Pheromone Synthesis via Organoboranes: A Convenient Stereospecific Synthesis of Racemic Disparlure, the Sex Pheromone of the Gypsy Moth (*Porthetria dispar L.*)

Herbert C. Brown*, D. Basavaiah

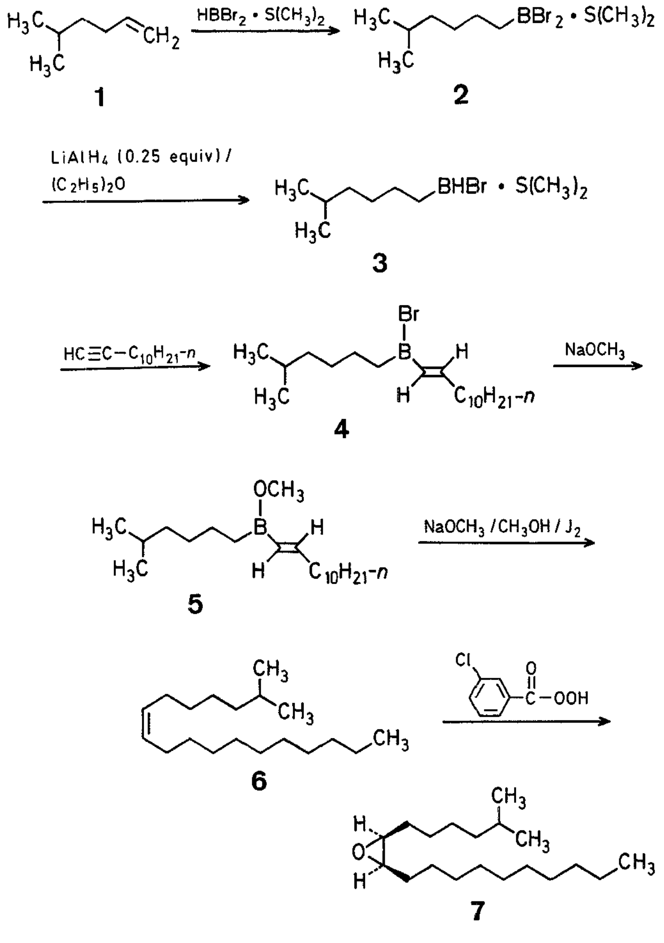
Richard B. Wetherill Laboratory, Purdue University, West Lafayette, Indiana 47907, U.S.A.

Disparlure, the sex attractant emitted by the female gypsy moth (*Porthetria dispar L.*), was identified as (*Z*)-7,8-epoxy-2-methyloctadecane (**7**) by Bierl and coworkers in 1970[1]. Since then, several syntheses of racemic and optically active forms of disparlure have been reported[2-11]. The key step in the synthesis of racemic disparlure is the generation of the *cisoid* C=C bond in the molecule. In earlier methods, this key step was achieved by Wittig olefination[2], protodesilylation of the appropriate vinylsilane[3], controlled hydrogenation of the corresponding disubstituted acetylenes[4,5], or selective ozonolysis of cyclooctadiene[6,7]. In continuation of our interest in the synthesis of insect pheromones using organoborane chemistry[12,13,14], we now report a convenient stereospecific synthesis of racemic disparlure via organoborane chemistry.

Organoboranes play an important role in developing new synthetic methodology in organic synthesis[15,16]. Recently, we have developed a simple, general, one-pot and stereospecific synthesis of (*Z*)-disubstituted alkenes via stepwise hydroboration[12]. We have now successfully employed this procedure for the synthesis of (*Z*)-2-methyl-7-octadecene (**6**) starting from readily available 5-methyl-1-hexene (**1**).

5-Methyl-1-hexene (**1**) was converted into 5-methyl-1-hexyldibromoborane-dimethyl sulfide (**2**) using dibromoborane-dimethyl sulfide[17]. Controlled hydridation[18] of **2** with lithium aluminum hydride in ether afforded the corresponding bromoborane **3**. Hydroboration of 1-dodecyne with **3** gave the corresponding vinylbromoborane **4**. Subsequent treatment with sodium methoxide, followed by iodination in the presence of sodium methoxide in methanol at room temperature produced (*Z*)-2-methyl-7-octadecene (**6**) in 55% yield. ^{13}C-N.M.R. analysis indicated >99% isomeric purity[19]. Treatment of **6** with *m*-chloroperbenzoic acid afforded (±)-disparlure (**7**) in 91% yield.

Thus, this procedure represents a simple and novel synthesis of racemic disparlure in two steps in 50% overall yield. It should be noted, however, that (+)-disparlure is ~10 times more effective as a gypsy moth attractant than (±)-disparlure[10]. We are presently exploring the possibilities of employing organoborane chemistry in the synthesis of other insect pheromones and biologically active molecules.



Boiling points were uncorrected. The G.L.C. analyses were carried out on Hewlett Packard 5750 research chromatograph (column 6 ft × 1/4 in packed with 10% SE-30 on Chromosorb W AW DMCS). ^{1}H-N.M.R. and ^{13}C-N.M.R. spectra were recorded on Varian T-60 and FT80A spectrometers respectively. 5-Methyl-1-hexene and 1-dodecyne were obtained from Wiley Organics and Farchan Acetylenes, respectively.

(*Z*)-2-Methyl-7-octadecene (6):

To 5-methyl-1-hexyldibromoborane-dimethyl sulfide [**2**; 30 mmol, obtained from 5-methyl-1-hexene (**1**; 2.94 g, 30 mmol) and dibromoborane-dimethyl sulfide (16.6 ml of 1.81 molar solution; 30 mmol)][17] are added dimethyl sulfide (3 ml) and ether (30 ml), followed by a slow addition of lithium aluminum hydride (8.15 ml of 0.92 molar solution; 7.5 mmol) under nitrogen[15]. The reaction mixture is stirred for 3 h at 0 °C and 1 h at room temperature. The resulting alkylbromoborane **3** is transferred into a solution of 1-dodecyne (6.42 ml, 30 mmol) in ether (10 ml) at 0 °C. The reaction is allowed to proceed 1 h at 0 °C and 1 h at room temperature. Then, the resulting vinylborane **4** is added to a 4.4 molar solution of sodium methoxide (34 ml, 150 mmol) in methanol at 0 °C. After 0.5 h at room temperature, the solvent ether is removed under reduced pressure and methanol (30 ml) was added. Iodine (7.62 g, 30 mmol) is added to this reaction mixture at 0 °C and stirred for 3 h at room temperature. Aqueous sodium thiosulfate solution (10 ml) is added, the reaction mixture is extracted with pentane (3 x 50 ml), and the extract is dried with anhydrous magnesium sulfate. The crude material contains ~17% of 1-dodecenyl iodide as an impurity, which can be separated nicely by careful distillation to afford (*Z*)-2-methyl-7-octadecene **(6)**; yield: 4.39 g (55%); b.p. 100–102 °C/0.05 torr (Ref.[6], b.p. 135–136 °C/1 torr); n_D^{20}: 1.4449 (Ref.[6], n_D^{20}: 1.4330); chemical purity: >98% by G.L.C.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 0.77$–1.01 (m, 9H); 1.13–1.62 (m, 23H); 1.91–2.18 (m, 4H); 5.36 ppm (m, 2H).

^{13}C-N.M.R. ($CDCl_3$/TMS): $\delta = 13.70$; 22.28; 22.50; 26.94; 27.02; 27.77; 29.20; 29.55; 29.86; 31.80; 38.81 (alkyl C); 129.31 ppm (C=C). The single vinylic carbon at $\delta = 129.31$ ppm reveals the absence of any significant amount of the corresponding (*E*)-isomer[19].

Disparlure (7):

Treatment of **6** with *m*-chloroperbenzoic acid according to the known procedure[2] affords (*Z*)-7,8-epoxy-2-methyloctadecane [**7**; (±)-disparlure]; yield: 91%; b.p. 117–118 °C/0.05 torr (Ref.[6], b.p. 142–143 °C/1 torr); n_D^{20}: 1.4462 (Ref.[6], n_D^{20}: 1.4460); chemical purity: >99% by G.L.C.

^{1}H-N.M.R. ($CDCl_3$/TMS): $\delta = 0.76$–0.99 (m, 9H); 1.06–1.71 (m, 27H); 2.76–2.94 ppm (m, 2H).

^{13}C-N.M.R. ($CDCl_3$/TMS): $\delta = 13.79$; 22.34; 22.56; 26.67; 26.92; 27.22; 27.88; 29.30; 29.58; 31.86; 38.88 (alkyl C); 55.78 ppm (2 oxirane ring C atoms).

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* Address for correspondence.

[1] B. A. Bierl, M. Beroza, C. W. Collier, *Science* **170**, 87 (1970).

[2] H. J. Bestmann, O. Vostrowsky, W. Stransky, *Chem. Ber.* **109**, 3375 (1976).

[3] W. Mychajlowskij, T. H. Chan, *Tetrahedron Lett.* **1976**, 4439.

[4] K. Eiter, *Angew. Chem.* **84**, 67 (1972); *Angew. Chem. Int. Ed. Engl.* **11**, 60 (1972).

[5] B. G. Kovalev, R. I. Ishchenko, V. A. Marchenko, M. P. Filippova, *Zh. Org. Khim.* **9**, 6 (1973).

[6] G. A. Tolstikov, V. N. Odinokov, R. I. Galeeva, R. S. Bakeeva, *Tetrahedron Lett.* **1978**, 1857.

[7] H. Klünenberg, H. J. Schäfer, *Angew. Chem.* **90**, 48 (1978); *Angew. Chem. Int. Ed. Engl.* **17**, 47 (1978).

[8] K. Mori, T. Takigawa, M. Matsui, *Tetrahedron Lett.* **1976**, 3953.

[9] S. Iwaki, S. Marumo, T. Saito, M. Yamada, K. Katagiri, *J. Am. Chem. Soc.* **96**, 7842 (1974).

[10] B. E. Rossiter, T. Katsuki, K. B. Sharpless, *J. Am. Chem. Soc.* **103**, 464 (1981).

[11] K. Mori, T. Ebata, *Tetrahedron Lett.* **22**, 4281 (1981).

[12] H. C. Brown, D. Basavaiah, *J. Org. Chem.* **47**, 3806 (1982).

[13] D. Basavaiah, H. C. Brown, *J. Org. Chem.* **47**, 1792 (1982).

[14] D. Basavaiah, *Heterocycles* **18**, 153 (1982).

[15] H. C. Brown, G. W. Kramer, A. B. Levy, M. M. Midland, *Organic Syntheses via Boranes*, Wiley-Interscience, New York, 1975.

[16] H. C. Brown, *Pure Appl. Chem.* **47**, 49 (1976).

[17] H. C. Brown, N. Ravindran, S. U. Kulkarni, *J. Org. Chem.* **45**, 384 (1980).

[18] S. U. Kulkarni, D. Basavaiah, M. Zaidlewicz, H. C. Brown, *Organometallics* **1**, 212 (1982).

[19] In a mixture of isomers, the vinylic carbons of (*Z*)-disubstituted alkenes can be distinguished from the corresponding carbons of (*E*)-alkenes: D. E. Dorman, M. Jautelat, J. D. Roberts, *J. Org. Chem.* **36**, 2757 (1971).