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Preliminary communication

HOMOGENEOUS TRANSITION-METAL CATALYSIS. CLEAVAGE OF THE C—N BOND OF TERTIARY AMINES BY ACID ANHYDRIDES IN THE PRESENCE OF TRANSITION METAL IONS

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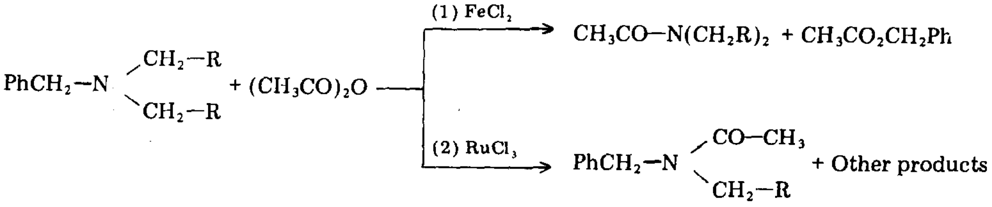
Summary

In the presence of transition metal chlorides, acid anhydrides are highly active in promoting the dealkylation of tertiary amines, and good yields of *N,N*-dialkylamides are obtained.

Although the dealkylation of tertiary amines by acid anhydrides has been known for some years [1,2], the reaction appears of limited applicability. In the course of studying the homogeneous catalysis exerted by transition metals on the reaction of amines, we have found that in the presence of appropriate catalysts tertiary amines can be dealkylated and acylated by acid anhydrides. The reaction can take two routes, as exemplified for *N,N*-dialkylbenzylamine as follows:



Only the principal reaction product is indicated for path 2; oxidation products such as aldehydes or acids have also been identified in some cases.

The results are shown in Table 1, and are briefly discussed below. *N,N*-Di-n-butylbenzylamine hardly reacts with acetic anhydride even on refluxing for 16 h. However upon heating in the presence of 20 mol% of $FeCl_2 \cdot 4H_2O$ (per amine) the benzyl group is displaced and quantitative yields of benzylacetate and of *N,N*-

(Fortsetzung s. S. C12)

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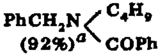
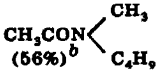
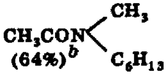
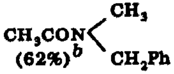
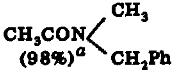
TABLE 1

THE DEALKYLATION OF TERTIARY AMINES BY ACID ANHYDRIDES

Exp. No.	Tertiary amines	Metal chloride (molar ratio to amine)	Acid anhydride (molar ratio to amine)	Temperature (°C)	Time (h.)	Product (Yield)
1	$PhCH_2N(n\text{-}C_4H_9)_2$	$FeCl_2 \cdot 4H_2O$ (20%)	$(CH_3CO)_2O$ (5/1)	160	16	$CH_3CON(C_4H_9)_2$ (96%)[a]
2	$PhCH_2N(n\text{-}C_4H_9)_2$	$FeCl_2 + 2Ph_3P$ (20%)	$(CH_3CO)_2O$ (5/1)	160	16	$CH_3CON(C_4H_9)_2$ (72%)[b] + $PhCH_2N{<}^{C_4H_9}_{COCH_3}$ (16%)[b] + amine unreact. (10%)[b]
3	$PhCH_2N(n\text{-}C_4H_9)_2$	$NiCl_2 \cdot 6H_2O$ (20%)	$(CH_3CO)_2O$ (5/1)	160	16	$CH_3CON(C_4H_9)_2$ (99%)[a]
4	$PhCH_2N(n\text{-}C_4H_9)_2$	$ZnCl_2$ (20%)	$(CH_3CO)_2O$ (5/1)	160	16	$CH_3CON(C_4H_9)_2$ (97%)[a]
5	$PhCH_2N(n\text{-}C_4H_9)_2$	$CoCl_2 \cdot 6H_2O$ (20%)	$(CH_3CO)_2O$ (5/1)	160	16	$CH_3CON(C_4H_9)_2$ (43%)[b] + amine unreact. (53%)[b]
6	$PhCH_2N(n\text{-}C_4H_9)_2$	$PdCl_2$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(C_4H_9)_2$ (39%) + $PhCH_2N{<}^{C_4H_9}_{COCH_3}$ (43%)[b]
7	$PhCH_2N(n\text{-}C_4H_9)_2$	$RhCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(C_4H_9)_2$ (10%)[b] + $PhCH_2N{<}^{C_4H_9}_{COCH_3}$ (65%)[b] + amine unreact. (9%)[b]
8	$PhCH_2N(n\text{-}C_4H_9)_2$	$RuCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(C_4H_9)_2$ (trace) + $PhCH_2N{<}^{C_4H_9}_{COCH_3}$ (97%)[a]
9	$PhCH_2N(n\text{-}C_4H_9)_2$	$RuCl_2(Ph_3P)_3$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$PhCH_2N{<}^{C_4H_9}_{COCH_3}$ (98%)[a]

10	$PhCH_2N(n\text{-}C_4H_9)_2$	$RuCl_3 \cdot 3H_2O$ (6%)	$(PhCO)_2O$ (3/1)	180	7	 $PhCH_2N{<}^{C_4H_9}_{COPh}$ (92%)[a]
11	$(n\text{-}C_4H_9)_3N$	$RuCl_3 \cdot 3H_2O$ (6%)	$(PhCO)_2O$ (3/1)	180	7	$PhCON(C_4H_9)_2$ (95%)[a]
12	$(n\text{-}C_4H_9)_3N$	$RuCl_3 \cdot 3H_2O$ (6%)	$(PhCO)_2O$ (3/1)	160	7	$PhCON(C_4H_9)_2$ + amine unreact. (70%)[b] (24%)[b]
13	$(n\text{-}C_4H_9)_3N$	$RuCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(C_4H_9)_2$ (37%)[a]
14	$(n\text{-}C_4H_9)_3N$	$RuCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (1/1)	160	7	$CH_3CON(C_4H_9)_2$ + $(C_4H_9)_2NCOC_3H_7$ (57%)[b] (10%)[b] + amine unreact. (19%)[b]
15	$(n\text{-}C_8H_{17})_3N$	$RuCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(C_8H_{17})_2$ (98%)[a]
16	$(n\text{-}C_4H_9)_2NCH_3$	$RuCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(C_4H_9)_2$ +  $CH_3CON{<}^{CH_3}_{C_4H_9}$ (40%)[b] (56%)[b]
17	$(n\text{-}C_6H_{13})_2NCH_3$	$RuCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(C_6H_{13})_2$ +  $CH_3CON{<}^{CH_3}_{C_6H_{13}}$ (30%)[b] (64%)[b]
18	$(PhCH_2)_2NCH_3$	$RuCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(PhCH_2)_2$ +  $CH_3CON{<}^{CH_3}_{CH_2Ph}$ (34%)[b] (62%)[b]
19	$(PhCH_2)_2NCH_3$	$FeCl_2 \cdot 4H_2O$ (20%)	$(CH_3CO)_2O$ (5/1)	160	16	 $CH_3CON{<}^{CH_3}_{CH_2Ph}$ (98%)[a]
20	$(PhCH_2)_3N$	$FeCl_2 \cdot 4H_2O$ (20%)	$(CH_3CO)_2O$ (5/1)	160	16	$CH_3CON(PhCH_2)_2$ + amine unreact. (25%)[b] (72%)[b]
21	$(PhCH_2)_3N$	$RuCl_3 \cdot 3H_2O$ (6%)	$(CH_3CO)_2O$ (3/1)	160	7	$CH_3CON(PhCH_2)_2$ (98%)[a]

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[a] The yield refers to the isolated product. [b] The yield was determined by GLC using an internal standard.

dibutylacetamide are obtained (exp. 1 in the Table 1). Similar results are obtained with other metal salts, such as $CoCl_2 \cdot 6H_2O$, $NiCl_2 \cdot 6H_2O$, $ZnCl_2$ [4] (exp. 3,4,5).

The $FeCl_2 \cdot 4H_2O$ is also a good catalyst for the reaction of *N,N*-dibenzylmethylamine (exp. 19) but it is less active in the case of tribenzylamine (exp. 20) (the conversion was about 37% after 16 h) probably because of the increased steric hindrance associated with the larger number of benzyl groups. The catalyst was ineffective with *N,N*-dibutylmethylamine or tributylamine. The variations in reactivity are rather similar to those obtained by others for reactions in the absence of metal salt [1], and a displacement reaction may take place, as proposed by Mariella [1].

Different results were obtained with $RuCl_3 \cdot 3H_2O$. When *N,N*-dibutylbenzylamine was heated with an excess of acetic anhydride in the presence of 6 mol% of $RuCl_3 \cdot 3H_2O$ *N,N*-butylbenzylacetamide was obtained in good yield and only a trace of *N,N*-dibutylacetamide was found (exp. 8). In contrast to the results with iron salt the n-butyl group was displaced instead of the benzyl group, and butyric acid and acetaldehyde were identified in the products. When tribenzylamine was used, in addition to dibenzylacetamide (98%), benzoic acid (about 35%) and a small amount of benzaldehyde were formed (exp. 21). When an equivalent molar ratio of tributylamine and acetic anhydride was used, about 10% yield of *N,N*-dibutylbutyramide was obtained (exp. 14).

The results suggest that ruthenium chloride induces an oxidation—reduction reaction in which the tertiary amine is oxidized and the acetic anhydride is reduced [5]. The mechanism could involve, as an initial step, the ruthenium catalysed oxidation of the tertiary amine to give an intermediated immonium ion complex, as previously suggested for other ruthenium-catalysed reactions of amines [3].

The presence of Ph_3P [6] along with $RuCl_3 \cdot 3H_2O$, or the use of $RuCl_2(Ph_3P)_3$ (exp. 9), gave similar results. However, Ph_3P led to some differences in the reactivity of the organic groups of the amine when iron chloride was used as catalyst. When two mol of the PPh_3 were used along with $FeCl_2 \cdot 4H_2O$, *N,N*-dibutylbenzylamine gave not only *N,N*-dibutylacetamide (74%) but also *N,N*-benzylbutylacetamide (16%) (exp. 2).

When acetic anhydride was used in place of benzoic anhydride analogous results were obtained (exp. 10, 12). When acetic acid, acetyl chloride or benzoyl chloride were used instead of acetic anhydride, as in exp. 13, the tributylamine was unchanged or *N,N*-dibutylacetamide was obtained in low yield.

General procedure

A mixture of the metal chloride (1.2×10^{-3} or 4×10^{-3} mol), the acid anhydride (6×10^{-2} or 10×10^{-2} mol), and the tertiary amine (2×10^{-2} mol), was stirred under nitrogen at room temperature until homogeneous solution was obtained. (If necessary gentle heating was used). The flask was then immersed in an oil bath at 160°C (for acetic anhydride) or 180°C (for benzoic anhydride). After 7 h (for $RuCl_3$, $RhCl_3$, $PdCl_2$ catalyst) or 16 h (for $FeCl_2$, $NiCl_2$, $ZnCl_2$, $CoCl_2$ catalyst), the mixture was cooled to room temperature and diethyl ether and NaOH 1 *N* were added. The ethereal layer contained the unreacted amines, amides, esters etc. From the aqueous layer the acids were isolated by acidification with hydrochloric acid and extraction with ether.

The products were identified by IR, NMR, GLC-mass spectra and GLC by comparison with authentic samples.

References

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5 The amount of acetaldehyde was determined and $RuCl_3 \cdot 3H_2O$ was used as catalyst.
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