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SYNTHESIS OF THE HONEY-BEE ATTRACTANT 13-HYDROXY-2-OXOTRIDECANE

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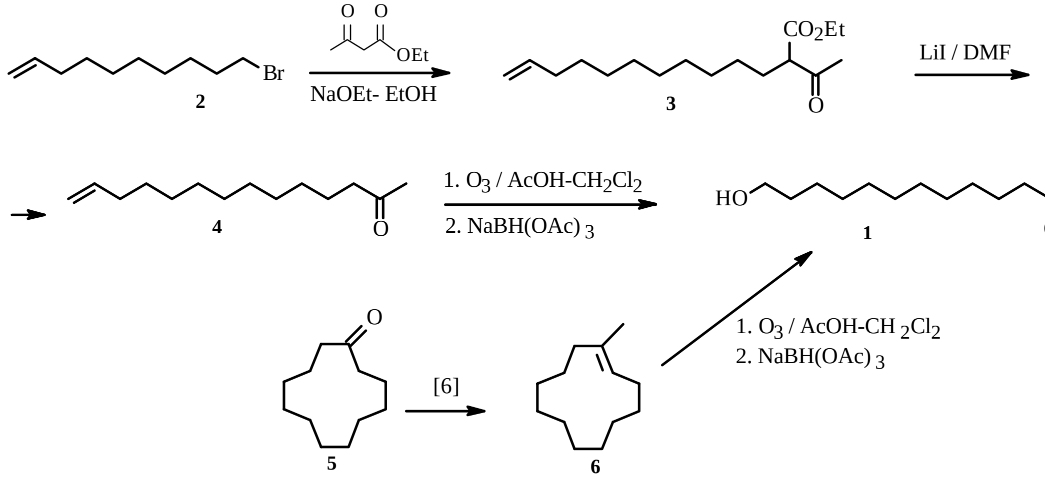
13-Hydroxy-2-oxotridecane, which is isolated from extract of Evodia hupehensis *Dode honey-bee eggs and actively attracts honey bees, is synthesized via ozonolysis of 1-methylcyclododecene and tetradec-13-en-2-one, the product from monoalkylation of the acetoacetic ester with 1-bromo-10-undecene followed by decarbethoxylation, with further reduction of the intermediate peroxides using NaBH(OAc)$_3$.*

Key words: bee attractant, acetoacetic ester, 1-bromo-10-undecene, 13-hydroxy-2-oxotridecane, bee, 1-methylcyclododecene, ozonolysis, tetradec-13-en-2-one, sodium triacetoxyborohydride, synthesis.

13-Hydroxy-2-oxotridecane (**1**) is isolated from extract of *Evodia hupehensis* Dode honey-bee eggs and actively attracts honey bees [1]. The synthesis of compound **1** via exhaustive ozonolysis of the double bonds in 2-methyl-1,13-tetradecadiene (prepared via condensation of 10-undecenylbromide and methylallylchloride) followed by selective reduction by NaBH(OAc)$_3$ of the aldehyde function in the intermediate 12-oxotridecanal has been reported [2].

We developed new approaches to the synthesis of attractant **1**. One of these is based on selective transformations of the product from monoalkylation of the acetoacetic ester with 1-bromo-10-undecene (**2**) from undecylenic acid by the literature method [3]. Decarbethoxylation of the unsaturated ketoester (**3**) under standard conditions [4] gives the key intermediate tetradec-13-en-2-one [**4**), ozonolysis of which followed by reduction of the peroxide with NaBH(OAc)$_3$ [5] avoids the preparation of the unstable 12-oxotridecanal and increases the overall yield of compound **1** (calculated based on bromide **2**) from 41 to 71%.



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A shorter and effective synthesis of **1** uses ozonolysis of 1-methylcyclododecene (**6**), prepared from cyclododecanone (**5**) according to the literature [6] and direct reduction of the peroxides using $NaBH(OAc)_3$. The yield was 98% based on starting olefine **6**.

EXPERIMENTAL

IR spectra were recorded on a UR-20 instrument as thin layers. NMR spectra were taken on a Bruker AM-300 spectrometer (working frequency 300.13 MHz for ^1H and 75.47 MHz for ^{13}C) in $CDCl_3$. The internal standard was chloroform (impurity of protonated solvent in PMR, δ 7.27 ppm; in ^{13}C NMR, the average $CDCl_3$ signal at δ 77.00 ppm). Chromatography was performed on a Chrom-5 instrument (column length, 1.2 m; stationary phase, SE-30 silicone (5%) on Chromaton N-AW-DMCS, 0.16-0.20 mm), working temperature 50-300°C, He carrier gas. Analytical data corresponded to those calculated.

Ethyl-2-acetyltridec-12-enoate (3). A solution of sodium ethylate [prepared from Na (0.85 g, $36.7 \cdot 10^{-3}$ g-at) in absolute EtOH (20 mL)] was treated under Ar at 20°C with acetoacetic ester (5.26 g, 40.4 mmole), heated to boiling, and treated with bromide **2** (4.05 g, 17.4 mmole). The reaction mixture was boiled for 18 h (TLC monitoring), cooled, and filtered through a Schott filter. The solid on the filter was washed with EtOH and evaporated. Yield of compound **3**, 4.38 g (89%). IR spectrum (KBr, ν, cm^{-1}): 920, 1010 (=C–H), 1050, 1275 (C–O–C), 1645 (C=C), 1715 (C=O, ketone), 1750 (C=O, ester), 3090 ($CH{=}CH_2$). PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 1.30 (3H, t, J = 6.5, $C\mathbf{H}_3CH_2O$), 1.20-1.40 (16H, m, H-3—H-10), 1.99 (2H, m, H-11), 2.18 (3H, s, H_3CCO), 3.33 (1H, t, J = 7.4, H-2), 4.15 (2H, q, J = 7.1, H_2CO), 4.85-5.00 (2H, m, $H_2C{=}$), 5.68-5.83 (1H, m, HC=).

^{13}C NMR ($CDCl_3$): 14.00 (q, $H_3\mathbf{C}CH_2O$), 28.61 (q, $H_3\mathbf{C}CO$), 27.28, 28.09, 28.81, 28.99, 29.06, 29.19, 29.34, 29.43 (t, C-3—C-10), 33.70 (t, C-11), 59.82 (d, C-2), 61.14 (t, CH_2O), 114.01 (t, C-13), 139.07 (d, C-12), 169.83 (s, C-1), 203.27 (s, $H_3\mathbf{C}CO$).

Tetradec-13-en-2-one (4). A solution of ester **3** (2.65 g, 9.4 mmole) in absolute DMF (27 mL) at room temperature was treated with LiI (3.27 g, 24.4 mmole), boiled until CO_2 evolution ceased (~12 h), cooled, extracted with methyl-*t*-butylether (200 mL), washed successively with saturated $Na_2S_2O_3$ and NaCl solutions, dried over Na_2SO_4, and evaporated. Yield of enone **4**, 1.60 g (81%). IR spectrum (KBr, ν, cm^{-1}): 920, 1010 (=C–H), 1650 (C=C), 1720 (C=O), 3020, 3090 ($CH{=}CH_2$). PMR spectrum ($CDCl_3$, δ, ppm, J/Hz): 1.22 (16H, br. s, H-4—H-11), 1.98 (2H, m, H-12), 2.08 (3H, s, H_3CCO), 2.37 (2H, t, J = 7.3, H-3), 4.83-4.98 (2H, m, $H_2C{=}$), 5.68-5.84 (1H, m, HC=).

^{13}C NMR ($CDCl_3$): 25.20 (t, C-4), 28.73, 29.10, 29.16, 29.18, 29.21, 29.26, 29.32 (t, C-5—C-11), 29.65 (q, C-1), 33.66 (t, C-12), 43.63 (t, C-3), 113.95 (t, C-14), 139.03 (d, C-13), 209.04 (s, C-2).

13-Hydroxy-2-oxotridecane (1). a. An ozone—oxygen mixture (ozonator production, 40 mmole O_3/h) was bubbled through a solution of olefine **4** (1.25 g, 14.4 mmole) and glacial AcOH (1.72 g, 28.7 mmole) in CH_2Cl_2 (40 mL) that was stirred at -4 to -2°C until 15 mmole of ozone was absorbed. The reaction mixture was purged with Ar, diluted with CH_2Cl_2 (20 mL), and treated with stirring (10°C) with a previously prepared suspension of $NaBH(OAc)_3$ [prepared by treating a solution of glacial AcOH (11.9 g, 198.0 mmole) in CH_2Cl_2 (20 mL) with a suspension of $NaBH_4$ (2.5 g, 66.0 mmole) in CH_2Cl_2 (100 mL) followed by stirring for 2 h]. The reaction mixture was heated to room temperature, stirred for 3 h, cooled to 10°C, and treated with NaOH solution (4.5 g in 100 mL water). The organic layer was separated, washed successively with saturated NH_4Cl solution and water, dried over Na_2SO_4, and evaporated. Yield of **1**, 1.25 g (98%), mp 54.0-54.5°C [2].

IR and PMR spectra were identical to those reported in the literature [2]. ^{13}C NMR spectrum ($CDCl_3$): 23.68 (t, C-10), 25.63 (t, C-3), 28.98, 29.21, 29.26, 29.26, 29.34, 29.41 (t, C-4—C-9), 29.67 (q, C-1), 32.58 (t, C-2), 43.67 (t, C-12), 62.69 (t, C-1), 209.56 (s, C-13).

b. Ozonolysis of cycloolefine **6** (1.00 g, 5.55 mmole) under the conditions described above gave **1** (1.06 g, 89%) identical to that obtained from experiment **a**.

REFERENCES

1. M. Gellert, Z. Rozsa, Z. Kovacz, K. Szendrei, R. A. Hussain, G. Reisch, and J. Reisch, *Herba Hung.*, **24**, 53 (1985).
2. V. N. Odinokov, G. Yu. Ishmuratov, I. M. Ladenkova, and G. A. Tolstikov, *Khim. Prir. Soedin.*, 270 (1990).

3. N. K. Khao, M. V. Mavrov, and E. P. Serebryakov, *Bioorg. Khim.*, **14**, 250 (1988).
4. G. A. Tolstikov, M. S. Miftakhov, and F. A. Valeev, *Zh. Org. Khim.*, **17**, 1441 (1981).
5. G. Yu. Ishmuratov, R. Ya. Kharisov, M. P. Yakovleva, O. B. Botsman, R. R. Muslukhov, and G. A. Tolstikov, *Izv. Akad. Nauk, Ser. Khim.*, 198 (1999).
6. J. Sicher, M. Svoboda, M. Pankova, and J. Zavada, *Collect. Czech. Chem. Commun.*, **35**, 3633 (1971).