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A Convenient Stereoselective Synthesis of a Sex Pheromone Component of the Southern Green Stink Bug, *Nezara viridula* (L.)

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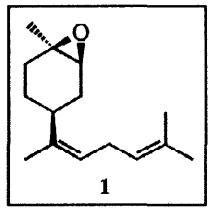
Abstract: (1'*S*,3'*S*,4'*R*,2*Z*)-(-)-2-(3',4'-Epoxy-4'-methylcyclohexyl)-6-methyl-2,5-heptadiene, a sex pheromone component of the southern green stink bug (*Nezara viridula* (L.)), was synthesized stereoselectively in four steps and 18% overall yield from (*S*)-4-methyl-3-cyclohexene-1-carboxylic acid.

The southern green stink bug, *Nezara viridula* (L.), is one of the most notorious agricultural pests distributed throughout the world, especially in tropical and neotropical regions. The sex pheromone released by males of this insect is known to consist mainly of (*Z*)-α-bisabolene, its *cis*-3',4'-epoxide **1**, and the corresponding *trans*-isomer **2**.[1] Significant damage caused by *N. viridula* (L.) to agricultural crops in both quantity and quality has prompted the synthesis of **1** and **2** with the aim to chemically control the population of this insect, and four synthetic works have already been reported to date.[1a,2] Our present communication describes the stereocontrolled synthesis of **1** accomplished in only four steps and 18% overall yield from (*S*)-4-methyl-3-cyclohexene-1-carboxylic acid **3**.



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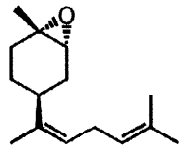

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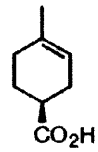

3

Our synthesis began with the bromolactonization of **3**, which was readily available *via* Helmchen's asymmetric Diels-Alder reaction[3] (Scheme 1). The resultant bromolactones, obtained as a mixture of γ-lactone **4** and δ-lactone **5** in a ratio of 1:1.3 in 86% combined yield, were treated without separation with the anion of 2-methyl-5-phenylthio-2-pentene (**6a**),[4] which brought about the lactone ring opening and concomitant epoxide ring formation to give **7a** in 81% yield. A similar reaction using **6b**[2c,5] was also successful, giving rise to 53% yield of **7b**, while in the case of **6c**[6] reductive elimination of the phenylseleno substituent occurred, resulting in the formation of **7c**. The α-phenylthio ketone **7a** produced as a 5:3 diastereomeric mixture was then allowed to react with methyllithium in THF to give a mixture which consisted of a pair of two *threo-vic*-phenylthioalcohols (*threo*-**8**), the corresponding two *erythro*-isomers (*erythro*-**8**), and a small amount of the substrate **7a**. Fortunately, *threo*-**8** was readily saparable from *erythro*-**8** by a silica gel column chromatography, which enabled us to isolate *threo*-**8** in 55% yield along with *erythro*-**8** and **7a** in 10% and 8% yields, respectively. The

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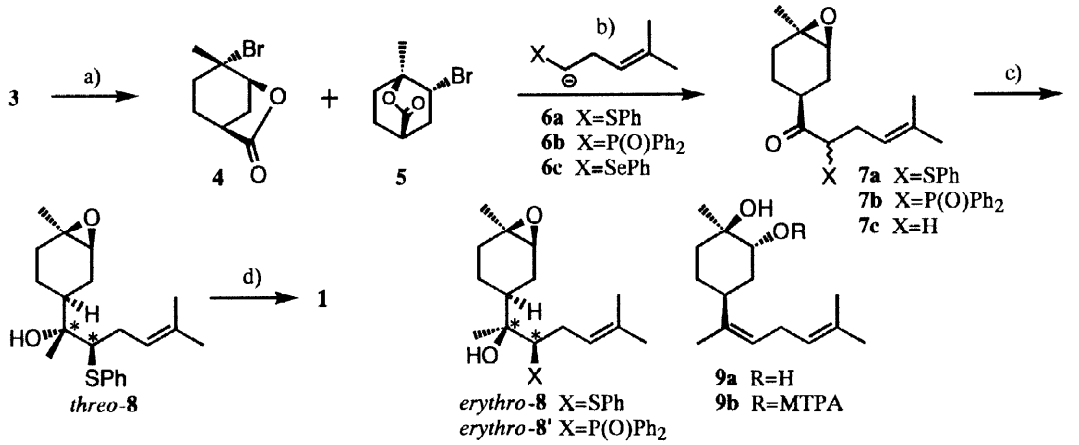

Scheme 1. *Reagents*: a) NBS, Na_2CO_3, DMF, rt (86%); b) **6a** (4-methyl-1-phenylthio-3-pentenyl-lithium), THF, -78°C to rt (81%); c) MeLi, THF, -78 to -50°C (55%); d) P_2I_4, Et_3N, CH_2Cl_2, 0°C (49%).

stereoselectivity observed in this conversion can be explained by the Felkin-Anh model.[6,7] Similar addition reactions to the α-phosphinyl ketone **7b** using MeLi, MeMgCl, MeLi-$CeCl_3$,[8a] MeMgCl-$CeCl_3$,[8a] MeMnCl,[8b] Me_3Al,[8b] $MeTiCl_3$,[8b] $LiAlMe_4$,[8c] Li_2ZnMe_4,[8c] or $MeZr(OBu)_3$[8d] as methyl donors, were also tried to obtain a mixture of chelation-controlled *erythro*-products (*erythro*-**8'**), which would lead to the desired (*Z*)-olefin **1** *via* base-induced stereospecific *syn*-elimination of diphenylphosphinic acid.[5] However, these attempts were not successful because of the epoxide ring opening or recovery of **7b** due to the enolization of this considerably acidic ketone. The mixture of the *threo*-isomers (*threo*-**8**) was finally treated with P_2I_4 (1.1 equiv) and Et_3N (5 equiv) in CH_2Cl_2 to afford, *via* stereospecific *anti*-elimination, **1** as a single isomer,[9] whose ^1H and ^{13}C NMR spectra (500 and 125 MHz, respectively) were identical with those reported previously.[2a] The optical purity of our synthetic sample ($[\alpha]_D^{22}$ -27.0° (*c*=1.60, CH_2Cl_2)) was determined to be 99% ee by ^1H NMR (500 MHz) analysis of **9b** which was obtained by *trans*-diaxial epoxide opening of **1** with dil. H_2SO_4-DMSO followed by MTPA-esterification of the resultant diol **9a**.

In conclusion, stereocontrolled synthesis of **1** was accomplished in four steps and 18% overall yield from the readily available carboxylic acid **3**. The conversion of **1** to the *trans*-isomer **2** is now in progress.

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References and Notes

1. a) Baker, R.; Borges, M.; Cooke, N. G.; Herbert, R. H. *J. Chem. Soc., Chem. Commun.* **1987**, 414-416; b) Aldrich, J. R.; Lusby, W. R. *Naturwissenschaften* **1989**, *76*, 173-175.
2. a) Marron, B. E.; Nicolaou, K. C. *Synthesis*, **1989**, 537-538; b) Tomioka, H.; Mori, K. *Biosci. Biotech. Biochem.* **1992**, *56*, 1001; c) Baptistella, L. H. B.; Aleixo, A. M. *Liebigs Ann. Chem.* **1994**, 785-789.
3. Poll, T; Sobczak, A.; Hartmann, H.; Helmchen, G. *Tetrahedron Lett.* **1985**, *26*, 3095-3098.
4. Amiaux, A.; Eman, A.; Dumont, N.; Krief, A. *Tetrahedron Lett.* **1975**, 1617-1620.
5. Hutton, G.; Jolliff, T.; Mitchellm H.; Warren, S. *Tetrahedron Lett.* **1995**, *36*, 7905-7908.
6. Leonard-Coppens, A. M.; Krief, A. *Tetrahedron Lett.* **1976**, 3227-3230.
7. The intermediate (*threo*-**8**) was a mixture of the two *threo*-diastereomers in a ratio of ca. 2:1, as judged by 500 MHz ^1H NMR analysis. The assignments of the relative stereochemistries were confirmed by the fact that *threo*- and *erythro*-**8** were converted into **1** and (*E*)-**1**, respectively, by the stereospecific *anti*-elimination described in the text.
8. a) Imamoto, T.; Takiyama, N.; Nakamura, K.; Hatajima, T.; Kamiya, K. *J. Am. Chem. Soc.* **1989**, *111*, 4392-4398; b) Taniguchi, M.; Fuji, H.; Oshima, K.; Utimoto, K. *Tetrahedron Lett.* **1992**, *33*, 4353-4356; c) Ashby, E.; Chao, L.-C.; Laemmle, J. *J. Org. Chem.* **1974**, *39*, 3258-3263; d) Weidmann, B.; Maycock, C. D.; Seebach, D. *Helv. Chim. Acta* **1981**, *64*, 1552-1557.
9. Denis, J. N.; Dumont, W.; Krief, A. *Tetrahedron Lett.* **1979**, 4111-4112.