Journal of Organometallic Chemistry, 235 (1982) 93—96
Elsevier Sequoia S.A., Lausanne — Printed in The Netherlands

SELECTIVE CONVERSION OF PRIMARY AMINES INTO *N,N*-DIMETHYLALKYL- OR *N,N*-DIALKYLMETHYL-AMINES WITH METHANOL AND $RuCl_2(Ph_3P)_3$

ANTONIO ARCELLI, BUI-THE-KHAI and GIANNI PORZI
Istituto Chimico "G. Ciamician" Università di Bologna, Via Selmi 2, Bologna (Italy)

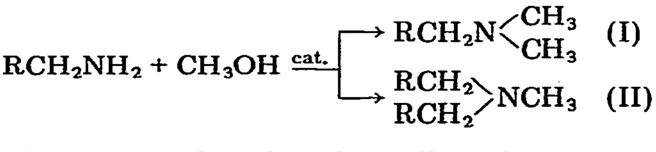
(Received March 8th, 1982)

Summary

N,N-dimethylalkyl- or *N,N*-dialkylmethyl-amines are selectively obtained from the reaction between aliphatic amines and methanol at 180°C for 7 h in the presence of $RuCl_2(Ph_3P)_3$ catalyst.

The alkylation of primary and secondary amines with alcohols promoted by $RhH(Ph_3P)_4$ was recently reported by Grigg et al. [1], and a method of obtaining *N*-alkylanilines by alkylation of aniline with alcohols in the presence of $RuCl_2(Ph_3P)_3$ catalyst was described by Watanabe [2]. In connection with our interest in the $RuCl_2(Ph_3P)_3$ catalyzed synthesis of secondary [3], tertiary, and heterocyclic amines [4,5], we now report another application of this catalyst in amine synthesis.

We have found that the reaction between methanol and primary aliphatic amines bearing an α-hydrogen atom gives two different products, depending on the conditions employed. By an appropriate choice of the amount of catalyst and the ratio of reactants, it is possible to obtain *N,N*-dimethylalkylamines (I) or *N,N*-dialkylmethylamines (II) selectively, as shown in the following Scheme:



$$RCH_2NH_2 + CH_3OH \xrightarrow{cat.} \begin{cases} RCH_2N(CH_3)_2 & \text{(I)} \\ (RCH_2)_2NCH_3 & \text{(II)} \end{cases}$$

The amine and methanol are allowed to react at 180°C for 7 h in a sealed glass tube in the presence of homogeneous catalyst $RuCl_2(Ph_3P)_3$.

A preliminary experiment carried out on benzylamine showed that the reaction does not occur with a satisfactory yield at the reflux temperature. Thus, using 6 mol% of catalyst and a 2.5 MeOH/benzylamine molar ratio, *N,N*-dibenzylmethylamine was recovered in 51% yield after 7 h, along with dibenzylamine (7%) and tribenzylamine (41%).

0022-328X/82/0000—0000/$02.75

Representative results are summarized in Table 1 and, some features of interest can be discussed. When the methanol was in large excess (15—30 molar ratio of MeOH/amine) and 1—1.3 mol% of catalyst (based on the amine) was used, *N*,*N*-dimethylalkylamine (I) was obtained in good yield (86—98%); the monomethylated product ($RNHCH_3$) was observed, in poor yield, only in the case of n-butyl and n-benzylamine. In contrast, use of a 2.5—5 molar ratio of MeOH/amine and 4—6.5 mol% of catalyst gave *N*,*N*-dialkylmethylamine (II) as the main product (72—93%); except the case of cyclohexylamine, symmetrical secondary (R_2NH) and tertiary (R_3N) amines were generally found in small amounts under these conditions. These by-products practically disappear if a larger amount of methanol is used (see n-butylamine) or the reaction time is prolonged (see n-dodecylamine).

From the results it appears that an increase in the length of the carbon chain of the starting primary amine leads to an increase in the catalyst percentage (from 4 to 6.5 mol%) required to give good yields of the corresponding *N*,*N*-dialkylmethylamine (II); this is presumably due to the increased bulk of the alkyl group linked to the nitrogen atom, as noted previously in the synthesis of symmetrical secondary and tertiary amine [3,4]. The results obtained with cyclohexylamine confirm that the reaction is sensitive to the steric hindrance in the amine; thus, while *N*,*N*-dimethylcyclohexylamine was obtained in 95% yield, *N*,*N*-dicyclohexylmethylamine was isolated in poor yield along with a moderate amount of dicyclohexylamine (see Table 1).

TABLE 1

SELECTIVE CONVERSION OF PRIMARY ALKYLAMINES INTO DIMETHYLALKYL- OR DIALKYLMETHYL-AMINES BY REACTION OF MeOH IN THE PRESENCE OF $RuCl_2(Ph_3P)_3$

Primary amine $R—NH_2$ R—	Reaction conditions [a]		Products (% yield) [b]		
	Mol% cat. [c]	Mol. ratio MeOH/amine	$RN(CH_3)_2$	R_2NCH_3	Other amines
n-Butyl	1	15	75	—	20 [d]
	1.3	15	86 (80)	—	15 [d]
	4	2.5	18	65	17 [e]
	4	5	19	75 (65)	—
n-Hexyl	1	15	82	18	—
	1.3	15	94 (88)	—	—
	4	2.5	7	72 (60)	15 [e]
n-Octyl	1	15	98 (90)	—	—
	6	2.5	12	86 (75)	—
n-Dodecyl	1	15	94 (86)	—	—
	6	2.5	15	65	16 [e]
	6.5 [f]	2.5	—	93 (80)	—
Cyclohexyl	1.3	15	95 (85)	—	—
	6.5 [f]	2.5	20	25	53 [g]
Benzyl	1	15	26	39	35 [d]
	1.3	30	95 (90)	—	—
	3	2.5	47	49	—
	6	2.5	16	81 (70)	—

[a] Reaction performed at 180°C for 7 h unless stated otherwise. [b] Determined by GLC analysis; in parentheses the yields of isolated products are reported. [c] Based on the amine used. [d] $RNHCH_3$. [e] R_2NH plus R_3N. [f] Reaction time 12 h. [g] R_2NH.

With a low percentage of the catalyst and in the presence of a large excess of methanol, no symmetrical secondary (R_2NH) and tertiary (R_3N) amines were ever found, while monomethylalkylamine ($RNHCH_3$) was detected in the reactions with n-butylamine (20%) and benzylamine (35%). In contrast when the reaction was carried out with a low MeOH/amine molar ratio and a higher percentage of the catalyst, R_2NH and R_3N were generally present, whilst $RNHCH_3$ was never detected.

In aid in elucidating the reaction path leading to dialkylmethylamine (II), it is useful to consider the results obtained in an additional experiment carried out on n-hexylamine using a 2.5 MeOH/hexylamine molar ratio and in the presence of 4 mol% of catalyst. Analysis of the products after 3 h showed *N,N*-dihexylmethyl- (28%) and dihexyl-amine (46%) to be present along with trihexyl- (14%) and *N*-methylhexyl-amine (10%); after 7 h the yield of *N,N*-dihexylmethylamine reached 72% at the expense of dihexylamine, which practically disappeared.

A possible explanation for the results is that the reactions involve the intermediates, $RNHCH_3$ and R_2NH in the formation of $RN(CH_3)_2$ and R_2NCH_3, respectively. However, in the path leading to R_2NCH_3 one cannot rule out (especially with a starting amine containing a small alkyl group) the presence of the intermediate $RNHCH_3$, which can be successively converted into R_2NCH_3, as previously observed under similar conditions [5].

The results, considered along with the mechanism suggested by Grigg [1] and Watanabe [2] for amine alkylation, lead us to suggest the following possible reaction routes:

$$\begin{tikzcd}
RCH_2NHCH_3 \arrow[d, "MeOH"', "cat."] & RCH_2NH_2 \arrow[l, "cat."', "MeOH"] \arrow[r, "cat."] & (RCH_2)_2NH \arrow[d, "cat."', "MeOH"] \\
RCH_2N(CH_3)_2 & & (RCH_2)_2NCH_3
\end{tikzcd}$$

(I) (II)

General procedure

A mixture of the primary alkylamine (6 mmol) and methanol (15—180 mmol) was sealed in a glass tube in the presence of $RuCl_2(Ph_3P)_3$ (0.06—0.39 mmol) and kept for 7 h at 180° C. The products were analyzed in GLC by comparison with authentic samples, and the yields were determined by use of an internal standard. The products derived from n-butyl-, n-dodecyl- and cyclohexyl-amine were identified by MS and ^1H NMR analysis.

The best results achieved for each substrate were confirmed for reactions involving a two-fold increase in the quantities of reactants. The purity of the products, isolated by distillation ($RN(CH_3)_2$) or by elution on alumina (R_2NCH_3), was checked by GLC using the following columns: 2 m × 2 mm, SE52 (5%) on Chromosorb W (for *N,N*-dimethylbenzylamine and *N,N*-dibenzylmethylamine) and 2 m × 2 mm, Versamid 900 and NaOH (0.5%) on Chromosorb G (for the other amines).

References

1 R. Grigg, T.R.B. Mitchell, S. Sutthivaiyakit and N. Tongpenyai, J. Chem. Soc. Chem. Comm. (1981) 611.
2 Y. Watanabe, Y. Tsuji and Y. Ohsugi, Tetrahedron Lett. 22 (1981) 2667.
3 Bui-the-Khai, C. Concilio and G. Porzi, J. Organometal. Chem. 208 (1981) 249.
4 Bui-the-Khai, C. Concilio and G. Porzi, J. Org. Chem. 46 (1981) 1759.
5 A. Arcelli, Bui-the-Khai and G. Porzi, J. Organometal. Chem., 231 (1982) C31.