residue which was distilled to give **ethyl epilupininate** (Vb); ν_{max}^{neat} (conspicuous peaks not present in ir of ethyl lupininate) 1320, 1260, and 1150 cm^{-1}.

Epilupinine (Vc).—The entire quantity of ethyl epilupininate (Vb) prepared from ethyl lupininate (4.22 g, 21.6 mmol), was dissolved in absolute ether (15 ml) and added to a solution of lithium aluminum hydride (200 g, 52.7 mmol) in ether (75 ml). After the mixture was heated under gentle reflux for 1 hr, it was hydrolyzed by successive additions of water (2 ml), 15% aqueous sodium hydroxide solution (2 ml), and finally water (6 ml). The hydrolyzate was passed through a filter, and the ethereal phase was separated and dried. Evaporation of the ether left a residue which crystallized in the refrigerator, **epilupinine** (Vc): yield 2.80 g (76.4% over two steps); mp 78–79° (lit.[10] mp 77–78°).

trans-**1-Bromomethylquinolizidine** (Vd).[8]—Epilupinine (2.27 g, 14.0 mmol) was dissolved in benzene (15 ml), treated with phosphorus tribromide (1 ml), and heated under reflux for 2 hr. The mixture was cooled (ice added) and basified by careful addition of a 20% aqueous potassium hydroxide solution (30 ml). After separation of the benzene layer, the aqueous layer was extracted with several small portions of benzene. The combined and dried benzene solutions were evaporated, and the residue was distilled to provide *trans*-**1-bromomethylquinolizidine** (Vd): yield 2.43 g (75.0%); bp 100° (1 mm); ν_{max}^{neat} 2940, 2860, 2800, 2760, 2680, 1470, 1445, 1400, 1370, 1350, 1300, 1285, 1275, 1260, 1250, 1230, 1215, 1190, 1170, 1130, 1115, 1075, 1055, 1020, 970, 945, 880, 865, 845, and 775 cm^{-1}; nmr ($CDCl_3$) δ 3.34 (apparent d, $J \cong 4$ Hz, 2 H of bromomethyl group), 2.67 (m, 4 H), and 2.2–1.2 (complex envelope, 12 H).

(±)-**Lamprolobine** (I).—Potassium (700 mg, 17.9 mg-atoms) was dissolved in absolute ethanol (40 ml) and added to glutarimide (2.00 g, 17.7 mmol), and the solution was heated under reflux for 1 hr before it was evaporated to a residue of N-potassioglutarimide. *trans*-1-Bromomethylquinolizidine (3.00 g, 12.9 mmol) dissolved in dimethylformamide (30 ml) was added to the N-potassioglutarimide, and the mixture was heated under gentle reflux for 0.5 hr. After the mixture was allowed to cool to room temperature, it was cautiously added to water (150 ml), and the whole was extracted with several volumes of ether. The combined and dried ether extracts were evaporated to a residue which was taken up in a minimum volume of benzene and carefully washed onto the top of a column of alumina (Woelm, nonalkaline). Elution of the column with benzene, followed by careful evaporation of the solvent, gave (±)-lamprolobine (I) as a colorless oil: yield 1.78 g (52.1%); mass spectrum *m/e* 264 (M^+); infrared spectrum (CCl_4) superimposable upon that determine from a sample[10] of authentic (−)-lamprolobine. The synthetic material was further characterized as its picrate salt and was recrystallized from ethanol; mp 192–193° (racemic compound, since (−)-lamprolobine picrate has mp 153–154°[2]).

Anal. Calcd for $C_{21}H_{27}N_5O_9$: C, 51.11; H, 5.52; N, 14.33. Found: C, 51.38; H, 5.43; N, 14.33.

Registry No.—(±)-I, 22142-02-5; (±)-I picrate, 22142-03-6; IIb, 491-42-9; IIIa, 491-40-7; IIIb, 493-10-7.

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A Short Synthesis of the Sex Pheromone of the Pink Bollworm Moth

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Contribution No. 571 from the Central Research Laboratories, 3M Company, St. Paul, Minnesota 55101

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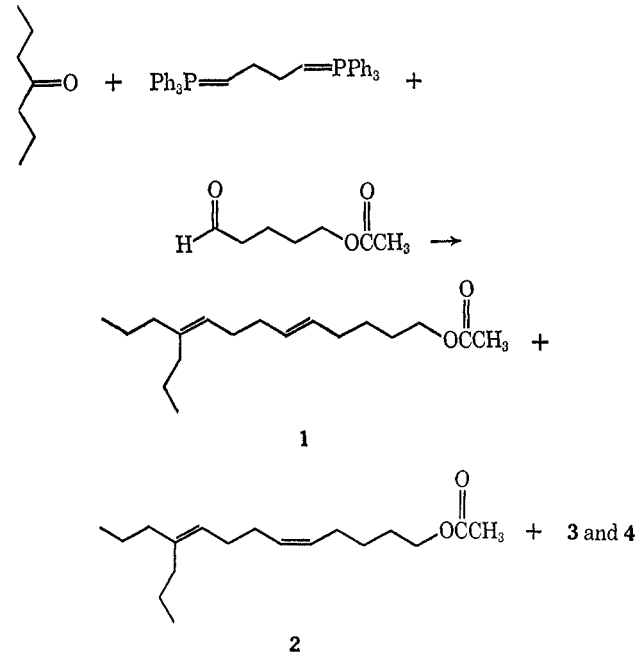
A valuable new technique for the survey of insect populations involves the use of sex pheromones to lure them to traps. The potency of these compounds is high; for example, the behavioral response threshold is in the region of 10^{-7}–10^{-11} g on the stimulus source for the silkworm moth, gypsy moth, and cabbage looper moth.[1]

In 1966, Jones, Jacobson, and Martin reported the isolation, structure determination, and synthesis of the sex pheromone of the pink bollworm moth, *Pectinophora gossypiella* (Saunders), 10-*n*-propyl-*trans*-5,9-tridecadienyl acetate (**1**).[2] This 11-step synthesis afforded a 0.2% overall yield. Another synthesis of this compound was reported[3] but the product was not biologically active, due to masking by the *cis* isomer.[4] A third synthesis was reported[5] involving seven steps and giving an 18% overall yield (1% overall conversion).



We have prepared compound **1** in 7% yield (overall conversion). The reaction of the difunctional Wittig reagent from tetramethylene-1,4-bistriphenylphosphonium bromide with 4-heptanone and 5-acetoxyvaleraldehyde gave the *cis*- and *trans*-10-*n*-propyl-5,9-tridecadienyl acetate (**1** and **2**) in addition to small amounts of 4,9-di-*n*-propyl-4,8-dodecadiene (**3**) and 5,9-tetradecadiene-1,14-diol diacetate (**4**). Isomerization of the mixture of **1** and **2** with selenium followed by silver nitrate–silica gel chromatography gives the pure *trans* isomer, while chromatography without isomerization affords the pure *cis* isomer and some pure *trans* isomer. The pure **1** from the Wittig reaction, the pure **1** from the isomerization reaction, and the isomerization product mixture were tested. Each gave a response in 75% of males exposed to the samples by the pipet method by which known pure **1** gives a 75% response.[4]

(1) H. H. Shorey, L. K. Gaston, and R. N. Jefferson, *Advan. Pest Control Res.*, **8**, 104 (1968).
(2) W. A. Jones, M. Jacobson, and D. F. Martin, *Science*, **152**, 1516 (1966); W. A. Jones and M. Jacobson, *ibid.*, **159**, 99 (1968).
(3) K. Eiter, E. Truscheit, and M. Boness, *Ann.*, **709**, 29 (1967).
(4) M. Jacobson, *Science*, **163**, 190 (1969).
(5) G. Pattenden, *J. Chem. Soc., C*, 2385 (1968).

Experimental Section[6]

5-Acetoxyvaleraldehyde.[7]—5-Bromo-*n*-pentyl acetate[8] (83.6 g, 0.40 mol), pyridine oxide (76.0 g, 0.80 mol), and sodium bicarbonate (67.2 g, 0.80 mol) were heated at reflux with vigorous stirring in toluene (500 ml) under nitrogen for 4 hr. The mixture was cooled and poured into water (2 l.). The organic layer was separated and the water layer was extracted with toluene. The combined toluene solution was distilled on a spinning-band column to give 28.6 g, (50%): bp 98° (12 mm); n^{28}D 1.4270; dinitrophenylhydrazone, mp 98–99° (lit.[9] mp 100°); nmr ($CDCl_3$) τ 0.23 (t, 1, J = 1.5 Hz), 5.93 (m, 2), 7.49 (m, 2), 7.96 (s, 3), and 8.31 (m, 4).

The same procedure was followed with 5-iodo-*n*-pentyl acetate to give the aldehyde in 40% yield.

Wittig Reaction.—An ether solution of phenyllithium[10] (0.040 mol, 1 *N*) was added to dry tetrahydrofuran (100 ml) under nitrogen. Dry tetramethylene-1,4-bistriphenylphosphonium bromide[11] (14.68 g, 0.020 mol) was added over 5 min at 0–5° and stirred for 5 min more to give a dark yellow color.[12] 4-Heptanone (2.28 g, 0.020 mol) was added over 3 min and stirred for 7 min more at 10°. 5-Acetoxyvaleraldehyde (2.88 g, 0.020 mol) was added over 2 min and stirred for 15 min at 10–18°. This was poured into water (500 ml) and extracted with ether. The extract was evaporated, and hexane (50 ml) was added to the residue to precipitate the triphenylphosphine oxide. The hexane solution was filtered, evaporated, and chromatographed on a column of Woelm acid-washed alumina. Elution with hexane gave 4,9-di-*n*-propyl-4,8-dodecadiene and biphenyl. The diene was purified by vpc, giving 206 mg (4.1%): n^{24}D 1.4618; nmr ($CDCl_3$) τ 4.87 (t, 2), 8.03 (m, 12), 8.61 (m, 8), and 9.13 (t, 12).

Anal. Calcd for $C_{18}H_{34}$: C, 86.3; H, 13.7. Found: C, 86.5; H, 13.5.

Elution with 20% chloroform in hexane gave a mixture of *cis*- and *trans*-10-*n*-propyl-5,9-tridecadienyl acetate, which was distilled [120° (0.05 mm)] giving 445 mg (8%).

Elution with 40% chloroform in hexane gave 5,9-tetradecadiene-1,14-diol diacetate (280 mg, 4.5%). A sample was purified by vpc: n^{24}D 1.4621; ir (neat) 1745 (ester C=O) and 966 cm^{-1} (*trans* C=C); nmr ($CDCl_3$) τ 4.63 (t, 4), 5.94 (t, 4), 7.9 (m, 8), 7.97 (s, 6), and 8.47 (m, 8). Thin layer chromatography on $AgNO_3$–silica gel[13] showed that all three geometrical isomers were present.

Anal. Calcd for $C_{18}H_{30}O_4$: C, 69.64; H, 9.74. Found: C, 69.71; H, 9.84.

Separation of *cis* and *trans* Isomers.—The 10-*n*-propyl-5,9-tridecadienyl acetate prepared above was chromatographed on a column of $AgNO_3$–silica gel[14] and eluted with 3% ether in hexane. The first fractions contained the pure *trans* isomer (110 mg, 2.0%): n^{24}D 1.4599 (lit.[5] n^{24}D 1.4610); ir (neat) 1745 and 966 cm^{-1}. The later fractions contained the pure *cis* isomer (300 mg, 5.3%): n^{24}D 1.4606; ir (neat) 1742 cm^{-1}; nmr ($CDCl_3$) τ 4.62 (t, 2), 4.88 (t, 1), 5.93 (t, 2), 7.97 (s, 3), 8.0 (m, 10), 8.6 (m, 8), and 9.12 (t, 6).

Anal. Calcd for $C_{18}H_{32}O_2$: C, 77.09; H, 11.50. Found: C, 77.27; H, 11.52. The isomer purity of the fractions was determined by thin layer chromatography on $AgNO_3$–silica gel, using sulfuric acid detection.

Conversion of *cis* to *trans* Isomer.[15]—10-*n*-Propyl-*cis*-5,9-tridecadienyl acetate (200 mg) and powdered selenium (10 mg) were heated in an evacuated sealed tube at 220–225° for 1 hr. Distillation at 0.1 mm and 120° afforded 190 mg of 10-*n*-propyl-*trans*-5,9-tridecadienyl acetate containing about 5% of the *cis* isomer by infrared analysis. The small amount of *cis* isomer was removed by chromatography on $AgNO_3$–silica gel as described above to give 170 mg (85%) of pure *trans* isomer.

Registry No.—1, 19889-82-8; 2, 10297-61-7; 3, 22142-01-4; 4, 22142-00-3.

Acknowledgment.—The author wishes to thank M. Jacobson for the biological evaluation, S. W. Bany for technical assistance, and J. J. McBrady for infrared and nmr interpretation.

(6) The nmr spectra were obtained on a Varian Associates A-60 spectrometer, and the vpc analyses and purifications were carried out on a 6 ft × 0.25 in. column containing 10% SE-30 on Chromosorb P or 5% Carbowax 20M on Anakrom ABS. Elemental analyses were performed by P. B. Olson of 3M Co., or Galbraith Laboratories, Inc.

(7) This method is similar to that used to prepare 4-acetoxybutanal from 4-bromobutanol acetate: L. D. Bergel'son, V. A. Vaver, A. A. Bezzubov, and M. M. Shemyakin, *Izv. Akad. Nauk SSSR, Ser. Khim.*, 1453 (1964); *Chem. Abstr.*, **64**, 14086*d* (1966).

(8) J. F. Oughton, U. S. Patent 3,112,330 (1963); *Chem. Abstr.*, **60**, P4011*h* (1964).

(9) E. Kobayashi and A. Yuzawa, Japanese Patent 3963 (1961); *Chem. Abstr.*, **59**, P2651*b* (1963).

(10) R. G. Jones, *Org. Reactions*, **6**, 353 (1951).

(11) L. Horner, H. Hoffman, W. Klink, H. Ertel, and U. G. Toscano, *Ber.*, **95**, 581 (1962).

(12) D. W. Dicker and M. C. Whiting, *J. Chem. Soc.*, 1944 (1958).

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(14) Prepared by drying a mixture of 20 g of silica gel and 60 ml of 10% aqueous $AgNO_3$ in a rotary evaporator and then heating in an oven at 105° for 1 hr.

(15) This procedure was adapted from that used to isomerize oleic acid: D. Swern and J. T. Scanlan, *Biochem. Prep.*, **3**, 118 (1963).

Improved Synthesis of Streptozotocin

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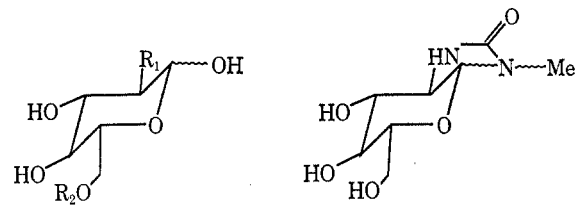
Streptozotocin[1] is a broad-spectrum antibiotic and an antitumor agent produced by *Streptomyces achromogenes*. Streptozotocin (**1**)[2] is an N-nitrosated methylurea derivative of D-glucosamine (**2**). We reinvestigated the synthesis of **1** because of its antibiotic properties, its structural simplicity, and its high cost of production by fermentation.



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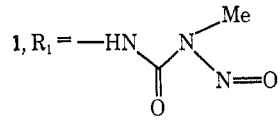
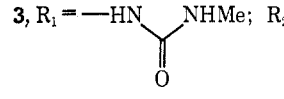
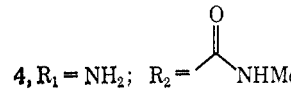


1, R_1 = —HN(Me)N=O; R_2 = H

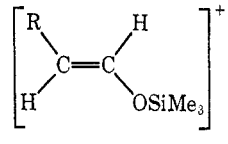
2, R_1 = —NH_2; R_2 = H



3, R_1 = —HN(C=O)NHMe; R_2 = H



4, R_1 = NH_2; R_2 = C(=O)NHMe



6, R = NH_2

7, R = NHCONHMe

(1) (a) J. J. Vavra, C. DeBoer, A. Dietz, L. J. Hanka, and W. T. Sokolski, *Antibiot. Ann.*, **1959–1960**, 230 (1960); (b) W. T. Sokolski, J. J. Vavra, and L. J. Hanka, *ibid.*, **1959–1960**, 241 (1960); (c) C. Lewis and A. R. Barbiers, *ibid.*, **1959–1960**, 247 (1960); (d) R. R. Herr, T. E. Eble, M. E. Bergy, and H. K. Jahnke, *ibid.*, **1959–1960**, 236 (1960); (e) M. E. Bergy, C. De Boer, A. Dietz, T. E. Eble, R. R. Herr, and L. E. Johnson, U. S. Patent 3,027,300 (March 27, 1962).

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