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N,N-DISUBSTITUTED LITHIUM BIS(CARBAMOYL)CUPRATE. A CONVENIENT COMPLEX FOR ONE-POT CONVERSIONS OF AMINES TO FORMAMIDES, OXAMIDES, CARBAMATES, AND OXAMIC ACIDS

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Summary

Lithium bis(carbamoyl)cuprates (**2**) were readily derived from secondary amines such as *N*-methylaniline, *N*-methylbenzylamine, and diethylamine, under mild carbonylation conditions (0°C, 1 atm of carbon monoxide), but diphenylamine and benzylphenylamine were unsuitable as the starting materials. The carbamoylcopper complexes **2** formed in ether were readily converted to the corresponding formamides, oxamides, carbamates, and oxamic acids by the appropriate treatment. The formation and stability of **2** depended much on the solvent used. The higher polarity effect of the solvent (DME, THF, and HMPA) made **2** less stable and caused concomitant evolution of carbon monoxide in further reactions. A palladium catalyst was found to be effective for cross-coupling reactions of **2** with iodobenzene or (*E*)-*β*-bromostyrene.

Introduction

Carbamoylmetal compounds formed by carbonylations of metal amides are of primary importance as reactive carbamoyl anion equivalents for direct introduction of a carbonyl functional group into organic compounds. Several carbamoylmetal compounds effecting useful organic reactions are known [1–6]. The simplest example is carbamoyllithium [2] formed from lithium amide and carbon monoxide at −78°C. However, the carbamoyllithium species, apart from those prepared by the lithiation of dialkylformamides [3] or by the transmetalation between carbamoylmercury compounds and n-butyllithium [1c], were liable to cause some tedious side reactions such as self-condensation, even at −78°C. Moreover, accessible lithium amides for carbonylation are limited by the structures of the organic part of the amides [2,6a] and by the basicity of the starting amines [6b]. While lithium carbamoyltricarbonylnickelates [4], formed from the reaction of lithium amide and $Ni(CO)_4$, is a useful carbamoyl anion source, and its high reactivity toward organic halides has been reported. However, the necessary use of $Ni(CO)_4$ is disadvantageous because of its

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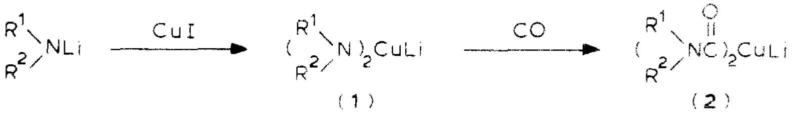
high toxicity. Cuprous amide [5] prepared from lithium amide and cuprous chloride required more severe conditions (60 atm CO, 180°C) to undergo carbonylation, and the scope of application for the reaction was limited by instability of the carbamoylcopper intermediate which decomposed to oxamide and metallic copper under these conditions. Alternatively, lithium bis(carbamoyl)cuprate [6], first reported by Saegusa et al. [6a], formed from the reaction of lithium bis(amino)cuprate with carbon monoxide was found to be a useful reagent for direct carbamoylation of organic halides. While the carbamoylcopper complex has promising possibilities as a carbamoyl anion source for synthetic organic reactions, further investigations concerning the properties and usefulness of the carbamoylcopper complex have not yet been undertaken. More information is necessary to extend the synthetic usefulness of the carbamoylcopper complex in organic synthesis. Here, we report the properties and the potential reactions of the carbamoylcopper complexes derived from secondary amines.

Results and discussion

Formation of lithium bis(carbamoyl)cuprates (2)

The usefulness of amines for the formation of **2** was examined by the reaction of lithium bis(amino)cuprates (**1**) with carbon monoxide in dry ether. The aminocopper complexes **1** derived from simple secondary amines such as *N*-methylaniline, *N*-methylbenzylamine, and diethylamine, absorbed smoothly two equivalents of carbon monoxide (based on copper) at 0°C under 1 atm of carbon monoxide, generating the corresponding carbamoylcopper complexes **2** (eq. 1, Tables 1–3). Usually, a reaction temperature of −40°C or more was required for the smooth absorption of



(1)

TABLE 1

SOLVENT EFFECTS ON THE REACTION OF **2a** WITH METHYL IODIDE [a]

Run	Solvents [b]	Yields (%) of *N*-methylacetanilide [c]
1	ether	72
2 [d]	ether	40
3	DME [e]	29
4	THF [e]	21
5	HMPA [f]	trace
6	benzene/DME [g] (10/1)	40

[a] Lithium bis(*N*-methyl-*N*-phenylamino)cuprate (**1a**), prepared from lithium *N*-methylanilide (1.87 mmol) and CuI (0. 935 mmol) in the solvent (5 ml), was allowed to react with carbon monoxide at 0°C for 2 h. The reaction mixture which contained lithium bis(*N*-methyl-*N*-phenylcarbamoyl)cuprate (**2a**) was treated with CH_3I (3.74 mmol), and then stirred for 3 h at 0°C and for 5 h at room temperature under carbon monoxide. [b] In all cases, the reaction mixture contained about 1.2 ml of n-hexane added as a solvent of n-butyllithium used. [c] Isolated yields based on *N*-methylaniline. [d] Triphenylphosphine (1.87 mmol) had been added before the reaction with carbon monoxide. [e] The evolution of CO was observed in the reaction with CH_3I. [f] Appreciable absorption of CO was not observed in the preparation of **2a**. [g] When the reaction mixture treated with CH_3I was warmed up to room temperature after being stirred for 3 h at 0°C, the evolution of CO was observed.

TABLE 2

CONVERSIONS OF **2** TO METHYL CARBAMATES (**5**) [a]

2		Yields (%) of products [b]	
R^1	R^2	**5**	**4**
CH_3	C_6H_5	66	31
C_2H_5	C_6H_5	61	33
C_3H_7	C_6H_5	59	31
C_2H_5	p-ClC_6H_4	61	32
C_2H_5	3,4-$Cl_2C_6H_3$	55	33
CH_3	o-$CH_3C_6H_4$	65	–
CH_3	m-$CH_3C_6H_4$	56	26
$CH_2CH{=}CH_2$	C_6H_5	56	28
CH_3	$CH_2C_6H_5$	61	29

[a] All reactions were carried out in dry ether. [b] Isolated yields based on the starting amines. [c] The product was not obtained in a pure form.

CO. Although the differences between aromatic amines and aliphatic amines were not crucial for the formation of **2**, the use of diphenylamine or benzylphenylamine as a starting material resulted in no CO absorption under our conditions. In the above two cases, the steric influence of the starting amine seemed to be decisive rather than the basicity of the amine; the corresponding aminocopper complex **1** is unstable.

Although aliphatic lithium amides undergo smooth carbonylation even at −78°C and, in some cases, relatively stable carbamoyllithium species are formed [2], the scope of the reaction is restricted for sterically hindered amides such as lithium

TABLE 3

REACTIONS OF **2** WITH CARBON DIOXIDE [a]

Run	2		Yields (%) of **6** [b]
	R^1	R^2	
1	CH_3	C_6H_5	53
2	C_2H_5	C_6H_5	55
3 [c]	C_2H_5	C_6H_5	9
4	CH_3	o-$CH_3C_6H_4$	51
5	CH_3	m-$CH_3C_6H_4$	56
6	C_2H_5	p-ClC_6H_4	59
7 [d]	C_2H_5	p-ClC_6H_4	55
8 [e]	C_2H_5	p-ClC_6H_4	56
9	C_2H_5	3,4-$Cl_2C_6H_3$	41
10	$CH_2CH{=}CH_2$	C_6H_5	44
11	CH_3	$CH_2C_6H_5$	51
12	$CH(CH_3)_2$	$CH(CH_3)_2$	42
13 [f]	C_6H_5	C_6H_5	trace
14 [f]	$CH_2C_6H_5$	C_6H_5	trace

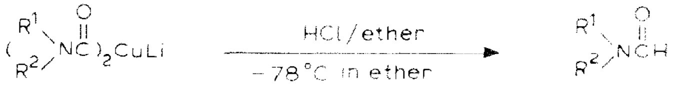
[a] Unless otherwise indicated, reactions were carried out at 0°C in ether and the reaction time was 2 h. [b] Isolated yields based on the starting amines. [c] The reaction was carried out at −78°C for 2 h. [d] After the reaction with carbon dioxide at −78°C for 1 h, the reaction system was allowed to stand at room temperature for 2 h. [e] The reaction was carried out at −20 to −30°C for 4 h. [f] Appreciable absorption of CO was not observed in the preparation of **2**.

diisopropylamide on account of the inherent instability of the carbamoyllithium. Furthermore, lithium amides prepared from less basic amines such as aromatic amines were shown to be ineffective for carbonylation [6b]. Therefore, the carbonylation of the aminocopper complex **1** provides an effective method for the formation of reactive carbamoyl anion equivalents which have many uses in organic chemistry. In fact, the successful coupling reaction of the carbamoylcopper complexes **2** with a variety of organic halides has been already demonstrated [6].

Unfortunately, **2** was found to be prone to carbon monoxide liberation in further reactions, therefore, the carbon monoxide should be pressurized [6a]. We investigated the conditions which make **2** unstable and promote CO liberation. For example, the hydrolysis of the carbamoylcopper complexes **2** with water resulted in nearly quantitative evolution of carbon monoxide, and only a trace amount of the corresponding formamide was obtained with the recovered material. Alternatively, the use of hydrochloric acid in water or acid in dry ethanol for the protolysis of **2** did not effect the preferential formation of the *N*-formyl product.

The polarity of the solvents used also affected the stability of **2**. In ether, the aminocopper complex **1a** derived from *N*-methylaniline absorbed almost 100% of the carbon monoxide (based on *N*-methylaniline) after 1 h at 0°C, and subsequent treatment of the carbamoylcopper complex **2a** generated with methyl iodide gave *N*-methylacetanilide in 72% isolated yield without detectable CO evolution. On the other hand, in tetrahydrofuran (THF), **1a** absorbed about 85% of CO after 2 h at 0°C and subsequent treatment with CH_3I caused CO evolution, ca. 55%, yielding 25% of the amide. Remarkably, neither absorption nor evolution of CO was observed in hexamethylphosphoramide (HMPA). Very slow CO absorption occurred when **1a** was treated with carbon monoxide in benzene; only 10% of CO was absorbed after 3 h at 0°C. The low solubility of **1a** in benzene is probably responsible for this slow reaction. The addition of a small amount (10%) of dimethoxyethane (DME) as a cosolvent for **1a** dramatically increased the rate of CO absorption; quantitative CO absorption was achieved after 0.5 h at 0°C. The solvent effects on the reaction of **2a** with methyl iodide are summarized in Table 1. The results allowed comparison of the solvent effect in facilitating CO evolution and gave the order HMPA > THF > DME > diethyl ether. This order is in fair agreement with that of polarity.

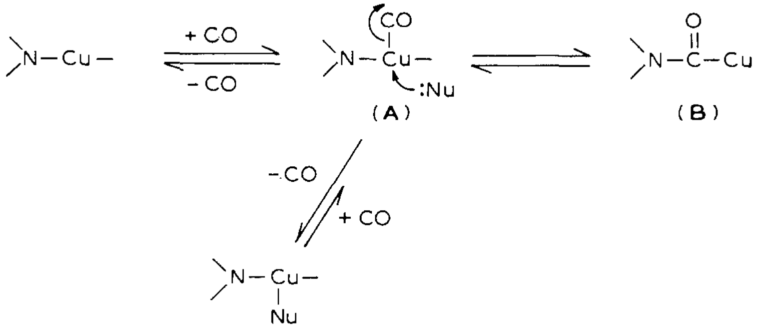
These findings suggest that the equilibrium lies between the carbamoylcopper complex **B** and the CO-coordinated copper complex **A** as shown in Scheme 1, and nucleophilic attack of electron donor molecules (represented by the symbol "Nu" in Scheme 1) such as water and polar aprotic solvents on the copper center, suppress the coordination of CO to the copper atom and facilitate the CO liberation from the CO-containing copper complex. Successful high-yield conversions of **2** to formamides (**3**), which were achieved by protolysis of **2** with HCl in dry ether (eq. 2),



$$(R^1R^2NC(O))_2CuLi \xrightarrow[-78^\circ C \text{ in ether}]{HCl/ether} R^1R^2NC(O)H \quad (2)$$

(2) (3)

$R^1 = CH_3$, $R^2 = C_6H_5$	91%
$R^1 = C_2H_5$, $R^2 = p\text{-}ClC_6H_4$	98%
$R^1 = CH_3$, $R^2 = CH_2C_6H_5$	89%
$R^1 = C_2H_5$, $R^2 = C_2H_5$	65%



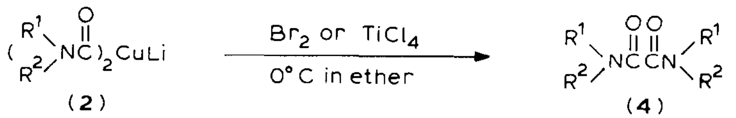
SCHEME 1

support the above suggestion. Thus, an optimum solvent or a solvent system, effecting successful formation and subsequent organic reactions of **2** (without loss of attached carbon monoxide groups) could be chosen when the reactions are conducted under carbon monoxide at atmospheric pressure.

Conversions of 2 to oxamides and carbamates

Previously we investigated the oxidation reactions of **2a** with a view to obtaining oxamide arising from oxidative coupling of carbamoyl groups on copper [6b]. The oxidation of **2a** with oxygen, however, gave a low oxamide yield. Improved results were obtained when nitrobenzene was used as the oxidant, but the yields of oxamide were still unsatisfactory (up to 45%). Therefore, we investigated other effective reagents for the high-yield synthesis of oxamides.

Bromine and titanium tetrachloride ($TiCl_4$) were found to be suitable and gave high-yield conversions of **2** to the corresponding oxamides (eq. 3). In addition to the

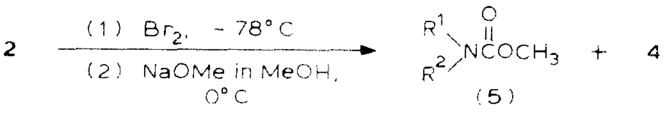


(3)

$R^1 = CH_3$, $R^2 = C_6H_5$	88–95%
$R^1 = C_2H_5$, $R^2 = p\text{-}ClC_6H_4$	79–91%
$R^1 = CH_3$, $R^2 = CH_2C_6H_5$	75–87%
$R^1 = C_2H_5$, $R^2 = C_2H_5$	75–89%

high oxamides yields, the reaction conditions (0°C, 1 atm CO) are much milder than those previously reported for carbonylations of amines or metal amides to form oxamides [5,7,8].

Since bromine has the ability to function not only as an oxidant, but also as a reagent for bromination, the formation of the oxamides may be partly attributable to the reaction of carbamoyl bromides, which were formed by bromination of **2**. Actually, the carbamoylcopper complexes **2** underwent bromination by bromine at low temperature (e.g. −78°C) to give the corresponding carbamoyl bromides although the reactions were accompanied by the competitive formations of oxamides. Thus, facile conversions of **2** to methyl carbamates could be achieved by subsequent treatment of the reaction mixtures with NaOMe (eq. 4, Table 2).



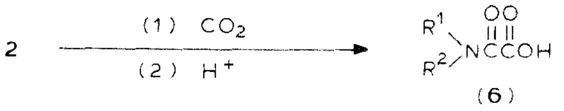
$$2 \xrightarrow[\text{(2) NaOMe in MeOH, } 0°\text{C}]{\text{(1) Br}_2\text{, } -78°\text{C}} R^1R^2NCOCH_3\ (5) + 4 \qquad (4)$$

As reported in the reaction between dimethylcarbamoylnickel carbonylate and mercuric chloride to produce oxamide [4a], the transmetalation between the carbamoylcopper complex **2** and $TiCl_4$, and the subsequent decomposition of the carbamoyltitanium complex formed, might possibly occur, and thereby contribute to the formation of oxamide when $TiCl_4$ was used as an oxidant. However, no conclusive evidence was obtained.

Reactions with carbon dioxide

There has been growing interest in the organic reactions of carbon dioxide with transition metal complexes [9]. Among the transition metal complexes, copper(I) complexes have been recently shown to support the organic reactions of carbon dioxide [10]. We have examined the reaction of the carbamoylcopper complexes **2** with carbon dioxide in order to extend the possibilities of synthetic utilization of both carbon dioxide and **2**.

The carbamoylcopper complexes **2** were found to react with carbon dioxide in ether, whereby CO_2 was smoothly absorbed at 1 atm pressure and 0°C, and the corresponding oxamic acids were obtained after hydrolysis (eq. 5). This reaction



$$2 \xrightarrow[\text{(2) } H^+]{\text{(1) } CO_2} R^1R^2NCOCOOH\ (6) \qquad (5)$$

appears to be the most straightforward method for the synthesis of oxamic acid derivatives since the oxamic acids are fragmented to the corresponding amines, CO, and CO_2. Unfortunately, however, concomitant evolutions of CO were observed in all cases during the reactions with CO_2, and this decreased the oxamic acid yields. Our attempts to improve the oxamic acid yields by optimizing the reaction conditions were unsuccessful. The results are summarized in Table 3.

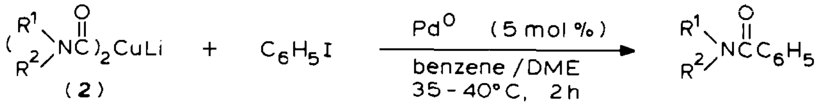
The nucleophilic attack of carbon dioxide on the copper center is an essential step prior to insertion in the reaction mechanism of CO_2 with **2**. Therefore, the displacement of CO coordinating to the copper atom by CO_2 would cause CO evolution.

Although the obtainable yields of oxamic acids are limited by the accompanying CO evolution, the yields based on converted amines were nearly quantitative because the reactions proceed without affording any detectable amounts of by-products except for recovered amines. Thus, this reaction can be used for preparative synthesis of oxamic acids.

Palladium-catalyzed cross-coupling reactions

Although a number of organic halides have been already examined in the reaction with the carbamoylcopper complexes [6], the situation was less favorable for aryl and vinyl halides. In the reaction of lithium bis(*N*-methyl-*N*-phenylcarbamoyl)cuprate (**2a**) with iodobenzene at room temperature, only 5% yield of *N*-methylbenzanilide was obtained after 84 h [6b]. As an improved result was obtained in the related reaction which involved bis(*N,N*-diethylcarbamoyl)cuprate [6a], transition metal catalysis sometimes prove effective in forcing cross-coupling reactions between organometallic compounds and unactivated organic halides [11,12]. Accordingly, we have examined the above reaction in the presence of a catalytic amount (5 mol%) of a transition-metal complex.

A Pd^0–PPh_3 complex *, a Ni^0–PPh_3 complex **, $NiBr_2(PPh_3)_2$, $RhCl(PPh_3)_3$, and $Co(OCOCH_3)_2$ were examined as catalysts, and only the palladium complex was found to be effective for the cross-coupling reaction. Cross-coupling between **2a** and iodobenzene in the presence of the palladium(0) catalyst (5 mol%) in ether stopped after 2 h at room temperature, and the CO-containing coupled product was isolated in 35% yield. The palladium catalyst in the catalytic cycle had possibly been inactivated before the reaction was complete. Attempts to optimize the reaction conditions could not improve the yield of the product, except when an excess of **2a**, based on iodobenzene, was used (**2a**/iodobenzene 2, 66% yield based on iodobenzene). Generally, palladium complexes have higher solubility in benzene, so we expected the palladium-catalyzed reaction to be accelerated when the reaction was conducted in benzene. We have, then, examined the palladium-catalyzed coupling reaction of **2a** with iodobenzene in benzene containing a small amount (7%) of DME as a cosolvent for the copper complex. At temperatures of 35–40°C, the reaction usually stopped in 0.5–1.0 h and the yield of the coupled product was improved up to 71% (eq. 6) although the results, obtained when aliphatic amines were used as starting materials, were not so satisfactory. Similarly, the palladium-catalyzed cross-coupling reaction of **2a** with (*E*)-β-bromostyrene did take place and the corresponding amide was isolated in 65% yield.



$$(R^1R^2NCO)_2CuLi + C_6H_5I \xrightarrow[\text{benzene/DME, 35-40°C, 2h}]{Pd^0\ (5\ mol\ \%)} R^1R^2NCOC_6H_5 \quad (6)$$

(2)

R^1	R^2	
$R^1 = CH_3$,	$R^2 = C_6H_5$	71%
$R^1 = C_2H_5$,	$R^2 = p\text{-}C_6H_4$	67%
$R^1 = CH(CH_3)_2$,	$R^2 = CH(CH_3)_2$	49%
$R^1 = C_2H_5$,	$R^2 = C_2H_5$	58%

Conclusion

Our results demonstrate the versatile applications of lithium bis(carbamoyl)-cuprate. In addition, superiority of the carbamoylcopper complex to other carbamoylmetal compounds previously reported has been shown especially for the formations of formamide and oxamide derivatives. The main disadvantage of this carbamoylcopper complex is the facile liberation of carbon monoxide to be utilized

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* Generated in situ by treating $PdCl_2(PPh_3)_2$ with 2 equivalents of $HAl(i\text{-}Bu)_2$ in the presence of 2 equivalents of PPh_3.

** Generated in situ by treating $Ni(acac)_2$ with 2 equivalents of $HAl(i\text{-}Bu)_2$ in the presence of 4 equivalents of PPh_3.

in organic reactions and this depended on the solvents used and could be suppressed to some extent by the use of ether or benzene/DME rather than THF or HMPA. Although there are some problems which require further investigation, the applications of this study will develop in synthetic organic chemistry.

Experimental

Melting points were measured with a Yanagimoto micro melting point apparatus and are uncorrected. ^{1}H NMR spectra were obtained with a JEOL PS-100 spectrometer using Me_4Si as internal standard. Infrared (IR) spectra were recorded on a JASCO IRA-1 spectrophotometer. Mass spectra were determined on a JEOL D-300 mass spectrometer. Elemental analyses were performed by the Service Center of the Elementary Analysis of Organic Compounds, Kyushu University. Column Chromatography was carried out on silica gel (70–230 mesh, Merck).

Materials and solvents

N-Ethyl-*p*-chloroaniline and *N*-ethyl-3,4-dichloroaniline were prepared according to the literature [13]. Other secondary amines used in this study as starting materials were commercial products and were purified before use by distillation or recrystallization. Cuprous iodide was purified using a literature procedure [14] and stored under nitrogen. Dichlorobis(triphenylphosphine)palladium(II) was prepared by heating sodium tetrachloropalladate with 2 equivalents of triphenylphosphine in methanol. Similarly, dibromobis(triphenylphosphine)nickel(II) was prepared from nickel bromide and 2 equivalents of triphenylphosphine in n-butanol. Nickel(II) acetylacetonate was purchased from a commercial source and dried (80°C, 0.1 mmHg) for 24 h before use. Chlorotris(triphenylphosphine)rhodium(I) and anhydrous cobalt(II) acetate were commercial products and were used directly. n-Butyllithium was purchased from a commercial source as a 15% solution in n-hexane and standardized by titration [15] before use. Diethyl ether and 1,2-dimethoxyethane (DME) were distilled from $LiAlH_4$ and stored over sodium wire. Benzene was distilled at atmospheric pressure and also stored over sodium wire. Hexamethylphosphoramide (HMPA) was stored over molecular sieves (4A). Tetrahydrofuran (THF) was freshly distilled from $LiAlH_4$ just before use.

All operations were performed under dry nitrogen.

*Preparation of carbamoylcopper complexes (**2**)*

Typical operations were performed on the following two scales (**A**, **B**).

A: A solution of 18.7 mmol of a secondary amine in 50 ml of a anhydrous solvent was placed in a 300 ml four-necked reaction vessel equipped with a balloon or a gas buret. 18.7 mmol of n-butyllithium in n-hexane was syringed with stirring at 0°C to this solution. After 15 min stirring, 9.35 mmol of purified cuprous iodide was added, and the mixture was stirred for a further 15–30 min at the same temperature. The reaction vessel containing the mixture was flushed several times with carbon monoxide. The mixture was usually stirred for 2 h under carbon monoxide at 0°C, and then subjected to further experiments.

B: The reaction was carried out on a one-tenth scale of **A** in a 20 ml reaction vessel.

Protolysis of 2 with HCl in ether

The reaction flask containing the copper complex **2**, prepared as described above for **B** in ether, was cooled to $-78°C$. 1.5 ml of HCl-saturated ether was added by syringe to the mixture and the resulting mixture was stirred for 0.5 h at the same temperature. The reaction mixture was allowed to warm to room temperature and then poured into water. The mixture was filtered through Celite-pad and completely extracted with ether. The ether extracts were combined, washed with 10% $NaHCO_3$, and dried over Na_2SO_4. Removal of ether under reduced pressure gave the pure *N*-formyl product.

The following products obtained were identified by comparisons of spectral data with those reported (*N*-benzyl-*N*-methylformamide) [16] or those for authentic materials: *N*-methyl-*N*-phenylformamide, *N*-ethyl-*N*-(4-chlorophenyl)formamide, *N,N*-diethylformamide.

Conversions to oxamides

To the copper complex **2**, prepared as for **B** in ether, $TiCl_4$ (1.87 mmol) or bromine (1.87 mmol) was added slowly with vigorous stirring at 0°C. The reaction mixture was stirred for 1 h at the same temperature and hydrolyzed with 1 *N* HCl. The mixture was filtered through Celite-pad and completely extracted with ether. The ether extracts were combined, washed with 10% $NaHCO_3$, dried over Na_2SO_4, and then concentrated under reduced pressure. The product was purified by column chromatography and/or recrystallization.

N,N'-Dimethyl-N,N'-diphenyloxamide. m.p. 107–110°C. Found: C, 71.43; H, 5.94; N, 10.33. $C_{16}H_{16}N_2O_2$ calcd.: C, 71.62; H, 6.01; N, 10.44%. MS: *m/e* 268 (M^+). ^1H NMR ($CDCl_3$): δ 3.05 (s, 6H, $2CH_3$), 6.75 ppm (m, 10H, aromatic). IR (nujol): 1680, 1660 cm^{-1}.

N,N'-Diethyl-N,N'-bis(4-chlorophenyl)oxamide. m.p. 100–101°C. Found: C, 59.24; H, 5.00; N, 7.78. $C_{18}H_{18}Cl_2N_2O_2$ calcd.: C, 59.19; H, 4.97; N, 7.67%. MS: *m/e* 364 (M^+). ^1H NMR ($CDCl_3$): δ 0.90 (t, 6H, $2CH_3$), 3.50 (q, 4H, $2CH_2$), 6.90 (d, 4H, aromatic), 7.30 ppm (d, 4H, aromatic). IR (nujol): 1680, 1660 cm^{-1}.

N,N'-Dibenzyl-N,N'-dimethyloxamide. Found: C, 72.82; H, 6.78; N, 9.31. $C_{18}H_{20}N_2O_2$ calcd.: C, 72.95; H, 6.80; N, 9.45%. MS: *m/e* 296 (M^+). ^1H NMR ($CDCl_3$): δ 2.90 (m, 6H, $2CH_3$), 4.40–4.60 (m, 4H, $2CH_2$), 7.30 ppm (m, 10H, aromatic). IR (neat): 1670, 1640 cm^{-1}.

N,N,N',N'-Tetraethyloxamide. Found: C, 60.11; H, 10.10; N, 13.73. $C_{10}H_{20}N_2O_2$ calcd.: C, 59.97; H, 10.17; N, 13.99%. MS: *m/e* 200 (M^+). ^1H NMR ($CDCl_3$): δ 1.10–1.30 (m, 12H, $4CH_3$), 3.15–3.55 ppm (m, 8H, $4CH_2$). IR (neat): 1640 cm^{-1}.

Conversions to methyl carbamates

The reaction flask containing the copper complex **2**, prepared as for **A** in ether, was cooled to $-78°C$ and Br_2 (18.7 mmol) in CCl_4 (15 ml) was added dropwise. After stirring for 1 h at $-78°C$, the reaction mixture was allowed to warm to 0°C. NaOMe (20 mmol) in MeOH was added and the resulting mixture was stirred for 5 h at 0°C. The reaction mixture was hydrolyzed with 1 *N* HCl and worked up as described above. The products were separated by column chromatography and purified by distillation.

Methyl N-methyl-N-phenylcarbamate. Found: C, 65.33; H, 6.80; N, 8.44. $C_9H_{11}NO_2$ calcd.: C, 65.44; H, 6.71; N, 8.48%. MS: *m/e* 165 (M^+). ^1H NMR

(CDCl$_3$): δ 3.25 (s, 3H, N–CH$_3$), 3.65 (s, 3H, O–CH$_3$), 7.20 ppm (m, 5H, aromatic). IR (neat): 1720 cm^{-1}.

Methyl N-ethyl-N-phenylcarbamate. Found: C, 66.88; H, 7.20; N, 7.75. $C_{10}H_{13}NO_2$ calcd.: C, 67.02; H, 7.31; N, 7.82%. MS: *m/e* 179 (M^+). ^{1}H NMR (CDCl$_3$): δ 3.15 (t, 3H, CH$_3$), 3.65 (s, 3H, O–CH$_3$), 3.70 (q, 2H, CH$_2$), 7.10–7.40 ppm (m, 5H, aromatic). IR (neat): 1720 cm^{-1}.

Methyl N-phenyl-N-propylcarbamate. m.p. 48–49°C. (Found: C, 68.40; H, 7.87; N, 7.23. $C_{11}H_{15}NO_2$ calcd.: C, 68.37; H, 7.82; N, 7.25%). MS: *m/e* 193 (M^+). ^{1}H NMR (CDCl$_3$): δ 0.85 (t, 3H, CH$_3$), 1.55 (sex, 2H, CH$_2$), 3.60 (t, 2H, N–CH$_2$), 3.65 (s, 3H, O–CH$_3$), 7.10–7.40 ppm (m, 5H, aromatic). IR (neat): 1720 cm^{-1}.

Methyl N-ethyl-N-(4-chlorophenyl)carbamate. Found: C, 56.19; H, 5.56; N, 6.57. $C_{10}H_{12}ClNO_2$ calcd.: C, 56.21; H, 5.66; N, 6.56%. MS: *m/e* 215 ($M^+ + 2$), 213 (M^+). ^{1}H NMR (CDCl$_3$): δ 1.10 (t, 3H, CH$_3$), 3.65 (s, 3H, O–CH$_3$), 3.65 (q, 2H, N–CH$_2$–), 7.10 (d, 2H, aromatic), 7.30 ppm (d, 2H, aromatic). IR (neat): 1715 cm^{-1}.

Methyl N-(3,4-dichlorophenyl)-N-ethylcarbamate. Found: C, 48.25; H, 4.45; N, 5.60. $C_{10}H_{11}Cl_2NO_2$ calcd: C, 48.41; H, 4.48; N, 5.65%. MS: *m/e* 247 (M^+). ^{1}H NMR (CDCl$_3$): δ 1.15 (t, 3H, CH$_3$), 3.70 (s, 3H, O–CH$_3$), 3.70 (q, 2H, CH$_2$), 7.00–7.50 ppm (m, 3H, aromatic). IR (neat): 1715 cm^{-1}.

Methyl N-methyl-N-(2-methylphenyl)carbamate. m.p. 40–41°C. Found: C, 67.03; H, 7.24; N, 7.84. $C_{10}H_{13}NO_2$ calcd.: C, 67.02; H, 7.31; N, 7.82%. MS: *m/e* 179 (M^+). ^{1}H NMR (CDCl$_3$): δ 2.20 (s, 3H, CH$_3$), 3.20 (s, 3H, N–CH$_3$), 3.60 (s, 3H, O–CH$_3$), 7.20 ppm (m, 4H, aromatic). IR (neat): 1720 cm^{-1}.

Methyl N-methyl-N-(3-methylphenyl)carbamate. Found: C, 67.06; H, 7.33; N, 7.80. $C_{10}H_{13}NO_2$ calcd.: C, 67.02; H, 7.31; N, 7.82%. MS: *m/e* 179 (M^+). ^{1}H NMR (CDCl$_3$): δ 2.35 (s, 3H, CH$_3$), 3.25 (s, 3H, N–CH$_3$), 3.70 (s, 3H, O–CH$_3$), 6.90–7.30 ppm (m, 4H, aromatic). IR (neat): 1715 cm^{-1}.

Methyl N-allyl-N-phenylcarbamate. Found: C, 68.96; H, 6.93; N, 7.26. $C_{11}H_{13}NO_2$ calcd.: C, 69.09; H, 6.85; N, 7.33%. MS: *m/e* 191 (M^+). ^{1}H NMR (CDCl$_3$): δ 3.70 (s, 3H, O–CH$_3$), 4.25 (dm, 2H, N–CH$_2$), 5.15 (dm, 2H, =CH$_2$), 5.90 (m, 1H, CH=), 7.10–7.40 ppm (m, 5H, aromatic). IR (neat): 1710 cm^{-1}.

Methyl N-benzyl-N-methylcarbamate. Found: C, 66.93; H, 7.32; N, 7.81. $C_{10}H_{13}NO_2$ calcd.: C, 67.02; H, 7.31; N, 7.81%. MS: *m/e* 179 (M^+). ^{1}H NMR (CDCl$_3$): δ 2.85 (s, 3H, N–CH$_3$), 3.70 (s, 3H, O–CH$_3$), 4.45 (s, 2H, CH$_2$), 7.25 ppm (m, 5H, aromatic). IR (neat): 1710 cm^{-1}.

N,N′-Diethyl-N,N′-diphenyloxamide. m.p. 94–95°C. Found: C, 73.02; H, 6.84; N, 9.44. $C_{18}H_{20}N_2O_2$ calcd.: C, 72.95; H, 6.80; N, 9.45%. MS: *m/e* 296 (M^+). ^{1}H NMR (CDCl$_3$): δ 0.90 (t, 6H, 2CH$_3$), 3.50 (q, 4H, CH$_2$), 6.80–7.40 ppm (m, 10H, aromatic). IR (nujol): 1650 cm^{-1}.

N,N′-Diphenyl-N,N′-dipropyloxamide. m.p. 83–84°C. Found: C, 73.93; H, 7.47; N, 8.67. $C_{20}H_{24}N_2O_2$ calcd.: C, 74.04; H, 7.46; N, 8.64%. MS: *m/e* 324 (M^+). ^{1}H NMR (CDCl$_3$): δ 0.70 (t, 6H, 2CH$_3$), 1.30 (m, 4H, 2CH$_2$), 3.40 (t, 4H, 2N–CH$_2$), 6.85–7.40 ppm (m, 10H, aromatic). IR (nujol): 1660, 1640 cm^{-1}.

N,N′-Bis(3,4-dichlorophenyl)-N,N′-diethyloxamide. m.p. 105–106°C. Found: C, 49.72; H, 3.76; N, 6.42. $C_{18}H_{16}Cl_4N_2O_2$ calcd.: C, 49.80; H, 3.71; N, 6.45%. MS: *m/e* 434 (M^+). ^{1}H NMR (CDCl$_3$): δ 0.95 (t, 6H, 2CH$_3$), 3.50 (q, 4H, 2CH$_2$), 6.80–7.50 ppm (m, 6H, aromatic). IR (nujol): 1670 cm^{-1}.

N,N′-Dimethyl-N,N′-bis(3-methylphenyl)oxamide. m.p. 77–78°C. Found: C, 72.73; H, 6.76; N, 9.39. $C_{18}H_{20}N_2O_2$ calcd.: C, 72.95; H, 6.80; N, 9.45%. MS: *m/e* 296 (M^+). ^{1}H NMR ($CDCl_3$): δ 2.30 (s, 6H, 2CH_3), 3.05 (s, 6H, 2N–CH_3), 6.50–7.30 ppm (m, 8H, aromatic). IR (nujol): 1665, 1655 cm^{-1}.

N,N'-Diallyl-N,N'-diphenyloxamide. m.p. 66–67°C. Found: C, 75.03; H, 6.31; N, 8.88. $C_{20}H_{20}N_2O_2$ calcd.: C, 74.97; H, 6.29; N, 8.74%. MS: *m/e* 320 (M^+). ^{1}H NMR ($CDCl_3$): δ 4.05 (dd, 4H, 2N–CH_2), 4.70–5.00 (m, 4H, 2=CH_2), 5.20–5.70 (m, 2H, 2CH=), 6.90–7.40 ppm (m, 10H, aromatic). IR (nujol): 1680, 1655 cm^{-1}.

Reactions with carbon dioxide

The reaction flask containing the copper complex **2**, prepared as for **A** in ether, was flushed several times with carbon dioxide and the mixture was stirred for 2 h at 0°C. The resulting mixture was hydrolyzed with 1 *N* HCl and filtered through Celite-pad and completely extracted with ether. The remaining amine was recovered from the aqueous layer to be alkalified. The ether extracts were combined and shaken with 0.5*N* NaOH. The aqueous layer was separated and acidified to pH 1 with concentrated hydrochloric acid. The oxamic acid formed was extracted with ether and the ether extracts were combined and dried over Na_2SO_4. Removal of ether under reduced pressure usually gave the pure oxamic acid.

N-Methyl-N-phenyloxamic acid. m.p. 123–124°C (dec). Found: C, 60.29; H, 5.10; N, 7.90. $C_9H_9NO_3$ calcd.: C, 60.33; H, 5.06; N, 7.82%. MS: *m/e* 179 (M^+). ^{1}H NMR (CD_3COCD_3): δ 3.30 (s, 3H, CH_3), 7.40 (m, 5H, aromatic), 11.00 ppm (br s, 1H, OH). IR (nujol): 1745, 1620 cm^{-1}.

N-Ethyl-N-phenyloxamic acid. m.p. 94–96°C (dec). Found: C, 62.02; H, 5.74; N, 7.30. $C_{10}H_{11}NO_3$ calcd.: C, 62.16; H, 5.74; N, 7.25%. MS: *m/e* 193 (M^+). ^{1}H NMR (CD_3COCD_3): δ 1.10 (t, 3H, CH_3), 3.80 (q, 2H, CH_2), 7.40 (m, 5H, aromatic), 10.60 ppm (br s, 1H, OH). IR (nujol): 1745, 1620 cm^{-1}.

N-Methyl-N-(2-methylphenyl)oxamic acid. m.p. 107–109°C (dec). Found: C, 62.12; H, 5.78; N, 7.17. $C_{10}H_{11}NO_3$ calcd.: C, 62.16; H, 5.74; N, 7.25%. MS: *m/e* 193 (M^+). ^{1}H NMR (CD_3COCD_3): δ 2.30 (s, 3H, CH_3), 3.15 (s, 3H, N–CH_3), 7.30 (m, 4H, aromatic), 10.40 ppm (br s, 1H, OH). IR (nujol): 1745, 1640 cm^{-1}.

N-Methyl-N-(3-methylphenyl)oxamic acid. m.p. 114–115°C (dec). Found: C, 62.19; H, 5.76; N, 7.31. $C_{10}H_{11}NO_3$ calcd.: C, 62.16; H, 5.74; N, 7.25%. MS: *m/e* 193 (M^+). ^{1}H NMR (CD_3COCD_3): δ 2.30 (s, 3H, CH_3), 3.25 (s, 3H, N–CH_3), 7.20 (m, 4H, aromatic), 10.90 ppm (br s, 1H, OH). IR (nujol): 1750, 1640 cm^{-1}.

N-(4-Chlorophenyl)-N-ethyloxamic acid. m.p. 132–134°C (dec). Found: C, 52.81; H, 4.48; N, 6.23. $C_{10}H_{10}ClNO_3$ calcd.: C, 52.76; H, 4.43; N, 6.15%. MS: *m/e* 229 ($M^+ + 2$), 227 (M^+). ^{1}H NMR (CD_3COCD_3): δ 1.10 (t, 3H, CH_3), 3.80 (q, 2H, CH_2), 7.40 (m, 4H, aromatic), 11.15 ppm (br s, 1H, OH). IR (nujol): 1755, 1620 cm^{-1}.

N-Allyl-N-phenyloxamic acid. Found: C, 64.15; H, 5.44; N, 6.79. $C_{11}H_{11}NO_3$ calcd.: C, 64.38; H, 5.40; N, 6.83%. MS: *m/e* 205 (M^+). ^{1}H NMR ($CDCl_3$): δ 4.25 (d, 2H, N–CH_2), 5.00–5.20 (m, 2H, =CH_2), 5.55–6.00 (m, 1H, CH=), 7.20 (m, 5H, aromatic), 10.00 ppm (s, 1H, OH). IR (neat): 1750, 1640 cm^{-1}.

N-Benzyl-N-methyloxamic acid. m.p. 91–92°C. Found: C, 62.12; H, 5.75; N, 7.28. $C_{10}H_{11}NO_3$ calcd.: C, 62.16; H, 5.74; N, 7.25%. MS: *m/e* 193 (M^+). ^{1}H NMR (CD_3COCD_3): δ 2.80 (s) and 3.00 (s) (3H, CH_3), 4.58 (s) and 4.60 (s) (2H, CH_2), 5.35 (m, 5H, aromatic), 7.80 ppm (s, 1H, OH). IR (nujol): 1745, 1600 cm^{-1}.

N,N-Diisopropyloxamic acid. m.p. 126–127 (dec). Found: C, 55.45; H, 8.77; N, 8.04. $C_8H_{15}NO_3$ calcd.: C, 55.47; H, 8.73; N, 8.09%. MS: *m/e* 173 (M^+). ^{1}H NMR (CD_3COCD_3): δ 1.25 (d) and 1.40 (d) (12H, $4CH_3$), 3.40–4.10 (m, 2H, $CH(CH_3)_2$), 11.60 ppm (s, 1H, OH). IR (nujol): 1745, 1590 cm^{-1}.

*Palladium-catalyzed cross-coupling of **2** with iodobenzene or (E)-β-bromostyrene*

The reaction flask containing the copper complex **2**, prepared as for **B** in benzene DME (15/1), was heated to 35–40°C. 2.0 mmol of iodobenzene or (*E*)-*β*-bromostyrene was added by syringe and 0.0935 mmol of a palladium(0) catalyst prepared in situ from $PdCl_2(PPh_3)_2$ and 2 equivalents of PPh_3 and 2 equivalents of HAl $(i\text{-}Bu)_2$ in 2 ml of benzene. After stirring for 2 h under carbon monoxide, the reaction mixture was hydrolyzed with 1 *N* HCl and worked up as described above. The crude product obtained was purified by column chromatography and/or distillation.

The products obtained from the reactions with iodobenzene were identified by comparison of spectral data with those of independently synthesized samples.

(E)-β-(N-Methyl-N-phenylcarbamoyl)styrene

Found: C, 80.81; H, 6.40; N, 5.79. $C_{16}H_{15}NO$ calcd.: C, 80.98; H, 6.37; N, 5.90%. MS: *m/e* 237 (M^+). ^{1}H NMR ($CDCl_3$): δ 3.40 (s, 3H, CH_3), 6.35 (d, 1H, =CHCO), 7.15–7.45 (m, 10H, aromatic), 7.65 ppm (d, 1H, PhCH=). IR (neat): 1665, 1615, 1595 cm^{-1}.

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