Homogeneous Catalytic Activation of C–N Bonds. Alkyl Exchange between Tertiary amines

By YOUVAL SHVO† and RICHARD M. LAINE*
(*Physical Organic Chemistry Department, SRI International, Menlo Park, CA* 94025)

Summary We have found that several transition metal cluster compounds act as homogeneous catalyst precursors in alkyl exchange reactions of tertiary amines; treatment of mixtures of Et_3N and Pr_3N with either $Ru_3(CO)_{12}$, $Os_3(CO)_{12}$, or $Ir_4(CO)_{12}$ and water leads to very efficient alkyl exchange.

WE have previously reported that $Rh_6(CO)_{16}$ serves as a precursor to a homogeneous metal catalyst that activates α- and β-C–H bonds of triethylamine and tri(n-propyl)amine such that deuterium exchange occurs when D_2O is used as the deuterium source.[1] We have since found that the precursors $Ru_3(CO)_{12}$ and $Os_3(CO)_{12}$ also provide homogeneous catalysts which catalyse deuterium exchange on Et_3N and Pr_3N with a similar selectivity to the rhodium catalyst.[2]

Murahashi *et al.* have studied the reactions of tertiary amines with the heterogeneous catalysts palladium and rhodium black which indicate that these catalysts also activate the α- and β-C–H bonds of tertiary amines.[3,4]

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† On sabbatical leave from Tel Aviv University.

TABLE. Extent of formation of mixed alkyl amines from catalytic alkyl exchange between Et_3N and Pr_3N.[a,b]

	T/°C	$Rh_6(CO)_{16}$	$Ir_4(CO)_{12}$	$Ru_3(CO)_{12}$	$Os_3(CO)_{12}$	Pd black
Et_2NPr	125	<0·1	1·2	8·9	6·2	—
$EtNPr_2$	125	<0·1	2·2	11·0	7·8	—
Et_2NPr[c]	150	0·2	6·2	22·8	26·7	1·6[d]
$EtNPr_2$[c]	150	0·6	7·1	25·6	28·4	1·6[d]

[a] The numerical values correspond to (mol mixed amine)/(total mol amine) × 100 and are reproducible to ±5% of the indicated value. Essentially all the nitrogen is recovered as tertiary amines. [b] Reaction conditions require heating a mixture of Et_3N (14 mmol) and Pr_3N (14 mmol), 0·1 ml H_2O, and 0·05 mmol catalyst under 100 lb in^{-2} N_2 at 125° or 150 °C for 3 h. [c] 0·1 mmol catalyst. [d] 0·075 mmol catalyst, 20 h reaction time.

The apparent mechanistic similarities between our homogeneously catalysed exchange reactions and Murahashi's heterogeneously catalysed exchange reactions suggested to us that it might be possible to model the reactions occurring on palladium black with the homogeneous catalysts.

If the modelling concept were valid then it seemed logical that the homogeneous catalysts should be capable of catalysing other tertiary amine/palladium black reactions. In particular, Murahashi has reported the novel alkyl

$$(C_4H_9)_3N + (C_6H_{13})_3N \rightleftharpoons (C_4H_9)_2NC_6H_{13} + (C_6H_{13})_2NC_4H_9 \quad (1)$$

exchange reaction (1). We report here that reaction (1) can be modelled with *homogeneous* catalysts derived from a variety of group 8 metal carbonyls and mixtures of Et_3N and Pr_3N. The data given in the Table show that the rhodium catalyst system has only slight activity for alkyl exchange. However, the precursors $Ru_3(CO)_{12}$, $Os_3(CO)_{12}$, and $Ir_4(CO)_{12}$ provide catalysts that are quite active for the alkyl exchange, as shown in equation (2). These results

$$Et_3N + Pr_3N \rightleftharpoons Et_2NPr + Pr_2NEt \quad (2)$$

represent the first examples of *homogeneous* catalytic activation of carbon–nitrogen single bonds.‡§ Moreover, our reaction conditions are considerably milder than those reported for the heterogeneous Pd catalyst. Thus, stationary state concentrations of the four amines were obtained after 3 h at 150 °C with $Ru_3(CO)_{12}$ or $Os_3(CO)_{12}$, while the heterogeneous Pd reaction needed 16 h at 200 °C.

In addition to requiring a metal catalyst, we find that the reaction does not proceed unless water is present. This and the work of Deeming *et al.*[5] and Shapley *et al.*[6] enable a reasonable mechanism involving prior C–H activation to be proposed for the C–N bond activation and alkyl exchange, as shown in equations (3)—(6). Moreover,

$$MeCH_2NEt_2 + \text{'M'} \rightleftharpoons (MeCH{=}NEt_2)^+MH^- \quad (3)$$

$$(MeCH{=}NEt_2)^+MH^- + H_2O \rightleftharpoons (MeCHO)(HNEt_2)MH^- + H^+ \quad (4)$$

$$(MeCHO)(HNEt_2)MH^- + MeCH_2CHO \rightleftharpoons (MeCH_2CH{=}NEt_2)^+MH^- + OH^- + MeCHO \quad (5)$$

$$(MeCH_2CH{=}NEt_2)^+MH^- \rightleftharpoons MeCH_2CH_2NEt_2 + \text{'M'} \quad (6)$$

the work of Deeming *et al.* and Shapley *et al.* suggests that 'M' is a cluster and that the iminium compound remains bound to the cluster until hydrolysis occurs. We have not observed free aldehyde or free amine in these reactions; however, this does not preclude the reactions from occurring with the amine and/or aldehydes remaining bound to the metals or, more likely, free amine and aldehyde may be present in too low concentrations to be detected. Indeed, $Pr_3N + Et_2NH$ gives Et_2NPr, while $Et_3N + EtCHO$ gives Et_2NPr when in reactions with $Ru_3(CO)_{12}$. We believe that a similar mechanism is likely for the heterogeneously catalysed reaction. Indeed, Murahashi has reported that palladium black *in the presence of acid* can be used for the heterogeneous catalysis of the hydrolysis of tertiary amines to aldehydes and secondary amines. These results further support our proposed mechanism for the reactions (1) and (2) and our proposal that the homogeneous metal-catalysed amine reactions can be used as models for the analogous reactions with heterogeneous catalyst.

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‡ In ref. 5, Deeming notes that the alkyl exchange of tertiary amines does occur with $Os_3(CO)_{12}$, but his results do not indicate catalysis.

§ Amine alkyl exchange can be brought about by the introduction of tetra-alkylammonium salts, although the conditions necessary are severe (300 °C). See H. K. Hofmeister and J. R. van Wazer, *J. Phys. Chem.*, 1965, **69**, 791.

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