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Ruthenium-catalysed ortho alkylation of hydroxyacetophenones; the functionalisation of ring C aromatic diterpenoids

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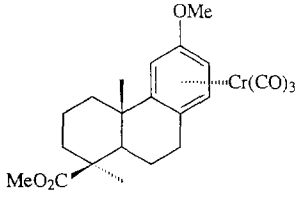
Abstract

Ortho C–H bond coupling of some 2-alkoxyacetophenones with olefins catalysed by ruthenium complexes results in a high yield of the ortho alkylated product, providing that a suitable protecting group is employed. No such protection was required for a para-alkoxy group; an activating effect was also observed. Bicyclic and tricyclic analogues react similarly.

Keywords: Alkoxyacetophenone; Ortho alkylation; Ruthenium

1. Introduction

We have described previously [1,2] the use of organotransition metal complexes as key intermediates in the cyclopentaannulation of podocarpic acid derivatives to afford ring C aromatic steroidal analogues. These approaches required the preparation and use of either an η^6-$Cr(CO)_3$ complex [1] or an η^1-$Mn(CO)_4$ complex [2]. For example, treatment of methyl 12-methoxypodocarpa-8,11,13-trien-19-oate with $Cr(CO)_6$ gave a mixture (4:1, 90%) of the diastereoisomeric α (**1**) and β (**2**) η^6 complexes. Attack of a carbanion preferentially at C14 followed by oxidative rearomatization of the η^5-cyclohexadienyl intermediate with iodine afforded a mixture (9:1, 93%) of the C14- (**3**) and C13- (**4**) alkylated regioisomers. Under Lewis acid conditions (2.2 molar equivalents $TiCl_4$, −78 °C) the mixture of **3** and **4** cyclised to give the tetracyclic indenenitrile (**5**) (14%) and the cyanoindanols (**6**) (84%).



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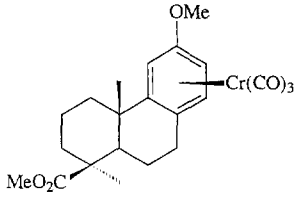

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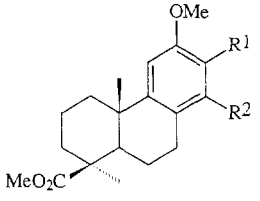
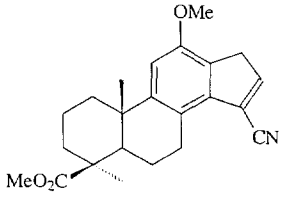


3: R^1 = H, R^2 = $CH(CN)CH_2\overline{CHO(CH_2)_2O}$

4: R^1 = $CH(CN)CH_2\overline{CHO(CH_2)_2O}$, R^2 = H



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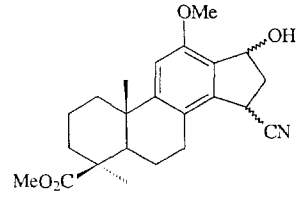

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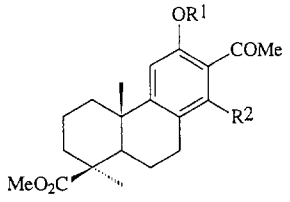
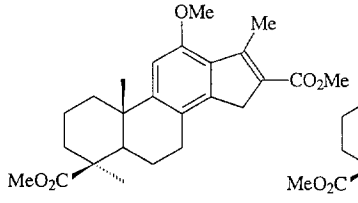
Alternatively, the ortho-manganated derivative **8** formed from treatment of the 13-acetyl diterpenoid arene **7** with $PhCH_2Mn(CO)_5$ could be converted into steroidal analogues in a one-pot sequence initiated by a C_{arene}–C coupling reaction with an alkene or an alkyne. Thus, refluxing **8** and methyl propenoate in benzene gave directly the indene **9** (48%) and the indanols **10** (50%).



7: R^1 = Me, R^2 = H
8: R^1 = Me, R^2 = $Mn(CO)_4$
41: R^1 = TBDMS, R^2 = H
42: R^1 = TBDMS, R^2 = $CH_2CH_2Si(OEt)_3$
43: R^1 = Me, R^2 = $CH_2CH_2Si(OEt)_3$



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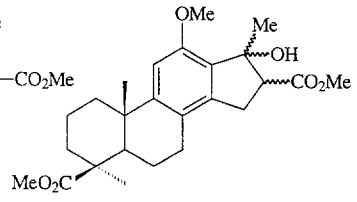

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This procedure was advantageous practically since the C_{13}–C_{17} bond construction which closes the five-membered ring occurs in situ following initial coupling of C14 with the terminal vinyl carbon of methyl propenoate, thus avoiding the separate cyclisation step required with the η^6-$Cr(CO)_3$-based chemistry. In both approaches, however, the transition metal is used in stoichiometric amounts relative to the diterpenoid. The use of a catalytic amount of a transition metal complex to promote initial coupling of the diterpenoid with an alkene (or alkyne) ligand would be preferable, since then the diterpenoid metal complex would not need to be pre-formed in a separate step. Moreover, in a catalytic process, liberation of the alkylated arene from the metal is an integral part of the cycle, and therefore no subsequent demetallation procedure is necessary. Murai and co-workers have reported the use of some ruthenium complexes to catalyse the coupling of an olefin (optimally a vinylsilane [3,4]) or an alkyne [5] with an ortho carbon of some acetophenones. This chemistry has been extended recently to include t-butylimine derivatives of aromatic aldehydes or ketones as substrates [6], and aromatic esters [7]. Alicyclic α,β-unsaturated carbonyl compounds (enones, amides, esters) also couple efficiently with vinyl silanes [8,9]. The catalysed process has found application in the step-growth copolymerisation of some substituted acetophenones and α,ω-dienes [10]. These results suggested that the procedure could also be applied to the alkylation of a podocarpane diterpenoid ketone at C14. Here we report the application of the catalysed coupling reaction to some 2- and 4-substituted acetophenones and to 6-methoxytetralone as model compounds, and to two diterpenoid ketones (some of these results have been communicated in preliminary form, see Ref. [11]).

2. Results and discussion

Our initial studies were directed towards the eventual alkylation of the 13-acetyl-12-methoxy diterpenoid **7** with methyl propenoate. However, refluxing the monocyclic model compound 2-methoxyacetophenone with methyl propenoate and a catalytic amount of $RuH_2(CO)(PPh_3)_3$ for 26 h in toluene gave no detectable coupled product. Similar treatment of the diterpenoid analogue **7** with methyl propenoate was also unsuccessful, as was the use of styrene as the olefin. The lack of reaction in these cases indicated that a study of the effect of substituents (particularly a methoxy group) on the acetophenone ring was warranted. In order to avoid potential interaction between ruthenium, the acetyl group, and an ortho substituent, leading perhaps to inhibition or quenching of the required catalytic cycle, 4-methoxyacetophenone was selected for the first study. The results are summarised in Table 1.

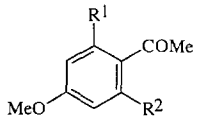
The use of $Ru(CO)_2(PPh_3)_3$ (2 mol%) as catalyst and a two-fold excess of styrene resulted in a 93% conversion (run 1). The coupled products **11** and **12** are derived respectively from the addition of either the terminal carbon or the benzylic alkene carbon to the ortho C–H bond of the aryl ketone. The ratio of **11**:**12** was close to that (76:11) found in a similar reaction using acetophenone itself, which gave the corresponding products **21** and **22** (90% combined yield). Increasing the amount of catalyst to 6 mol% relative to 4-methoxyacetophenone resulted in the bis alkylated compounds **13** and **14** becoming the major products (run 2). This result differs from that obtained from a similar reaction with acetophenone in which the monoalkylated adducts **21** and **22** were present in the (percentage) ratio of 74:9, the bis adducts **23** and **24** being formed in minor amount only (12:3.5 respectively). The regiochemistry of the bis styrene adducts **13** and **14** was confirmed readily by NMR as a consequence of the

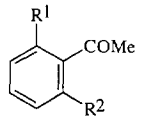
Table 1
Reactions of 4-methoxyacetophenone catalysed by $Ru(CO)_2(PPh_3)_3$

Run	Olefin/molar equivalents	Catalyst (mol%)	Time (h)	Yield (%) [a]	Products [b]
1	Styrene/2	2	24	93	**11** (82%) **12** (11%)
2	Styrene/2	6	48	100	**11** (9%) **12** (1.5%) **13** (72.5%) **14** (17%)
3	CH_2=$CHSiMe_3$/5	6	41	100	**15** (90%) **16** (5%)
4	CH_2=$CHSiMe_3$/5	2	48	100	**15** (60%) **16** (34%)
5	CH_2=$CHSiMe_3$/1.5	2	24	76	**15** (49%) **16** (15%)
6	CH_2=$CHSi(OMe)_3$/1	2	24	36	**17** (36%)
7	CH_2=$CHSi(OMe)_3$/1	6	24	100	**17** (95%)
8	CH_2=$CHSi(OEt)_3$/1	2	24	97	**18** (95%)

[a] GC yield based on remaining ketone; [b] ratio based on GC.

presence of the methoxy group. The major bis product showed only one upfield C–H resonance due to C3 at 112 ppm in the ^{13}C NMR spectrum, and H3 was a singlet at 6.62 ppm in the ^1H NMR spectrum. Hence the major component must be the symmetrical adduct **13**. The minor bis product **14** showed separate signals for C3 and C5, at 111.5 and 111.9 ppm respectively, in the ^{13}C spectrum, while in the ^1H spectrum the signals due to H3 and H5 occurred at 6.82 and at 6.83 ppm.





11: R^1 = H, R^2 = CH_2CH_2Ph
12: R^1 = H, R^2 = $CH(CH_3)Ph$
13: R^1 = R^2 = CH_2CH_2Ph
14: R^1 = $CH(CH_3)Ph$, R^2 = CH_2CH_2Ph
15: R^1 = R^2 = $CH_2CH_2SiMe_3$
16: R^1 = H, R^2 = $CH_2CH_2SiMe_3$
17: R^1 = H, R^2 = $CH_2CH_2Si(OMe)_3$
18: R^1 = H, R^2 = $CH_2CH_2Si(OEt)_3$
19: R^1 = H, R^2 = CH_2CH_3
20: R^1 = CH_2CH_3, R^2 = $CH_2CH_2SiMe_3$

21: R^1 = H, R^2 = CH_2CH_2Ph
22: R^1 = H, R^2 = $CH(CH_3)Ph$
23: R^1 = R^2 = CH_2CH_2Ph
24: R^1 = $CH(CH_3)Ph$, R^2 = CH_2CH_2Ph
25: R^1 = R^2 = $CH_2CH_2SiMe_3$
26: R^1 = H, R^2 = $CH_2CH_2SiMe_3$
27: R^1 = H, R^2 = $CH_2CH_2Si(OMe)_3$
28: R^1 = H, R^2 = $CH_2CH_2Si(OEt)_3$

Reaction of 4-methoxyacetophenone with 5 molar equivalents of vinyltrimethylsilane and 6 mol% catalyst (run 3) followed a similar trend. After 41 h reflux the bis compound **15** predominated (90%), the mono adduct **16** being formed in minor amount only (5%). Also present were **19** (1%) and **20** (4%), derived from protodesilylation of **15** and **16** respectively. The molecular formulae of the ethylated by-products **19** and **20** were confirmed by accurate mass measurements of the molecular ions in their mass spectra, ruling out the alternative possibility of carbonyl insertion into an Ru–H intermediate, which could lead to aldehydes of the same molar mass. The analogous reaction with acetophenone gave mainly bis product **25** (57%) together with a significant amount of the mono adduct **26** (36%). Reaction of 4-methoxyacetophenone with only 2 mol% catalyst gave mono (34%) and bis (60%) adducts, suggesting that it is the amount of catalyst which controls the relative amounts of these compounds (side-products **19** and **20** were present in 1% and 4% yields respectively (run 4)). It is interesting to note, however, that the bis product was still the major component, whereas from an analogous reaction with acetophenone the proportion of mono adduct **25** was slightly higher (2 mol% $Ru(CO)_2(PPh_3)_3$, 5 equivalents vinyltrimethylsilane, 48 h; mono **26** (49%) and bis **25** (52%)). These results can be rationalised by the electron-donating effect of the para methoxy group. After the initial olefin insertion, followed by reductive elimination to give the mono adduct, the ruthenium can remain coordinated to the carbonyl oxygen. Rotation about the C_{aryl}–$C_{C=O}$ bond would bring the ruthenium closer to the second ortho C–H bond so that it can then be cleaved. If the aromatic ring is electron-rich due to the presence of both a methoxy group and the alkyl sidechain from the first coupling, then rotation/insertion is apparently favoured over competitive decomplexation leading to the mono product. In an attempt to increase the relative yield of the mono adduct only 1.5 molar equivalents of vinyltrimethylsilane were used, together with 2 mol% catalyst and a shorter reflux time (24 h) (run 5). However, the bis adduct was still formed in more than three times the amount of the mono adduct. Significantly, the side-products **19** and **20** were now present in 3% and 10% yields respectively. A study by Murai et al. of the quantitative analysis of the differing reactivities of some substituted acetophenones supports the notion of bond

Table 2
Reactions of 4-acetoxyacetophenone (**29**) catalysed by $RuH_2(CO)(PPh_3)_3$

Run	Olefin/molar equivalents	Catalyst (mol%)	Time (h)	Yield (%) [a]	Products [b]
9	$CH_2=CHSi(OEt)_3$/3	2	24	1.5	**30** (1.5)
10	$CH_2=CHSi(OEt)_3$/5	6	24	66	**30** (60) **31** (6)

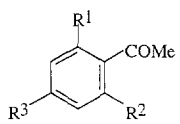
[a] GC yield based on remaining ketone; [b] ratio based on GC.

rotation competitive with decomplexation [12]. It was suggested that a large proportion of a dialkylated product results from rapid C–C bond rotation to bring the coordinated ruthenium closer to the second ortho C–H bond, and not from an alternative sequence involving decomplexation and then re-complexation of the active catalyst to the mono adduct. Weber and co-workers have reported [10] that a piperidino group para to the ketone results in shorter reaction times for the catalytic alkylation reaction, indicating rate enhancement by an electron-donating resonance effect.

Although trimethoxyvinylsilane with 2 mol% catalyst for 24 h gave only 36% conversion of 4-methoxyacetophenone into the mono adduct **17** (run 6), increasing the amount of catalyst to 6 mol% resulted in a 95% yield of this adduct only (run 7). Triethoxyvinylsilane gave a superior result; only 2 mol% catalyst for 24 h was required to obtain the mono adduct **18** in 95% yield (run 16).

For further support of the dependence of the reactivity on the electron density in the benzene ring, the reaction catalysed by $RuH_2(CO)(PPh_3)_3$ was examined using 4-acetoxyacetophenone (**27**) (Table 2).

Even with this more active catalyst, a reaction time of 24 h gave only 1.5% conversion of this less electron-rich substrate into the desired mono adduct **30** (run 9). However, increasing the amount of catalyst to 6 mol% and refluxing for the same length of time resulted in a 66% conversion into **30** (60%), together with a small amount of the bis adduct **31** (run 10). Although the decreased reactivity could be due to the electron withdrawing nature of the *p*-OCOMe functionality relative to *p*-OMe, inhibition of the catalytic cycle by competitive chelation of the ruthenium by the two oxygen atoms of the ester cannot be discounted.



29: $R^1 = R^2 = H$, $R^3 = OCOMe$
30: $R^1 = H$, $R^2 = CH_2CH_2Si(OEt)_3$, $R^3 = OCOMe$
31: $R^1 = R^2 = CH_2CH_2Si(OEt)_3$, $R^3 = OCOMe$

Changing the carbonyl functionality to an amide, i.e. refluxing 3-methoxy-*N*,*N*-dimethylbenzamide with 2 mol% $Ru(CO)_2(PPh_3)_3$ and triethoxyvinylsilane for 24 h, gave no coupled product. However, it has recently been reported [9] that coupling does occur in excellent yield with an alicyclic α,β-unsaturated amide under similar conditions. This difference between the aryl and vinyl systems is highlighted further by the success of the coupling reaction of triethoxyvinylsilane with methyl 1-cyclohexenecarboxylate; the corresponding aryl system (methyl benzoate) failed to give any adduct [7,9]. The use of a 3-acetyl group (i.e. 3-methoxyacetophenone) instead of the 3-amido group and treatment with 2 mol% $Ru(CO)_2(PPh_3)_3$ and vinyltrimethylsilane (5 equivalents) in a closed system for 48 h gave a 57% conversion into two coupled products. The major regioisomer was derived from addition to C2, as reported by Murai and co-workers using triethoxyvinylsilane [13].

Reactions with 2-methoxyacetophenone, an appropriate model for the eventual reaction using the diterpenoid **7**, are summarised in Table 3.

The most striking observation is the lower yields of products from most runs (excluding run 16), even after prolonged reaction times and using an excess of both the catalyst and the vinyl silane. For example, treatment of this ortho methoxy ketone with vinyltrimethylsilane and 6 mol% catalyst for 24 h gave only 43% conversion (run 11), and three products were formed. GC-MS analysis of the crude reaction mixture indicated the unexpected presence of a disubstituted benzene (i.e. without the methoxy group) and additionally a bis adduct. The retention times and mass spectra of these products were identical with those of compounds **25** and **26** isolated from the reaction of acetophenone itself with vinyltrimethylsilane. The presence of the methoxy substituent ortho to the carbonyl group had thus resulted in the formation of coupled products lacking the ether group; that is, hydrodemethoxylation had occurred. The desired product **32** was formed in only 24% yield. Although doubling the reaction time to 48 h (run 12) increased the yield of **32** slightly (to 28%), the two side products were again present in significant amounts.

The cleavage of the ortho methoxy group in the course of the alkylation reaction was not restricted to the use of vinyltrimethylsilane as the olefin. Thus, trimethoxyvinylsilane and 6 mol% catalyst (run 13) resulted in only 53% conversion, of which 30% was the

Table 3
Reactions of 2-methoxyacetophenone catalysed by $Ru(CO)_2(PPh_3)_3$

Run	Olefin/molar equivalents	Catalyst (mol%)	Time (h)	Yield (%) [a]	Products [b]
11	CH_2=CHSiMe$_3$/5	6	24	43	**32** (24) **26** (9) **25** (10)
12	CH_2=CHSiMe$_3$/5	6	48	45	**32** (28) **26** (8) **25** (7)
13	CH_2=CHSi(OMe)$_3$/5	6	24	53	**33** (30) **27** (22)
14	CH_2=CHSi(OEt)$_3$/1	2	24	15	**34** (5) **28** (10)
15	CH_2=CHSi(OEt)$_3$/5	6	48	75	**34** (29) **28** (45)
16	CH_2=CHSi(OEt)$_3$/5	6 [c]	24	91	**34** (29) **28** (62)

[a] GC yield based on remaining ketone; [b] ratio based on GC; [c] $RuH_2(CO)(PPh_3)_3$.

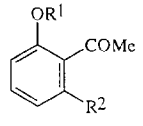
desired coupled product **33**. Although increasing the reaction time to 48 h and using triethoxyvinylsilane (run 15) resulted in a higher conversion (75%) of the substrate, a large amount (45%) of the desmethoxy alkylated compound **28** was formed, the desired product **34** being obtained in a yield similar to that afforded by trimethoxyvinylsilane. In an attempt to decrease the amount of demethoxylation, the relative amounts of both the vinyl silane and catalyst were decreased, as was the reaction time (run 14). These conditions compare directly with those using 4-methoxyacetophenone (Table 1, run 8), from which the coupled product was obtained in 95% yield and cleavage of the methoxy group did not occur. However, with 2-methoxyacetophenone as substrate these conditions resulted in only 15% conversion, and only 5% was the desired adduct **34**. The other product (10%) had a retention time (GC) and mass spectrum characteristic of **28**. Treatment of the ortho methoxy acetophenone with triethoxyvinylsilane and $RuH_2(CO)(PPh_3)_3$ (6 mol%) as catalyst for 24 h resulted in a 91% conversion into two products (run 16). However, only 29% was **34**, **28** being present in 62% yield. Thus, use of the more active catalyst resulted in a higher yield of the unwanted desmethoxy adduct **28**.

Steric effects could account for the decreased reactivity of the ortho methoxy substrate. Chelation of the carbonyl oxygen to the σ(arene)-bound ruthenium requires a bond rotation which could result in an unfavourable interaction between the methyl bonded to the carbonyl and the methyl group of the ortho ether. Such interaction can, however, be relieved by O–CH_3 rotation so that the ether methyl group is no longer proximal to the methyl ketone, allowing the desired alkylation to proceed. Alternatively, the oxygen atom of the methyl ether could provide a second and stabilizing coordination site for the ruthenium, so that insertion into the ortho C–H bond does not occur. The formation of some of the desired product **34** indicates an equilibrium between species involving the doubly oxygenated ruthenium (cf. acetylacetonato complexes) and singly coordinated ruthenium, the desired C–H bond insertion proceeding from the latter.

Cleavage of the methoxy group does not occur unless the vinyl silane is present (in the case of $Ru(CO)_2(PPh_3)_3$). Thus, refluxing 2-methoxyacetophenone and 6 mol% $Ru(CO)_2(PPh_3)_3$ in toluene for 48 h returned only starting material. Correspondingly, the use of excess triethoxyvinylsilane (and 6 mol% catalyst) increased the amount of the hydrodemethoxylation product (45%) (run 15). A decrease in the molar ratio of both the catalyst and the triethoxyvinylsilane resulted in less hydrodemethoxylation (run 14), although only a small yield of the desired adduct was formed. These results imply that cleavage of the methyl ether follows the alkylation step, and that a ruthenium hydride is an obligatory intermediate in the hydrodemethoxylation. After reductive elimination to give the saturated side chain, hydride transfer from the vinyl silane would give a doubly-oxygenated ruthenium hydride species, the demethoxylated product then being formed by insertion and hydride transfer. Of those aromatic ketones reported by Murai and co-workers [4] not to undergo the catalysed alkylation reaction, most contained substituents with lone pairs of electrons that were close to the carbonyl functionality.

If the failure of 2-methoxyacetophenone to couple with olefins to give a single product is due to the relatively small size of the methyl group, then increasing the bulk of the alkyl group may successfully hinder the (unwanted) chelation between the ketone and the ortho oxygen atom. Conversely, however, a larger substituent on the ether oxygen atom may result in a steric interaction with the methyl ketone, thus disfavouring the ruthenium-containing conformer required for C–H bond cleavage.

A number of derivatives of 2-hydroxyacetophenone were therefore synthesised, and their reactions with vinyltriethoxysilane were examined (Table 4). The use of an isopropyl ether [14] favoured the coupling reaction, but some hydrodeisopropylation occurred after a reaction time of 24 h (run 17). Decreasing the reaction time to 9 h (run 18) resulted in only a slightly lower yield of the unwanted product **28**, and, more significantly, in a lower yield also (60%) of the desired adduct **36**. Quantitative conversion of 2-isopropoxyacetophenone was achieved using excess olefin, although the side product was then present in 17% yield. Thus the isopropyl ether ortho to the ketone had not disfavoured the conformer required for the C–H bond activation, but the results were not yet optimal. A t-butyldimethylsilyl ether [15] proved to be the most effective in promoting the alkylation reaction, using either of the ruthenium catalysts and an excess of the vinyl silane (runs 20 and 21). No product from hydrodesilyloxylation was detected (GC-MS), and a quantitative yield of the 2-silyloxy alkylated adduct **38** was obtained. A benzyl ether [16], however, offered no advantage over a methyl ether and cleavage of the benzyloxy group was also observed. The use of 6 mol% catalyst resulted in an elevated yield of **28** from hydrodebenzylation, the desired adduct **40** being formed in only 29% yield. The various carbon ethers described are mildly electron-donating, which may have facilitated the eventual hydrodealkylation process observed from **35** and **39**. A less electron-donating group would result in less electron density on the ortho ether oxygen. However, neither the acetate [17] nor tosylate [18,19] derivatives of 2-hydroxyacetophenone reacted with vinyltriethoxysilane in the presence of either ruthenium catalyst.



32: R^1 = Me, R^2 = $CH_2CH_2SiMe_3$
33: R^1 = Me, R^2 = $CH_2CH_2Si(OMe)_3$
34: R^1 = Me, R^2 = $CH_2CH_2Si(OEt)_3$
35: R^1 = ^iPr, R^2 = H
36: R^1 = ^iPr, R^2 = $CH_2CH_2Si(OEt)_3$
37: R^1 = TBDMS, R^2 = H
38: R^1 = TBDMS, R^2 = $CH_2CH_2Si(OEt)_3$
39: R^1 = CH_2Ph, R^2 = H
40: R^1 = CH_2Ph, R^2 = $CH_2CH_2Si(OEt)_3$

The 12-TBDMS diterpenoid derivative **41** required 4 mol% $RuH_2(CO)(PPh_3)_3$ and an excess of triethoxyvinylsilane with a reaction time of 36 h to give the coupled adduct **42** in 98% isolated yield. In accord with the results for the catalysed alkylation reaction of **37** (the corresponding monocycle), no product from hydrodesilyloxylation was detected from any of the reactions on the diterpenoid **41**.

Table 4
Coupling reactions of derivatives of 2-hydroxyacetophenone

Run	Substrate	Olefin/ molar equivalents [a]	Catalyst (mol%)	Time (h)	Yield [d]	Products [e]
17	**35**	1	2 [b]	24	97	**36** (78) **28** (19)
18	**35**	1	2 [b]	9	77	**36** (60) **28** (17)
19	**35**	5	2 [b]	16	100	**36** (83) **28** (17)
20	**37**	5	2 [b]	24	100	**38**
21	**37**	5	2 [c]	12	100	**38**
22	**39**	3	2 [b]	24	17	**40** (8) **28** (8)
23	**39**	5	6 [c]	1	96	**40** (29) **28** (68)

[a] CH_2=CHSi(OEt)$_3$; [b] $Ru(CO)(PPh_3)_3$; [c] $RuH_2(CO)(PPh_3)_3$; [d] GC yield based on remaining ketone; [e] ratio based on GC.

The effectiveness of an ortho t-butyldimethylsilyloxy group was demonstrated further by comparison with the results from reaction of the 12-methoxy diterpenoid (**7**). The use of 6 mol% $RuH_2(CO)(PPh_3)_3$ and triethoxyvinylsilane (5 molar equivalents) for 7 days resulted in only 24% conversion of **7** into the adduct **43**. This result is in accord with those from corresponding reactions of 2-methoxyacetophenone with various vinyl silanes, for which yields of the desired coupled product were 24–30%. The crude mixture from **7** also contained side products which were not characterised, but which appeared to have lost the 12-methoxy group and then to have coupled at either C12 or C14 or both.

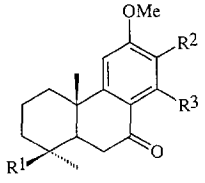
Although methyl 13-acetyl-12-methoxypodocarpa-8,11,13-trien-19-oate (**7**) gave only a moderate yield (25%) of the coupled product, the use of 13-acetyl-12-methoxy-7-oxopodocarpa-8,11,13-trien-19-oate (**44**) was investigated, since the extra chelation site at C7 may prevent the proposed unwanted doubly-oxygenated ruthenium complex being formed between the 12-OMe and 13-COMe substituents. Alternatively, a cooperative directing effect involving the 13-COMe and 7-oxo moieties may favour the desired outcome. Such an effect has been established for the tetracarbonylmanganese complex of a diterpenoid diketone. However, treatment of **44** with triethoxyvinylsilane (3 molar equivalents) and $RuH_2(CO)(PPh_3)_3$ (2 mol%) for 48 h resulted in only a trace amount (^{1}H NMR) of the coupled product. This lack of reaction may have been due to the low solubility of **44** in toluene, since a suspension remained throughout. A similar reaction with the 13-methoxycarbonyl analogue of **45** (100 mg), triethoxyvinylsilane (5 molar equivalents) and 6 mol% $Ru(CO)_2(PPh_3)_3$ for

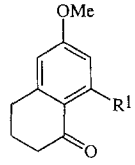
Table 5
Catalytic reactions with the diterpenoid **46** using $Ru(CO)_2(PPh_3)_3$

Run	Olefin/molar equivalents	Catalyst (mol%)	Time (h)	Yield [a]	Product
24	CH_2=CHSi(OEt)$_3$/1	2	17	0	
25	CH_2=CHSi(OEt)$_3$/1	2	48	0	
26 [c]	CH_2=CHSi(OEt)$_3$/1	2	24	0	
27	CH_2=CHSi(OEt)$_3$/5	4	48	0	
28	CH_2=CHSi(OEt)$_3$/5	2 [b]	24	0	
29	CH_2=CHSi(OEt)$_3$/5	6	48	100	**47**
30	CH_2=CHSi(OEt)$_3$/5	6	48	94	**50**
31	CH_2=CHSiMe$_3$/5	2 [b]	24	84	**48**

[a] Isolated yield; [b] $RuH_2(CO)(PPh_3)_3$; [c] C(19) methyl ether (**49**).

48 h also resulted in only a trace amount of the product. The failure of both of these reactions may be attributed to the sterically hindered C14 site in these diketone substrates.





44: R^1 = CO_2Me, R^2 = COMe, R^3 = H
45: R^1 = CO_2Me, R^2 = CO_2Me, R^3 = H
46: R^1 = CO_2Me, R^2 = R^3 = H
47: R^1 = CO_2Me, R^2 = H, R^3 = $CH_2CH_2Si(OEt)_3$
48: R^1 = CO_2Me, R^2 = H, R^3 = $CH_2CH_2SiMe_3$
49: R^1 = CH_2OMe, R^2 = H, R^3 = H
50: R^1 = CH_2OMe, R^2 = H, R^3 = $CH_2CH_2Si(OEt)_3$

51: R^1 = H
52: R^1 = $CH_2CH_2Si(OEt)_3$

The removal of the carbonyl substituent from C13, as in **46**, allows the catalysed alkylation reaction to proceed at C14 via coordination of ruthenium to the C7 oxygen atom. The bicyclic compound **51** served as a model for the diterpenoid system, and afforded the adduct **52** in 92% yield after refluxing for 38 h with triethoxyvinylsilane and 2 mol% $Ru(CO)_2(PPh_3)_3$. The results for the diterpenoid analogue **46** are summarised in Table 5. However, under conditions similar to those used for alkylation of the bicyclic compound **51**, but with a reaction time of 17 h (run 24), no coupling product resulted; increasing the reaction time to 48 h similarly gave no reaction (run 25). Since the reaction potentially could have been inhibited by the competitive coordinating ability of the C19 ester the 19-methoxymethyl ether **49** was employed, but again the alkylation was unsuccessful (run 26). Using the reagents in excess also did not effect the coupling reaction (run 27), nor did changing the catalyst to the more reactive $RuH_2(CO)(PPh_3)_3$ and using an excess of the vinyl silane (run 28). Gratifyingly, however, using 6 mol% $Ru(CO)_2(PPh_3)_3$ with an excess of the vinyl silane for 48 h afforded the coupled product **47** from the C19 methoxycarbonyl diterpenoid **46** in quantitative yield (run 29). Under the same conditions the C19 methyl ether **49** gave the desired adduct **50** in 94% yield (run 30). Subsequent experiments on **46** have shown that the success of the reaction in the case of the diterpenoids is dependent on the scale of the reaction and that a minimum weight of catalyst is required in order to obtain good yields of the coupled adducts (e.g. run 31). Thus, using vinyltrimethylsilane (5 molar equivalents), the 7-oxo diterpenoid **46** and only 2 mol% $RuH_2(CO)(PPh_3)_3$ gave an 84% conversion into the adduct **48**.

In summary, the ruthenium-catalysed coupling of acetophenone with a vinyl silane has been shown to be applicable to a range of functionalised and structurally diverse aryl ketone substrates. It was necessary to convert 2-hydroxyacetophenone and its congeners into the 2-t-butyldimethylsilyloxy ether derivatives in order to obtain a high yield of the ortho 2-(tri-alkoxysilyl)ethyl adduct. Successful extension of this chemistry to diterpenoid substrates opens the way for transformation of the alkyl silane adducts into functionalized ortho side-chains suitable for use in cyclopentaannulation of the natural products.

3. Experimental

For general experimental details, see Ref [1].

*3.1. Methyl 13-acetyl-12-(((1,1-dimethylethyl)dimethylsilyl)oxy) podocarpa-8,11,13-trien-19-oate (**41**)*

Methyl 13-acetyl-12-hydroxypodocarpa-8,11,13-trien-19-oate (2.0 g, 6.05 mmol), DBU (1.4 g, 9.1 mmol) and TBDMSCl (1.4 g, 9.1 mmol) were dissolved in benzene (30 ml). A precipitate of the amine hydrochloride was observed after heating for a short time. The resultant yellow solution was refluxed for 5 h, after which time the cooled reaction mixture was washed with water, HCl (0.1 mol l^{-1}), aqueous sodium hydrogencar-

bonate, and dried ($MgSO_4$). The crude yellow solid was then percolated through a short column of silica gel (hexanes:ether, 2:1) to give methyl 13-acetyl-12-(((1,1-dimethylethyl)dimethylsilyl)oxy)podocarpa-8,11,13-trien-19-oate (2.59 g, 96%) (**41**) as white microcrystals, m.p. 103–104 °C. ν_{max} 1716 (C=O, ester), 1662 (C=O, ketone), 1462 (C=C), 863 cm^{-1} (Si–C). δ(H) 0.23, s, 3H, Si*Me*; 0.24, s, 3H, Si*Me*; 0.99, s, 9h, CMe_3; 1.01, s, 3H, H(20); 1.08, td, 13.55, 3.95 Hz, 1H, H(3ax); 1.27, s, 3H, H(18); 1.39, td, 13.2, 3.95 Hz, 1H, H(1ax); 1.50, dd, 12.2, 1.22 Hz, 1H, H(5); 1.62–1.66, m, 1H, H(2eq); 1.93, qd, 13.1, 5.4 Hz, 1H, H(6ax); 1.99, qt, 13.8, 3.6 Hz, 1H, H(2ax); 2.08, bd, 12.9 Hz, 1H, H(3eq); 2.17, dd, 13.9, 6.1 Hz, 1H, H(6eq); 2.28, bd, 13.5 Hz, 1H, H(1eq); 2.57, s, 3H, C(O)CH_3; 2.68, ddd, 16.3, 12.8, 6.0 Hz, 1H, H(7ax); 2.86, dd, 16.5, 4.2 Hz, 1H, H(7eq); 3.66, s, 3H, 12-OCH_3; 6.75, s, 1H, H(11); 7.33, s, 1H, H(14). δ(C) −4.1, SiMe_2; 18.26, *C*Me$_3$; 19.7, C(2); 21.0, C(6); 22.7, C(20); 25.9, CMe_3; 28.4, C(18); 30.9, C(7); 31.3, C(O)CH_3; 37.5 C(3); 38.7, C(10); 39.3, C(1); 44.0, C(4); 51.0, 19-OCH_3; 52.4, C(5); 117.1, C(11); 128.3, C(13); 128.4, C(8); 130.5, C(14); 152.8, C(9); 153.5, C(12), 177.7, C(19); 199.9, 13-*C*(O)Me. *m/z* 445 (5, $M^+ + 1$), 387 (100, M − ^{t}Bu). Found: ($M^+ + 1$), 445.2787. $C_{26}H_{41}O_4Si$ calc.: (M + 1), 445.2774.

3.2. General procedure for the ruthenium-catalysed reactions

To an oven-dried 10 ml round-bottomed flask was added the catalyst, an aryl ketone, an olefin and toluene (3 ml). A reflux condenser equipped with a vacuum adapter was attached to the reaction flask. After three freeze–pump–thaw cycles the apparatus was flushed with nitrogen for 5 min and a balloon of nitrogen was fitted for the duration of the reaction. The mixture was then heated to reflux (sand bath temperature 155 °C) for the specified time, and the solution was cooled to room temperature. Toluene and any remaining olefin were then removed by rotary evaporation. The residue was passed through a short column (7 cm × 0.7 cm ID) of silica gel (hexanes:ether, 2:1) to remove any remaining ruthenium complex(es). A small sample of the crude material was retained for GC and GC-MS analyses. The product was then purified by flash chromatography.

3.3. Reaction of acetophenone with styrene

Acetophenone (0.100 g, 0.833 mmol), styrene (0.173 g, 1.665 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (0.048 g, 0.050 mmol) were refluxed for 48 h and the products isolated by flash chromatography (silica gel; benzene) to give (i) a mixture [4] of 1-(2-(2-phenylethyl)phenyl)ethanone (**21**) (74.5%) and 1-(2-(1-phenylethyl)phenyl)ethanone (**22**) (9%) as a colourless oil; (ii) a mixture of 1-(2,6-bis(2-phenylethyl)phenyl)ethanone (**23**) (12%) and 1-(2-(2-phenylethyl)-6-(1-phenylethyl)phenyl)ethanone) (**24**) (3.5%) as a colourless oil. ν_{max} 1695 (C=O), 1258 (C=C), 700 cm^{-1}. δ(H) 1.60, d, 3H, 7.2 Hz, CH_3 (minor); 2.35, s, 6H, C(O)CH_3; 2.72–2.94, m, 12H, PhCH_2; 4.18, q, 1H, 7.2 Hz, C–*H* (minor); 7.07–7.35, m, 14H, Ar–*H*. δ(C) 22.4, *C*H_3 (minor); 32.9, C(O)*C*H_3; 35.5, Ph–CH_2; 37.9, Ph–CH_2; 41.1, *C*–H (minor); 125.4, 126.1, 127.2, 127.8, 128.4, 128.6, 129.0, 136.3, 141.4, (Ar–*C*); 208.0, (C=O). *m/z* 328 (2, M^+), 310 (90, M − H_2O), 219 (60, 310 − $PhCH_2$), 91 (100, $PhCH_2$). Found: ($M^+ + H$), 329.1910. $C_{24}H_{25}O$ calc.: (M + H), 329.1905.

3.4. Reactions of 4-methoxyacetophenone

3.4.1. With styrene

4-Methoxyacetophenone (0.100 g, 0.67 mmol), styrene (0.139 g, 1.33 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (0.038 g, 0.050 mmol) were refluxed for 48 h. Reduced-pressure distillation gave:

(i) a mixture of 1-(4-methoxy-2-(2-phenylethyl)phenyl)ethanone (**11**) (9%) and 1-(4-methoxy-2-(1-phenylethyl)phenyl)ethanone (**12**) (1.5%) as a colourless oil. ν_{max} 1673 (C=O), 1601 (C=C), 1247 cm^{-1} (C–O). δ(H) 1.57, d, 7.11 Hz, 3H, CH_3 (minor); 2.42 s, 3H, C(O)CH_3 (minor); 2.54, s, 3H, C(O)CH_3 (major); 2.82–2.90, m, 2H, PhCH_2; 3.16–3.23, m, 2H, PhCH_2; 3.77, s, 3H, OCH_3 (minor); 3.79, s, 3H, OCH_3 (major); 5.15, q, 1H, 7.07 Hz, C–*H* (minor); 6.67, d, 2.58 Hz, 2H, H(3); 6.75, dd, 8.63, 2.64 Hz, 2H, H(5); 7.13–7.32, m, 10H, Ar–*H*; 7.61, d, 8.6 Hz, 1H, H(6) (minor); 7.74, d, 8.63 Hz, 1H, H(6) (major). δ(C) 21.9, *C*H_3 (minor); 29.2, C(O)*C*H_3; 37.2, Ph*C*H_2; 37.8, Ph*C*H_2; 39.3, *C*–H (minor); 55.3, O*C*H_3; 109.8, C(5) (minor); 110.9, C(5) (major); 115.1, C(3) (minor); 116.9, C(3) (major); 125.8, 128.2, 128.6, 129.7, 131.5, 132.6, 145.1, 145.7, (Ar–*C*); 161.0, C(4); 199.5, (C=O) (minor); 201.1, (C=O) (major). *m/z* 254 (15, M^+), 239 (100, M − Me), 91 (40, $PhCH_2$). Found: M^+, 254.13054. $C_{24}H_{25}O$ calc.: M, 254.13068;

(ii) a mixture of 1-(4-methoxy-2,6-bis(2-phenylethyl)phenyl)ethanone (**13**) (72.5%) and 1-(4-methoxy-2-(2-phenylethyl)-6-(1-phenylethyl)phenyl)ethanone) (**14**) (17%) as a colourless oil. ν_{max} 1693 (C=O), 1600 (C=C) and 699 cm^{-1}. δ(H) 1.62, d, 7.1 Hz, 3H, CH_3 (minor); 2.18, s, 3H, C(O)CH_3 (minor); 2.38, s, 3H, C(O)CH_3 (major); 2.78–2.94, m, 12H, PhCH_2; 3.75, s, 6H, OCH_3; 4.2, q, 7.05 Hz, 1H, C–*H* (minor); 6.62, s, 2H, H(3) (major); 6.82, s, 1H, H(3) (minor); 6.83, s, 1H, H(5) (minor); 7.18–7.35, m, 20H, (Ar–*H*). δ(C) 22.9, *C*H_3; 33.1, C(O)*C*H_3; 35.6, Ph*C*H_2; 37.8, Ph*C*H_2; 41.0, *C*–H; 55.1, O*C*H_3; 115.5, C(3); 111.9, C(5); 112.6, C(3) (major); 126.0, 126.5, 127.7, 127.9, 128.3, 135.1, 138.0, 138.4, 141.3, 143.2, 145.2, (Ar–*C*);

159.0, C(4); 207.9, (C=O) (major); 208.5, (C=O) (minor). m/z 358 (10, M^+), 343 (100, $M-CH_3$). Found: M^+, 358.1929. $C_{25}H_{26}O_2$ calc.: M, 358.1933.

3.4.2. With vinyltrimethylsilane

4-Methoxyacetophenone (0.1 g, 0.67 mmol), vinyltrimethylsilane (0.34 g, 3.35 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (12.6 mg, 0.0134 mmol) were refluxed for 48 h. Flash chromatography (silica gel, hexanes:benzene, 1:1) gave:

(i) 1-(4-methoxy-2-(2-(trimethylsilyl)ethyl)-phenyl)ethanone (**15**) (34%) as a brown oil. ν_{max} 1676 (C=O), 1601 (C=C), 1259 and 835 cm^{-1} (Si–C). δ(H) 0.043, s, 9H, $SiMe_3$; 0.75–0.83, m, 2H, $CH_2CH_2SiMe_3$; 2.56, s, 3H, $C(O)CH_3$; 2.84–2.92, m, 2H, $CH_2CH_2SiMe_3$; 3.79, s, 3H, OCH_3; 6.75, dd, 8.6, 2.6, Hz, 1H, H(5); 6.78, d, 2.6 Hz, 1H, H(3); 7.73, d, 8.56 Hz, 1H, H(6). δ(C) −1.8, $SiMe_3$; 19.1, $CH_2CH_2SiMe_3$; 27.6 $CH_2CH_2SiMe_3$; 29.3, $C(O)CH_3$; 55.5, OCH_3; 110.2, C(5); 116.0, C(3); 129.3, C(1); 132.6, C(6); 149.8, C(2); 162.1, C(4); 199.5, (C=O). m/z 250 (26, M^+), 235 (100, M − Me), 177 (35, $M-SiMe_3$), 73 (65, $SiMe_3$). Found: M^+, 250.1389. $C_{14}H_{22}O_2Si$ calc.: M, 250.1387;

(ii) 1-(4-methoxy-2,6-bis((2-trimethylsilyl)ethyl)phenyl)ethanone (**16**) (60%) as a brown oil. ν_{max} 1694 (C=O), 1247, 860 and 835 cm^{-1} (Si–C). δ(H) 0.022, s, 9H, $SiMe_3$; 0.76–0.85, m, 2H, $CH_2CH_2SiMe_3$; 2.40–2.49, m, 2H, $CH_2CH_2SiMe_3$; 2.45, s, 3H, $C(O)CH_3$; 3.79, s, 3H, OCH_3; 6.58, s, 2H, H(3,3′). δ(H) −1.9, $SiMe_3$; 19.2, $CH_2CH_2SiMe_3$; 27.6 $CH_2CH_2SiMe_3$; 33.2, $C(O)CH_3$; 55.1, OCH_3; 111.3, C(3); 133.9, C(1); 142.2, C(2); 159.8, C(4); 208.0, (C=O). m/z 250 (21, M^+), 235 (78, M − Me), 177 (35, $M-SiMe_3$), 73 (100, $SiMe_3$). Found: M^+, 350.2099. $C_{19}H_{34}O_2Si_2$ calc.: M, 350.2097.

3.4.3. With trimethoxyvinylsilane

4-Methoxyacetophenone (0.1 g, 0.67 mmol), trimethoxyvinylsilane (0.1 g, 0.67 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (0.0372 g, 0.0402 mmol) were refluxed for 24 h. Flash chromatography (silica gel, benzene) gave 1-(4-methoxy-2-(2-(trimethoxysilyl)ethyl)phenyl)ethanone (**17**) (95%) as a colourless oil. ν_{max} 1670 (C=O), 1085 cm^{-1} (Si–O). δ(H) 0.93–1.01, m, 2H, $CH_2CH_2Si(OMe)_3$; 2.52, s, 3H, $C(O)CH_3$; 2.93–3.02, m, 2H, $CH_2CH_2Si(OMe)_3$; 3.58, s, 9H, $Si(OMe)_3$; 3.81 s, 3H, OCH_3; 6.73, dd, 1H, 8.5, 2.6 Hz, H(5); 6.76, d, 1H, 7.24 Hz, H(3); 7.70, d, 1H, 8.44 Hz, H(6). δ(C) 11.4, $CH_2CH_2Si(OMe)_3$; 28.2, $CH_2CH_2Si(OMe)_3$; 29.2, $C(O)CH_3$; 50.5, $Si(OMe)_3$; 55.2, OCH_3; 110.7, C(5); 116.1, C(3); 129.2, C(1); 132.7, C(6); 148.6, C(2); 162.1, C(4); 199.5, (C=O). m/z 298 (7, M^+), 266 (100, M − MeOH), 121 (65, $Si(OMe)_3$). Found: M^+, 298.1233. $C_{14}H_{22}O_5Si$ calc.: M, 298.1237.

3.4.4. With triethoxyvinylsilane

4-Methoxyacetophenone (0.1 g, 0.67 mmol), triethoxyvinylsilane (0.128 g, 0.67 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (0.0126 g, 0.0134 mmol) were refluxed for 24 h. Flash chromatography (silica gel; hexanes:ether, 4:1) gave 1-(2-(2-(triethoxysilyl)ethyl)-4-methoxyphenyl)ethanone (**18**) (95%) as a colourless oil. ν_{max} 1676 (C=O), 1602 (C=C), 1078 cm^{-1} (Si–O). δ(H) 0.91–1.0, m, 2H, $CH_2CH_2Si(OEt)_3$; 1.25, t, 9H, 6.99 Hz, OCH_2CH_3; 2.51, s, 3H, $C(O)CH_3$; 2.94–3.03, m, 2H, $CH_2CH_2Si(OEt)_3$; 3.81, s, 3H, OCH_3; 3.82, q, 6H, 7.0 Hz, OCH_2CH_3; 6.71, dd, 1H, 8.6, 2.6 Hz, H(5); 6.78, d, 1H, 2.6 Hz, H(3); 7.69, d, 1H, 8.6 Hz, H(6). δ(C) 12.5, $CH_2CH_2Si(OEt)_3$; 18.2, OCH_2CH_3; 28.0, $CH_2CH_2Si(OEt)_3$; 29.2, $C(O)CH_3$; 55.2, OCH_3; 58.3, OCH_2CH_3; 110.5, C(5); 116.0, C(3); 129.4, C(1); 132.5, C(6); 148.7, C(2); 162.0, C(4); 199.4, (C=O). m/z 340 (5, M^+), 294 (100, M − EtOH), 279 (40, 294 − Me). Found: M^+, 340.1692. $C_{17}H_{28}O_5Si$ calc.: M, 340.1706.

3.5. Reaction of 1-(4-(acetyloxy)phenyl)ethanone

1-(4-(Acetyloxy)phenyl)ethanone (0.1 g, 0.56 mmol), triethoxyvinylsilane (0.350 g, 1.68 mmol) and carbonyldihydrotris(triphenylphosphine)ruthenium (0.031 g, 0.034 mmol) were refluxed for 24 h and the product isolated by reduced-pressure distillation to give 1-(4-acetyloxy-2-(2-(triethoxysilyl)ethyl)phenyl)ethanone (**30**) (60%) as a colourless oil, b.p. 105 °C/0.60 mm Hg. ν_{max} 1768 (C=O, ester), 1658 (C=O, ketone), 1077 cm^{-1} (Si–O). δ(H) 0.88–0.97, m, 2H, $CH_2CH_2Si(OEt)_3$; 1.22, t, 9H, 7.0 Hz, OCH_2CH_3; 2.25, s, 3H, $OC(O)CH_3$; 2.52, s, 3H, $C(O)CH_3$; 2.88–2.97, m, 2H, $CH_2CH_2Si(OEt)_3$; 3.79, q, 6H, 7.0 Hz, OCH_2CH_3; 6.96, dd, 1H, 8.4, 2.46 Hz, H(5); 6.98, d, 1H, 2.2 Hz, H(3); 7.64, d, 1H, 8.4 Hz, H(6). δ(C) 12.5, $CH_2CH_2Si(OEt)_3$; 18.2, OCH_2CH_3; 20.9, $OC(O)CH_3$; 27.3, $CH_2CH_2Si(OEt)_3$; 29.6, $C(O)CH_3$; 58.3, OCH_2CH_3; 118.7, C(5); 123.3, C(3); 130.7, C(6); 133.7, C(1); 147.4, (2); 152.6 C(4); 168.8, (C=O) ester; 200.4, (C=O) ketone. m/z 368 (5, M^+), 322 (100, M − EtOH), 280 (98, 322 − CH_2=C=O), 43 (60, $COCH_3$). Found: M^+, 368.1646. $C_{18}H_{28}O_6Si$ calc.: M, 368.1655.

3.6. Reactions of 2-methoxyacetophenone

3.6.1. With vinyltrimethylsilane

2-Methoxyacetophenone (0.109 g, 0.762 mmol), vinyltrimethylsilane (0.38 g, 3.81 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (0.043 g, 0.0457 mmol) were refluxed for 48 h. Flash chromatography (silica gel; hexanes:ether, 10:1) gave 1-(2-methoxy-6-(2-(trimethylsilyl)ethyl)phenyl)ethanone (**32**)

(28%) as a colourless oil. ν_{max} 1697 (C=O), 1597, 1467 (C=C), 1260 (C–O–C), 1247, 860, 834 cm^{-1} (Si–C). δ(H) 0.013, s, 9H, SiMe_3; 0.73–0.82, m, 2H, $CH_2CH_2SiMe_3$; 2.43–2.52, m, 2H, $CH_2CH_2SiMe_3$; 2.47, s, 3H, C(O)CH_3; 3.79, s, 3H, OCH_3; 6.72, d, 8.27 Hz, 1H, H(3); 6.82, d, 8.25 Hz, 1H, H(5); 7.22, t, 8.25 Hz, 1H, H(4). δ(C) −1.91, SiMe_3; 19.4, $CH_2CH_2SiMe_3$; 27.0, $CH_2CH_2SiMe_3$; 32.4, C(O)CH_3; 55.5, OCH_3; 108.1, C(3); 121.3, C(5); 129.8, C(4); 130.6, C(1); 143.2, C(6); 156.0, C(2); 205.6, (C=O). m/z 250 (25, M^+), 235 (100, M − Me), 73 (90, $SiMe_3$). Found: M^+, 250.1390. $C_{14}H_{22}O_2Si$ calc.: M, 250.1389.

3.6.2. With trimethoxyvinylsilane

2-Methoxyacetophenone (0.109 g, 0.76 mmol), trimethoxyvinylsilane (0.564 g, 3.81 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (0.043 g, 0.0456 mmol) were refluxed for 24 h and the product isolated by fractional reduced-pressure distillation (Kugelrohr) to give 1-(2-methoxy-6-(2-(trimethoxysilyl)ethyl)phenyl)ethanone (**33**) (30%) as a colourless oil. ν_{max} 1693 (C=O), 1073 cm^{-1} (Si–O). δ(H) 0.89–0.97, m, 2H, $CH_2CH_2Si(OMe)_3$; 2.47, s, 3H, C(O)CH_3; 2.52–2.61, m, 2H, $CH_2CH_2Si(OMe)_3$; 3.53, s, 9H, Si(OMe)$_3$; 3.78 s, 3H, OCH_3; 6.72, d, 1H, 7.8 Hz, H(3); 6.82, d, 1H, 7.72 Hz, H(4); 7.72, t, 1H, 7.80 Hz, H(3). $\delta(C)_C$ 11.8, $CH_2CH_2Si(OMe)_3$; 25.8, $CH_2CH_2Si(OMe)_3$; 32.3, C(O)CH_3; 50.4, Si(OMe)$_3$; 55.5, OCH_3; 108.3, C(3); 121.3, C(5); 129.9, C(4); 130.6, C(1); 142.1, C(6); 156.0, C(2); 205.5, (C=O).

3.6.3. With triethoxyvinylsilane

2-Methoxyacetophenone (0.109 g, 0.762 mmol), triethoxyvinylsilane (0.725 g, 3.81 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (0.043 g, 0.046 mmol) were refluxed for 48 h. Flash chromatography (silica gel; benzene:hexanes, 3:1) and then p.l.c. (hexanes:ethyl acetate, 9:1) gave 1-(6-(2-(triethoxysilyl)ethyl)-2-methoxyphenyl)ethanone (**34**) (29%) as a colourless oil. ν_{max} 1684 (C=O), 1078 cm^{-1} (Si–O). δ(H) 0.87–0.96, m, 2H, $CH_2CH_2Si(OEt)_3$; 1.21, t, 9H, 6.99 Hz, OCH_2CH_3; 2.48, s, 3H, C(O)CH_3; 2.54–2.63, m, 2H, $CH_2CH_2Si(OEt)_3$; 3.79, s, 3H, OCH_3; 3.81, q, 6H, OCH_2CH_3; 6.73, d, 8.25 Hz, 1H, H(3); 6.84, d, 8.25 Hz, 1H, H(5); 7.23, t, 8.25 Hz, 1H, H(4). δ(C) 13.01, $CH_2CH_2Si(OEt)_3$; 18.3, OCH_2CH_3; 26.0, $CH_2CH_2Si(OEt)_3$; 32.4, C(O)CH_3; 55.5, OCH_3; 58.4, OCH_2CH_3; 108.2, C(3); 121.4, C(5); 129.4, C(4); 142.4, C(6); 155.9, C(2); 205.6, (C=O); C(1) not detected. m/z 340 (7, M^+), 294 (100, −EtOH). Found: M^+, 340.1710. $C_{17}H_{28}O_5Si$ calc.: M, 340.1706.

3.7. Reaction of 1-(2-(1-methylethoxy)phenyl)ethanone (35)

1-(2-(1-Methylethoxy)phenyl)ethanone (**35**) (0.1 g, 0.56 mmol), triethoxyvinylsilane (0.54 g, 2.8 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (0.0106 g, 0.0112 mmol) were refluxed for 16 h. Flash chromatography (silica gel; benzene) gave 1-(6-(2-(triethoxysilyl)ethyl)-2-(1-methylethoxy)phenyl)ethanone (**36**) (83%) as a brown oil. ν_{max} 1698 (C=O), 1261 (C–O), 1078 cm^{-1} (Si–O). δ(H) 0.86–0.94, m, 2H, $CH_2CH_2Si(OEt)_3$; 1.16, d, 6H, 6.0 Hz, C(Me)$_2$H; 1.26, t, 9H, 7.04 Hz, OCH_2CH_3; 2.45, s, 3H, C(O)CH_3; 2.52–2,60, m, 2H, $CH_2CH_2Si(OEt)_3$; 3.78, q, 6H, 7.0 Hz, OCH_2CH_3; 4.50, sp, 1H, 6.05 Hz, OC(Me)$_2H$; 6.69, d, 1H, 7.7 Hz, H(3); 6.78, d, 1H, 7.65 Hz, H(5); 7.16, t, 1H, 7.7 Hz, H(4). δ(C) 12.9, $CH_2CH_2Si(OEt)_3$; 18.2, OCH_2CH_3; 22.0, OC(Me)$_2$H; 26.1, $CH_2CH_2Si(OEt)_3$; 32.4, C(O)CH_3; 58.3, OCH_2CH_3; 70.5, OC(Me)$_2$H; 110.5, C(3); 121.1, C(5); 130.6, C(4); 142.6; (6); 154.3, C(2); 205.7, (C=O); C(1) not detected. m/z 368 (5, M^+), 322 (100, M − EtOH), 163 (75, Si(OEt)$_3$). Found: M^+, 368.2017. $C_{19}H_{32}O_5Si$ calc.: M, 368.2019.

3.8. Reaction of 1-(2-(((1,1-dimethylethyl)dimethylsilyl)oxy)phenyl)ethanone (37)

1-(2-(((1,1-Dimethylethyl)dimethylsilyl)oxy)phenyl)ethanone (**37**) (0.1 g, 0.4 mmol), triethoxyvinylsilane (0.38 g, 2 mmol) and carbonyldihydrotris(triphenylphosphine)ruthenium (0.00733 g, 0.008 mmol) were refluxed for 12 h. Reduced-pressure distillation gave 1-(6-(2-(triethoxysilyl)ethyl)-2-(((1,1-dimethylethyl)dimethylsilyl)-oxy)phenyl)ethanone (**38**) (100%) as a brown oil, b.p. 90 °C/0.2 mm Hg. ν_{max} 1701 (C=O), 1081 (Si–O) and 840 cm^{-1} (Si–C). δ(H) 0.15, s, 6H, SiMe_2; 0.83–0.92, m, 2H, $CH_2CH_2Si(OEt)_3$; 0.92, s, 9H, CMe_3; 1.18, t, 9H, 7.04 Hz, OCH_2CH_3; 2.45, s, 3H, C(O)CH_3; 2.50–2.59, m, 2H, $CH_2CH_2Si(OEt)_3$; 3.77, q, 6H, 7.0 Hz, OCH_2CH_3; 6.60, d, 1H, 7.8 Hz, H(3); 6.80, d, 1H, 7.8 Hz, H(5); 7.09, t, 1H, 7.8 Hz, H(4). δ(C) −4.4, SiMe_2; 12.9, $CH_2CH_2Si(OEt)_3$; 17.9, CMe$_3$; 18.2, OCH_2CH_3; 25.5, CMe_3; 26.1, $CH_2CH_2Si(OEt)_3$; 32.5, C(O)CH_3; 58.3, OCH_2CH_3; 116.3, C(3); 121.6, C(5); 129.5, C(4); 133.5, C(1); 142.2; (6); 151.6, C(2); 205.7, (C=O). m/z 440 (< 1, M^+), 383 (100, M − ^{t}Bu), 337 (7, 383 − EtOH). Found: M^+, 440.2373. $C_{22}H_{40}O_5Si_2$ calc.: M, 440.2414.

3.9. Reaction of 1-(2-(phenylmethoxy)phenyl)ethanone (39)

1-(2-(Phenylmethoxy)phenyl)ethanone (**39**) (0.1 g, 0.442 mmol), (0.1 g, 0.4 mmol), triethoxyvinylsilane (0.520 g, 2.73 mmol) and carbonyldihydrotris(triphenylphosphine)ruthenium (0.025 g, 0.0273 mmol) were refluxed for 24 h. Reduced-pressure distillation gave 1-(6-(2-(triethoxysilyl)ethyl)-2-(phenylmethoxy)phenyl)ethanone (**40**) (28%) as a brown oil, b.p. 130 °C/0.30 mm Hg. ν_{max} 1697 (C=O), 1079 (Si–O), 734 cm^{-1}. δ(H) 0.90–0.99, m, 2H, $CH_2CH_2Si(OEt)_3$;

1.22, t, 9H, 6.94 Hz, OCH_2CH_3; 2.50, s, 3H, $C(O)CH_3$; 2.57–2.66, m, 2H, $CH_2CH_2Si(OEt)_3$; 3.83, q, 6H, 7.0 Hz, OCH_2CH_3; 5.05, s, 2H, OCH_2Ph; 6.77, d, 1H, 8.3 Hz, H(3); 6.86, d, 1H, 8.2 Hz, H(5); 7.20, t, 1H, 8.2 Hz, H(4); 7.30–7.71, m, 5H, Ar–H. δ(C) 12.9, $CH_2CH_2Si(OEt)_3$; 18.2, OCH_2CH_3; 26.2, $CH_2CH_2Si(OEt)_3$; 32.4, $C(O)CH_3$; 58.3, OCH_2CH_3; 70.3, OCH_2Ph; 109.5, C(3); 121.6, C(5); 129.8, C(4); 127.0, 127.8, 128.3, 128.4, 131.9, 132.1 (Ar–C); 136.5, C(1); 142.4, C(6); 154.6, C(2); 205.4, (C=O). *m/z* 416 (2, M^+), 325 (30, M − $PhCH_2$), 279 (35, 325 − EtOH), 91 (100, $PhCH_2$). Found: M^+, 416.2019. $C_{23}H_{32}O_5Si$ calc.: M, 416.2019.

3.10. Reaction of 3,4-dihydro-6-methoxy-1(2H)-naphthalenone (51)

3,4-Dihydro-6-methoxy-1(2*H*)-naphthalenone (**51**) (0.1 g, 0.57 mmol), triethoxyvinylsilane (0.108 g, 0.57 mmol) and dicarbonyltris(triphenylphosphine)ruthenium (10.8 mg, 0.0114 mmol) were refluxed for 38 h. Flash chromatography (silica gel; benzene:ether, 8:1) gave 8-(2-(triethoxysilyl)ethyl)-3,4-dihydro-6-methoxy-1(2*H*)-naphthalenone (**52**) (92%) as a brown oil. ν_{max} 1668 (C=O), 1596 (C=C), 1078 cm^{-1} (Si–O). δ(H) 0.88–0.96, m, 2H, $CH_2CH_2Si(OEt)_3$; 1.19, t, 9H, 7.05 Hz, OCH_2CH_3; 1.99, p, 6.6 Hz, 2H, H(3); 2.52, t, 2H, 6.5 Hz, H(2); 2.83, t, 6.1 Hz, 2H, H(4); 3.04–3.13, m, 2H, $CH_2CH_2Si(OEt)_3$; 3.76, s, 3H, OCH_3; 3.80, q, 6H, 7.0 Hz, OCH_2CH_3; 6.49, d, 1H, 2.50 Hz, H(5); 6.59, d, 1H, 2.5 Hz, H(7). δ(C) 11.94, $CH_2CH_2Si(OEt)_3$; 18.2, OCH_2CH_3; 22.8; C(3); 28.9, $CH_2CH_2Si(OEt)_3$; 31.6, C(2); 40.8, C(4); 55.0, OCH_3; 58.1, OCH_2CH_3; 110.8, C(5); 114.8, C(7); 121.5, C(8a); 148.4, C(4a); 150.9, C(8); 161.9, C(6); 197.9, (C=O). *m/z* 366 (5, M^+), 320 (100, M − EtOH). Found: M^+, 366.1867. $C_{18}H_{30}O_5Si$ calc.: M, 366.1863.

3.11. Reactions of methyl 12-methoxy-7-oxopodocarpa-8,11,13-trien-19-oate (46)

3.11.1. With triethoxyvinylsilane

Methyl 12-methoxy-7-oxopodocarpa-8,11,13-trien-19-oate (**46**) (0.2 g, 0.630 mmol), triethoxyvinylsilane (0.60 g, 3.15 mmol) and carbonyldihydrotris(triphenylphosphine)ruthenium (0.0116 g, 0.0126 mmol) were refluxed for 24 h and the product isolated by flash chromatography (silica gel; hexanes:ether, 2:1) to give methyl 14-(2-(triethoxysilyl)ethyl)-12-methoxy-7-oxopodocarpa-8,11,13-trien-19-oate (90%) (**47**) as an orange oil. ν_{max} 1727 (C=O, ester), 1670 (C=O, ketone), 1078 (Si–O), 1280 cm^{-1} (C–O–C). δ(H) 0.89–0.98, 2H, $CH_2CH_2Si(OEt)_3$; 1.00, s, 3H, H(20); 1.02, td, 13.7, 3.7 Hz, 1H, H(3ax); 1.18, s, 3H, H(18); 1.19, t, 9H, 7.0 Hz, OCH_2CH_3; 1.45, td, 13.1, 3.8 Hz, 1H, H(1ax); 1.60, bd, 14.1 Hz, 1H, H(2eq); 1.89–1.95, m, 2H, H(5), H(2ax); 2.27–2.31, m, 2H, H(1eq), H(3eq); 2.80, dd, 17.9, 3.3 Hz, 1H, H(6eq); 3.01–3.39, m, 3H, H(6ax), $CH_2CH_2Si(OEt)_3$; 3.69, s, 3H, 19-OCH_3; 3.84, s, 3H, 12-OCH_3; 3.89, q, 7.0 Hz, 6H, OCH_2CH_3; 6.67, d, 2.5 Hz, 1H, H(11); 6.77, d, 2.5 Hz, 1H, H(13). δ(C) 12.1, $CH_2CH_2Si(OEt)_3$; 18.2, OCH_2CH_3; 19.7, C(2); 21.3, C(20); 27.7, C(18); 29.4, $CH_2CH_2Si(OEt)_3$; 37.2, C(6), 39.03, C(3) C(1); 39.3, C(10); 43.7, C(4); 49.3, C(5); 51.3, 19-OCH_3; 55.0, 12-OCH_3; 58.2, OCH_2CH_3; 108.3, C(11); 113.8, C(13); 122.4, C(8); 150.8, C(14); 158.4, C(9); 162.4, C(12); 176.8, C(19); 198.4, C(7). *m/z* 506 (5, M^+), 460 (100, M − EtOH), 163 (15, $Si(OEt)_3$). Found: M^+, 506.2694. $C_{27}H_{42}O_7Si$ calc.: M, 506.2700.

3.11.2. With vinyltrimethylsilane

Methyl 12-methoxy-7-oxopodocarpa-8,11,13-trien-19-oate (**46**) (0.2 g, 0.630 mmol), vinyltrimethylsilane (0.317 g, 3.17 mmol) and carbonyldihydrotris(triphenylphosphine)ruthenium (11.6 mg, 0.0126 mmol) were refluxed for 24 h and the product isolated by flash chromatography (silica gel; hexanes:ether, 2:1) to give methyl 12-methoxy-14-(2-(trimethylsilyl)ethyl)-7-oxopodocarpa-8,11,13-trien-19-oate (**48**) (84%) as a yellow oil. ν_{max} 1727 (C=O ester), 1667 (C=O ketone), 862, 835 cm^{-1} (Si–C). δ(H) 0.072, s, 9H, $SiMe_3$; 0.78–0.88, 2H, $CH_2CH_2SiMe_3$; 0.091, s, 3H, H(20); 1.10, td, 13.5, 4.2 Hz, 1H, H(3ax); 1.25, s, 3H, H(18); 1.52, td, 13.5, 4.3 Hz, 1H, H(1ax); 1.69, bd, 14.0 Hz, 1H, H(2eq); 1.99, dd, 1H, H(5); 2.0, qt (partially obscured), 13.9, 4.5 Hz, 1H, H(2ax); 2.28, m, 2H, H(1eq), H(3eq); 2.89, dd, 14.0, 4.3 Hz, 1H, H(6eq); 2.94–3.07, m, 2H, $CH_2CH_2SiMe_3$; 3.19, dd, 17.9, 14.4 Hz, 1H, H(6ax); 3.68, s, 3H, 19-OCH_3; 3.84, s, 3H, 12-OCH_3; 6.63, d, 2.6 Hz, 1H, H(11); 6.76, d, 2.6 Hz, 1H, H(13). δ(C) −1.809, $SiMe_3$; 18.8, $CH_2CH_2SiMe_3$; 19.8, C(2); 21.4, C(20); 27.7, C(18); 30.9, $CH_2CH_2SiMe_3$; 37.2, C(6); 39.08, C(3); 39.13, C(1); 39.3, C(10); 43.8, C(4); 49.4, C(5); 51.4, 19-OCH_3; 55.1, 12-OCH_3; 108.2, C(11); 113.7, C(13); 122.4, C(8); 152.8, C(14); 158.5, C(9); 162.4, C(12); 176.8, C(19); 198.7, C(7). *m/z* 416 (90, M^+), 401 (95, M − 15), 343 (100, M − $SiMe_3$), 73 (50, $SiMe_3$). Found: M^+, 416.2380. $C_{24}H_{36}O_4Si$ calc.: M, 416.2383.

3.12. 14-(2-(Triethoxysilyl)ethyl)-12,19-dimethoxypodocarpa-8,11,13-trien-7-one (50)

12,19-Dimethoxypodocarpa-8,11,13-trien-7-one (**49**) (0.1 g, 0.331 mmol), triethoxyvinylsilane (0.315 g, 1.66 mmol) and dicarbonyltris(triphenylphosphine)-ruthenium (18.8 mg, 0.0331 mmol) were refluxed for 48 h and the product isolated by flash chromatography (silica gel; hexanes:ether, 2:1) to give 14-(2-(triethoxysilyl)ethyl)-12,19-dimethoxypodocarpa-8,11,13-trien-

7-one (**50**) (94%) as an orange oil. ν_{max} 1668 (C=O ketone), 1278 (C–O–C alkyl), 1104 (C–O–C aryl), 1078 (Si–O), 860 cm^{-1} (Si–C). δ(H) 0.90–0.98, 2H, $CH_2CH_2Si(OEt)_3$; 0.97, s, 3H, H(18); 1.05, td, 13.5, 4.0 Hz, 1H, H(3ax); 1.16, s, 3H, H(20); 1.22, t, 9H, 7.0 Hz, OCH_2CH_3; 1.54, td, 13.1, 4.0 Hz, Hz, 1H, H(1ax); 1.61–1.73, m, 2H, H(2eq) and H(2ax); 1.78, bs, 1H, H(3eq); 1.84, dd, 10.2, 6.2 Hz, 1H, H(5); 2.23, bd, 1H, H(1eq); 2.66–2.78, m, 2H, H(6eq) and H(6ax); 3.0–3.11, m, 2H, $CH_2CH_2Si(OEt)_3$; 3.29, s, 3H, 19-OCH_3; 3.28 (partially obscured), 3.48, 2d, 9.2 Hz, 2H, H(19); 3.79, s, 3H, 12-OCH_3; 3.85, q, 7.0 Hz, 6H, OCH_2CH_3; 6.63, d, 2.5 Hz, 1H, H(11); 6.70, d, 2.5 Hz, 1H, H(13). δ(C) 12.3, $CH_2CH_2Si(OEt)_3$; 18.2, OCH_2CH_3; 18.8, C(2); 23.7, C(20); 26.9, C(18); 29.0, $CH_2CH_2Si(OEt)_3$; 36.0, C(3), 37.5, C(10); 37.6, C(6); 38.6, C(1) and C(4); 48.4, C(5); 55.0, 12-OCH_3; 58.2, OCH_2CH_3; 59.3, 19-OCH_3; 75.7, C(19); 107.3, C(11); 113.3, C(13); 122.7, C(8); 150.7, C(14); 159.7, C(9); 162.4, C(12), 198.4, C(7). *m/z* 492 (2, M^+), 446 (100, M − EtOH). Found: M^+, 492.2907. $C_{27}H_{44}O_6Si$ calc.: M, 492.2907.

*3.13. Methyl 13-acetyl-12-(((1,1-dimethylethyl)dimethylsilyl)oxy)podocarpa-8,11,13-trien-19-oate (**42**)*

Methyl 13-acetyl-12-(((1,1-dimethylethyl)dimethylsilyl)oxy)podocarpa-8,11,13-trien-19-oate (**41**) (0.888 g, 2 mmol), triethoxyvinylsilane (0.60 g, 8 mmol) and carbonyldihydrotris(triphenylphosphine)ruthenium (37 mg, 0.04 mmol) were refluxed for 24 h, then more carbonyldihydrotris(triphenylphosphine)ruthenium (37 mg, 0.04 mmol) was added and refluxing continued for a further 12 h. Flash chromatography (silica gel; hexanes:ether, 2:1) gave methyl 13-acetyl-14-(2-(triethoxysilyl)ethyl)-12-(((1,1-dimethylethyl)dimethylsilyl)oxy)podocarpa-8,11,13-trien-19-oate (**42**) (1.251 g, 98%) as a brown oil. ν_{max} 1728 (C=O, ester), 1702 (C=O, ketone,) 1463 (C=C), 1078 (Si–O), 852 cm^{-1} (Si–C). δ(H) 0.17, s, 3H, Si*Me*; 0.18, s, 3H, Si*Me*; 0.83–0.87, m, 2H, $CH_2CH_2Si(OEt)_3$; 0.94, s, 9H, CMe_3; 1.01, s, 3H, H(20); 1.06, td, 13.8, 4.35 Hz, 1H, H(3ax); 1.24, t, 9H, 7.0 Hz, OCH_2CH_3; 1.27, s, 3H, H(18); 1.34, td, 13.2, 3.95 Hz, 1H, H(1ax); 1.48, d, 11.1 Hz, 1H, H(5); 1.57–1.64, m, 1H, H(2eq); 1.91, qd, 12.8, 5.3 Hz, 1H, H(6ax); 1.98, qt, 13.9, 3.7 Hz, 1H, H(2ax); 2.09, bd, 12.8 Hz, 1H, H(3eq); 2.24, dd (partially obscured), 13.8, 6.1 Hz, 1H, H(6eq); 2.27, bd, 13.3 Hz, 1H, H(1eq); 2.43–2.59, m, 3H, H(7ax) and $CH_2CH_2Si(OEt)_3$; 2.47, s, 3H, C(O)CH_3; 2.86, dd, 16.7, 4.0 Hz, 1H, H(7eq); 3.66, s, 3H, 19-OCH_3; 3.84, q, 7.0 Hz, 6H, OCH_2CH_3; 6.60, s, 1H, H(11). δ(C) −4.4, Si*Me*; −4.3, Si*Me*; 11.76, $CH_2CH_2Si(OEt)_3$; 18.1, CMe_3; 18.3, OCH_2CH_3; 19.9, C(2); 20.9, C(6); 22.8, C(20); 23.0, C(7); 25.6, CMe_3; 27.9, $CH_2CH_2Si(OEt)_3$; 28.3, C(18); 32.7, C(O)CH_3; 37.3, C(3); 38.7, C(10); 39.7, C(1); 43.8, C(4); 51.2, 19-OCH_3; 52.0, C(5); 58.2, OCH_2CH_3; 113.7, C(11); 126.3, C(13); 131.6, C(8); 139.6, C(14); 149.5, C(9); 150.0, C(12); 177.7, C(19); 206.6, 13-C(O)Me. *m/z* 634 (2, M^+), 588 (15, M − EtOH), 577 (100, M − ^{t}Bu), 163 (45, $Si(OEt)_3$). Found: (M^+), 634.3707. $C_{34}H_{58}O_7Si_2$ calc.: M, 634.3721.

*3.14. Methyl 13-acetyl-14-(2-(triethoxysilyl)ethyl)-12-methoxypodocarpa-8,11,13-trien-19-oate (**43**)*

Methyl 13-acetyl-12-methoxypodocarpa-8,11,13-trien-19-oate (**7**) (0.2 g, 0.580 mmol), triethoxyvinylsilane (0.552 g, 2.90 mmol) and carbonyldihydrotris(triphenylphosphine)ruthenium (32 mg, 0.0349 mmol) were refluxed for 7 days. Flash chromatography (silica gel: benzene; then hexanes:ether, 1:1) gave methyl 13-acetyl-14-(2-(triethoxysilyl)ethyl)-12-methoxypodocarpa-8,11,13-trien-19-oate (**43**) (24%) as a brown oil. ν_{max} 1727 (C=O ester), 1698 (C=O ketone), 1079 cm^{-1} (Si–O). δ(H) 0.85–0.95, 2H, $CH_2CH_2Si(OEt)_3$; 1.04, s, 3H, H(20); 1.07, td, 13.4, 4.3 Hz, 1H, H(3ax); 1.25, s, 3H, H(18); 1.26, t, 9H, 7.0 Hz, OCH_2CH_3; 1.37, td, 13.5, 3.7 Hz, 1H, H(1ax); 1.47, d, 1H, H(5); 1.56–1.64, m, 1H, H(2eq); 1.90, qd, 12.9, 5.2 Hz, 1H, H(6ax); 1.97, qt, 13.9, 3.4 Hz, 1H, H(2ax); 2.18–2.27, m, 3H, H(1eq), H(3eq), H(6eq); 2.45, s, 3H, $COCH_3$; 2.46–2.57, m, 3H $CH_2CH_2Si(OEt)_3$, H(7ax); 2.99, dd, 17.1, 4.0 Hz, H(7eq); 3.63, s, 3H, 19-OCH_3; 3.72, s, 3H, 12-OCH_3; 3.80, q, 7.0 Hz, 6H, OCH_2CH_3; 6.68, s, 1H, H(11). δ(C) 11.9, $CH_2CH_2Si(OEt)_3$; 18.3, OCH_2CH_3; 19.9, C(2); 20.9, C(6); 22.7, C(20); 23.1, C(7); 27.9, $CH_2CH_2Si(OEt)_3$; 28.4, C(18); 32.6, $COCH_3$; 37.4, C(3); 39.2, C(10); 39.8, C(1); 43.9, C(4); 49.4, C(5); 51.2, 19-OCH_3; 55.1, 12-OCH_3; 58.2, OCH_2CH_3; 105.8, C(11); 125.6, C(13); 130.6, C(8); 139.6, C(14); 150.2, C(9); 153.8 C(12); 177.7, C(19); 206.3, 13-C(O)Me. *m/z* 534 (2, M^+), 488 (100, M − EtOH). Found: M^+, 534.3006. $C_{29}H_{46}O_7Si$ calc.: M, 534.3013.

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