etherate in THF (10 ml). The solution was stirred at room temperature for 2 hr and cooled in an ice bath and 0.953 g (0.053 mol) of 1-phenyl-1-(1-pyrrolidino)-1-propene in THF (10 ml) was added dropwise. The solution was stirred at room temperature for 5 hr and cooled and a solution of 1 *N* sodium hydroxide (4 ml) was added simultaneously with a solution of 30% hydrogen peroxide (3 ml). The solution was stirred for 12 hr, poured into a saturated sodium chloride solution, and extracted with three 50-ml portions of 1 *M* hydrochloric acid and the combined acid extracts were made basic by the addition of sodium hydroxide pellets. The basic solution was extracted with ether and dried ($MgSO_4$) and the solvent was removed in vacuo. Crystallization of the residue from hexane afforded 0.207 g (20%) of *dl-threo*-**1b**.

**Reduction of 2-(1-pyrrolidino)-1-phenyl-1-propanone.** The sodium borohydride reduction of the amino ketone in methanol afforded a mixture of *dl-threo-* and *dl-erythro*-**3b** in high yields. The *dl*-threo and *dl*-erythro amino alcohols (Table IV) could be isolated in low yields from the mixture by fractional crystallization from hexane.

**Benzoate Esters 2 and 4.** A solution of benzoic anhydride (0.01 mol), pyridine (2 ml), and amino alcohol (ca. 0.002 mol) was heated on a steam bath for 2–24 hr. The solution was poured into a mixture of saturated sodium bicarbonate (50 ml) and ether (25 ml). The solution was magnetically stirred for ca. 1 hr, extracted with three 50-ml portions of ether, and dried ($MgSO_4$) and the solvent was removed in vacuo. The oily benzoates were purified by chromatography over alumina.

**Acknowledgments.** We are pleased to acknowledge the partial support of the Research Corporation for a Frederick Gardner Cottrell grant and a grant for partial support from the University of Northern Colorado Faculty Research and Publications Committee. We are indebted to Colorado State University for the use of their Beckman IR-12 spectrophotometer for the infrared studies.

**Registry No.**—*threo*-**1a**, 56571-81-4; *erythro*-**1a**, 56571-82-5; *threo*-**1b**, 56571-83-6; *erythro*-**1b**, 56571-84-7; *threo*-**2a**, 56571-85-8; *erythro*-**2a**, 56571-86-9; *threo*-**2b**, 56571-87-0; *erythro*-**2b**, 56571-88-1; *threo*-**3a**, 56571-89-2; *erythro*-**3a**, 56571-90-5; *threo*-**3b**, 56571-91-6; *erythro*-**3b**, 56571-92-7; *threo*-**4a**, 56571-93-8; *erythro*-**4a**, 56571-94-9; *threo*-**4b**, 56571-95-0; *erythro*-**4b**, 56571-96-1; *trans*-1-phenyl-1-propene oxide, 23355-97-7; pyrrolidine, 123-75-1; piperidine, 110-89-4; 1-phenyl-2-(1-piperidino)-1-propene, 56571-97-2; 1-phenyl-1-(1-piperidino)-1-propene, 25076-80-6; 1-phenyl-1-(1-pyrrolidino)-1-propene, 31889-28-8; 2-(1-pyrrolidino)-1-phenyl-1-propanone, 19134-50-0.

## References and Notes

(1) For previous paper in this series see M. K. Meilahn and M. E. Munk, *J. Org. Chem.*, **34**, 1440 (1969).
(2) M. K. Meilahn, C. N. Statham, J. L. McManaman, and M. E. Munk, Abstracts, First Rocky Mountain Regional Meeting of the American Chemical Society, Fort Collins, Colo., June 1972, p 39.
(3) Taken in large part from the senior research project of C. N. Statham, University of Northern Colorado, 1972.
(4) M. E. Munk, M. K. Meilahn, and P. Franklin, *J. Org. Chem.*, **33**, 3480 (1968).
(5) The term threo and erythro as used in this paper indicate *dl*-threo and *dl*-erythro.
(6) Footnote 7, ref 4, defines the term "rotamer" as used in this paper.
(7) These interactions have been previously discussed and Figures 1 and 2 in ref 4 show these interactions.
(8) M. E. Munk and Y. K. Kim, *J. Am. Chem. Soc.*, **86**, 2213 (1964).

# Reactions of Amines. XVIII. The Oxidative Rearrangement of Amides with Lead Tetraacetate[1,2]

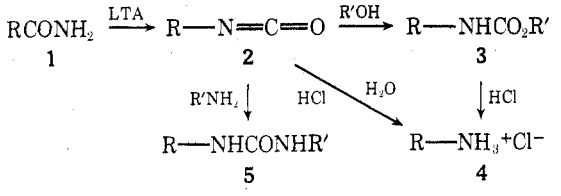
Henry E. Baumgarten,* Howard L. Smith, and Andris Staklis

*Department of Chemistry, University of Nebraska—Lincoln, Lincoln, Nebraska 68588*

*Received July 17, 1974*

Fourteen primary amides of varying structures were converted to isocyanates by treatment with lead tetraacetate. Generally the isocyanates were not isolated but were converted to carbamates by using a reaction solvent such as benzyl or, preferably, *tert*-butyl alcohol. Alternatively, the reaction was run in dimethylformamide and the isocyanate was converted to the *unsym*-urea by treatment with *tert*-butylamine. The carbamates could be easily cleaved to the corresponding amines (as the hydrochlorides) by treatment with HCl in alcohol, ether, or acetic acid. The rearrangement was shown to proceed with retention of configuration about the migrating carbon atom.

Some years ago we reported[3] the oxidative rearrangement of *N*-aminooxindole to 3-cinnolinol using lead tetraacetate (LTA) as the oxidant. Because this rearrangement appeared to resemble in some aspects the classical Hofmann rearrangement of *N*-halo amides, we next showed[4] that the rearrangement of *N*-aminooxindole could be carried out via the *N*-chloro derivative. These observations led logically to the conclusion and subsequent demonstration[5] that a Hofmann-like oxidative rearrangement of amides (**1**) could be brought about with LTA. By a somewhat different




pattern of reasoning Beckwith[6-9] and his coworkers came independently to the same conclusion. They have described in some detail their investigations of this quite general and immensely practical version of the Hofmann rearrangement.[10]

Even earlier Tscherniac[11] had noted an apparent similarity in the behavior of iodosobenzene and the hypohalites and reported the first example known to us of a Hofmann-like rearrangement using a two-electron oxidant other than positive halogen. This communication describes some of our efforts to explore the scope and limitations of the rearrangement as a practical synthetic method.

As was reported in the preliminary communication,[5] the rearrangement can be run very rapidly in dimethylformamide solution in such as a way as to permit isolation of the intermediate isocyanate (**2**) or to proceed directly via acid hydrolysis to the amine hydrochloride (**4**). However, for many amides isolation of **2** is tedious, if not difficult,[6] and acid-catalyzed hydrolysis of **2** without isolation may result in lower yields of **4** than may be obtained by the less direct routes described here. Nevertheless, the use of dimethylformamide is very advantageous in those rearrangements involving a subsequent reaction with an amine to form a urea[5] (**5**) or a subsequent cyclization of the isocyanate

Table I
Yields of Carbamates and Amine Hydrochloride from the Reactions

$$RCONH_2 + LTA + PhCH_2OH \xrightarrow{Et_3N} RNHCO_2CHPh \xrightarrow[HCl]{HCl} RNH_3Cl$$

| Registry no. | R | Scale,[a] mol | Solvent | Temp,[a] °C | Yield, %,[b] carbamate | Yield, %,[b] amine hydrochloride |
|---|---|---|---|---|---|---|
| 56700-65-3 | Cyclobutyl | 0.01 | DMF | | 66 | |
| 7107-58-6 | Cyclohexyl | 0.01 | MeCN | 40, 80 | 76 | |
| | Cyclohexyl | 0.01 | DMF[c] | 25, 120 | 67 | |
| | Cyclohexyl | 0.03 | DMF | 25, 120 | 72[d] | 63[h] |
| 39896-97-4 | Benzyl | 0.01 | DMF | 0, 60 | 65[e] | 54[i] |
| | Benzyl | 0.01 | DMF[c] | 25, 68 | 64 | |
| | Benzyl | 0.01 | MeCN[c] | 60, 60 | 38 | |
| 3422-02-4 | Phenyl | 0.01 | DMF[c,d] | 25, 75 | 33[f] | |

[a] First temperature given is that of oxidation step; second, that of conversion of isocyanate to carbamate. [b] Based on amide. [c] Benzyl alcohol added at start of reaction. [d] $Et_3N$ not used. [e] Mp 95–95.5° (lit.[52] mp 90–91°). [f] Mp 62–63° (lit.[53] mp 64°). [g] Mp 77° (lit.[53] mp 78°). [h] Mp 205–207° (lit.[42] mp 203–204°). [i] Mp 245–247° (lit.[43] mp 246–250°).

group with some other functional group in the same molecule.[9] Dimethylformamide appears to serve both as a good solvent and as a catalyst for the oxidative rearrangement.[5]

In our experiments the rearrangement of amides proceeded slowly in pure benzene, chloroform, and methylene chloride, although the reaction in these solvents could be accelerated by addition of alcohols, triethylamine, or pyridine. Beckwith and coworkers have used benzene–aliphatic acid and benzene–alcohol mixtures successfully in preparing acylamines[7] and carbamates,[8] respectively. The former solvent–reactant mixture gave a relatively slow reaction and the latter a relatively fast reaction.[10] We found that the rearrangement also took place slowly in pure acetic acid. This solvent has been used (usually with benzene) in the preparation of acylamines,[7] but again the times given for disappearance of LTA are quite long compared with those in dimethylformamide[5] or benzene–alcohol mixtures.[8]

Although the use of alcohols as solvent–reactants has certain easily demonstrated disadvantages, we have chosen to concentrate our attention on their use for two reasons: (1) the rearrangement reaction is or can be made quite rapid in the alcohols, and (2) the resultant carbamates (3) afford excellent intermediates for clean, high-yield conversion to the corresponding amines or to other useful products. The principal disadvantages in the use of alcohols as solvent–reactants are the preferential oxidation of the alcohol (rather than the amide) in some instances,[5,8] and the difficulty that is sometimes encountered in cleaving primary alkyl carbamates.[12] Thus, for example, LTA reacts with methanol at the reflux temperature at approximately the same rate (or faster) that it reacts with some amides. Acott, Beckwith, and Hassanali[8] have used primary and secondary alcohols successfully with a number of amides and benzene–alcohol mixtures with those for which the alcohol oxidation appeared to be faster than the oxidative rearrangement. They did not obtain satisfactory results with *tert*-butyl alcohol, possibly because their reactions conditions were not optimized. Although simple alkyl carbamates are not readily hydrolyzed in alkaline solutions,[12] acid-catalyzed hydrolysis is generally very satisfactory. Therefore, we have concentrated our attention on alcohols that yield very easily cleaved carbamates, benzyl alcohol and, especially, *tert*-butyl alcohol.

The benzyl carbamates were prepared by oxidative rearrangement of the amide in DMF or acetonitrile solution with LTA, followed by reaction with benzyl alcohol (catalyzed by triethylamine). The carbamates could be hydrolyzed with hydrogen chloride in acetic acid. The results are given in Table I. The reaction was satisfactory with aliphatic amides on a small scale but less so on a large scale, probably because of difficulties associated with the isolation of the product. Benzamide gave unsatisfactory results in this system. Because the concurrent development of the use of *tert*-butyl alcohol appeared to be more promising, the use of benzyl alcohol was not studied further.

The procedure that appears to us to be the simplest and most effective means to date for obtaining amine hydrochlorides from simple amides via LTA oxidation consists of the preparation of the *tert*-butyl carbamates (3, R′ = *t*-Bu) followed by cleavage of the carbamate to the corresponding amine hydrochloride by treatment with anhydrous hydrogen chloride. The *tert*-butyl carbamates were obtained in good to excellent yields by treating the appropriate amide (1) in anhydrous *tert*-butyl alcohol with LTA at the reflux temperature.[13] This procedure has the advantage of giving a stable, solid intermediate product (3) that can be purified by recrystallization or chromatography and then readily and quickly converted to the amine hydrochloride when required.

When cyclohexanecarboxamide was treated with LTA in refluxing *tert*-butyl alcohol for 3 hr, the yield of *tert*-butyl *N*-cyclohexylcarbamate was 64%, but, when phenylacetamide was treated in the same way for only 1 hr, a yield of 83% of *tert*-butyl *N*-benzylcarbamate was obtained. The slower of the two successive reactions, oxidative rearrangement of the amide and addition of the alcohol to the isocyanate, is almost certainly the alcohol–isocyanate reaction in all the examples studied. However, there are a number of catalysts which may be used to accelerate this reaction. Although we have found no study of the catalysis of the *tert*-butyl alcohol–isocyanate reaction, a comparison of the effectiveness of various catalysts for the *n*-butyl alcohol–phenyl isocyanate reaction has been reported.[15,16] The following order of increasing catalyst effectiveness was determined by comparing reaction rates: triethylamine ≪ stannic chloride < di-*n*-butyltin dilaurate.[17] Use of any of these catalysts raised the yield of *tert*-butyl *N*-cyclohexylcarbamate to 80–87%, probably by accelerating the alcohol–isocyanate reaction and minimizing, thereby, the competitive dehydration reaction.[18] The yields of *tert*-butyl carbamates from aromatic carboxamides were not improved by these catalysts, probably because the aryl isocyanates react with *tert*-butyl alcohol almost as rapidly as they are formed. The lower yields of *tert*-butyl carbanilates are attributed to side reactions other than those brought about alcohol dehydration.

The oxidation of aliphatic primary amides with LTA in anhydrous *tert*-butyl alcohol proceeded quite selectively at the amide function except for cinnamamide and *trans*-2-

Table II
Yields of *tert*-Butyl Carbamates and Amine Hydrochlorides Obtained from the Reactions

$$RCONH_2 + LTA + t\text{-}BuOH \xrightarrow{\text{catalyst}} RNHCO_2\text{-}t\text{-}Bu \quad (1)$$

$$RNHCO_2\text{-}t\text{-}Bu + HCl \longrightarrow RNH_3Cl \quad (2)$$

| Registry no. | R | Scale, mol | Catalyst | Reaction time for carbamate formation, hr[n] | Yield,[a] *tert*-butyl carbamate, % | Yield,[a] amine hydrochloride, % |
|---|---|---|---|---|---|---|
| 1503-98-6 | Cyclobutyl | 0.277 | $Et_3N$ | 10.0 | 87.2 | 81.5[n] |
| | Cyclobutyl | 0.006 | *d* | 3.0 | *b* | 81.9 |
| | Cyclobutyl | 0.03 | *m* | | 72.6 | |
| 1122-56-1 | Cyclohexyl | 0.01 | None | 3.0 | 63.5 | |
| | Cyclohexyl | 0.01 | $Et_3N$[i] | 1.3 | 79.9[f] | |
| | Cyclohexyl | 0.01 | $Et_3N$[i] | 1.5 | 79.4[f,h] | |
| | Cyclohexyl | 0.01 | $Et_3N$ | 3.0 | 86.8 | |
| | Cyclohexyl | 0.10 | $Et_3N$ | 9.0 | 77.6 | 72.8 |
| | Cyclohexyl | 0.01 | $SnCl_4$ | 1.0 | 84.5 | |
| | Cyclohexyl | 0.01 | $SnCl_4$ | 1.5 | 83.4[f] | |
| | Cyclohexyl | 0.01 | *d* | 3.0 | 80.4 | |
| | Cyclohexyl | 0.03 | *m* | | 30 | |
| 1503-87-3 | Cyclohexylmethyl | 0.10 | $Et_3N$ | 10.0 | 77.9 | |
| 56760-76-0 | 1,2,2-Trimethyl-3-carbomethoxy-1-cyclopentyl | 0.0086 | $SnCl_4$ | 19.0 | 87.1 | 78.3 |
| | 1,2,2-Trimethyl-3-carbomethoxy-1-cyclopentyl | 2.13 | *d* | 13.0 | *b* | 80.7 |
| 103-81-1 | Benzyl | 0.01 | None | 0.8 | 88.8[f] | |
| | Benzyl | 0.10 | None | 1.0 | 83.5 | |
| | Benzyl | 0.10 | *d* | 3.0 | *b* | 90.0 |
| | Benzyl | 0.10 | $Et_3N$ | 10.0 | 88.7 | 86.1 |
| 102-93-2 | 2-Phenethyl | 0.1 | $Et_3N$ | 10.0 | 83.3 | 74.6 |
| 939-88-8 | *trans*-2-Phenylcyclopropyl | 0.01 | None | 2.5 | 12.9[l] | |
| 98-92-0 | 3-Pyridyl | 0.01 | None | 1.5 | 78.9[e] | |
| | 3-Pyridyl | 0.01 | None | 2.0 | *e* | 73.0[c] |
| | 3-Pyridyl | 0.01 | $Et_3N$ | 7.0 | 61.7 | |
| 55-21-0 | Phenyl | 0.01 | None | 0.5 | 76.2 | |
| | Phenyl | 0.1 | None | 1.0 | *e* | 76.8 |
| | Phenyl | 0.1 | None | 1.5 | 75.2[g] | |
| | Phenyl | 0.3 | None | 2.0 | *e* | 82.7[k] |
| | Phenyl | 0.05 | None | 2.5 | 89.1[j] | |
| | Phenyl | 0.01 | $Et_3N$ | 10.5 | 68.6 | |
| | Phenyl | 0.1 | *d* | 3.0 | *b* | 75.5 |
| | Phenyl | 0.03 | *m* | | 75.5 | 75.5 |
| 619-56-7 | 4-Chlorophenyl | 0.01 | None | 1.0 | 70.6 | |
| | 4-Chlorophenyl | 0.01 | $SnCl_4$ | 3.0 | 68.3 | |
| | 4-Chlorophenyl | 0.03 | *d* | 10.0 | *b* | 71.5 |
| | 4-Chlorophenyl | 0.03 | *m* | | 70.5 | |
| 619-80-7 | 4-Nitrophenyl | 0.01 | None | 0.5 | 73.1 | |
| | 4-Nitrophenyl | 0.01 | None | 1.0 | 78.5 | |
| | 4-Nitrophenyl | 0.01 | None | 3.0 | 78.9 | |
| | 4-Nitrophenyl | 0.01 | $SnCl_4$ | 24.0 | 77.7 | 75.4[c] |
| | 4-Nitrophenyl | 0.03 | *m* | | 35.0 | |
| 2008-58-4 | 2,6-Dichlorophenyl | 0.03 | None | 1.0 | *b* | 74.8[c] |
| | 2,6-Dichlorophenyl | 0.01 | $SnCl_4$ | 10.0 | 81.6 | |
| 4380-68-1 | 2,4,6-Trimethylphenyl | 0.01 | $SnCl_4$ | 9.0 | 78.3 | |

[a] Yields are based on the amide. [b] The carbamate was not isolated. [c] "Free" amine. [d] Di-*n*-butyltin dilaurate. [e] The carbamate was purified with activated alumina. [f] The carbamate was precipitated by adding *tert*-butyl alcohol solution to ice water. [g] The carbamate was precipitated by adding acetone solution to ice water. [h] The LTA was added as a 10% acetic acid paste. [i] Added after 15 min at reflux. [j] A fivefold excess of amide was used; yield based on LTA. [k] A threefold excess of amide was used; yield based on LTA. [l] 37% of starting amide recovered. [m] $Et_3N$ used as oxidative rearrangement catalyst (see Experimental Section). [n] Optimum reaction times were not determined; some times are greater than necessary to obtain the maximum yield.

phenylcyclopropanecarboxamide, which suffered some attack at the double bond and three-ring, respectively. Apparently isolated olefinic bonds are not oxidized under similar conditions.[8] The yields of *tert*-butyl carbamate were usually in the range 80–90%. Aromatic amides also gave good yields (60–80%) of *tert*-butyl carbanilates despite the formation of colored by-products, the nature of which was not determined. Our results are summarized in Table II.

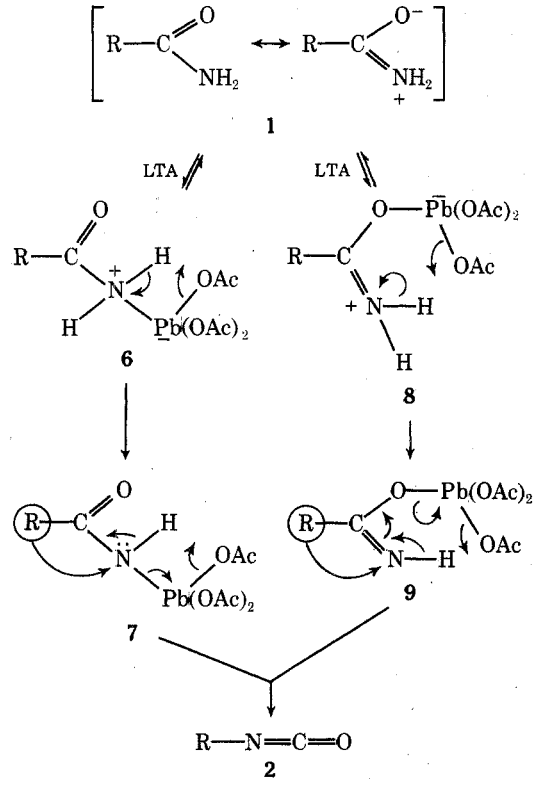
Although Acott, Beckwith, and Hassanali[8] obtained at best a 37% yield of ethyl *N*-pyridylcarbamate from the oxidative rearrangement of nicotinamide in ethyl alcohol or ethyl alcohol–benzene, we experienced no difficulty in preparing the *tert*-butyl carbamate in yields up to 79%.

*N*-Carbo-*tert*-butoxy protective groups[19] have been removed by treatment of the derivative, usually a peptide, with anhydrous hydrogen chloride in ether,[5] diethyl phos-

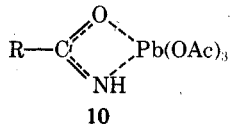
phite,[20] benzene,[20] or nitromethane,[21] as well as with other acids.[22] Although most of the *tert*-butyl carbamates lost the carbo-*tert*-butoxy group when treated with anhydrous hydrogen chloride in ether, we found that cleavage proceeded most satisfactorily in anhydrous ethanol to give high yields of the corresponding amine hydrochloride (Table II).[23]

Incomplete kinetic studies still in progress[25] indicate that in 0.01 M solutions in 1:1 methylene chloride–*tert*-butyl alcohol at 22° the rate of reaction (as measured by disappearance of LTA) is accelerated by the addition of pyridine as a catalyst by roughly a factor of 2–3 at 50% completion of the reaction. However, variations in the rate of this same order of magnitude may result from the use of different batches of LTA (or of *tert*-butyl alcohol in different stages of dryness). It is not known at this time whether pyridine[8,26] (and other bases such as triethylamine[5] and DMF[5]) serves as a catalyst or as a scavenger of acetic acid. Acetic acid does appear to depress the rate of this reaction as it does for other LTA oxidations of organic nitrogen compounds.[27,28] Fortunately, at the reflux temperature of *tert*-butyl alcohol these rate variations are not particularly important, and catalysts for the oxidative rearrangement are not required in practical applications of the method, provided that the amides and solvents used are reasonably dry and the LTA reasonably free from excess acetic acid.

The detailed mechanism of the oxidative rearrangement of amides cannot be specified on the basis of available evidence, although simplified mechanisms have been suggested.[5,8] Two reasonable alternatives consistent with available evidence are summarized in sequences **1** → **6** → **7** → **2** and **1** → **8** → **9** → **2**. These two alternatives could be considered



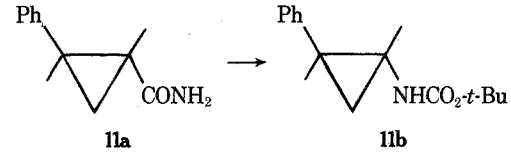

extreme forms of a third alternative in which the lead atom is bonded to both oxygen and nitrogen in the RCONH-$Pb(OAc)_3$ complex (**10**).




In view of the proposed[29] eight-coordinate, distorted dodecahedral structure for LTA in the crystal, **10** would be a reasonable structure. At the time of rearrangement the structure might be distorted toward either **7** or **9**, especially under the influence of nucleophilic solvents (alcohols) or presumed catalysts (pyridine, DMF).

It is also possible that a discrete nitrene intermediate may result from the decomposition of **7**, **9**, or **10**; however, attempts to demonstrate the existence of the nitrene by trapping experiments on the presumed nitrene obtained from the oxidation of urethane ($EtO_2CNH_2$) with LTA were unsuccessful. Although carboethoxynitrene (from the azide) has been trapped with cyclohexene,[30] cyclohexane,[30] and benzene,[31,32] we have obtained none of the expected cycloaddition or insertion products from the reaction of urethane with LTA in the presence of these hydrocarbons. Acott, Beckwith, and Hassanali[6] reported a similar failure with cyclohexane and urethane. Unfortunately, these negative results provide less than compelling evidence of the absence of an intermediate nitrene, for in our experiments urethane was not oxidized by LTA at an appreciable rate and ultimately the oxidant was consumed in other reactions, presumably with the solvents present. However, attempts to trap the presumed nitrene intermediate in the oxidative rearrangement of cyclohexanecarboxamide with cyclohexane or benzamide with dimethyl sulfoxide[33] also failed. In the latter solvent the principal product was the *sym*-urea.

On the reasonable assumption that the oxidative rearrangement of amides, like the Hofmann[34] and Curtius[35] reactions, proceeds with retention of configuration, Acott, Beckwith, and Hassanali[8] assigned the 17 $\beta$ configuration to the methyl carbamate obtained from 3$\beta$-acetoxyandrost-5-ene-17$\beta$-carboxamide. We have established that the reaction does indeed proceed with retention of configuration by the sequence shown in Chart I and by the conversion of *trans*-2-phenylcyclopropanecarboxamide (**11a**) into *tert*-butyl *N*-(*trans*-2-phenylcyclopropyl)carbamate (**11b**) albeit in low yield. After this work had been completed Si-



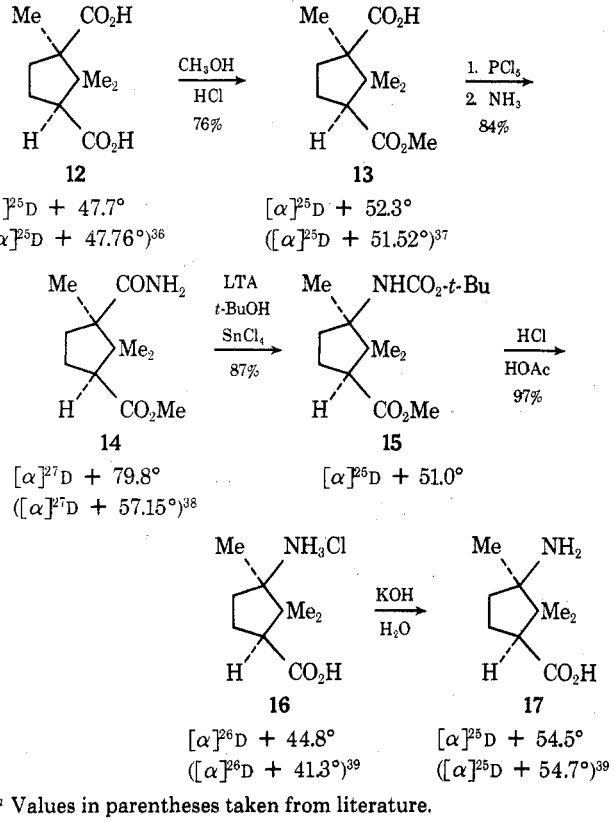

mons[26] reported the apparently stereospecific conversion of *exo*-3-carbamyl-*exo*-2-norborneol to norbornyl[2,3-*d*]-2-oxazolidinone.

From the foregoing discussion it is clear that the oxidative rearrangement of amides using LTA in *tert*-butyl alcohol affords a useful alternative to the classical Hofmann, Schmidt, Curtius, and Lossen rearrangements. The question then arises as to whether or not some other two-electron oxidant, such as iodosobenzene diacetate,[2] might give even better results. A number of other oxidants will be compared in a subsequent communication; however, for most (but not all) purposes LTA appears to be the reagent of choice based on cost, availability, ease of use, and overall results.

## Experimental Section

All melting points are uncorrected. The NMR spectra were observed with a Varian A-60 spectrophotometer. Infrared spectra were observed with Perkin-Elmer Models 137 and 237 spectrometers. *tert*-Butyl alcohol was dried by refluxing over calcium hydride (approximately 10 g/l.) for 4–10 hr, followed by distillation. *N,N*-Dimethylformamide (DMF) was dried by refluxing over calcium oxide (approximately 50 g/l.), followed by distillation. Tri-

**Chart I**
**Stereochemistry of Oxidative Rearrangement**[a]




[a] Values in parentheses taken from literature.

ethylamine was dried by refluxing over barium oxide, followed by distillation and storage over potassium hydroxide. Acetonitrile (practical grade) and benzyl alcohol were dried by refluxing over phosphorus pentoxide for several hours, followed by distillation. Di-*n*-butyltin dilaurate was purchased from K & K Laboratories, Inc. Lead tetraacetate (LTA) (Arapahoe Chemical Co.) was stored in a desiccator over sulfuric acid (which removes most of the acetic acid stabilizer). The reagent was added as a dry powder in most reactions and directly from the reagent bottle (added in 10% excess to allow for the acetic acid present) in a few instances.

***tert*-Butyl Carbamates. General Procedures.** Most of the reactions were carried out using 0.1 or 0.01 molar equiv of amide and LTA and no catalyst *for the oxidation step*. The 0.1-mol reactions were carried out by warming 250–500 ml of anhydrous *tert*-butyl alcohol with the appropriate amide until dissolution was complete. The reaction flask was equipped with a mechanical stirrer and a reflux condenser protected with a drying tube. The 0.01-mol reactions were run in 50 ml of anhydrous *tert*-butyl alcohol. The reaction flask was equipped with a magnetic stirrer and reflux condenser, protected with a drying tube. When stannic chloride or di-*n*-butyltin dilaurate was used as a catalyst for the isocyanate–alcohol reaction, the catalyst was added via a syringe prior to LTA addition (for example, see the preparation of *tert*-butyl *N*-cyclohexylcarbamate). When triethylamine was used as the catalyst, it was added via a pipette 0.25–2 hr after the addition of LTA (for example, see the preparation of *tert*-butyl *N*-benzylcarbamate). In all reactions, the LTA was weighed as rapidly as possible and added to the *tert*-butyl alcohol–amide solution in one lot. The reaction temperature was then raised to reflux as rapidly as possible.

After the reaction, the *tert*-butyl alcohol was removed on a bench evaporator. The residue was extracted with ether, which was then filtered through Celite. The lead diacetate remaining in the reaction flask was agitated and washed with several portions of ether to remove any entrained carbamate.

In the early experiments, the ethereal filtrate was reduced in volume and washed with 300 ml of 10% potassium carbamate to remove the acetic acid. This was found later to be unnecessary. The ethereal filtrate was evaporated and the carbamate was recrystallized from Skellysolve B (bp 60–69°). If the carbamate was not to be purified, the ethereal filtrate was evaporated, the residue was dissolved in anhydrous ethanol, and the carbamate was converted to the amine hydrochloride as described below. The carbamates were isolated whenever stannic chloride or triethylamine was used as a catalyst, since recovery of the amine hydrochloride was otherwise difficult. Purification of *N*-aryl carbamates was effected by column chromatography in a few instances.

In several small-scale (1–2 g) experiments the *N*-alkyl carbamates were recovered by pouring the cooled mixture into ice water. A modification of the method was found to be effective in recovering *tert*-butyl carbanilates without purification using a column of alumina. After the reaction of the benzamide and LTA was complete, the *tert*-butyl alcohol was removed, the residue was extracted with acetone, and the extract was filtered to remove lead diacetate. The volume of the filtrate was reduced and the concentrated acetone solution was poured into water. The carbanilate which precipitated was considerably cleaner than that obtained when the reaction mixture (*tert*-butyl alcohol as solvent) was poured into water.

The foregoing general procedures are illustrated below with three typical amides: cyclohexanecarboxamide, phenylacetamide, and benzamide. Other examples are summarized in Table II. Properties of the carbamates are given in Table III.

In several experiments triethylamine was used as a catalyst for both the oxidative rearrangement and the alcohol–isocyanate reaction. This procedure would appear to be useful when it is necessary to use the mildest conditions possible. To a solution (or suspension) of 0.03 mol of the amide and 0.03 mol of dry, powdered LTA in 70 ml of dry *tert*-butyl alcohol warmed with stirring to 50° on the steam bath (thermometer in the reaction mixture), 10 ml of triethylamine was added very slowly (ca. one drop every 3–4 sec) with no additional heating. The initial reddish color of the reaction solution faded to colorless (or pale pink) within a few minutes. At this point, the conversion to the isocyanate was essentially complete and the remainder of the triethylamine could be added more rapidly. The reaction mixture was allowed to stand up to several days to permit the isocyanate to react with the *tert*-butyl alcohol. The disappearance of the isocyanate infrared peak at ca. 2260 $cm^{-1}$ could be used as a qualitative test for completeness of conversion. The reaction mixture was evaporated at room temperature to a volume of ca. 30 ml, and this solution was poured into a mixture of crushed ice and 15 ml of acetic acid [to neutralize triethylamine and prevent precipitation of lead(II) salts]. After a few minutes the white or tan urethane was collected by filtration, air dried, and recrystallized from petroleum ether. Examples of carbamates made by this procedure are cited in Table II.

***tert*-Butyl *N*-Cyclohexylcarbamate.** A mixture composed of 1.27 g (0.01 mol) of cyclohexanecarboxamide, 50 ml of anhydrous *tert*-butyl alcohol, and 0.2 ml of stannic chloride, in a 100-ml flask fitted with a magnetic stirrer and a reflux condenser with a drying tube, was stirred at 50° until dissolution of the amide was complete. The addition of 4.43 g (0.01 mol) of LTA was carried out as rapidly as possible, after which the reaction mixture was refluxed for 1 hr. The *tert*-butyl alcohol was removed, the residue was extracted with ether, and the ethereal extract was filtered through Celite, reduced in volume to 15 ml, and diluted with 150 ml of Skellysolve B, whereupon the *tert*-butyl *N*-cyclohexylcarbamate precipitated, yield 1.68 g (84.4%), mp 76–78°.

In another experiment using the same quantities of reagents, 0.1 ml of stannic chloride, and a reflux time of 1.5 hr, the cooled reaction mixture was poured directly into ice water. The carbamate was collected by filtration and recrystallized from Skellysolve B, yield 1.66 g (83.4%), mp 76–78°.

In another experiment 4.87 g (0.01 mol plus 10%) of LTA taken directly from the reagent bottle was added to 1.27 g (0.01 mol) of cyclohexanecarboxamide in 60 ml of anhydrous *tert*-butyl alcohol. After the mixture had been heated under reflux for 15 min, 2.0 ml of triethylamine was added and the mixture was heated under reflux for an additional 1.5 hr. The cooled reaction mixture was poured into ice water, and the carbamate was collected and recrystallized from Skellysolve B, yield 1.58 g (79.4%), mp 76–78°.

***tert*-Butyl *N*-Benzylcarbamate.** A mixture of 1.35 g (0.01 mol) of phenylacetamide and 4.43 g (0.01 mol) of LTA in 25 ml of *tert*-butyl alcohol (no added catalyst) was heated rapidly to reflux and held there for 1 hr. After cooling, the reaction mixture was poured into 250 ml of ice water. The carbamate was recovered by filtration and recrystallized from Skellysolve B, yield 1.84 g (88%), mp 53–54°.

***tert*-Butyl carbanilate** was prepared by treating 2.42 g (0.02 mol) of benzamide with 8.86 g (0.02 mol) of LTA in 50 ml of anhydrous *tert*-butyl alcohol. The reaction mixture was refluxed for 1.5 hr, the alcohol was removed, the residue was extracted with acetone, and the resultant mixture was filtered through Celite to re-

Table III
Properties of Carbamates, $RNHCO_2$-*t*-Bu

| Registry no. | R | Mp, °C | Infrared, $cm^{-1}$ [a] ν (NH) | ν (C=O) | Anal., % C Calcd (found) | H Calcd (found) | N Calcd (found) | NMR ($CCl_4$), δ, ppm δ (*t*-Bu)[f] | δ (NH)[g] | δ(R) |
|---|---|---|---|---|---|---|---|---|---|---|
| 56700-66-4 | c-$C_4H_7$ | 79–80 | 3450 | 1710 | 63.13 (63.00) | 10.00 (10.10) | 8.18 (8.20) | 1.42 | 4.80 | 1.65–2.30[h] (6 H m, ring $CH_2$'s), 4.10 (1 H m, CHN) |
| 3712-40-1 | c-$C_6H_{11}$ | 77.5–79 | 3450 | 1705 | 66.29 (66.40) | 10.62 (10.43) | 7.03 (6.96) | 1.40 | 5.40 | 0.96–2.10[h] (10 H m, ring $CH_2$'s), 4.02 (1 H m, CHN) |
| 56700-67-5 | c-$C_6H_{11}CH_2$ | 50–51 | 3455 | 1705 | 67.56 (67.52) | 10.87 (10.81) | 6.57 (6.69) | | | |
| 42116-44-9 | $C_6H_5CH_2$ | 53–54[b] | 3455 | 1710 | | | | 1.46 | 4.78 | 4.24 (2 H d, $CH_2$), 7.21 (5 H s, $C_6H_5$) |
| 38427-90-6 | $C_6H_5CH_2CH_2$ | 55–56 | 3455 | 1710 | 70.55 (70.61) | 8.65 (8.66) | 6.33 (6.22) | | 4.50 | 2.71 (2 H t, *J* = 13 Hz, $CH_2$) 3.21 (2 H t, *J* = 13 Hz, $CH_2$), 7.11 (5 H s, $C_6H_5$) |
| 3422-01-3 | $C_6H_5$ | 134–135.5[c] | 3460 | 1715 | | | | 1.52 | 6.60 | 7.32 (5 H t, $C_6H_5$) |
| 18437-66-6 | 4-$ClC_6H_4$ [d] | 105–106 | 3435 | 1730 | 58.02 (57.91) | 6.20 (6.16) | 6.16 (6.35) | 1.49 | 6.58 | 7.2 (4 H s, $C_6H_4$) |
| 18437-63-3 | 4-$NO_2C_6H_4$ | 110.5–111.5 | 3435 | 1735 | 55.45 (55.66) | 5.92 (5.92) | 11.76 (11.69) | 1.57 | 7.02 | 7.64 (2 H d, *J* = 9 Hz, *o*-CH), 8.25 (2 H d, *J* = 9 Hz, *m*-CH) |
| 56700-68-6 | 2,6-$Cl_2C_6H_3$ [e] | 96–97 | 3430 | 1735 | 50.39 (50.61) | 5.00 (4.97) | 5.34 (5.53) | 1.50 | 6.12 | 7.21 (3 H m, $C_6H_3$) |
| 56700-69-7 | 2,4,6-$Me_3C_6H_2$ | 70–71 | 3440 | 1720 | 71.45 (71.32) | 9.00 (9.01) | 5.95 (6.02) | 1.41 | 6.17 | 2.11 (6 H s, 2,6-$Me_2$), 2.21 (3 H s, 4-Me), 6.69 (2 H s, $C_6H_2$) |
| 56700-70-0 | 3-$C_5H_4N$ | 117–118 | 3440 | 1710 | 61.83 (62.11) | 7.27 (7.33) | 14.42 (14.41) | | | |

[a] In $CHCl_3$. [b] Lit.[40] mp 57–58°. [c] Lit.[41] mp 136.3–136.5°. [d] Calcd: Cl, 15.57. Found: Cl, 15.50. [e] Calcd: Cl, 27.05. Found: Cl, 26.90. [f] 9 H s. [g] 1 H s, broad. [h] At 60 MHz.

move the lead diacetate. After removal of the acetone, the carbanilate was dissolved in ether, and the ethereal solution was reduced to 75 ml and put on a 2.5 × 50 cm column of activated alumina (80 g) in Skellysolve B (bp 60–69°). After elution with 300 ml of Skellysolve B, followed by 750 ml of ether, 2.98 g (77.3%) of the carbanilate was recovered, mp 134–135.5°. Further elution with 150 ml of 10% methanol–ether yielded 0.294 g (12.1%) of benzamide: mp 127–128.5°; ir ($CHCl_3$) 3510, 3400, 1680, 1580, 1475 $cm^{-1}$. No other compounds were characterized.

For ordinary preparative purposes the above procedure could be simplified by passing the ethereal solution (without concentration) through 100 g of activated alumina in a Büchner funnel.

In another experiment *tert*-butyl carbanilate was prepared by adding 44.34 g (0.1 mol) of LTA to 12.11 g (0.1 mol) of benzamide in *tert*-butyl alcohol. The reaction mixture was refluxed for 1.5 hr, the alcohol was removed, the residue was extracted with acetone, and the extract was filtered. The volume of filtrate was reduced until the carbanilate was just kept in solution. The solution was poured into 750 ml of ice water. The carbanilate was recrystallized from Skellysolve B, yield 14.52 g (75.2%), mp 134–136°.

**Conversion of *tert*-Butyl Carbamates to Amine Hydrochlorides. General Procedure.** The *tert*-butyl carbamate was dissolved in the minimum volume of anhydrous ethanol (approximately 35 ml for 0.01-mol reactions, and 150 ml for 0.10-mol reactions). Anhydrous hydrogen chloride was passed into the solution for 1.5–2 hr. The reaction flask was fitted with a magnetic stirrer and a reflux condenser, protected with a drying tube. The volume of ethanol was reduced, and the amine salt was brought out by the addition of ether and recovered by filtration. Subsequent fractions were recovered by removing the ether, reducing the volume of ethanol, and adding more ether. If methanol was substituted for ethanol, two layers sometimes formed at this stage, complicating recovery. If necessary, the amine salts were recrystallized from methanol or ethanol. A large quantity of decolorizing carbon was used to purify the aromatic amine hydrochlorides (2–3 g/10 g of amine hydrochloride) when the carbanilate had not been purified prior to cleavage. This procedure was used in most of the examples in Table II, and was more satisfactory than the following for unpurified carbamates.

Alternatively, dry hydrogen chloride could be passed into a solution of *tert*-butyl carbamate in anhydrous ether (ca. 150 ml/g of carbamate) for 10–15 min. Usually the solution became filled with a fine, white precipitate, which was collected by filtration and dried in over sulfuric acid under mild vacuum, yields 79–90%.

Purification of solid aromatic amines was best carried out by neutralizing the crude hydrochloride with aqueous potassium hydroxide and recrystallizing the amine from Skellysolve B (bp 60–69°).

The amine hydrochlorides obtained gave the following melting points: cyclobutyl, 183–184° (Anal. Calcd for $C_4H_{10}ClN$: C, 44.66; H, 9.37; Cl, 32.95; N, 13.02. Found: C, 44.54, H, 9.35; Cl, 32.68; N, 13.13); cyclohexyl, 205–207° (lit.[42] mp 203–204°); benzyl, 247–248° (lit.[43] mp 246–250°); 2-phenethyl, 218–219° (lit.[44] mp 217°); aniline, 196–198° (lit.[45] mp 198°). The free amines gave the following melting points: *p*-chloroaniline, mp 69–71° (lit.[46] mp 70–71°); *p*-nitroaniline, mp 146–148° (lit.[47] mp 145°); 2,6-dichloroaniline, mp 37–37.5° (lit.[48] mp 39°).

***cis*-3-Carbomethoxy-1,2,2-trimethylcyclopentanecarboxylic acid (13).** *d*-Camphoric acid (12) (Aldrich) was recrystallized[49] from ether: mp 187–188°; $[\alpha]^{20}D$ +47.7° (*l* 2, *c* 0.04, etha-

Table IV
Preparation of Ureas, RNHCONH-*t*-Bu

| Registry no. | R | Yield, % | Mp, °C | Lit. mp, °C | Infrared, $cm^{-1}$ [a] $\nu$(NH) | $\nu$(C=O) |
|---|---|---|---|---|---|---|
| 5336-24-3 | *tert*-Butyl | 96 | 240 ± 2[b] | 242–243[c] | 3440 | 1680 |
| 2387-23-7 | Cyclohexyl | 88 | 226 ± 2[b] | 227[d] | 3440 | 1668 |
| 5472-16-2 | Cyclohexylmethyl | 74 | 150–151[e] | | 3440 | 1670 |
| 56700-71-1 | 2-Methyl-2-phenylpropyl | 97 | 192–193[f] | | 3435 | 1665 |

[a] In $CHCl_3$ solution. [b] On Koeffler hot bench calibrated to accuracy shown. [c] R. N. Lacy, *J. Chem. Soc.*, 1633 (1960). [d] B. Brauner, *Ber.*, **12**, 1875 (1879). [e] Anal. Calcd for $C_{12}H_{24}N_2O$: C, 67.89; H, 11.39; N, 13.20. Found: C, 67.57; H, 11.56; N, 12.91. [f] Anal. Calcd for $C_{15}H_{24}N_2O$: C, 72.53; H, 9.68; N, 11.28. Found: C, 72.27, H, 9.75; N, 11.61.

nol) [lit.[49] mp 187°; lit.[36] $[\alpha]^{20}D$ +47.76° (*l* 2, *c* 0.93, ethanol)]. Anhydrous hydrogen chloride was passed into a stirred solution of 20.02 g (0.100 mol) of **12** in 250 ml of methanol for 2 hr. The methanol was evaporated and the residue was taken up in 5% aqueous sodium bicarbonate. The sodium bicarbonate solution was added until effervescence ceased, then 100 ml of 5% aqueous sodium hydroxide was added. The diester was removed by extraction with ether and discarded. The aqueous layer was acidified with 10% hydrochloric acid and extracted with ether. The ethereal extract was dried ($MgSO_4$) and evaporated, and the residue was recrystallized from Skellysolve B (bp 60–69°): yield 16.2 (76%); mp 77.0–77.5°; $[\alpha]^{25}D$ +52.3° (*l* 2, *c* 0.04, ethanol) [lit.[37] mp 75–76°; $[\alpha]^{25}D$ +51.52° (*l*, *c* not given)]; ir ($CHCl_3$) 3490, 1720 $cm^{-1}$ (acid C=O and ester C=O, broad peak).

***cis*-3-Carbamoyl-2,2,3-trimethylcyclopentanecarboxylate (14).** To 10.5 g (0.049 mol) of **13** susupended in 60 ml of petroleum ether was added 12 g (0.057 mol) of phosphorus pentachloride, and the mixture was stirred for 1 hr at room temperature. To 250 ml of anhydrous acetonitrile, which had been saturated with anhydrous ammonia at −30°, was added dropwise the mixture of acid chloride and phosphoryl chloride in petroleum ether. The temperature was kept at −35° until addition was complete. The mixture was stirred for 10 min following addition of the acid chloride, the acetonitrile was removed on a bench evaporator, and the residue was taken up in hot ethyl acetate. The solution was filtered through Celite and evaporated. The amide was recrystallized from ethyl acetate: yield 8.83 g (84%); mp 141–142°; $[\alpha]^{27}D$ +79.8° (*l* 2, *c* 0.025, ethanol) (lit.[38] mp 139°, $[\alpha]^{27}D$ +57.15°); ir ($CHCl_3$) 3540, 3410, 2950 (broad), 1725, 1660, 1580 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.70 (3 H s, $CH_3O$), 2.83 (1 H m), 1.5–2.5 (4 H m), 1.30 (3 H s), 1.21 (3 H s), 0.86 (3 H s).

***tert*-Butyl *N*-(*cis*-1,2,2-trimethyl-3-carbomethoxy-1-cyclopentyl)carbamate (15)** was prepared from 1.85 g (0.0086 mol) of **14**, using stannic chloride (0.1 ml) as a catalyst for the alcohol–isocyanate reaction. The reaction mixture was heated under reflux for 19 hr. After removal of the *tert*-butyl alcohol, the residue was taken up in ether and washed with 100 ml of 10% potassium carbonate. The carbamate was recrystallized from Skellysolve B (bp 60–69°); yield 2.5 g (87.1%); mp 78.8–79.2°; $[\alpha]^{25}D$ +51.0° (*l* 2, *c* 0.029, ethanol); ir ($CHCl_3$) 3450, 1715 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 3.68 (3 H s, $CH_3O$), 2.63 ( 1 H m), 2.0 (4 H m), 1.41 (9 H s), 1.33 (3 H s), 1.11 (3 H s), 0.85 (3 H s). Anal. Calcd for $C_{15}H_{27}O_4N$: C, 63.13; H, 9.54, N, 4.91. Found, 63.11; H, 9.46; N, 4.99.

***cis*-3-Amino-2,2,3-trimethylcyclopentanecarboxylic Acid Hydrochloride (16).** A mixture of 2.00 g (0.0070 mol) of **15** and a solution of 10 ml of hydrochloric acid (37%) and 15 ml of glacial acetic acid was heated under reflux for 11 hr, after which the acetic acid, methanol, and water were removed. The amine salt was recrystallized from ethanol and brought out by adding ether: yield 1.41 g (97%); mp 254–256°; $[\alpha]^{26}D$ +44.8° (*l* 2, *c* 0.028, water) [lit.[39] mp 261–222°; $[\alpha]^{26}D$ +41.3° (*c* 0.1, water)]; NMR ($D_2O$) $\delta$ 4.80 (5 H s), 3.00 (1 H m), 2.15 (4 H d), 1.40 (3 H s), 1.20 (3 H s), 1.09 (3 H s).

***cis*-3-Amino-2,2,3-trimethylcyclopentanecarboxylic Acid (17).** To 20 ml of 3% aqueous potassium hydroxide was added 1.57 g (0.0075 mol) of **16**. The water was carefully evaporated until the amino acid precipitated. The amino acid was recovered by filtration and washed with water: yield 0.973 g (97%); $[\alpha]^{25}D$ +54.5° (*l* 2, *c* 0.0202, water) [lit.[39] $[\alpha]^{25}D$ +54.7° (*c* 0.05, water)].

***tert*-Butyl *N*-(*trans*-2-phenylcyclopropyl)carbamate** was prepared by treating *trans*-2-phenylcyclopropanecarboxamide (1.61 g, 0.01 mol) with 4.43 g (0.01 mol) of LTA in *tert*-butyl alcohol. After removal of the alcohol and filtration of the ethereal extract, the ethereal filtrate was evaporated and the residue was taken up in hot Skellysolve B (bp 60–69°). The solution was cooled, and the crystalline mixture, which was removed by filtration, was recrystallized from Skellysolve B (bp 60–69°). The solid which was insoluble in Skellysolve B was identified as *trans*-2-phenylcyclopropanecarboxamide (0.594 g, 36.9%): mp 189–191°; ir ($CHCl_3$) 3515, 3405, 1675, 1585 $cm^{-1}$. Only 0.30 g (12.9%) of the carbamate was recovered: mp 80–81° (lit.[50] mp 80–82°); ir ($CHCl_3$) 3440, 2915, 1715, 1590, 1355 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 7.2 (5 H s), 4.96 (1 H s), 2.69 (1 H m), 2.05 (1 H m), 1.46 (9 H s), 1.13 (2 H m).

**3-Aminopyridine.** The oxidation of 12.2 g (0.100 mol) of nicotinamide with 44.39 (0.100 mol) of LTA in 500 ml of *tert*-butyl alcohol was carried out with no catalyst present. The mixture was heated under reflux for 2 hr, and the *tert*-butyl alcohol was removed. To the gummy, red residue was added 400 ml of ether in 100-ml portions, each of which was filtered through Celite to remove the lead diacetate. The combined ethereal filtrates were reduced to a volume of 50 ml and placed on a 4.5 × 25 cm column of 250 g of activated alumina in ether. The column was eluted with 2.5 l. of ether, from which the carbamate was recovered and dissolved in 500 ml of methanol. Anhydrous hydrogen chloride was passed into the solution for 2 hr, after which the mixture was stirred overnight.

The volume of methanol was reduced to 50 ml, 200 ml of ether was added, and the amine dihydrochloride was collected by filtration. The dihydrochloride was neutralized with 10 g of potassium hydroxide in 100 ml of water, and the solution was saturated with sodium chloride and extracted with 250 ml of chloroform. The chloroform extracts were dried ($MgSO_4$), filtered, and reduced to a volume of 75 ml. Addition of 75–100 ml of petroleum ether (bp 30–60°) and cooling yielded 6.87 g (73.1%) of 3-aminopyridine: mp 60–61.5° (lit.[51] mp 64°); ir ($CHCl_3$) 3370, 3380, 1620, 1580 $cm^{-1}$; NMR ($CDCl_3$) $\delta$ 8.1 (2 H m), 7.0 (2 H m), 3.85 (2 H s).

***tert*-Butyl Isocyanate.** To a solution of 10.0 g (0.100 mol) of *tert*-butyl carboxamide in 100 ml of dry DMF was added 44.3 g (0.100 mol) of lead tetraacetate. The mixture was distilled through a 2-ft, heated Vigreux column (with magnetic stirring of the reaction mixture in the still pot). The fraction boiling at 83–85° (lit.[54] bp 85.5°) was collected, yield 4.4 g (44%). When the oil bath temperature reached 150° the distillation was stopped. The infrared spectrum ($CCl_4$) of the distillate showed the expected peaks at 2980 [$\nu$(CH)], 2260 [$\nu$(N=C=O)], 1540 (*t*-Bu), and 1365 $cm^{-1}$ (*t*-Bu) and no amide $\nu$(C=O) absorption. An infrared spectrum of the still pot residue showed an intense band at 2260 $cm^{-1}$, indicating that not all of the isocyanate was recovered from the reaction mixture.

**Alkyl *tert*-Butyl Ureas. General Procedure.** A solution of 0.02 mol of the amide in 100 ml of dry DMF was stirred while 8.86 g (0.02 mol) of dry LTA was added. The addition caused the solution to become light red. As the reaction progressed to completion the temperature rose to ca. 60° and the color faded. When the solution became colorless, 7 ml of *tert*-butylamine was added. Although the product could be isolated by removing the DMF under reduced pressure, usually the solution was poured over ca. 100 g of crushed ice and water, and the urea was collected and washed thoroughly with water The yields and properties of the ureas are summarized in Table IV.

**Benzyl Carbamates. General Procedure.** A solution of 0.01 mol of the amide in 20–30 ml of dry DMF or dry acetonitrile was stirred while 4.43 g (0.01 mol) of LTA was added. The reaction mixture was kept at the initial temperature (Table I) for 20–90 min, then heated at the final temperature overnight (10–12 hr). The reaction mixture was cooled and poured into 500 ml of ice water. The carbamate was collected and recrystallized from Skellysolve B. For reaction at the 0.1-mol scale, the volume of the reaction mixture was reduced before it was poured into 1 l. of water.

**Hydrolysis of Benzyl Carbamates.** The benzyl carbamates, prepared as described, were hydrolyzed by refluxing a solution of

the purified carbamates in a mixture of glacial acetic acid and concentrated (37%) hydrochloric acid for 2–4 hr. After removal of the solvent mixture by distillation, the amine salt was taken up in methanol and precipitated by adding ether. The results for these preparations are summarized in Table I.

**Registry No.**—**1** (R = $C_6H_5CMeEt$), 828-40-0; **4** (R = cyclobutyl), 6291-01-6; **4** (R = cyclohexyl), 4998-76-9; **4** (R = 1,2,2-trimethyl-3-carbomethoxy-1-cyclopentyl, 56700-72-2; **4** (R = benzyl), 3287-99-8; **4** (R = 2-phenethyl), 156-28-5; **4** (R = 3-pyridyl), 462-08-8; **4** (R = phenyl), 142-04-1; **4** (R = 4-chlorophenyl), 20265-96-7; **4** (R = 4-nitrophenyl), 100-01-6; **4** (R = 2,6-dichlorophenyl), 608-31-1; **12**, 124-83-4; **13**, 29607-02-1; **14**, 56760-77-1; **15**, 56760-78-2; **16**, 56700-74-4; **17**, 56700-79-3; *tert*-butyl 1,2,2-trimethyl-3-carboethoxy-1-cyclopentylcarbamate, 56700-73-3; *tert*-butyl *trans*-2-phenylcyclopropylcarbamate, 56700-75-5; lead tetraacetate, 546-67-8; benzyl alcohol, 100-51-6; *tert*-butyl alcohol, 75-65-0; hydrochloric acid, 7647-01-0; *tert*-butylamine, 75-64-9.

**Supplementary Material Available.** The experimental procedures used to prepare the amides **1** will appear following these pages in the microfilm edition of this volume of the journal. Photocopies of the supplementary material from this paper only or microfiche (105 × 148 mm, 24× reduction, negatives) containing all of the supplementary material for the papers in this issue may be obtained from the Business Office, Books and Journals Division, American Chemical Society, 1155 16th St., N.W., Washington, D.C. 20036. Remit check or money order for $4.00 for photocopy or $2.50 for microfiche, referring to code number JOC-75-3554.

## References and Notes


(1) (a) Part XVII: H. E. Baumgarten, D. F. McLaen, and H. W. Taylor, Jr., *J. Org. Chem.*, **36**, 3668 (1971). (b) This work was supported in part by Public Health Service Grant CA-3090 from the National Cancer Institute and Grant GM-13122 from The National Institute of General Medical Sciences, and Grants GP-4915 and GP-28261 from the National Science Foundation.
(2) Abstracted from the Ph.D. Theses of A. Staklis, 1964, and H. L. Smith, 1970, which may be consulted for additional details.
(3) H. E. Baumgarten, P. L. Creger, and R. L. Zey, *J. Am. Chem. Soc.*, **82**, 3977 (1960).
(4) H. E. Baumgarten, W. F. Wittman, and G. J. Lehmann, *J. Heterocycl. Chem.*, **6**, 333 (1969).
(5) H. E. Baumgarten and A. Staklis, *J. Am. Chem. Soc.*, **87**, 1141 (1965).
(6) B. Acott, A. L. J. Beckwith, A. Hassanali, and J. W. Redmond, *Tetrahedron Lett.*, 4039 (1965).
(7) B. Acott, A. L. J. Beckwith, and A. Hassanali, *Aust. J. Chem.*, **21**, 185 (1968).
(8) B. Acott, A. L. J. Beckwith, and A. Hassanali, *Aust. J. Chem.*, **21**, 197 (1968).
(9) A. L. J. Beckwith and R. J. Hickman, *J. Chem. Soc. C*, 2756 (1968).
(10) An illustration of the ease, simplicity, and good yield possible with this rearrangement has been given in an elementary experiment in W. W. Linstromberg and H. E. Baumgarten, "Organic Experiments for a Brief Course", 2nd ed, D. C. Heath, Boston, Mass., 1970, p 227.
(11) J. Tscherniac, *Ber.*, **36**, 218 (1903).
(12) A. Hassner and C. Heathcock, *Tetrahedron*, **20**, 1037 (1964).
(13) Despite the persistence in the folklore of organic chemistry of the myth that *tert*-alkyl carbamates cannot be readily prepared from tertiary alcohols and isocyanates because of the tendency of the latter to dehydrate the former (D. J. Pasto and C. R. Johnson, "Organic Structure Determination", Prentice-Hall, Englewood Cliffs, N.J., 1969, p 359; R. L. Shriner, R. C. Fuson, and D. Y. Curtin, "The Systematic Identification of Organic Compounds", 5th ed, Wiley, New York, N.Y., 1965, p 241), we found no difficulty in effecting this preparation in good to excellent yields. The effects of the structure of the alcohol and of the isocyanate on this reaction have been reviewed.[14]
(14) R. G. Arnold, J. A. Nelson, and J. J. Verbanc, *Chem. Rev.*, **57**, 47 (1957); J. H. Saunders and R. J. Slocombe, *Ibid.*, **43**, 203 (1948); cf. also S. R. Sandler and W. Karo, "Organic Functional Group Preparations", Vol. II, Academic Press, New York, N.Y., 1971, p 224.
(15) F. Hostetler and E. F. Cox, *Ind. Eng. Chem.*, **52**, 609 (1960).
(16) J. Burkus, *J. Org. Chem.*, **26**, 779 (1961).
(17) Presumably the tin compounds function as catalysts by coordination with the oxygen of the isocyanate, thereby making the carbonyl carbon more positive and more susceptible to attack by the weakly nucleophilic *tert*-butyl alcohol. The mechanism of triethylamine catalysis has been discussed by Burkus.[16]
(18) Catalysis of the dehydration of a small amount of the *tert*-butyl alcohol by the isocyanate would not be important, were it not for the water formed which hydrolyses the isocyanate to yield the amine, which reacts rapidly with a second molecule of isocyanate to form the *sym*-disubstituted urea. Formation of the latter is also the basis of the need for absolutely anhydrous reagents and conditions throughout the reaction.
(19) L. A. Carpino, *Acc. Chem. Res.*, **6**, 191 (1973).
(20) G. W. Anderson and A. C. McGregor, *J. Am. Chem. Soc.*, **79**, 6180 (1957).
(21) F. C. McKay and N. F. Albertson, *J. Am. Chem. Soc.*, **79**, 4686 (1957).
(22) Reference 19, footnote 12.
(23) We made no attempt to determine whether the *tert*-butyl group was eliminated as *tert*-butyl chloride[20] or isobutylene.[19,24] In no instance did this by-product interfere with isolation or purification of the amine hydrochloride.
(24) L. F. Carpino, *J. Am. Chem. Soc.*, **79**, 98 (1957).
(25) T. Masters, M.S. Thesis, University of Nebraska—Lincoln, May 1975.
(26) S. S. Simons, Jr., *J. Org. Chem.*, **38**, 414 (1973).
(27) L. K. Dyall, J. O. M. Evans, and J. E. Kemp, *Aust. J. Chem.*, **21**, 409 (1968).
(28) A. Stojiljković, V. Andrejević, and M. L. Mihailovk, *Tetrahedron*, **23**, 721 (1967).
(29) B. Kamenar, *Acta Crystallogr., Sect. A*, **16**, 34 (1963).
(30) W. Lwowski and T. W. Mattingly, *Tetrahedron*, 227 (1962).
(31) K. Hafner and C. Konig, *Angew. Chem.*, **75**, 89 (1963).
(32) W. Kwowski, T. J. Marichich, and T. W. Mattingly, Jr., *J. Am. Chem. Soc.*, **85**, 1200 (1963).
(33) L. Horner and A. Christman, *Ber.*, **96**, 388 (1963).
(34) E. S. Wallis and J. F. Lane, *Org. React.*, **3**, 267 (1946).
(35) P. A. S. Smith, *Org. React.*, **3**, 337 (1946).
(36) W. Hartmann, *Ber.*, **21**, 222 (1888).
(37) A. Haller, *C. R. Acad. Sci.*, **114**, 1518 (1892).
(38) A. Haller, *C. R. Acad. Sci.*, **141**, 697 (1905).
(39) W. A. Noyes and R. S. Potter, *J. Am. Chem. Soc.*, **37**, 201 (1915).
(40) L. A. Carpino, *J. Am. Chem. Soc.*, **79**, 4430 (1957).
(41) A. R. Choppin and J. W. Rogers, *J. Am. Chem. Soc.*, **70**, 2967 (1948).
(42) O. Wallachi, *Justus Liebigs Ann. Chem.*, **343**, 46 (1905).
(43) N. Konovalon, *Ber.*, **28**, 1861 (1895).
(44) J. Bertram and H. Walbavon, *J. Prakt. Chem.*, **50**, 556 (1894).
(45) F. Ullmann, *Ber.*, **31**, 1699 (1898).
(46) F. Beilstein and A. Kurbatow, *Justus Liebigs Ann. Chem.*, **176**, 29 (1875).
(47) V. Merz and C. Ris, *Ber.*, **19**, 1753 (1886).
(48) F. Beilstein and A. Kurbatow, *Justus Liebigs Ann. Chem.*, **196**, 219 (1879).
(49) O. Aschan, *Ber.*, **27**, 2003 (1894).
(50) C. Kaiser, B. M. Lester, C. L. Zirkle, A. Burger, C. S. Davis, T. J. Delia, and L. Zirngibl, *J. Med. Pharm. Chem.*, **5**, 1243 (1962).
(51) A. Phillips, *Justus Liebigs Ann. Chem.*, **288**, 263 (1895).
(52) D. Ben-Ishai and A. Berger, *J. Org. Chem.*, **17**, 1564 (1952).
(53) H. V. Soden and W. Rojahn, *Ber.*, **34**, 3809 (1901).
(54) B. Brauner, *Ber.*, **12**, 1875 (1879).