

SYNTHESIS OF OPTICALLY ACTIVE PHEROMONES WITH AN EPOXY RING,
(+)-DISPARLURE AND THE SALTMARSH CATERPILLAR MOTH
PHEROMONE [(Z,Z)-3,6-cis-9,10-EPOXYHENEICOSADIENE]

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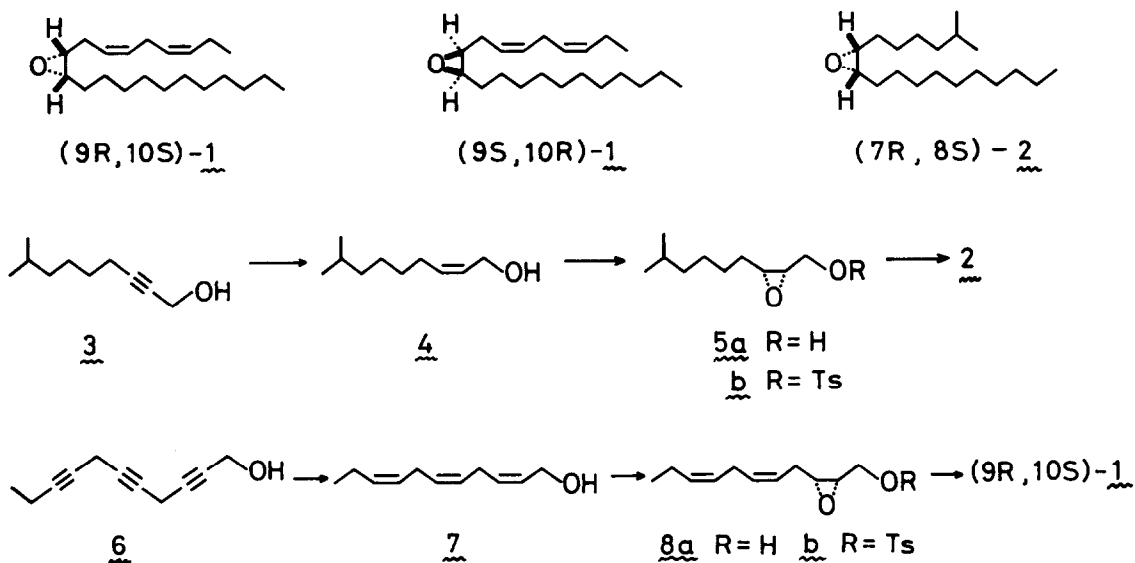
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Abstract : (+)-Disparlure 2 and the saltmarsh caterpillar moth pheromone enantiomers 1 were synthesized and the stereochemistry of the naturally occurring 1 was shown to be 9S, 10R.

(Z,Z)-3,6-cis-9,10-Epoxyheneicosadiene 1 was identified by Hill and Roelofs as one of the three components of the sex pheromone emitted by females of the saltmarsh caterpillar moth, Estigmene acrea (Drury).¹⁾ Importance in insect life of optically active epoxides such as juvenile hormones and disparlure 2 made us to synthesize both (9S, 10R)- and (9R, 10S)-1 so as to establish the stereochemistry of the natural pheromone.

As a model experiment, we first attempted a simple synthesis of (+)-disparlure 2, the pheromone of the gypsy moth (Porthetria dispar).^{2,3)} Our strategy was to employ the Sharpless asymmetric epoxidation⁴⁾ (4 → 5a) and the coupling of an epoxy tosylate with lithium dialkylcuprate⁵⁾ as two key-reactions. An acetylenic alcohol 3 was semi-hydrogenated ($H_2/Pd-BaSO_4/quinoline/MeOH$) to give (Z)-4 (91.6% yield). This was epoxidized [$Ti(Oi-Pr)_4$ -diethyl L-(+)-tartrate-t-BuOOH/ CH_2Cl_2 , -20° , 18 hr]⁴⁾ to (2S, 3R)-5a (80.8% yield) [α_D^{21} -2.55° ($c=2.43$, $CHCl_3$)].⁶⁾ The corresponding tosylate 5b was reacted with ($n-C_9H_{19}$)₂CuLi (1.4eq) in ether at -20° for 3 hr to give (7R, 8S)-(+)-disparlure 2 (47% yield after TLC purification), [α_D^{21} $+1.1^\circ \pm 0.5^\circ$ ($c=2.3$, CCl_4)], identical with an authentic sample.³⁾

For the synthesis of 1, a triynol 6 was prepared from ethyl bromide and propargyl alcohol in the conventional manner. This was hydrogenated ($H_2/P-2-Ni/H_2N(CH_2)_2NH_2-EtOH$)⁷⁾ to 7 (23.7% yield after careful purification on a Merck Lobar column). Asymmetric epoxidation [$Ti(Oi-Pr)_4$ -diethyl L-(+)-tartrate-t-BuOOH/ CH_2Cl_2 , -20° , 26hr]⁴⁾ of 7 yielded (2S, 3R)-8a (54.8% yield after chromatographic purification on a Merck Lobar column), [α_D^{23} -8.30° ($c=0.964$, $CHCl_3$)].⁸⁾ The corresponding tosylate (2S, 3R)-8b was treated with ($n-C_{10}H_{21}$)₂CuLi (1.0 eq) in ether at -20° for 1.5 hr to give (9R, 10S)-1 (43.8% yield after TLC purification), [α_{230} $+77.1^\circ$, [α_{240} $+42.9^\circ$, [α_{260} $+20.0^\circ$, [α_{280} $+14.3^\circ$; CD $\Delta\epsilon$ $+0.23$ (205 nm)].⁹⁾ Similarly, by employing diethyl D-(-)-tartrate instead of L-(+)-isomer, 7 afforded (2R, 3S)-8a (60.3% yield), [α_D^{23} $+8.02^\circ$ ($c=1.16$, $CHCl_3$)].⁸⁾ Treatment of the corresponding



tosylate ($2R$, $3S$)- $8b$ with $(n\text{-C}_{10}\text{H}_{21})_2\text{CuLi}$ gave $(9S, 10R)\text{-}1$ (33.9% yield), $[\alpha]_{230}\text{-}43.3^\circ$, $[\alpha]_{240}\text{-}33.3^\circ$, $[\alpha]_{260}\text{-}20.8^\circ$, $[\alpha]_{280}\text{-}15.0^\circ$; CD $\Delta\epsilon\text{-}0.18$ (205 nm). Since the natural pheromone exhibited negative ORD and CD curves,¹⁰⁾ $(9S, 10R)\text{-}$ stereochemistry was assigned to the saltmarsh caterpillar moth pheromone. Bioassay of the enantiomers is now under way by Prof. W.L. Roelofs.¹¹⁾

REFERENCES AND FOOTNOTES

- 1) A.S. Hill and W.L. Roelofs, *J. Chem. Ecol.*, in the press.
- 2) An independent synthesis of $(+)\text{-}2$ by a different route (asymmetric epoxidation-oxidation-Wittig reaction-hydrogenation) has recently been reported: B.E. Rossister, T. Katsuki and K.B. Sharpless, *J. Am. Chem. Soc.*, **103**, 464 (1981).
- 3) For previous syntheses of $(+)\text{-}2$ see, K. Mori "The Synthesis of Insect Pheromones," pp 146-151 in J. ApSimon (ed.) "The Total Synthesis of Natural Products, Vol. 4", John Wiley & Sons, New York (1981).
- 4) T. Katsuki and K.B. Sharpless, *J. Am. Chem. Soc.*, **102**, 5974 (1980).
- 5) G.H. Posner, "An Introduction to Synthesis Using Organocopper Reagents," Chapter 3, John Wiley & Sons, New York (1980).
- 6) This was highly optically pure as judged by the $^1\text{H-NMR}$ measurement of the corresponding acetate (50 mg) in the presence of $\text{Eu}(\text{hfc})_3$ (60 mg) in CCl_4 [CH-O : racemate, 5.00 (m) and 5.30 (m); ($2S, 3R$)-isomer, δ 4.99 (m)].
- 7) C.A. Brown and V.K. Ahuja, *J.C.S. Chem. Comm.*, 553 (1973).
- 8) So far this epoxidation is known to give highly optically pure epoxides without exception.⁴⁾ Direct determination of the optical purity of $8a$ was not attempted due to the scarcity of the material.
- 9) $^1\text{H-NMR}$ δ (100MHz, C_6D_6) 0.92 (6H, t, $J=7\text{Hz}$), 1.14-1.59 (20H, br. s), 1.78-2.42 (4H, m), 2.58-2.96 (4H, m), 5.25-5.68 (4H, m); $^{13}\text{C-NMR}$ δ (25MHz, CDCl_3) 14.08, 14.21, 20.57, 22.69, 25.73, 26.29, 26.63, 27.80, 29.36, 29.58, 31.92, 56.36, 57.12, 124.28, 126.71, 130.74, 132.17. The $^1\text{H-NMR}$ spectrum was identical with that of the natural pheromone¹⁾. Careful examination of the olefinic carbon region of the expanded $^{13}\text{C-NMR}$ spectrum revealed the presence of three small signals at δ 123.77, 128.57 and 131.00 with intensities of about 6% of those of the major signals. This implies that the *cis-trans* isomeric purity of our synthetic 1 is about 91% [$100\text{-}(6/2) \times 3$].
- 10) W.L. Roelofs, Personal communication to K.M. dated November 14, 1978.
- 11) We thank Professors W.L. Roelofs, K.B. Sharpless, and the late Dr. A.S. Hill for exchange of informations. Our thanks are due to Drs. T. Umemura and M. Horiba, Sumitomo Chemical Co., for ORD and CD measurements.

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