

Palladium-catalysed Intramolecular Arylation: a New Synthesis of Munduserone

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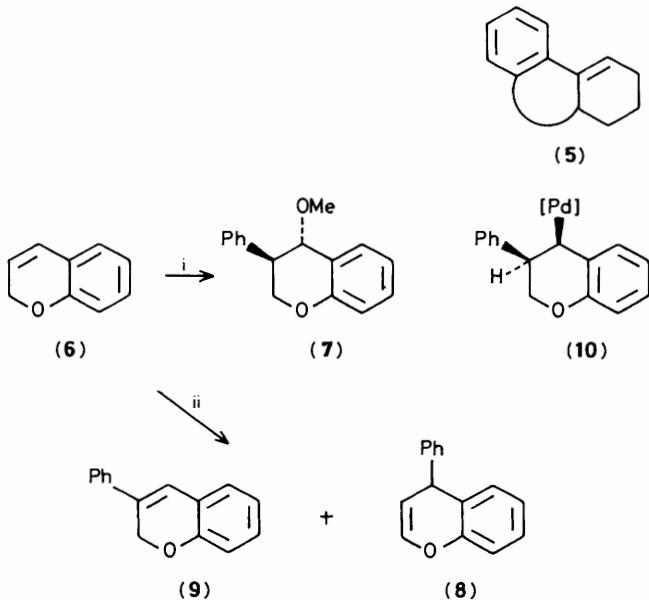
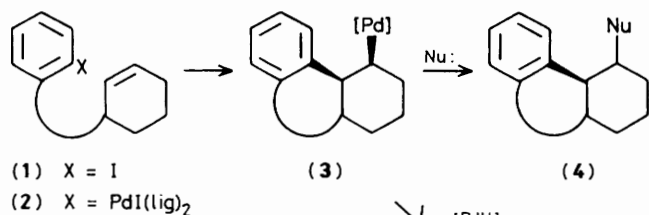
Treatment of the aryl iodides (**11**) with palladium acetate gave the tetracyclic stilbenes (**13**) via a formal but stereochemically disallowed Heck reaction; the method was exploited to synthesise (\pm)-munduserone (**21**).

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 known¹ 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-methanol² 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)

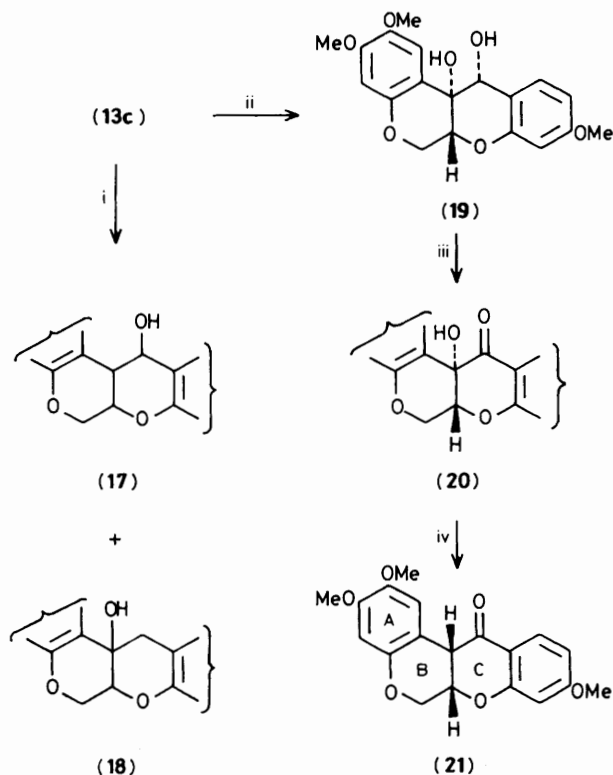
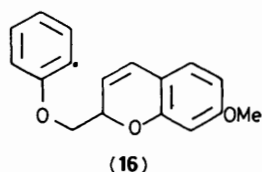
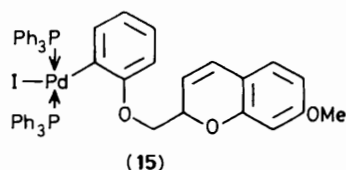
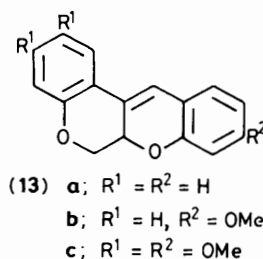
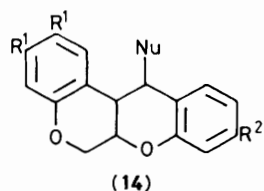
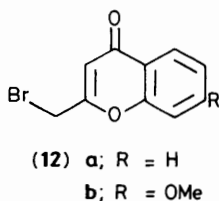
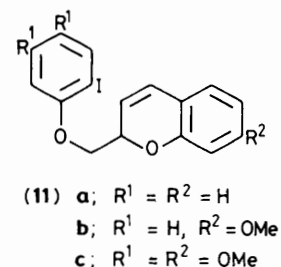
since *syn*-elimination from an intermediate (**10**) is not possible. No methoxy-containing products were observed.

We thus examined the parallel intramolecular case. Treatment of (**11a**) [readily obtained from 2-bromomethylchromone³ (**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 crystallography⁴ 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**) \rightarrow (**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, Li₂PdCl₄, MeOH; ii, PhI, Pd(OAc)₂, Ph₃P, Et₃N, MeCN-MeOH, 50 °C.



Scheme 2. Reagents and conditions: i, BH₃-Me₂S; ii, OsO₄, NMMO; iii, MnO₂; iv, Zn, AcOH.

system (13) and this has been exploited to provide a new synthesis of the rotenoid (±)-munduserone⁵ (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 regioselectivity 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

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