

Conformations of Bark Beetle Pheromones: The Importance of the Medium

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The conformational composition of ipsenol (**1**) and ipsdienol (**2**) has been investigated by ¹H NMR and IR spectroscopy of solutions in CCl₄, CFCl₃ and MeOH. The relative energies of the stable conformations have been estimated by molecular mechanics calculations (MMPMI). In CCl₄ and CFCl₃ (to mimic the gas phase) the dominant conformations are those with an *anti* conformation of the carbon-carbon chain. For both compounds, the hydroxy group hydrogen is partly hydrogen bonded to the butadiene fragment of the molecules. In methanol, a conformation with a *gauche* rotamer around the C⁴-C⁵ bond is important in addition to the *anti* conformation. The conformational change takes place in a region of the molecule which has been shown to be important for the effect of the pheromone.

Insect pheromones are of great interest and importance both from an applied and a scientific point of view. Characteristically, pheromone molecules trigger biological responses at very low concentrations. A single molecule or a few molecules interacting with a receptor cell may result in nerve impulse responses.¹ The precise mechanism for the interaction between the pheromone molecule and the receptor cell is still unknown. Combined chemical and biological efforts have been applied to the elucidation of this mechanism, chemically by studying the effect of often subtle changes in the pheromone molecule, biologically by electrophysiological and biochemical studies.²⁻⁶ The general opinion today is that the pheromone molecule interacts with a membrane-bound receptor protein. It is further believed that the active site in the protein is specific for one type of pheromone.

On interaction with the pheromone molecule, the receptor protein undergoes a conformational change which triggers the chain of events leading to the nerve impulse.⁷ If this is the case, the stereochemistry of the pheromone molecule must be one of the important factors for its mode of action. The structure of the protein is unknown and the shape of the active site is therefore inaccessible.

The pheromone molecules reach the receptor cell through pores in the cuticle wall of the sensory organ, the sensilla.⁸ They may then pass either through microtubules in the sensilla liquor or directly through the sensilla liquor to the cell membrane. Thus, before a pheromone molecule reaches the receptor protein it has changed medium from the non-polar gas-phase to the highly polar hydrogen-bonding aqueous phase in the insect. As the conformational composition of the pheromone in the protein is unknown,

we envisaged that a study of the conformation of pheromones in different media might give an insight into the importance of the medium for the conformational composition. The shape of the molecules might also give a clue as to the shape of the active site in the receptor protein. Furthermore, one would observe which parts of the pheromone molecule are subject to changes in the conformation. These changes might then be correlated with the results from chemical modifications of the molecule in which the important structural details have been mapped.

We have studied two bark beetle pheromones, ipsenol (**1**) and ipsdienol (**2**) from this point of view. The structure-activity correlations have been studied for ipsdienol by comparison with a series of analogous compounds. The important structural details appear to be the hydroxy group and the two double bond systems (C²-C³ and C⁸-C⁷-C⁶-C⁹).⁹ Furthermore, the conformational composition of these molecules is accessible by IR and NMR spectroscopy and we have complemented the spectroscopic investigation with molecular mechanics calculations.

The spectroscopic studies were carried out in CFCl₃ or CCl₄ (to mimic the gas-phase) or in MeOH-*d*₄ (to simulate the aqueous phase inside the insect).

Results

The investigations were carried out on the racemic mixtures of ipsenol and ipsdienol. In Fig. 1, (*R*)-**1** and (*S*)-**2** are shown. The ¹H NMR parameters for **1** and **2** are given in Tables 1–4 and the IR data in the Experimental part. The molecular mechanics calculations were performed in the default dipole-dipole electrostatic mode (program MMPMI).¹⁰ For ipsdienol (**2**) the calculations were performed for nine low-energy conformations (three staggered

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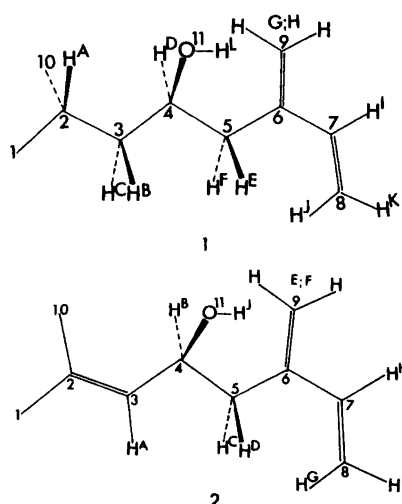


Fig. 1. Ipsenol (1) and ipsdienol (2) with annotations used in text and Tables.

rotamers around the C⁴-O¹¹ bond and three around the C⁴-C⁵ bond). For all nine conformations the minimum energy for the rotamers around the C²-C³-C⁴-C⁵ and C⁴-C⁵-C⁶-C⁷ dihedral angles were found by driving these two angles. The angles, energies and dipole moments for the totally relaxed minimum energy conformations are given in Table 5.

Table 1. Proton chemical shifts for ipsenol (1) (δ ppm from SiMe₄), see Fig. 1 for proton assignments.

| Solvent | H _A | H _B | H _C | H _D | H _E | H _F | H _G ; H _H | H _I | H _J | H _K | H _L | CH ₃ (C ¹ , C ¹⁰) |
|-----------------------------|----------------|----------------|----------------|----------------|----------------|----------------|---------------------------------|----------------|----------------|----------------|----------------|---|
| CFCl ₃ | 1.858 | 1.420 | 1.200 | 3.730 | 2.143 | 2.443 | 5.106; 5.052 | 6.325 | 5.226 | 5.069 | 1.217 | 0.948; 0.919 |
| MeOH- <i>d</i> ₄ | 1.819 | 1.353 | 1.255 | 3.809 | 2.361 | 2.332 | 5.090; 5.054 | 6.398 | 5.251 | 5.066 | - | 0.921; 0.876 |

Table 2. Proton-proton coupling constants (Hz) for ipsenol (1), see Fig. 1 for the proton assignments.

| Solvent | J _{A,Me} | J _{AB} | J _{AC} | J _{BC} | J _{BD} | J _{CD} | J _{DL} | J _{DE} | J _{DF} | J _{EF} | J _{GH} | J _{IJ} | J _{IK} | J _{JK} |
|-----------------------------|-------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| CFCl ₃ | 6.65 | 5.17 | 8.85 | -13.86 | 9.19 | 3.80 | 2.89 | 9.13 | 3.32 | -13.57 | 1.31 | 17.55 | 10.86 | ca. 0 |
| MeOH- <i>d</i> ₄ | 6.72 | 4.79 | 9.25 | -13.87 | 9.32 | 3.61 | - | 6.79 | 5.91 | -13.85 | - | 17.66 | 10.77 | 0 |
| | 6.57 | | | | | | | | | | | | | (unknown) |

Table 3. Proton chemical shifts for ipsdienol (2) (δ /ppm from SiMe₄), see Fig. 1 for the proton assignments.

| Solvent | H _A | H _B | H _C | H _D | H _E , H _F | H _G | H _H | H _I | H _J | CH ₃ (C ¹ , C ¹⁰) |
|-----------------------------|----------------|----------------|----------------|----------------|---------------------------------|----------------|----------------|----------------|----------------|---|
| CFCl ₃ | 5.140 | 4.408 | 2.353 | 2.334 | 5.053 | 5.256 | 6.327 | 5.023 | 1.062 | 1.659, 1.715 |
| MeOH- <i>d</i> ₄ | 5.136 | 4.508 | 2.500 | 2.290 | 5.052, 5.014 | 5.279 | 6.384 | 5.066 | - | 1.633, 1.535 |

Table 4. Proton-proton coupling constants (Hz) for ipsdienol (2). See Fig. 1 for the proton assignments.

| Solvent | J _{AB} | J _{AMe} | J _{BC} | J _{BD} | J _{BJ} | J _{CD} | J _{GH} | J _{GI} | J _{GJ} | J _{HI} |
|-----------------------------|-----------------|------------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| CFCl ₃ | 8.48 | 1.1 | 4.88 | 8.16 | 2.51 | -13.85 | 17.69 | - | - | 10.70 |
| MeOH- <i>d</i> ₄ | 8.85 | 1.45; 1.43 | 6.42 | 7.11 | - | -13.71 | 17.64 | 1.11 | 0.57(t) | 10.82 |

For ipsenol (1) a less extensive calculation scheme was performed. The purpose was to probe the energetics on rotating the single bonds of the carbon skeleton and thereby identify the low-energy rotamers. This was necessary in order to analyse the ¹H NMR spectra. Rotation of the C⁴-C⁵-C⁶-C⁷ angle with the carbon-carbon single bond chain in the all-*anti* conformation and the angle C⁸-C⁷-C⁶-C⁹ set at 180° indicated a flat energy minimum for rotation around the C⁵-C⁶ bond, ca. 5 kcal mol⁻¹ lower than the maximum at 0°. This angle was therefore relaxed in the subsequent calculations. The angle C⁸-C⁷-C⁶-C⁹ was kept at 180°. The results from the subsequent calculations of nine conformers are summarised in Table 6. The results in Table 6 do not represent all possible combinations of staggered conformations around C²-C³, C³-C⁴, C⁴-C⁵ and C⁴-O¹¹ (81 conformations) but only those necessary for analyses of the NMR spectra.

Discussion

The conformational composition of ipsdienol (2, Table 5) is defined by the rotamer composition around five single bonds (C³-C⁴, C⁴-C⁵, C⁵-C⁶, C⁶-C⁷ and C⁴-O¹¹, not including the CH₃ groups) and for ipsenol (1) around six single bonds (C²-C³, C³-C⁴, C⁴-C⁵, C⁵-C⁶, C⁶-C⁷ and C⁴-O¹¹). The vicinal coupling constants in the ¹H NMR

Table 5. Relative energies and dipole moments of stable conformations of ipsdienol (2) as calculated by MMPMI.¹⁰ All geometry parameters were relaxed during the calculations. See Fig. 1 for notation of atoms.

| Conformer | Angles as defined by atom No. | | | | | <i>E</i> /kcal mol ⁻¹ (relative) | Mol fraction (%) | Dipole moment/D |
|--------------|-------------------------------|---------|-----------------------|---------|---------|--|------------------|-----------------|
| | 2-3-4-5 | 3-4-5-6 | 3-4-11-H ^J | 4-5-6-7 | 8-7-6-9 | | | |
| 1 | -152.9 | 61.6 | 51.9 | 65.8 | -161.3 | 1.63 | 2.4 | 1.374 |
| 2 | -152.8 | 61.5 | -173.7 | 65.0 | -160.6 | 2.02 | 1.2 | 1.741 |
| 3 | -152.0 | 60.5 | -53.0 | 67.1 | -163.0 | 0.93 | 7.7 | 1.796 |
| 4 | -162.8 | -178.2 | 50.0 | -85.5 | -172.4 | 0 | 36.2 | 1.680 |
| 5 | -162.7 | 175.3 | -169.3 | -86.0 | -171.1 | 0.05 | 33.3 | 1.572 |
| 6 | -159.4 | 174.9 | -50.7 | -94.3 | 137.9 | 0.45 | 17.1 | 1.997 |
| 7 | -164.2 | -62.4 | 48.1 | -74.5 | 156.3 | 2.31 | 0.8 | 1.254 |
| 8 | -171.2 | -63.3 | -173.3 | -72.4 | 151.6 | 3.10 | 0.2 | 1.961 |
| 9 | -165.0 | -64.0 | -54.3 | -71.3 | 154.1 | 2.08 | 1.1 | 2.033 |
| ^a | -160.4 | 175.5 | -158.2 | -73.3 | 177.2 | 0 | | |
| ^b | -165.7 | 177.3 | -158.1 | +105.1 | 164.5 | 2.81 | | |

^aMNDO calculation, using coordinates for conformer 5 as input coordinates. ^bMNDO calculations. Start geometry as for conformation 5 but C⁴-C⁵-C⁶-C⁷ at 90°. MMPMI used to generate start coordinates for MNDO. All geometry parameters relaxed for the MNDO calculations.

Table 6. Relative energies of stable conformations of ipsenol (1) as calculated by MMPMI.¹⁰ The angle C⁸-C⁷-C⁶-C⁹ kept at 180°. See Fig. 1 for notation of atoms.

| Conformer | Angles as defined by atom No. | | | | | <i>E</i> /kcal mol ⁻¹ (relative) |
|-----------|-------------------------------|---------|---------|-----------------------|---------|--|
| | 1-2-3-4 | 2-3-4-5 | 3-4-5-6 | 3-4-11-H ^L | 4-5-6-7 | |
| 1 | -176 | 170 | 60 | -173 | 94 | 0.95 |
| 2 | -177 | 174 | 180 | -172 | 92 | 0.00 |
| 3 | -177 | 176 | -60 | -176 | 92 | 1.14 |
| 4 | -172 | 60 | 177 | -161 | 95 | 1.41 |
| 5 | -143 | -60 | -178 | -168 | 93 | 2.40 |
| 6 | -178 | 180 | 176 | 60 | 94 | 0.92 |
| 7 | -178 | 180 | 176 | -60 | 96 | 0.32 |
| 8 | 60 | -175 | 178 | 173 | 92 | 1.63 |
| 9 | -60 | -172 | 176 | -173 | 91 | 1.30 |

spectra contain information on the rotational compositions around all these bonds except for C⁵-C⁶ and C⁶-C⁷.

We will assume the dihedral angle C⁸-C⁷-C⁶-C⁹ to be close to 180°. This is supported by both theoretical and experimental investigations on isoprene, which show the *anti* conformer to be ca. 2.5 kcal mol⁻¹ more stable than a *gauche* form.^{11,12} The composition around the C⁵-C⁶ bond was estimated from calculations. For both compounds, molecular mechanics calculations indicated flat energy minima for the C⁴-C⁵-C⁶-C⁷ angle around ca. 70° or ca. -80° (Tables 5 and 6). However, the molecular mechanics program does not always give reliable results for the substituted butadiene system represented by C⁸-C⁷-C⁶-C⁹-C⁵.¹³ Therefore, we also carried out a semiempirical molecular-orbital calculation (MNDO)¹⁴ for conformer 5 (Table 5). The result from this (Table 5) gave almost the same geometric parameters as the MMPMI calculation. However, if the dihedral angle C⁴-C⁵-C⁶-C⁷ used as input was ca. +100°, the MNDO calculation gave a heat of formation of 2.81 kcal mol⁻¹ above that of conformer 5 (Table

5). From inspection of space-filling models it is, furthermore, evident that the butadiene fragment must be at angles close to those of Table 5. We will therefore, with the uncertainties of the calculations, assume the results for this fragment to be reasonable.

The rotational compositions around the other bonds were determined from the vicinal coupling constants. The coupling constants for each rotamer were obtained by the use of Haasnoot's treatment of the angular and polar dependence of these constants.¹⁵ From Tables 5 and 6 it is evident that the proton-proton dihedral angles may not be exactly 60 or 180°. Around 60°, the change in vicinal coupling constant is ca. 0.15 Hz/° (from the Karplus equation).¹⁶ It should therefore be stressed that the present method only gives an estimate of the rotamer composition. However, for non-crystalline molecules as complex as those studied here, we know of no other method that will give even an estimate, especially for molecules in solution.

The rotamers of **1** (around C²-C³, C³-C⁴, C⁴-C⁵ and C⁴-O¹¹) and **2** (around C⁴-C⁵ and C⁴-O¹¹) are shown in

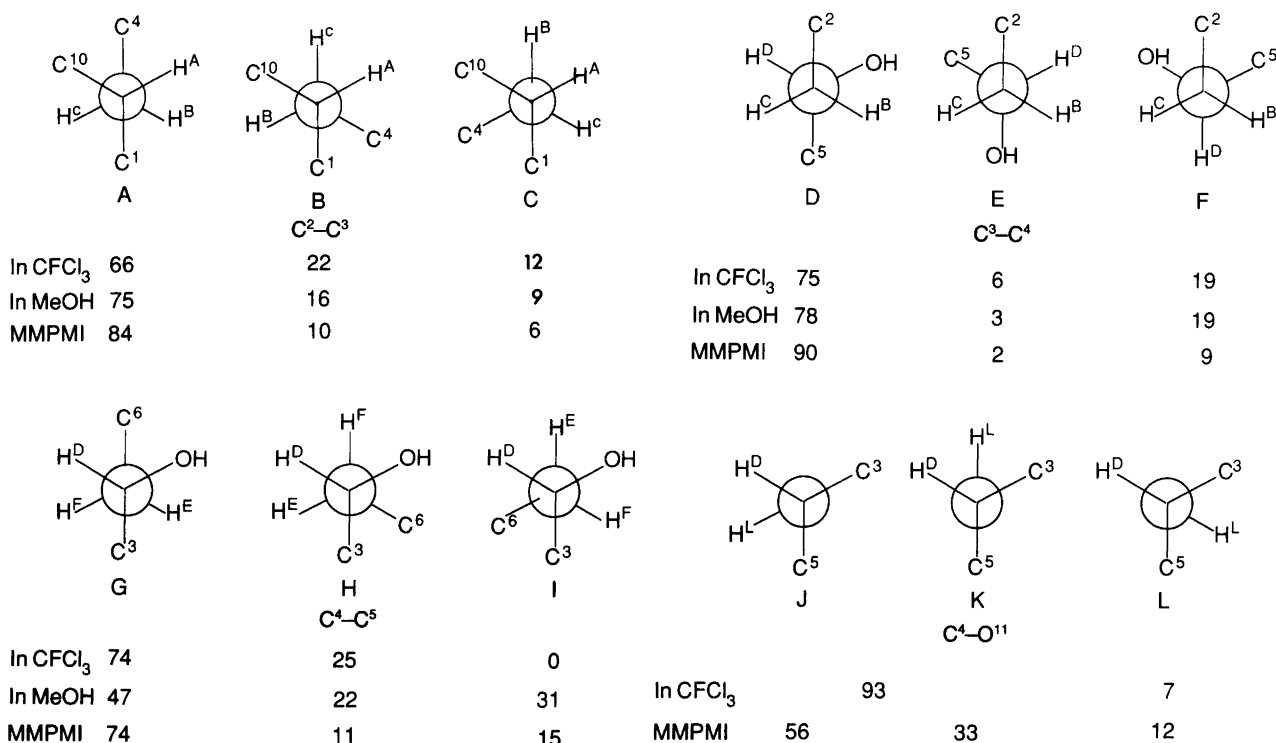


Fig. 2. Rotamers of ipsenol (1) around C²-C³, C³-C⁴, C⁴-C⁵ and C⁴-O¹¹. Numbers are rotamer compositions (%) obtained from ¹H NMR data on CFCl₃ and MeOH-*d*₄ solutions and from molecular mechanics calculations. MMPMI results are shown for the molecules in the all-*anti* conformation except for the depicted angles (and C⁴-C⁵-C⁶-C⁷).

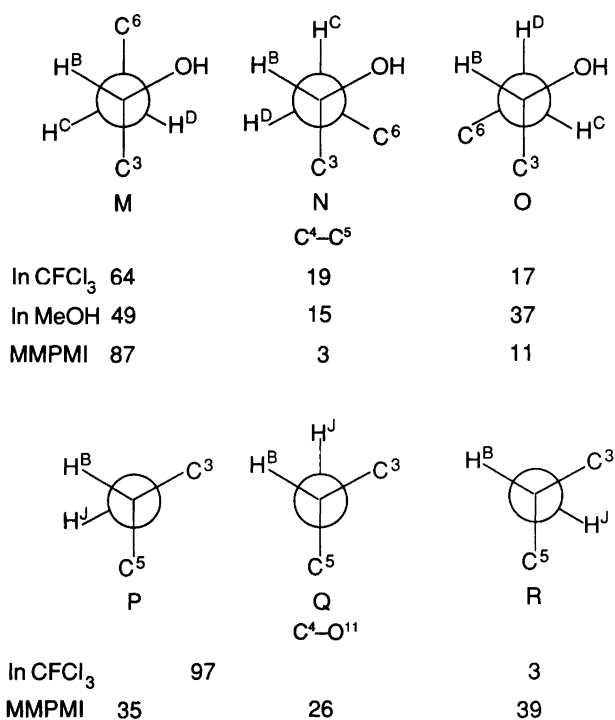


Fig. 3. Rotamers of ipsdienol (2) around C⁴-C⁵ and C⁴-O¹¹. Numbers are rotamer compositions (%) from ¹H NMR data on CFCl₃ and MeOH-*d*₄ solutions and from molecular mechanics calculations.

Figs. 2 and 3, respectively. From the observed and calculated vicinal coupling constants,¹⁵ the rotamer compositions were calculated and these are also shown.

For ipsdienol (2) the conformation around the C³-C⁴ bond must also be considered. This fragment is similar to allyl alcohol in which only three conformations are important: the two (energetically equivalent) *gauche* and the *cis* (looking at the OH group/C=C bond). In ipsdienol, the allylic fragment C²-C³-C⁴-O¹¹ is substituted with two methyl groups, creating a situation different from that of allyl alcohol. Estimation of the energy on rotation of the C³-C⁴ bond by molecular mechanics¹⁰ showed two low-energy rotamers, one at C²-C³-C⁴-C⁵ ca. -170° and one at -80°, separated by a low maximum at -120° (0.5 kcal mol⁻¹ over the minima). Major maxima were at 0 and 120° (5.5 and 4.5 kcal mol⁻¹, respectively). The angle C²-C³-C⁴-C⁵ at -170 and -80° corresponds to angles H^A-C³-C⁴-H^B of 136 and -143°, respectively. The vicinal coupling constants J_{AB} will be approximately the same for these two rotamers from a slightly modified Garbisch equation: $J_{est.} = 12 \cos^2 \varphi + 2.6 \sin^2 \varphi$ ^{17,18} giving $J_{AB} = 7.5$ and 8.6 Hz, respectively. The observed coupling constants were 8.48 Hz (CFCl₃) and 8.85 Hz (MeOH-*d*₄). It should be noted that from the equation above, $J_{est.}$ increases from 7.5 Hz for $\varphi = 136^\circ$ to 8.9 Hz for $\varphi = 145^\circ$. The only conclusion possible for the rotamer composition around C²-C³-C⁴-C⁵ is therefore that this is either ca. -170° or ca. -80° and that the observed vicinal coupling constant was not sensitive to the solvent used.

The only rotamer compositions left are those around C^4-O^{11} . For the molecules in $CFCl_3$ solution, information on this point is obtained from the coupling constants J_{DL} (for ipsenol **1**) and J_{BJ} (for ipsdienol **2**). The rotamers are shown in Figs. 2 and 3 with two *gauche* rotamers (*J*, *K* for **1**; *P*, *Q* for **2**) and one *anti* (*L* for **1**; *R* for **2**) rotamer. We will use the coupling constants $J_{anti} = 12.0$ Hz and $J_{gauche} = 2.2$ Hz to estimate these compositions.¹⁸ This, together with the data in Tables 2 and 4 show the rotamer composition for C^4-O^{11} to consist of 93% *gauche* (*J* and *K*) for ipsenol and 97% *gauche* (*P* and *Q*) for ipsdienol. The NMR spectra do not contain further information on this point and attempts to differentiate between the two *gauche* rotamers by NOE experiments failed.

However, the OH-stretch region of the IR spectra contains some further information. For **2**, two bands are observed at 3617 cm^{-1} (60%) and 3583 cm^{-1} (40%), 34 cm^{-1} apart. This shift is large enough to indicate the presence of an internal hydrogen bond to the π -electron system.¹⁹ We have earlier shown that intramolecular hydrogen bonds are not formed in allylic alcohols.¹⁸ For both **1** and **2** the hydrogen bonding must therefore be towards the butadiene system. From Oki's studies of unsaturated alcohols, the C^6-C^9 double bond appears the most likely receptor for such a bond (being part of a 4-butenol system.²⁰ For the *gauche* C-OH rotamers of **2**, only *P* has the correct geometry for a hydrogen bond to the butadiene system. If we assume this rotamer to be completely hydrogen bonded, the areas of the two OH bands observed for **2** give an indication of the relative populations of the two *gauche* rotamers (ca. 60/40, ignoring the small amounts of *anti* rotamer for the moment).

The IR spectrum of ipsenol showed three overlapping OH bands: 3627 cm^{-1} (15%), 3606 cm^{-1} (10%) and 3592 cm^{-1} (75%). The areas are approximate only, owing to the overlap of the bands. From comparison of the IR and NMR results the 3727 cm^{-1} band is assigned to the free *gauche* rotamer (*K*), the one at 3606 cm^{-1} to *anti* (*L*) and that at 3592 cm^{-1} to the hydrogen-bonded rotamer *J* (Fig. 2). The ratio of the hydrogen-bonded to the free *gauche* rotamers is thus ca. 75/15 (*J/K*). For ipsdienol this ratio was only 40/60. The explanation of this large difference may be that in **2** there exists a repulsion between the lone pair electrons of the OH group and the π -electrons of the C^2-C^3 double bond in the hydrogen bonded rotamer *P*.²¹

Only two rotamers around C^4-C^5 have the correct geometry for intramolecular hydrogen bonds, *G* and *H* for ipsenol and *M* and *N* for ipsdienol. However, the rotamers *H* and *N* require the rotamer to be *anti* around the C^4-O^{11} bond. From the NMR data we know that this rotamer has a low population for both compounds. The major intramolecular hydrogen-bonded conformers will therefore be conformer **5** for ipsdienol (Table 5, Fig. 4) and conformer **2** for ipsenol (Table 6).

If we now compare the results from the NMR and IR investigations of ipsdienol with those from the molecular mechanics calculations (Tables 5 and 6) we find a reason-

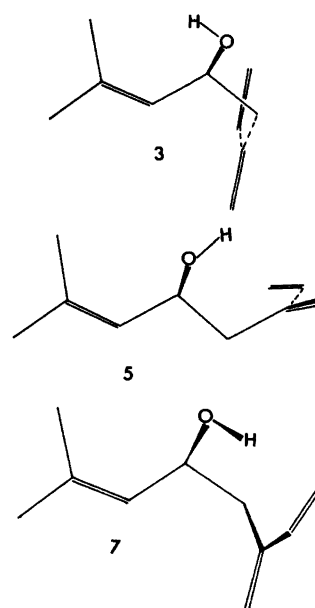


Fig. 4. The three stable conformations of the carbon-carbon chain of ipsdienol (**2**). The numbers refer to the conformations of Table 5.

able agreement. However, the calculations underestimate the proportion of the *gauche* rotamers *H* and *N* (around C^4-C^5) and overestimate the proportions of the rotamers *L* and *R* (around C^4-O^{11} , Figs. 2 and 3). For the composition around the C^3-C^4 bond, the calculations and the NMR results are in good agreement (see above). We therefore conclude that calculations on molecules as complex as those discussed here give only an estimate of the conformational composition.

These results are all concerned with the molecules in a non-polar gas-like medium: the molecular mechanics calculations ignore interactions with the medium and $CFCl_3$ or CCl_4 are non-polar non-hydrogen bonding solvents. Inside the insects, the medium will be polar and hydrogen bonding. The results from the investigations in methanol are therefore relevant to this situation. The most striking difference between the results from the two solvents is the change in the compositions around the C^4-C^5 bond: from a dominance of the *anti* rotamers in $CFCl_3$ to important contributions from rotamers *I* and *O* in methanol (Figs. 2 and 3, respectively). Together with this there will also be a change in the rotamer compositions around the C^4-O^{11} bonds as the intramolecular hydrogen bonds are broken and the pheromones become hydrogen bonded to the polar solvent. This change is not observable in MeOH and the complete conformational compositions of the pheromones in the polar medium are therefore not obtainable from our data.

There may be several reasons for the variation in the composition around C^4-C^5 . Changing the medium from a non-polar to a polar one will favour conformations with a higher dipole moment. From Table 5, the conformations with rotamer *O* (conformers 7, 8 and 9) do have higher

dipole moments than those with rotamer *M* (conformers 4, 5, 6) and are therefore stabilised by an increase in the polarity of the medium. The differences in dipole moments are, however, rather small and we believe the change in intra- and inter-molecular hydrogen bonding to be more important. Going from CFCl_3 to MeOH, the internal hydrogen bonds stabilising rotamers *G* (for 1)? and *M* (for 2) are broken. Instead, new intermolecular hydrogen bonds are formed between the hydroxy groups of the pheromones and methanol. Furthermore, hydrogen bonds will also be formed from the hydroxy groups of methanol to the π -electrons of the pheromones. Intermolecular hydrogen bonds with π -electrons as acceptor groups are not strong, typical shifts as for the hydroxy-stretch frequency being from 70 to 100 cm^{-1} corresponding to a ΔH of ca. 2 kcal mol^{-1} for such a bond.¹⁹ These interactions are nevertheless sufficient to explain the observed changes in the molecular compositions. The three conformations of the carbon chain of ipsdienol are presented in Fig. 4, represented by configurations 3, 5 and 9 (Table 5). The conformers of ipsenol are analogous to these.

Conclusions

From the results of the investigations in CFCl_3 and methanol, the *anti* conformations of ipsenol (1) and ipsdienol (2) appear to be the dominant ones in the gas phase. Inside the insects with a polar, hydrogen-bonding environment, the conformations with a *gauche* rotamer around C^4 – C^5 (rotamer *I* for ipsenol, Fig. 2, *O* for ipsdienol, Fig. 3) are important. These changes take place around the part of the pheromones that earlier investigations have shown to be central for the effect on the insect.⁹ The results may therefore be of consequence for considerations on the shape of the receptor site in the insect.

Experimental

The NMR spectra were recorded on a Bruker 500 MHz spectrometer with a numerical resolution of 0.1 Hz. The NMR assignments were based on a series of double resonance experiments. The IR spectrometer used was Nicolet 20SXC FT-IR. The overlapping bands were resolved graphically. The procedure for obtaining the spectra has been reported.²³ Ipsenol and ipsdienol (racemic mixtures) from Borregaard Industries Ltd. were used as obtained, 95 and 97% pure, respectively.

Ipsenol. IR [4.5 mM in CCl_4 , ν_{max} , $\nu_{1/2}(\text{A}^\circ)$]: 3627, 16.9 (830 $\text{M}^{-1} \text{cm}^{-2}$); 3606, 20 (estm.) (500 $\text{M}^{-1} \text{cm}^{-2}$); 3593, 37.7 (3921 $\text{M}^{-1} \text{cm}^{-2}$).

Ipsdienol. IR [3.9 mM in CCl_4 , ν_{max} , $\nu_{1/2}(\text{A}^\circ)$]: 3617, 14.0 (2320 $\text{M}^{-1} \text{cm}^{-2}$); 3583, 35.5 (1549 $\text{M}^{-1} \text{cm}^{-2}$).

Theoretical investigations. Calculations were performed on an Olivetti M24 computer. Molecular mechanics calcula-

tions utilised the MMPMI program. This consists of MM2 (Allinger, N. L. *QCPE* Program No. 395) and MMP1 (Allinger, N. L. *QCPE* Program No. 318) molecular mechanics program²⁴ implemented by Serena Software, Bloomington, Indiana, USA. PCMODEL from Serena Software was used for input files for the MMPMI program and for obtaining the ^1H NMR coupling constants by the Haasnoot method.¹⁵

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