react.) ^{1}H NMR showed that the presumed 6-Cl had hydrolyzed to give (at least predominantly) 7-OH (and the starting material which had remained after the irradiation had hydrolyzed to give *exo*-5-OH).

Benzophenone-Sensitized Irradiation of *exo*-5-Cl in Wet CD_3CN. A solution of 43 mg (0.19 mmol) of *exo*-5-Cl and 13 mg (0.07 mmol) of benzophenone in 0.5 mL of CD_3CN containing 2% D_2O in a Pyrex NMR tube was irradiated with 16 300-nm lamps in the Rayonet. It was monitored during the irradiation by ^{1}H NMR. After 6 h of irradiation, approximately 70% of the starting material had reacted. Five products (which accounted for about 60% of the lost starting material) were observed. These products (along with the percentage of the identified product which they represented) were *exo*-5-OH (18%), 6-OH (9%), *exo*-5-$NDCOCD_3$ (15%), *anti*-4-Cl (25%), and 6-Cl (33%). A trace of 7-OH, the solvolysis product of 6-Cl, was also present. Some small, unidentified ^{1}H NMR resonance were also observed.

Acetone-Sensitized Irradiation of *exo*-5-Cl in Wet CD_3CN. A solution of 34 mg (0.15 mmol) of *exo*-5-Cl in 0.5 mL of CD_3CN containing 10% acetone-d_6 and 3% D_2O in a Pyrex NMR tube was irradiated with 16 300-nm lamps in the Rayonet. The experiment was monitored periodically by ^{1}H NMR. After 6.0 h of irradiation, approximately 55% of the starting material had reacted. Five products were observed (which appeared to represent more than 90% of the reacted starting material). These products (along with the percentages of the observed product which they represented) were *exo*-5-OH (25%), 6-OH (12%), *exo*-5-$NDCOCD_3$ (13%), *anti*-4-Cl (22%), and 6-Cl (29%).

Direct Irradiation of *exo*-5-Cl. A solution of 28 mg (0.12 mmol) of *exo*-5-Cl in 0.5 mL of CD_3CN containing 2% D_2O in a quartz NMR tube was examined by ^{1}H NMR both before and after 21 h in the dark. No change during this period was observed. The solution was then irradiated with 12 254-nm lamps in the Rayonet and examined periodically by ^{1}H NMR. After 1.5 h of irradiation 50% of the starting material had reacted. Four products (which in total accounted for only 50% of the loss of starting material) were observed. These products were *exo*-5-OD (53%), *endo*-5-Cl (21%), 6-OD (16%) (believed to be a secondary product arising from the *exo*-5-OD), and *exo*-5-$NDCOCD_3$ (10%). No other products could be identified; however, the ^{1}H NMR spectrum was consistent with the speculation that any other specific products must be minor relative to those which were identified. After 8 h of irradiation over 70% of starting material had been lost. Little change in the relative proportions of the products was seen (except that the relative amount of 6-OH had increased). A trace of *anti*-4-Cl was detected at this time; however, it is not possible to state that this could not have been present in the starting material. Irradiation was continued to 100 h. Little additional change occurred (probably because of the development of a brown film on the inside walls of the NMR tube).

Acknowledgment. We are indebted to the National Science Foundation (Grants CHE80-11933 and CHE83-09927) for support of this work.

Registry No. *syn*-4-OH, 72204-35-4; *anti*-4-Cl, 75947-49-8; 5-K, 102306-40-1; *exo*-5-OAc, 102306-38-7; *endo*-5-OAc, 102418-45-1; *exo*-5-OH, 102306-39-8; *endo*-5-OH, 102418-46-2; *exo*-5-Cl, 102306-41-2; *endo*-5-Cl, 102418-47-3; *exo*-5-$NHCOCH_3$, 102306-42-3; *endo*-5-$NHCOCH_3$, 102418-48-4; *exo*-5-$NDCOCD_3$, 102306-46-7; 6-OH, 102306-43-4; 6-K, 102306-44-5; 6-Cl, 102306-45-6; 7-OH, 102418-49-5.

Carbonylation of β-Aminoethanols, Diols, and Diol Amines†

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Oxazolidinones are prepared from the palladium-catalyzed carbonylation of β-aminoethanols under mild conditions. With *N*-alkyl-substituted substrates, conditions for double carbon monoxide incorporation to give morpholinediones have been discovered. Cyclic carbonates can be prepared from the carbonylation of diols. The carbonylation of *N*-phenyl-1-aminopropane-2,3-diol can give either the carbonate or oxazolidinone as the major product depending on the reaction conditions.

Oxazolidinones are an important class of heterocyclic compounds which have many biological uses.[1] Their preparation normally involves the use of dangerous phosgene or phosgene-based reagents. An attractive alternative to phosgene is carbon monoxide; recently, several groups have reported on the use of carbon monoxide to prepare carbamates and carbonates.[2,3] We report that oxazolidinones can be readily prepared from the palladium-catalyzed carbonylation of β-amino alcohols under mild conditions. We have also discovered conditions for double carbonylation of β-aminoethanols containing *N*-alkyl substituents to give morpholine-2,3-diones.

Results

The reaction of *N*-alkyl-β-amino alcohols with carbon monoxide in the presence of 4–10 mol % of $PdCl_2$ with $CuCl_2$ as oxidant and NaOAc as based in ethylene glycol dimethyl ether (DME) gives 75–95% yields of the oxazolidinone (Table I). The reaction conditions are mild; only

Table I. Catalytic Reactions[a]

β-amino alcohols			oxazolidinone yield, %
R_1	R_2		
n-Bu	Ph		94[c]
t-Bu	Ph		83[c]
n-Bu	CH_3		95[b]
Me	H		77[b]
$CH_3C{=}O$	H		34[c]
Ph	H	$PdCl_2/CuCl_2/NEt_3$/room temp	48[c]

[a] 4–10 mol % of $PdCl_2$ was used with 2 equiv of base and oxidant. Mixture was heated at 80 °C overnight except for the last example. [b] Isolated yield. [c] GC yield based on added internal standard.

† Contribution No. 3893.

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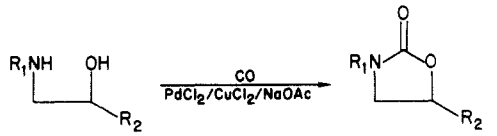
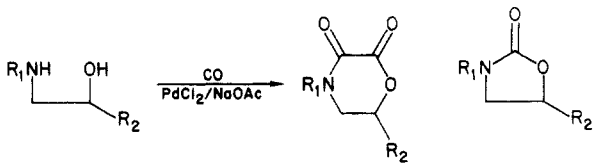


3 atm of carbon monoxide is needed at 80 °C overnight. Two equivalents of $CuCl_2$ and NaOAc are needed for catalytic activity. No oxazolidinones are produced in the absence of the palladium catalyst. Therefore, copper alkoxides and amides, if formed in these reactions, do not give oxazolidinones under these mild conditions.[4] The reaction does not work well with primary β-aminoethanols such as 2-aminoethanol.

The reaction is less effective for *N*-phenyl and *N*-acetyl substrates (Table I). With 2-anilinoethanol, NEt_3 as base gives higher yield than with NaOAc as base. Lower yields result at 80 °C for 2-anilinoethanol. The lower yields for these derivatives are most likely due to side reactions with $CuCl_2$ since the carbonylation of these substrates with $PdCl_2$ proceeds in excellent yields (vide infra, Table II).

The palladation reaction is an efficient one. With a *stoichiometric* amount of $PdCl_2$, the carbonylation proceeds at room temperature (Table II) under 3 atm of carbon monoxide and 2 equiv of base. With *N*-alkyl



substituents, there are two major products. With (*N*-methylamino)ethanol the major product is 4-methylmorpholine-2,3-dione,[5] with the minor product being the oxazolidinone. The morpholinedione is not produced from the oxazolidinone since the latter does not react with CO and $PdCl_2$/NaOAc in DME. With (*N*-*n*-butylamino)-1-methylethanol, a 33% of the morpholine-2,3-dione is prepared along with a 26% yield of the oxazolidinone. A third product is also obtained; however, we have not been able to identify this product. This material does not have a carbonyl group as indicated by infrared spectroscopy and therefore is not derived from a carbonylation reaction. The replacement of $PdCl_2$ with $Pd(OAc)_2$ in this reaction gives a cleaner reaction; 52% of the morpholine-2,3-dione and 35% of the oxazolidinone are obtained without the formation of the side product.

Similar observations are noted for the carbonylation of (*N*-*n*-butylamino)-1-phenylethanol with $PdCl_2$; unfortunately, we have not been able to separate the three components. ^{13}C NMR and infrared spectroscopy suggest the presence of the morpholine-2,3-dione and GC analysis indicates a 38% yield of the oxazolidinone.[6]

The oxazolidinone is the major product when the carbonylation of β-(*N*-alkylamino)ethanol is performed at 80 °C. Yields range from 78% to 100% (Table II).

Double carbonylation does not proceed with the (*N*-acetylamino)- and (*N*-phenylamino)ethanols. An exception to the double carbonylation of (*N*-alkylamino)ethanol at room temperature is the reaction with (*N*-*tert*-butylamino)-1-phenylethanol; a quantitative yield of the oxazolidinone is obtained.

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Table II. Carbonylation of β-Amino Alcohols

β-amino alcohol		temp,[d]	morpholinedione	oxazolidinone
R_1	R_2	°C	yield, %	yield, %
Ph	H	rt	0	100[c]
$CH_3C{=}O$	H	rt	0	91[b]
CH_3	H	rt	47–57	0–13[b]
		80	11	78[b]
n-Bu	CH_3	rt	33	26[c]
		80	0	100[c]
t-Bu	Ph	rt	0	100[c]
n-Bu	Ph	rt	*e*	38[c]
		80	0	86[c]

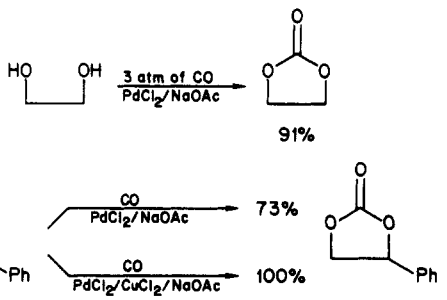
[a] All reactions were stirred overnight. One equivalent of $PdCl_2$ and two equivalents of base were used. [b] Isolated yield. [c] GC yield based on added internal standard. [d] Room temperature = rt. [e] Not determined.

Table III. Carbonylation of a Diol Amine[a]

1-(*N*-phenylamino)-propane-2,3-diol	oxazolidinone yield, %	carbonate yield, %
$PdCl_2/NEt_3$	10–22	78–90
cat. $PdCl_2/CuCl_2/NEt_3$	18	56
$PdCl_2$/NaOAc	56	42
cat. $PdCl_2/CuCl_2$/NaOAc	77	20

[a] One equivalent of $PdCl_2$ and two equivalents of base were used in the stoichiometric reactions. In the catalytic reactions, 4–10 mol % of $PdCl_2$ was used along with two equivalents of $CuCl_2$. All yields were isolated yields. All reactions were stirred at room temperature for 3–4 days.

The reaction is also effective for the preparation of carbonates from diols. We have found that ethylene glycol and 1-phenylethanediol react with a stoichiometric amount of $PdCl_2$ and 2 equiv of NaOAc as base at room temperature to give 91% and 73% of the respective carbonates.



No double carbonylation product is observed. With 1-phenylethanediol, the reaction can be made catalytic in palladium with the addition of $CuCl_2$. Without the palladium catalyst, only a 6% yield of the carbonate is formed. Attempts to make the reaction with ethylene glycol catalytic in palladium fail probably due to the interaction of ethylene glycol with $CuCl_2$; no carbonate is formed.

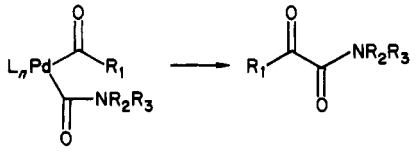
The carbonylation of 1-(*N*-phenylamino)propane-2,3-diol with $PdCl_2$ gives a mixture of the carbonate and the oxazolidinone (Table III). Again, the reaction conditions are mild. The carbonate is the major product when NEt_3 is the base. This carbonate would be difficult to prepare by conventional methodology; protection and deprotection of the nitrogen would be needed. The ratios of carbonate to oxazolidinone are smaller in the catalytic reactions compared with the ratios obtained in the stoichiometric reactions. The catalytic reactions may be going through intermediate copper alkoxide and amide complexes. The carbonate is not converted to the oxazolidinone when treated with $PdCl_2$/NaOAc/$CuCl_2$ or when treated with NEt_3.

The reaction of 1-(*N*-*n*-butylamino)propane-2,3-diol with a stoichiometric amount of $PdCl_2$ and NaOAc as base at

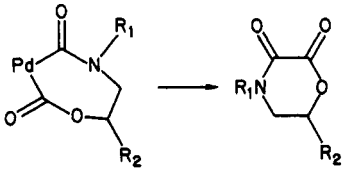
room temperature gives a mixture which could not be effectively separated. This mixture consists of the carbonate, the oxazolidinone, and the morpholinedione. As with (*N*-alkylamino)ethanol, the reaction with 1-(*N*-*n*-butylamino)propane-2,3-diol is cleaner when performed at higher temperatures. An 87% yield of the oxazolidinone is obtained at 80 °C.

Discussion

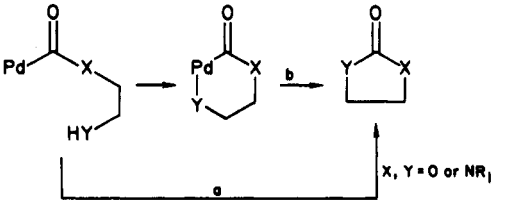
The carbonylation of amines with palladium chloride to give ureas is a known reaction.[7] We have extended this reaction to the preparation of oxazolidinone from β-aminoethanol. With *N*-alkyl-substituted substrates at room temperature, the major product is derived from double carbon monoxide incorporation[8] while *N*-phenyl-substituted substrates lead to only the oxazolidinone. Interestingly, this observation is similar to that observed for the palladium-catalyzed carbonylation of aryl halides with amines to give α-keto amides. α-Keto amides are formed when secondary amines with alkyl groups are employed whereas the organic amide is the only product with aniline.[8e] The formation of α-keto amides in these cases is believed to proceed by reductive elimination of palladium bis(acyl) intermediates.[9] Similarly, oxalate synthesis from



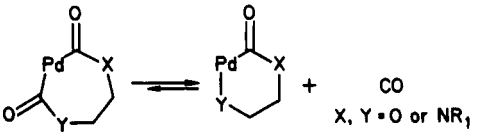
CO and alcohol has been suggested for the metals rhodium and palladium to involve a dicarboalkoxy metal intermediate.[10] The formation of morpholinedione most likely involves a cyclic bis(acyl)palladium species.



The formation of the bis(acyl) may be derived from nucleophilic attack of a palladium carbonyl intermediate similar to that proposed in the α-keto amide synthesis or may be derived from intermediate palladium amide/alkoxide complexes. An analogous thiolatonickel compound $[Ni(SCH_2CH_2OH)_2]$ has been isolated from the Ni-catalyzed carbonylation of 2-mercaptoethanol to give cyclic *O,S*-ethylene thiocarbonate.[11] We have demonstrated the CO insertion into a Pt–N bond to give a carboxamido complex.[12] Carbon monoxide insertion into metal alkoxides are known.[13] We are studying the carbonylation of platinum amides and alkoxides as a model system for this chemistry and results will be reported. Oxazolidinone may be derived from the complexes shown. Nucleophilic



attack of amides and alcohols on acyl metal complexes (step a) to give new carbon–nitrogen and carbon–oxygen bonds is a well-known reaction.[14] Reductive elimination of a metal acyl/alkoxide complex similar to that proposed above (step b) has been demonstrated.[15] With *N*-alkyl-substituted substrates, the oxazolidinone is the major product at higher temperature (80 °C). This is most likely due to the shift of the equilibrium toward the monoacyl at higher temperature.



With *N*-phenyl-, *N*-acetyl-, andd *N*-*tert*-butyl-substituted substrates, the oxazolidinone is the only product. A possible reason for this may be the lower nucleophility of these substrates. It is known that aniline does not react with cationic platinum carbonyl complexes.[16]

Experimental Section

Melting points were taken on a Thomas Hoover capillary apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 9830 spectrophotometer. ^1H and ^{13}C NMR spectra were performed on a QE-300 Nicolet spectrometer. Mass spectra were recorded on a VGMM 770 double focusing high-resolution instrument. Anhydrous ethylene glycol dimethyl ether was obtained from Aldrich and used without further purification. All amines were degassed and stored over 4A molecular sieves under nitrogen in the drybox. The preparations of 2-(*N*-*n*-butylamino)-1-methylethanol, 2-(*N*-*tert*-butylamino)-1-phenylethanol, and 2-(*N*-*n*-butylamino)-1-phenylethanol were from modification of the literature procedure.[17]

Preparation of 1-(*N*-*n*-Butylamino)propane-2,3-diol. To 80 mL of refluxing *n*-butylamine was added dropwise 22 mL (0.33 mol) of glycidol. The mixture was refluxed overnight. Excess *n*-butylamine was distilled at atmospheric pressure, and the product was distilled at 3.5 mm (bp 132–135 °C). Thus collected was 28.6 g (0.19 mol, 59%) of a colorless viscous liquid: ^1H NMR (CD_2Cl_2) δ 4.2 (br s, 3 H), 3.72 (m, 1 H), 3.52 (dd, J = 4, 11 Hz, 1 H), 3.45 (dd, J = 6, 11 Hz, 1 H), 2.64 (dd, J = 4, 12 Hz, 1 H), 2.55 (m, 3 H), 1.46 (m, 2 H), 1.35 (m, 2 H), 0.92 (t, J = 7 Hz, 3 H); ^{13}C NMR (CD_2Cl_2) 70.5, 65.5, 52.7, 49.7, 32.1, 20.5, 13.8 ppm; IR (neat) 3308 br, 2956 s, 2927 s, 2861 s, 1460 s, 1097 s, 1045 s cm^{-1}. Anal. Calcd for $C_7H_{17}O_2N$: C, 57.11; H, 11.64. Found: C, 57.05; H, 11.67.

Preparation of 1-(*N*-Phenylamino)propane-2,3-diol. To 182 mL of aniline at 80–85 °C was slowly added 26 mL (0.390 mol) of glycidol. After addition, the mixture was kept at 80–90

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°C for 2 h. The excess aniline was distilled at 4–5 mm, and then the product was distilled at 0.10 mm (bp 174 °C). Thus obtained was 49.9 g (0.30 mol, 76%) of product. This material can be recrystallized from hot toluene: mp 48–52 °C; ^{1}H NMR (Me_2SO-d_6) δ 7.04 (dd, J = 8, 7.4 Hz, 2 H), 6.57 (d, J = 8 Hz, 2 H), 6.49 (t, J = 7.3 Hz, 1 H), 5.36 (t, J = 5.6 Hz, 1 H), 4.73 (d, J = 4.9 Hz, 1 H), 4.57 (t, J = 5.6 Hz, 1 H), 3.61 (m, 1 H), 3.38 (t, J = 5.6 Hz, 2 H), 3.14 (ddd, J = 12.7, 6.3, 5.2 Hz, 1 H), 2.88 (ddd, J = 12.8, 6.5, 5.2 Hz, 1 H); ^{13}C NMR (CD_2Cl_2) 47.0, 65.1, 71.0, 113.6, 118.0, 129.4, 148.6 ppm. Anal. Calcd for $C_9H_{13}O_2N$: C, 64.65; H, 7.84. Found: C, 64.42;, H, 7.95.

General Procedure for Carbonylation Reactions. A 12-oz Fischer–Porter bottle was charged under nitrogen in the drybox, evacuated, and pressurized with 3 atm of carbon monoxide. After the reaction, the mixture was either analyzed by GC on a 6 ft × $^1/_8$ in. 10% SP2100 on 100/120 Supelcoport stainless steel column by using *o*-xylene or *m*-diethylbenzene as internal standard or it was worked up by filtration, washed with $CHCl_3$, solvent removed by rotary evaporation, and the residue purified by column chromatography on silica gel. Authentic samples for GC analyses were obtained either from (1) previous preparation runs, (2) reaction of amino alcohols with diethyl carbonate, or (3) commercial sources.

2-(*N*-*n*-Butylamino)-1-methylethanol and CO. After reacting 0.80 g (6.10 mmol) of 2-(*N*-*n*-butylamino)-1-methylethanol, 1.0 g (5.68 mmol) of $PdCl_2$, and 1.0 g (12.19 mmol) of NaOAc in 50 mL of DME with CO at room temperature overnight, the mixture was worked up as usual. Chromatography with 50% EtOAc/hexane yielded 0.350 g (1.89 mmol, 33%) of the morpholinedione as a light yellow oil: ^{1}H NMR (C_6D_6) δ 3.78 (m, 1 H), 3.07 (m, 1 H), 2.95 (m, 1 H), 2.44 (dd, J = 13, 10 Hz, 1 H), 2.14 (dd, J = 13, 3 Hz, 1 H), 1.07 (m, 4 H), 0.80 (t, J = 7 Hz, 3 H), 0.72 (d, J = 6 Hz, 3 H); ^{13}C NMR ($CDCl_3$) 157.0, 153.4, 73.3, 50.7, 47.2, 28.9, 19.9, 17.7, 13.5 ppm; IR (neat) 1762 s, 1685 s cm^{-1}. Analytically pure material can be obtained after Kugelrohr to give a colorless liquid. Anal. Calcd for $C_9H_{15}NO_2$: C, 58.36; H, 8.16. Found: C, 58.63; H, 8.15. Also obtained from the column was 0.697 g of a mixture which included the oxazolidinone. The mixture was dissolved in methylene chloride and 0.112 g of *o*-xylene added as internal standard. GC analysis indicated 1.48 mmol (26%) of the oxazolidinone. When this reaction was repeated at 80 °C overnight, GC analysis with 0.341 g of *o*-xylene as internal standard indicated 5.8 mmol (100%) of the oxazolidinone.

In a similar run but using 0.10 g (0.57 mmol) of $PdCl_2$ and 1.65 g (12.27 mmol) of $CuCl_2$ instead of the stoichiometric amount of $PdCl_2$ and heating at 80 °C overnight, 0.914 mg (5.8 mmol, 95%) of the oxazolidinone was isolated after the usual workup and column chromatography with 1% MeOH/$CHCl_3$: ^{1}H NMR ($CDCl_3$) δ 4.6 (m, 1 H), 3.62 (t, J = 8 Hz, 1 H), 3.2 (m, 2 H), 3.08 (dd, J = 8, 7 Hz, 1 H), 1.5 (m, 2 H), 1.39 (d, J = 6 Hz, 3 H), 1.32 (m, 2 H), 0.91 (t, J = 7 Hz, 3 H); IR (neat) 1753 s cm^{-1}; high-resolution mass spectrum calcd for $C_8H_{15}NO_2$ 157.1102, found 157.1097.

1-(*N*-*n*-Butylamino)propane-2,3-diol and CO. After reacting 1.60 g (10.88 mmol) of 1-(*N*-*n*-butylamino)propane-2,3-diol, 2.0 g (11.36 mmol) of $PdCl_2$, and 2.0 g (24.4 mmol) of NaOAc in 65 mL of DME with CO at 80 °C overnight, the mixture was worked up, and residue was column chromatographed with 10% MeOH/EtOAc. Thus obtained was 1.909 g (9.5 mmol, 87%) of the oxazolidinone as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 4.6 (m, 1 H), 3.84 (dd, J = 3, 12 Hz, 1 H), 3.64 (dd, J = 3, 12 Hz, 1 H), 3.57 (t, J = 9 Hz, 1 H), 3.46 (dd, J = 7, 9 Hz, 1 H), 3.2 (d of t, J = 2, 7 Hz, 2 H), 1.50 (m, 2 H), 1.33 (m, 2 H), 0.93 (t, J = 7 Hz, 3 H); IR (neat) 1734 s cm^{-1}; ^{13}C NMR ($CDCl_3$) 158.3, 73.7, 62.9, 46.0, 43.8, 29.3, 19.8, 13.6 ppm; high-resolution mass spectrum calcd for $C_8H_{15}NO_3$ 173.1052, found 173.1061. The material is identical with that obtained from the reaction of diethyl carbonate with 1-(*N*-*n*-butylamino)propane-2,3-diol.

1-Phenylethane-2,3-diol and CO. After reacting 0.40 g (2.9 mmol) of 1-phenylethane-2,3-diol, 0.05 g (0.28 mmol) of $PdCl_2$, 0.50 g (6.10 mmol) of NaOAc, and 0.80 g (5.95 mmol) of $CuCl_2$ with CO at room temperature for 4 days, 0.218 g of *o*-xylene was added, and GC analysis indicated 2.9 mmol (100%) of the carbonate. In another run, 0.50 g of $PdCl_2$ was used instead of $PdCl_2/CuCl_2$ (mixture was stirred at room temperature overnight) and column chromatography eluted with 50% EtOAc/hexane gave 349 mg (2.1 mmol, 73%) of the carbonate: ^{1}H NMR ($CDCl_3$) δ 7.43 + 7.35 (m, 5 H), 4.34 (t, J = 9 Hz, 1 H), 4.80 (t, J = 9 Hz, 1 H), 5.67 (t, J = 9 Hz, 1 H); IR (neat) 1814 s cm^{-1}; high-resolution mass spectrum calcd for $C_9H_8O_3$ 164.0473, found 164.0476.

1-Phenyl-1-aminopropane-2,3-diol and CO. After reacting 2.00 g (11.98 mmol) of 1-phenyl-1-aminopropane-2,3-diol, 2.40 g (13.64 mmol) of $PdCl_2$, 2.40 g (23.76 mmol) of NEt_3 in 50 mL of DME with CO at room temperature for 3 days, the mixture was worked up. The residue was column chromatographed with 50% EtOAc/hexane. Thus obtained was 1.80 g (9.3 mmol, 78%) of the carbonate as white crystals: mp 63–64 °C; ^{1}H NMR (Me_2SO-d_6) δ 7.07 (dd, J = 8, 7.5 Hz, 2 H), 6.64 (d, J = 7.8 Hz, 2 H), 6.56 (t, J = 7.2 Hz, 1 H), 5.89 (t, J = 6.3 Hz, 1 H), 4.93 (m, 1 H), 4.57 (t, J = 8 Hz, 1 H), 3.56 (dd, J = 6.7, 8.2 Hz, 1 H), 3.38 (m, 2 H); ^{13}C NMR (CD_2Cl_2) 154.8, 147.6, 129.4, 118.6, 113.4, 75.8, 67.4, 46.2 ppm; IR (KBr) 1782 s cm^{-1}. Anal. Calcd for $C_{10}H_{11}O_3N$: C, 62.17; H, 5.74. Found: C, 62.00; H, 5.75. Also obtained was 0.539 g (2.8 mmol, 22%) of the oxazolidinone as white crystals: mp 118–121 °C; ^{1}H NMR (Me_2SO-d_6) δ 7.56 (d, J = 8 Hz, 2 H), 7.37 (t, J = 8 Hz, 2 H), 7.10 (t, J = 7 Hz, 1 H), 5.20 (t, J = 5.7 Hz, 1 H), 4.68 (m, 1 H), 4.07 (t, J = 9 Hz, 1 H), 3.82 (dd, J = 6, 9 Hz, 1 H), 3.55 (ddd, J = 12.3, 5.7, 4.2 Hz, 1 H), 3.67 (ddd, J = 12.3, 5.5, 3.5 Hz, 1 H); IR (KBr) 1735 m, 1728 s, 1712 s cm^{-1}. Anal. Calcd for $C_{10}H_{11}O_3N$: C, 62.17; H, 5.74. Found: C, 62.08; H, 5.93. This material was identical with that prepared from the diol amine and diethyl carbonate.[18]

(*N*-Methylamino)ethanol and CO. After reacting 0.50 g (6.66 mmol) of *N*-methylethanol amine, 1.0 g (5.68 mmol) of $PdCl_2$, and 1.0 g (12.19 mmol) of NaOAc in 50 mL of DME with CO at 80 °C overnight, the mixture was worked up and chromatographed with 5% MeOH/$CHCl_3$ to remove 443 mg (4.43 mmol, 78% based on $PdCl_2$ used) of the oxazolidinone [^{1}H NMR ($CDCl_3$) δ 4.32 (t, J = 8 Hz, 2 H), 3.57 (t, J = 8 Hz, 2 H), 2.89 (s, 3 H); IR (neat) 1754 cm^{-1} (lit. 1746 cm^{-1})[19]] and 80 mg (0.63 mmol, 11%) of the morpholinedione: 98–99 °C (lit. 98 °C)[5]; ^{1}H NMR ($CDCl_3$) δ 4.54 (t, J = 5 Hz, 2 H), 3.71 (t, J = 5 Hz, 2 H), 3.12 (s, 3 H); IR ($CHCl_3$ 1766 s, 1693 s cm^{-1}. When this reaction was run with 0.050 g (0.29 mmol) of $PdCl_2$ and 1.8 g (13.4 mmol) of $CuCl_2$ instead of stoichiometric $PdCl_2$, 0.529 g (5.2 mmol, 77%) of the oxazolidinone was isolated.

2-(*N*-*n*-Butylamino)-1-phenylethanol and CO. After reacting 1.10 g (5.98 mmol) of 2-(*N*-*n*-butylamino)-1-phenylethanol, 1.00 g (5.68 mmol) of $PdCl_2$, and 1.00 g (12.19 mmol) of NaOAc in 75 mL of DME with CO at room temperature overnight, 0.296 g of *m*-diethylbenzene was added as internal standard. GC analysis indicated 38% yield of the oxazolidinone. When this reaction was repeated at 80 °C, GC analysis indicated an 86% yield of the oxazolidinone.

(*N*-Acetylamino)ethanol and CO. After reacting 0.30 g (2.9 mmol) of (*N*-acetylamino)ethanol, 0.50 g (2.8 mmol) of $PdCl_2$, and 0.50 g (6.1 mmol) of NaOAc in 10 mL of DME with CO at room temperature overnight, the mixture was filtered through silica gel with $CHCl_3$. The solvent from the filtrate was removed by rotary evaporation to yield 0.338 g (2.62 mmol, 91%) of the oxazolidinone: ^{1}H NMR ($CDCl_3$) δ 4.44 (t, J = 8 Hz, 2 H), 4.04 (t, J = 8 Hz, 2 H), 2.55 (s, 3 H); IR ($CHCl_3$) 1786 s, 1704 s cm^{-1} (lit. 1785 s, 1695 s cm^{-1});[19] high-resolution mass spectrum calcd for $C_5H_7NO_3$ 129.0425, found 129.0428.

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Registry No. CO, 630-08-0; $PdCl_2$, 7647-10-1; $CuCl_2$, 7447-39-4; 2-(*N*-*n*-butylamino)-1-phenylethanol, 6273-86-5; 2-(*N*-*tert*-butylamino)-1-phenylethanol, 18366-40-0; 2-(*N*-*n*-butylamino)-1-methylethanol, 25250-77-5; 2-(*N*-methylamino)ethanol, 109-83-1; 2-(*N*-acetylamino)ethanol, 142-26-7; 2-(*N*-phenylamino)ethanol, 122-98-5; 3-butyl-5-phenyl-2-oxazolidinone, 17539-81-0; 3-*tert*-butyl-5-phenyl-2-oxazolidinone, 100994-72-7; 3-butyl-5-methyl-

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2-oxazolidinone, 95891-61-5; 3-methyl-2-oxazolidinone, 19836-78-3; 3-acetyl-2-oxazolidinone, 1432-43-5; 3-phenyl-2-oxazolidinone, 703-56-0; 4-methyl-2,3-morpholinedione, 7624-61-5; 4-butyl-6-methyl-2,3-morpholinedione, 100994-73-8; 1-(*N*-*n*-butylamino)-propane-2,3-diol, 60278-95-7; *n*-butylamine, 109-73-9; glycidol, 556-52-5; 1-(*N*-phenylamino)propane-2,3-diol, 5840-15-3; aniline, 62-53-3; 3-butyl-5-(hydroxymethyl)-2-oxazolidinone, 100994-74-9; 1-phenylethanediol, 93-56-1; 4-phenyl-1,3-dioxalan-2-one, 4427-92-3; 3-phenyl-5-(hydroxymethyl)-2-oxazolidinone, 29218-21-1; 4-[*N*-(phenyl)methylamino]-1,3-dioxolan-2-one, 100994-75-0.

Organoselenium Chemistry. Alkylation of Acid, Ester, Amide, and Ketone Enolates with Bromomethyl Benzyl Selenide and Sulfide: Preparation of Selenocysteine Derivatives

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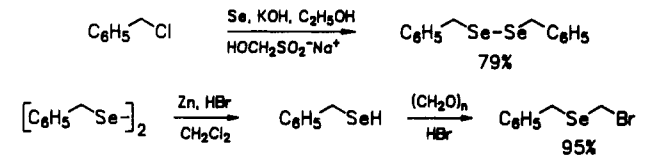
Bromomethyl benzyl selenide has been prepared and used for the alkylation of several carboxylic acid and amide dianions and certain ketones and ester enolates. Clean reaction could not be achieved for ketones and esters whose alkylation products were subject to selenolate elimination. The selenide reacted 18 times more slowly than bromomethyl benzyl sulfide, which alkylated ketones in fair yield even in some cases where the selenide failed. The bromomethyl benzyl sulfide alkylation products gave α-methylene ketones upon oxidation to sulfoxide and thermolysis. Several protected amino acid enolates (valine, alanine, and glycine) were alkylated with bromomethyl benzyl selenide. The product from glycine, **5b**, was converted to the protected dehydroalanine **11** by oxidation and to the protected selenocystine **10** by using bromine cleavage of the benzyl selenide. Halogen reagents (Br_2, SO_2Cl_2) were shown to very efficiently and generally convert benzyl selenides to selenenyl halides, which were converted to diselenides or selenides by reduction or alkylation.

We have long been interested in selenium as a "disposable" element in the construction of complex organic molecules and also as an inherent and crucial atom in important biomolecules. During our work on selenenic acids related to the active site of the seleno-enzyme glutathione peroxidase,[1c,2] we required a series of selenocysteine analogues, and α-alkylation of protected amino acids with a halomethyl selenide seemed the most effective route to them. Although the utilization of halomethyl sulfides as alkylating reagents has a long history,[1d,3] the related selenides had been only infrequently used,[4] and appeared to be much less satisfactory.[1d]

Scheme I



We have now developed an efficient synthesis of bromomethyl benzyl selenide and have found it to be a versatile reagent for the alkylation of several classes of enolates. The choice of a benzyl group was dictated by the requirement that the selenium be subsequently deprotected in the presence of other functional groups. From earlier studies on the chemistry of the halomethyl sulfides[1d] we had also observed that the benzyl sulfides were considerably more reactive than the phenyl analogues, and this proved true for the selenides as well. We here report the application of bromomethyl benzyl selenide and sulfide for the convenient preparation of a protected selenocystine and a series of related molecules and for the preparation of several α-methylene carbonyl compounds. This work also features a highly efficient oxidative removal of the benzyl protecting group from selenium.

Results and Discussion

Our preparation of bromomethyl benzyl selenide followed literature precedent (Scheme I).[4,5] Reduction of dibenzyl diselenide with zinc gave the selenol, which was converted directly to the bromide in 95% overall yield by treatment with paraformaldehyde. The selenide formed could not be effectively purified by distillation or other means, but was suitable for use (>95% pure) if pure di-

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