N-Alkylation of Nitriles with Tricarbonylchromium Complexes of Benzyl and Related Alcohols as Synthetic Intermediates. Further Development of the Ritter Reactions

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Summary The *in situ* generation of various carbenium ions, temporarily stabilized by an organometallic unit situated in the α-position, in the presence of nitriles has allowed the ready preparation of amides in high yields even from primary alcohol precursors, thus extending the scope of the Ritter reaction.

The condensation of a nitrile with a tertiary alcohol or olefin derived from such an alcohol has been extensively studied by Ritter and his co-workers. The reaction involves attack of the nitrile group on the carbenium ion produced by the action of sulphuric acid and, after hydrolysis, yields an amide.[1] Tertiary alcohols generally give very high yields, but moderate to very poor yields are obtained with secondary or primary alcohols.[2] This important limitation, resulting from the stabilization of the intermediate carbenium ions, may be overcome, in some instances, *via* organometallic transition metal intermediates, as exemplified here.

The remarkably enhanced stability of carbenium ions adjacent to organo-transition metal units is of great interest.[3] While considerable attention has been centred upon the magnitude and possible modes of this stabilization, the potential utility of these cations in organic synthesis has remained essentially unexplored.[4] The *in situ* generation of α-carbenium ions from (η^6-benzyl alcohol)tricarbonylchromium complexes (**1**) at −15 °C with H_2SO_4 under N_2, followed by rapid reaction with an excess of nitrile allowed the ready preparation of the amide complexes (**2**) in high yields, see equation (1). Some characteristic properties of the *N*-benzylamide complexes (**2**) are in Tables 1 and 2.

$$\begin{array}{c}[(\eta^6\text{-}R^1C_6H_4CR^2R^3OH)Cr(CO)_3] + R^4CN \\ (\mathbf{1}) \quad \Big\downarrow H_2SO_4,\ -15\ ^\circ C \\ [(\eta^6\text{-}R^1C_6H_4CR^2R^3NHCOR^4)Cr(CO)_3] \\ (\mathbf{2})\end{array} \qquad (1)$$

The following features of this method should be noted. (i) Only a few minutes are needed for the reaction, which compares favourably with 20—40 h usually required previously. (ii) High yields have been obtained with the complexed primary alcohols (Table 1). The pK_{R^+} value for $(PhCH_2^+)Cr(CO)_3$ is −11·8[5] compared with the values for the uncomplexed benzyl cation of < − 17·3[6] and other related wholly organic carbenium ions such as Ph_3C^+ (−6·6) and Ph_2CH^+ (−13·4).[7] These data provide clear evidence

Table 1. Yields and m.p.s of the *N*-benzylamide complexes (**2**; $R^1 = R^2 = R^3 = H$) obtained from (**1**).

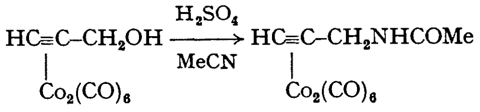
R^4	M.p./°C	Yield/%	R^4	M.p./°C	Yield/%
Me	94	99	$CH_2{=}CH$	93	98
Ph	132	78	$PhCH_2$	138	78
$ClCH_2$	108	98	o-MeC_6H_4	159	83
Pr^n	97	96			

TABLE 2. Yields and m.p.s of the *N*-substituted benzyl amide complexes (**2**; R^4 = Me or Ph) obtained from (**1**).

			R^4 = Me		R^4 = Ph	
R^1	R^2	R^3	M.p./°C	Yield/%	M.p./°C	Yield/%
p-Me	H	H	106	95	136	89
p-MeO	H	H	88	94	122	81
p-MeO	Me	H	138	99	125	84
H	Ph	H	170	82	—	0
H	Me	Me	—	0	—	0

that the $Cr(CO)_3$ group stabilizes carbenium ions to a considerable extent and account for the experimental results. (iii) Tertiary alcohols give rise to carbenium ions that are so stable they are unreactive with nitriles, while the reactivity of secondary alcohols depends on the nitrile substrate (Table 2). Therefore, these organometallic complexes provide useful selective species which complement those available from the free ligand. (iv) In the conventional Ritter reaction several nitriles have been reported to give poor yields[8] (*e.g.* $ClCH_2CN$, 21%; Pr^nCN, 50%; and *o*-MeC_6H_4CN, 35%). We have obtained much higher yields here. (v) Since the $Cr(CO)_3$ group may lead to asymmetry in the co-ordinated molecule, new stereospecific reactions may be induced. For example, reaction of '*endo*' tricarbonyl(indan-1-ol)chromium (racemic: m.p, 105 °C; optically pure 1*S*, m.p. 110 °C, $[\alpha]_D^{25} + 60°$, *c* 2·07, $CHCl_3$[9]) with MeCN led to the '*exo*' amide derivative in pure form (racemic: m.p. 142 °C, yield 89%; optically active 1*R*, m.p. 155 °C, $[\alpha]_D^{25} + 143°$, *c* 1·88, $CHCl_3$). Total inversion of the stereochemistry of the chiral 1-atom took place. (vi) Decomplexation by photochemical oxidation in ether gives rise to the free ligand quantitatively.[10]

This temporary complexation method may be easily extended to other organometallic systems of synthetic interest, for example (prop-2-ynylic alcohol)Co_2CO_6.[4a] Since the activating unit is introduced[11] and removed[12] efficiently under mild conditions, these complexes appear to be ideally suited for utilization as electrophilic propynyl synthons.



$$\underset{\displaystyle Co_2(CO)_6}{HC{\equiv}C\text{–}CH_2OH} \xrightarrow[MeCN]{H_2SO_4} \underset{\displaystyle Co_2(CO)_6}{HC{\equiv}C\text{–}CH_2NHCOMe} \qquad (2)$$

(**3**) (**4**)

Reaction of the cation derived from the primary alcohol (**3**) with MeCN led to [$(HC{\equiv}C\text{–}CH_2NHCOMe)Co_2(CO)_6$] (**4**), m.p. 97 °C, in a similar manner to the $Cr(CO)_3$ series; see equation (2). Acid-catalysed rearrangements which are troublesome with uncomplexed propynylic alcohols are avoided in this reaction.[13]

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