Palladium-catalysed Intramolecular Arylation: a New Synthesis of Munduserone

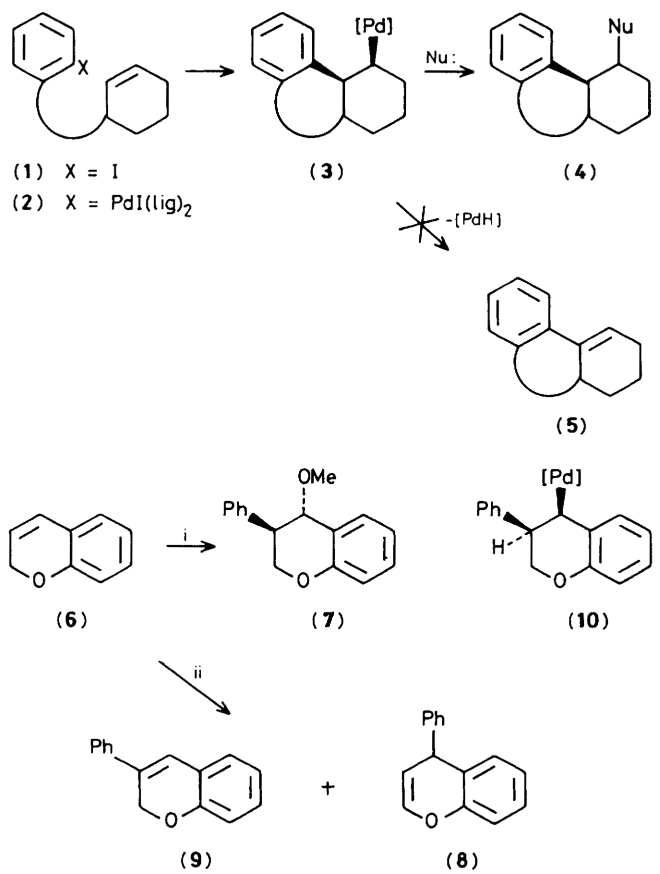
Peter C. Amos and Donald A. Whiting*
Chemistry Department, The University, Nottingham NG7 2RD, U.K.

Treatment of the aryl iodides (**11**) with palladium acetate gave the tetracyclic stilbenes (**13**) *via* a formal but stereochemically disallowed Heck reaction; the method was exploited to synthesise (±)-munduserone (**21**).

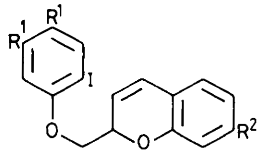
Aryl iodides of general type (**1**) would, under the conditions of the Heck reaction, be expected to generate an aryl palladium species (**2**), leading on through *syn* addition to an intermediate (**3**). This intermediate would lack the *syn* Pd–H stereochemistry necessary for elimination to an alkene (**5**), but could yield a substitution product (**4**) by reaction with a suitable nucleophile. Intermolecular reactions following such a course are known[1] and in agreement we have observed that treatment of 2*H*-chromene (**6**) with phenylmercury(II) chloride and dilithium palladium tetrachloride in methanol gives the methoxy adduct (**7**). In contrast however 2*H*-chromene (**6**) reacted with iodobenzene and palladium acetate in acetonitrile–methanol[2] to give 4-phenyl-4*H*-chromene (**8**) and, unexpectedly, 3-phenyl-2*H*-chromene (**9**). Chromenes (**9**) and (**8**) were obtained in 54% and 1% yield, respectively, using 50 mol% palladium acetate; at 100 mol% the yields were 23% and 10%. The former could arise by *syn*-addition–*syn*-elimination, but the latter must arise by a different mechanism (see below) since *syn*-elimination from an intermediate (**10**) is not possible. No methoxy-containing products were observed.

We thus examined the parallel intramolecular case. Treatment of (**11a**) [readily obtained from 2-bromomethylchromone[3] (**12a**)] with palladium acetate gave the stilbene (**13a**), (58%), m.p. 109—110 °C. The methoxychromenes (**11b**) and (**11c**) afforded stilbenes (**13b**), m.p. 138—139 °C, and (**13c**), m.p. 135—136 °C, in similar yields. An intermediate aryl organopalladium iodide was intercepted in the case of (**11b**) and shown by *X*-ray crystallography[4] to be (**15**); refluxing (**15**) in toluene gave (**13b**) (90%). No products of type (**14**) were observed.

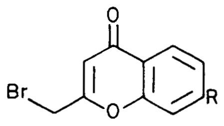
Since this nominal 'intramolecular Heck reaction' is stereochemically disallowed, an alternative pathway involving homolysis, (**15**) → (**16**), followed by radical addition, looks an attractive alternative mechanism, and a radical pathway may also account for the formation of (**9**) from (**6**). Whatever its course the reaction provides a simple entry into the tetracyclic



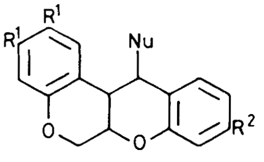
Scheme 1. *Reagents and conditions:* i, PhHgCl, Li_2PdCl_4, MeOH; ii, PhI, $Pd(OAc)_2$, Ph_3P, Et_3N, MeCN–MeOH, 50 °C.



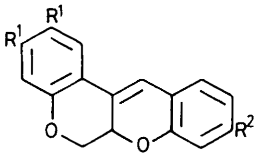
(11) a; $R^1 = R^2 = H$
b; $R^1 = H$, $R^2 = OMe$
c; $R^1 = R^2 = OMe$



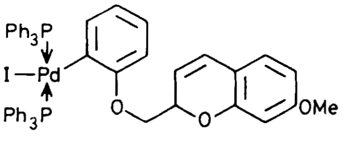
(12) a; R = H
b; R = OMe



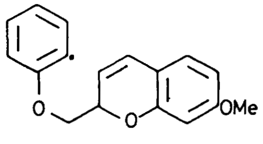
(14)



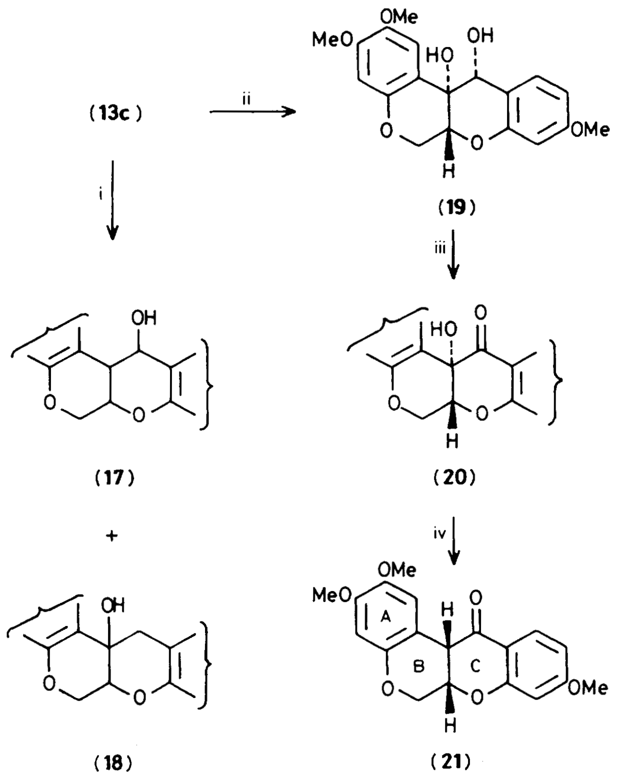
(13) a; $R^1 = R^2 = H$
b; $R^1 = H$, $R^2 = OMe$
c; $R^1 = R^2 = OMe$



(15)



(16)



Scheme 2. *Reagents and conditions:* i, BH_3–Me_2S; ii, OsO_4, NMMO; iii, MnO_2; iv, Zn, AcOH.

system (**13**) and this has been exploited to provide a new synthesis of the rotenoid (±)-munduserone^5 (**21**).

Reaction of (**13c**) with borane–dimethyl sulphide was disappointingly unspecific, giving stereoisomers of both (**17**) and (**18**), while bulkier boranes failed to react. To overcome the regiospecificity problem, the unsaturated compound (**13c**) was treated with osmium tetraoxide–*N*-methylmorpholine *N*-oxide (NMMO) to yield the diol (**19**); oxidation to the rotenolone (**20**) was followed by zinc-effected deoxygenation to yield (±)-munduserone (**21**) [20% from (**13c**)] identified by ^1H n.m.r. comparison with other rotenoids.^{6} The stereochemistry of (**19**) and (**20**) follows from related chemistry of natural rotenone and isorotenone;^{7} the *cis*-B/C fusion apparent in munduserone is the thermodynamically favoured stereochemistry.^{8}

We thank S.E.R.C. and Wellcome Research Laboratories (Berkhamsted) for a C.A.S.E. award (P. C. A.).

Received, 21st November 1986; Com. 1660

References

1 *Inter alia:* A. Kasahara, T. Izumi, K. Endo, T. Takeda, and M. Ookita, *Bull. Chem. Soc. Jpn.*, 1974, **47**, 1967; H. Horino, M. Arai, and N. Inoue; *ibid.*, 1974, **47**, 1683; H. Horino and N. Inoue, *J. Chem. Soc., Chem. Commun.*, 1976, 500.

2 S. Cacchi and G. Palmieri, *Synthesis*, 1984, 575.

3 H. A. Offe, *Berichte*, 1938, **71B**, 1837.

4 We thank Dr. M. J. Begley for this information; details will be included in a full paper.

5 N. Finch and W. D. Ollis, *Proc. Chem. Soc.*, 1960, 176.

6 D. J. Adam, L. Crombie, and D. A. Whiting, *J. Chem. Soc. (C)*, 1966, 542; D. G. Carlson, D. Weisleder, and W. H. Tallent, *Tetrahedron*, 1973, **29**, 2731.

7 L. Crombie and P. J. Godin, *J. Chem. Soc.*, 1961, 2861.

8 L. Crombie, P. J. Godin, K. S. Siddalingaiah, and D. A. Whiting, *J. Chem. Soc.*, 1961, 2876.