Insect Sex Attractants. II. The Synthesis of a Highly Potent Gypsy Moth Sex Attractant and Some Related Compounds[1]

MARTIN JACOBSON AND WILLIAM A. JONES

Entomology Research Division, Agricultural Research Service,
U.S. Department of Agriculture, Beltsville, Maryland

Received January 15, 1962

(+)-12-Acetoxy-*cis*-9-octadecen-1-ol, a highly potent sex attractant for the male gypsy moth (*Porthetria dispar*), has been synthesized and designated "gyplure." A homolog, two analogs, and the *trans* form of gyplure were also prepared, and their activity is compared with that of the natural attractant.

During an investigation to determine the structure of the naturally occurring sex attractant secreted by the female gypsy moth (*Porthetria dispar*),[2] a model compound was needed for microoxidation studies. It was necessary that such a compound possess sixteen or eighteen carbon atoms, primary hydroxyl, secondary acetoxyl, an unbroken chain of at least four methylene groups, and a double bond having, preferably, a *cis* configuration. Ricinoleic acid (12-hydroxy-*cis*-9-octadecenoic acid), readily available commercially in pure form, appeared to be ideal for use as a starting material for the preparation of the required compound.

Ricinoleic acid was quantitatively reduced with lithium aluminum hydride to the corresponding alcohol,[3] which is now commercially available, and this was acetylated in 62% yield with acetyl chloride in refluxing benzene (containing pyridine) to the 1,12-diacetate. Saponification with refluxing ethanolic potassium hydroxide removed only the primary acetyl group,[4] giving a 90% yield of (+)-12-acetoxy-*cis*-9-octadecen-1-ol (Ib). The compound shows blue fluorescence in ultraviolet light, as does the natural lure, is remarkably stable to heat, and does not appear to decompose when stored at room temperature for at least a year.

Male gypsy moths in large numbers were lured to field traps containing as little as 10^{-5} microgram of Ib, and the compound was attractive at 10^{-12} microgram in laboratory bioassay tests (Table I).[5] It therefore compares very favorably in activity with the natural attractant, identified as (+)-10-acetoxy-*cis*-7-hexadecen-1-ol (Ia), and has been designated "gyplure." Ease of preparation and extreme potency have made gyplure an excellent inexpensive substitute for the crude benzene extract of female gypsy moth tips in field traps.[6]

Attempts to isomerize gyplure to the *trans* form by irradiation with ultraviolet light were unsuccessful and resulted in the recovery of unchanged material. Isomerization was achieved, albeit in 28% yield, by treatment with a mixture of sodium nitrite and nitric acid according to the procedure of Kass and Radlove.[7] The principal significant bands in the infrared spectrum of gyplure were at 3400 and 1022 cm.$^{-1}$ (hydroxyl) and at 1746 and 1240 cm.$^{-1}$ (acetate carbonyl); the *trans* isomer contained, in addition, a band at 967 cm.$^{-1}$. In contrast to the *cis* form, the *trans* isomer was much less attractive to male gypsy moths in the laboratory and trapped no males in the field at a concentration of 250 milligrams. A *cis* configuration is therefore necessary for attractiveness in this type of compound. The propoxy and butoxy analogs of gyplure, prepared by a similar procedure, were completely unattractive to male gypsy moths in both laboratory and field tests, which showed that the presence of an acetoxy group is also necessary for activity.

TABLE I

COMPARATIVE ATTRACTANCY OF GYPLURE AND ITS HOMOLOGS TO MALE GYPSY MOTHS

Compound	Attractancy, μgrams	
	Laboratory	Field
Ia (natural)	10^{-12}	10^{-7}
Ib (gyplure)	10^{-12}	10^{-5}
trans-Gyplure	10^{4}	$>2.5 \times 10^{5}$
Ic	10^{-2}	10

The recent isolation[8] of lesquerolic acid [(+)-14-hydroxy-*cis*-11-eicosenoic acid], the C_{20} homolog of ricinoleic acid, from *Lesquerella lasiocarpa* seed oil prompted us to prepare (+)-14-acetoxy-*cis*-11-eicosen-1-ol (Ic) for gypsy moth attractancy tests.

---

[1] Reported in part as a Communication, *J. Org. Chem.*, **25**, 2074 (1960).

[2] M. Jacobson, M. Beroza, and W. A. Jones, *Science*, **132**, 1011 (1960); *J. Am. Chem. Soc.*, **83**, 4819 (1961).

[3] S. P. Ligthelm, E. von Rudloff, and D. A. Sutton, *J. Chem. Soc.*, 3187 (1950).

[4] The secondary acetyl group was extremely resistant to saponification with refluxing ethanolic alkali, and it was necessary to use diethylene glycol-potassium hydroxide mixture at 120° to break this linkage. This unusual stability now appears to be due in some way to the position of the secondary acetyl group with respect to the double bond, since the same behavior was noted during the attempted saponification of the natural lure (10-acetoxy-*cis*-7-hexadecen-1-ol[2]) and of 14-acetoxy-*cis*-11-eicosen-1-ol.

[5] Field tests were carried out as described by J. M. Corliss, Yearbook of Agriculture (Insects), 694 (1952). The assistance of Mr. E. C. Paszek, U.S. Department of Agriculture, Nashua, N. H., in carrying out these tests is gratefully acknowledged. Laboratory bioassay tests were carried out by the method of B. C. Block, *J. Econ. Entomol.*, **53**, 172 (1960).

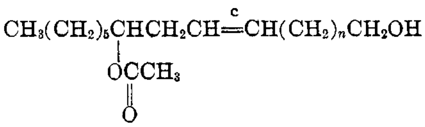
[6] F. Acree, M. Beroza, R. F. Holbrook, and H. L. Haller, *ibid.*, **52**, 82 (1959).

[7] J. P. Kass and S. B. Radlove, *J. Am. Chem. Soc.*, **64**, 2253 (1942).

[8] C. R. Smith, Jr., T. L. Wilson, T. K. Miwa, H. Zobel, R. L. Lohmar, and I. A. Wolff, *J. Org. Chem.*, **26**, 2903 (1961).

With lesquerolic acid as starting material, the sequence of reactions used previously to prepare gyplure gave Ic in 60% over-all yield. Its degree of attractiveness to male gypsy moths was considerably below that of gyplure (Table I).

The order of attractiveness appears to be Ia > Ib (gyplure) > Ic. The activity of gyplure homologs of lower chain length is being investigated.



$CH_3(CH_2)_5\underset{\underset{\underset{O}{\|}}{OCCH_3}}{\overset{|}{C}}HCH_2CH\overset{c}{=}CH(CH_2)_nCH_2OH$

Ia. $n = 5$
b. $n = 7$ (gyplure)
c. $n = 9$

Experimental[9]

Ricinoleyl Alcohol.—Lithium aluminum hydride reduction of ricinoleic acid (Kahlbaum) by the procedure of Ligthelm, *et al.*,[8] gave a quantitative yield of the corresponding alcohol, b.p. 175° (0.5 mm.), n^{25}_D 1.4704, $[\alpha]^{30}_D$ +5.3° (*c* 1.0, chloroform) [lit.,[8] b.p. 178° (0.5 mm.), n^{25}_D 1.4700, $[\alpha]^{24}_D$ +5.7° (undiluted)].

1,12-Diacetoxy-*cis*-9-octadecene.—To a solution of 12.0 g. of ricinoleyl alcohol and 8.5 ml. of dry pyridine in 50 ml. of anhydrous benzene was added, with stirring and ice-cooling, a solution of 7.32 g. (10% excess) of acetyl chloride in 20 ml. of benzene. The mixture was refluxed on the steam bath for 2 hr., cooled, washed successively with dilute hydrochloric acid, dilute potassium hydroxide, and water, and dried over sodium sulfate. Removal of solvent and distillation of the residual oil gave 9.7 g. (62%) of colorless, mobile liquid, b.p. 180° (1.3 mm.), n^{25}_D 1.4519, $[\alpha]^{30}_D$ +8.7° (*c* 1.0, chloroform), showing blue fluorescence in ultraviolet light.

Anal. Calcd. for $C_{22}H_{40}O_4$: C, 71.68; H, 10.94. Found: C, 71.52; H, 11.06.

(+)-12-Acetoxy-*cis*-9-octadecen-1-ol (Gyplure).—A solution of 8.0 g. of the diester above, 1.2 g. of potassium hydroxide, 3 ml. of water, and 15 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, and the residue was distilled to give 6.4 g. (90%) of colorless, somewhat-viscous liquid, b.p. 182° (0.5 mm.), n^{25}_D 1.4607, $[\alpha]^{30}_D$ +7.4° (*c* 1.0, chloroform), showing blue fluorescence in ultraviolet light.

Anal. Calcd. for $C_{20}H_{38}O_3$: C, 73.56; H, 11.74. Found: C, 73.36; H, 11.70.

(+)-12-Acetoxy-*trans*-9-octadecen-1-ol.—Gyplure (0.5 g.) was dissolved in 20 ml. of petroleum ether (b.p. 60–70°), a small crystal of iodine was added, and the solution was irradiated with an ultraviolet lamp (30-watt, 3660 Å.) for 1.5 hr. while being cooled with an electric fan to prevent evaporation. The solution was filtered, dried over sodium sulfate, and evaporated to dryness. The colorless liquid remaining showed an infrared spectrum identical with that of gyplure and was considered to be unchanged material.

A mixture of 10 g. of gyplure and 60 ml. of a 15% solution of sodium nitrite in 50% nitric acid was shaken occasionally over a period of 2 hr. and then allowed to stand at room temperature for 66 hr. The mixture was extracted with several portions of ether, and the combined ether solution was washed with water and dried. Removal of the solvent left 10.8 g. of viscous, yellow liquid whose infrared spectrum showed the presence of nitrate ester in addition to *trans* unsaturation. It was therefore dissolved in a solution containing 1.6 g. of potassium hydroxide, 1.5 ml. of water, and 15 ml. of 95% ethanol, and refluxed on the steam bath for 1.5 hr. The solution was diluted with 8 volumes of water and extracted with ether. The ether solution was washed with water, dried, and evaporated to dryness, and the residual red oil was distilled to give 2.8 g. (28%) of yellow oil, b.p. 178° (0.5 mm.), n^{25}_D 1.4625, showing pale blue fluorescence in ultraviolet light.

Anal. Calcd. for $C_{20}H_{38}O_3$: C, 73.56; H, 11.74. Found: C, 73.30; H, 11.78.

1,12-Dipropoxy-*cis*-9-octadecene.—This was prepared in 92% yield from 24 g. of ricinoleyl alcohol and 17.3 g. of propionyl chloride by the procedure used to prepare the diacetoxy compound. A slightly yellow liquid, b.p. 184° (0.2 mm.), n^{25}_D 1.4527, was obtained.

Anal. Calcd. for $C_{24}H_{44}O_4$: C, 72.67; H, 11.18. Found: C, 72.75; H, 11.19.

(+)-12-Propoxy-*cis*-9-octadecen-1-ol.—This was prepared in 50% yield by the selective saponification of the primary ester grouping, as described above for the preparation of gyplure. A colorless liquid, b.p. 172–175° (0.25 mm.), n^{25}_D 1.4596, was obtained.

Anal. Calcd. for $C_{22}H_{42}O_3$: C, 74.51; H, 11.94. Found: C, 74.39; H, 12.06.

1,12-Dibutoxy-*cis*-9-octadecene.—This was prepared in 87% yield from 24 g. of ricinoleyl alcohol and 19.9 g. of butyryl chloride by the procedure already given. A slightly yellow liquid, b.p. 187° (0.1 mm.), n^{25}_D 1.4533, was obtained.

Anal. Calcd. for $C_{26}H_{48}O_4$: C, 73.53; H, 11.38. Found: C, 73.39; H, 11.46.

(+)-12-Butoxy-*cis*-9-octadecen-1-ol.—This was prepared in 68% yield by the selective saponification of the dibutoxy compound. A colorless liquid, b.p. 177–179° (0.25 mm.), n^{25}_D 1.4601, was obtained.

Anal. Calcd. for $C_{24}H_{46}O_3$: C, 75.33; H, 12.11. Found: C, 75.28; H, 12.00.

(+)-14-Acetoxy-*cis*-11-eicosen-1-ol.—The lithium aluminum hydride reduction of lesquerolic acid[10] gave a 68% yield of the corresponding alcohol as a pale yellow oil. Treatment of the undistilled product with acetyl chloride and pyridine, by the procedure given above, gave the diacetate, in 97% yield, as a pale yellow, mobile oil, which was then selectively saponified with one molar equivalent of potassium hydroxide to give the desired product in 65% yield. Distillation yielded a colorless, viscous oil, b.p. 185° (0.3 mm.), showing blue fluorescence in ultraviolet light.

Anal. Calcd. for $C_{24}H_{42}O_3$: C, 76.13; H, 11.18. Found: C, 75.93; H, 11.08.

---

(9) Boiling points are uncorrected.

(10) We are indebted to I. A. Wolff, Northern Utilization Research and Development Laboratory, U.S. Department of Agriculture, Peoria, Illinois, for a sample of the sodium salt of lesquerolic acid.