H(1′ax), H(2′ax), H(2′eq), H(6′ax)), 1.65 (p, $J = 7.4$ Hz, $CH_3CH_2CH_2CH_2$), 1.91 (bd, $J = 13.7$ Hz, H(3′eq)), 2.02 (bdd, $J = 13.2$, 6.8 Hz, H(6′eq)), 2.33 (bd, $J = 12.5$ Hz, H(1′eq)), 2.75–2.96 (m, H(7′ax), H(7′eq)), 3.27 (d, $J = 9.1$ Hz, H(19′)), 3.35 (s, 19′-OMe), 3.56 (d, $J = 9.1$ Hz, H(19′)), 3.74 (s, 12′-OMe), 3.78 (s, $CHCO_2Bu$), 3.79(6) (s, $CHCO_2Bu$), 3.80(4) (s, 12′-OMe), 4.07–4.16 (m, OCH_2CH_2), 6.88 (s, H(11′)), 6.90 (s, H(11′)), 7.00(9) (s, H(14)), 7.01 (s, H(14)), 7.06 (td, $J = 8.1$, 1.1 Hz, H(5)), 7.11 (td, $J = 8.1$, 1.1 Hz, H(5)), 7.13 (td, $J = 8.2$, 1.2 Hz, H(6)), 7.18 (td, $J = 8.1$, 1.2 Hz, H(6)), 7.29 (bd, $J = 8.0$ Hz, H(7)), 7.35 (bd, $J = 8.0$ Hz, H(7)), 7.66 (bd, $J = 7.7$ Hz, H(4)), 7.80 (bd, $J = 8.0$ Hz, H(4)), 8.19 (bs, NH). ^{13}C-NMR: δ −0.68, Me_3Si), 13.7 (CH_3CH_2), 19.2 (C(2′)), 19.3 (C(6′)), 25.6 (C(20′)), 27.6 (C(18′)), 30.1 (C(7′)), 30.7 (CH_3CH_2), 30.9 ($CH_3CH_2CH_2$), 31.7 (CH_3CH_2), 36.0 (C(3′)), 36.5(8) ($CHCO_2Bu$), 36.6(4) ($CHCO_2Bu$), 38.1 (C(10′)), 38.2 (C(4′)), 39.0 (C(1′)), 51.3 (C(5′)), 55.6 (12′-OMe), 55.8 (12′-OMe), 59.4 (19′-OMe), 64.0 (CH_2OCO), 64.6 (CH_2OCO), 75.9 (C(19′)), 107.7 (C(11′)), 109.3 (C(3)), 109.4 (C(3)), 110.4 (C(7)), 110.6 (C(7)),118.2 (C(4)), 118.7 (C(4)), 119.0 (C(13′)), 119.1 (C(13′)), 119.4 (C(13′)), 121.4 (C(5)), 122.0 (C(6)), 122.4 (C(6)), 127.3(0) (C(8′)), 127.3(5) (C(8′)), 127.3(9) (C(3a)), 127.9 (C(3a)), 131.5 (C(2)), 131.7 (C(2)), 131.8(7) (C(14′)), 131.9(4) (C(14′)), 135.4 (C(7a)), 135.9(5) (C(7a)), 151.1 (C(9)), 155.2(5) (C(12)), 172.4 (C=O), 173.9 (C=O). IR (cm^{-1}); m/z: 589 [64, M^+], 532 [22, $M - Bu^{\bullet}$], 517 [100, $M - Me_2Si{=}CH_2$], 443 (18), 414 [74, $M - Me_3SiH - BuOCO^{\bullet}$].

3.16. Thermolysis of pentacarbonyl[(2-(3,3-dimethylbutynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**15**)

3.16.1. In dibutyl ether

A solution of pentacarbonyl[(2-(3,3-dimethylbutynyl)phenylamino)(13-(12,19-dimethoxy-podocarpa-8,11,13-triene))carbene]chromium (**15**) (0.222 g, 0.335 mmol) in dibutyl ether (6 ml) was freeze–pump–thaw cycled three time and then heated to 90°C under a continuous flow of nitrogen for 2 h. The mixture was filtered and the solvent was removed to give a orange oil which was dissolved in Et_2O–water (2:1 v/v, 30 ml) and photolysed under air for 18 h using a Wotan sunlamp. The greenish yellow solution was diluted with Et_2O and washed with water. PLC (hexanes–Et_2O, 2:1; two elutions) followed by analytical TLC (hexanes–Et_2O, 1:1 then 2:1, two elutions) failed to improve product purity. Mass spectroscopy showed that butyl 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(1,1-dimethylethyl)-1*H*-indole-3-acetate (**23**) was one component of the mixture.

3.16.2. In toluene

A solution of pentacarbonyl[(2-(3,3-dimethylbutynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**15**) (0.168 g, 0.253 mmol) in C_6H_5Me (10 ml) was freeze–pump–thaw cycled three times and then heated to 85°C for 2 h under a continuous flow of nitrogen. Removal of the solvent gave a orange oil which was dissolved in Et_2O and photolysed under air in sunlight. The colourless solution was filtered and PLC (hexanes–Et_2O, 1:1) gave 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(1,1-dimethylethyl)-1*H*-indole-3-acetic acid (**24**) (22.1 mg, 17%) as a colourless glass. Found: $M^{+\bullet}$, 517.3191. Calc. for $C_{33}H_{43}NO_4$: 517.3192. IR (cm^{-1}): ν_{max} 1705 (C=O). ^{1}H-NMR: δ 0.96 (s, $C(CH_3)_3$), 1.04 (m, H(3′ax)), 1.07 (s, H(18′)), 1.08 (s, H(18′)), 1.26(7) (s, H(20′)), 1.27 (s, H(20′)), 1.49 (bd, $J = 12.7$ Hz, H(5′)), 1.54 (ddd, $J = 13.0$, 13.0, 3.6 Hz, H(1′ax)), 1.60–1.80 (m, H(2′ax), H(2′eq), H(6′ax)), 1.91 (bd, $J = 13.5$ Hz,

H(3′eq)), 2.02 (bdd, $J = 12.5$, 6.6 Hz, H(6′eq)), 2.34 (bd, $J = 12.6$ Hz, H(1′eq)), 2.80 (ddd, $J = 16.7$, 11.2, 7.3 Hz, H(7′ax)), 2.92 (bdd, $J = 16.7$, 6.0 Hz, H(7′eq)), 3.28(2) (d, $J = 9.0$ Hz, H(19′)), 3.28(7) (d, $J = 9.0$ Hz, H(19′)), 3.35(2) (s, 19′-OMe), 3.35(5) (s, 19′-OMe), 3.55 (d, $J = 9.1$ Hz, H(19′)), 3.63 (s, C*H*CO_2H), 3.65 (s, C*H*CO_2H), 3.75 (s, 12′-OMe), 6.91 (s, H(11′)), 7.08 (td, $J = 7.0$, 1.4 Hz, H(5)), 7.09 (s, H(14′)), 7.15 (t, $J = 7.1$ Hz, H(6)), 7.31 (d, $J = 8.0$ Hz, H(7)), 7.76 (bd, $J = 7.4$ Hz, H(4)), 7.88 (dd, $J = 8.0$, 3.3 Hz, H(4), 8.14, bs, NH), 8.15 (bs, NH), COOH, b, not detected. ^{13}C-NMR: δ 19.1(6) (C(2′)), 19.2(4) (C(6′)), 25.6(2) (C(20′)), 25.6(3) (C(20′)), 27.7 (C(18′)), 28.5 ((*C*H_3)$_3$C), 30.0(7) (C(7′)), 30.1(0) (C(7′)), 35.7 ((CH$_3$)$_3$*C*), 36.0 (C(3′)), 38.1 (C(10′)), 38.3 (C(4′)), 39.095 (C(1′)), 51.1 (C(5′)), 51.2 (C(5′)), 52.8(0) (*C*HCO_2H), 52.8(6) (*C*HCO_2H), 55.9(1) (12′-OMe), 55.9(7) (12′-OMe), 59.4 (19′-OMe), 75.9(2) (C(19′)), 75.9(6) (C(19′)), 107.7 (C(11′)), 107.8 (C(11′)), 108.9(5) (C(3a)), 109.0(2) (C(3)), 110.5 (C(7)), 119.0 (C(13′)), 119.5(3) (C(4)), 119.5(7) (C(4)), 121.7 (C(5)), 122.3(0) (C(6)), 122.3(5) (C(6)), 127.2 (C(8′)), 128.0 (C(3a)), 132.4 (C(14′)), 134.7(8) (C(2)), 134.8(5) (C(2)), 135.8(6) (C(7a)), 135.9(1) (C(7a)), 152.0 (C(9′)), 154.9 (C(12′)), 155.0 (C(12′)), 175.0 (C=O), 175.2 (C=O). MS; *m*/*z*: 517 [22, M$^+$], 460 [100, M − *t*-Bu$^\bullet$].

3.17. Thermolysis of pentacarbonyl[(2-(heptyn-1-yl)-phenylamino)(13-(12,19-dimethoxy-podocarpa-8,11,13-triene))carbene]chromium (16)

A solution of pentacarbonyl[(2-(heptyn-1-yl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**16**) (0.222 g, 0.328 mmol) in dibutyl ether (8 ml) was freeze–pump–thaw cycled three times and then was heated to 85°C under a continuous flow of nitrogen for 2 h. The solvent was removed and the residual orange oil was dissolved in Me_2CO–H_2O (3:1 v/v, 20 ml) and stirred at r.t. for 24 h to oxidise any chromium residues. The solution was extracted with CH_2Cl_2 (80 ml) and washed with water (50 ml). PLC (hexanes–Et_2O, 2:1) gave 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-3-(hexan-1-one)-1*H*-indole (**25**) (71.6 mg, 44%) as a pale orange glass. Found: M$^+$$^\bullet$, 501.3256. Calc. for $C_{33}H_{43}NO_3$: 501.3243. IR (cm^{-1}): ν_{max} 3322 (NH), 1667 (C=O). ^{1}H-NMR: δ 0.80 (t, $J = 7.3$ Hz, C*H*$_3$CH$_2$CH$_2$), 1.01–1.16 (m, H(3′ax), CH$_3$C*H*$_2$C*H*$_2$), 1.07 (s, H(18′)), 1.26 (s, H(20′)), 1.45 (dd, $J = 12.4$, 1.8 Hz, H(5′)), 1.46 (ddd, $J = 12.9$, 3.8 Hz, H(1′ax)), 1.56 (p, $J = 7.4$ Hz, PrC*H*$_2$CH$_2$), 1.64–1.80 (m, H(2′ax), H(2′eq), H(6′ax)), 1.91 (bd, $J = 13.5$ Hz, H(3′eq)), 2.02 (bdd, $J = 13.3$, 7.1 Hz, H(6′eq)), 2.35 (bd, $J = 12.5$ Hz, H(1′eq)), 2.43 (t, $J = 7.6$ Hz, ArCOC*H*$_2$), 2.76 (ddd, $J = 16.7$, 11.4, 7.2 Hz, H(7′ax)), 2.86 (bdd, $J = 16.7$, 5.8 Hz, H(7′eq)), 3.28 (d, $J = 9.1$ Hz, H(19′)), 3.35 (s, 19′-OMe), 3.55 (d, $J = 9.1$ Hz, H(19′)), 3.76 (s, 12′-OMe), 6.82 (s, H(11′)), 6.96 (s, H(14′)), 7.22–7.25 (seven lines), H(6), H(5)), 7.34 (ddd, $J = 6.7$, 1.7, 0.5 Hz, H(7), 8.35 (three lines), H(4)), 8.69 (bs, NH). ^{13}C-NMR: δ 14.0 (*C*H$_3$CH$_2$), 19.1 (C(2′)), 19.2 (C(6′)), 22.3 (CH$_3$*C*H$_2$), 24.8 (*C*H$_2$CH$_2$CO), 25.5 (C(20′)), 27.7 (C(18′)), 30.0 (C(7′)), 31.6 (CH$_3$CH$_2$*C*H$_2$), 35.9 (C(3′)), 38.0(5) (C(10′)), 38.3 (C(4′)), 39.0(5) (C(1′)), 41.3 (CO*C*H$_2$), 51.2 (C(5′)), 55.5 (12′-OMe), 59.4 (19′-OMe), 75.9 (C(19′)), 107.2 (C(11′)), 110.5(5) (C(7)), 115.9(5) (C(3)), 118.8 (C(13′)), 122.0 (C(5), C(3a)), 122.2 (C(4)), 123.0 (C(6)), 127.3 (C(8′)), 132.4 (C(14′)), 135.0(5) (C(2)), 140.4 (C(7a)), 153.0 (C(9′)), 155.1 (C(12′)), 199.1 (C=O). MS; *m*/*z*: 501 [49, M$^+$], 470 [100, M − MeO$^\bullet$], 430 [62, M − $C_5H_{11}$$^\bullet$].

3.18. Thermolysis of pentacarbonyl[(2-(ethynyl)-phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (14)

A solution of pentacarbonyl[(2-(ethynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (**14**) (0.181 g, 0.298 mmol) in dibutyl ether (5 ml) was freeze–pump–thaw cycled three times and then was heated to 85°C under a continuous flow of nitrogen for 1.5 h. Removal of solvent gave a brown oil. PLC (hexanes–Et_2O, 1:1 and then 2:1, two elutions) gave 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)-3-(pentan-2-one)-1*H*-indole (**27**) (9.9 mg, 7%) as a colourless oil. Found: M$^+$$^\bullet$, 487.3083. Calc. for $C_{32}H_{41}NO_3$: 487.3086. IR (cm^{-1}): ν_{max} 3407 (NH), 1705 (C=O). ^{1}H-NMR: δ 0.81 (t, $J = 7.4$ Hz, C*H*$_3$CH$_2$), 1.04 (ddd, $J = 13.7$, 4.3 Hz, H(3′ax)), 1.06 (s, H(18′)), 1.25 (s, H(20′)), 1.47 (dd, $J = 12.9$, 1.8 Hz, H(5′)), 1.49 (ddd, $J = 13.1$, 3.6 Hz, H(1′ax)), 1.53 (sx, $J = 7.3$ Hz, CH$_3$C*H*$_2$), 1.62–1.82 (m, H(2′ax), H(2′eq), H(6′ax)), 1.91 (bd, $J = 13.4$ Hz, H(3′eq)), 2.01 (bdd, $J = 13.3$, 7.1 Hz, H(6′eq)), 2.33 (bd, $J = 12.3$ Hz, H(1′eq)), 2.40 (t, $J = 7.3$ Hz, CH$_2$C*H*$_2$CO), 2.79 (ddd, $J = 16.7$, 11.4, 7.2 Hz, H(7′ax)), 2.89 (bdd, $J = 16.7$, 5.7 Hz, H(7′eq)), 3.27 (d, $J = 9.1$ Hz, H(19′), 3.35 (s, 19′-OMe), 3.55 (d, $J = 9.1$ Hz, H(19)), 3.79 (s, 12′-OMe), 3.83 (s, ArC*H*$_2$CO), 6.90 (s, H(11)), 7.07 (s, H(14)), 7.12 (td, $J = 7.8$, 7.5, 0.9 Hz, H(5)), 7.19 (td, $J = 8.0$, 7.5, 1.1 Hz, H(6)), 7.37 (bd, $J = 8.0$ Hz, H(7)), 7.50 (bd, $J = 7.8$ Hz, H(4)), 8.61 (bs, NH). ^{13}C-NMR: δ 13.7 (*C*H$_3$CH$_2$), 17.2 (CH$_3$*C*H$_2$), 19.1(5) (C(2′)), 19.2(5) (C(6′)), 25.5 (C(20′)), 27.6(5) (C(18′)), 30.1 (C(7′)), 35.9 (C(3′)), 38.1 (C(10′)), 38.2 (C(4′)), 39.0 (C(1′)), 40.4 (CH$_2$*C*H$_2$CO), 43.2 (Ar*C*H$_2$O), 51.2 (C(5′)), 55.7 (12′-OMe), 59.4 (19′-OMe), 75.9 (C(19′)), 106.7 (C(3)), 107.7 (C(11′)), 110.7(5) (C(7)), 118.3 (C(13′)), 118.6 (C(4)), 119.6 (C(5)), 122.0 (C(6)), 127.6(5) (C(3a), C(8′)), 128.6 (C(2)), 131.2 (C(14′)), 135.5 (C(7a)), 151.3 (C(9′)), 155.0 (C(12′)), 210.3 (C=O). MS; *m*/*z*: 487 [23, M$^+$], 416 [100, M − PrCO$^\bullet$], 248 (28).

3.19. Synthesis and thermolysis of pentacarbonyl[(2-(phenylethynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (17)

A solution of acetyl bromide in CH_2Cl_2 (0.277 g of CH_3COBr per millilitre, 0.47 ml, 1.06 mmol) was added to a solution of the benzyltriethylammonium acylate **12** (0.693 g, 1.05 mmol) in CH_2Cl_2 (15 ml) at −30°C in a foil-covered flask under nitrogen. The solution was stirred at −30°C for 1 h then cooled to −78°C. A solution of 2-(phenylethynyl)aniline (**5**) (0.213 g, 1.10 mmol) and Et_3N (0.154 ml, 1.10 mmol) in CH_2Cl_2 (10 ml) was added and the temperature was held at −78°C for 2 h before warming to r.t. TLC showed that pentacarbonyl[(2-(phenylethynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]-chromium (**17**) had been produced. The solvent was removed using an oil pump connected via a cold trap to the flask and dibutyl ether (20 ml) was added to the yellow–orange residue under nitrogen. The mixture was heated to 85°C for 1.5 h under nitrogen then the product was diluted with water and stirred overnight at r.t. The product was extracted with Et_2O, washed with water and dried. PLC (hexanes–Et_2O, 2:1) followed by PTLC of individual fractions (hexanes–Et_2O, 2:1) gave (i) butyl 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(phenyl)-1*H*-indole-3-acetate (**31**) (47 mg, 7.5%) as a colourless glass. Found: $M^{+\bullet}$, 593.3501. Calc. for $C_{39}H_{47}NO_4$: 593.3505. IR (cm^{-1}): ν_{max} 3401 (NH), 1729 (C=O). ^{1}H-NMR: δ 0.81(7) (t, $J = 7.4$ Hz, C*H*$_3$CH$_2$), 0.82(2) (t, $J = 7.4$ Hz, C*H*$_3$CH$_2$), 1.04 (m, H(3′ax)), 1.04(3) (s, H(18′)), 1.06 (s, H(18′)), 1.21–1.28 (m, CH$_3$C*H*$_2$), 1.23 (s, H(20′)), 1.26 (s, H(20′)), 1.43 (dd, $J = 12.3$, 1.6 Hz, H(5′)), 1.46 (dd, $J = 12.3$, 1.7 Hz, H(5′)), 1.50–1.58 (m, H(1′ax), CH$_3$CH$_2$C*H*$_2$), 1.61–1.77 (m, H(2′ax), H(2′eq), H(6′ax)), 1.89 (bd, $J = 13.3$ Hz, H(3′eq)), 1.99 (bdd, $J = 12.9$, 6.5 Hz, H(6′eq)), 2.31 (bd, $J = 12.4$ Hz, H(1′eq)), 2.69–2.85 (m, H(7′ax), H(7′eq)), 3.25 (d, $J = 9.1$ Hz, H(19′)), 3.26 (d, $J = 9.1$ Hz, H(19′)), 3.34(0) (s, 19′-OMe), 3.34(5) (s, 19′-OMe), 3.54 (d, $J = 9.0$ Hz, H(19′)), 3.71 (s, 12′-OMe), 3.72 (s, 12′-OMe), 4.10(5) (t, $J = 6.7$ Hz, PrC*H*$_2$O), 4.11(1) (t, $J = 6.7$ Hz, PrC*H*$_2$O), 5.33(0) (s, C*H*Ph), 5.33(5) (s, C*H*Ph), 6.87(0) (s, H(11′)), 6.87(4) (s, H(11′)), 6.99 (td, $J = 7.5$, 1.1 Hz, H(5)), 7.12 (s, H(14′)), 7.13 (s, H(14′)), 7.14 (td, $J = 7.7$, 1.1 Hz, H$_{para}$), 7.16–7.22 (m, H(6)), 7.23–7.26 (m, H$_{ortho}$, H$_{meta}$), 7.35 (bdd, $J = 8.3$, 0.7 Hz, H(7)), 7.53 (bdd, $J = 7.5$, 0.8 Hz, H(4)), 7.54 (bdd, $J = 7.5$, 0.8 Hz, H(4)), 8.52 (s, NH), 8.54 (s, NH). ^{13}C-NMR: δ 13.6 (*C*H$_3$CH$_2$), 19.0 (CH$_3$*C*H$_2$), 19.1(5) (C(2′)), 19.2 (C(6′)), 25.5 (C(20′)), 27.6 (C(18′)), 30.0 (C(7′)), 30.6 (CH$_3$CH$_2$*C*H$_2$), 35.9 (C(3′)), 38.1 (C(10′)), 38.1(5) (C(4′)), 39.0 (C(1′)), 48.9 (*C*HPh), 51.2(4) (C(5′)), 51.2(8) (C(5′)), 55.7 (12′-OMe), 59.4 (19′-OMe), 64.8 (Pr*C*H$_2$OCO), 75.8(6) (C(19′)), 75.9(1) (C(19′)), 107.8 (C(11′)), 109.6(8) (C(3)), 109.7(4) (C(3)), 110.6 (C(7)), 118.2 (C(13′)), 119.4 (C(4)), 121.4 (C(5)), 121.8 (C(6)), 126.4 (C$_{para}$), 127.3 (C(8′)), 127.5 (C(3a)), 128.0(4) (C$_{ortho}$), 128.0(7) (C$_{ortho}$), 128.3 (C$_{meta}$), 128.4(5) (C$_{meta}$), 131.9 (C(14′)), 133.9 (C(2)), 135.8 (C$_{ipso}$), 139.1 (C(7a)), 139.2 (C(7a)), 151.5 (C(9′)), 155.3 (C(12′)), 173.3 (C=O). MS; *m*/*z*: 593 [66, M^+], 493 [100, M − BuOCO$^\bullet$]; and (ii) 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-3-(benzyl)-1*H*-indole (**30**) (37 mg, 7%) as a colourless glass. Found: $M^{+\bullet}$ 493.2987. Calc. for $C_{34}H_{39}NO_2$: 493.2981. ^{1}H-NMR: δ 1.02 (ddd, $J = 13.6$, 13.6, 3.9 Hz, H(3′ax)), 1.03 (s, H(18′)), 1.23 (s, H(20′)), 1.43 (dd, $J = 12.6$, 1.7 Hz, H(5′)), 1.48 (ddd, $J = 13.0$, 13.0, 3.8 Hz, H(1′ax)), 1.61–1.80 (m, H(2′ax), H(2′eq), H(6′ax)), 1.89 (bd, $J = 13.6$ Hz, H(3′eq)), 1.95 (bdd, $J = 13.4$, 6.7 Hz, H(6′eq)), 2.31 (bd, $J = 12.3$ Hz, H(1′eq)), 2.61–2.75 (m, H(7′ax), H(7′eq)), 3.24 (d, $J = 9.1$ Hz, H(19′)), 3.33 (s, 19′-OMe), 3.53 (d, $J = 9.1$ Hz, H(19′)), 3.79 (s, 12′-OMe), 4.20 (d, $J = 16.7$ Hz, CHPh), 4.25 (d, $J = 16.7$ Hz, CHPh), 6.88 (s, H(11′)), 7.02 (td, $J = 7.4$, 0.7 Hz, H(5)), 7.04 (s, H(14′)), 7.14 (bt, $J = 7.6$ Hz, H$_{para}$), 7.16 (td, $J = 7.0$, 1.0 Hz, H(6)), 7.23 (three lines, H$_{ortho}$, H$_{meta}$). 7.37 (bd, $J = 8.1$ Hz, H(7)), 7.41 (bd, $J = 7.9$ Hz, H(4)), 8.75 (bs, NH). ^{13}C-NMR: δ 19.1 (C(2′)), 19.2 (C(6′)), 25.5 (C(20′)), 27.6 (C(18′)), 30.0 (C(7′)), 31.0 (*C*H$_2$Ph), 35.9 (C(3′)), 38.0(5) (C(10′)), 38.1 (C(4′)), 39.0 (C(1′)), 51.3 (C(5′)), 55.8 (12′-OMe), 59.4 (19′-OMe), 75.8 (C(19′)), 110.6 (C(11′)), 110.6 (C(7)), 111.4 (C(3)), 118.7 (C(13′)), 119.1 (C(4)), 119.2 (C(5)), 121.8 (C(6)), 125.5 (C$_{para}$), 127.5 (C(8′)), 128.2 (C$_{ortho}$), 128.3 (C$_{meta}$), 129.0 (C(3a)), 131.2 (C(14′)), 132.6(5) (C(2)), 135.5(5) (C$_{ipso}$), 141.9 (C(7a)), 150.8 (C(9′)), 154.9 (C(12′). MS; *m*/*z*: 493 [100, M^+], 416 [12, M − Ph$^\bullet$].

3.20. Synthesis and thermolysis of pentacarbonyl[(2-(ferrocenylethynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (18)

A solution of acetyl bromide in CH_2Cl_2 (0.71 ml, 0.152 g of CH_3COBr per millilitre, 0.88 mmol) was added to a solution of benzyltriethylammonium acylate **12** (0.573 g, 0.872 mmol) in CH_2Cl_2 (12 ml) cooled to −30°C in a foil-covered flask under nitrogen. The solution was stirred at −30°C for 1 h then cooled to −78°C. A solution of 2-(ethynylferrocene)aniline (**8**) (0.274 g, 0.910 mmol) and Et_3N (134 μl, 0.961 mmol) in CH_2Cl_2 (10 ml) was added and the temperature was held at −78°C before warming to r.t. TLC (hexanes–Et_2O, 1:1) showed that pentacarbonyl[(2-(ferrocenylethynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]-chromium (**18**) had been produced. The solvent was removed using an oil pump connected via a cold trap to the flask, and dibutyl ether (20 ml) was then added to the yellow–orange residue. The mixture was heated to 85°C for 2 h, cooled and filtered through Celite. Radial chromatography (hexanes–Et_2O, 1:1) followed by PLC

(hexanes–Et_2O, 1:1) gave an inseparable mixture of butyl 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(ferrocenyl)-1H-indole-3-acetate (**33**) (97.8 mg, 16%) and 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(2-ferrocenylmethyl)-1*H*-indole (**32**) (41.9 mg, 8%). Found: $M^{+\bullet}$, 701.3232. Calc. for $C_{43}H_{51}FeNO_4$: 701.3299 (**33**). Found: $M^{+\bullet}$, 601.2682. Calc. for $C_{38}H_{43}FeNO_2$: 601.2643 (**32**). IR (cm^{-1}): ν_{max} 3401 (NH), 1736 (C=O), 1107 (C–O–C). ^{1}H-NMR: δ 0.83–0.90 (m, CH_3CH$_2$), 1.03–1.06 (m, H(3′ax)), 1.05 (s, H(18′)), 1.08 (s, H(18′)), 1.21–1.28 (m, CH$_3$CH_2), 1.23 (s, H(20′)), 1.25 (s, H(20′)), 1.26 (s, H(20′)), 1.38 (bt, $J = 13.0$ Hz, H(5′)), 1.47 (b, H(1′ax)), 1.50–1.75 (m, CH$_3$CH$_2$CH$_2$, H(2′ax), H(2′eq), H(6′ax)), 1.92 (bd, $J =$ 12.8 Hz, H(3′eq)), 1.93 (b, H(6′eq)), 2.25–2.33 (m, H(1′eq)), 2.63–2.66 (m, H(7′ax), H(7′eq)), 3.24 (d, $J =$ 9.0 Hz, H(19′)), 3.26 (d, $J = 9.0$ Hz, H(19′)), 3.34 (s, 19′-OMe), 3.36 (s, 19′-OMe), 3.54 (d, $J = 9.0$ Hz, H(19′)), 3.56 (d, $J = 9.0$ Hz, H(19′)), 3.68 (s, 12′-OMe), 3.69 (s, 12′-OMe), 3.70 (s, 12′-OMe), 3.71 (s, 12′-OMe), 3.75–3.81 (m, CH$_2$CH_2O), 4.09 (three lines, $J = 1.4$ Hz, H(2″)), 4.18 (s, Cp), 4.25 (m, H(2″)), 4.29 (m, H(1″)), 4.36 (bs, CH$_2$Fc), 4.58 (three lines, $J = 1.1$ Hz, H(1″)), 4.60 (three lines, $J = 1.1$ Hz, H(1″)), 5.94 (s, COC*H*Fc), 5.95 (s, COC*H*Fc), 6.67 (s, H(11′)), 6.70 (s, H(11′)), 6.71 (dd, $J = 7.9$, 0.8 Hz, H(5)), 6.91–7.11 (m, H(5), H(6)), 7.15 (d, $J = 8.3$ Hz, H(6)), 7.23 (s, H(14′)), 7.25 (s, H(14′)), 7.31 (d, $J = 8.5$ Hz, H(7)), 7.38 (d, $J = 8.3$ Hz, H(7)), 7.87 (d, $J = 8.2$ Hz, H(4)), 7.95 (d, $J = 8.2$ Hz, H(4)), 7.80–8.00 (b, NH). ^{13}C-NMR: δ 13.7 (*C*H$_3$CH$_2$), 14.1 (*C*H$_3$CH$_2$), 19.1 (CH$_3$*C*H$_2$), 19.3 (C(2′)), 19.5 (C(6′)), 25.6 (C(20′)), 25.6(5) (C(20′)), 27.7 (C(18′)), 29.9 (C(7′)), 30.0(9) (C(7′)), 30.1 (*C*H$_2$Fc), 30.2 (*C*H$_2$Fc), 30.6 (CH$_3$CH$_2$*C*H$_2$), 35.5 (C(3′)), 35.9 (C(3′)), 38.0(5) (C(10′)), 38.1 (C(4′)), 38.2 (C(4′)), 39.0 (C(1′)), 39.1 (C(1′)), 51.2 (C(5′)), 51.3 (*C*HFc), 55.1 (12′-OMe), 55.2 (12′-OMe), 55.4 (12′-OMe), 55.5 (12′-OMe), 59.4 (19′-OMe), 64.6 (CO$_2$*C*H$_2$), 66.8 (C$_5$H$_4$Fe), 66.9 (C$_5$H$_4$Fe), 67.0 (C$_5$H$_4$Fe), 67.2 (C$_5$H$_4$Fe), 67.3 (C$_5$H$_4$Fe), 67.4 (C$_5$H$_4$Fe), 67.5 (C$_5$H$_4$Fe), 68.1 (Cp), 68.2 (C$_5$H$_4$Fe), 68.3 (C$_5$H$_4$Fe), 68.5 (Cp), 68.8 (C$_5$H$_4$Fe), 68.9 (C$_5$H$_4$Fe), 69.3 (C$_5$H$_4$Fe), 69.4 (C$_5$H$_4$Fe), 69.5 (C$_5$H$_4$Fe), 69.9 (C$_5$H$_4$Fe), 75.6 (C(19′)), 75.8(5) (C(19′)), 75.9 (C(19′)), 106.5 (C(11′)), 106.7 (C(11′)), 106.9 (C(11′)), 107.0 (C(11′)), 107.3 (C(3)), 107.5 (C(3)), 110.2 (C(7)), 110.4 (C(7)), 110.8 (C(7)), 110.0 (C(7)), 117.7 (C(13′)), 117.9 (C(13′)), 118.0 (C(13′)), 118.6 (C(4)), 118.9 (C(4)), 119.0 (C(4)), 120.9 (C(5)), 121.0 (C(5)), 121.6 (C(6)), 121.7 (C(6)), 126.8 (C(8′)), 127.1 (C(8′)), 127.3 (C(8′)), 127.4 (C(8′)), 128.7 (C(3a)), 128.8 (C(3a)), 129.0 (C(3a)), 129.7 (C(3a)), 131.7 (C(14′)), 131.8 (C(14′)), 133.1 (C(2)), 133.1(7) (C(2)), 133.2 (C(2)), 133.3 (C(2)), 135.6 (C(7a)), 135.7 (C(7a)), 151.1 (C(9′)), 151.3 (C(9′)), 151.6 (C(9′)), 155.0(9) (C(12′)), 155.1(4) (C(12′)), 155.2 (C(12′)), 155.2(5) (C(12′)), 172.9 (C=O), 173.0 (C=O). MS; m/z: 701 [100, $M^{+\bullet}$ (**32**)], 601 [100, $M^{+\bullet}$ (**33**)].

3.21. Synthesis and thermolysis of pentacarbonyl-[(2-(pyridylethynyl)phenylamino)(13-(12,19-dimethoxypodocarpa-8,11,13-triene))carbene]chromium (19)

A solution of acetyl bromide in CH_2Cl_2 (0.51 ml, 0.151 g of CH_3COBr per millilitre, 0.63 mmol) was added to a solution of benzyltriethylammonium acylate **12** (0.407 g, 0.619 mmol) in CH_2Cl_2 (10 ml) cooled to −30°C in a foil-covered flask under nitrogen. The solution was stirred at −30°C for 1 h then cooled to −78°C. A solution of 2-(2′-pyridinylethynyl)aniline (**9**) (0.127 g, 0.654 mmol) and Et_3N (100 μl, 0.717 mmol) in CH_2Cl_2 (10 ml) was added and the temperature was held at −78°C for 2 h before warming the mixture to r.t. TLC showed that pentacarbonyl[(2-(2′-pyridylethynyl)phenylamino)(13 - 912,19 - dimethoxypodocarpa-8,11,13-triene)) carbene]chromium (**19**) was present, but only as a minor component. The solvent was removed using an oil pump connected via a cold trap to the flask and dibutyl ether (15 ml) was added to the yellow–brown residue under nitrogen. The mixture was heated to 85°C for 1 h then the product was extracted with Et_2O and the extract was washed with water and dried. Flash chromatography gave a pale yellow oil which was purified by PLC (hexanes–Et_2O, 1:1, three elutions) followed by analytical TLC (hexanes–Et_2O, 1:1, 5 elutions) to give (i) an inseparable mixture (19.7 mg) of butyl 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(2-pyridyl)-1*H*-indole-3-acetate (**35**) (3%) and (ii) 2-[13′-(12′,19′-dimethoxypodocarpa-8′,11′,13′-triene)]-α-(2-pyridylmethyl)-1*H*-indole (**34**) (3%). Found: $M^{+\bullet}$, 594.3460. Calc. for $C_{38}H_{46}N_2O_4$: 594.3458 (**35**). Found: $M^{+\bullet}$, 494.2938. Calc. for $C_{33}H_{38}N_2O_2$: 494.2933 (**34**). IR (cm^{-1}): ν_{max} 3393 (NH), 1731 (C=O). ^{1}H-NMR: δ 0.81 (t, $J = 7.4$ Hz, CH$_2$CH_3), 1.02 (m, H(3′ax)), 1.03 (s, H(18′)), 1.04(6) (s, H(18′)), 1.05(5) (s, H(18′)), 1.23 (s, H(20′)), 1.25 (s, H(20′)), 1.42 (six lines, H(5′)), 1.47 (ddd, $J =$ 12.6, 12.6, 3.9 Hz, H(1′ax)), 1.55 (p, $J =$ CH$_3$CH_2CH$_2$), 1.61–1.80 (m, H(2′ax), H(2′eq), H(6′ax)), 1.89 (bd, $J =$ 13.6 Hz, H(3′eq)), 1.98 (bdd, $J = 13.4$, 6.8 Hz, H(6′eq)), 2.30 (bd, $J = 12.5$ Hz, H(1′eq)), 2.64–2.88 (m, H(7′ax), H(7′eq)), 3.24 (d, $J = 9.1$ Hz, H(19′)), 3.25 (d, $J = 9.1$ Hz, H(19′)), 3.33(6) (s, 19′-OMe), 3.34(3) (s, 19′-OMe), 3.34(5) (s, 19′-OMe), 3.54 (d, $J = 9.1$ Hz, H(19′)), 3.55 (d, $J = 9.1$ Hz, H(19′)), 3.67(4) (s, 12′-OMe), 3.67(9) (s, 12′-OMe), 3.76 (s, 12′-OMe), 4.14 (t, $J = 6.7$ Hz, CH_2CO$_2$Bu), 4.41 (s, CH_2Py), 5.49 (s, C*H*CO$_2$Bu), 5.50 (s, C*H*CO$_2$Bu), 6.86 (s, H(11′)), 6.87 (s, H(11′)), 7.00–7.19 (m, H(14′), H(5), H(6), H(5″)), 7.35 (bd, $J = 7.9$ Hz, H(7)), 7.39 (dd, $J = 8.0$, 1.5 Hz, H(3″)), 7.44–7.50 (m, H(4″)), 7.58 (bd, $J = 7.9$ Hz, H(4)), 8.57–8.60 (m, NH, H(6″)), 8.76 (s, NH). ^{13}C-NMR: δ 13.6 (*C*H$_3$CH$_2$), 19.0 (C(2′)), 19.1 (*C*H$_2$CH$_3$), 19.2 (C(2′)), 25.5 (C(20′)),

27.6 (C(18′)), 30.0 (C(7′)), 30.5 ($CH_3CH_2CH_2$), 34.0 (CH_2Py), 35.9 (C(3′)), 38.0(4) (C(10′)), 38.0(9) (C(4′)), 38.1(4) (C(4′)), 39.0 (C(1′)), 51.2 (C(5′)), 51.8 (BuO_2CCHPy), 55.5(5) (12′-OMe), 55.5(7) (12′-OMe), 55.7 (12′-OMe), 59.4 (19′-OMe), 64.8 ($COOCH_2$), 75.8 (C(19′)), 107.5(8) (C(11′)), 107.6(3) (C(11′)), 108.4 (C(3)), 108.5 (C(3)), 110.0 (C(7)), 110.7 (C(7)), 117.9(5) (C(13′)), 118.4 (C(13′)), 119.1 (C(4)), 119.2(5) (C(4)), 119.5 (C(5″)), 120.8 (C(5″)), 121.3 (C(5)), 121.3(5) (C(5)), 121.5 (C(6)), 121.8 (C(6)), 122.5 (C(6)), 123.0 (C(3″)), 127.2 (C(8′)), 127.5(5), C(8′)) (127.6, C(3a) (128.7, C(3a)), 131.2(5) (C(14′)), 132.0 (C(14′)), 132.1 (C(14′)), 133.1 (C(2)), 134.3(8) (C(2)), 134.4(3) (C(2)), 135.6 (C(7a)), 135.8 (C(7a)), 136.2(5) (C(4″)), 136.4(5) (C(4″)), 148.7(7) (C(6″)), 148.8(1) (C(6″)), 151.0 (C(9′)), 151.6 (C(9′)), 154.9 (C(12′)), 155.2 (C(12′)), 159.4 (C(2″)), 172.6 (C=O). MS; m/z: 594 [100, $M^{+\bullet}$ (**35**)], 494 [100, $M^{+\bullet}$ (**34**)].

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