The flies were allowed to feed on a diet containing 1% of the candidate chemosterilant and the sterilizing effect was determined from the extent of hatch of eggs which were periodically collected.[8] With the exception of compounds IV, V, VI, XV, and XVI, the remaining 20 compounds were active as chemosterilants toward at least one species of the insects. Additional tests with the active compounds at lower concentrations indicated that none of them was as effective as tepa or apholate.[8] Characteristically, the derivatives of 2-methylaziridine were all inactive.[9] Most surprising, however, was the lack of activity of the trisaziridinyl XVI, especially because the related bisaziridinyl XIII was active toward all three insect species.

Experimental[10]

General Method for Acylaziridines.—To a mixture of 8.6 g. (0.20 mole) of ethylenimine in 150 ml. of methylene chloride and 8.0 g. (0.20 mole) of sodium hydroxide in 50 ml. of water was added dropwise with moderate stirring 0.20 equiv. of the acid chloride. The temperature was maintained between −10° and 0° during the addition and then allowed to rise to 15° during a 1-hr. period. The organic layer was washed with a saturated sodium chloride solution, dried with magnesium sulfate, and the methylene chloride was removed by distillation under vacuum. The resulting product was either distilled or recrystallized when possible from the appropriate solvent. The physical constants and solvents are given in Table I.

1,1′-(1,2-Cyclobutanedicarbonyl)bisaziridine.—The 1,2-cyclobutanedicarbonyl chloride was prepared in the usual manner by allowing 14.4 g. (0.10 mole) of 1,2-cyclobutanedicarboxylic acid to react with 60 g. (0.50 mole) of thionyl chloride in 50 ml. of dry benzene. The yield of the dichloride was 16 g. (88%), b.p. 51° (0.2 mm.).

To 11 g. (0.25 mole) of ethylenimine in 100 ml. of methylene chloride and 6.7 g. (0.166 mole) of sodium hydroxide in 40 ml. of water was slowly added with stirring 15 g. (0.083 mole) of 1,2-cyclobutanedicarbonyl chloride in 75 ml. of methylene chloride. The temperature was held between −10 and 0° during the addition and allowed to rise to 20° during a 1-hr. period. The organic layer was dried with magnesium sulfate and the solvent removed by evaporation under vacuum to give 10 g. of a light green oil which was distilled, b.p. 100° (0.2 mm.), $n^{25}\text{D}$ 1.5180.

Anal. Calcd. for $C_{10}H_{14}N_2O_2$: N, 14.43. Found: N, 14.25.

N-(2-Chloroethyl)phthalimide.—To a mixture of 12.9 g. (0.30 mole) of ethylenimine in 150 ml. of methylene chloride and 12 g. (0.30 mole) of sodium hydroxide in 100 ml. of water was added slowly with stirring 30.5 g. (0.15 mole) of phthaloyl chloride in 360 ml. of methylene chloride. The temperature was maintained between −5 and 0° during the addition and allowed to rise to 12° within a 1-hr. period. The organic layer was dried with magnesium sulfate and the solvent was removed by evaporation under vacuum. The solid residue after two recrystallizations from methanol weighed 14 g. and melted at 81–82.5° (lit.[11] m.p. 81°).

Anal. Calcd. for $C_{10}H_8ClNO_2$: C, 57.29; H, 3.84; Cl, 16.92; N, 6.68. Found: C, 57.49; H, 3.86; Cl, 16.70; N, 6.41.

N-(2-Chloropropyl)phthalimide.—This compound was obtained in the same way as N-(2-chloroethyl)phthalimide except 2-methylaziridine was substituted for ethylenimine. From 0.30 mole of phthaloyl chloride was obtained, after recrystallization from methanol, 21 g. of product, m.p. 97–98° [N-(2-chloropropyl)phthalimide, lit.[12] m.p. 97.5–98; N-(1-chloro-2-propyl)-phthalimide, lit.[13] m.p. 56–58°].

Anal. Calcd. for $C_{11}H_{10}ClNO_2$: C, 59.07; H, 4.51; Cl, 15.85; N, 6.26. Found: C, 59.11; H, 4.56; Cl, 16.04; N, 6.24.

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[8] Detailed procedures and results of the biological evaluation will be published elsewhere. For a description of methods used in comparative screening of chemosterilants, see H. K. Gouck, M. M. Crystal, A. B. Bořkovec, and D. W. Meifert, *J. Econ. Entomol.*, **56**, 506 (1963).

[9] A. B. Bořkovec and C. W. Woods, *Advan. Chem. Ser.*, **41**, 47 (1963).

[10] All melting points are corrected.

[11] H. Wenker, *J. Am. Chem. Soc.*, **59**, 422 (1937).

[12] L. Smith and B. Platon, *Ber.*, **55**, 3151 (1922).

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Insect Sex Attractants. V. The Synthesis of Some Additional Compounds Related to Gyplure

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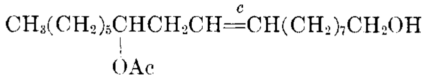
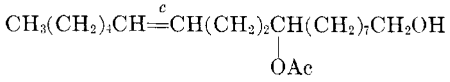
In continuation of a program to synthesize compounds related to gyplure (*d*-12-acetoxy-*cis*-9-octadecen-1-ol)[1] (I), a potent sex attractant for the male gypsy moth (*Porthetria dispar*), we have prepared *d*-9-acetoxy-*cis*-12-octadecen-1-ol (II), as well as the *trans* form of I by a procedure different from that previously reported.[1]



$$\underset{\displaystyle\text{OAc}}{CH_3(CH_2)_5\underset{|}{C}HCH_2CH\overset{c}{=}CH(CH_2)_7CH_2OH}$$

I



$$CH_3(CH_2)_4CH\overset{c}{=}CH(CH_2)_2\underset{\displaystyle\text{OAc}}{\underset{|}{C}H}(CH_2)_7CH_2OH$$

II

The starting material for the synthesis of II was *d*-9-hydroxy-*cis*-12-octadecenoic acid, isolated from *Strophanthus kombe* seed oil by a modification of the method of Gunstone.[2] Reduction of this acid with lithium aluminum hydride gave *cis*-12-octadecene-1,9-diol, which was acetylated, with acetyl chloride in refluxing benzene containing pyridine, to the 1,9-diacetate. Saponification with one mole of ethanolic potassium hydroxide gave a product shown by gas chromatography to be 80% II and 20% of the 1,9-diol.

In contrast with the poor yield (28%) of the *trans* isomer of I obtained previously[1] by the nitrous acid elaidinization of gyplure, an over-all yield of 54% of the pure *trans* form was realized by subjecting ricinelaidyl alcohol[3] to acetylation and selectively saponifying the diacetate.

None of the compounds prepared elicited a typical sexual response from male gypsy moths when tested in the laboratory by the method of Block.[4,5] Although these substances are to be tested in field traps during male moth flight, their lack of activity in the laboratory makes it extremely unlikely that males will be attracted in the field.

The biological test results help to confirm the belief that, in compounds of this type, an acetoxy group situated in a position β to a *cis* double-bonded carbon is necessary for attractiveness to male gypsy moths.[1]

Experimental[6]

9-Hydroxy-*cis*-12-octadecenoic Acid.—Powdered *Strophanthus kombe* seed[7] (454 g.) was extracted in a Soxhlet extractor with

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[1] M. Jacobson and W. A. Jones, *J. Org. Chem.*, **27**, 2523 (1962).

[2] F. D. Gunstone, *J. Chem. Soc.*, 1274 (1952).

[3] M. A. McCutchon, R. T. O'Connor, E. F. DuPré, L. A. Goldblatt, and W. G. Bickford, *J. Am. Oil Chemists' Soc.*, **36**, 450 (1959).

[4] B. C. Block, *J. Econ. Entomol.*, **53**, 172 (1960).

[5] These tests were conducted by Mr. C. Collier, Plant Pest Control Division, U. S. Department of Agriculture, Falmouth, Mass.

[6] Melting points are corrected; boiling points are uncorrected. Mention of trade names or proprietary products does not necessarily constitute endorsement by the Department of Agriculture.

[7] Obtained from S. B. Penick and Co., New York, N. Y.

Skellysolve A and the extract was freed of solvent to give 155.4 g. (34%) of green semisolid, which was refluxed with 5% ethanolic potassium hydroxide to obtain 135 g. of mixed acids as a green semisolid and 35 g. of yellow, waxy, unsaponifiable fraction. A solution of the acids in 1350 ml. of acetone was kept overnight at −45°, the separated white solid filtered and discarded, and the filtrate evaporated to dryness, leaving 63 g. of greenish yellow liquid. This was refluxed for 3 hr. with 200 ml. of methanol saturated with hydrogen chloride, freed of solvent, and the residue was dissolved in ether, washed successively with 10% sodium carbonate and water, and dried over sodium sulfate. Removal of solvent and distillation of the residual oil (63.4 g.) gave the following 3 fractions: (1) 33.2 g. of pale yellow oil, b.p. 153–170° (0.3 mm.); (2) 9.8 g. of pale yellow oil, b.p. 170–180° (0.3 mm.); (3) 3.0 g. of yellow oil, b.p. 180–185° (0.3 mm.). Fractions 2 and 3 were each dissolved separately in a solution of 10 g. of potassium hydroxide, 3 ml. of water, and 100 ml. of 95% ethanol, and the mixtures were refluxed for 2 hr., diluted with several volumes of water, extracted once with ether, acidified to congo red with 5% hydrochloric acid, and extracted with several portions of ether. The ether solutions were washed with water, dried, and freed of solvent, yielding 7.8 g. and 3.0 g. of viscous orange oil from fractions 2 and 3, respectively. These oils (7.2 g. and 2.4 g.) were chromatographed in 1-g. batches on 80 g. of silicic acid (Merck) prewashed with 150 ml. of 70% ethyl acetate in isooctane and 200 ml. of isooctane. The columns were each eluted with 400 ml. of 10% ethyl acetate in isooctane followed by 400 ml. of 25% ethyl acetate in isooctane. Removal of solvent from the latter eluates gave the product as 4.3 g. of pale yellow oil ($n^{25.5}\text{D}$ 1.4708), and crystals from fraction 2, and 1.5 g. of identical material from fraction 3.

Anal. Calcd. for $C_{18}H_{34}O_3$: C, 72.43; H, 11.48. Found: C, 71.34; H, 10.98.

***cis*-12-Octadecene-1,9-diol.**—To a stirred solution of 2 g. of lithium aluminum hydride in 75 ml. of anhydrous ether was added slowly, with cooling, a solution of 5.1 g. of 9-hydroxy-*cis*-12-octadecenoic acid in 60 ml. of anhydrous ether. After addition was complete (0.75 hr.), the mixture was treated carefully with 50 ml. of water followed by 75 ml. of 10% sulfuric acid. The separated ether layer was washed with water, dried over sodium sulfate, and freed of solvent, leaving 4.8 g. (100%) of the diol as a gas chromatographically pure pale yellow oil, $n^{25}\text{D}$ 1.4718, that solidified after standing for 1 month at room temperature. A small amount was crystallized from pentane–acetone (1:1) and washed with hexane, m.p. 53–54°.

Anal. Calcd. for $C_{18}H_{36}O_2$: C, 75.99; H, 12.76. Found: C, 76.38; H, 12.78.

1,9-Diacetoxy-*cis*-12-octadecene.—To a solution of 4.7 g. of the diol and 4 ml. of dry pyridine in 25 ml. of anhydrous benzene was added dropwise (12 drops/min.), with stirring and ice cooling, a solution of 4 g. of acetyl chloride in 15 ml. of benzene. The mixture was refluxed on a steam bath for 2 hr., cooled, washed successively with dilute hydrochloric acid, dilute potassium hydroxide, and water, and dried over sodium sulfate. Removal of the solvent left 5.76 g. (95%) of yellow, mobile liquid; a portion (5.04 g.) of this was distilled to give the gas chromatographically pure diester (4.1 g.) as a pale yellow, mobile liquid, b.p. 176–177° (0.1 mm.), $n^{25}\text{D}$ 1.4520.

Anal. Calcd. for $C_{22}H_{40}O_4$: C, 71.69; H, 10.94. Found: C, 71.38; H, 11.18.

An additional 1.15 g. of 95% pure diester was obtained by combining the undistilled portion with the distillation residue and chromatographing the mixture on 80 g. of prewashed silicic acid. The column was eluted with 400 ml. of isooctane followed by 400 ml. of 5% ethyl acetate in isooctane. Removal of solvent from the latter eluate left the diester.

9-Acetoxy-*cis*-12-octadecen-1-ol (II).—A solution of 5.0 g. of the previously mentioned diester, 1 g. of potassium hydroxide, 2 ml. of water, and 20 ml. of 95% ethanol was refluxed on the steam bath for 1.5 hr., then diluted with several volumes of water and extracted with ether. The ether solution was washed with water, dried, and evaporated to dryness; the residue (4.1 g., 93%) distilled as a colorless oil, b.p. 184° (0.4 mm.), $n^{25}\text{D}$ 1.4621, that was shown by gas chromatography to consist of 80% II and 20% 1,9-diol.

Anal. Calcd. for $C_{20}H_{38}O_3$: C, 73.56; H, 11.74. Found: C, 73.10; H, 11.84.

Ricinelaidyl Alcohol.—To 50 g. of ricinoleyl alcohol, maintained at 60°, was added with rapid stirring 3.4 ml. of 2 *M* sodium nitrite solution and 2.2 ml. of 40% nitric acid. Heating and stirring was continued for 3 hr., after which the reaction mixture was poured into 500 ml. of water contained in a separatory funnel. The ricinelaidyl alcohol was extracted with ether, which was washed free of acid with water, and dried over sodium sulfate. Removal of the solvent left 50 g. of a yellow oil that solidified completely at room temperature. It was dissolved in 10 volumes of pentane–acetone (1:1), allowed to crystallize overnight at −5°, and the colorless solid (25.5 g.) was recrystallized from hexane, m.p. 51.5° (lit.[3] m.p. 53.0–53.4°).

Anal. Calcd. for $C_{18}H_{36}O_2$: C, 75.99; H, 12.76. Found: C, 76.77; H, 12.79.

1,12-Diacetoxy-*trans*-9-octadecene.—This was prepared in 92% yield from 47.3 g. of ricinelaidyl alcohol and 30 g. of acetyl chloride by the procedure already given. A colorless, mobile liquid, b.p. 181° (0.4 mm.), $n^{26}\text{D}$ 1.4497, was obtained (lit.[3] b.p. 166–167° at 0.085 mm.).

Anal. Calcd. for $C_{22}H_{40}O_4$: C, 71.69; H, 10.94. Found: C, 72.00; H, 11.09.

12-Acetoxy-*trans*-9-octadecen-1-ol (*trans*-Gyplure).—The product obtained in 92% yield by selective saponification of the diacetoxy compound was distilled to give a colorless, somewhat viscous liquid, b.p. 167–168° (0.1 mm.), $n^{26}\text{D}$ 1.4579. A portion (703 mg.) of this liquid was chromatographed on 80 g. of silicic acid (prewashed as previously described), and eluted with 400 ml. of 5% ethyl acetate in isooctane followed by 400 ml. of 10% ethyl acetate in isooctane. The latter eluate yielded 486 mg. (69% of the distilled product) of gas chromatographically pure product.

Anal. Calcd. for $C_{20}H_{38}O_3$: C, 73.56; H, 11.74. Found: C, 74.21; H, 11.14.

Basically Substituted Derivatives of 4-Hydroxy-2,3,6-trimethoxy-5H-benzocyclohepten-5-one

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Since the proposal of the tropolone ring system by Dewar in 1945,[1] a great number of compounds containing the tropolone and tropone structures were prepared and some of these compounds were tested for their chemotherapeutic activity. We prepared several substituted benzotropones (Table I) for evaluation of their pharmacodynamic properties. The starting material for the synthesis of these compounds, 4-hydroxy-2,3,6-trimethoxy-5H-benzocyclohepten-5-one[2] (A, formula in Table I where R = H and R′ = OCH_3), was obtained by oxidation of pyrogallol to the substituted benzotropolone, purpurogallin,[3] followed by treatment of the latter with dimethyl sulfate. Compounds **1–3** of Table I were obtained by the addition of A to an equivalent of sodium isopropoxide in isopropyl alcohol followed by the appropriate basically substituted alkyl chloride. Compounds **4–8** were prepared by heating A with an excess of the appropriate alkylenediamine in toluene or xylene for about 24 hr. The products were isolated and purified in the form of oxalic acid salts.

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(1) For review articles on the subject see T. Nozoe in "Nonbenzenoid Aromatic Compounds," D. Ginsburg, Ed., Interscience Publishers, Inc., New York, N. Y., 1959, p. 339, and P. L. Pauson, *Chem. Rev.*, **55**, 9 (1955).

(2) J. A. Barltrop and J. S. Nicholson, *J. Chem. Soc.*, 116 (1948).

(3) T. W. Evans and W. M. Dehn, *J. Am. Chem. Soc.*, **52**, 3647 (1930).