Registry No.—**1**, 28917-02-4; **2a**, 33780-61-9; **2b**, 33777-15-0; **3a**, 33777-16-1; **3b**, 33777-17-2; **3c**, 33777-18-3; **3d**, 33777-19-4; **3e**, 33777-20-7; **3f**, 33777-21-8; **4a**, 33777-22-9; **4a** acetate, 33777-23-0; **4b**, 33777-24-1; **4c**, 33777-25-2; **4d**, 33777-26-3; **4e**, 33780-62-0; **4f**, 33780-63-1; **4g**, 33780-64-2.

Acknowledgments.—This work was supported by NIH Grants Al-00226 and FR 5 S01 RRO5621. The authors also wish to thank Dr. T. C. McMorris for helpful discussions.

Synthesis of Imino Derivatives of *Cecropia* Juvenile Hormone[1]

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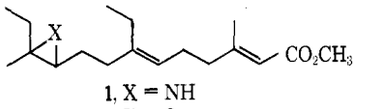
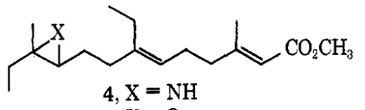
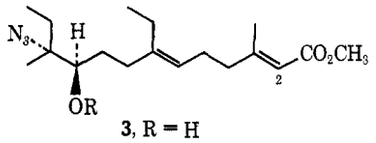
In connection with our studies of the effects of the juvenile hormones[2] of *Hyalophora cecropia* on insect metamorphosis, we were encouraged to devise an efficient synthesis for the imino analog **1**, particularly in view of a report[3a] of the preparation of **1**, by an undetailed method,[3b] and of its interesting biological properties.



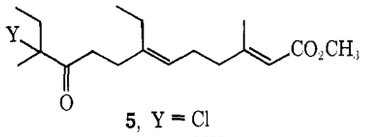
1, X = NH
2, X = O



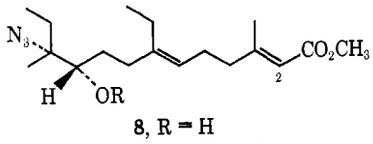
4, X = NH
11, X = O



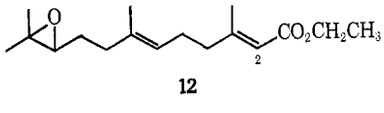
3, R = H
9, R = SO_2CH_3



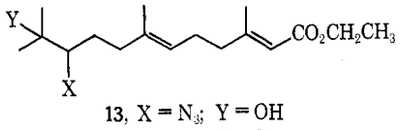
5, Y = Cl
6, Y = NH_2
7, Y = N_3



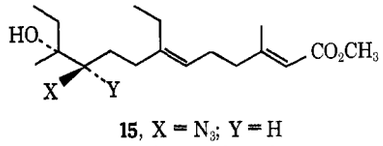
8, R = H
10, R = SO_2CH_3



12



13, X = N_3; Y = OH
14, X = OH; Y = N_3



15, X = N_3; Y = H
16, X = H; Y = N_3

Initial attempts to prepare **1** from the racemic Röller juvenile hormone **2** *via* opening of the epoxide ring with either azide ion or with hydrazoic acid under a variety of conditions failed, although a later variation (see below) did allow the preparation of **1** by this method but in poor yield. In this connection it was found that treatment of **2** with excess lithium azide in dimethoxyethane–acetic acid at 25° for 24 hr failed to give any of the required azido alcohol **3** (*cf.* 3b).

An efficient synthesis of the racemic imino C_{18} juvenile hormone (JH) analogs **1** and **4** was developed starting with the available chloro ketone **5**.[4] Since initial attempts to convert **5** to the amino ketone **6** were unsuccessful, we prepared the corresponding azido ketone **7** from the chloro ketone **5** in 90% yield using sodium azide in dimethylformamide (100° for 3 hr). Reduction of **7** with 1 equiv of sodium borohydride in methanol gave a mixture of the diastereoisomeric azido alcohols **3** and **8** (ratio 3:2), which was separated by thin layer chromatography in an overall combined yield of 65% from **5**. Each pure alcohol was separately converted into its corresponding azido mesylate using methanesulfonyl chloride in triethylamine–pentane[5] (yield 80–85% after purification *via* preparative tlc). The final conversion of the azido mesylates **9** and **10** into the aziridines **1** and **4**, respectively, was best carried out by reduction using hydrazine hydrate and Raney nickel in ethanol.[6] Preparative tlc of the reduction products gave **1** (62% yield) and **4** (55% yield) in high purity. Use of an alternative reduction system, cobaltous bromide–dipyridyl–sodium borohydride,[7] also gave the aziridines, but some selective saturation[8] of the α,β-unsaturated ester double bond also occurred. The two aziridines **1** and **4** could be differentiated by glc and by the different chemical shift of the C-11 methyl in their nmr spectra.

The diastereoisomeric azido alcohols **3** and **8**, and thus the aziridines derived from them, were assigned their stereochemistry on the basis of the correlations with the synthetic trans,trans,cis hormone **2** and the all-trans isomer **11**, respectively,[4] providing also an alternative synthesis of the imino JH analogs. These correlations were established using an epoxide opening

(1) Contribution No. 5 from the Research Laboratory of Zoecon Corp. This work was presented in part at the XXIII International Congress of Pure and Applied Chemistry, Boston, Mass., July 1971.

(2) H. Röller, K. H. Dahm, C. C. Sweeley, and B. M. Trost, *Angew. Chem., Int. Ed. Engl.*, **6**, 179 (1967); A. S. Meyer, H. A. Schneidermann, E. Hanzmann, and J. H. Ko, *Proc. Nat. Acad. Sci. U. S.*, **60**, 853 (1968).

(3) (a) Report by Dr. E. J. Corey at the International Conference on Juvenile Hormones, Basel, Switzerland, Oct 1970; (b) L. M. Riddiford, A. M. Ajami, E. J. Corey, H. Yamamoto, and J. E. Anderson, *J. Amer. Chem. Soc.*, **93**, 1815 (1971).

(4) P. Loew, J. B. Siddall, V. L. Spain, and L. Werthemann, *Proc. Nat. Acad. Sci. U. S.*, **67**, 1462, 1824 (1970).

(5) R. K. Crossland and K. L. Servis, *J. Org. Chem.*, **35**, 3195 (1970).

(6) R. D. Guthrie and D. Murphy, *J. Chem. Soc.*, 5288 (1963); K. Ponsold, *Chem. Ber.*, **97**, 3524 (1964).

(7) K. Ponsold, *J. Prakt. Chem.*, **36**, 148 (1967).

(8) T. Satoh, J. Nanba, and S. Suzuki, *Chem. Pharm. Bull.*, **19**, 817 (1971).

method developed initially with the model epoxide **12**.[9] When **12** was treated with an excess of lithium azide and acetic acid (azide:acid = 2:1) in hexamethylphosphoramide (HMPA) at room temperature for 6 days, the azido alcohols **13** and **14** were isolated in yields of 42 and 18%, respectively. At 95° (20 hr) only **14** could be isolated (in 11% yield) and no other product could be identified. At the higher temperature some 2-ene isomerization also occurred. Reaction of racemic *Cecropia* hormone **2** under the above conditions in HMPA (7 days at 25°) gave the azido alcohols **3** (20% yield) and **15** (60% yield). At 105° (19 hr) only **3** could be isolated in 10% yield (with some isomerization to cis at Δ^2). Similarly, the all-trans epoxide **11** at room temperature gave *only* the azido alcohols **8** (17% yield) and **16** (41% yield) with no detectable **3** or **15**.

To establish the trans nature of the epoxide ring opening under our reaction conditions, cyclohexane epoxide was treated with lithium azide–acetic acid (2:1) in HMPA (4 days at room temperature). The only product was shown to be *trans*-2-azidocyclohexanol, identical with material prepared as described[10] in the literature with sodium azide in refluxing aqueous dioxane. However, it is necessary to point out that the epoxide **12** was recovered unchanged under the latter conditions and treatment of **12** with lithium azide in HMPA in the absence of acetic acid at room temperature gave a mixture which contained a negligible proportion of the required ring-opening product **14**. Thus the above correlations depend in some way on the presence of acid in the reaction mixture used for the epoxide ring opening.

The biological properties of the aziridines **1** and **4** have been investigated in detail and the results are reported in part elsewhere.[1]

Experimental Section

Infrared spectra were determined with a UNICAM SP 200 G infrared spectrophotometer; nmr spectra were obtained using a Varian T-60 spectrometer with TMS as internal standard. The gas chromatograph used was a Hewlett-Packard Model 402 equipped with flame detector. Microanalyses were performed by Bernhardt Microanalytical Laboratories, Elbach, West Germany.

Methyl 11-Azido-3,11-dimethyl-7-ethyl-10-oxo-2-*trans*,6-*trans*-tridecadienoate (7).—To 4.32 g (13.2 mmol) of chloro ketone **5**[4] in 40 ml of dry dimethylformamide under argon was added 0.91 g (14 mmol) of sodium azide and the mixture was heated at 90° for 6 hr. After sitting overnight at room temperature, the suspension was poured into water and extracted three times with pentane–ether (9:1). The combined organic fractions were washed with saturated sodium chloride, dried ($MgSO_4$), and evaporated to give the azido ketone **7** (4.0 g, 91% yield): ir (CCl_4) 2100 ($-N_3$), 1720 (ester C=O), 1710 (shoulder, ketone C=O), 1650 cm^{-1} (C=C); nmr ($CDCl_3$) δ 1.40 (s, 3, CH_3CN_3), 2.18 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.72 (s, 3, $COOCH_3$), 5.10 (m, 1, C=C**H**), and 5.72 ppm (broad s, 1, C=C**H**COOR).

Anal. Calcd for $C_{18}H_{29}N_3O_3$: C, 64.45; H, 8.72; N, 12.53. Found: C, 64.27; H, 8.69; N, 12.49.

Reduction of Azido Ketone 7.—To 4.0 g of the ketone **7** in 25 ml of methanol was added 300 mg of sodium borohydride. After 45 min, reduction was quenched by the addition of ether and water, the aqueous phase was twice more extracted with ether, and the combined ether fractions were washed to neutrality (saturated sodium chloride). After drying ($MgSO_4$) 3.85 g of crude alcohol mixture was recovered. The diastereoisomers **3** and **8** were separated by use of preparative tlc: each 1 m × 20 cm plate (1.3 mm PF silica gel) was charged with 250 mg of the mixture of **3** and **8** and was developed five times with 12% ether in hexane. In this manner, it was possible to obtain from the above mixture 1.43 g of pure **3** (larger R_f) and 1.09 g of pure **8** (smaller R_f). This recovery (2.52 g) represents a 62% overall yield from azido ketone **7**.

Both diastereoisomers were completely characterized. **3** had ir (film) 3510 (OH), 2100 (N_3), 1720 (ester C=O), and 1640 cm^{-1} (C=C); nmr ($CDCl_3$) δ 0.97 (t, 6, J = 7 Hz, CH_3CH_2–), 1.23 (s, 3, CH_3CN_3), 2.18 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.72 (s, 3, $COOCH_3$), 5.14 (m, 1, C=C**H**), and 5.71 ppm (broad s, 1, C=C**H**COOR).

Anal. Calcd for $C_{18}H_{31}N_3O_3$: C, 64.06; H, 9.26; N, 12.45. Found: C, 64.25; H, 9.13; N, 12.44.

8 had ir (film) 3510 (OH), 2100 (N_3), 1720 (ester C=O), and 1640 cm^{-1} (C=C); nmr δ 0.97 (t, 6, J = 7 Hz, CH_3CH_2–), 1.28 (s, 3, CH_3CN_3), 2.17 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.71 (s, 3, $COOCH_3$), 5.15 (m, 1, C=C**H**), and 5.72 ppm (broad s, 1, C=C**H**COOR).

Anal. Calcd for $C_{18}H_{31}N_3O_3$: C, 64.06; H, 9.26; N, 12.45. Found: C, 64.26; H, 9.24; N, 12.40.

Conversion of Azido Alcohols 3 and 8 to the Methanesulfonates 9 and 10.—The azido alcohol **3** (1.14 g, 3.4 mmol), dissolved in 33 ml of 0.3 M triethylamine in pentane, was cooled to −10° under argon, and 0.58 ml (7.5 mmol) of methanesulfonyl chloride was added dropwise. After 1 hr the gummy suspension was poured into ice and ether, and the organic phase was washed successively with cold 5% hydrochloric acid, saturated sodium bicarbonate, and saturated sodium chloride solutions. After drying ($MgSO_4$), 1.45 g of crude material was isolated and applied directly to three 1 m × 20 cm silica gel PF preparative plates (1.3 mm thickness). After developing with 20% ethyl acetate in hexane, 1.09 g (2.64 mmol) of pure azido mesylate **9** (R_f 0.29) could be recovered (78% yield): ir (CCl_4) 2100 (N_3), 1720 (C=O), 1650 (C=C), 1365 and 1190 cm^{-1} (OSO_2); nmr ($CDCl_3$) δ 0.98 (t, 6, J = 7 Hz, CH_3CH_2–), 1.28 (s, 3, CH_3CN_3), 2.17 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.15 (s, 3, CH_3SO_2O), 3.72 (s, 3, $COOCH_3$), 4.60 (t, 1, J = 6 Hz, HCOMs), 5.15 (m, 1, C=C**H**), and 5.71 ppm (broad s, 1, C=C**H**COOR).

Anal. Calcd for $C_{19}H_{33}N_3O_5S$: C, 54.92; H, 8.01; N, 10.11; S, 7.70. Found: C, 54.86; H, 7.97; N, 10.21; S, 7.80.

The preparation of the second diastereoisomer **10** was identical with that of **9**. Thus 0.90 g (2.67 mmol) of azido alcohol **8** gave 0.96 g (2.30 mmol, 86% yield) of pure azido mesylate **10**: ir (film) 2100 (N_3), 1720 (ester C=O), 1640 (C=C), 1350, and 1180 cm^{-1} (OSO_2); nmr ($CDCl_3$) δ 0.98 (t, 6, J = 7 Hz, CH_3CH_2–), 1.37 (s, 3, CH_3CN_3), 2.18 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.15 (s, 3, CH_3SO_2O), 3.72 (s, 3, $COOCH_3$), 4.64 (t, 1, J = 6 Hz, HCOMs), 5.17 (m, 1, C=CH), and 5.72 ppm (broad s, 1, C=C**H**COOR).

Anal. Calcd for $C_{19}H_{33}N_3O_5S$: C, 54.92; H, 8.01; N, 10.11; S, 7.70. Found: C, 55.05; H, 8.00; N, 10.26; S, 7.94.

Methyl 3,11-Dimethyl-10,11-*cis*-imino-7-ethyl-2-*trans*,6-*trans*-tridecadienoate (1).—To 1.10 g (2.65 mmol) of mesylate **9** in 30 ml of ethanol under argon was added 2 ml of 85% hydrazine hydrate and about 0.2 g of Raney nickel. After stirring for 3 hr at room temperature the catalyst was filtered off and ether and saturated sodium chloride were added to the filtrate. The organic phase was washed to neutrality with brine and dried ($MgSO_4$). The crude product (712 mg) was purified by chromatography on two 1 m × 20 cm preparative silica gel plates (1.3 mm thickness PF), developed with a benzene–methanol–diethylamine system (94:5.4:0.6), to give 483 mg (62% yield) of the aziridine **1**: ir (film) 1720 (ester C=O) and 1640 cm^{-1} (C=C). nmr ($CDCl_3$) δ 0.98 (t, 6, J = 7 Hz, CH_3CH_2), 1.22 [s, 3, CH_3C–N(imino)], 2.18 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.72 (s, 3, $COOCH_3$), 5.14 (m, 1, C=C**H**), and 5.72 ppm (broad s, 1, C=C**H**COOR); mass spectrum (70 eV) m/e (rel intensity) M^+ 293 (1), 180 (13), 98 (100).

Anal. Calcd for $C_{18}H_{31}NO_2$: C, 73.67; H, 10.65; N, 4.77. Found: C, 73.48; H, 10.51; N, 4.60.

Methyl 3,11-Dimethyl-10,11,*trans*-imino-7-ethyl-2-*trans*,6-*trans*-tridecadienoate (4).—Azido mesylate **10** (0.88 g, 2.12 mmol) on reduction with hydrazine hydrate and Raney nickel in ethanol as above gave 0.54 g of crude **4**. Preparative tlc gave 339 mg (55% yield) of pure **4**: ir (film) 1720 (ester C=O) and 1640 cm^{-1} (C=C); nmr ($CDCl_3$) δ 0.97 (t, 6, J = 7 Hz, CH_3CH_2), 1.15

(9) R. J. Anderson, C. A. Henrick, and J. B. Siddall, unpublished work. The corresponding methyl ester has been prepared; see W. S. Bowers, M. J. Thompson, and E. C. Uebel, *Life Sci.*, **4**, 2323 (1965); E. E. van Tamelen, M. A. Schwartz, E. J. Hessler, and A. Storni, *Chem. Commun.*, 409 (1966).

(10) C. A. VanderWerf, R. H. Heisler, and W. E. McEwen, *J. Amer. Chem. Soc.*, **76**, 1231 (1954).

[s, 3, CH_3C–N(imino)], 2.18 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.71 (s, 3, $COOCH_3$), 5.12 (m, 1, C=CH), and 5.72 (broad s, 1, C=CHCOOR); mass spectrum (70 eV) m/e M^+ 293.

Anal. Calcd for $C_{18}H_{31}NO_2$: C, 73.67; H, 10.65; N, 4.77. Found: C, 73.42; H, 10.46; N, 4.89.

Reduction of 9 and 10 with Cobaltous Bromide–Sodium Borohydride.—An alternate method of reduction of the mixture of azido mesylates (**9** and **10**) was also investigated. The reducing agent[7] was first prepared as follows: 146 mg (0.67 mmol) of anhydrous cobaltous bromide was dissolved in 10 ml of absolute ethanol (blue solution) and 312 mg (2 mmol) of dipyridyl was added (orange solution). To this solution at 0° under argon was added 76 mg (2 mmol) of sodium borohydride (blue-black solution). In a second flask, 35 mg (0.085 mmol) of a mixture of azido mesylates **9** and **10** was dissolved in 0.8 ml of dry ethanol at 0° under argon and to this solution was added dropwise 0.7 ml of the reducing solution. After 0.5 hr, the solution was poured into ether and water, and the organic phase was washed to neutrality (saturated sodium chloride) and dried ($MgSO_4$). The residue was applied to one 20 × 20 cm silica gel plate (0.5 mm thickness) and developed with a benzene–methanol–diethylamine system (94:5.4:0.6); 7 mg (R_f 0.29) of aziridines **1** and **4** was recovered. However, some saturation of the α,β-unsaturated ester function also occurred (to the extent of about 25%).

Ring Opening of 12 with Lithium Azide–Acetic Acid.—The epoxide **12** (100 mg, 0.36 mmol), lithium azide (175 mg, 3.6 mmol), and acetic acid (0.10 ml, 1.8 mmol) were stirred together in 4 ml of dry hexamethylphosphoramide for 6 days at room temperature under argon. Hexane–ether (95:5) and water were added and the phases were separated; the organic phase was washed to neutrality (saturated NaCl) and dried ($MgSO_4$) and the solvent was removed. The crude residue was applied to one 20 × 20 cm preparative silica gel plate (1.3 mm thickness) and developed twice with 20% ethyl acetate in hexane. The upper product band (R_f 0.38, 19 mg) was shown to be **14** and the lower band (R_f 0.30, 46 mg) the position isomer **13**. In addition, 5 mg of starting material **12** was recovered.

Isomer **13** had ir (CCl_4) 3630, 3590, 3520 (m, OH), 2110 (N_3), 1725 (ester C=O), 1655 cm^{-1} (C=C); nmr ($CDCl_3$) δ 1.23 [s, 6, $(CH_3)_2COH$], 1.27 (t, 3, J = 7 Hz, CH_3CH_2O–), 1.63 (broad s, 3, CH_3C=C), 2.17 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.12 (d of d, 1, HCN$_3$), 4.17 (q, 2, J = 7 Hz, $-CH_2O-$), 5.20 (m, 1, C=CH), and 5.70 ppm (broad s, 1, C=CHCOOR).

Anal. Calcd for $C_{17}H_{29}N_3O_3$: C, 63.13; H, 9.04; N, 12.99. Found: C, 63.31; H, 9.12; N, 12.92.

Isomer **14** had ir (CCl_4) 3590 (OH), 2110 (N_3), 1725 (ester C=O), and 1650 cm^{-1} (C=C); nmr ($CDCl_3$) δ 1.30 [s, 6, $(CH_3)_2CN_3$], 1.63 (broad s, 3, CH_3C=C), 2.18 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.35 (m, 1, HCOH), 4.18 (q, 2, J = 7 Hz, $-CH_2O-$), 5.20 (m, 1, C=CH), and 5.71 ppm (broad s, 1, C=CHCOOR).

Anal. Calcd for $C_{17}H_{29}N_3O_3$: C, 63.13; H, 9.04; N, 12.99. Found: C, 63.04; H, 8.94; N, 13.10.

On treatment of the two isomers separately with acetic anhydride–pyridine at room temperature for 6 hr, the top band (*i.e.*, **14**) gave an acetate [ir (CCl_4) 1740 cm^{-1} (acetate C=O); nmr ($CDCl_3$) δ 2.13 (s, 3, CH_3COO)] while the lower band gave only recovered starting material **13** (*via* infrared).

Ring Opening of 2 and 11.—Synthetic juvenile hormone **2**[4] (60 mg, 0.20 mmol), lithium azide (350 mg, 7.2 mmol), and glacial acetic acid (0.20 ml, 3.6 mmol) were dissolved in 4 ml of dry hexamethylphosphoramide and stirred under argon for 7 days at room temperature. Pentane–ether (95:5) and water were then added, and the organic phase was washed with 2 M sodium carbonate and saturated sodium chloride, dried ($MgSO_4$), and evaporated. The residue was placed on one 20 × 20 cm silica gel plate (1.3 mm PF) and developed with 12% ethyl acetate in hexane three times. In this manner two products were isolated: **3** (14 mg, 20% yield) and the position isomer **15** (40 mg, 59% yield). Azido alcohol **3** was identical with the faster eluting isomer obtained above from reduction of azido ketone **7**. Isomer **15** was completely characterized: ir (CCl_4) 3630, 3590, 3520 (broad multiplet, OH), 2110 (N_3), 1725 (ester C=O), and 1655 cm^{-1} (C=C); nmr ($CDCl_3$) δ 0.93 (t, 3, J = 7 Hz, CH_3CH_2–), 0.98 (t, 3, J = 7 Hz, CH_3CH_2), 1.15 (s, 3, CH_3COH), 2.18 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.22 (d of d, 1, HCN$_3$), 3.72 (s, 3, $COOCH_3$), 5.15 (m, 1, C=CH), and 5.72 ppm (broad s, 1, C=CHCOOR).

Anal. Calcd for $C_{18}H_{31}N_3O_3$: C, 64.06; H, 9.26; N, 12.45. Found: C, 64.29; H, 9.12; N, 12.30.

Similarly, the all-trans isomer **11**[4] (53 mg, 0.18 mmol), lithium azide (350 mg, 7.2 mmol), and glacial acetic acid (0.20 ml, 3.6 mmol) were dissolved in 4 ml of dry hexamethylphosphoramide and stirred for 9 days. Work-up as above gave a residue which was applied to one 20 × 20 cm silica gel plate (1.3 mm PF) and developed eight times with 10% ethyl acetate in hexane. Again, two bands were recovered and identified. The upper band was shown to be identical with that of the azido alcohol **8** (10 mg, 17% yield) and the lower band (25 mg, 41% yield) was shown to be that of the position isomer **16**: ir (CCl_4) 3630, 3590, 3530 (broad multiplet, OH), 2110 (N_3), 1730 (ester C=O), and 1655 cm^{-1} (C=C); nmr ($CDCl_3$) δ 0.93 (t, 3, J = 7 Hz, CH_3CH_2–), 0.98 (t, 3, J = 7 Hz, CH_3CH_2–), 1.18 (s, 3, CH_3COH), 2.18 (d, 3, J = 1 Hz, CH_3C=CCOOR), 3.18 (d of d, 1, HCN$_3$), 3.72 (s, 3, $COOCH_3$), 5.16 (m, 1, C=CH), and 5.71 ppm (broad s, 1, C=CHCOOR).

Anal. Calcd for $C_{18}H_{31}N_3O_3$: C, 64.06; H, 9.26; N, 12.45. Found: C, 64.22; H, 9.10; N, 12.20.

***trans*-2-Azidocyclohexanol.**—To 3.9 g (0.08 mol) of lithium azide and 2.3 ml (0.04 mol) of glacial acetic acid in 20 ml of hexamethylphosphoramide was added 2.0 g (0.02 mol) of cyclohexane oxide and the milky suspension was stirred at room temperature for 4 days. Pentane–ether (95:5) and 2 M sodium carbonate were added, the layers were separated, and the organic phase was washed to neutrality. After drying ($MgSO_4$), the solvent was removed and the residue was distilled, bp 95° (0.5 mm). This product (both prior to and after distillation) was homogeneous on three vpc columns (2 m 3% OV-225, 98°; 4 m 20% UCON 90M, 170°; 2 m 3% PDEAS, 100°) and was identical in all respects with a sample of *trans*-2-azidocyclohexanol prepared as described,[10] with sodium azide in hot aqueous dioxane.

Registry No.—**1**, 33780-87-9; **3**, 33780-88-0; **4**, 33780-89-1; **7**, 33780-90-4; **8**, 33780-91-5; **9**, 33780-92-6; **10**, 33886-27-0; **13**, 33886-28-1; **14**, 33780-93-7; **15**, 33780-94-8; **16**, 33780-95-9; *trans*-2-azidocyclohexanol, 10027-78-8.

The Synthesis of *trans*-3′-Methylnicotine[1a]

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Recently Rueppel and Rapoport reported that *dl*-1,3-dimethylpyrrolinium-3-$^{14}CH_3$ chloride (**1**) is incorporated into 3′-methylnicotine (**2**) by *Nicotiana glutinosa*.[2] The asymmetric center at C-2′ was assigned the *S* configuration on the basis of ORD and CD studies. However, the configuration at C-3′ remained unassigned. The superimposition of the nmr spectrum of *dl-trans*-3′-methylnicotine, synthesized in the present study, with the nmr spectrum of the biosynthesis product[3] establishes the absolute stereochemistry of the biosynthesis product as 2′*S*,3′*S* (**2a**). The nmr spectrum of **2a** displays in addition to the assignable signals for the NCH_3, CCH_3, and aromatic protons, a series of signals between δ 2.6 and 1.4 ppm integrating for five protons and a multiplet centered near δ 3.2 ppm integrating for one proton. The nmr spectrum of

(1) (a) Presented in part at the 162nd Meeting of the American Chemical Society, Washington, D. C., Sept 1971. (b) NDEA Predoctoral Fellow and American Foundation for Pharmaceutical Education Fellow.

(2) M. L. Rueppel and H. Rapoport, *J. Amer. Chem. Soc.*, **92**, 5528 (1970).

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