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Conformationally Constrained Analogues of (*Z*)-5-Decenyl Acetate, a Pheromone Component of *Agrotis segetum*

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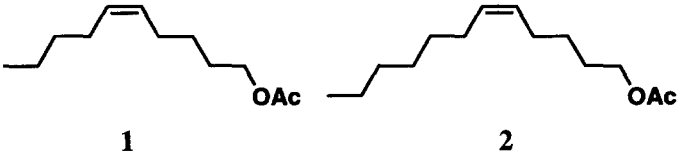
Abstract—Conformationally constrained analogues of (*Z*)-5-decenyl acetate (**1**), a pheromone component of the turnip moth, *Agrotis segetum*, have been synthesized and tested by using electrophysiological single-cell recordings. In the constrained analogues the terminal alkyl chain in **1** has been incorporated in a six-membered (**3** and **4**) or five-membered (**6**) ring system. These cyclic compounds are also conformationally constrained analogues of the previously deduced bioactive conformations of the corresponding chain-elongated analogues **2** and **5**. The electrophysiological activities of the constrained analogues are found to be significantly lower than that of the natural pheromone component **1**, most probably due to steric repulsive interactions between the analogue and the receptor, and also lower than the activities of the corresponding chain-elongated analogues of **1**. It is concluded that the flexibility of the terminal chains in **2** and **5** is essential for the possibility of the receptor to accommodate these parts of the chain-elongated analogues in their bioactive conformations. Copyright © 1996 Elsevier Science Ltd

Introduction

(*Z*)-5-Decenyl acetate (**1**) is a pheromone component of the turnip moth, *Agrotis segetum*.[1–3] In a number of previous studies, we have investigated structure–activity relationships for analogues of **1**, employing single-cell electrophysiology and molecular mechanics calculations.[4–14] On the basis of these studies we have concluded that the biologically active conformation of **1** is a *cisoid* conformation with all-*anti* alkyl chains, as shown in Figure 1(a). We have also concluded that the receptor for **1** does not tolerate any increase of the molecular size in the direction of the terminal terminal C—C bond.[6] Furthermore, in studies of chain-elongated analogues of **1** we have been able to rationalize their electrophysiological activities in terms of the conformational energies required by the analogues to mimic the proposed biologically active conformation of **1**.[7,8] For instance, in order to structurally mimic the proposed bioactive conformation of **1**, the terminal alkyl chains of the chain-elongated analogues were concluded to form a loop as shown in Figure 1(b) for (*Z*)-5-dodecenyl acetate (**2**). Conformational energies for such a loop formation, calculated by the molecular mechanics method, were shown to correlate extremely well with observed relative electrophysiological activities implying that the relative activities of the chain-elongated analogues of **1** are largely determined by the energies required to acquire the bioactive conformation.[4,8] This further implies that the receptor is able accommodate the bulk of the loops.

In the case of **2** the observed activity decrease was found to be due to repulsive steric interactions between the methylene groups in the 7 and 11 positions in the bioactive conformation of **2** [see Fig. 1(b)]. In order to test the conclusion that the terminal chains of chain-elongated analogues of **1** adopt a loop conformation in the bioactive conformation, we have in a recent study prepared and tested the 7-oxa and 9-oxa analogues of **1** and the 7-oxa and 11-oxa analogues of the chain-elongated analogue **2**.[14] By replacing one of the methylene groups in the 7 and 11 positions in **2** by an oxygen atom, the energy requirements for loop formation decrease significantly due to smaller steric repulsive interactions between an oxygen atom and a methylene group compared with the corresponding repulsions between two methylene groups. Thus, if the bioactive conformation of chain-elongated analogues involves a loop conformation, the decrease of the electrophysiological activity on chain-elongation of the oxa-analogues should be significantly smaller than that observed for chain-elongation of **1** to **2**. This was shown to be the case.[14] In addition, it was found that the molecular mechanics calculated energies for loop



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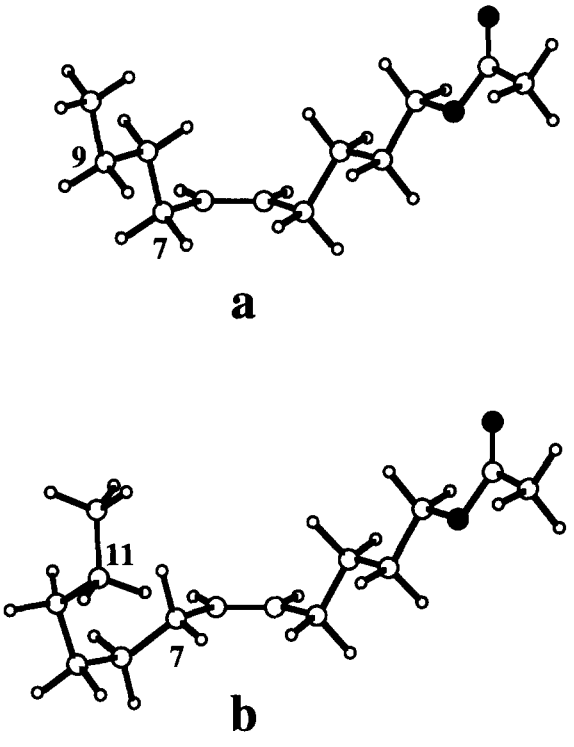
Key words: Structure–activity, *Agrotis segetum*, cyclic analogues, single-cell recordings, pheromone component.



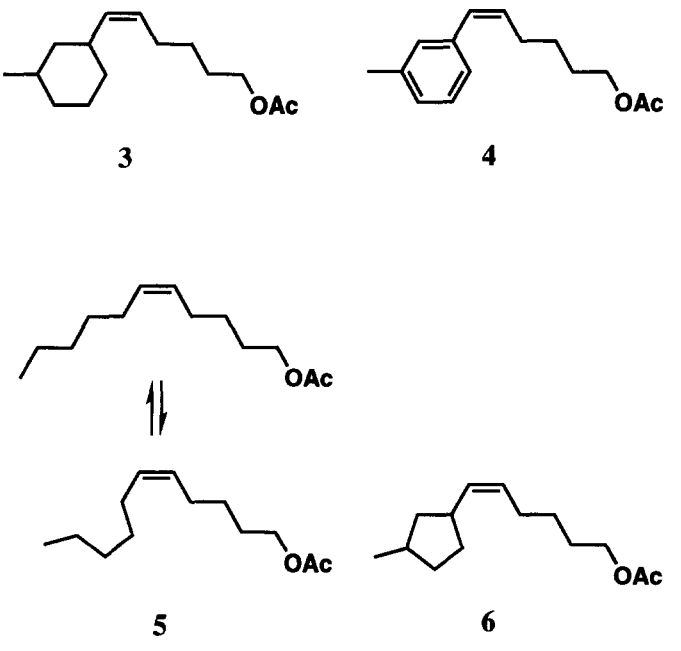


Figure 1. The deduced bioactive conformations of (a) **1** and (b) **2**.

formation of the terminal chains in the oxa-analogues closely parallel the observed activities. These results strongly support a loop conformation of the terminal chain in the active conformation of **2**.

On the basis of these studies the receptor seems to be able to accommodate the bulk of a loop as in the proposed bioactive conformation of **2** shown in Figure 1(b). However, in recent studies on alkyl substituted analogues of **1**, we have found that the terminal alkyl chain of **1** interacts with the receptor with a very high degree of steric complementarily.[9-11] In particular, the introduction of methyl groups in the 7 and 9 positions of **1** [see Fig. 1(a)], corresponding to the first and the last methylene groups of the loop in Figure 1(b), leads to a significant reduction of the electrophysiological activity, which was interpreted as being due to steric repulsive interactions between the methyl groups and the receptor.

In order to further probe the dimensions and properties of the receptor in the vicinity of the receptor-bound terminal chain of **1**, we have in the present work studied the cyclic analogues **3**, **4** and **6**. These compounds are conformationally constrained mimics of **1** in a conformation with an all-*anti* terminal chain. Compounds **3** and **4** are also conformationally constrained analogues of the loop conformation of **2** in its suggested biologically active conformation (Figure 1b), whereas **6** mimics the proposed loop conformation of the one-carbon chain-elongated analogue **5**.

Results and Discussion

Synthesis

As shown in Figure 2, the cyclic analogues **3**, **4** and **6** were prepared from the (*Z*)-alkenyl cuprate **8**.[9,15] Michael addition of **8** to 2-cyclohexenone afforded **9** in 47% yield.[16] At this point we were searching for a stereoselective approach for equatorial methylation of the cyclohexanone derivative **9**. The reagent of choice was found to be MeLi–Me_2CuLi, which has previously proven to give good stereoselectivity for unhindered conformationally biased cyclohexanones.[17] Methylation with this reagent gave a 9:1 mixture of *cis/trans* dialkyl-substituted cyclohexane derivative **10**. Removal of the tertiary alcohol group took place quantitatively when the alcoholate anion of **10** was phosphorylated with diethylphosphorochloridate followed by reductive cleavage of the ester group by the addition of the ester to a solution of lithium in dry ethyl amine.[18] Completion of the synthesis of compound **3** was accomplished by removal of the ethoxyethyl group followed by acetylation.

The synthesis of compound **6** was accomplished in a similar manner, but with 2-cyclopentenone in place of 2-cyclohexenone. The stereochemical control in the methylation step of the cyclopentenone derivative was, as expected, inferior to that of the cyclohexanone derivative. The product was a 55:45 mixture of the *cis* and *trans* isomers, which were not separable by preparative GC.

The synthesis of **4** was carried out according to the procedure of Jabri et al.[19] Transmetallation from **8** to the corresponding alkenyl zinc halide, followed by

addition of 3% $Pd(PPh_3)_4$ and 3-iodotoluene afforded the conjugate product with retained stereochemistry.

The product was acetylated and purified by silica gel chromatography (83% yield from **8**) and finally purified by preparative GC to obtain the final product in > 99% purity.

Single-cell electrophysiology

The activities of compounds **1-6** were determined by single-cell electrophysiology using the olfactory receptor cell specifically tuned to (*Z*)-5-decenyl acetate, present in the antennal sensilla type SWI of *A. segetum*.[3] Relative single-cell activities for compounds **1–6**, including corrections for differences in volatilities (see Experimental), are shown in Figure 3.

All analogues display reduced activities compared with that of **1**. Compound **3** is essentially inactive, while compounds **2** and **4–6** show 600, 830, 13 and 130 times lower activities, respectively, than the natural pheromone component **1**. The conformational energies required for **2**, **4** and **6** to mimic the proposed biologically active conformation of **1** [Fig. 1(a)] were calculated by the molecular mechanics method employing the MM2(91) force-field.[20] The details of the computational methodology have previously been described.[8] The calculated conformational energies required by the conformationally constrained analogues **3**, **4** and **6** to mimic the bioactive conformation of **1** were in all cases less than 1 kcal/mol higher than that calculated for **1**.

Compound **3** was tested as its racemate, but as the pure *cis* isomer. The strongly preferred conformation of this isomer is the diequatorial one, which closely mimics an all-*anti* conformation of the terminal chain of **1**. The conformational energy for **3** to adopt the proposed bioactive conformation is, as described above, low. Thus, it must be concluded that the

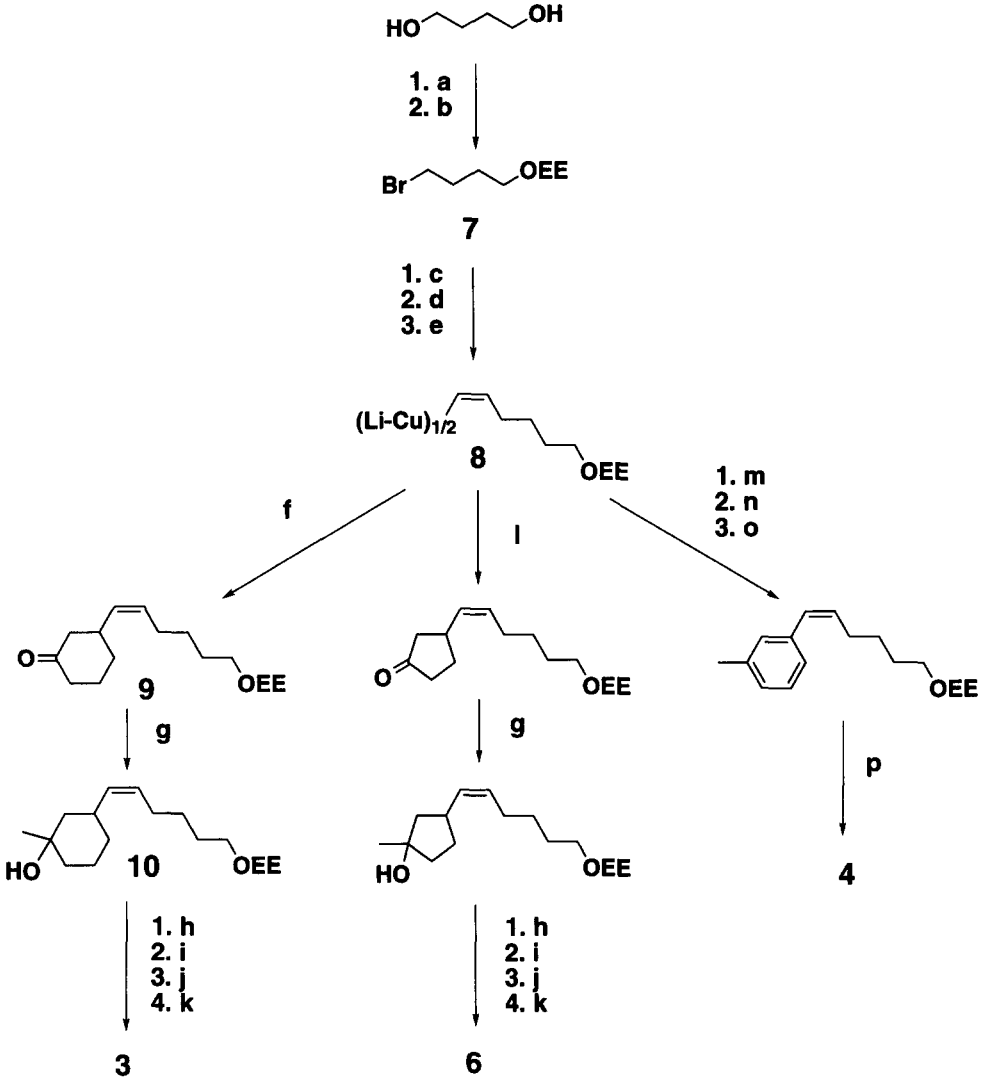


Figure 2. Synthetic schemes for compounds **3**, **4** and **6**. EE = ethoxyethyl. (a) 48% HBr, benzene, reflux; (b) ethyl vinyl ether, CH_2Cl_2, 15 °C; (c) Li, ether, −15 °C; (d) CuBr-Me_2S, −40 °C; (e) acetylene, −40 °C; (f) 2-cyclohexen-1-one, ether, −70 °C; (g) MeLi-Me_2CuLi, ether, −78 °C; (h) BuLi, THF, 0 °C; (i) $ClPO(OEt)_2$, TMEDA, 0 °C; (j) Li, $EtNH_2$, ^{t}BuOH, THF, 0 °C; (k) HOAc/AcCl, 35 °C; (l) 2-cyclopenten-1-one, ether, −70 °C; (m) $ZnBr_2$, THF, −40 °C; (n) 3% $Pd(PPh_3)_4$; (o) 3-iodo-toluene, −20 °C; (p) HOAc/AcCl, 35 °C.

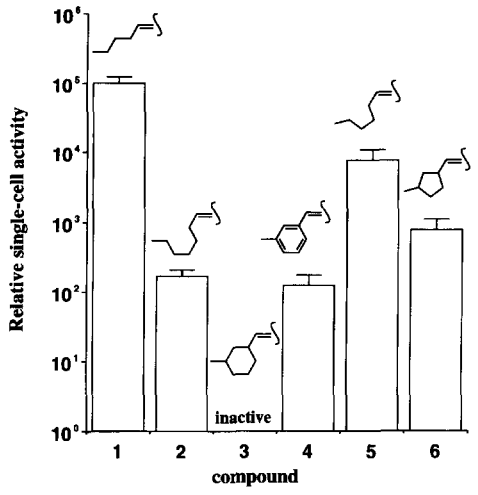


Figure 3. Relative single-cell activities (+SEM) for compounds **1–6**. The data shown are corrected for differences in volatility.

inactivity of **3** most probably is due to strong repulsive steric interactions between the methylene groups of the cyclohexane ring system and the receptor. Monomethyl substitution in positions 7 and 9 of compound **1** results in activity decreases by factors of 45 and 10, respectively.[9] Thus, the repulsive interactions between **3** and the receptor are larger than the combined effects of 7- and 9-methyl substitution in **1**.

In spite of the high structural similarity of **2** in its suggested loop conformation [Fig. 1(b)] and **3** and the much higher conformational energy of the bioactive conformation of **2**,[8] compound **2** is significantly more active than **3**. As the evidence presented above for the presence of a loop conformation of the terminal alkyl chain in the bioactive conformation of **2** is, in our opinion, strong, the inactivity of **3** underscores the very restricted dimensions of the receptor cavity. Thus, we conclude that the terminal chain in **2** uses its flexibility to adjust to the available receptor space in an induced fit with the receptor, whereas the much more rigid diequatorially substituted cyclohexane ring is too bulky to be accommodated.

In compound **4** the terminal chain in **1** is replaced by a methyl-substituted aromatic ring which due to its planar structure may be expected to be able to avoid repulsive steric interactions with the receptor. Although **4** is equally active to **3**, it is significantly less active than **1** (Fig. 3). The reduced activity of **4** can not be explained by a prohibitively high conformational energy of its bioactive conformation, as described above. The low activity of **4** is probably due to a combination of steric repulsive interactions with the receptor in the region about the aromatic 4, 5 and 6 positions and the strong electrostatic field of the phenyl ring interfering with a proper interaction between the (*Z*)-double bond and its receptor site.

Compound **6** (tested as a 55/45 mixture of the racemic *cis/trans* isomers) which mimics the proposed loop conformation of **5**, displays a slightly lower activity than **5**. However, it is still 130 times less active than **1**. It is clear that also for this, in comparison to **3**, less bulky cyclic analogue of **1** steric repulsions with the receptor are present, although not as strong as for **3**. The combined reductions of activity due to methyl groups in the 7 and 9 positions of **1** (see above) correspond essentially to the observed activity drop of compound **6** compared with **1**.

Conclusions

The results of the present study support our earlier findings of a very high complementarity between the receptor and the terminal alkyl chain of its natural substrate. The high flexibility of the terminal alkyl parts of **2** and **5** is essential for the possibility of the receptor to accommodate these chains in their proposed bioactive loop conformations. Locking such a loop conformation into a five- or six-membered ring-system, the resulting relative rigidity of the terminal part of the analogue makes an induced fit between the ligand and the receptor less feasible which leads to strongly reduced activity.

Experimental

All reactions of air- and water-sensitive materials were performed in anhydrous solvents and under a nitrogen atmosphere in oven-dried glassware. Analytical TLC was carried out on precoated plates (silica gel, 60 F254) and spots were visualized with iodine vapor. The crude pheromone products were purified by flash chromatography with TLC silica gel 60H. Flash chromatographed products were further purified by preparative GC using a 6 m × 4 mm 15% OV-351 column. Analytical GC was performed with a Varian 3400 capillary GC fitted with a DB-Wax 30-m column. The purity of the isolated final products was > 99%. No sample contained any detectable amount (< 0.05%) of the natural pheromone component (**1**). ^{1}H and ^{13}C NMR spectra were recorded on a Varian XL-300 spectrometer. Spectra were recorded with TMS as the internal standard in ^{2}H-chloroform. High resolution mass spectra were recorded on a Jeol JMS-SX 102 spectrometer.

Compound **5** is a gift from Dr C. Löfstedt, Department of Ecology, University of Lund, Sweden.

4-(1-Ethoxyethoxy)-butyl bromide (7). 1,4-Butanediol (45 mL, 0.5 mol) and 48% HBr (63 mL, 0.55 mol) in benzene (800 mL) were heated at reflux for 5 h, while the water formed was trapped by using a Dean–Stark separator. The solvent was removed and the crude residue dissolved in anhydrous methylene chloride (200 mL). The mixture was cooled on ice, then ethyl vinyl ether (48 mL, 0.5 mol) was added slowly, keeping the solution temperature between 10 and 16 °C. After 1 h of stirring, the colorless solution was washed with 5% Na_2CO_3 (50 mL) dried by Na_2CO_3 and $MgSO_4$. The solvent was removed and the product distilled in carefully base-washed glassware to give 45 g (40%

yield, bp 58–68 °C/0.7 mm Hg) of pure **7**. ^{1}H NMR: δ 1.0–1.3 (6H, m, CH_3), 1.4–2.1 (4H, m, CH_2), 3.2–3.7 (6H, m, CH_2Br, CH_2O), 4.7 (1H, q, OCHO).

Lithium bis[(Z)-6-(1-ethoxyethoxy)-hex-1-enyl] cuprate (8). A solution of **7** (22.5 g, 0.1 mol) in ether (60 mL) was added dropwise at −15 °C to freshly cut small chips of lithium in ether (20 mL). The grayish turbid solution was stirred for another hour at 0 °C and then transferred to a graduated glass cylinder and stored at −15 °C overnight, allowing cloudy material to precipitate. The pale yellow clear solution of the lithium compound was titrated by the method of Watson and Eastham[21] and 30 mL (25 mmol) of the solution was slowly transferred to a well-stirred suspension of CuBr–Me_2S complex (2.88 g, 14 mmol) in ether (50 mL) at −40 to −50 °C. The almost clear colorless solution was stirred for 30 min, then acetylene (0.6 L, 25 mmol) was bubbled slowly into the reaction mixture. After stirring of the resulting dark green solution for 30 min at −25 °C, the (Z)-alkenyl cuprate solution was ready for use in the subsequent steps.

6-(cis-3-methylcyclohexyl)-(Z)-5-hexenylacetate(3). To an ether solution (100 mL) of cuprate **8** (10 mmol) at −70 °C was added cyclohexanone (1.0 g, 10 mmol). The mixture was warmed to −10 °C (1 h) and then quenched by addition of 25 mL of satd NH_4Cl. Hexane (50 mL) was added, the precipitate filtered off and the organic layer dried over $MgSO_4$ and then the solvent was evaporated. Chromatography of the residue on silica gel with petroleum ether:ethyl acetate (4:1) as eluent afforded **9** as a light yellow oil (1.3 g, 47% yield). R_f (hexane:ethyl acetate 4:1) 0.20.

Methyl lithium (15 mmol) was added dropwise to CuI (0.9 g, 5 mmol) in ether (20 mL) at −10 °C. After 10 min of stirring, the solution was cooled to −78 °C and **9** (4.7 mmol) dissolved in ether (10 mL) was added. The mixture was allowed to warm to −10 °C and quenched by pouring the mixture into satd NH_4Cl. The mixture was then treated with hexane, the precipitate filtered off and the organic layer dried and evaporated to give a colorless oil. GC analysis indicated a 9:1 mixture of the *cis* and *trans*-dialkylsubstituted cyclohexane derivative. R_f (hexane:ethyl acetate 4:1) 0.12. This crude product (**10**, 4.7 mmol) was dissolved in THF (20 mL) and treated with butyllithium (2.4 mL in hexane, 5 mmol) at 0 °C. The solution was stirred for 15 min and *N,N,N′,N′*-tetramethylethylenediamine (5 mL) followed by diethylphosphorochloridate (0.7 g, 4.7 mmol) was added. The mixture was stirred at 20 °C for 2 h, worked up with cold 1 M NH_4OH and ether, the organic layers dried and concentrated to give the phosphorylated ester in quantitative yield. R_f (hexane:ethyl acetate 1:1) 0.08. The residue was dissolved in THF (10 mL and *tert*-butyl alcohol (1.5 g, 20 mmol). This solution was added to an ice-cooled, argon protected solution of lithium (0.35 g, 50 mmol) in dry ethylamine (15 mL). The dark-blue solution was stirred for 30 min, then the mixture was quenched with water and the product isolated by ether extraction. The crude colorless oil was acetylated with a mixture of acetic acid:acetyl chloride 10:1 at 35 °C overnight. The mixture was then poured into ice-water, extracted with ether, washed with $NaHCO_3$, dried over $MgSO_4$ and the solvent evaporated. The residue was chromatographed on SiO_2 with petroleum ether:ethyl acetate (20:1) as eluent to give a 9:1 mixture of *cis*- and *trans*-**3** (1.0 g, 85% yield from **9**). Purification by preparative GC (6 m × 4 mm 15% OV351 column, He = 130 mL/min, 175 °C) gave the pure *cis* isomer (*cis*-isomer 91%, R_t = 33 min; *trans*-isomer 9% R_t = 38 min). ^{1}H NMR: δ 0.64–1.00 (m, 2H), 0.87 (d, 3H, J = 6.5Hz, CH_3-eq), 1.21–1.46 (m, 5H), 1.51–1.75 (m, 6H), 2.02–2.10 (m, 2H,=$CHCH_2$), 2.04 (s, 3H, $COCH_3$), 2.17–2.31 (m, 1H, CHCH=), 4.06 (t, 2H, J = 6.7 Hz, CH_2O), 5.13–5.29 (m, 2H, CH=CH). ^{13}C NMR: δ 21.1, 22.9, 26.0, 26.2, 27.0, 28.2, 32.3, 32.9, 34.7, 36.5, 42.1, 64.5, 127.1, 136.6, 171.2. High-resolution CI MS for $C_{15}H_{30}O_2N$ ($M+NH_4^+$) calcd 256.2276, found 256.2285.

Mixture of 6-(*cis*-3-methylcyclopentyl)-(Z)-5-hexenyl acetate and 6-(*trans*-3-methylcyclopentyl)(Z)-5-hexenyl acetate (6). This compound was obtained from **8** and 2-cyclopentenone according to the general procedure described for the preparation of **3** (0.9 g, 88% yield). ^{1}H NMR: δ 0.97 (d, J = 6.4 Hz), 0.98 (d, J = 6.7 Hz, 3H, CH_3- eq. and ax.), 4.06 (dt, 2H, CH_2O). ^{13}C NMR: δ 20.9, 21.0, 21.4, 26.2, 26.2, 26.9, 28.2, 32.9, 33.5, 33.9, 34.2, 34.7, 35.0, 36.6, 38.5, 41.7, 43.4, 64.5, 127.2, 127.4, 136.3, 136.5, 171.2. High-resolution CI mass spectrum for $C_{14}H_{28}O_2N$ ($M+NH_4^+$). Calcd: 242.2120. Found: 242.2126.

6-(3-Methylphenyl)-(Z)-5-hexenyl acetate (4). Zinc bromide (2.5 g, 11 mmol) was dissolved in THF (10 mL) and then slowly added to a solution of **8** (10 mmol) in ether (50 mL) and THF (10 mL) at −40 °C. To the dark brownish solution was added after 15 min at −20 °C a mixture of 3-iodotoluene (1.8 g, 8 mmol) and $Pd(PPh_3)_4$ (0.4 g, 0.3 mmol) in THF (10 mL). The solution was allowed to warm gradually to 15 °C during 1 h and then it was quenched with saturated NH_4Cl. The product was worked up and acetylated in the same manner as described for compound **2**, followed by flash chromatography with petroleum ether:ethyl acetate (4:1) as eluent, yielding 1.9 g (83%) of **4**. ^{1}H NMR: δ 1.47–1.59 (m, 2H, =$CCCH_2$), 1.60–1.73 (m, 2H, CH_2CO), 2.04 (s, 3H, $COCH_3$), 2.34–2.42 (m, 2H, =CCH_2), 2.36 (s, 3H, $ArCH_3$), 4.07 (t, 2H, J = 6.7 Hz, CH_2O), 5.64 (dt, 1H, $J_{CH=CH}$ = 11.7 Hz J_{CHCH_2} = 7.2 Hz, =$CHCH_2$), 6.42 (d, 1H, $J_{CH=CH}$ = 11.7 Hz, ArCH=C), 7.04–7.10 (m, 3H), 7.20–7.26 (t, 1H, ArH). ^{13}C NMR: δ 21.0, 21.5, 26.4, 28.2, 28.3, 64.4, 125.8, 127.3, 128.1, 129.4, 129.5, 132.1, 137.6, 137.7, 171.2; high-resolution MS for $C_{15}H_{20}O_2$. Calcd: 232.1463. Found: 232.1458.

Electrophysiology

The activities of compounds **1–6** were determined by single-cell electrophysiology.[22] The olfactory receptor-cell specifically tuned to (Z)-5-decenyl acetate, present

in the antennal sensilla type SW1 of *A. segetum*, was used.[3,23,24] The method was modified according to van der Pers and den Otter[25] and has been previously described.[5,8]

The stimulus amounts used for **1** were 10^{-4} μg to 1 μg, for compounds **2** and **3** 10^{-1} μg to 100 μg and for compounds **4**, **5** and **6** 10^{-2} μg to 100 μg, in decadic steps. For each stimulus loading, 10 replicates were recorded and the mean value of the number of action potentials generated during 1 s from the onset of stimulation was used in the construction of dose–response curves. The errors were expressed as standard errors of the mean (SEM). The electrophysiological activity of each compound in relation to that of **1** is expressed as the reciprocal of the relative quantities required to elicit the same response from the receptor as the natural pheromone component **1**.

Differences in volatility for compounds **2–6** were taken into account by correcting the activities by using relative vapor pressures as previously described.[5,7,14] The correction factors used for compounds **2–6** are 7, 7, 24, 42 and 2.5, respectively.

Molecular mechanics calculations

Conformational energies were calculated by using the molecular mechanics program MM2(91), developed by Allinger and co-workers[20] and implemented in the molecular modeling package MacMimic/MM2(91).[26]

Acknowledgments

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References

1. Bestmann, H. J.; Vostrowsky, O.; Koschatzky, K. H.; Platz, H.; Brosche, T.; Kantardjiew, I.; Rheinwald, M.; Knauf, W. *Angew. Chem.* **1978**, *90*, 815.

2. Arn, H.; Städler, E.; Rauscher, S.; Buser, H. R.; Mustaparta, H.; Esbjerg, P.; Philipsen, H.; Zethner, O.; Struble, D. L.; Bues, R. *Z. Naturforsch.* **1980**, *35c*, 986.

3. Löfstedt, C.; van der Pers, J. N. C.; Löfquist, J.; Lanne, B. S.; Appelgren, M.; Bergström, G.; Thelin, B. *J. Chem. Ecol.* **1982**, *8*, 1305.

4. Bengtsson, M.; Liljefors, T.; Hansson, B. S. *Bioorg. Chem.* **1987**, *15*, 409.

5. Bengtsson, M.; Liljefors, T.; Hansson, B. S.; Löfstedt, C.; Copaja, S. V. *J. Chem. Ecol.* **1990**, *16*, 667.

6. Jönsson, S.; Liljefors, T.; Hansson, B. S. *J. Chem. Ecol.* **1991**, *17*, 1381.

7. Liljefors, T.; Thelin, B.; van der Pers, J. N. C.; Löfstedt, C. *J. Chem. Soc. Perkin Trans. II* **1985**, 1957.

8. Liljefors, T.; Bengtsson, M.; Hansson, B. S. *J. Chem. Ecol.* **1987**, *13*, 2023.

9. Jönsson, S.; Liljefors, T.; Hansson, B. S. *J. Chem. Ecol.* **1991**, *17*, 103.

10. Jönsson, S.; Liljefors, T.; Hansson, B. S. *J.* Chem. Ecol. **1991**, *17*, 1381.

11. Jönsson, S.; Liljefors, T.; Hansson, B. S. *J.* Chem. Ecol. **1992**, *18*, 637.

12. Wenqi, W.; Bengtsson, M.; Hansson, B. S.; Liljefors, T.; Löfstedt, C.; Prestwich, G.; Sun, W.-C.; Svensson, M. *J.* Chem. Ecol. **1993**, *19*, 143.

13. Jönsson, S.; Malmström, T.; Liljefors, T.; Hansson, B. S. *J.* Chem. Ecol. **1993**, *19*, 459.

14. Gustavsson, A.-L.; Liljefors, T.; Hansson, B. S. *J. Chem. Ecol.* **1995**, *21*, 815.

15. Gardette, M.; Alexakis, A.; Normant, J. F. *Tetrahedron* **1985**, *41*, 5887.

16. Alexakis, A.; Cahiez, G.; Normant, J. F. *Tetrahedron* **1980**, *36*, 1961.

17. Still, W. C.; Macdonald, T. L. *Tetrahedron. Lett.* **1976**, *31*, 2659.

18. Ireland, R. E.; Muchmore, D. C.; Hengartner, U. *J. Am. Chem. Soc.* **1972**, *94*, 5098.

19. Jabri, N.; Alexakis, A.; Normant, J. F. *Bull. Soc. Chim. Fr.* **1983**, *11*, 321.

20. Burkert, U.; Allinger, N. L. *Molecular Mechanics*; American Chemical Society: Washington DC, 1982.

21. Watson, S. C.; Eastham, J. F. *J. Organomet. Chem.* **1967**, *9*, 165.

22. Kaissling, K.-E. In *Biochemistry of Sensory Functions*; Jaenicke, L., Ed.; Springer-Verlag: Berlin, 1974; p 243.

23. Hallberg, E. *Cell Tissue Res.* **1981**, *218*, 209.

24. Van der Pers, J. N. C.; Löfstedt, C. *Physiol. Entomol.* **1983**, *8*, 203.

25. Van der Pers, J. N. C.; Den Otter, C. J. *J. Insect Physiol.* **1978**, *24*, 337.

26. MacMimic/MM2(91), Version 2.0, Instar Software, Ideon Research Park, S-223 70 Lund Sweden.

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