Intramolecular Nucleophilic Substitutions of Co-ordinated Aryl Halides. A Preparation of Chromans

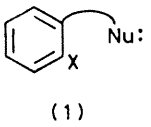
By ROY P HOUGHTON* and MARTYN VOYLE
(*Department of Chemistry, University College, Cardiff* CF1 1XL)
and RAYMOND PRICE
(*Imperial Chemical Industries Ltd , Organics Division, Blackley, Manchester* M9 3DA)

Summary 3-(*o*-Fluorophenyl)propan-1-ol can be cyclised readily to chroman either through chromium tricarbonyl complexes or (as also with substituted fluorophenylpropanols) by the action of the (η^6-benzene)(η^5-ethyltetramethylcyclopentadienyl)rhodium(III) cation

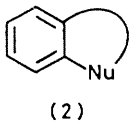
INTRAMOLECULAR nucleophilic substitutions with *ortho*-substituted aryl halides (**1**) in which the substituent contains a nucleophilic nitrogen, oxygen, or sulphur atom (Nu) generally proceed too slowly for this process to be used for the synthesis of heterocycles (**2**) However, it seemed possible that conversions of the type (**1**) → (**2**) could be carried out readily *via* π-bonded metal complexes, for it has been established that co-ordination of the arene ring of an aryl halide with metals such as chromium(0) and ruthenium(II) activates the halide towards nucleophilic substitution [1,2] We are currently examining this idea, and here we report its application to the preparation of chromans

The complex (**3a**)† was prepared from the parent fluoro alcohol (**6a**) by the action of trispyridinetricarbonylchromium(0) and boron trifluoride–ether [3] Addition of potassium t-butoxide to a solution of this complex in dimethyl sulphoxide at room temperature resulted in almost immediate cyclisation to give the chroman complex

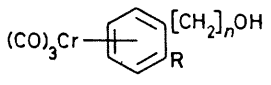
† All new compounds had microanalytical and/or spectroscopic data consistent with their assigned structures



(1)

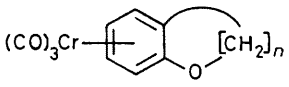


(2)



(3)

	n	R
a;	3	F
b;	2	F
c;	2	OMe
d;	2	$OCHMe_2$

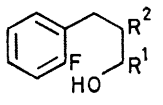


(4)

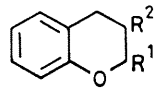
a ; $n = 3$
b ; $n = 2$

$(\eta^5\text{-EtMe}_4C_5)(\eta^6\text{-}C_6H_6)Rh^{2+}$

(5)

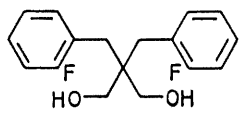


(6)

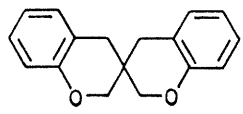


(7)

	R^1	R^2
a;	H	H
b;	Me	H
c;	H	CH_2OH
d;	H	$o\text{-F}\cdot C_6H_4\cdot CH_2$

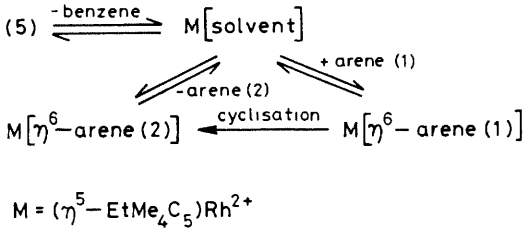


(8)



(9)

(**4a**; 75% yield after purification) which was identical (i.r., n.m.r., t.l.c.) with a sample prepared directly from chroman. Mild oxidation of (**4a**) by iodine in diethyl ether gave chroman in virtually quantitative yield. In contrast with this very rapid cyclisation, treatment of the parent fluoro alcohol with potassium t-butoxide in dimethyl sulphoxide gave a solution of the corresponding alkoxide anion whose ^{1}H n.m.r. spectrum was unchanged after 100 h at room temperature. Evidently, co-ordination with a chromium tricarbonyl residue considerably enhances the rate of intramolecular nucleophilic substitution.



SCHEME

In order to modify the system so that heterocycle formation would be metal-*catalysed* (as distinct from metal-*promoted*), the complexed rhodium(III) cation (**5**) was prepared as its hexafluorophosphate(v) salt.[4] On the basis of studies by Maitlis and his co-workers,[5] it was predicted that in solution the co-ordinated benzene in this cation would be reversibly displaced by arenes of type (**1**) *via* an intermediate solvated species. A metal-facilitated intramolecular nucleophilic substitution would then be followed by a similar displacement of the cyclised product (**2**) by the starting arene (**1**) (see the Scheme).

In accordance with this prediction, the hexafluorophosphate(v) salt was found to catalyse the cyclisations of the fluoro alcohols (**6**; **a**—**d**) to the corresponding chromans (**7**) under relatively mild conditions. With concentrations of $4{\cdot}6 \times 10^{-2}$ M and 28×10^{-2} M of the salt and the fluoro alcohol respectively, and nitromethane which contained (initially) 20% (v/v) of acetone as the solvent, the cyclisations proceeded to the extent of 57—88% during 24 h at 80 °C. Under the same conditions the diol (**8**) gave the previously unknown spiro compound [(**9**) 90% yield after purification]. All the cyclisations were also catalysed by the corresponding tetrafluoroborate salt, but (unexpectedly) the rates of cyclisation were lower than with the hexafluorophosphate salt. ^{1}H N.m.r. studies suggest that this is because the co-ordinated arenes, *e.g.* benzene, are displaced from the rhodium by the solvent less readily when the gegen-ion is BF_4^- than when it is PF_6^-.

Attempts to use the chromium(0) and rhodium(III) systems described above for the analogous preparation of five-membered oxygen heterocycles were unsuccessful. For example, the action of sodium isopropoxide in propan-2-ol on the chromium tricarbonyl complex (**3b**) gave the product (**3d**) of intermolecular nucleophilic substitution, even though this reagent steadily converted (15 h, room temperature) the higher homologue (**3a**) into (**4a**). Similarly, treatment with sodium methoxide in methanol gave (**3c**), while the action of potassium t-butoxide in dimethyl sulphoxide gave a mixture of products from which no pure compound was isolated. Presumably the absence of the product (**4b**) of intramolecular nucleophilic substitution in these reactions is the direct result of the strain associated with the bicyclic intermediate that would be formed initially by nucleophilic attack of the alkoxide oxygen atom on the benzene ring.

We thank S.R.C. for a CASE award, and I.C.I. Ltd., Organics Division, for generous financial assistance.

(*Received*, 4*th July* 1980; *Com.* 724.)

[1] See A. C. Knipe, S. J. McGuinness, and W. E. Watts, *J. Chem. Soc., Chem. Commun.*, 1979, 842, and references cited therein.
[2] M. A. Bennett and T. W. Matheson, *J. Organomet. Chem.*, 1979, **175**, 87.
[3] K. Öfele, *Chem. Ber.*, 1966, **99**, 1732.
[4] N. A. Bailey, E. H. Blunt, G. Fairhurst, and C. White, *J. Chem. Soc., Dalton Trans.*, 1980, 829.
[5] C. White, S. J. Thompson, and P. M. Maitlis, *J. Chem. Soc., Dalton Trans.*, 1977, 1654.