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.

Acknowledgment. We acknowledge support of this work by the National Institute of General Medical Sciences (GM 25143) and the National Science Foundation (CHE 77-22493). We also gratefully acknowledge the assistance of Mr. John Kozlowski with the NMR experiments.

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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(2) P. A. S. Smith and D. R. Baer, *Org. React.*, **11**, 157 (1960); H. Söll in "Methoden der organische Chemie (Houben-Weyl)", Vol. **11/2**, E. Müller, Ed., George Thieme Verlag, Stuttgart, 1958, pp 163–70.

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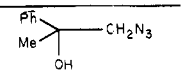
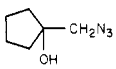
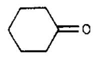
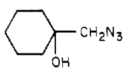
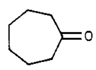
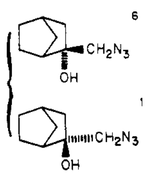
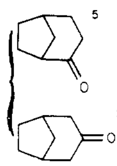
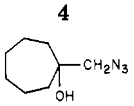
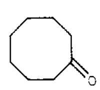
Table I. Reaction of β-Azido Alcohols with Nitrosonium Tetrafluoroborate in Acetonitrile at 0 °C

azido alcohol	product (yield, %)
 **1**	$PhCH_2COCH_3$, $PhCOCH_2CH_3$ (50) (trace)
 **2**	 (10)
 **3**	 (22)
 **4**	 (overall 38)[5]
 **5**	 (24)

reactions involve the same number of steps. Therefore, at present, the only difference between the two reactions lies in the protic (Tiffeneau[2]) vs. aprotic (our reaction) conditions. In fact, also in our reactions, from the present results, migratory aptitudes are typical of carbonium ion rearrangements, e.g., aryl migrates in preference to alkyl (1, Table I).

Experimental Section

General Methods. Solvents were purified and dried by standard procedures. ^{1}H NMR spectra were run in the indicated solvents on a Varian EM 360L spectrometer, and chemical shifts (δ) are measured from internal tetramethylsilane as reference. Infrared spectra were run on a Perkin-Elmer 337 spectrometer.

1-Azido-2-phenylpropan-2-ol (1). To a solution of 1-phenyl-1-methylethylene oxide[6] in 65 mL of dioxane at reflux (4.0 g, 30 mmol) was added dropwise sodium azide (40% molar excess) dissolved in 15 mL of water. The mixture was refluxed for an additional 23 h. The two layers were then separated, and the water layer was further extracted with dioxane. The combined dioxane extract was evaporated, and the residue was distilled in vacuo: yield 3.4 g (64%); bp 104–105 °C (6 torr); 55:45 mixture of 1 and 2-phenyl-2-azidopropan-1-ol. The two isomers were separated by column chromatography (silica gel; 1:1 petroleum ether–ethyl ether) whereby 1 was eluted first: ^{1}H NMR (CCl_4) δ 1.57 (s, 3 H, CH_3), 2.51 (s, 1 H, OH), 3.50 (AB system, 2 H, $J_{AB} = 13$ Hz, CH_2N_3), 7.59 (m, 5 H, C_6H_5); IR (CCl_4) 3430, 2105, 1275 cm^{-1}.

Anal. Calcd for $C_9H_{11}N_3O$: C, 61.00; H, 6.26. Found: C, 60.89; H, 6.18.

1-(Azidomethyl)cyclopentan-1-ol (2). The reaction was carried out as in the case of 1 with 3.4 g (35 mmol) of methylenecyclopentane oxide[7] for 16 h at reflux: yield 4.2 g (85%); bp 60–61 °C (8 torr); ^{1}H NMR (CCl_4) δ 1.60 (m, 8 H, cyclopentyl), 2.45 (br s, 1 H, OH), 3.32 (s, 2 H, CH_2N_3); IR (film) 3395, 2100, 1285 cm^{-1}.

Anal. Calcd for $C_6H_{11}N_3O$: C, 51.04; H, 7.85. Found: C, 51.20; H, 7.77.

1-(Azidomethyl)cyclohexan-1-ol (3). The reaction was carried out as in the case of 1 with 2.0 g (18 mmol) of methylenecyclohexane oxide[8] for 22 h at reflux: yield 1.2 g (43%); bp 69–70 °C (8 torr); ^{1}H NMR (CCl_4) δ 1.50 (m, 10 H, cyclohexyl), 1.98 (br s, 1 H, OH), 3.21 (s, 2 H, CH_2N_3); IR (film) 3410, 2100, 1285 cm^{-1}.

Anal. Calcd for $C_7H_{13}N_3O$: C, 54.17; H, 8.44. Found: C, 54.23; H, 8.19.

***exo*- and *endo*-2-(Azidomethyl)norbornan-2-ols (4).** The reaction was carried out as in the case of 1 with a 1:6 mixture of *exo*-2-methylene- and *endo*-2-methylenenorbornane oxide[9] for 23 h at reflux: yield 4.5 g (67%); bp 82–83 °C (6 torr); IR (CCl_4) 3410, 2100, 1280 cm^{-1}.

Anal. Calcd for $C_8H_{13}N_3O$: C, 57.47; H, 7.83. Found: C, 57.21; H, 7.96.

1-(Azidomethyl)cycloheptan-1-ol (5). The reaction was carried out as in the case of 1 starting from 4.0 g (32 mmol) of methylenecycloheptane: yield 3.4 g (66%); bp 128–129 °C (22 torr); ^{1}H NMR (CCl_4) δ 1.56 (m, 12 H, cycloheptyl), 2.55 (br s, 1 H, OH), 3.20 (s, 2 H, CH_2N_3); IR (film) 3410, 2100, 1280 cm^{-1}.

Anal. Calcd for $C_8H_{15}N_3O$: C, 56.78; H, 8.93. Found: C, 56.23; H, 8.98.

General Procedure for the Treatment of β-Azido Alcohols with Nitrosonium Tetrafluoroborate. To a solution of the azido alcohol (ca. 0.5 M) in acetonitrile at 0 °C was added, with stirring, slightly less than the equimolar amount of crystalline nitrosonium tetrafluoroborate. After 5 min the mixture was analyzed by VPC to determine the yields (see Table I) of ketones which were then isolated by standard procedures. Physical data for the ketones exactly matched those for authentic samples either commercially available or prepared by literature methods. Yields of isolated ketones approach those given in Table I when the reactions were carried out on large quantities (several grams) of azido alcohols.

Acknowledgment. We are grateful to CNR, Roma, for financial support.

Registry No. **1**, 1961-65-5; **2**, 72939-17-4; **3**, 57770-11-3; *exo*-**4**, 72939-18-5; *endo*-**4**, 72939-19-6; **5**, 72939-20-9; $PhCH_2COCH_3$, 103-79-7; $PhCOCH_2CH_3$, 93-55-0; cyclohexanone, 108-94-1; cycloheptanone, 502-42-1; bicyclo[3.2.1]octan-2-one, 5019-82-9; bicyclo[3.2.1]octan-3-one, 14252-05-2; cyclooctanone, 502-49-8; 1-phenyl-1-methylethylene oxide, 2085-88-3; 2-phenyl-2-azidopropan-1-ol, 72939-21-0; methylenecyclopentane oxide, 185-60-4; methylenecyclohexane oxide, 185-70-6; *exo*-methylenenorbornane oxide, 16282-10-3; *endo*-methylenenorbornane oxide, 16282-11-4; methylenecycloheptane, 185-85-3.

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Raman Spectrum of a Malonic Anhydride

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Despite the simplicity of its molecular structure, malonic anhydride has been an elusive molecule for more than 70 years. Various substituted malonic anhydrides have been obtained, but these are polymeric.[1-4] More recently, a monomeric diethylmalonic anhydride was claimed,[5] on the

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