Tetrahedron Letters No. 26, pp 2401 - 2402.
0040-4039/79/0622-2401$02.00/0
© Pergamon Press Ltd. 1979. Printed in Great Britain.

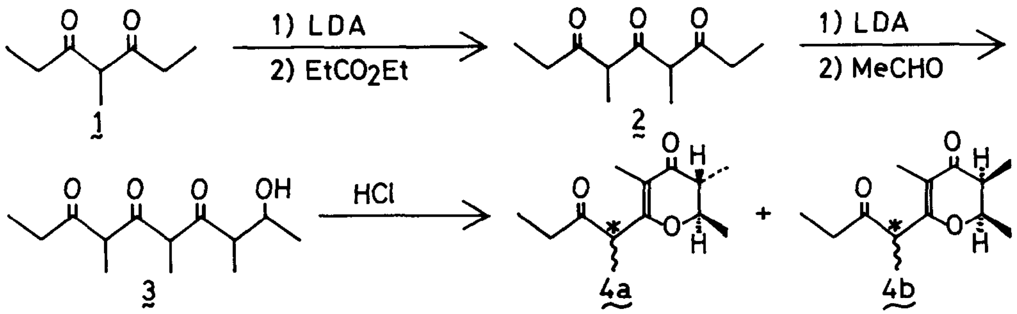
SYNTHESIS OF A STEREOISOMERIC MIXTURE OF 2,3-DIHYDRO-2,3,5-TRIMETHYL-6-(1-METHYL-2-OXOBUTYL)-4H-PYRAN-4-ONE, THE PHEROMONE OF THE DRUGSTORE BEETLE

Masayuki Sakakibara and Kenji Mori*

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

Abstract : Reaction of acetaldehyde with the trianion of 4,6-dimethylnonane-3,5,7-trione followed by acidification yielded a stereoisomeric mixture of the pheromone of *Stegobium paniceum* L.

The sex pheromone produced by the female drugstore beetle, *Stegobium paniceum* L., was recently isolated,[1] and the structure 4b was assigned to it on the basis of chemical and spectroscopic evidence.[2] Here we record a simple biomimetic synthesis of 4b as a mixture of two diastereomeric racemates. The synthetic scheme shown below is based on the recent progress in the chemistry of di- and trianions.[3-7]



Diethyl ketone was acylated with ethyl propionate in the presence of sodium hydride to give 1 in 81% yield, bp 82-85°/14mm, n_D^{20} 1.4388. This (20mmol) was dissolved in THF-HMPA (4:2.4) and converted to a dianion by the addition of LiNPr$^i_2$ (2.2eq) at -70° under Ar. The mixture was warmed to -30° during 30 min and cooled again to -70°. Ethyl propionate (20mmol) in THF was added to yield 2. After 1 hr LiNPr$^i_2$ (1.1eq) in THF was added at -70° to generate a trianion of 2. After another hr acetaldehyde (22mmol) was added at -70° and the mixture was warmed to -30° during 1 hr. Then the mixture containing 3 was acidified with excess 10% HCl-MeCN (1:1) and left to stand for 18 hr at room temperature. The products were extracted with n-hexane and purified by silica gel column chromatography. Elution with n-hexane-ether yielded the *trans*-isomer 4a first, and then the desired *cis*-isomer **4b** was obtained. These were further purified by preparative TLC (Merck Kieselgel 60 F_{254}) to give pure **4a** (109mg)[8] and **4b** (100mg)[9] as oils. The configurational assignment of the *vic*-dimethyl groups of **4a** and **4b** was made possible by inspection of their PMR spectra: the signal due to the proton at C-2 of **4a** was observed at δ 4.02 as 1H dq (J=14 and 7Hz), while that of **4b** was observed at δ 4.46 as 1H dq (J=7 and 3Hz). The small J-value (3Hz) indicated the 2,3-*cis*-stereochemistry of **4b**. The IR, UV, NMR and mass spectral data of **4b** were identical with the published data of the natural pheromone.[2] The structure of the drugstore beetle pheromone was thus established as **4b**. Biological evaluation of our synthetic **4b** is now underway by Professor W.E. Burkholder, University of Wisconsin-Madison.[10]

Acknowledgements. We thank Professors W.E. Burkholder, H. Fukami and Y. Kuwahara for their interests.

REFERENCES AND FOOTNOTES

1. Y. Kuwahara, H. Fukami, S. Ishii, F. Matsumura and W.E. Burkholder, *J. Chem. Ecol*. **1**, 413 (1975).
2. Y. Kuwahara, H. Fukami, R. Howard, S. Ishii, F. Matsumura and W.E. Burkholder, *Tetrahedron* **34**, 1769 (1978). Although the formulas **4a** and **4b** represent only one enantiomer, they are taken to mean a diastereomeric mixture of racemates with unknown configuration at the side-chain methyl group. The absolute stereochemistry of the natural pheromone is unknown.
3. T.T. Howarth, G.P. Murphy and T.M. Harris, *J. Am. Chem. Soc*. **91**, 517 (1969).
4. T.M. Harris and G.P. Murphy, *ibid*. **93**, 6708 (1971).
5. S.N. Huckin and L. Weiler, *ibid*. **96**, 1082 (1974).
6. Idem., *Canad. J. Chem*. **52**, 1343 (1974).
7. For an application of dianion chemistry in pheromone synthesis see: K. Mori, M. Sasaki, S. Tamada, T. Suguro and S. Masuda, *Heterocycles* **10**, 111 (1978).
8. PMR data of **4a**: δ (60MHz, $CDCl_3$) 1.05 (3H, t, J=7Hz), 1.10 (3H, d, J=7Hz), 1.31 (3H, d, J=7Hz), 1.38 (3H, d, J=7Hz), 1.79 (3H, s), 2.0-2.7 (3H, m, containing 2H, q (J=7Hz) at 2.45), 3.62 (1H, q, J=7Hz), 4.02 (1H, dq, J=14 and 7Hz).
9. Spectral data of **4b**: $IR_{\nu max}$(film) 2970 (m), 2920 (m), 2860 (m), 1723 (vs), 1660 (vs), 1605 (vs), 1450 (m), 1385 (s), 1363 (m), 1340 (s), 1215 (m), 1145 (s), 1120 (m), 1090 (m), 1050 (m), 1015 (w), 1000 (w), 960 (w), 910 (w), 705 (w) cm^{-1} ; UV λmax (EtOH) 273 nm (ε 10900); PMR δ(60MHz, $CDCl_3$) 1.05 (3H, d, J=7Hz), 1.06 (3H, t, J=7Hz), 1.30 (6H, d, J=7Hz), 1.79 (3H, s), 2.1-2.7 (3H, m, containing 2H, q (J=7Hz) at 2.48), 3.67 (1H, q, J=7Hz), 4.46 (1H, dq, J=7 and 3Hz); CMR δ(25.05 MHz, $CDCl_3$) 7.897, 9.360, 12.724 & 12.812, 15.707 & 15.883, 33.873, 43.730, 49.200 & 49.405, 77.223 & 77.515, 109.458 & 109.516, 168.984, 196.948 & 197.036, 207.011 & 207.420. In the CMR spectrum of **4b**, some signals (e.g. Me at C-2, Me α to the side-chain CO, etc.) were observed as doublets due to the presence of the two diastereomers originating from the different configuration at the asterisked asymmetric carbon in the side-chain of **4b**.
10. This paper is Part XXXIII of "Pheromone Synthesis" by K. Mori. Part XXXII, K. Sato, T. Nakayama and K. Mori, *Agric. Biol. Chem*., in the press.

(Received in Japan 24 March 1979)