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A Study of the Palladium-Catalysed Carbonylation of *N*-Chloroamines

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The suitability of three routes to primary (1°) and secondary (2°) *N*-chloroamines for carbonylation to carbamoyl chlorides and isocyanates using palladium catalysts is explored. Free nitrogen bases inactivate the catalyst, which at 65 atm CO pressure and ambient temperature achieves up to 75% conversion of 2°-chloroamines to product, but only 30–45% for 1°-chloroamines. Triphenylphosphine enhances the yield and rate of CO uptake at an optimum Pd : PPh_3 ratio of 1 : 2. *N,N*-Dichloroamines do not carbonylate under the same conditions and have no influence on the carbonylation of *N*-chloroamines. Chloroamines having long alkyl chains (C_{12}–C_{18}), which need to be prepared using the HOCl route, give good yields of 2°-carbamoyl chlorides but lower yields of the 1°-compounds because of the detrimental effect of HCl generated in the formation of isocyanates. Attempts to isolate an intermediate complex by reacting $(PPh_3)_3Pd(CO)$ with Me_2NCl give $(PPh_3)_2PdCl_2$. A high-pressure IR study of the reactions using Pd, $PdCl_2$, and $(PPh_3)_2PdCl_2$ shows $[(PPh_3)_2Pd(CO)Cl]^+$ as the only identifiable carbonyl complex detected in solution.

INTRODUCTION

The traditional synthetic route to isocyanates, used extensively in the manufacture of urethane polymers, and carbamoyl chlorides, used as acylating agents, involves the highly toxic compound phosgene (reaction (1)) (*1*). Also, stringently controlled conditions are required to avoid significant by-product formation of ureas, arising from disubstitution.

$$RNH_2 + COCl_2 \xrightarrow{-HCl} RNHCOCl \xrightarrow{-HCl} RNCO \qquad (1)$$

$$RR'NH + COCl_2 \xrightarrow{-HCl} RR'NCOCl \xrightarrow[-HCl]{RR'NH} RR'NCONRR'. \qquad (2)$$

Optimisation of the strongly exothermic reaction (1) requires efficient mixing and the presence of excess phosgene, requiring subsequent removal from the reaction products. A further disadvantage of this route is that hydrogen chloride produced may consume up to two-thirds of the added amine as the amine hydrochloride. In the production of carbamoyl chlorides from primary amines, formation of isocyanates (by reaction (1)) causes further loss of amine.

Carbonylation of amines offers an alternative route to isocyanates, but a variety of other products may also be simultaneously produced, including formamides, ureas, and oxamides (*2–5*). Many transition metal complexes, e.g., complexes of nickel and palladium, catalyse these reactions which involve nucleophilic attack of amines at the carbon of coordinated carbon monoxide. For example, amides and ureas result from the use of carbonyl complexes of manganese, cobalt, and nickel at 150–270°C and 100–300 atm pressure of carbon monoxide (*6*). The products formed depend on the nature of the amine used. Aromatic amines give ureas predominantly (*7*), whereas aliphatic amines give *N*-for-

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myl derivatives. For some amines double carbonylation occurs to produce oxamides (*8*), i.e.,

$$RNH_2 \xrightarrow{+PdCl_2} RNHCONHR + RNHCOCONHR$$

where $R = C_{10}H_{21}$, temp = 180°C, pressure = 100 atm.

Processes for the catalytic formation of aromatic isocyanates involve aromatic nitrocompounds subjected to 200°C and 300 atm. pressure of carbon monoxide (*9*). Nitrene complexes are thought to be intermediates in these systems and to react subsequently with carbon monoxide to yield isocyanates.

$$ArNO_2 \xrightarrow[-2CO_2]{+2CO} ArN \xrightarrow{CO} ArNCO.$$

Alternatively, urethanes can be produced directly by the palladium-catalysed carbonylation of aromatic amines in the presence of ethanol (*10*). A notable disadvantage, however, is the need to reoxidise the palladium metal formed to the +II state and the consequent use of carbon monoxide/air mixtures for this purpose.

$$PhNH_2 + EtOH \xrightarrow[CO/O_2]{PdCl_2, CsI} PhNHCOOEt$$

at 160°C for 1 h. Also amines and carbon monoxide undergo stoichiometric reactions with palladium(II) chloride to form isocyanates or urethanes in the presence of alcohols, conditions being mild and yields moderate to good (*11, 12*). The palladium is commonly reduced to palladium metal and requires oxidation by air or copper(II) to return the metal to its original state.

An alternative route to isocyanates involves the use of *N*-haloamines, e.g., *N*-chloroamines, which with nickel tetracarbonyl produce ureas in a stoichiometric reaction (*13*). Nickel is converted to nickel(II) chloride. A minor by-product from this reaction is the carbamoyl chloride, which indicates that a possible mechanism involves generation of the carbamoyl ligand RR'N-CO-, previously trapped in the complex $Li[Ni(CO)_3CONMe_2]$ (*14*). The reaction becomes catalytic, forming carbamoyl halides, when palladium or palladium chloride are used at 50°C and 60 atm carbon monoxide for 20 h (*15*).

$$RR'NCl + CO \rightarrow RR'NCOCl.$$

A detailed investigation of this reaction is reported here.

EXPERIMENTAL

Amines were, in general, obtained from Aldrich, Fluka, and B.D.H. and fatty acid amines were obtained from Akzo Chemie. They were used without further purification. Triphenylphosphine was purchased from B.D.H., and palladium(II) chloride and ethanoate were purchased from Aldrich. Sodium hypochlorite, *N*-chlorosuccinimide, and the organic solvents used were all supplied by B.D.H. Ltd. Solvents were dried using a 3A molecular sieve and were stored under nitrogen.

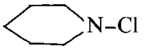
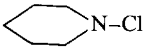
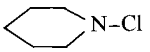
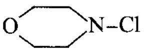
General high-pressure studies were undertaken in stainless-steel vessels having glass linings. A Rockhurst Engineers autoclave, equipped with a MagneDrive stirrer, and Parr autoclaves were used throughout, but for IR spectral studies at high pressures, a titanium vessel (*16*) with CaF_2 windows was used in association with a Perkin–Elmer 235 spectrometer. Pressure measurements were made using a Wikka pressure transducer, the output being recorded on an X-Y plotter.

Reaction between N-Chloroamines and Carbon Monoxide in the Presence of Palladium Ethanoate and Triphenylphosphine

N-Chloropiperidine was prepared by adding cold aqueous sodium hypochlorite (0.12 mol) to piperidine hydrochloride (12.2 g, 0.10 mol) in ice water (100 cm^3) over 15 min. After a further 15 min at ambient temperature, the mixture was extracted with diethyl ether (4 × 50 cm^3) and then the combined

TABLE 1

Total Yields of Carbamoyl Chlorides/Isocyanates from Carbonylation of *N*-Chloroamines

N-Chloroamine	Pressure (atm)	Reaction time (h)	Catalyst	Concentration (mmol)	% Yield[a]
	50	21	$PdCl_2$, $Pd(OAc)_2$	0.1	75
	50	21	$(PPh_3)_2PdCl_2$	0.1	85
	50	21	$PdCl_2/PPh_3$	0.1/0.2	84
	50	21	$PdCl_2/PPh_3$	0.1/0.2	62
$(CH_3)_3CH_2C(CH_3)_2CNHCl$	60	29	$PdCl_2/PPh_3$	0.1/0.2	33
$(CH_3)_3CNHCl$	50	21	$PdCl_2/PPh_3$	0.1/0.2	37
$(CH_3)_3CNHCl$	65	48	$(PPh_3)_2PdCl_2$	0.1	38

[a] Yields are based on the amount of amine used. For 1°-amines,carbamoyl chloride and isocyanate products were converted to disubstituted *N,N'*-ureas to determine the total yield.

extracts were washed successively with 8% sulphuric acid, 5% sodium hydroxide solution, and water, before drying with anhydrous magnesium sulphate.

The chloropiperidine solution was placed in an autoclave with palladium(II) ethanoate (0.224 g, 10 mmol) and triphenylphosphine (0.52 g, 20 mmol), and the equipment was flushed with carbon monoxide. After increasing the CO pressure to 50 atm the reaction mixture was stirred rapidly for 21 h at ambient temperature. After venting the carbon monoxide, the reaction mixture was filtered, and the solvent was removed *in vacuo*. The product was distilled at 100°C and 12 Torr pressure to give a colourless liquid, identified as piperidyl carbamoyl chloride by comparison (NMR and IR) with an authentic sample prepared via the phosgene route. The yield was 84%.

Other carbamoyl chlorides were prepared using the same method (see Tables 1–4). Product solutions of primary amines were converted into ureas by reaction with an amine, followed by purification by recrystallisation. This method allowed the total yield of the carbonylation process to carbamoyl chlorides and isocyanates to be obtained.

Reaction of Chloroamines with Carbon Monoxide in the Presence of Bases

The general experimental procedure was as above, except that the bases listed in Table 2 were included in the reaction mixture. The *N*-chloroamines used were derived from *t*-octylamine and *t*-butylamine, and the carbonylated products were isolated as disubstituted ureas.

Effect of N,N-Dichloroamines on the Carbonylation Reaction

N,N-Dichloro-*t*-octylamine was prepared by treatment of the parent amine (0.2 mol) with excess *N*-chlorosuccinimide (0.25 mol) in diethyl ether at room temperature, and the mixture was stirred until the ν(N–H) peak at 3410 cm^{-1} had disappeared. The dichloroamine and a mixture with *N*-chloro-*t*-octylamine were reacted with CO as described above, and the final solutions were treated in the same way. No product was obtained from the *N,N*-dichloroamine reaction.

The Effect of Carbon Monoxide Pressure on the Rate of Reaction

N-Chloro-*t*-octylamine (0.1 mol) in diethyl ether (100 cm^3) was placed in the

TABLE 2

Total Yields of Carbamoyl Chlorides/Isocyanates Produced by the Carbonylation of *N*-Chloroamines in the Presence of Bases[a]

N-Chloroamine	Base	Yield %[b]
$(CH_3)_3CH_2C(CH_3)_2CNHCl$	Et_3N	0
$(CH_3)_3CH_2C(CH_3)_2CNHCl$	Pyridine	0
$(CH_3)_3CH_2C(CH_3)_2CNHCl$	$(CH_3)_3C(CH_3)_2CNH_2$[c]	0
$(CH_3)_3CNHCl$	Et_3N	0
$(CH_3)_3CNHCl$	—	35
$(CH_3)_3CNHCl$	$NaHCO_3$	36
$(CH_3)_3CH_2C(CH_3)_2CNHCl$	—	40
$(CH_3)_3CH_2C(CH_3)_2CNHCl$	$KHCO_3$	42

[a] *N*-Chloroamine 0.1 mol in diethylether (150 ml); palladium(II) ethanoate (0.224 g, 1.0 mmol); triphenylphosphine (0.52 g, 2.0 mmol); 50 atm carbon monoxide; room temperature for 18 h; base (0.13 mol).

[b] Yields are based on the amount of amine used. For 1°-amines, carbamoyl chloride and isocyanate products were converted to disubstituted *N,N'*-ureas to determine the total yield.

[c] The base (0.15 mol) was in excess by 0.05 mol in the initial chlorination to prepare *N*-chloro-*t*-octylamine (0.1 mol).

autoclave together with palladium ethanoate (0.224 g, 1 mmol) and triphenylphosphine (0.52 g, 1 mmol), and the system was flushed several times with carbon monoxide before pressurisation to the required pressure in the range 7–55 atm. The mixture was stirred rapidly at room temperature, and the pressure was monitored with time. Using initial pressures of 6.8, 13.6, 27.2, and 54.5 atm, initial rates of carbon monoxide uptake (calculated at STP) were 2.14, 4.84, 6.18, and 7.36 × 10^{-5} mol min^{-1}, respectively. The pressures measured for the reaction of *N*-chloropiperidine (0.1 mol), palladium(II) chloride (0.885 g, 5 mmol) in benzene (100 cm^3) at ambient temperature after 0-, 1-, 2-, 3-, 4-, 5-, 7-, 10-, 14-, 21-h reaction periods were 51.0, 49.9, 48.8, 47.5, 46.2, 44.9, 43.0, 41.8, 40.8, and 39.6 atm, respectively.

The Effect of Palladium : Phosphine Ratio on the Reaction Rate

The experimental procedure was similar to that described immediately above, and similar quantities of reagents were used. Palladium : phosphine ratios of 1 : 0, 1 : 1, 1 : 2, 1 : 3, 1 : 4, and 1 : 5 were used, giving initial rates of CO uptake at STP of 2.61, 3.88, 6.62, 5.22, 5.18, 5.04 × 10^{-5} mol min^{-1}.

Attempted Preparation and Carbonylation of N,N'-Dichloro-1,6-diaminohexane

1,6-Diaminohexane (11.6 g, 0.1 mol) in water (150 cm^3) was treated with hydrochloric acid until the pH became 6.5–7, then added to cold sodium hypochlorite solution with rapid stirring. The product was solvent-extracted into diethyl ether (3 × 50 cm^3), which was dried over magnesium sulphate. Carbonylation of this solution was attempted over 14 h, at 50 atm CO pressure and ambient temperature using palladium(II) ethanoate (0.224 g, 1 mmol) and triphenylphosphine (0.52 g, 2 mmol) as the catalyst. The loss of pressure was very small, the final mixture contained palladium metal in suspension and only a small amount of carbonylated material. The main component was unreacted *N*-chloroamine.

Preparation of N-Chloroamines Derived from Fatty Acid Amines

Route 1. The most widely applicable route, the reaction of an amine hydrochloride with sodium hypochlorite at <0°C, was not applicable to fatty acid amines because of their limited solubility in cold water. This is particularly so for 2°-amines and leads to ineffective chlorination (see Tables 3 and 4).

Route 2. The use of N-chlorinating agents such as *N*-chlorosuccinimide proved unsuitable. Stirring this reagent with the amine in chloroform at room temperature for 24 h (*17*) gave some chloroamine, but the presence of free amines in solution prevented its subsequent catalytic carbonylation. The chlorination is relatively slow, and this route requires the removal of both free amine and succinimide. The preferred preparative method for chloroamines is as follows.

Route 3. Hypochlorous acid was generated by the addition of hydrochloric acid to

TABLE 3

Yields of Carbamoyl Chlorides Derived from Long-Chain *N*-Chlorodialkylamines

System[a]	% Yield[b]
Di(*n*-hexadecyl)NCl/Pd$(OCOCH_3)_2$/PPh_3	75
Di(coco)NCl/Pd$(OCOCH_3)_2$/PPh_3	73
Di(*n*-octadecyl)NCl/Pd$(OCOCH_3)_2$/PPh_3	72
Di(*n*-hexadecyl)NCl[c]/Pd$(OCOCH_3)_2$/PPh_3	0
Di(*n*-octadecyl)NCl[c]/Pd$(OCOCH_3)_2$/PPh_3	0
Di(*n*-hexadecyl)NCl/$PdCl_2$	68
Di(*n*-octadecyl)NCl/$PdCl_2$	67
Di(*n*-hexadecyl)NCl[d]/Pd$(OCOCH_3)_2$/PPh_3	10
Di(*n*-hexadecyl)NCl[d]/Pd$(OCOCH_3)_2$/PPh_3	11

[a] *N*-Chloroamine (0.02 mol); palladium compound (0.2 mmol); triphenylphosphine (0.4 mmol); 50 atm, room temperature, 14 h.

[b] Yields are based on the amount of amine used.

[c] *N*-Chloroamine prepared from amine and *N*-chlorosuccinimide.

[d] *N*-Chloroamine prepared from amine hydrochloride and NaOCl solution.

Dicocoamine is derived from cocoa plant materials and is a mixture having C_{12}, C_{14}, and C_{16} alkyl chains.

sodium hypochlorite at − 10 to 0°C, then subsequently solvent-extracted into methyl ethyl ketone. This reagent was added to the amine dissolved in chloroform, the mixture being kept at − 10°C.

Various solvents were tested for extraction of the hypochlorous acid, including diethyl ether, methyl ethyl ketone, chloroform, and dichloromethane, but methyl ethyl ketone was found the most suitable. About 70–80% of the hypochlorite was converted to usable hypochlorous acid, concentrated solutions up to 1.6 *M* could be prepared, and solutions were stable for several days if kept below 0°C. Generally, the reagent was freshly prepared before use. The chlorinated solvents proved less effective at extracting the hypochlorous acid, and diethyl ether underwent a vigorous reaction on several occasions causing the solvent to boil. Though the solvent was initially peroxide-free, the solution had an induction period typical of a radical reaction. Consequently, diethyl ether was not used except at the start of the study, even though concentrated solutions of HOCl were produced and successful chlorination of amines was achieved in this medium.

Hypochlorous acid was generated by the dropwise addition of cold concentrated hydrochloric acid into sodium hypochlorite solution at − 10–0°C, in the presence of methyl ethyl ketone and with vigorous stirring to prevent local overheating and liberation of chlorine. The dropwise addition of acid was stopped when the pH of the aqueous layer was 6–6.5, virtually all the hypochlorite having been converted into HOCl. The reaction mixture was allowed to separate into two layers and the organic layer removed. The remaining aqueous layer was extracted with further portions of organic solvent and the combined extracts were dried over calcium chloride. The concentration of HOCl was determined by iodometry, but since solutions were slighlty yellow in colour suggesting the presence of some chlorine con-

TABLE 4

Total Yields of Carbamoyl Chlorides/Isocyanates Derived for Long-Chain *N*-Chloroalkylamines

System[a]	% Yield[b]
(*n*-Dodecyl)NHCl/Pd$(OCOCH_3)_2$/PPh_3	35
(*n*-Hexadecyl)NHCl/Pd$(OCOCH_3)_2$/PPh_3	37
(*n*-Octadecyl)NHCl/Pd$(OCOCH_3)_2$/PPh_3	35
(*n*-Dodecyl)NHCl/$PdCl_2$	33
(*n*-Hexadecyl)NHCl/$PdCl_2$	32
(*n*-Octadecyl)NHCl/$PdCl_2$	30
(*n*-Hexadecyl)NHCl[c]/Pd$(OCOCH_3)_2$/PPh_3	Trace
(*n*-Hexadecyl)NHCl[d]/Pd$(OCOCH_3)_2$/PPh_3	32

[a] *N*-Chloroamine (0.02 mol); palladium salt (0.2 mmol); triphenylphosphine (0.4 mmol); 50 atm, room temperature, 14 h.

[b] Yields are based on the amount of amine used. For 1°-amines, carbamoyl chloride and isocyanate products were converted to N,N′-disubstituted ureas to determine the total yield.

[c] *N*-Chloroamine prepared from amine hydrochloride and NaOCl solution.

[d] *N*-Chloroamine prepared from amine and *N*-chlorosuccinimide.

tamination, the HOCl content was overestimated. The solutions could not be obtained without some chlorine being present and were used without further purification because of the practical difficulties in removing chlorine.

Fatty acid amines are readily soluble at −10°C in very few solvents, methyl ethyl ketone not being one. Consequently, a mixed solvent system, chloroform–methyl ethyl ketone, was used at −10°C, the HOCl solution being added dropwise to the amine dissolved in chloroform. The exothermic reaction required efficient cooling and rapid stirring. The resulting solution of *N*-chloro amine was, in the case of 2°-amines, purified by washing with a 10% aqueous solution of sodium hydroxide, 5% sulphuric acid, and drying over calcium chloride. For 2°-amines, the chlorination was undertaken using a 5% excess of HOCl, but not for 1°-amines where an excess leads to *N,N*-dichloroamines. The *N*-chloroamines can be isolated by removal of the solvent *in vacuo* as off-white waxy solids.

Carbonylation of 2°-Fatty N-Chloroamines

A solution of the chloroamine (0.02 mol) was diluted with methyl ethyl ketone to 150 cm^3 and placed in the autoclave with palladium ethanoate (0.045 g, 0.2 mmol) and triphenylphosphine (0.10 g, 0.4 mmol). The equipment was flushed with carbon monoxide and pressurised to 50 atm, and the solution was stirred at ambient temperature for 14 h. Solvent extraction of the reaction mixture with hot 40–60°C petroleum ether selectively dissolved the carbamoyl chloride product, together with unreacted *N*-chloroamine, leaving any amine hydrochloride. The extract was evaporated to dryness *in vacuo,* the residue was dissolved in cloroform, and the solution was chromatographed on a 15- to 20-cm column of Kieselgel 60 using chloroform as the elutant. Traces of the *N*-chloroamine eluted first and were followed by the carbamoyl chloride, obtained as a pale yellow waxy solid by removal of the solvent. Yields based on the amount of amine used are given in Table 3. Carbamoyl chlorides were characterised by elemental analysis and IR spectroscopy. For di(*n*-octadecyl)carbamoyl chloride, we found: C, 75.2; H, 11.8; N, 2.30; Cl, 5.95. $(C_{18}H_{37})_2NCOCl$ requires C, 76.0; H, 12.8; N, 2.40; Cl, 6.07%. For di(*n*-hexadecyl)carbamoyl chloride, we found: C, 76.0; H, 13.4; N, 2.90; Cl, 6.50. $(C_{16}H_{33})_2NCOCl$ requires C, 75.0; H, 12.6; N, 3.03; Cl, 6.71%. Authentic samples of the carbamoyl chlorides were prepared from the amine using phosgene solutions in toluene (12.5% w/w) at low temperature. A 50% excess of phosgene gave yields of 40–50%. The products all showed a characteristic carbamoyl carbonyl absorption at *ca.* 1735 cm^{-1}.

Carbonylation of 1°-Fatty N-Chloroamines

The three methods described above were each used to obtain a solution of an *N*-chloroamine (0.02 mol) for subsequent carbonylation using the same conditions as those described above for 2°-chloroamines. At the end of the reaction, following the solvent extraction using petroleum ether, the solvent was replaced by chloroform and excess aniline added. After reflux for several hours to ensure complete conversion of the carbamoyl chloride/isocyanate mixture into an *N*-phenylurea derivative, the reaction mixture was extracted several times with dilute hydrochloric acid, followed by washing with water to remove excess aniline as the hydrochloride salt. Solvent was removed *in vacuo,* and the solid residue was solvent-extracted with 40–60°C petroleum ether to leave an off-white powder, the insoluble urea derivative. This was dissolved in chloroform and either purified by recrystallisation or column chromatography using Kieselgel 60. Products were characterised by elemental analysis, ^{1}H NMR, and IR spectroscopy. Yields are given in Table 4. For $C_{18}H_{37}NHCONHPh$, we found: C, 77.8; H, 12.1; N, 7.22. $C_{25}H_{44}N_2O$ requires C, 77.3; H, 11.4; N, 7.20%. Authentic samples of the ureas were prepared by reaction of phenyl isocyanate and the appropriate amine. Preparation from phosgene gave low yields only (10–20%). Characteristic ν(N–H) and ν(C=O) absorptions occurred at 3210 and 1660 cm^{-1}, respectively.

Reaction of N-chlorodiethylamine with Carbonyl-tris(triphenylphosphine) Palladium(0)

The palladium complex was prepared from palladium(II) ethanoate and triphenylphosphine in methanol under a carbon monoxide atmosphere (*18*). *N*-Chlorodiethylamine was prepared from diethylammonium chloride and sodium hypochlorite (Route 1 above), the compound being extracted into chloroform, and washed with dilute sulphuric acid, dilute sodium hydroxide, and water, before drying over calcium chloride. The solution was degassed by freeze/thaw cycles *in vacuo*. The *N*-chloroamine (0.01 mol) in chloroform (5 cm^3) was added to a chloroform (20 cm^3) solution of the palladium carbonyl (5 mmol) and the mixture was stirred at ambient temperature for 24 h, the reaction being followed by IR spectroscopy. Filtration of the solution, followed by partial removal of the solvent and addition of hexane gave a pale yellow solid identified as $Pd(PPh_3)_2Cl_2$. We found: C, 63.1; H, 6.20; Cl, 10.4; P, 8.25; Pd, 16.0. $C_{36}H_{30}Cl_2P_2Pd$ requires C, 61.6; H, 4.30; Cl, 10.1; P, 8.84; Pd, 15.1%. The IR spectrum was identical to an authentic sample of $Pd(PPh_3)_2Cl_2$, present as a mixture of the two geometric isomers.

RESULTS AND DISCUSSION

The effects of carbon monoxide pressure, catalyst precursor, and added phosphine on the palladium-catalysed carbonylation of chloroamines are investigated and quantified. Initial studies used chloroamines having short alkyl chains, but the work is extended later to fatty acid *N*-chloroamines. The former are prepared by reaction of the amine hydrochlorides at 0°C with aqueous sodium hypochlorite, followed by solvent extraction of the chloroamine into diethyl ether. The same method could not be used for the fatty acid amines because of their insolubility in water. Instead, hypochlorous acid was generated in the presence of a suitable solvent, e.g., methyl ethyl ketone, by the reaction of sodium hypochlorite with hydrochloric acid at −10° to 0°C, then reacted with the fatty amine dissolved in chloromethane in an exothermic reaction below 0°C.

The results shown in Table 1 clearly show that palladium(II) compounds are effective catalysts for the carbonylation of *N*-chloroamines, confirming the work of Saegusa *et al.* (*15*), since in the absence of the metal compound the *N*-chloroamine is recovered unchanged. For *N*-chloropiperidine, the yield of the metal-catalysed reaction is enhanced from 75 to 84% by the presence of triphenylphosphine. Yields from primary chloroamine reactions are, however, less than half the yields for secondary chloroamines, the primary amines being recovered predominantly as hydrochloride salts. The source of the amine is intriguing as it is unlikely to arise from the original chlorination reaction product, which was washed with aqueous acid prior to use. Unfortunately, an excess of sodium hypochlorite cannot be used in this preliminary stage to ensure complete reaction to form monochloroamines, because of the possibility of further reaction to form dichloroamines.

$$R\mathrm{NH_2} + \mathrm{NaOCl} \rightarrow R\mathrm{NHCl} + \mathrm{NaOH}$$

$$R\mathrm{NHCl} + \mathrm{NaOCl} \rightarrow R\mathrm{NCl_2} + \mathrm{NaOH}.$$

Also, dichloroamines do not undergo carbonylation under the conditions used in these experiments (see later section), so their formation would lead only to low overall conversion to carbonylated products. Recovery of the amine as the hydrochloride salt implies a source of hydrogen in the high-pressure reaction or extraneous water or hydrogen in the carbon monoxide gas supply as possibilities. However, the chloroamine solutions were dried over calcium chloride prior to use to minimise this source of water.

Since amines appear to be generated in the reactions, it was relevant to determine the effect of bases in general on the course of the carbonylation reactions. Indeed, bases may have a beneficial effect in removing HCl formed, thereby minimising side reactions or promoting loss of HCl from *R*NH-COCl to form isocyanates. However, Saegusa *et al.* (*15*) found that pyridine was not a suitable solvent for the carbonylation stage.

The results of studies using *N*-chloro-*t*-octylamine and *N*-chloro-*t*-butylamine with nitrogen bases and hydrogen carbonates are presented in Table 2. Clearly, nitrogen bases completely suppress the reaction and are found to have this effect even in small amounts. A logical explanation is the preferential coordination of the nitrogen base to palladium(II), thereby restricting its conversion to the active catalytic species, presumably a palladium(0) complex, and the reaction of the *N*-chloroamine. These results may also explain the lower yield obtained when *N*-chloromorpholine is used in place of *N*-chloropiperidine (Table 1 and Ref. (*15*)). The oxygen atom present in the former amine may function as a σ-donor and hence reduce the activity of the catalyst. Similarly, the reduced yield observed by Saegusa *et al.* (*15*) when the reaction solvent was changed from benzene to 1,2-dimethoxyethane or acetonitrile may arise for the same reason. The insoluble inorganic bases have little effect on the yield of carbonylated products and on the amount of amine hydrochloride formed, as expected on the basis of the above sequence of reactions.

Since amines kill the catalytic reaction, the presence of free amines in the *N*-chloroamine can be eliminated as the source of the by-product primary amine salts. The absence of amines was demonstrated also by a GLC study. A further potential complication is the reaction between *N*-chloroamines and the parent amines to form hydrazinium salts (*19*),

$$RR'NCl + R''NH_2 \rightarrow RR'NNHR'' \cdot HCl,$$

but no evidence was found for their formation.

Since dichloroamines form readily from the monochloroamines in the presence of hypochlorite, the former will be common contaminants in the *N*-chloroamine reagents. Consequently, it was relevant to study the carbonylation of an *N,N*-dichloroamine in order to assist interpretation of the results.

Attempts were made to carbonylate *N,N*-dichloro-*t*-octylamine but with no success. The dichloroamine was recovered unchanged, no pressure changes were detected, and no new carbonyl stretching frequencies were detected in the infrared spectrum. When a mixture of the dichloro- and chloroamine was used, carbonylation proceeded normally (as indicated by CO consumption and by IR spectral studies), although no attempt was made to isolate the product because of the potential hazards arising from the dichloroamine. Carbonylation was indicated by a fall in pressure and the presence of a characteristic carbonyl stretching frequency (1740 cm^{-1}) due to the carbamoyl chloride.

The conditions used (50 atm CO, 18°C, 18 h) for these reactions are generally too mild for any reaction of the dichloroamine to occur, although the compounds are known to react with tetracarbonylnickel (*20*) at 20°C to produce *N,N'*-dialkylureas, which have a characteristic IR stretching frequency at ca. 1660 cm^{-1}. No absorption is observed in this IR region for the palladium-catalysed reaction.

The following equilibrium is reported to occur between the mono- and dichloroamines (*21*):

$$2RNHCl \rightleftharpoons RNCl_2 + RNH_2.$$

In an experiment in which *t*-octylamine was mixed with dichloro-*t*-octylamine at ambient temperature in diethyl ether, no ν(NH) stretching frequency due to the *N*-chloroamine was detected at 3260 cm^{-1} over several days. Thus if this equilibrium does occur, it must lie well to the right. Indeed the poisoning effect of free amines on the carbonylation reactions and the fact that carbonylation reactions of *N*-chloroamines occur up to 81% yield indicate that this reaction is only of minor importance if it occurs at all.

Carbon monoxide pressures decrease rapidly during the initial stages of the reactions, and a plot of the logarithm of the pressure against time shows an almost linear relationship during this period of time (5 h). Using different initial pressures of CO, the rate of reaction is found to be strongly pressure dependent below 50 atm, increasing with increase in pressure; but at about 50 atm, the rate becomes independent of pressure. The initial dependence on pressure probably relates to the formation of the active carbonyl catalyst species for which a minimal pressure is necessary for efficient conversion from the metal precurser. Once the active catalyst has formed, the reaction is independent of pressure, and the carbonylation stage represents a fast process.

For the mixed palladium–phosphine system, the initial rate of CO uptakes depends on the triphenylphosphine content up to a Pd : P ratio of 1 : 2. Excess of phosphine relative to this ratio does not have a detrimental effect on the reaction rate and probably reflects the ability of CO to displace phosphines from palladium complexes, particularly those of Pd(0), under high-pressure conditions. It may be expected that excess phosphine would decrease the availability of coordinatively unsaturated species and so reduce their reaction with *N*-chloroamines. This has not been found to occur. Three possible explanations are as follows. The phosphine ligands may be labile and the number of coordinatively unsaturated species may not be significantly reduced by excess phosphine. Alternatively, excess phosphine may be removed by reaction with the *N*-chloroamine, which is present in much larger quantity, according to

$$RR'\mathrm{N{-}Cl} + \mathrm{PPh_3} \rightarrow [\mathrm{Ph_3P{=}N}RR']^{+}\mathrm{Cl}.$$

If the latter reaction occurred to any large extent, all free phosphine resulting from labile cleavage from the active catalyst would be consumed, and the catalytic process would slow as the concentration of palladium–phosphine complex decreases. There was no evidence that this occurred, and, indeed, the pale yellow colour of the final solution was typical of solutions of palladium–phosphine complexes. Finally, the reaction may proceed by nucleophilic attack by the chloroamine at a coordinated CO group, the chloroamine not requiring a vacant coordination site at the metal.

Carbonylation of Fatty Acid Chloroamines

Three routes to the chloroamines were explored: the reactions of (i) an amine hydrochloride with sodium hypochlorite at <0°C, (ii) *N*-chlorosuccinimide with an amine, and (iii) hypochlorous acid with an amine. The last route was found to be the most successful (as discussed later), the chlorination being undertaken in a mixed solvent system. The hypochlorous acid in methyl ethyl ketone was added at −10°C to the amine in chloromethane solution. It was found essential that the amine be fully dissolved for high conversion of the fatty acid amine to the chloroamine; hence chloromethane was needed as the solvent. Residual amine was removed from the resulting chloroamine solution by washing with dilute sodium hydroxide solution, before drying over calcium chloride. For secondary amines, the chlorination was undertaken using a 5% excess of HOCl, but for primary amines excess was avoided to prevent formation of dichloroamines. In general, the chloroamines of fatty acids can be isolated by removal of the solvent to give waxy solids.

Carbonylation was attempted using 50 atm carbon monoxide pressure, at room temperature, over 14 h. The carbamoyl chloride product was purified by a combination of solvent extraction and column chromatography to give pale yellow waxy solids, which were characterised by IR spectroscopy and elemental analysis. Product identification was confirmed by comparison with authentic material produced by the phosgene route. Yields varied between 0 and 75% and depended on the route used to obtain the chloroamine. *In situ* generation using *N*-chlorosuccinimide and di(*n*-hexadecyl)amine gave a reagent that failed to produce any carbonylated product, although chlorination did occur as indicated by the presence of a ν(N–Cl) stretching frequency band at ca. 750 cm $^{-1}$. The presence of free amine was undoubtedly the cause of catalyst deactivation, the palladium being recovered as the metal. The low yields of carbamoyl chlorides from carbonylation of *N*-chloroamines prepared via the amine hydrochloride–sodium hypochlorite route also relate to the poor chloroamine production. The reaction between the insoluble amine hydrochloride and aqueous sodium hypochlorite is not efficient unless the amine salt is in solution.

For carbonylation of secondary *N*-chloroamines prepared from hypochlorous acid in methyl ethyl ketone, yields of carbamoyl chlorides were good, although slightly lower than those obtained for the lower alkyl chloroamines (Table 1) and by Saegusa *et al.* (*15*) for piperidine. However, the calculated yields may be low because of the method used to assay the hypochlorous acid solution, viz. iodometry. The presence of free chlorine, arising from the hypochlorite, will lead to an overestimate of the amount of hypochlorite present, and hence to an underestimate of the yield of carbonylated product based on the amount of amine used. Only minor differences in yields were observed for the three long-chain amines used. Dicocoamine is a mixture of amines having *n*-dodecyl, *n*-tetradecyl, and *n*-hexadecyl alkyl chains and contains some molecules having two different substituents. The yield for this amine was based on an average relative molecular mass of all combinations.

The experimental procedure for the carbonylation of primary *N*-chloroamines was the same as that for the secondary compounds, except that the resultant products were refluxed with an excess of aniline for several hours to convert the carbamoyl chloride/isocyanate mixture into *N*-phenyl urea derivatives. This procedure allowed the total yields (Table 4) of the carbonylation reaction to be measured. Carbonylation occurs only poorly for primary amines (yields 30–37%) and, as discussed earlier, the amine hydrochloride route to the chloroamine leads to little eventual carbonylation. The hypochlorous acid route produced yields similar to those obtained for other primary chloroamines having shorter alkyl groups (Table 1),but in the present case IR spectral studies show the presence of both isocyanates and carbamoyl chlorides. The former compound arises from elimination of HCl from the carbamoyl chloride, according to

$$R\mathrm{NHCOCl} \rightarrow R\mathrm{N{=}C{=}O} + \mathrm{HCl}$$

The HCl generated is detrimental to the yields obtained from primary chloroamines due to the formation of amine hydrochlorides that always accompanies its production.

$$R\mathrm{NHCl} + 2\mathrm{HCl} \rightarrow R\mathrm{NH_3^+Cl^-}.$$

The salt is a major by-product of the carbonylation reaction. Another contributory factor to the low yield may be the low electron donating ability/nucleophilicity of primary chloroamines to palladium even compared with the secondary chloroamines, where the electron donating effects of two alkyl groups tend to offset the electron withdrawing effect of chlorine. The reaction sequence is thought to involve a coordination or nucleophilic attack step.

$$\mathrm{Pd}L_n + RR'\mathrm{N{-}Cl} \rightarrow \mathrm{Pd}L_m(RR'\mathrm{N{-}Cl})$$

or

$$\mathrm{Pd}L_x(\mathrm{CO}) + RR'\mathrm{N{-}Cl} \rightarrow \overset{-}{\mathrm{Pd}}L_x\{\mathrm{CO}\overset{+}{\mathrm{N}}(RR')\mathrm{Cl}\}.$$

In the case of primary chloroamines (R'=H) the equilibrium would lie more to the left compared to that for secondary chloroamines.

In an attempt to prepare intermediate complexes involved in the catalytic reaction, carbonyltris(triphenylphosphine) palladium (*18*) was reacted with *N*-chlorodialkylamines in chloroform at ambient temperature over 24 h and the carbonyl stretching region of the IR spectrum was monitored. The metal carbonyl absorption at 1955 cm^{-1} soon disappeared after the addition of the chloroamine, and the final product obtained was $Pd(PPh_3)_2Cl_2$. No attempt was made here to isolate and identify the nitrogen-containing product. Similar results are found for reactions of other metal carbonyl complexes, e.g., octacarbonyldicobalt and tetracarbonylnickel, where the chloroamine acts as an oxidising reagent for the low valent metal, and metal dichloride complexes are formed. Intermediate carbamoyl complexes of the type isolated for nickel, i.e., $Li^+[Me_2NCONi(CO)_3]^-$[14], may be involved, but in the presence of additional chloroamine will react further to form metal dichloride complexes, viz.

$$Pd(PPh_3)_2(RR'NCO)Cl + RR'NCl \rightarrow Pd(PPh_3)_2Cl_2 + RR'NCONRR'.$$

The above carbamoyl palladium complex has been prepared by different routes (*22*), involving carbonylation of a mixture of $Pd(PPh_3)_2Cl_2$ and amine, and also from dialkylcarbamoyl chlorides with zero-valent compounds such as $Pd(PPh_3)_4$. Interestingly, using the latter route the main metal complex produced is the dichloride complex as formed in the present work.

Carbamoyl complexes of palladium derived from primary amines have a low stability under acidic conditions (*22*). Since the carbonyl chloride products of the carbonylation reactions eliminate HCl when forming isocyanates, the low yields of the reaction may be attributed to decomposition of an intermediate palladium carbamoyl complex by HCl to give the amine salt.

$$L_2Pd(Cl)CONRR' + 2HCl \rightarrow [L_2Pd(Cl)CO]Cl + RR'NH_2Cl.$$

An *in situ* examination of the carbonylation process by IR spectroscopy was undertaken using three forms of palladium, the metal, palladium(II) chloride, and dichlorobis(triphenylphosphine)palladium(II). Spectra were recorded in the 2500–1400 cm^{-1} region for reactions with *N*-chlorodimethylamine in chloroform solution. Using a freshly prepared sample of the metal and a carbon monoxide pressure of 65 atm, new absorptions appeared at 1680(s), 1715(s), and 1755 cm^{-1}. After 15 min, no further changes to these absorptions occurred, but two carbonyl peaks were observed at ca. 2100 and ca. 2160 cm^{-1}, assigned to a carbonyl complex and dissolved CO, respectively. The 1715 cm^{-1} peak (due to Me_2NCOCl) strengthened with progress of the reaction, but on release of the pressure, the 2100 and 2160 cm^{-1} absorptions disappeared. The most feasible type of complex to have a carbonyl stretching absorption as high as 2100 cm^{-1} is a cationic complex of the type $[L_2Pd(CO)Cl]^+$, known to form from palladium(II) chloride complexes in a carbon monoxide atmosphere (*23, 24*). However, the nature of L here is unknown.

Using palladium(II) chloride and 65 atm carbon monoxide, new absorptions only appeared at 50°C after 15 min. A broad peak at 1680 cm^{-1} and an unresolved shoulder at ca. 1760 cm^{-1} developed and remained unchanged both on increasing the pressure to 100 atm and on removing the pressure completely. When $Pd(PPh_3)_2Cl_2$ was used, initial reaction with carbon monoxide (65 atm) produced three new absorptions at 2120(m), 1755(w), and 1670(w) cm^{-1}. After 15 min, the first peak decreased in intensity, whereas the other two became stronger. A new peak at 1715(w,sh) cm^{-1} appeared and continued to grow. After a further 15 min, the three peaks coalesced and their total intensity increased greatly. On increasing the CO pressure to 100 atm, there was no further increase in intensity of this peak, although the peak ca. 2100 cm^{-1} increased from weak to medium intensity. When the high-pressure gas was released, the 2100

cm^{-1} absorption disappeared, but the 1670, 1715, and 1755 cm^{-1} absorptions remained.

Absorptions at 2120 and 1715 cm^{-1} are assigned to $[(PPh_3)_2Pd(CO)Cl]^+$ (*24*) and Me_2NCOCl, respectively. The absorption at 1670 cm^{-1} is almost certainly due to $Me_2NCONMe_2$, but the 1755 cm^{-1} absorption cannot be assigned. This last absorption occurs at too high a frequency to be assigned to a nitrogen-bound carbonyl group and is too low to arise from $COCl_2[\nu(CO)$ 1827 $cm^{-1}]$ (*25*). A strong possibility, however, is that it is due to the ester $Me_2NCOOEt$ formed between Me_2NCOCl and the ethanol stabiliser in the chloroform solvent.

CONCLUSIONS

N-Chloroamines undergo carbonylation reactions catalysed by palladium compounds to produce carbamoyl chlorides. Yields up to 85% are achieved using secondary amine derivatives, but for primary amine derivatives yields are halved. For long-chain primary amines (C_{12}–C_{18}) yields are typically 32–35%. Triphenylphosphine generally enhances the yield for palladium(II) chloride and ethanoate when used in a 1 : 2 Pd : P ratio, although nitrogen bases stop the process. *N,N'*-Dichloroamines failed to carbonylate.

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