

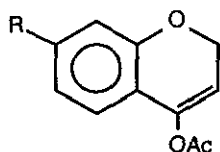
PALLADIUM CATALYSED ARYLATION OF CHROM-3-EN-4-OL ACETATES VIA THEIR TRIBUTYLTIN ENOLATES

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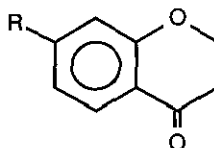
Dedicated with admiration and respect to Professor Sir Derek Barton on the occasion of his 70th birthday.

Abstract — Arylation of *in situ* generated chrom-3-en-4-ol tributyltin enolates with aryl bromide in the presence of a catalytic amount of $\text{PdCl}_2[(\text{o-tolylphosphine})_3]_2$ gives moderate to good yields of the corresponding isoflavanones.

Selective monoarylation of chroman-4-ones is a highly desirable synthesis of isoflavanones and of their further elaborated structures. A variety of arylation methods have been described, but they generally require special reagents or drastic reaction conditions totally incompatible with sensitive functionalities¹. In our first approach directed towards the synthesis of variously substituted isoflavanones, we have described the use of pentavalent organobismuth derivatives². However the generality of the method was limited by the number of available bismuth derivatives. Among the newer methods of arylation³, the palladium mediated arylations have been most widely used. Heck's arylation has been applied to the synthesis of isoflavanones⁴. However, it requires toxic arylmercury derivatives and stoichiometric amounts of the expensive palladium acetate to generate *in situ* the arylpalladium reagents. These drawbacks are avoided in a recently reported reaction: the palladium catalysed arylation of *in situ* generated tributyltin enolates⁵. We now describe our results on the extension of this procedure to the arylation of chroman-4-ones. The enol acetates 1 and 2 of chroman-4-one 3 and of 7-benzyloxychroman-4-one 4 respectively were prepared by condensation of the chroman-4-one with isopropenyl acetate in the presence of *p*-toluenesulfonic acid.



1: R = H

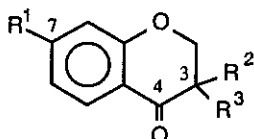
2: R = $\text{C}_6\text{H}_5\text{CH}_2\text{O}$ 

3: R = H

4: R = $\text{C}_6\text{H}_5\text{CH}_2\text{O}$

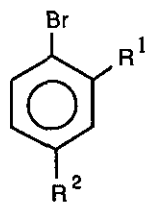
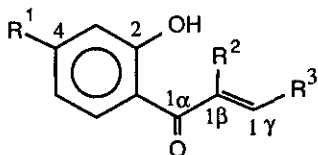
A series of aryl bromides were reacted with the enol acetate and tributyltin methoxide in the presence of a catalytic amount of dichloro-bis-(tri-*o*-tolylphosphine)palladium⁶. The best yields of isoflavanones were obtained when a lesser amount of the aryl bromide was used (1.5 eq. of the enol acetate and 1 eq. of the aryl bromide). When equimolar amounts were used, significant quantities of biaryl derivatives were detected.

Table 1. Isoflavanones Prepared by the Palladium Catalysed Arylation.



Formula	R ¹	R ²	R ³	Ref.
6	H	C ₆ H ₅	H	8
7	H	C ₆ H ₅	C ₆ H ₅	9
9	H	4'-MeO-C ₆ H ₄	H	4b
10	H	4'-MeO-C ₆ H ₄	4'-MeO-C ₆ H ₄	12
12	H	2'-MeO-C ₆ H ₄	H	12
15	H	4'-Me-C ₆ H ₄	H	4b
17	H	C ₆ H ₅ -CH ₂	H	10
18	C ₆ H ₅ CH ₂ O	C ₆ H ₅	H	11
19	C ₆ H ₅ CH ₂ O	C ₆ H ₅	C ₆ H ₅	2

16: C₆H₅-CH₂Br



5: R¹ = R² = H

8: R¹ = H, R² = MeO

13: R¹ = H, R² = R³ = 2-MeOC₆H₄ (Ref. 12)

11: R¹ = MeO, R² = H

20: R¹ = C₆H₅CH₂O, R² = R³ = C₆H₅ (Ref. 12)

14: R¹ = H, R² = Me

Isoflavanone and 7-benzyloxyisoflavanone were obtained in good yields together with small amounts of the α,α -diphenyl derivatives. Lower yields were obtained in the case of substituted isoflavanones, as partial thermal decomposition of chrom-3-en-4-ol acetate occurred as well as competing side

reactions leading to small amounts of diphenylated products, e.g. 3,3-diphenylchroman-4-one, 2-hydroxy- α -(2'-methoxyphenyl)chalcone and 3,3-di-(4'-methoxyphenyl)chroman-4-one. The unexpected formation of the chalcones **13** and **20** probably arises through aryl migration and ring opening of the 3,3-diarylchroman-4-one.

Table 2. Palladium Catalysed Reactions of Tributyltin Enolates **1** and **2**.

Substrate	Aryl Bromide	Reaction Conditions ⁶	Products (%) ^a
1	5	A, 4h	6 (61), 7 (2), 3 (14)
1	5	B, 7h	6 (52), 7 (3), 3 (24)
1	8	A, 20h	9 (26), 10 (10), 3 (40)
1	11	A, 25h	12 (33), 13 (8), 3 (43)
1	11	B, 28h	12 (24), 13 (7), 3 (34)
1	14	A, 20h	15 (38), 3 (42)
1	16	A, 22h	17 (30), 3 (63)
2	5	A, 12h	18 (42), 19 (9), 20 (5), 4 (32)
2	5	B, 22h	18 (49), 19 (3), 20 (6), 4 (32)

a - All yields are based on the enol acetate.

The reaction was also extended to the synthesis of homoisoflavanone, through reaction with benzyl bromide. However, only a modest yield (30%) of the homoisoflavanone was obtained, which in this case does not compete favourably with existing methodology⁷.

Although only moderate yields are obtained for the synthesis of substituted isoflavanones, this represents nevertheless the first direct entry to the 2'-substituted isoflavanones, from chroman-4-ones, thus allowing further elaboration to pterocarpanes and rotenoids. Further studies are now under way to improve the yields of this new synthetic approach.

ACKNOWLEDGEMENTS

This work was made possible by a CNRS-NBST-RIA Exchange Fellowship to P.H.S.

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6. **In a typical experiment** : a stirred solution of the chrom-3-en-4-ol acetate, tributyltin methoxide and aryl or benzyl halide in anhydrous toluene (5ml per g of enol acetate) was heated under argon at 100°C for the time indicated. The solvents were distilled off and the oily residue partitioned by flash column chromatography (eluant : gradient of hexane-methylene dichloride). **Conditions A** : 1 molar eq. of the aryl bromide, 1.5 molar eq. of the enol acetate and 1.5 molar eq. of Bu₃SnOMe; **Conditions B** : 1 molar eq. of the aryl bromide, 1 molar eq. of the enol acetate and 1.5 molar eq. of Bu₃SnOMe.
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12. **10** : mp 186°C (methanol-hexane), $\nu_{\max}(\text{CHCl}_3)$ 1701, 1682 and 1626 cm⁻¹; $\lambda_{\max}(\text{CHCl}_3)$ 252(12 987) and 320(4 204) nm(ϵ); δ (CDCl₃ - 270 MHz) 7.99 - 6.73(12H, m, ArH), 5.48(1H, d, J 11.72 Hz, H-2A or H-2B), 4.12(1H, d, J 11.72 Hz, H-2B or H-2A), 3.76(3H, s, OCH₃), and 3.74(3H, s, OCH₃); m/z 360 (M⁺, 69), 253(12), 240(100) and 225(35).
- 12** : oil, $\nu_{\max}(\text{CHCl}_3)$ 1690 and 1606 cm⁻¹; δ (CDCl₃ - 270 MHz) 7.94 - 7.91(1H, m, H-5), 7.46 - 7.39(1H, m, H-6), 7.25 - 6.84(6H, m, ArH), 4.63 - 4.27(3H, m, H-3 and H-2), and 3.71(3H, s, OCH₃); m/z 254 (M⁺, 49), 223(4), 134(100), 119(72), 91(53), and 65(12).
- 13** : mp 81-82°C (95% ethanol); $\nu_{\max}(\text{CHCl}_3)$ 1633, 1590 and 1488 cm⁻¹; $\lambda_{\max}(\text{CHCl}_3)$ 245(16 418) and 343(11 027) nm(ϵ); δ (CDCl₃ - 270 MHz) 12.30(1H, s, sh. ex-D₂O, OH), 7.90 - 7.87(1H, dd, J 8.06 and 1.83 Hz, H-5), 7.31(1H, s, H-1), 7.44 - 6.80(11H, m, ArH), 3.71(3H, s, OCH₃), and 3.53(3H, s, OCH₃); m/z 360 (M⁺, 6), 329(100), 312(11), 253(7), 121(11), and 91(8).
- 20** : mp 116-117°C (ethanol), $\nu_{\max}(\text{CHCl}_3)$ 1622 cm⁻¹; $\lambda_{\max}(\text{CHCl}_3)$ 246(16 966) and 340(20 065) nm(ϵ); δ (CDCl₃ - 270 MHz) 12.76(1H, s, sh. ex-D₂O, OH), 7.77 - 7.18(18H, m, ArH), 6.48(1H, s, H-1), and 5.30(2H, s, O-CH₂Ph); m/z 406 (M⁺, 19), 329(100), 180(8), 91(71).

Received, 23rd March, 1988