mp 125–126 °C: $^1$H NMR ($CCl_4$) δ 10.08 (2 H, d), 8.95 (1 H, m), 8.17 and 8.12 (3 H, overlapping s and d); IR (KBr) 3062, 1662, 1518, 1432, 1220, 1190 cm$^{-1}$. Anal. Calcd for $C_{16}H_6O_2F_{10}$: C, 45.73; H, 1.44. Found: C, 45.86; H, 1.47.

**1,3-Azulenedicarboxylic acid (5).** A mixture of **2** (64 mg, 0.2 mmol), 2 mL of ethanol, and 2 mL of 10% aqueous KOH was shaken until complete dissolution occurred. The mixture was then heated at 50–60 °C for 8 h. After the solution was cooled and 4 mL of $H_2O$ was added, the solution was brought to pH ~1 with dilute HCl. The fluffy red precipitate was filtered, washed with water and ether, and dried in vacuo to give the brick-red product (41 mg, 0.18 mmol, 95%). No true melting point was observed, although decomposition occurred above 260–270 °C (lit. mp 254–258 °C,[8] 268 °C[9]): $^1$H NMR ($D_2O$ + NaOH) δ 9.26 (2 H, d), 8.43 (1 H, s), 7.7–7.2 (3 H, m); IR (KBr) 2900 (s, bd), 2710, 2530, 1660, 1515, 1460, 1240, 775 cm$^{-1}$. Anal. Calcd for $C_{12}H_8O_4$: C, 66.66; H, 3.73. Found: C, 66.37; H, 3.73.

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**Registry No.** **2**, 73017-87-5; **3**, 73017-88-6; **4**, 73017-89-7; **5**, 38303-39-8; azulene, 275-51-4.

## Protected Diaminomethane

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Recently there has been a certain amount of interest in compounds of the general form **1**. Such compounds were

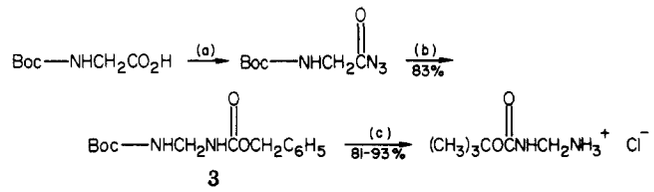
$$R^1C(O)NHCH(NH_2)R^2$$
**1**

first synthesized by Bergmann and Zervas,[1] and the *N*-(1-aminoalkyl) carboxamide linkage has received some attention in protein modification work.[2] More recently, these compounds have developed as key intermediates in our carboxyl-terminal peptide degradation[3] and have proven useful for providing "mock" amino-terminal residues in the retro-inverso peptide concept.[4] There are thus a number of applications in which one would like to introduce an (aminomethyl)amino group into peptides or proteins (eq 1).

$$RC(O)OH + \text{“}NH_2CH_2NH_2\text{”} \rightarrow RC(O)NHCH_2NH_2 + H_2O \quad (1)$$

The parent compound, diaminomethane, although known as the dihydrochloride,[5] is not sufficiently stable in the mono- or unprotonated form to survive the conditions required to use it as a reagent, despite reports to the contrary.[6] We have found, however, that compounds of the form **1** are remarkably stable to aqueous conditions, despite their thin disguise as masked aldehydes. A detailed report dealing with this point will be forthcoming, but we would here like to describe the synthesis, characterization, and aqueous solution stability of a hitherto unknown, simple protected form of diaminomethane, [(*tert*-butoxycarbonyl)amino]methylamine hydrochloride **2**, stable for use in many of the reactions of protein chemistry, and perhaps in general organic synthesis as well.

Scheme I[a]




[a] (a) $(O_2N\text{-}p\text{-}C_6H_4O)_2PO—N_3$, EtOAc, $Et_3N$; (b) Δ, $C_6H_5CH_2OH$; (c) $H_2$, Pd/C, HCl (1 equiv), $CH_3OH$.

$$(CH_3)_3COC(O)NHCH_2NH_3^+Cl^-$$
**2**

The synthesis of **2** is shown in Scheme I. Boc-glycine is converted to its azide by using bis(*p*-nitrophenyl)-phosphoryl azide, and the resulting material is rearranged in the presence of benzyl alcohol to give the diprotected methylenediamine derivative **3**. Hydrogenolysis in the presence of 1 equiv of HCl yields the hydrochloride **2** (for NMR spectrum and microanalysis see Experimental Section). This synthesis has also been used to prepare radiolabeled **2** by starting with radiolabeled glycine (see Experimental Section).

A similar route has also been used to prepare other amino acid derivatives of type **1**, although the method fails for $R^2$ = phenyl; in this case, one must resort to a different procedure.[8] We considered the possibility of beginning with the less expensive Z-glycine and carrying out the Curtius rearrangement in the presence of *tert*-butyl alcohol. Attempts in this direction were frustrated by the presence of traces of water even in scrupulously dried *tert*-butyl alcohol, probably from decomposition of the alcohol under the reaction conditions, and moderate yields of symmetrical ureas were obtained. Low yields in the synthesis of *tert*-butyl carbamates via the Curtius rearrangement in *tert*-butyl alcohol have been encountered by others, and special methods have been developed to deal with this problem.[9,10] Because of the high yields of the synthesis shown in Scheme I, however, these other alternatives were not explored.

The free base form of **2** could be prepared by neutralization and extraction into ether. This material is therefore also accessible for use in synthesis in nonaqueous solvents.

Some preliminary kinetic experiments were carried out to determine the stability of **2** in aqueous solution by simply dissolving this compound in $D_2O$ and following the decay of its spectrum. By this technique, **2** was found to decay to *tert*-butyl carbamate, formaldehyde hydrate, and ammonia with a rate constant of $(2.4 \pm 0.3) \times 10^{-4}$ s$^{-1}$. A detailed kinetic and mechanistic study of the hydrolysis reaction of compounds of type **1**, including a pH dependence, is in progress. However, stability data reported here and the ability to extract this material into nonaqueous solution show that this compound should be useful in synthetic operations.

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## Experimental Section

**General Procedures.** Melting points were taken on a Büchi melting point apparatus and are uncorrected. Proton NMR spectra were taken on a Varian EM-360 instrument unless otherwise noted. Scintillation counting was performed on a Beckman LS-100 liquid scintillation system in 10 mL of Aquasol (New England Nuclear).

***N*-Carbobenzoxy-*N'*-(*tert*-butoxycarbonyl)diaminomethane (3).** In a dry 250-mL flask fitted with a stirrer and a drying tube were combined Boc-glycine (1.75 g, 0.01 mol), dry ethyl acetate (100 mL), and triethylamine (1.4 mL, 0.01 mol), and the solution was cooled to 0 °C. Then bis(*p*-nitrophenyl)-phosphoryl azide[7] (3.65 g, 0.01 mol) was added and the mixture stirred at 0 °C for 45 min. The precipitated triethylammonium bis(*p*-nitrophenyl) phosphate was filtered and washed with ether, and the filtrate was immediately washed with ice water (2 × 50 mL) to remove the remaining salt and dried for 1 h ($MgSO_4$) at 0 °C. The solution was filtered into a dry 250-mL flask and the solvent removed in vacuo at <30 °C. Dry benzyl alcohol (10.3 mL, 0.1 mol) was added to the residual oil, and the flask was suspended in an oil bath at 75 °C. Vigorous gas evolution occurred within 2–3 min and was mostly complete in 10 min. After 4.5 h, the solvent was removed in vacuo by using a short-path still. The semisolid residue was freed of residual benzyl alcohol by drying over $P_2O_5$ in vacuo at 56 °C to constant weight. Recrystallization of the crude product gave 2.33 g (83%) of **3**: mp 114–5 °C; NMR ($CDCl_3$) δ 1.40 (s, 9 H), 4.50 (t, 2 H, $J$ = 6 Hz), 5.15 (s, 2 H), 5.3–5.9 (br, 2 H), 7.41 (s, 5 H). Anal. Calcd: C, 59.98; H, 7.19; N, 10.00. Found: C, 60.17; H, 7.21; N, 10.10.

***N*-[(*tert*-Butoxycarbonyl)amino]methylamine Hydrochloride (2).** **3** (560 mg, 2 mmol) was dissolved in 15 mL of absolute methanol and 100 mg of 5% Pd/C catalyst was added, followed by 2.0 mL (1 equiv) of 1.0 N HCl. The flask was rinsed with an additional 5 mL of methanol. The flask was attached to an atmospheric pressure hydrogenation apparatus, cooled to 0 °C, and subjected to a stream of hydrogen without stirring for 5 min. The ice bath was then removed, stirring was begun, and the effluent hydrogen stream was monitored for $CO_2$ every 5 min by using a solution of $Ba(OH)_2$. When the test for $CO_2$ was negative (30–45 min), the solution was filtered through Celite, and the filter rinsed with methanol (5 mL) followed by water (20 mL). The methanol was then removed on a rotary evaporator at ≤35 °C, the remaining aqueous solution was quickly extracted with ether to remove *tert*-butyl carbamate and starting material, and the remaining aqueous solution was lyophilized to yield an amorphous white powder in 81–93% yield. The product gave a single spot on TLC (silica gel, 4:1:1 1-butanol/acetic acid/water, $R_f$ 0.66) which was positive to fluorescamine and chlorine 1% starch–potassium iodide. The melting behavior was unusual, possibly reflecting decomposition: the compound melts to a core at 128.5–130 °C, then remains otherwise unchanged to 280 °C; NMR ($Me_2SO$-$d_6$) δ 1.40 (s, 11 H), 4.18 (br, 2 H), 8.2 (br, 3.5 H). Anal. Calcd: C, 39.45; H, 8.28; N, 15.34. Found: C, 39.24; H, 8.50; N, 15.50.

The free amine was isolated by dissolving **2** (53.5 mg, 0.298 mmol) in 1 M $NaHCO_3$ (5 mL) and extracting with ether. Drying and concentration of the ether layer gave an oil (69%): NMR ($CDCl_3$) δ 1.42 (s, 10 H), 4.18 (d, 2 H), 5.60 (br, 0.72 H).

**Hydrolysis of 2.** **2** (20 mg) was dissolved in $D_2O$ (0.5 mL) and the solution was filtered into an NMR tube. Spectra of the solution were taken at 2-min intervals on a Varian FT-80 instrument for the first 40 min, and then were spaced gradually further apart. The data were stored on disks for later use. The rate of decay of the *tert*-butyl singlet of **2** and the rates of appearance of the *tert*-butyl singlet of *tert*-butyl carbamate and the methylene of formaldehyde hydrate were determined by fitting the progress curves to a first-order exponential, using a nonlinear least-squares technique.

**Boc-[2-$^3$H]glycine (4).** This material was synthesized by using a modification of the procedure of Schnabel.[11] Into a 50-mL beaker were placed glycine (1.50 g, 0.02 mol) and 8 mL of dioxane. To this was added 1 mL of an aqueous solution of [2-$^3$H]glycine (Amersham, 1 mCi, specific activity 21 Ci/mmol), followed by 3 mL of water used to rinse the vial. To the resulting solution was added *tert*-butoxycarbonyl azide (3.3 g, 23 mmol), the pH was adjusted to 10 with 4 N NaOH, and the pH was maintained at that value for 6 h by using a pH-stat. The solution was then extracted with ether, the pH lowered to 3.0 with 6 N HCl, NaCl added to saturation, and the solution extracted with ethyl acetate. The ethyl acetate was washed with brine, dried, filtered, and concentrated. The resulting material was triturated with hexane to give 2.72 g (77%) of **4**, mp 87–88.5 °C (lit.[11] 94–95 °C), specific activity 0.0505 Ci/mol (theoretical 0.0500). This material could be used uneventfully to synthesize radiolabeled **2**.

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**Registry No.** **2**, 73017-97-7; **2**·HCl, 73017-98-8; **3**, 73017-99-9; **4**, 4530-20-5; glycine, 56-40-6.

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# Reaction of Primary β-Azido Tertiary Alcohols with Nitrosonium Salts. A Rearrangement Related to the Tiffeneau Reaction

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It was reported that alkyl azides generate carbonium ions on treatment with nitrosonium salts under aprotic conditions.[1] We now wish to report that primary β-azido tertiary alcohols under similar conditions give ketones in what constitutes an alternative to the Tiffeneau reaction.[2] Thus, starting from a ketone (phenyl methyl ketone, cyclopentanone, cyclohexanone, cycloheptanone, and norcamphor) we arrived at its epoxide in a 60–70% yield by the method of Corey and Chaykovsky.[3] Alternatively, the epoxide was arrived at by peracid oxidation of the appropriate olefin. The epoxide was then transformed into the β-azido alcohol (Table I) on treatment with sodium azide in 70% yield.[4]

As regards the nitrosonium reaction, when the azido alcohol **1** was treated with slightly less than 1 molar equiv of nitrosonium tetrafluoroborate in carefully dried acetonitrile at 0 °C, benzyl methyl ketone was rapidly obtained in 50% yield in addition to traces of phenyl ethyl ketone (Table I). The other data in Table I show that this method can be applied, unchanged, to ring enlargements, working with both monocyclic (**2**, **3**, **5**) and bicyclic[5] (**4**) systems.

However, the yields of homologated ketones are low, ranging from 10 to 38% (Table I). For comparison, the β-amino alcohols corresponding to our azido alcohols gave homologated ketones with 60–70% yields under Tiffeneau conditions.[2,5] Both the Tiffeneau[2] and our homologation

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