ELSEVIER

Journal of Organometallic Chemistry 506 (1996) 339–341

Journal of Organometallic Chemistry

Preliminary communication

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

Paul W.R. Harris, Paul D. Woodgate *

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

Received 17 July 1995

Abstract

Reaction of 2-, 3-, or 4-hydroxyacetophenone with a catalytic amount of a ruthenium complex and excess of a vinyltrialkoxysilane results in *ortho* alkylation in high yield, providing that a suitable protecting group is used. Bicyclic and tricyclic analogues react similarly.

Keywords: Hydroxyacetophenone; *Ortho* alkylation; Ruthenium; Catalysis

We have reported previously on the cyclopentaannulation of ring C aromatic tricyclic diterpenoids promoted by the formation and reaction of transition metal-containing intermediates, leading to ring C aromatic steroidal analogues. For example, nucleophile attack on the η^6-$Cr(CO)_3$ complexes **1** [1] from the podocarpic acid derivative **2** leads mainly to the regioisomer **3** [2], which can be cyclized to **4**. In another approach, the cyclomanganated 13-acetyl diterpenoid **5** underwent decarbonylation and then reaction with ethene to give **6** [3], while the 7-oxo analogue **7** yielded Heck-type adducts **8** (59%) and **9** (28%) [4]. These results demonstrated the unique capability of the transition metal mediated chemistry to direct functionalisation of the diterpenoid at C-14, a site not directly accessible in the free arene. However, a procedure which is catalytic in a transition metal would offer significant advantages. A ruthenium-catalysed procedure for the *ortho* alkylation of some acetophenones and 2-alkylacetophenones has been described [5]. We now report the application of this method to some derivatives of 2-, 3-, and 4-hydroxyacetophenone and to 6-methoxytetralone, and to the diterpenoid ketones **10** and **11**.

Since competitive intramolecular chelation of ruthenium by a β-hydroxy ketone could either limit the turnover in the catalytic cycle [5], or prevent the *ortho* alkylation completely, a number of phenol-protecting groups were investigated. Thus (Table 1), refluxing 2-methoxyacetophenone (**12**) and $Ru(CO)_2(PPh_3)_3$ (6 mol%) with either trimethylvinylsilane or triethoxyvinylsilane in toluene for 48 h gave the *ortho* alkylation products **13** or **14** in 25–30% yield. Also present, however, were small amounts of adducts resulting from hydrodemethoxylation.

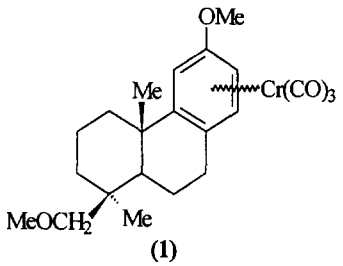
The benzyl ether **15** did not give an improved yield. An isopropyl group provided good protection against chelation, **17** affording **18** in 83% yield, but some hydrodealkoxylation still occurred. A t-butyldimethylsiloxy (TBDMS) group offered optimum efficiency, **19** giving **20** quantitatively. In all cases only the regioisomer resulting from coupling at the terminal carbon of the vinylsilane was formed. No reaction occurred with either 2-acetoxyacetophenone- or 2-*p*-toluenesulfonyloxyacetophenone.

The methyl ethers **21** and **24** of 3- or 4-hydroxyacetophenone reacted satisfactorily (Table 2), although bis alkylation also occurred with excess trimethylvinylsilane. However, the use of one equivalent of triethoxyvinylsilane with **24** and $Ru(CO)_2(PPh_3)_3$ gave only monoalkylation **27** in 94% yield. 4-Acetoxyacetophenone (**28**) afforded **29** from $CH_2 = CHSi(OEt)_3$ in 60% yield, together with the bis adduct **30** (6%).

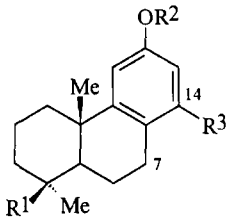
6-Methoxytetralone (**31**) afforded **32** in 92% yield. Gratifyingly, the 7-oxo-12-methoxy diterpenoid **11** gave the analogous C-14 substituted product, requiring only 2 mol% of $RuH_2(CO)(PPh_3)_3$ [5] and 24 h to give **33**

* Corresponding author.

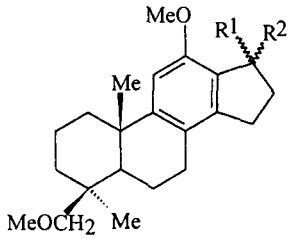
SSDI 0022-328X(95)05893-1

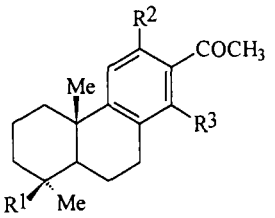


(1)



(**2**: $R^1 = CH_2OMe$, $R^2 = Me$, $R^3 = H$
3: $R^1 = CH_2OMe$, $R^2 = Me$, $R^3 = Nu$)





(**4**: R^1, $R^2 = O$
6: $R^1 = Me$, $R^2 = OH$)

(**5**: $R^1 = CH_2OMe$, $R^2 = OMe$, $R^3 = Mn(CO)_4$
10: $R^1 = CO_2Me$, $R^2 = OMe$, $R^3 = H$
34: $R^1 = CO_2Me$, $R^2 = OMe$, $R^3 = H$
35: $R^1 = CO_2Me$, $R^2 = OMe$, $R^3 = CH_2CH_2Si(OEt)_3$
36: $R^1 = CO_2Me$, $R^2 = H$, $R^3 = CH_2CH_2Si(OEt)_3$
37: $R^1 = CO_2Me$, $R^2 = OTBDMS$, $R^3 = H$
38: $R^1 = CO_2Me$, $R^2 = OTBDMS$, $R^3 = CH_2CH_2Si(OEt)_3$)

from $CH_2=CHSi(OEt)_3$ in 90% yield. As expected, the *ortho* methoxy diterpenoid ketone **34** reacted only slowly with $CH_2=CHSi(OEt)_3$ and $RuH_2(CO)(PPh_3)_3$ (6 mol%), affording **35** in only 24% yield after refluxing for 7 days, and the 12-demethoxy compound **36** was also produced. Again, however, a TBDMS ether proved much more suitable, **37** giving **38** in 98% yield after 36 h with 4 mol% $RuH_2(CO)(PPh_3)_3$.

The ruthenium-catalysed method clearly offers a more efficient entry to C-14 alkylated ring C aromatic diter-

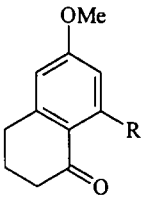
Table 1

Substrate	Alkene, mol equivalent	Catalyst, mol%	Time, h	Product(s), %
12	$CH_2=CHSiMe_3$, 5	$Ru(CO)_2(PPh_3)_3$, 6	48	**13**, 29; [a]
12	$CH_2=CHSi(OEt)_3$, 5	$Ru(CO)_2(PPh_3)_3$, 6	48	**14**, 25; [b]
15	$CH_2=CHSi(OEt)_3$, 5	$RuH_2(CO)(PPh_3)_3$, 6	24	**16**, 28; [b]
17	$CH_2=CHSi(OEt)_3$, 5	$Ru(CO)_2(PPh_3)_3$, 2	16	**18**, 83; [b]
19	$CH_2=CHSi(OEt)_3$, 5	$RuH_2(CO)(PPh_3)_3$, 2	12	**20**, 100

[a] Some 2-ethylacetophenone and 2-ethyl-6-(2-trimethylsilylethyl)acetophenone also. [b] Some 2-(2-triethoxysilylethyl)acetophenone also.

Table 2

Substrate	Alkene, mol equivalent	Catalyst, mol%	Time, h	Product(s), %
21	$CH_2=CHSiMe_3$, 5	$Ru(CO)_2(PPh_3)_3$, 2	48	**22**, 8; **23**, 57
24	$CH_2=CHSiMe_3$, 5	$Ru(CO)_2(PPh_3)_3$, 2	48	**25**, 34; **26**, 60
24	$CH_2=CHSi(OEt)_3$, 1	$Ru(CO)_2(PPh_3)_3$, 2	24	**27**, 94
28	$CH_2=CHSi(OEt)_3$, 5	$RuH_2(CO)(PPh_3)_3$, 6	24	**29**, 60; **30**, 6

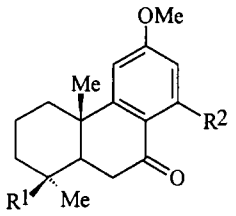


(**31**: R = H
32: R = $CH_2CH_2Si(OEt)_3$)

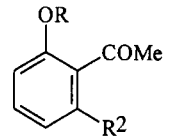
penoids than those requiring a transition metal complex to be prepared and then used stoicheiometrically. Since the transformation of C–Si(OR)$_n$ into heteroatom functionalised alkyl carbon has been reported [6–9], this chemistry opens the way for annulation reactions leading to ring C aromatic steroidal analogues with either a carbocyclic or heterocyclic ring D.

References

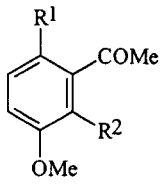
[1] R.C. Cambie, G.R. Clark, A.C. Gourdie, P.S. Rutledge, and P.D. Woodgate, *J. Organomet. Chem., 297* (1985) 177.
[2] R.C. Cambie, P.S. Rutledge, R.J. Stevenson, and P.D. Woodgate, *J. Organomet. Chem., 471* (1994) 133.
[3] R.C. Cambie, M.R. Metzler, C.E.F. Rickard, P.S. Rutledge, and P.D. Woodgate, *J. Organomet. Chem., 426* (1992) 213.
[4] R.C. Cambie, M.R. Metzler, P.S. Rutledge, and P.D. Woodgate, *J. Organomet. Chem., 429* (1992) 59.
[5] F. Kakiuchi, S. Sekine, Y. Tanaka, A. Kamatani, M. Sonoda, N. Chatani, and S. Murai, *Bull. Chem. Soc., Jpn., 68* (1995) 62.
[6] A. Hosomi, I. Susumi, and H. Sakurai, *Chem. Lett.*, (1981) 243.
[7] A. Sakurai, M. Ando, N. Kawada, K. Sato, and A. Hosomi, *Tetrahedron. Lett., 27* (1986) 75.
[8] K. Tamao, T. Kakai, T. Iwahara, R. Kanatani, J. Yoshida, and M. Kumada, *Tetrahedron, 39* (1983) 983.
[9] K. Tamao, N. Ishida, T. Tanaka, and M. Kumada, *Organometallics, 2* (1983) 1694.



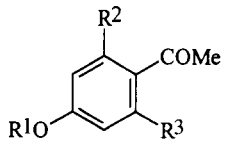
(**7**: $R^1 = CH_2OMe$, $R^2 = Mn(CO)_4$
8: $R^1 = CH_2OMe$, $R^2 = CH_2CH_2CO_2Me$
9: $R^1 = CH_2OMe$, $R^2 = CH{=}CHCO_2Me$
11: $R^1 = CO_2Me$, $R^2 = H$
33: $R^1 = CO_2Me$, $R^2 = CH_2CH_2Si(OEt)_3$)



(**12**: $R^1 = Me$, $R^2 = H$
13: $R^1 = Me$, $R^2 = CH_2CH_2SiMe_3$
14: $R^1 = Me$, $R^2 = CH_2CH_2Si(OEt)_3$
15: $R^1 = CH_2Ph$, $R^2 = H$
16: $R^1 = CH_2Ph$, $R^2 = CH_2CH_2Si(OEt)_3$
17: $R^1 = {}^iPr$, $R^2 = H$
18: $R^1 = {}^iPr$, $R^2 = CH_2CH_2Si(OEt)_3$
19: $R^1 =$ TBDMS, $R^2 = H$
20: $R^1 =$ TBDMS, $R^2 = CH_2CH_2Si(OEt)_3$)



(**21**: $R^1 = R^2 = H$
22: $R^1 = CH_2CH_2SiMe_3$, $R^2 = H$
23: $R^1 = H$, $R^2 = CH_2CH_2SiMe_3$)



(**24**: $R^1 = Me$, $R^2 = H$
25: $R^1 = Me$, $R^2 = H$, $R^3 = CH_2CH_2SiMe_3$
26: $R^1 = Me$, $R^2 = R^3 = CH_2CH_2SiMe_3$
27: $R^1 = Me$, $R^2 = H$, $R^3 = CH_2CH_2Si(OEt)_3$
28: $R^1 = Ac$, $R^2 = R^3 = H$
29: $R^1 = Ac$, $R^2 = H$, $R^3 = CH_2CH_2Si(OEt)_3$
30: $R^1 = Ac$, $R^2 = R^3 = CH_2CH_2Si(OEt)_3$)