

equation (eq 4). Table II presents our "predictions" for

$$\Delta H_v = (1.15 \pm 0.07)n_c + RT \quad (4)$$

$$\sigma = 0.70$$

the four hydrocarbons discussed earlier. Quick perusal shows the average discrepancy is ca. 0.6 kcal/mol. This quantity is small enough, that we feel this method can be useful in predicting  $\Delta H_v$  in cases where experimental data do not exist.

**Acknowledgment.** We thank the following individuals for helpful discussion: Drs. E. S. Domalski, V. Fried, F. Gornick, A. Greenberg, P. M. Haberfield, H. P. Hopkins, Jr., C. L. Liotta, H. M. Rosenstock, F. J. Stillinger, J. J. Topping, and D. Van Vechten. We also thank Messrs. C. C. Bowen and T. Ladon for their calculational assistance and the University of Maryland Computer Center for a gift of computer time. Finally, we thank the U.S. Department of Energy, Office of Environment, for Contract No. 80EV10373.000 (awarded to J.F.L.) and the University of Missouri-St. Louis for partial support of this research.

**Registry No.** 1-Hexyne, 693-02-7; 1-octene, 111-66-0; phenylacetylene, 501-65-5; mesitylene, 108-67-8; 1-butyne, 107-00-6; 2-butyne, 503-17-3; 1,2-butadiene, 590-19-2; 1,3-butadiene, 106-99-0; 1-butene, 106-98-9; (Z)-2-butene, 590-18-1; (E)-2-butene, 624-64-6; isobutene, 115-11-7; cyclobutane, 287-23-0; butane, 106-97-8; isobutane, 75-28-5; cyclopentene, 142-29-0; spiropentane, 157-40-4; pentene, 109-67-1; (Z)-2-pentene, 627-20-3; (E)-2-pentene, 646-04-8; 2-methyl-1-butene, 563-46-2; 3-methyl-1-butene, 563-45-1; 2-methyl-2-butene, 513-35-9; cyclopentane, 287-92-3; pentane, 109-66-0; 2-methylbutane, 78-78-4; benzene, 71-43-2; cyclohexane, 110-83-8; 1-hexene, 592-41-6; (Z)-2-hexene, 7688-21-3; (E)-2-hexene, 4050-45-7; (Z)-3-hexene, 7642-09-3; (E)-3-hexene, 13269-52-8; 2-methyl-1-pentene, 763-29-1; 3-methyl-1-pentene, 760-20-3; 4-methyl-1-pentene, 691-37-2; 2-methyl-2-pentene, 625-27-4; (Z)-3-methyl-2-pentene, 922-62-3; (E)-3-methyl-2-pentene, 616-12-6; (Z)-4-methyl-2-pentene, 691-38-3; (E)-4-methyl-2-pentene, 674-76-0; 2-ethyl-1-butene, 760-21-4; 2,3-dimethyl-1-butene, 563-78-0; 3,3-dimethyl-1-butene, 558-37-2; 2,3-dimethyl-2-butene, 563-79-1; methylcyclopentane, 96-37-7; cyclohexane, 110-82-7; hexane, 110-54-3; 2-methylpentane, 107-83-5; 3-methylpentane, 96-14-0; 2,2-dimethylbutane, 75-83-2; 2,3-dimethylbutane, 79-29-8; cycloheptatriene, 544-25-2; toluene, 108-88-3; 1-methylcyclohexene, 591-49-1; 1-heptene, 592-76-7; 4-methylheptane, 589-53-7; 3-ethylhexane, 619-99-8; 2,2-dimethylhexane, 590-73-8; 2,3-dimethylhexane, 584-94-1; 2,4-dimethylhexane, 589-43-5; 2,5-dimethylhexane, 592-13-2; 3,3-dimethylhexane, 563-16-6; 3,4-dimethylhexane, 583-48-2; 3-ethyl-2-methylpentane, 609-26-7; 3-ethyl-3-methylpentane, 1067-08-9; 2,2,3-trimethylpentane, 564-02-3; 2,2,4-trimethylpentane, 540-84-1; 2,3,3-trimethylpentane, 560-21-4; 2,3,4-trimethylpentane, 565-75-3; propylbenzene, 103-65-1; isopropylbenzene, 98-82-8; 1-methyl-2-ethylbenzene, 611-14-3; 1-methyl-3-ethylbenzene, 620-14-4; 1-methyl-4-ethylbenzene, 622-96-8; 1,2,3-trimethylbenzene, 526-73-8; 1,2,4-trimethylbenzene, 95-63-6; 1,3,5-trimethylbenzene, 108-67-8; propylcyclohexane, 1678-92-8; nonane, 111-84-2; butylbenzene, 104-51-8; iso-butylbenzene, 538-93-2; sec-butylbenzene, 135-98-8; tert-butylbenzene, 98-06-6; cis-decahydronaphthalene, 493-01-6; trans-decahydronaphthalene, 493-02-7; 1-decene, 872-05-9; butylcyclohexane, 1678-93-9; decane, 124-18-5; heptylcyclohexane, 5617-41-4; (Z)-3-methyl-3-hexene, 4914-89-0; (E)-3-methyl-3-hexene, 3899-36-3; 2,4-dimethyl-1-pentene, 2213-32-3; 4,4-dimethyl-1-pentene, 762-62-9; 2,4-dimethyl-2-pentene, 625-65-0; (Z)-4,4-dimethyl-2-pentene, 762-63-0; (E)-4,4-dimethyl-2-pentene, 690-08-4; 3-methyl-2-ethyl-1-butene, 7357-93-9; 2,3,3-trimethyl-1-butene, 594-56-9; 1,1-dimethylcyclopentane, 1638-26-2; cis-1,2-dimethylcyclopentane, 1192-18-3; trans-1,2-dimethylcyclopentane, 822-50-4; cis-1,3-dimethylcyclopentane, 2532-58-3; trans-1,3-dimethylcyclopentane, 1759-58-6; ethylcyclopentane, 1640-89-7; methylcyclohexane, 108-87-2; cycloheptane, 291-64-5; heptane, 142-82-5; 2-methylhexane, 591-76-4; 3-methylhexane, 589-34-4; 3-ethylpentane, 617-78-7; 2,2-dimethylpentane, 590-35-2; 2,3-dimethylpentane, 565-59-3; 2,4-dimethylpentane, 108-08-7; 3,3-dimethylpentane, 562-49-2; 2,2,3-trimethylbutane, 464-06-2; 1,3,5,7-cyclooctatetraene, 629-20-9; styrene, 100-42-5; ethylbenzene, 100-41-4; o-xylene, 95-47-6; m-xylene, 108-38-3; p-xylene, 106-42-3; 1-ethylcyclohexene, 1453-24-3; (Z)-2,2-dimethyl-3-hexene, 690-92-6; (E)-2,2-dimethyl-3-hexene, 690-93-7; 2-methyl-3-ethyl-1-pentene, 19780-66-6; 2,4,4-trimethyl-1-

pentene, 107-39-1; 2,4,4-trimethyl-2-pentene, 107-40-4; propylcyclopentane, 2040-96-2; ethylcyclohexane, 1678-91-7; 1,1-dimethylcyclohexane, 590-66-9; cis-1,2-dimethylcyclohexane, 2207-01-4; trans-1,2-dimethylcyclohexane, 6876-23-9; cis-1,3-dimethylcyclohexane, 638-04-0; trans-1,3-dimethylcyclohexane, 2207-03-6; cis-1,4-dimethylcyclohexane, 624-29-3; trans-1,4-dimethylcyclohexane, 2207-04-7; cyclooctane, 292-64-8; octane, 111-65-9; 2-methylheptane, 592-27-8; 3-methylheptane, 589-81-1; isoprene, 78-79-5; indene, 95-13-6; 2,3-dihydroindene, 496-11-7; cis-bicyclo[4.3.0]nonane, 4551-51-3; trans-bicyclo[4.3.0]nonane, 3296-50-2;  $\alpha$ -pinene, 80-56-8;  $\beta$ -pinene, 127-91-3; cyclopentadiene, 542-92-7; 1,2,3,4-tetrahydronaphthalene, 119-64-2;  $\alpha$ -phellandrene, 99-83-2; cis-stilbene, 645-49-8; hexadecane, 544-76-3; dodecylcyclohexane, 1795-17-1; (+)-limonene, 5989-27-5; dipentene, 138-86-3; 6,6-dimethylfulvene, 2175-91-9; 1,1-diphenylethylene, 530-48-3; undecane, 1120-21-4; dodecane, 112-40-3; decylbenzene, 104-72-3; hexadecene, 629-73-2; 3,3-diethylpentane, 1067-20-5; 2,2,3,3-tetramethylpentane, 7154-79-2; 2,2,3,4-tetramethylpentane, 1186-53-4; 2,2,4,4-tetramethylpentane, 1070-87-7; 2,3,3,4-tetramethylpentane, 16747-38-9; 2-methylnonane, 871-83-0; 5-methylnonane, 15869-85-9; 2,2,5,5-tetramethylheptane, 61868-47-1; 2,2,4,4,5-pentamethylhexane, 60302-23-0; 3,3,6,6-tetramethyloctane, 62199-46-6; 4,4,6,6-tetramethylnonane, 74286-93-4; 3,5-dimethyl-3,5-diethylheptane, 74286-94-5; 5,5,7,7-tetramethylundecane, 74286-95-6; 5-butylidocosane, 55282-16-1; 11-butylidocosane, 13475-76-8; 11-decylidocosane, 55320-06-4; bicyclopentyl, 5685-46-1; cyclodecane, 293-96-9; cycloundecane, 294-41-7; cyclotridecane, 295-02-3; 1-methylcyclopentene, 693-89-0; 3-methylcyclopentene, 1120-62-3; 4-methylcyclopentene, 1759-81-5.

**Supplementary Material Available:** Tables containing the names and heats of vaporization of the 138 compounds used to derive eq 1-4 and a comparison of the predicted and experimental values for an additional 44 compounds (5 pages). Ordering information is given on any current masthead page.

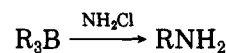
### A Convenient Synthesis of Alkyl Amines via the Reaction of Organoboranes with Ammonium Hydroxide

George W. Kabalka,\* Kunda A. R. Sastry,  
Gary W. McCollum, and Hiroaki Yoshioka

Chemistry Department, University of Tennessee, Knoxville,  
Tennessee 37916

Received May 20, 1981

The synthesis of amines has long been of interest due to their physiological activity and their potential as organic intermediates. Brown reported that organoboranes could be utilized to produce amines by treating them with chloramine<sup>1</sup> or hydroxylamine-O-sulfonic acid.<sup>2</sup> The re-



actions involve the regiospecific replacement of the boron atom by the amino group. These reactions have not been utilized extensively, presumably due to the cumbersome preparation and inherent instability of chloramine<sup>3</sup> and the expense of hydroxylamine-O-sulfonic acid.

In recent years, we have had success in carrying out reactions in systems where the reagents are generated in situ.<sup>4,5</sup> For example, organoboranes will react with iodide

(1) Brown, H. C.; Heydkamp, W. R.; Baeuer, E.; Murphy, W. S. *J. Am. Chem. Soc.* 1964, 86, 3565.




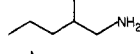


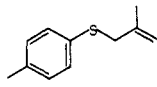
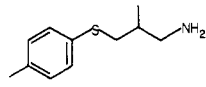
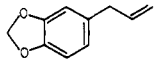
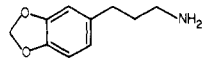
(2) Rathke, M. W.; Inoue, N.; Varma, K. R.; Brown, H. C. *J. Am. Chem. Soc.* 1966, 88, 2870.

(3) Schmitz, V. E.; Schramm, S.; Flamme, W.; Bicker, U. *Z. Anorg. Allg. Chem.* 1973, 396, 178.

(4) Kabalka, G. W.; Sastry, K. A. R.; Hsu, H.; Hylarides, M. D. *J. Org. Chem.* 1981, 46, 3113.

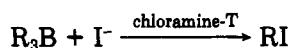
(5) Kabalka, G. W.; Gooch, E. E. *J. Org. Chem.* 1981, 46, 2582.

Table I. Conversion of Alkenes to the Corresponding Amine<sup>a</sup>

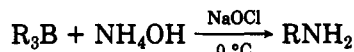
alkene	product	% yield <sup>b,c</sup>
$\text{CH}_3(\text{CH}_2)_5\text{CH}=\text{CH}_2$	$\text{CH}_3(\text{CH}_2)_6\text{CH}_2\text{NH}_2$	95 (92)
$\text{CH}_3(\text{CH}_2)_7\text{CH}=\text{CH}_2$	$\text{CH}_3(\text{CH}_2)_8\text{CH}_2\text{NH}_2$	84 (78)
		91 (72)
		72 (58)
		72 (78)
		85 (59)
		96 (86) <sup>d</sup>
$\text{CH}_3\text{OC}(=\text{O})\text{-(CH}_2)_5\text{CH}=\text{CH}_2$	$\text{CH}_3\text{OC}(=\text{O})\text{-(CH}_2)_6\text{CH}_2\text{NH}_2$	76 (49)

<sup>a</sup> The alkenes were converted to the corresponding organoboranes by reaction with  $\text{BH}_3\text{-THF}$ . <sup>b</sup> Isolated yields based on ammonium hydroxide. The yields listed are based on reactions utilizing 1 equiv of ammonium hydroxide per equivalent of organoborane. <sup>c</sup> Yields in parentheses are isolated yields based on 2 equiv of ammonium hydroxide per equivalent of organoborane. <sup>d</sup> See ref 12.

ion in the presence of a mild oxidizing agent such as chloramine-T.<sup>5</sup> The reaction presumably proceeds through the intermediacy of iodine monochloride or some form of electropositive iodine.

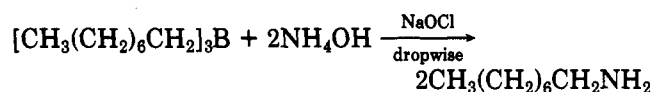


We report that organoboranes react with ammonium hydroxide in the presence of sodium hypochlorite (bleach).



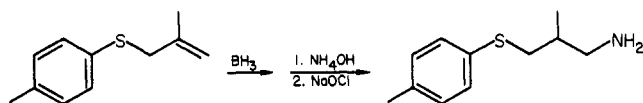
The reaction presumably proceeds via the in situ formation of chloramine.<sup>6</sup> The reaction provides a convenient synthesis for a variety of amines from readily available starting materials.

The organoborane is prepared via hydroboration, aqueous ammonium hydroxide is added, and then aqueous sodium hypochlorite (bleach) is added to the mixture. The



alkyl amines are formed in good yield. Our results parallel those obtained by Brown in that two of the alkyl groups in the trialkylborane may be converted to the corresponding amine.

The mild and convenient conditions of this reaction make it ideally suited for the synthesis of functionally substituted molecules. Thus 3-(*p*-tolylthio)-2-methyl-1-propene is readily converted to the corresponding amine in a one-pot synthesis.



Our results are summarized in Table I.

(6) Coleman, G. H.; Johnson, H. C. *Inorg. Synth.* 1939, 1, 59.

## Experimental Section

Routine NMR spectra were recorded on a Varian Associates T-60 spectrometer. All chemical shifts are reported in parts per million downfield from  $\text{Me}_4\text{Si}$ . The mass spectra were obtained with a HP-5982-A gc-mass spectrometer.

Commercially available samples (Aldrich) of 1-octene, 1-decene, 2-methyl-1-pentene, norbornene, cyclohexene, saffrole, methyl 10-undecenoate were distilled prior to use. 5-Benzyloxy-1-pentene and 3-(*p*-tolylthio)-2-methyl-1-propene were prepared according to published procedures.<sup>7</sup>

**Hydroboration. General Procedure.** The alkene (30 mmol) was dissolved in 10 mL of THF in a dry, 100-mL,  $\text{N}_2$ -flushed, round-bottomed flask equipped with a septum inlet and a magnetic stirring bar. The solution was cooled to  $0^\circ\text{C}$  and  $\text{BH}_3\text{-THF}$  (10 mmol, 5.2 mL of a 1.9 M solution) was added via syringe. The solution was stirred for 1–3 h and allowed to warm to room temperature.

**Amination. General Procedure.** The organoborane (10 mmol) was cooled to  $0^\circ\text{C}$  while maintaining a nitrogen atmosphere, aqueous ammonium hydroxide (10 mmol, 4.9 mL of a 2.05 M solution) was added, and aqueous sodium hypochlorite (bleach; 12 mmol, 15.39 mL of a 0.78 M solution)<sup>8</sup> was then added dropwise. (A light, white precipitate normally forms at this stage.) The mixture was stirred at  $0^\circ\text{C}$  for 15 min and then allowed to warm to room temperature.

The reaction mixture was made acidic with hydrochloric acid (10%) and then extracted with two 50-mL portions of ether. The aqueous layer was then made alkaline with sodium hydroxide (3 N) and the product extracted with two 75-mL portions of ether. The ether layers were combined, washed with saturated aqueous sodium chloride solution, and dried over anhydrous potassium hydroxide. Removal of the solvent yielded the product amine.

The aminations were repeated with 2 equiv of ammonium hydroxide. The yields are summarized in Table I.

**1-Aminooctane.** 1-Octene (30 mmol, 3.37 g) was hydroborated with  $\text{BH}_3\text{-THF}$  (10 mmol) for 1 h. The amination was carried out as described in the general procedure to yield 1.23 g (95%) of 1-aminooctane: melting point of picrate derivative,  $110^\circ\text{C}$  (lit.<sup>9</sup> mp  $112^\circ\text{C}$ ); NMR ( $\text{CDCl}_3$ )  $\delta$  0.95 (m, 3 H,  $\text{CH}_3$ ), 1.1–1.6 (envelope, 12 H, alkyl), 2.1 (s, 2 H,  $\text{NH}_2$ ), 2.36–2.7 (br s, 2 H,  $\text{CH}_2\text{NH}_2$ ).

**1-Aminodecane.** 1-Decene (30 mmol, 4.21 g) was hydroborated with  $\text{BH}_3\text{-THF}$  (10 mmol) for 1 h. The amination was carried out as described in the general procedure to yield 1.31 g (84%) of 1-aminodecane: melting point of picrate derivative,  $118^\circ\text{C}$  (lit.<sup>9</sup> mp  $118^\circ\text{C}$ ); NMR ( $\text{CDCl}_3$ )  $\delta$  0.95 (m, 3 H,  $\text{CH}_3$ ), 1.1–1.4 (envelope, 16 H, alkyl), 1.8–1.9, (br s, 2 H,  $\text{NH}_2$ ), 2.7–2.9 (br t, 2 H,  $\text{CH}_2\text{NH}_2$ ).

**Aminocyclohexane.** Cyclohexene (30 mmol, 2.46 g) was hydroborated with  $\text{BH}_3\text{-THF}$  (10 mmol) at  $50^\circ\text{C}$  for 3 h. The amination was carried out as described in the general procedure to yield 0.90 g (91%) of aminocyclohexane: melting point of picrate derivative,  $159^\circ\text{C}$  (lit.<sup>10</sup> mp  $158\text{--}159^\circ\text{C}$ ); mass spectrum,  $m/e$  99.2 (calcd 99.2); NMR ( $\text{CDCl}_3$ )  $\delta$  1.0–2.0 (br m, 11 H, cyclohexyl), 1.3 (s, 2 H,  $\text{NH}_2$ ), 2.4–2.8 (br m, 1 H,  $\text{CHNH}_2$ ).

**1-Amino-2-methylpentane.** 2-Methyl-1-pentene (30 mmol, 2.53 g) was hydroborated with  $\text{BH}_3\text{-THF}$  (10 mmol) for 1 h. The amination was carried out as described in the general procedure to yield 0.72 g (72%) of 1-amino-2-methylpentane: melting point of the picrate derivative,  $148.5^\circ\text{C}$ ; mass spectrum,  $m/e$  101.1 (calcd 101.1); NMR ( $\text{CDCl}_3$ )  $\delta$  0.8–1.0 (m, 6 H,  $\text{CH}_3$ ), 1.1–1.6 (m, 5 H, alkyl), 1.8–2.0 (m, 2 H,  $\text{NH}_2$ ), 2.5–2.7 (br t, 2 H,  $\text{CH}_2\text{NH}_2$ ).

**2-Aminonorbornene.** Norbornene (30 mmol, 2.83 g) was hydroborated with  $\text{BH}_3\text{-THF}$  (10 mmol) at  $25^\circ\text{C}$  for 2 h. The amination was carried out as described in the general procedure to yield 0.80 g (72%) of 2-aminonorbornene: melting point of picrate derivative,  $172^\circ\text{C}$  (lit.<sup>11</sup> mp  $174^\circ\text{C}$ ); mass spectrum,  $m/e$  111.4 (calcd 111.1); NMR ( $\text{CDCl}_3$ )  $\delta$  0.8–1.85 (br m, 8 H, alkyl),

(7) Kabalka, G. W.; Gooch, E. E. *J. Org. Chem.* 1980, 45, 3578.

(8) We used commercial grade bleach. The concentration of sodium hypochlorite was determined by using the procedure published by Ayres, G. H. "Quantitative Chemical Analysis," Harper and Row: New York, 1968; p 668.

(9) Adamson, D. W.; Kenner, J. *J. Chem. Soc.* 1934, 838.

(10) Breuer, G.; Schnitzer, J. *Monatsh. Chem.* 1936, 68, 301.

(11) Alder, K.; Stein, G. *Justus Liebigs Ann. Chem.* 1936, 525, 183.

2.0 (br s, 1 H, bridgehead), 2.1 (s, 2 H, NH<sub>2</sub>), 2.2 (s, 1 H, bridgehead), 2.8 (m, 1 H, CHNH<sub>2</sub>).

**3-(*p*-Tolylthio)-2-methyl-1-aminopropane.** 3-(*p*-Tolylthio)-2-methyl-1-propene (12 mmol, 2.14 g) was hydroborated with BH<sub>3</sub>-THF (4 mmol) for 1 h. The amination was carried out as described in the general procedure to yield 0.67 g (85%) of 3-(*p*-tolylthio)-2-methyl-1-aminopropane; mass spectrum, *m/e* 195.3 (calcd 195.3); NMR (CDCl<sub>3</sub>) δ 1.1 (t, 3 H, CH<sub>3</sub>), 1.4-1.8 (m, 3 H, CH and NH<sub>2</sub>), 2.2 (s, 3 H, ArCH<sub>3</sub>), 2.5-3.0 (br m, 4 H, CH<sub>2</sub>S and CH<sub>2</sub>NH<sub>2</sub>), 7.1 (A<sub>2</sub>X<sub>2</sub>', 4 H, ArH).

**3-[3,4-(Methylenedioxy)phenyl]-1-aminopropane.** Safrole (30 mmol, 4.87 g) was hydroborated with BH<sub>3</sub>-THF (10 mmol) for 1 h. The amination was carried out as described in the general procedure to yield 1.71 g (96%) of 3-[3,4-(methylenedioxy)phenyl]-1-aminopropane;<sup>12</sup> melting point of picrate derivative, 150 °C; mass spectrum, *m/e* 179.7 (calcd 179.2); NMR (CDCl<sub>3</sub>) δ 1.5-2.2 (m, 6 H, Ar CH<sub>2</sub>CH<sub>2</sub>CH<sub>2</sub>NH<sub>2</sub> and NH<sub>2</sub>), 2.5-2.7 (m, 2 H, CH<sub>2</sub>NH<sub>2</sub>), 5.9 (s, 2 H, OCH<sub>2</sub>O), 6.7 (s, 3 H, ArH).

**Methyl 11-Aminoundecanoate.** Methyl 10-undecenoate (30 mmol, 5.95 g) was hydroborated with BH<sub>3</sub>-THF (10 mmol) for 1 h. The amination was carried out as described in the general procedure to yield 1.64 g (76%) of methyl 11-aminoundecanoate; melting point of picrate derivative, 112 °C; mass spectrum, *m/e* 215 (calcd 215.3); NMR (CDCl<sub>3</sub>) δ 1.1-1.6 (s, 16, alkyl), 1.8-2.4 (m, 4 H, CH<sub>2</sub>C=O and NH<sub>2</sub>), 2.6-2.9 (m, 2 H, CH<sub>2</sub>NH<sub>2</sub>), 3.7 (s, 3 H, OCH<sub>3</sub>).

**Acknowledgment.** We thank the Department of Energy (DE-AS05-80-EV10363) for support of this research.

**Registry No.** 1-Octene, 111-66-0; 1-decene, 872-05-9; cyclohexene, 110-83-8; 2-methyl-1-pentene, 763-29-1; norbornene, 498-66-8; 3-(*p*-tolylthio)-2-methyl-1-propene, 54844-24-5; safrole, 94-59-7; methyl 10-undecanoate, 111-81-9; triacetylborane, 3248-78-0; tridecylborane, 1188-96-1; tricyclohexylborane, 1088-01-3; tri(2-methylpentan-1-yl)borane, 1188-50-7; tri-2-norbornylborane, 14289-75-9; tri[3-(*p*-tolylthio)-2-methylpropan-1-yl]borane, 78498-53-0; tri[3-(1,3-benzodioxol-5-yl)propan-1-yl]borane, 78498-54-1; tri[(10-carboxymethoxy)decane-1-yl]borane, 63399-92-8; 1-aminooctane, 111-86-4; 1-aminooctane picrate, 78498-55-2; 1-aminodecane, 2016-57-1; 1-aminodecane picrate, 78498-56-3; aminocyclohexane, 108-91-8; aminocyclohexane picrate, 17623-38-0; 1-amino-2-methylpentane, 13364-16-4; 1-amino-2-methylpentane picrate, 78498-57-4; 2-aminonorborene, 822-98-0; 2-aminonorborene picrate, 1485-53-6; 3-(*p*-tolylthio)-2-methyl-1-aminopropane, 78498-58-5; 3-[3,4-(methylenedioxy)phenyl]-1-aminopropane, 78498-59-6; 3-[3,4-(methylenedioxy)phenyl]-1-aminopropane picrate, 78498-60-9; 1-[3,4-(methylenedioxy)phenyl]-2-aminopropane, 4764-17-4; methyl 11-aminoundecanoate, 28691-27-2; methyl 11-aminoundecanoate picrate, 78498-61-0; ammonium hydroxide, 1336-21-6.

(12) The product contains approximately 15% of the 2-amino derivative. This is a result of the decrease in regioselectivity of the hydroboration reaction due to the inductive effect of the phenyl ring. Primary amines synthesized via this method normally contain only small amounts of the 2-amino isomer.

#### Aminoglycoside Antibiotics. 4. Regiospecific Partial Synthesis of Ribostamycin and 4''-Thioribostamycin

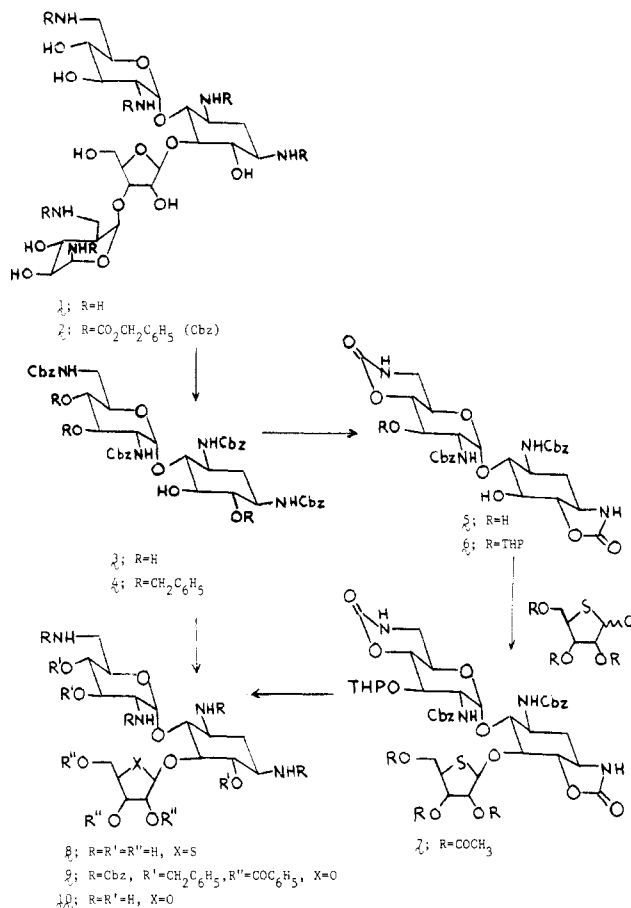
Virendra Kumar and William A. Remers\*

Department of Pharmaceutical Sciences, University of Arizona, Tucson, Arizona 85721

Received April 8, 1981

In an earlier paper in this series we described the regiospecific synthesis of ribostamycin (10) from neamine.<sup>1</sup> This synthesis was based on protecting the functional groups of neamine in such a manner that only the 5-

Scheme I



hydroxyl group was free for glycosidic linking with a suitable 1-ribosyl chloride. In order to obtain the appropriately protected neamine derivative (6), we treated tetra-*N*-(carbobenzyloxy)neamine (3) with sodium hydride to give a bis(cyclic carbamate) derivative 5, which had both the 6- and 3'-hydroxyl groups free (see Scheme I). Selective protection of the 3'-hydroxyl group was surprisingly effective with dihydropyran and *p*-toluenesulfonic acid. The product 6 was obtained in 80% yield. In fact, all of the steps in the synthesis of ribostamycin went in satisfactory yield except for the final deprotection, which gave 19% for the sequence of alkaline hydrolysis and catalytic hydrogenolysis.<sup>1</sup>

With a good synthesis of 6 accomplished, it was desirable to establish its further utility for aminoglycoside synthesis. One structure that interested us was the 4''-thio analogue 8 of ribostamycin. No thioaminoglycosides had been prepared prior to the start of our investigation (although one investigation<sup>2</sup> has been published in the meantime). We anticipated that the 4''-thio analogue would be biologically active by analogy to the good antibacterial activity observed when 4-thioribose was used in place of ribose in certain purine nucleosides.<sup>3,4</sup> Thus, 2,3,5-tri-*O*-acetyl-4-thioribosyl 1-chloride was prepared by the published method<sup>5</sup> and treated with 6, mercuric cyanide, and Drierite in methylene chloride. The reaction went to completion and workup gave 58% of protected 4''-thioribostamycin derivative 7, obtained as a single anomer. This anomer is presumed to be β according to the trans rule.<sup>3</sup> Deprotection by barium hydroxide hydrolysis and catalytic hy-

(2) Kavadias, G.; Droghini, R. *Can. J. Chem.* 1978, 56, 2743.

(3) Bobek, M.; Whistler, R. L.; Block, A. *J. Med. Chem.* 1970, 13, 411.

(4) Bobek, M.; Whistler, R. L.; Block, A. *J. Med. Chem.* 1972, 15, 168.

(5) Urbas, B.; Whistler, R. L. *J. Org. Chem.* 1966, 31, 813.

(1) Kumar, V.; Remers, W. A. *J. Org. Chem.* 1978, 43, 3327.