Carbonylation of Amines with Carbon Monoxide and Silver Acetate[1]

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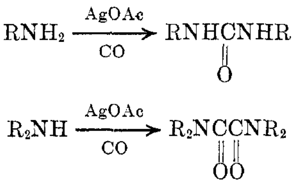
Facile and almost quantitative carbonylation of primary and secondary amines was performed at room temperature with a combination of carbon monoxide and silver acetate. The carbonylation product obtained depended upon the structure of the amine. Primary amines gave the corresponding *N,N'*-dialkylureas and secondary amines gave *N,N,N',N'*-tetraalkyloxamides. Carbamoylsilver derivatives, $AgC(=O)NR_1R_2$, resulting from carbon monoxide insertion into transiently formed silver–nitrogen bonds have been proposed as intermediates in the reaction.

Although the affinity of carbon monoxide to group Ib metal atoms (Cu, Ag, and Au) has been demonstrated by the formation of metal halide carbonyls, *e.g.*, $CuCl(CO)$,[2] little attention has been paid to the carbonylation of organic compound using group Ib metal compound. Recently, several interesting carbonylation reactions of copper compounds involving carbon monoxide insertion and subsequent ligand coupling have been reported by us. These include carbonate[3] and oxamide[4] formation by carbonylation of cupric alkoxides and cuprous amide, respectively. Symmetrical ketone formation by the carbonylation of organocopper complex is another example.[5] As for the carbonylation by silver compound, our previous communication[1] has reported *N,N,N',N'*-tetraethyloxamide formation by the carbonylation of diethylamine with carbon monoxide and silver acetate. However, the yield of oxamide was not high in this report. The present report is concerned with the facile and quantitative carbonylation of primary and secondary amines with a combination of carbon monoxide and silver acetate.

Results and Discussion

Primary and secondary amines underwent facile and quantitative carbonylation with a combination of carbon monoxide and silver acetate at room temperature (Table I). It is important to note that two carbonylation products were formed depending upon the structure of the amine.



$$\mathrm{RNH_2 \xrightarrow[CO]{AgOAc} RNH\underset{\underset{\displaystyle O}{\|}}{C}NHR}$$

$$\mathrm{R_2NH \xrightarrow[CO]{AgOAc} R_2N\underset{\underset{\displaystyle O}{\|}}{C}\underset{\underset{\displaystyle O}{\|}}{C}NR_2}$$

Primary amines gave predominantly the corresponding *N,N'*-dialkylureas, whereas secondary amines produced tetraalkyloxamides. Formamides were formed in small amounts; *e.g.*, in the carbonylation of diethylamine, *N,N*-diethylformamide was produced in a yield of 5% and *N*-butylformamide was detected in a yield of 3% in the case of *n*-butylamine.

Several variables of the reaction conditions were examined in the carbonylation of diethylamine. The results combined with the previous ones are summarized as follows.

(i) The amine/silver acetate ratio was important to the oxamide yield. Although the best yield of oxamide was only 40% in the ratio of 1:1,[1] an almost quantitative yield was obtained by increasing this ratio to 10:1.

(ii) Among the silver salts used (AgOAc, $AgNO_3$, AgCl, AgCN, and AgSCN), silver acetate was the most effective.[1]

(iii) Other metal acetates such as $Cu(OAc)_2$, $Zn(OAc)_2$, $Cd(OAc)_2$, $Co(OAc)_2$, and $Ni(OAc)_2$ were ineffective. $Pd(OAc)_2$ showed a slight activity.

(iv) High carbon monoxide pressure was not necessary. Carbonylation took place at a carbon monoxide pressure as low as 5 kg/cm^2.

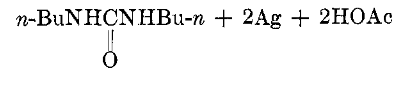
(v) Lower reaction temperature (0° ~ room temperature) was favorable for the oxamide formation and higher reaction temperature (100–160°) diminished the yield of oxamide.[1]

(vi) Triethylamine, tetrahydrofuran, and 1,2-dimethoxyethane could be used as a reaction solvent, but pyridine and *N,N,N',N'*-tetramethylethylenediamine reduced the yield of oxamide remarkably.[1]

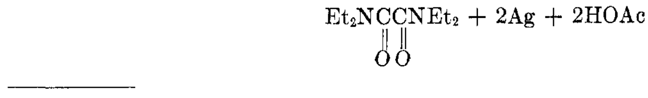
Examples of carbonylation reactions using transition metal compounds in which two carbonyl groups are coupled together are rare[6] and the transition metals used have been limited to group VIII. Thus, it is particularly interesting that oxamide is produced quantitatively by silver acetate under mild reaction conditions.

The determination of the stoichiometry of the reaction has provided insight into the mechanism. In the carbonylation of *n*-butylamine and diethylamine with carbon monoxide–silver acetate, metallic silver and acetic acid were formed together with the respective carbonylation products (Table II).

The yields of silver metal and acetic acid were in good agreement with those of the carbonylation products calculated on the basis of the following equations.



$$\mathrm{2AgOAc + 2\mathit{n}\text{-}BuNH_2 + CO \longrightarrow \mathit{n}\text{-}BuNH\underset{\underset{\displaystyle O}{\|}}{C}NHBu\text{-}\mathit{n} + 2Ag + 2HOAc}$$



$$\mathrm{2AgOAc + 2Et_2NH + 2CO \longrightarrow Et_2N\underset{\underset{\displaystyle O}{\|}}{C}\underset{\underset{\displaystyle O}{\|}}{C}NEt_2 + 2Ag + 2HOAc}$$

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(1) A preliminary report has appeared: T. Saegusa, T. Tsuda, K. Isayama, K. Nishijima, and Y. Isegawa, *Tetrahedron Lett.*, 1641 (1968).

(2) "Gmelins Handbuch der Anorganischen Chemie," Verlag Chemie GMBH, Weinheim/Bergstr., 1958, Kupfer, Teil B, Lieferung 1, p 240.

(3) T. Saegusa, T. Tsuda, and K. Isayama, *J. Org. Chem.*, **35**, 2976 (1970).

(4) T. Saegusa, T. Tsuda, K. Nishijima, and K. Isayama, *Tetrahedron Lett.*, 3379 (1968).

(5) T. Tsuda, K. Nishijima, and T. Saegusa, unpublished work.

(6) N. L. Bauld, *Tetrahedron Lett.*, 1841 (1963); G. Booth and J. Chatt, *J. Chem. Soc. A*, 634 (1966); J. Tsuji and N. Iwamoto, *Chem. Commun.*, 380 (1966); S. Fukuoka, M. Ryang, and S. Tsutsumi, *J. Org. Chem.*, **33**, 2973 (1968).

TABLE I

CARBONYLATION OF AMINES BY SILVER SALT AND CO[a]

Silver salt (mmol)	Registry no.	Amine (mmol)	Solvent (ml)	CO, kg/cm²	Time, hr	Yields of products, %[b] urea	oxamide
AgOAc (10)	109-73-9	n-$C_4H_9NH_2$ (50)	$N(C_2H_5)_3$ (7)	85	15.5	~100	
AgOAc (10)	107-11-9	$CH_2{=}CHCH_2NH_2$ (50)	$N(C_2H_5)_3$ (7)	85	15.5	73	
$AgNO_3$ (10)		n-$C_4H_9NH_2$ (100)		80	9.5	68	3
$AgNO_3$ (10)		$CH_2{=}CHCH_2NH_2$ (100)		80	6	60	Trace
AgOAc (10)	124-40-3	$(CH_3)_2NH$ (50)	$N(C_2H_5)_3$ (7)	80	33	Trace	~100
AgOAc (20)	109-89-7	$(C_2H_5)_2NH$ (200)	$N(C_2H_5)_3$ (20)	100	19.5		91
AgOAc (10)	111-92-2	$(n$-$C_4H_9)_2NH$ (50)		55	19.5	Trace	82

[a] The reaction was carried out at room temperature in a stainless steel tube with mechanical shaking. [b] The yield is based on silver salt. About the reaction stoichiometry; see the text.

TABLE II

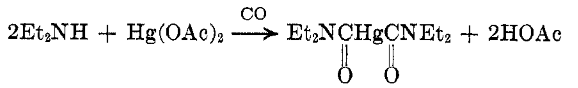
STOICHIOMETRY OF CARBONYLATION OF AMINE[a]

AgOAc, mmol	Amine (mmol)	CO, kg/cm²	Time, hr	Yields of products, %[b] Oxamide	Urea	Acetic acid	Silver metal
10	n-$C_4H_9NH_2$ (100)	55	19.5		91	93	92
20	$(C_2H_5)_2NH$ (200)	100	5	90		Not determined	89
20	$(C_2H_5)_2NH$ (100)	90	7	74		72	Not determined

[a] The reaction was carried out at room temperature in a stainless steel tube with mechanical stirring. [b] The yield is based on silver acetate.

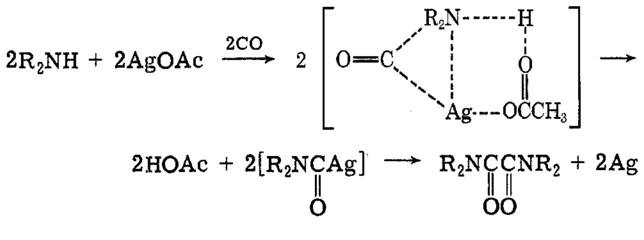
Although different carbonylation products were obtained from each, primary and secondary amines showed the same stoichiometry. This fact suggests that a commom intermediate is formed in these reactions.

It is significant to note here that mercuric acetate reacts with secondary amines in the presence of carbon monoxide to form stable carbamoylmercuric compounds with the release of acetic acid.[7]



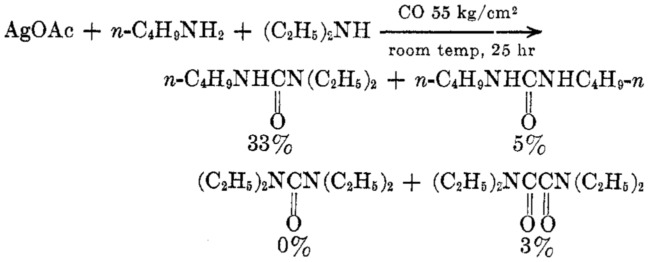
$$2Et_2NH + Hg(OAc)_2 \xrightarrow{CO} Et_2N\underset{\underset{O}{\|}}{C}Hg\underset{\underset{O}{\|}}{C}NEt_2 + 2HOAc$$

Carbamoylsilver may be the key reaction intermediate of the present study. In the carbonylation of secondary amines, the carbon monoxide insertion into a transient silver–nitrogen bond could give rise to a carbamoylsilver derivative with the liberation of acetic acid. In the *N*,*N*-dialkylcarbamoylsilver complexes, the nitrogen atom has no abstractable hydrogen and therefore the coupling of the two carbamoyl groups occurs to give oxamide and metallic silver.



In the case of primary amines, the nitrogen atom of the carbamoylsilver species has one hydrogen atom. The abstraction of the hydrogen and the scission of the carbon–silver bond in carbamoylsilver may take place simultaneously to produce the corresponding alkyl isocyanate. Then the isocyanate would react rapidly with another molecule of primary amine to give the urea. In the carbonylation of primary amines with carbon monoxide–silver nitrate, a small amount of *N*,*N'*-dialkyloxamide was formed, which was probably derived from coupling of the carbamoylsilver species.

The carbonylation of an equimolar mixture of *n*-butylamine and diethylamine is compatible with an isocyanate intermediate.



$$AgOAc + n\text{-}C_4H_9NH_2 + (C_2H_5)_2NH \xrightarrow[\text{room temp, 25 hr}]{\text{CO 55 kg/cm}^2} \underset{33\%}{n\text{-}C_4H_9NH\underset{\underset{O}{\|}}{C}N(C_2H_5)_2} + \underset{5\%}{n\text{-}C_4H_9NH\underset{\underset{O}{\|}}{C}NHC_4H_9\text{-}n} + \underset{0\%}{(C_2H_5)_2N\underset{\underset{O}{\|}}{C}N(C_2H_5)_2} + \underset{3\%}{(C_2H_5)_2N\underset{\underset{O}{\|}}{C}\underset{\underset{O}{\|}}{C}N(C_2H_5)_2}$$

N,*N'*-Di-*n*-butylurea and *N*-*n*-butyl- *N'*,*N'*-diethylurea were found, but *N*,*N*,*N'*,*N'*-tetraethylurea could not be detected. These facts exclude the possibility of urea formation by the attack of amine on carbamoylsilver. *n*-Butylamine apparently reacts with silver acetate faster than it does with diethylamine to give *n*-butyl isocyanate, which then is attacked by the unreacted diethylamine to produce the unsymmetrical urea as the main product. The formation of *N*,*N*,*N'*,*N'*-tetraethyloxamide indicates the intermediacy of diethylcarbamoylsilver. However, because of its inability to give an isocyanate intermediate, *N*,*N*,*N'*,*N'*-tetraethylurea formation is impossible.

The carbonylation of an equimolar mixture of silver acetate, diethylamine, and organic halide such as ethyl bromide and allyl chloride did not change the yield of oxamide, and *N*,*N*-diethylpropionamide and *N*,*N*-diethylvinylacetamide were not detected. This result suggests that the carbonylation reaction may occur very rapidly in the silver acetate–amine complex.

Experimental Section

Reagents.—Silver acetate and other metal acetates were commercial reagents and were used without further purification. Commercial metal acetates which contain the water of hydration were dehydrated by heating *in vacuo*. Amines except dimethylamine were refluxed and distilled over KOH. Dimethylamine was generated by adding its aqueous solution to anhydrous

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[7] U. Schoellkopf and F. Gerhart, *Angew. Chem.*, **78**, 675 (1966).

calcium carbonate, and was dried by passing through NaOH pellets and condensed at Dry Ice temperature. Carbon monoxide was obtained from a commercial cyclinder.

General Procedure of Carbonylation.—Silver salt, amine, and solvent, if used, were placed in a 50-ml stainless steel tube under nitrogen, into which carbon monoxide gas was compressed at room temperature. The tube was closed and heated. After reaction, carbon monoxide was released, and the organic layer was separated from the precipitated silver metal by centrifugation. The silver metal was washed several times with ether. The organic layer, combined with the ether washings, was concentrated and analyzed by glpc (9-ft column of Silicon DC 200 on Celite 545). Urea and oxamide were identified by comparison of ir spectra and glpc retention times with those of authentic samples. The authentic samples of oxamides were prepared from oxalyl chloride and amine. The authentic symmetrical ureas were obtained by the reaction of phosgene and amine. The authentic unsymmetrical ureas were synthesized from carbamoyl chloride and amine.

Stoichiometry of the Carbonylation Reaction. Determination of Silver Metal Deposited and Acetic Acid Liberated.—After reaction, the precipitated silver metal was separated by centrifugation and washed several times with the amine used in the reaction. Then silver metal was oxidized to silver nitrate by concentrated nitric acid and titrated with ammonium thiocyanate using ferric ammonium sulfate as an indicator. The acetic acid liberated in the reaction was determined by glpc analysis of the separated organic layer combined with the amine washings (9-ft column of PEG 20M on Celite 545).

Registry No.—CO, 630-08-0; AgOAc, 563-63-3; $AgNO_3$, 7761-88-8.

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endo-7-Aminomethylbicyclo[3.3.1]nonan-3-ones from Rearrangement of 1-N-Substituted *N*-Haloadamantanamines by Aluminum Chloride[1]

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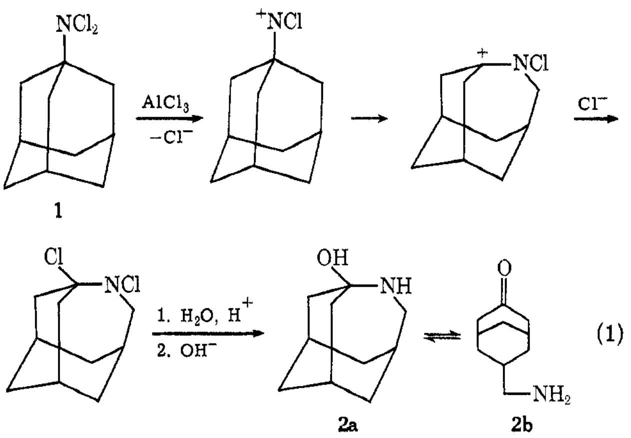
Treatment of *N*-chloro-*N*-ethyl-1-adamantanamine (**3**) with aluminum chloride afforded rearranged product which was isolated as *endo*-*N*-ethyl-7-aminomethylbicyclo[3.3.1]nonan-3-one (**4**) after acid hydrolysis. The configurational and conformational aspects of the isomeric alcohols obtained by hydride reduction are treated. The response of 3-methoxy-4-azahomoadamantanes to hydrolysis and hydride reduction was investigated. Rearrangement of *N*-chloro- and *N*,*N*-dibromo-1-adamantanamines yielded *endo*-7-aminomethylbicyclo[3.3.1]-nonan-3-one (**2**). Evidence is presented concerning the nature of the carbinolamine–amino ketone equilibrium for **2** and **4**.

Several rearrangements of *N*-haloamines have been characterized.[3] Most noted is the Hofmann–Löffler cyclization *via* an amminium radical.[4] α-Amino ketones are generated by the action of base on *N*,*N*-dichloro-*sec*-alkylamines, presumably by a pathway analogous to the Neber rearrangement.[5] Nitrenium ions have been proposed as intermediates in the Stieglitz rearrangement of *N*-halo- and *N*,*N*-dihalotritylamines.[6]

Evidence for the existence of a discrete electron-deficient nitrogen of this type was obtained[6] through studies of *N*-chloroalkylamine rearrangements in the presence of silver salts. Gassman's group,[6] as well as other investigators,[7] found that alkyl migration to nitrogen occurred with a strained ring system whose carbon analog is known to undergo carbonium ion rearrangement quite readily. Similar transformations of primary *N*-haloamines in the presence of aluminum chloride were observed when nitrogen was adjacent to a bicyclic[8] or tricyclic[9] ring system. For example, *N*,*N*-dichloro-1-adamantanamine (**1**) was converted to 7-aminomethylbicyclo[3.3.1]nonan-3-one (**2b**) by rearrangement followed by hydrolysis.[9] The postulated mechanism is depicted in eq 1. An analogous rearrangement was recently reported for *N*-acetyl-*N*-chloro-1-adamantanamine.[10]



(1)

The objective of the present work was to determine the effect of variation in the substitutent on rearrangement of 1-N-substituted *N*-haloadamantanamines. The chemical behavior of various compounds obtained in this study was examined. In addition, carbinolamine–ketoamine equilibria and stereochemical aspects were investigated.

Results and Discussion

Most of our attention was devoted to the rearrangement of *N*-chloro-*N*-ethyl-1-adamantanamine (**3**). Synthesis of **3** was accomplished by hydride reduction of

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[1] Paper V, "Adamantanes and Related Compounds;" for the preceding publication in the series see ref 9; presented at the 163rd National Meeting of the American Chemical Society, Boston, Mass., April 1972.

[2] Postdoctoral, 1970–1971.

[3] P. Kovacic, M. K. Lowery, and K. W. Field, *Chem. Rev.*, **70**, 639 (1970).

[4] M. E. Wolff, *ibid.*, **63**, 55 (1963).

[5] H. E. Baumgarten and F. A. Bower, *J. Amer. Chem. Soc.*, **76**, 4561 (1954).

[6] P. G. Gassman, *Accounts Chem. Res.*, **3**, 26 (1970).

[7] H. H. Wasserman, H. W. Adickes, and O. E. de Ochoa, *J. Amer. Chem. Soc.*, **93**, 5586 (1971).

[8] P. Kovacic, M. K. Lowery, and P. D. Roskos, *Tetrahedron*, **26**, 529 (1970).

[9] P. Kovacic, J.-H. Liu, P. D. Roskos, and E. M. Levi, *Chem. Commun.*, 1034 (1970); *J. Amer. Chem. Soc.*, **93**, 5801 (1971).

[10] T. Sasaki, S. Eguchi, T. Kiriyama, and H. Suzuki, *Syn. Commun.*, **1**, 267 (1971).