Journal of Organometallic Chemistry, 384 (1990) C6–C8
Elsevier Sequoia S.A., Lausanne – Printed in The Netherlands
JOM 20565PC

Preliminary communication

Regioselective hydroxylation of (η^6-arene)tricarbonylchromium(0) complexes of diterpenoids

Richard C. Cambie, Paul I. Higgs, Peter S. Rutledge, and Paul D. Woodgate *

Department of Chemistry, University of Auckland, Private Bag, Auckland (New Zealand)

(Received October 9th, 1989)

Abstract

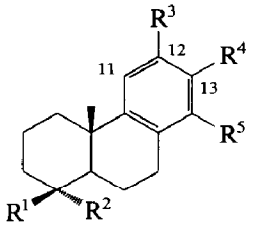
A novel procedure has been developed for the regioselective hydroxylation of ring-C aromatic diterpenoids via their (η^6-arene)tricarbonylchromium(0) complexes. Lithiation-cupration-oxidation gives good yields from methoxyarene complexes having an unhindered *ortho* position.

Introduction of an oxygen function *ortho* to a methoxy group on an arene ring is a route to catechol derivatives, which can then be cleaved oxidatively between the oxygenated carbon atoms. We have used this approach in studies directed towards the synthesis of the naturally-occurring biologically active nagilactones **A** and **C**, and their analogues [1]. Although treatment of lithiated arenes with molecular oxygen in THF provides a direct route to phenols [2], experience in our laboratory and elsewhere [3] has shown that such oxidation reactions can be not only capricious but occasionally explosive. Methods devised to overcome the potential instability of a hydroperoxide intermediate include conversion of an aryllithium to an arylboron species prior to oxidation with H_2O_2 [4] or the use of bis(trimethylsilyl)peroxide as oxidant [5]. Recently, regioselective hydroxylation at C(2) of 3-methoxyestra-1,3,5(10)-trienes has been achieved [6] by *ortho* lithiation of their diastereomic (η^6-arene)$Cr(CO)_3$ complexes followed by reaction with MoOPH [7] and decomplexation.

Lithiated (η^6-arene)$Cr(CO)_3$ complexes of monocyclic arenes have also been used for the attachment of carbon electrophiles onto aromatic rings, although successful reaction required transmetallation to give either an arylcopper or an arylpalladium derivative prior to trapping with the electrophile [8]. We now report the use of a novel lithiation-cupration-oxidation sequence to convert the diterpenoid methyl ethers **1** and **2** into catechol derivatives and the demethoxy compound **3** into a phenol.

* Author to whom correspondence should be addressed.

0022-328X/90/$03.50



(**1**: $R^1 = R^2 = Me$; $R^3 = H$; $R^4 = OMe$; $R^5 = {}^iPr$

2: $R^1 = MeO_2C$; $R^2 = Me$; $R^3 = OMe$; $R^4 = R^5 = H$

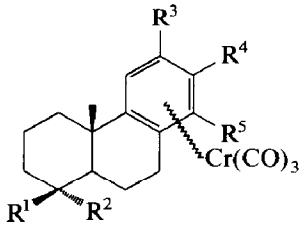
3: $R^1 = Me$; $R^2 = CH_2OMe$; $R^3 = R^5 = H$; $R^4 = {}^iPr$

4: $R^1 = R^2 = Me$; $R^3 = OMe$; $R^4 = {}^iPr$; $R^5 = H$

9: $R^1 = R^2 = Me$; $R^3 = OH$; $R^4 = OMe$; $R^5 = {}^iPr$

10: $R^1 = MeO_2C$; $R^2 = Me$; $R^3 = OMe$; $R^4 = OH$; $R^5 = H$

11: $R^1 = Me$; $R^2 = CH_2OMe$; $R^3 = OH$; $R^4 = {}^iPr$; $R^5 = H$)



(**5**: $R^1 = R^2 = Me$; $R^3 = H$; $R^4 = OMe$; $R^5 = {}^iPr$

6: $R^1 = MeO_2C$; $R^2 = Me$; $R^3 = OMe$; $R^4 = R^5 = H$

7: $R^1 = Me$; $R^2 = CH_2OMe$; $R^3 = R^5 = H$; $R^4 = {}^iPr$

8: $R^1 = R^2 = Me$; $R^3 = OMe$; $R^4 = {}^iPr$; $R^5 = H$)

Treatment of the diterpenoids **1**, **2**, **3**, and **4** with hexacarbonylchromium(0) in Bu_2O/THF under reflux afforded the (η^6-arene)$Cr(CO)_3$ complexes **5** (54%), **6** (74%) [9], **7** (60%), and **8** (55%) as mixtures of diastereomers. By use of the published procedure [6] (4 mol equiv. BuLi, THF/TMEDA, −78°C; 10 mol equiv. MoOPH, −40°) the complexes **5** derived from 13-methoxytotara-8,11,13-triene (**1**) were converted into the 12-hydroxy derivative **9** in only 18% isolated yield after decomplexation. Use of t-BuLi increased the yield of **9** only slightly, to 25%. However, incorporation of a transmetallation step to give an arylcopper intermediate prior to oxidation (5 mol equiv. t-BuLi, THF/TMEDA, −78°C; 5 mol equiv. $CuBr \cdot SMe_2$; 10 mol equiv. MoOPH) increased the yield of the phenol **9** to 66%. Use of only 2 mol equiv. of each of the reagents resulted in recovery of the parent diterpenoid ligand **1**.

By use of the successful sequence, the complexes **6** derived from methyl 12-methoxypodocarpa-8,11,13-trien-19-oate (**2**) gave the 13-hydroxy derivative **10** in 60% yield. In the case of the complexes **7** from dehydroabietic acid **3** (which lacks an *ortho*-methoxy group to promote lithiation) the yield of the 12-hydroxy derivative **11** was only 16%. Attempted oxygenation at the hindered C(11) site of the complexes **8** from 12-methoxyabieta-8,11,13-triene (**4**) was unsuccessful.

Thus, transmetallation of an aryllithium to an arylcopper promotes regioselective *ortho* hydroxylation of (η^6-arene)$Cr(CO)_3$ complexes of diterpenoid methoxyarenes at an unhindered site. The sequence is less successful for an alkyl-substituted arene.

References

1 R.C. Cambie, G.R. Clark, C.E.F. Rickard, P.S. Rutledge, G.R. Ryan, and P.D. Woodgate, Aust. J. Chem., 41 (1988) 1171.
2 H. Gilman, L.C. Cheney, and B.H. Willis, J. Am. Chem. Soc., 61 (1939) 951.
3 For examples, see D.S. Kemp and D.R. Buckler, J. Org. Chem., 54 (1989) 3647; E. Vedejš, H. Mastalen, G.P. Meier, and D.W. Powell, J. Org. Chem., 46 (1981) 5253.
4 G. Sauer, J. Heindl, and H. Wachtel, Tetrahedron Lett., 29 (1988) 6425.
5 M. Taddei and A. Ricci, Synthesis, (1986) 633.
6 J.C. Gill, B.A. Marples, and J.R. Traynor, Tetrahedron Lett., 28 (1987) 2643.
7 E. Vedejs and S. Larsen, Org. Syn., 64 (1986) 127.
8 P.J. Beswick, S.J. Leach, N.F. Masters, and D.A. Widdowson, J. Chem. Soc. Chem. Commun., (1984) 46.
9 R.C. Cambie, G.R. Clark, A.C. Gourdie, P.S. Rutledge, and P.D. Woodgate, J. Organomet. Chem., 297 (1985) 177.