OXIDATION OF ALCOHOLS BY TRANSITION METAL COMPLEXES PART V.[1] SELECTIVE CATALYTIC MONOALKYLATION OF ARYLACETONITRILES BY ALCOHOLS

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Summary. Selective catalytic monoalkylation of arylacetonitriles by primary alcohols can be achieved at $\leqslant 100^{o}$ using a catalyst prepared in situ from rhodium trichloride, triphenylphosphine and sodium carbonate. $RuH_2(PPh_3)_4$ is a more effective catalyst for this process.

Alkylation of the active methylene group of arylacetonitriles (1) is usually effected by the use of strong base and alkyl halides[2,3] or dimethyl sulphate[3]. Phase transfer methods have also been used.[4] Dialkylation can be readily achieved[5] and may be an important side reaction in monoalkylation procedures. A few examples of high temperature base catalysed alkylation of arylacetonitriles by alcohols are known.[6]

Our previous work on the catalytic N-alkylation of amines by alcohols[7] led us to study (Table 1) the transition metal catalysed C-alkylation of arylacetonitriles by alcohols (1→2).
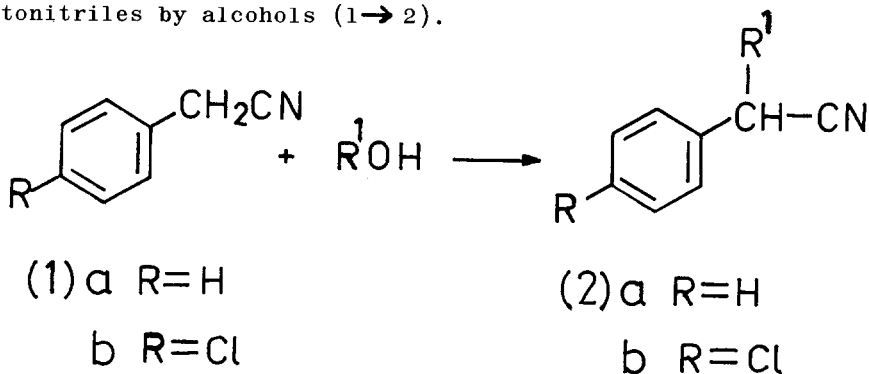

(1) a R=H
    b R=Cl

(2) a R=H
    b R=Cl

Table 1. Catalytic ethylation of (1a)

Catalyst[b]	Time (h)	Yield (%) of (2a; R^1 = Et)[c]
$RuH_2(PPh_3)_4$	11	78
$RuH_2(PPh_3)_4$	24	92
$RhH(PPh_3)_4$	48	75
$RhCl_3 \cdot 3H_2O$-PPh_3[d]	48	86
$RhCl(PPh_3)_3$	96	75
$IrCl_3$-PPh_3[d]	48	9

a. reactions carried out in boiling ethanol under a nitrogen atmosphere in the presence of sodium carbonate (110 mole %).

b. 5 mole % catalyst based on (1; R=H)

c. % yield estimated by glc (4m, 5% SGR at 150° or 2m, 15% carbowax 20M at 170°), using mesitylene as internal standard.

d. metal chloride: phosphine molar ratio 1:5

Table 1 shows $RuH_2(PPh_3)_4$ to be the most active catalyst examined followed by a catalyst prepared in situ from rhodium trichloride, triphenylphosphine and sodium carbonate. Variation of substrate and alcohol were briefly studied using the "in situ" rhodium catalyst (Table 2).

Table 2. Alkylation of arylacetonitriles by alcohols[a]

Substrate	Alcohol	Time (h)	Product (%)[b]
1a	EtOH	48	2a, R^1 = Et (71.5)
1a	MeOH	72	2a, R^1 = Me (35)
1b	EtOH	24	2b, R^1 = Et (68.5)
1b	$PhCH_2OH$	132	2b, R = CH_2Ph (55)
4	MeOH	24	5a (30)
4	EtOH	24	5b (78)

a. 5 mole % catalyst, $RhCl_3 \cdot 3H_2O$-PPh_3-Na_2CO_3 molar ratio 1:5:22. Reactions carried out in boiling alcohol (MeOH, EtOH) or at 100° ($PhCH_2OH$).

b. isolated yields

Introduction of a p-chlorosubstituent (1b) accelerates the ethylation procedure (Table 2). 2-Propanol failed to alkylate (1a). When benzyltrimethyl ammonium hydroxide (110 mole%) was used in place of sodium carbonate for the reaction of (1a) with methanol in the presence of 5 mole % of the "in situ" rhodium catalyst, benzyl transfer occurred to give (3; 31.5%). The dinitrile (4) undergoes cyclisation and alkylation leading to enaminonitriles (5). Thorpe-Ziegler cyclisation of some dinitriles by potassium hydride to give enaminonitriles has been reported.[8] The attempted alkylation of (6a) using the

(3)

(4)

(5) a R=CH$_3$
     b R=C$_2$H$_5$
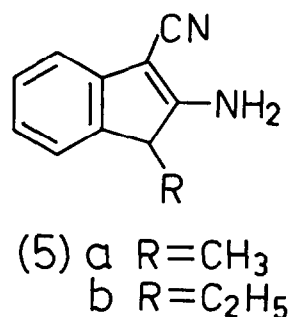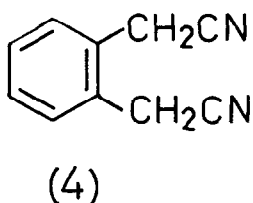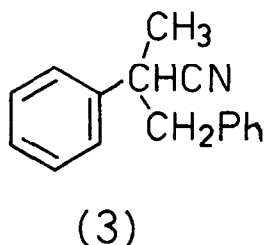
"in situ" rhodium catalyst and ethanol (24h, 78°) led to a mixture of (6b; 16%), (7a; 6.5%) and (8a, 7%). With methanol (12h, 64°) only the isoquinolines (7b; 32%) and (8b; 34.5%) were obtained. The assignment of structures to isomers (7a,b) and (8a,b) is based on their ^{1}H-nmr spectra (CDCl$_3$) and those of their acyl derivatives, in particular on the chemical shift of H$_A$ e.g. (7a; H$_A$ δ 6.22), (8a; H$_A$ δ 6.27), (7c; H$_A$ δ 7.98) (8c; H$_A$ δ 6.80). The isoquinolines are formed in the absence of transition metal.
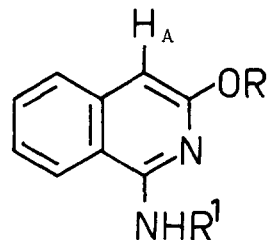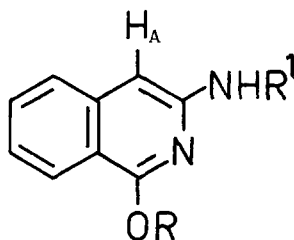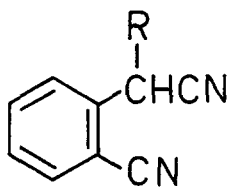
(6)a R=H
   b R=C$_2$H$_5$

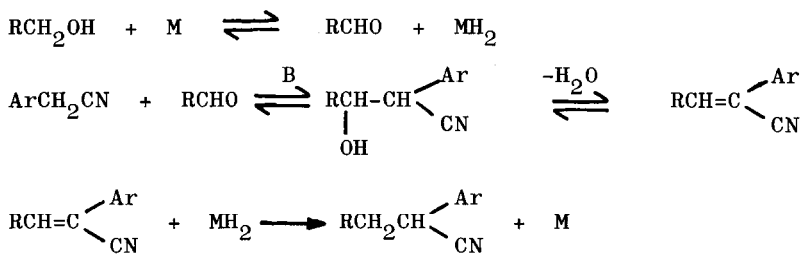(7)a R=C$_2$H$_5$, R^1=H
   b R=CH$_3$, R^1=H
   c R=C$_2$H$_5$, R^1=COCH$_3$

(8)a R=C$_2$H$_5$, R^1=H
   b R=CH$_3$, R^1=H
   c R=C$_2$H$_5$, R^1=COCH$_3$

<u>Scheme</u>

$$RCH_2OH + M \rightleftharpoons RCHO + MH_2$$

$$ArCH_2CN + RCHO \underset{B}{\rightleftharpoons} RCH-CH\begin{smallmatrix}Ar\\CN\end{smallmatrix} \underset{-H_2O}{\rightleftharpoons} RCH=C\begin{smallmatrix}Ar\\CN\end{smallmatrix}$$
$$\qquad\qquad\qquad\qquad\ \ OH$$

$$RCH=C\begin{smallmatrix}Ar\\CN\end{smallmatrix} + MH_2 \longrightarrow RCH_2CH\begin{smallmatrix}Ar\\CN\end{smallmatrix} + M$$

(9)

The precise nature of the active catalyst is uncertain but the mechanism shown in the scheme accords with our previous work.[1,7] The arylacrylonitrile intermediate (9) was detected in reactions catalysed by both the "in situ" rhodium catalyst and more particularly in those catalysed by $RuH_2(PPh_3)_4$. Thus in the reaction of (1a) with ethanol catalysed by $RuH_2(PPh_3)_4$, the intermediate (9; R=Me, Ar=Ph) was present to the extent of ca. 35% after 2 h. [^{1}H-nmr $\delta(CDCl_3)$ 2.22 (d, 3H, CHMe) and 6.94 (q, 1H, C<u>H</u>Me)].

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