A Stereoselective Synthesis of Racemic \((E)-7,8\)-Epoxy-2-methyloctadecane, the Geometrical Isomer of Racemic Disparlure'

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After the completion of our synthesis of the optically active disparlure (1),1 we became interested in preparing its geometrical isomer \(\text{[(E)-7, 8-epoxy-2-methyl-octadecane, 2]}\) in order to test its possible biological activity as a pheromone inhibitor.2 Although the synthesis of 2 as racemic3 or optically active4 forms were reported previously, we felt it necessary to develop a new and efficient stereoselective route to 2. Herein we record our results.

n-Decanal (3) was treated with vinylmagnesium bromide to give 4 in 85% yield. This was mixed with 47% hydrobromic acid to give a bromide (5). For the preparation of the required \((E)\)-olefin (8) we employed Kondo’s method.5 Thus the bromide was heated with triethyl phosphite to give a phosphonate (6). This was alkylated with 5-methylhexyl bromide to yield 7 in 73% yield. The \((E)\)-olefin (8) was obtained in 67% yield from 7 by reduction with lithium aluminum hydride. Oxidation of 8 with m-chloroperbenzoic acid gave \((E)-7, 8\)-epoxy-2-methyl-octadecane in 81% yield. The biological test is now under way by Prof. J. P. Vité, University of Freiburg.

EXPERIMENTAL

All bps were uncorrected. IR spectra refer to films. NMR spectra were recorded with TMS as an internal standard.

1-Dodecen-3-ol (4)

A solution of vinylmagnesium bromide was prepared from magnesium (13 g) and a large excess of vinyl bromide in tetrahydrofuran (300 ml) in the usual manner. n-Decanal (42 g) was added to the Grignard reagent under stirring at \(10^\circ C\). Then the reaction mixture was heated under reflux for 2 hr and poured into ice-cooled ammonium chloride solution. The aqueous solution was extracted with ether. The extract was washed with water and sodium bicarbonate solution, dried over magnesium sulfate and concentrated. The residue was distilled to give 42.1 g (85%) of 4, bp \(99\sim100^\circ C (4 \text{ mmHg})\); \(n^D_0\) \(1.4479\); IR \(\nu_{\max} \text{ cm}^{-1}: 3350 \text{ (s)}, 2925 \text{ (s)}, 2850 \text{ (s)}, 1640 \text{ (w), 1465 (m), 1420 (w), 995 (m), 920 (m); NMR } \delta \text{ (60 MHz, CDCl}_3\) \(0.95 \text{ (3H, t), 1.35 (16H, bs), 4.20 (1H, m), 5.10 \sim 5.45 \text{ (2H, m), 5.75 \sim 6.35 (1H, m). Anal. Found: C, 78.32; H, 12.81. Calcd. for C}_{12}\text{H}_{21}O: C, 78.19; H, 13.13%}

2-Dodecenyl bromide (5)
The allyl alcohol (4, 21 g) was added dropwise to the stirred aqueous hydrobromic acid \((47\%, 150 \text{ ml})\) at room temperature and the mixture was stirred for 3 hr at \(50^\circ C\). The organic layer was separated and the aqueous layer was extracted with chloroform. The combined organic solution was washed with water and sodium bicarbonate solution, dried over magnesium sulfate and concentrated in vacuo. The residue was distilled to give 24.0 g \((85\%)\) of 5, bp \(105\sim107^\circ C \text{ (4 mmHg)}\); \(n^D_0\) \(1.4742\); IR \(\nu_{\max} \text{ cm}^{-1}: 2925 \text{ (s), 2850 \text{ (s), 1660 (w), 1460 (m), 1440 (w), 1380 (w), 1205 (s), 965 (m); NMR } \delta \text{ (60 MHz, CDCl}_3\) \(0.9 (3H, t), 1.30 \text{ (14H, bs), 2.0 \sim 2.2 (2H, m), 3.80 \sim 3.95 (2H, m), 5.6 \sim 5.85 (2H, m). Anal. Found: C, 58.35; H, 9.38. Calcd. for C}_{12}\text{H}_{23}Br: C, 58.30; H, 9.31%}

Diethyl 2-dodecenylphosphonate (6)
The bromide \((5, 20 \text{ g})\) was added dropwise to the stirred triethylphosphoric acid \((47\%, 150 \text{ ml})\) at room temperature and the mixture was stirred for 3 hr at \(140^\circ C\). The organic layer was separated and the aqueous layer was extracted with chloroform. The combined organic solution was washed with water and sodium bicarbonate solution, dried over magnesium sulfate and concentrated in vacuo. The residue was distilled to give 24.0 g \((85\%)\) of 6, bp \(124.5^\circ C (0.2 \text{ mmHg}); \nu_{D} \nu_{D} \text{ cm}^{-1}: 1.4484; 1.4844; \text{ IR } \nu_{\max} \text{ cm}^{-1}: 2930 \text{ (s), 2860 (s), 1470 (m), 1445 (m), 1400 (m), 1260 (s), 1165 (m), 1100 (m), 1050 (s), 1030 (s), 960 (s), 830 (w), NMR } \delta \text{ (60 MHz, CDCl}_3\) \(0.9 \text{ (3H, t), } J=6\text{ Hz), 1.20 \sim 1.45 (20H, m), 1.90 \sim 2.2 (2H, m), 2.55 (2H, dd, } J_1=6, J_2=21 \text{ Hz), 4.08 (2H, q, } J=7\text{ Hz), 4.12 (2H, q, } J=7\text{ Hz) 5.40 \sim 5.60 (2H, m). Anal. Found: C, 58.32; H, 10.83. Calcd. for C}_{16}\text{H}_{33}O_3P: C, 63.16; H, 10.86%}

Diethyl 1-(5'-methylhexyl)2-dodecenylphosphonate (7)
A solution of n-butyllithium in n-hexane \((1.6 \text{ m, 19 ml})\) was added dropwise to a stirred and cooled solution of 6 \((8.4 \text{ g})\) in dry tetrahydrofuran \((80 \text{ ml})\) at \(-60^\circ C\). The mixture was stirred for 1 hr at \(-60^\circ C\). Then a solution of 5-methylhexyl bromide \((4.9 \text{ g})\) in dry tetrahydrofuran \((15 \text{ ml})\) was added during 30 min at \(-60 \sim -50^\circ C\). The mixture was stirred for 30 min at \(-60^\circ C\) and then allowed to stand at room temperature for 1 hr. The mixture was poured into ice and brine. The organic layer was separated and the aqueous layer was extracted with ether. The combined
organic solution was dried over magnesium sulfate and concentrated in vacuo. The residue was distilled to give 7.9 g (73%) of 7, bp 162-164°C (0.1 mmHg); \( n_D^{15.5} = 1.4478 \); IR \( \nu_{\text{max}} \text{ cm}^{-1} \: 2930 (s), 2860 (s), 1470 (m), 1395 (w), 1370 (w), 1260 (s), 1170 (w), 1100 (w), 1060 (s), 1030 (s), 960 (s); NMR \( \delta \) (100 MHz, CDCl\(_3\)): 0.89 (9H, m), 1.21 (29H, m), 2.01 (2H, m), 2.18-2.40 (1H, m), 4.05 (4H, q, \( J=7.5 \text{ Hz} \)), 5.0-5.6 (2H, m); MS \( m/e \): 402 (M\(^+\)).

(E)-2-Methyl-7-octadecene (8)

A solution of the phosphonate (7, 5g) in dry ether (50ml) was added dropwise to a stirred and ice-cooled suspension of lithium aluminum hydride (0.71g) in dry ether (150ml). The mixture was stirred for 3 hr at 10-15°C and then the excess of the hydride was decomposed by successive addition of water (1ml) and 5% hydrochloric acid (10ml). The ether layer was dried over magnesium sulfate and concentrated in vacuo. The residue was distilled to give 2.21g (67%) of 8, bp 118-120°C (0.2 mmHg); \( n_D^{15.5} = 1.4839 \); IR \( \nu_{\text{max}} \text{ cm}^{-1} \: 2940 (s), 2860 (s), 1470 (m), 1390 (w), 1370 (w), 965 (m), 730 (w); NMR \( \delta \) (100 MHz, CDCl\(_3\)): 0.83 (6H, d, \( J=6 \text{ Hz} \)), 0.85 (3H, t, \( J=6 \text{ Hz} \)), 1.21-1.5 (27H, m), 2.55-2.63 (2H, m); MS \( m/e \): 266 (M\(^+\)); GLC (Column, QF-1, 1.5 m \times 3 mm i.d., at 203°C; Carrier gas, N\(_2\), 0.8 kg/cm\(^2\)): \( t_R \) 6.1 min. Anal. Found: C, 80.46; H, 13.50. Calcd. for C\(_{19}\)H\(_{38}\): C, 80.78; H, 13.56%.

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REFERENCES

2) J. P. Vité, Personal communication to K. M. dated November 5, 1976.