Table I. Palladium(0)-Catalyzed Cyclization of 2-Halo-*N*-allylanilines to 3-Substituted Indoles

aniline	product	yld, %[a]	charac-terizn	aniline	product	yld, %[a]	charac-terizn
2-iodo-*N*-allyl	3-methylindole	87	*b*	2-iodo-*N*-(2-methylallyl)	no reaction		
2-bromo-*N*-allyl	3-methylindole	60	*b*	2-bromo-4-methyl-*N*-allyl	3,5-dimethylindole	77	*f*
2-iodo-*N,N*-diallyl	1-allyl-3-methyl-indole	87	*c*	2-bromo-4-carb-ethoxy-*N*-allyl	3-methyl-5-carb-ethoxyindole	50	*g*
2-iodo-*N*-(3-methylallyl)	3-ethylindole	51	*d*	2-bromo-3,4-di-methoxy-*N*-allyl	3-methyl-5,6-di-methoxyindole	66	*g*
2-iodo-*N*-(3,3-dimethylallyl)	3-isopropylindole	73	*e*	2-iodo-*N*-(2-carb-ethoxyallyl)	3-carbethoxy-quinoline	49	*c*
2-iodo-*N*-(cyclo-hex-2-enyl)	no reaction						

[a] Yields are of isolated purified products. [b] Identical in all respects with authentic material. [c] Identical with material prepared by an alternate route. [d] Mp 37 °C (lit.[12] mp 37 °C). [e] Spectra identical with literature.[13] [f] Mp 75 °C (lit.[14] mp 75 °C). [g] These compounds have satisfactory IR and NMR spectra and acceptable elemental analyses or high-resolution exact-mass measurements.

aniline to 3-carbethoxyquinoline.

Experimental Section

The palladium acetate, tris(2-tolyl)phosphine, acetonitrile, and allyl bromide were obtained commercially and used without further purification. The triethylamine was distilled from KOH. The requisite 2-haloanilines were prepared by literature procedures.[1] NMR spectra were obtained with a Varian EM-360 instrument, and infrared spectra were obtained with a Beckman 4240 instrument. A typical procedure for each type of reaction is given below.

Preparation of 2-Iodo-*N*-allylaniline. 2-Iodoaniline (1.0 g, 4.54 mmol) was dissolved in 20 mL of dry tetrahydrofuran (THF) in a 100-mL round-bottom flask with a sidearm, and the flask was flushed with argon and cooled to −78 °C. Lithium diisopropylamide (4.5 mmol) (from 4.6 mmol of diisopropylamine and 4.6 mmol of *n*-butyllithium) in 5 mL of THF was slowly added, and the resulting mixture was allowed to warm to 0 °C over 10 min. After the resulting solution was recooled to −78 °C, allyl bromide (0.43 mL, 5.0 mmol) was added and the solution was stirred for 10 min, allowed to warm to room temperature, and stirred for 2 h at that temperature. The reaction mixture was partitioned between ether and saturated NaCl solution, and the ether phase was dried over anhydrous $MgSO_4$. After removal of solvent under vacuum, the crude material was purified by medium-pressure liquid chromatography (silica gel), using hexane as eluant. 2-Iodo-*N*-allylaniline (1.06 g, 89%) was obtained as a clear oil: NMR ($CDCl_3$) δ 3.55 (d, J = 6 Hz, 2, NCH_2), 4.09 (br s, 1, NH), 4.8–5.2 (m, 2, CH_2=C), 5.5–5.9 (m, 1, CH=C), 6.0–6.35 (m, 2, Ar H), 6.7–7.6 (m, 4, Ar H).

1-Allyl-3-methylindole was prepared from 3-methylindole and allyl bromide by using the same procedure to give 0.81 g (62%): NMR ($CDCl_3$) δ 2.35 (s, 3, CH_3), 4.25 (m, 2, NCH_2), 4.6–6.16 (m, 2, CH_2=C), 5.3–6.0 (m, 1, CH=C), 6.60 (s, 1, indole 2 H), 7.0–7.6 (m, 4, Ar H).

Cyclization of 2-Iodo-*N*-(3,3-dimethylallyl)aniline to 3-Isopropylindole. A Fischer–Porter aersol compatibility tube (3.5 × 13 cm) was charged with 0.287 g (1.00 mmol) of the iodoaniline, 2.2 mg (0.01 mmol) of $Pd(OAc)_2$, 0.21 mg (1.5 mmol) of NEt_3, and 6 mL of CH_3CN. The bottle was capped with a rubber serum cap, clamped into place by the pressure bottle head supplied with the unit, and flushed several times with argon. The mixture was heated at 110 °C for a total of 72 h. After 24 h and 48 h, the mixture was cooled to room temperature, an additional 2.2 mg of $Pd(OAc)_2$ and 0.07 mL of Et_3N in 1 mL of CH_3CN was added, and the mixture was reheated to 110 °C. After completion, the crude product was purified by medium-pressure liquid chromatography, eluting with 4:1 hexane/ether to give 3-isopropylindole[13] (0.116 g, 73%).

Cyclization of 2-Bromo-4-carbethoxy-*N*-allylaniline to 3-Methyl-5-carbethoxyindole. The reaction was run as above except 0.02 equiv of tris(2-tolyl)phosphine (based on substrate) was added in addition to the rest of the components. An additional 0.02 equiv of this phosphine was added with each subsequent addition of $Pd(OAc)_2$. From 0.32 g (1.12 mmol) of the allylaniline was obtained 0.113 g (49%) of 3-methyl-5-carbethoxyindole: NMR (CCl_4) δ 1.48 (t, J = 7 Hz, 3, CH_3CH_2O), 2.38 (s, 3, CH_3), 4.45 (q, J = 7 Hz, 2, CH_3CH_2O), 6.95 (s, 1, indole 2 H), 7.25 (d), 7.90 (d of d), 8.35 (s, 3, Ar H), 9.00 (br, 1, NH); IR (CCl_4) 3330 (NH), 1700 (C=O) cm^{-1}.

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Registry No. 2-Iodo-*N*-allylaniline, 73396-87-9; 2-iodoaniline, 615-43-0; 1-allyl-3-methylindole, 1914-05-2; 3-methylindole, 83-34-1; allyl bromide, 106-95-6; 2-iodo-*N*-(3,3-dimethylallyl)aniline, 73396-88-0; 3-isopropylindole, 16886-00-3; 2-bromo-4-carbethoxy-*N*-allylaniline, 73396-89-1; 3-methyl-5-carbethoxyindole, 73396-90-4; 2-bromo-*N*-allylaniline, 73396-91-5; 2-iodo-*N,N*-diallylaniline, 73396-92-6; 2-iodo-*N*-(cyclohex-2-enyl)aniline, 73396-93-7; 2-iodo-*N*-(2-methylallyl)aniline, 73396-94-8; 2-bromo-4-methyl-*N*-allylaniline, 73396-95-9; 2-bromo-3,4-dimethoxy-*N*-allylaniline, 73396-96-0; 2-iodo-*N*-(2-carbethoxyallyl)aniline, 73396-97-1; 3-ethylindole, 1484-19-1; 3,5-dimethylindole, 3189-12-6; 3-methyl-5,6-dimethoxyindole, 73396-98-2; 3-carbethoxyquinoline, 50741-46-3; Pd(O), 7440-05-3.

(12) R. H. Cornforth and R. Robinson, *J. Chem. Soc.*, 680 (1942).
(13) B. Cardillo, G. Casnati, A. Ponchi, and A. Ricca, *Tetrahedron*, **23**, 3771 (1967).
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Osmium-Catalyzed Vicinal Oxyamination of Olefins by *N*-Chloro-*N*-metallocarbamates

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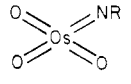
We have previously reported four procedures for the vicinal oxyamination of olefins. One method employs stoichiometric amounts of preformed (*tert*-alkylimido)-osmium compounds (**1a**).[1] The other methods are catalytic in osmium. Two of the catalytic methods rely on Chloramine-T (TsNClNa) for the in situ regeneration of the imidoosmium species **1b**.[2,3] These procedures produce



1a, R = *tert*-alkyl
b, R = Ts
c, R = R′OCO

(1) Sharpless, K. B.; Patrick, D. W.; Truesdale, L. K.; Biller, S. A. *J. Am. Chem. Soc.* **1975**, *97*, 2305. Chong, A. O.; Oshima, K.; Sharpless, K. B. *Ibid.* **1977**, *99*, 3420. Patrick, D. W.; Truesdale, L. K.; Biller, S. A.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2628.

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Table I. Reactivity of Styrene with Different Ethyl *N*-Chloro-*N*-metalocarbamates[a]

metallic salts	reaction time,[b] h
$HgCl_2$, $Hg(NO_3)_2$, $Hg(OAc)_2$, $AgNO_3$, $Zn(OAc)_2$	<2
$Cd(OAc)_2$, $Cd(NO_3)_2$, $Cu(OAc)_2$	5-10
$Zn(NO_3)_2$, $CdCl_2$, $ZnCl_2$	10-20

[a] In all the cases reported in Table I the yield (GLC) of hydroxy carbamate was greater than 95%. Blank experiments (no OsO_4 added) showed no reaction of styrene with the ethyl *N*-chloro-*N*-metallocarbamate. [b] Disappearance of the styrene from the reaction mixture.

Table II. Reactivity of (*E*)-5-Decene with Different Ethyl *N*-Chloro-*N*-metallocarbamates[a]

metallic salts	reaction time,[b] h
$HgCl_2$, $Hg(NO_3)_2$, $Hg(OAc)_2$	24
$AgNO_3$	~80
$Zn(OAc)_2$	proceeds very slowly

[a] In all the cases except one [$Zn(OAc)_2$] reported in Table II the yield (GLC) of hydroxy carbamate was greater than 90%. Blank experiments (no OsO_4 added) showed no reaction of (*E*)-5-decene with the ethyl *N*-chloro-*N*-metallocarbamates. [b] Disappearance of (*E*)-5-decene from the reaction mixture.

vicinal hydroxy *p*-toluenesulfonamides. In some cases the sulfonamide moiety may be acceptable or even desirable, but in others the difficulties associated with removing sulfonamide protecting groups will restrict the usefulness of these oxyaminations. This fact provided incentive for developing an analogous osmium-catalyzed procedure which effects cis addition of hydroxyl (OH) and carbamate (ROCONH) moieties across the olefinic linkage. This method employs *N*-chloro-*N*-argentocarbamates for the in situ regeneration of the imidoosmium species **1c**.[4a,b] β-Amino alcohols with BOC and *t*-BOC protecting groups on the nitrogen are accessible directly from the corresponding olefins. Recently, we have found even more effective osmium-catalyzed procedures by using different kinds of *N*-chloro-*N*-metallocarbamates in conjunction with the addition of Et_4NOAc to the reaction mixtures.

N-Chloro-*N*-metallocarbamates are generated in situ by reaction of the corresponding *N*-chlorosodiocarbamates with the corresponding metallic salt in acetonitrile. A great variety of metallic salts were added to the ethyl *N*-chloro-*N*-sodiocarbamate and their reactivity was tested in the reaction with styrene (Table I). All the oxyamination reactions described in this work were performed at room temperature.

The metallic salts which were most reactive with styrene were then tested with the less reactive substrate (*E*)-5-decene (Table II).

It is clear from the results in Table II that the mercury(II) salts give the most powerful oxyamination reagents. However, this carbamate-based procedure is amenable to further improvement by adding Et_4NOAc[4c] or by using an excess of the metallic salt[4d] (Table III and Figure 1). In Figure 1 the time course of olefin consumption has been

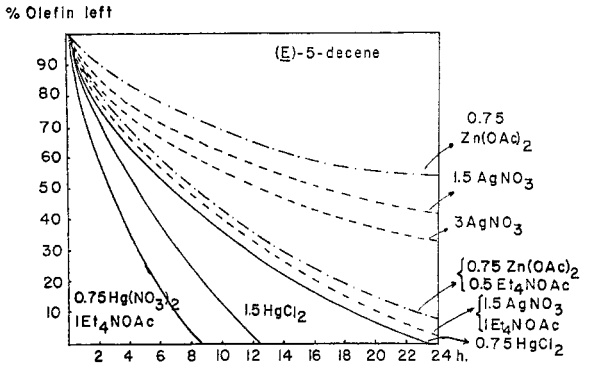

Figure 1. Reactivity of (*E*)-5-decene with different ethyl *N*-chloro-*N*-metallocarbamates.

Table III. Effect of Et_4NOAc or Excess Metallic Salt in Reaction of (*E*)-5-Decene with Ethyl *N*-Chloro-*N*-sodiocarbamates

metallic salt (mol)	reaction time,[a] h
$HgCl_2$ (0.75)	24
$HgCl_2$ (1.5)	12
$HgCl_2$ (0.75) + Et_4NOAc[b] (1)	8
$Hg(NO_3)_2$ (0.75)	24
$Hg(NO_3)_2$ (0.75) + Et_4NOAc (1)	8
$Hg(OAc)_2$ (0.75)	24
$Hg(OAc)_2$ (0.75) + Et_4NOAc[b] (1)	8
$AgNO_3$ (1.5)	80
$AgNO_3$ (3.0)	60
$AgNO_3$ (1.5) + Et_4NOAc[b] (1.5)	18
$AgNO_3$ (1.5) + Et_4NOAc (1)	24
$AgNO_3$ (1.5) + Et_4NOAc (0.5)	40
$Zn(OAc)_2$ (0.75)	proceeds very slowly
$Zn(OAc)_2$ (0.75) + Et_4NOAc[b] (1)	15
$Zn(OAc)_2$ (0.75) + Et_4NOAc[b] (0.5)	24

[a] Disappearance of (*E*)-5-decene from the reaction mixture. [b] (*E*)-5-Decene remains in the reaction mixture after all the oxidant has been consumed.

plotted for the various metal salts with and without added Et_4NOAc.

The *N*-chlorosodiocarbamates, essential components in these oxyaminations, are prepared from the carbamates according to a convenient method developed by Campbell and co-workers.[5] For the simplicity of one flask operation, we sometimes use the crude *N*-chlorosodiocarbamates which result after evaporation of the methanol (i.e., the step in their[5] procedure calling for trituration of the crude salt with ether is omitted). However, the crude salts (i.e., not ether washed) give slightly lower yields of hydroxy carbamate (Table IV).

There are conflicting statements in the literature about the stability of these *N*-chlorosodiocarbamates.[6] On one occasion, when EtOCONNaCl was prepared on a 250-mmol scale it decomposed rapidly (but not explosively), turning dark and releasing heat and gases. However, we had earlier

(2) Sharpless, K. B.; Chong, A. O.; Oshima, K. *J. Org. Chem.* **1976**, *41*, 177.

(3) Herranz, E.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2544. Herranz, E.; Sharpless, K. B., submitted for publication in *Org. Synth.*

(4) (a) Herranz, E.; Biller, S. A.; Sharpless, K. B. *J. Am. Chem. Soc.* **1978**, *100*, 3596. (b) Herranz, E.; Sharpless, K. B., submitted for publication in *Org. Synth.* (c) For a discussion of the beneficial effect of Et_4NOAc on these osmium-catalyzed processes, see: Akashi, K.; Palermo, R. E.; Sharpless, K. B. *J. Org. Chem.* **1978**, *43*, 2063. (d) This beneficial effect of using excess of the metallic salt had also been observed previously (see ref 4a).

(5) Bremmer, D. H.; Campbell, M. M.; Johnson, G. *J. Chem. Soc., Perkin Trans. 1* **1976**, 1918. Campbell, M. M.; Johnson, G. *Chem. Rev.* **1978**, *78*, 65.

(6) Saika, D.; Swern, D. *J. Org. Chem.* **1968**, *33*, 4548. These authors describe preparation of the sodium, potassium, and silver salts of *N*-chlorocarbamates. They state that contrary to literature reports (Chabrier, P. *C. R. Hebd. Seances Acad. Sci.* **1942**, *214*, 362) the sodium and potassium salts do not decompose on heating below 250 °C.

Table IV. Isolated Yields of Hydroxy Carbamates Using Different Oxyamination Reagents and Different Olefins[a]

example	olefin	oxyamination reagent[b]	reaction time, h[c]	% yield[d]
1	(*E*)-5-decene[e]	*t*-BuOC(O)NClNa + $AgNO_3$	40	36
2	(*E*)-5-decene	EtOC(O)NClNa + $AgNO_3$ + Et_4NOAc	24	68
3	(*E*)-5-decene	EtOC(O)NClNa + $Hg(NO_3)_2$	24	78
4	(*E*)-stilbene	$EtOC(O)NH_2$ + Ag_2O + *t*-BuOCl	18	65 (122–123.5 °C)
5	(*E*)-stilbene	crude EtOC(O)NClNa + $AgNO_3$	18	69
6	(*E*)-stilbene	crude *t*-BuOC(O)NClNa + $AgNO_3$	10	83 (137–138 °C)
7	(*E*)-stilbene	*t*-BuOC(O)NClNa + $AgNO_3$	10	87
8	1-methylcyclohexene[f,g,i]	EtOC(O)NClNa + $Hg(NO_3)_2$ + Et_4NOAc	40	38
9	2-methyl-2-heptene[f,g,i]	EtOC(O)NClNa + $Hg(NO_3)_2$ + Et_4NOAc	24	46
10	1-phenylcyclohexene[f,i]	EtOC(O)NClNa + $Hg(NO_3)_2$ + Et_4NOAc	36	34
11	3-methyl-2-cyclohexenone[f,h,i]	EtOC(O)NClNa + $AgNO_3$ + Et_4NOAc	36	37

[a] All the reactions were performed on 1 mmol of the olefin (except example 3 which was on a 5-mmol scale and examples 4 and 5 which were on a 100-mmol scale) as described in detail under General Procedures. All new compounds exhibited appropriate spectral and analytical data except in the case of the products from 1-methylcyclohexene and 3-methyl-2-cyclohexenone where the carbon analysis was slightly off. [b] Unless otherwise noted (i.e., examples 5 and 6) the sodium salts of the *N*-chlorocarbamates were purified by washing with ether. [c] Time required for complete disappearance of olefin. [d] All yields are for isolated pure substances and are based on the initial moles of olefin. For solid products the melting points are given after the yields. [e] The reaction proceeds very slowly. After 40 h some olefin remains in the reaction mixture and starch–iodide paper gives a positive test. [f] These hydroxy carbamates are not very stable on silica gel. [g] An organomercury complex also forms in these cases. [h] The reaction does not proceed to completion; unreacted olefin remains in the reaction mixture. [i] In the case of these trisubstituted olefins, the only product regioisomer detected was that with the nitrogen attached to the less substituted olefinic carbon.

prepared this same chloramine salt on a 100-mmol scale without incident. Before we knew how to deal safely with the *N*-chlorosodiocarbamates, we developed an in situ procedure in which the entire reaction sequence is carried out in acetonitrile, obviating the need for dealing with the dry *N*-chlorosodiocarbamates.

Our investigations[7] on the stability of the *N*-chlorosodiocarbamates revealed that acidic conditions (leading to contamination by the *N*-chlorocarbamate) were responsible for the spontaneous decomposition of these salts at room temperature. This led us to modify Campbell's procedure for preparing *N*-chloro-*N*-sodiocarbamates by adding 5% more NaOH than the calculated amount, thereby assuring that all the *N*-chlorocarbamate in the reaction mixture is neutralized. No spontaneous decomposition has occurred in the batches of *N*-chloro-*N*-sodiocarbamates prepared in this way.

Table IV shows the isolated yields of hydroxy carbamate obtained by using different oxyamination reagents with different olefins. When the most effective carbamate-based reagent ($Hg(NO_3)_2$, ROCONNaCl, and Et_4NOAc in the correct amount) is applied to trisubstituted olefins, the hydroxy carbamates are obtained. However, the yields are rather poor, because there is competitive formation of an organomercury complex.[9] The in situ procedure is very convenient because of its simplicity; however, the yields obtained are always a little bit lower than when the *N*-chloro-*N*-sodiocarbamate-based procedures are used. The in situ procedure is best suited for mono- and simple disubstituted olefins. When the steric hindrance of the olefin increases, *N*-chloro-*N*-sodiocarbamate-based procedures should be used. In Scheme I the different procedures are listed in order of increasing reactivity.

Scheme I. Carbamate-Based Oxyamination Systems in Order of Increasing Reactivity

increasing reactivity ↓

ROC(O)NH_2 + *t*-BuOCl + Ag_2O (1.5:1.5:0.75)
ROC(O)NClNa + $AgNO_3$ (1.5:1.5)
ROC(O)NClNa + $AgNO_3$ (1.5:3)
ROC(O)NClNa + $AgNO_3$ + Et_4NOAc (1.5:1.5:1)
ROC(O)NClNa + $Hg(NO_3)_2$ (1.5:0.75)
ROC(O)NClNa + $Hg(NO_3)_2$ (1.5:1.5)
ROC(O)NClNa + $Hg(NO_3)_2$ + Et_4NOAc (1.5:0.75:1)

The third procedure in Scheme I is the general procedure recommended in our previous publication.[4a] It is fine for most mono- and disubstituted olefins but is not effective for trisubstituted olefins. Only the more reactive procedures toward the bottom of Scheme I are capable of oxyaminating trisubstituted olefins, and with this type of olefin even the best method has never given the oxyamination product in better than 46% isolated yield (example 9, Table IV). All of the procedures in Scheme I fail with tetrasubstituted olefins. In summary, we recommend these new, more reactive procedures [especially ROCONClNa + $Hg(NO_3)_2$ + Et_4NOAc (1.5:0.75:1.0)] for all trisubstituted olefins and also for any mono- and disubstituted olefins which are found to give poor results with the less reactive procedures in Scheme I (cf. examples 1 and 3 in Table IV).

Experimental Section

Unless stated otherwise, all reagents and chemicals were obtained commercially and were used without further purification.

General Procedure for Preparing *N*-Chloro-*N*-sodiocarbamates.[5] To an ice-cold stirred solution or suspension of 50 mmol of the carbamate in 40 mL of reagent-grade methanol was added 5.63 mL (5.4 g, 50 mmol) of *tert*-butyl hypochlorite. After 15 min a methanolic solution (25 mL) of sodium hydroxide (2.15 g, 52.5 mmol) was added dropwise over a period of several minutes.[10] The ice bath was removed and stirring was continued for 10 min. Then the solvent was removed on a rotary evaporator (bath <60 °C) and the resulting white solid residue (crude *N*-chloro-*N*-sodiocarbamate) was triturated with dry ether and

(7) Our own experiences showed that when two different samples of EtOCONNaCl (one prepared by Campbell's method[5] and the other by Swern's method[8]) were heated slowly in an oil bath with a magnetic stirrer and the temperature was between 110 and 120 °C rapid decomposition occurred in both cases. The solid that remained gave an IR spectrum identical with the IR spectrum of a sample of pure sodium isocyanate and gave a negative starch–iodide test. The evolved gases are strong oxidants and give a positive starch–iodide test.

(8) Foglia, T. A.; Swern, D. *J. Org. Chem.* **1966**, *31*, 3625. The *N*-chlorocarbamate is produced by reaction of the *N,N*-dichlorocarbamate with the carbamate. Neutralization with NaOH in methanol provides the *N*-chlorosodiocarbamate.

(9) At present we do not know the structure of these organomercury complexes, but control experiments show that they form equally well in the absence of the osmium catalyst. The presence of acetonitrile is necessary for the formation of the organomercury complexes. We do know that when heated they decompose to give imidazoline derivatives.

(10) A 5% excess of NaOH was used to ensure that the *N*-chloro-*N*-sodiocarbamates would be in a basic environment. The NaOH was obtained from J. T. Baker Chemical Co. and was 97.9% pure.

collected by filtration to afford the *N*-chloro-*N*-sodiocarbamates.

The salts prepared and isolated in this way were dry. The IR spectra of the compounds indicated the absence of water of hydration. The *N*-chloro-*N*-sodiocarbamates are hygroscopic and should be stored in a desiccator in a freezer (ca. −20 °C). When stored in this way at low temperature these reagents were stable for at least 6 months.

General Procedure for the Catalytic Hydroxyamination of Olefins Using *N*-Chloro-*N*-sodiocarbamates and Various Metallic Salts with or without Added Et_4NOAc. A one-necked, round-bottomed flask (25 mL) equipped with a magnetic stirrer was charged with 1.5 mmol of the desired *N*-chloro-sodiocarbamate,[11] the appropriate number of equivalents of a metallic salt (i.e., a stoichiometric amount + 5% excess), and 10 mL of reagent-grade acetonitrile. After the mixture was stirred at room temperature for ~5 min, a milky brown suspension resulted. To this suspension was added 81 μL (4.5 mmol) of water, 1 mmol of olefin, and 0.01 mmol of OsO_4 as a solution in *tert*-butyl alcohol.[3] The mixture was stirred at room temperature for ~5 min and then, if planned, 1 mmol of Et_4NOAc was added; stirring was continued at room temperature until the olefin disappeared from the reaction mixture. In case an excess of metallic salt had been used, the appropriate number of equivalents of saturated sodium chloride solution was added to precipitate the remaining metallic ion [e.g., 0.25 mL (1.5 mmol) if the excess was twice the necessary number of equivalents]. The solid salts were removed by filtration. The filtrate was refluxed for several hours (3–6) with 2 mL of 5% aqueous sodium sulfite. The workup is identical with that described immediately below for the in situ procedure.

In Situ Procedure for the Catalytic Hydroxyamination of Olefins. A one-necked, round-bottomed flask (25 mL) equipped with a magnetic stirrer was placed in an ice bath and charged with a solution of 1.5 mmol of the desired carbamate in 10 mL of reagent-grade acetonitrile. To this ice-cold solution was added 1.7 mL (1.6 g, 1.5 mmol) of *tert*-butyl hypochlorite, and the mixture was stirred for 5 min. Then 1.7 g (0.75 mmol) of silver oxide was added, and stirring was continued for 10 min. To the resulting suspension was added 1 mmol of the olefin, 0.1 mL of an OsO_4 solution in *tert*-butyl alcohol, and 40 μL (2.2 mmol) of water. After 5 min, the ice bath was removed and stirring was continued at room temperature until the olefin had been consumed. Filtration of the reaction mixture gave a solution that was refluxed for several hours (3–6) with 2 mL of 5% aqueous sodium sulfite. The resulting mixture was concentrated in a rotary evaporator, and the largely aqueous residue was extracted with two 10-mL portions of methylene chloride. The organic phase was dried ($MgSO_4$) and concentrated to give the crude hydroxycarbamate. When mixtures were formed, chromatography on silica gel was used to separate the regioisomers. When only one hydroxy carbamate was produced, recrystallization of the crude reaction product was the preferred method of purification.

Acknowledgment. We are grateful to the National Science Foundation (CHE77-14628), Hoffmann-La Roche, and Eli Lilly for financial support.

Registry No. *t*-BuOC(O)NClNa, 73210-14-7; EtOC(O)NClNa, 17510-52-0; $EtOC(O)NH_2$, 51-79-6; $HgCl_2$, 7487-94-7; $Hg(NO_3)_2$, 10045-94-0; $Hg(OAc)_2$, 1600-27-7; $AgNO_3$, 7761-88-8; $Zn(OAc)_2$, 557-34-6; $Cd(OAc)_2$, 543-90-8; $Cd(NO_3)_2$, 10325-94-7; $Cu(OAc)_2$, 142-71-2; $Zn(NO_3)_2$, 7779-88-6; $CdCl_2$, 10108-64-2; $ZnCl_2$, 7646-85-7; Ag_2O, 20667-12-3; styrene, 100-42-5; (*E*)-5-decene, 7433-56-9; (*E*)-stilbene, 103-30-0; 1-methylcyclohexene, 591-49-1; 2-methyl-2-heptene, 627-97-4; 1-phenylcyclohexene, 771-98-2; 3-methyl-2-cyclohexenone, 1193-18-6; *tert*-butyl *threo*-[6-(5-hydroxy)decyl]carbamate, 67341-06-4; ethyl *threo*-[6-(5-hydroxy)decyl]carbamate, 73210-15-8; ethyl *threo*-[1-(2-hydroxy-1,2-diphenyl)ethyl]carbamate, 73197-89-4; *tert*-butyl *threo*-[1-(2-hydroxy-1,2-diphenyl)ethyl]carbamate, 67366-52-3; ethyl *cis*-[1-(2-hydroxy-2-methyl)cyclohexyl]carbamate, 73197-90-7; ethyl [3-(2-hydroxy-2-methyl)heptyl]carbamate, 73197-91-8; ethyl *cis*-[1-(2-hydroxy-2-phenyl)cyclohexyl]carbamate, 73197-92-9; ethyl *cis*-[1-(2-oxo-6-hydroxy-6-methyl)cyclohexyl]carbamate, 73197-93-0; Et_4NOAc, 1185-59-7; OsO_4, 20816-12-0.

(11) Either the crude or the ether-washed *N*-chlorosodiocarbamate can be used. The difference in the isolated yield of hydroxycarbamate is generally small (cf. examples 6 and 7 in Table IV).

Conversion of Carbalkoxymethyl Groups to γ-Oxocrotonate Derivatives

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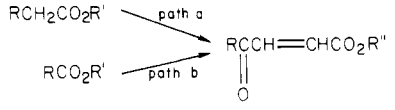
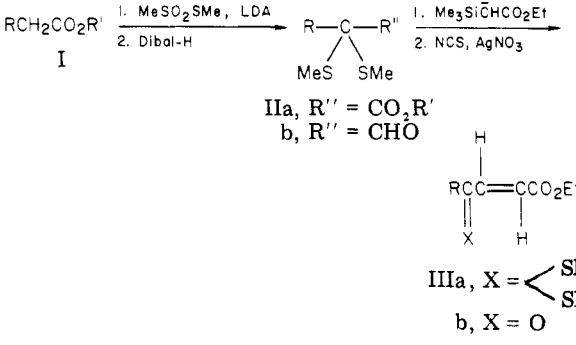
In the course of our ongoing effort directed toward the total synthesis of (±)-brefeldin A,[1] we required an efficient means of transforming a carbalkoxymethyl group to a ketone-protected γ-oxocrotonate unit that ultimately could be deprotected under mild, selective conditions. Surprisingly, there are few published methods[2] for effectively carrying out this overall process (eq 1, path a) in contrast



(1)

with the numerous procedures[3] that are available for converting a carbalkoxyl group to the corresponding γ-oxocrotonate derivative (eq 1, path b). In that γ-oxygenated crotonate derivatives are widespread in nature,[4] an efficient method for accomplishing this complementary conversion undoubtedly would be quite useful.

A sequence of reactions that we have found to be particularly well suited for our brefeldin synthesis and which appears to be generally applicable for effecting the carbalkoxymethyl → γ-oxocrotonate transformation is shown in eq 2. As can be seen from the examples given in Table



(2)

I, the yields on the average are quite high (ca. 85%) at each stage with the exception of the thioketal hydrolysis, for which the yields vary from 55 to 71%.[5] The synthetic advantages afforded by such a protected ketone function, which can be introduced in a single step[6] and hydrolyzed

(1) For our previous work in this area, see: R. Baudouy, P. Crabbé, A. E. Greene, C. Le Drian, and A. F. Orr, *Tetrahedron Lett.*, 2973 (1977).

(2) (a) E. J. Corey, R. H. Wollenberg, and D. R. Williams, *Tetrahedron Lett.*, 2243 (1977); ref 1. (b) See also P. Montellano and C. K. Hsu, *ibid.*, 4215 (1976).

(3) (a) E. J. Corey and R. H. Wollenberg, *Tetrahedron Lett.*, 4705 (1976); (b) P. A. Bartlett, *J. Am. Chem. Soc.*, **98**, 3305 (1976); (c) P. Bakuzis, M. L. F. Bakuzis and T. Weingartner, *ibid.*, **100**, 2371 (1978), and references cited therein.

(4) For examples of γ-oxygenated crotonate natural products, see: K. C. Nicolaou, *Tetrahedron*, **33**, 683 (1977); S. Masamune, *Aldrichimica Acta*, **11**, 23 (1978). See also, footnote 1 in ref 3 b.

(5) (a) E. J. Corey and B. Erickson, *J. Org. Chem.*, **36**, 3553 (1971). For related examples, see: (b) E. W. Colvin, T. A. Purcell, and R. A. Raphael, *J. Chem. Soc., Perkin Trans.*, 1718 (1976); (c) D. Seebach, B. Seuring, H.-O. Kalinowski, W. Lubosch, and B. Renger, *Angew. Chem., Int. Ed. Engl.*, **16**, 264 (1977); (d) K. F. Burri, R. A. Cardone, W. Y. Chen, and P. Rosen, *J. Am. Chem. Soc.*, **101**, 7068 (1979).

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