12. Synthesis of Blattellastanoside A, a Steroid Glucoside Isolated as the Aggregation Pheromone of the German Cockroach

By Kenji MORI and Kunio FUKAMATSU

Department of Agricultural Chemistry, The University of Tokyo,
1-1-1 Yayoi, Bunkyo-ku, Tokyo 113

(Communicated by Masanao MATSUI, M. J. A., March 12, 1993)

Abstract: β -Sitosterol (**7**) was converted to blattellastanoside A [**5**, 1-(6 α -chloro-4 β , 5 β -epoxy-5 β -stigmastan-3 β -yl)- β -D-glucopyranoside], the structure proposed for the arrestant component of the aggregation pheromone of the German cockroach, *Blattella germanica* L. Our synthetic **5** was identical with the natural product on the basis of ^1H and ^{13}C NMR spectral comparison, HPLC analysis and pheromone activity.

Key words: Aggregation pheromone; blattellastanoside A, synthesis of; German cockroach; glucoside; steroid.

The aggregation pheromone of the German cockroach (*Blattella germanica* L.) is excreted with its frass and marks its harboring place.¹⁾ In 1990 Sakuma and Fukami identified the hydrochlorides of ammonia, methylamine, dimethylamine, trimethylamine, and 1-dimethylamino-2-methyl-2-propanol as the attractant components of the aggregation pheromone.²⁾ They then demonstrated the presence of the arrestant components in the frass.³⁾ Their work culminated in the isolation of two arrestant components, which were shown to be steroid glucosides and named as blattellastanosides A and B.⁴⁾ The pheromone activity of the former was ca. 70 times stronger than that of the latter. Their structures were first proposed as **1** and **2**, respectively (Fig. 1).⁴⁾ These proposals were modified shortly afterwards, and the structures **3** and **4** were the next candidates.⁵⁾ Our synthetic studies on the compounds related to **1–4** including a synthesis of **3**, however, indicated the incorrectness of the proposed structures.⁶⁾

Very recently, Sakuma and Fukami reported new structures **5** and **6** for blattellastanosides A and B, respectively.⁷⁾ Herein we announce the first synthesis of **5**, which was proved to be identical with the natural blattellastanoside A by the comparison of its physical and biological properties. The outline of our synthesis is shown in Fig. 2. Commercially available stigmasterol was converted to β -sitosterol (**7**) in 70% overall yield (4 steps) according to Steele and Mosettig.⁸⁾ Epoxidation of **7** with *m*-chloroperbenzoic acid (MCPBA) gave epoxy alcohol **8** as a 4:1 mixture of the desired α -epoxide and its β -isomer in accord with the known result with cholesterol.⁹⁾ Treatment of **8** with hydrogen chloride in chloroform was followed by oxidation of the product to give nicely crystalline chloro ketol **9**, m.p. 224–226°C; $[\alpha]_D^{25} = +1.63^\circ$ ($c=0.57$, CHCl_3), in 64% yield after recrystallization. The β - and axial orientation of the chlorine substituent of **9** was supported by its ^1H NMR spectrum, in which the signal due to the equatorial proton at C-6 appeared at $\delta=3.84$ (br. t, $J=2.6$ Hz). Dehydration of **9** with hydrochloric acid in acetic acid caused epimerization at C-6 to give **10**, m.p. 106–108°C; $[\alpha]_D^{25} = +59.2^\circ$ ($c=0.98$, CHCl_3), with an axial proton at C-6 ($\delta=4.67$, ddd, $J=12.6, 5.0, 1.8$ Hz). The α , β -unsaturated ketone **10** was reduced with lithium tri(*t*-butoxy)aluminum hydride to generate a β - and quasi-equatorial hydroxy group at C-3. The resulting allylic alcohol was epoxidized with MCPBA to give the corresponding β -epoxide **12** produced by *cis*-epoxidation as assisted by the β -oriented

Acknowledgment. We thank Dr. M. Sakuma, Pesticide Research Institute (Kyoto University), for exchange of information, and the spectral and HPLC comparison as well as bioassay of our synthetic **5**. Financial support of this work by Fuji Chemical Industries, Ltd. is acknowledged with thanks.

Fig. 2. Synthesis of blattellastanoside A. Reagents: (a) MCPBA, CH_2Cl_2 ; (b) HCl , CHCl_3 ; (c) Jones CrO_3 , Me_2CO ; (d) concd. HCl , AcOH ; (e) $\text{LiAl}(\text{O}t\text{-Bu})_3\text{H}$, THF ; (f) Ac_2O , Et_3N , DMAP , CH_2Cl_2 ; (g) $(i\text{-Bu})_2\text{AlH}$, CH_2Cl_2 ; (h) PCC , CH_2Cl_2 ; (i) $\text{Hg}(\text{CN})_2$, $\text{C}_6\text{H}_6/\text{MeNO}_2$; (j) NaOMe , MeOH/THF .

References

- 1) Ishii, S., and Kuwahara, Y.: Appl. Ent. Zool., 2, 203–217 (1967).
- 2) Sakuma, M., and Fukami, H.: ibid., 25, 355–368 (1990).
- 3) —: ibid., 26, 223–235 (1991).
- 4) —: Nippon Nōgeikagaku Kaishi, 66, 442 (1992).
- 5) Sakuma, M., and Fukami, H.: Presented as Poster-44 at the 9th Annual Meeting of International Society of Chemical Ecology, July 6–9, Kyoto, Japan, Abstract of Papers, p. 74 (1992).
- 6) Mori, K., Fukamatsu, K., and Kido, M.: Liebigs Ann. Chem. (to be submitted).
- 7) Sakuma, M., and Fukami, H.: Tetrahedron Lett. (in press).
- 8) Steele, J. A., and Mosettig, E.: J. Org. Chem., 28, 571–572 (1963).
- 9) Fieser, L. F., and Fieser, M.: Reagents in Organic Synthesis. John Wiley and Sons, Inc., New York, p. 136 (1967).
- 10) We thank Dr. M. Kido (Otsuka Pharmaceutical Co., Ltd.) for the X-ray analysis of 13. Details will be reported in the forthcoming full paper.
- 11) ^1H NMR spectrum of 5 (300 MHz, CDCl_3): $\delta=0.68$ (s, 3H, 18-H), 0.81 (d, $J=6.5$ Hz, 3H, 26-H), 0.83 (d, $J=6.5$ Hz, 3H, 27-H), 0.85 (t, $J=7.3$ Hz, 3H, 29-H), 0.91 (d, $J=6.5$ Hz,

3H, 21-H), 0.80–1.48 (m), 1.50–1.70 (m), 1.80–1.95 (m, 1H, 16 α -H), 2.00 (br.d, J =12.5 Hz, 1H, 12 β -H), 2.25 (dt, J =12.5, 4.0 Hz, 1H, 7 β -H), 3.35–3.50 (m, 2H, 2'-H and 5'-H), 3.55–3.70 (m, 2H, 3'-H and 4'-H), 3.81 (d, J =3.5 Hz, 1H, 4-H), 3.80–3.95 (m, 2H, 6'-H), 4.25 (br.s, $W_{1/2}$ =10.5 Hz, 1H, 3-H), 4.44 (dd, J =12.5, 4.0 Hz, 1H, 6-H), 4.60 (d, J =7.6 Hz, 1H, 1'-H). ^{13}C NMR spectrum of **5** (125 MHz, CDCl_3): 1; δ c 30.1, 2; 23.5, 3; 72.2, 4; 56.1, 5; 67.5, 6; 58.5, 7; 41.7, 8; 35.8, 9; 48.3, 10; 38.3, 11; 21.4, 12; 39.5, 13; 42.7, 14; 55.5, 15; 24.2, 16; 28.1, 17; 56.2, 18; 12.0, 19; 18.6, 20; 36.1, 21; 18.6, 22; 33.9, 23; 26.2, 24; 45.8, 25; 29.1, 26; 19.8, 27; 19.0, 28; 23.1, 29; 12.0, 1'; 101.8, 2'; 73.6, 3'; 76.3, 4'; 69.8, 5'; 75.7, 6'; 61.9.