14. Investigations of the Molecular Surface of a Few Sandalwood-Odor Molecules and Related Structures: Conformational Calculations on Sandalwood Odorants. VI[1])

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Dedicated to Prof. Dr. *C. H. Eugster* on the occasion of his 70th birthday

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The calculated molecular surfaces for some Sandalwood-odor molecules and structurally similar inactive compounds were compared with the calculated mean surface obtained from five Sandalwood odorants included in the set, and their individual agreement and deviations were estimated. Especially the investigation of selected parts of the surfaces seems very promising in finding structure subunits which might be important for an association to a possible receptor site.

1. Introduction. – In continuation of our earlier studies about the structure-odor relationship of Sandalwood-odor compounds [1–3], it could be shown, that the investigation of molecular surfaces furnishes interesting insights into structure-activity relationships. These studies are especially useful in cases where an association of biological active molecules at a suitable receptor site is important but the structure of the complementory receptor surface is unknown. A comparison of the molecular surfaces of different active as well as inactive molecules may lead to informations about a common structure element which is responsible for the biological activity. There exist some different theories about odor perception [4–7], but neither the general molecular mechanism of olfaction nor the structure of any fragrance receptor is known so far. As many different Sandalwood odorants are known [8] [9], a study of the molecular surface seems to be promising to gain more insight into the molecular basis of Sandalwood fragrance. An attempt of a surface analysis on other odor molecules was done a few years ago [10].

In earlier studies [11], it was pointed out that, typically for Sandalwood-odor molecules, a polar group at one end of the molecule is connected to a large hydrophobic part[2]). For an evaluation of the geometries and the molecular-surface structures which might be of importance for an association at a convenient receptor site, we performed molecular calculations on some selected Sandalwood-odor molecules and compared the molecular surfaces of various active and inactive molecules. Results of the study are reported in this paper.

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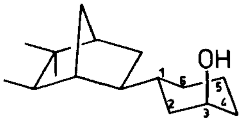
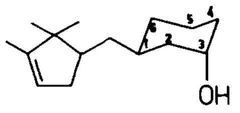
[1]) The method of calculation was published in detail in [1].

[2]) A detailed review of some structural elements of this type of molecules was given recently [12].

2. Compounds Used in This Study. – For the present study, a few Sandalwood-odor molecules were compared with other, mostly structurally very similar, but nevertheless inactive compounds. Especially, the group of the *exo*-isocamphanylcyclohexanols (*e.g.* 3a-**1**) [13], the [(trimethylcyclopentenyl)methyl]cyclohexanols (*e.g.* 3a-**2**) [14], and the [(trimethylcyclopentenyl)ethyl]cyclohexanols (*e.g.* 3a-**3**) [14] was of interest[3]. In all these compounds, ten different positions of the OH group at the cyclohexane moiety are possible[3]. The rigid molecule 6α-(*tert*-butyl)-*trans*-perhydronaphthalen-2α-ol (**4**) [15] was used as standard. The *exo*- and *endo*-isobornylcyclohexan-3(a)-ols **5** and **6** [16] which are rather similar to *exo*-isocamphanylcyclohexan-3(a)-ol 3a-**1** were included in the study. Additionally β-santalol (**7**), the main component of the natural East-Indian Sandalwood oil, and its analogues dihydro-β-santalol (**8**) [17] [18] and (*E*)-β-santalol (**9**) [19] were also taken into account.



3a-**1**[3]



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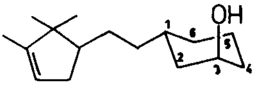

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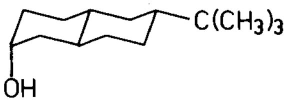

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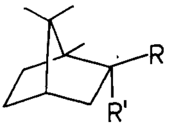
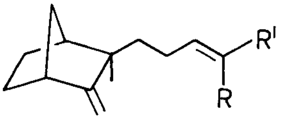
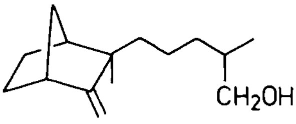
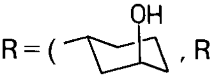
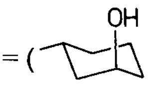






5 R=( , R'=H

6 R=H, R'=(

7 R=CH_2OH, R'=CH_3
9 R=CH_3, R'=CH_2OH

8

Compound **4** was chosen as standard, because it is definitely the most rigid structure of all given molecules. As the two rings of the perhydronaphthalene system are *trans*-configurated, only one conformation is possible. Moreover, the rotation of the *t*-Bu group leads to identical conformations. The OH-group rotation can be neglected, as it does not

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[3] The prefixes '2a-', '3a-', *etc.* denote the axial position of the OH group at C(2), C(3), *etc.* of the cyclohexane ring; similarly, '2e-', '3e-', *etc.* are used for the corresponding equatorial OH groups.

change the shape of the molecule considerably. Besides these 'structural advantages' of **4**, its fragrance is described to be a very pure Sandalwood-like odor [15].

The *exo*-isocamphanylcyclohexanols 3a-**1** and 5a-**1** and the two isobornylcyclohexanols **5** and **6** possess somewhat less rigid structures. They all have only one freely rotating C–C bond, which leads to three different conformations. The inversion of the cyclohexane ring causes an axial position of the bulky residue within the ring instead of an equatorial one. Due to the resulting steric interactions between both ring systems, only two conformations exist within the energetically favorable range of *ca.* 5 kcal/mol from the absolute energy minimum. According to *Demole* [16], only two of the ten isomeric *exo*-isocamphanylcyclohexanols **1** possess pronounced Sandalwood odor, *i.e.* 3a- and 5a-**1**. Two others, 3e- and 4a-**1**, are only reminiscent of Sandalwood odor. Also the substitution pattern of the bicyclic ring system is important for creating an odor sensation as compound **6** is described to be odorless [16].

In analogy, among the [(trimethylcyclopentenyl)methyl]cyclohexanols **2**, only two compounds show a distinct Sandalwood odor, *i.e.* 2a- and 5a-**2**. In contrast to this group, the [(trimethylcyclopentenyl)ethyl]cyclohexanols **3** are mainly odorless; two compounds, 6a- and 2a-**3**, are described to be reminiscent of Sandalwood fragrance [16].

As the natural odor standard, β-santalol (**7**) was taken into account. The four freely rotating C–C bonds in **7** lead to a large number, at least 3^4 different conformations. This rather large flexibility does not allow us to use **7** as a standard molecule for the molecular-surface comparison. Also compounds **8** and **9** are rather flexible molecules with a large number of conformers which have to be considered. The naturally occurring dihydro-β-santalol (**8**) [18] possesses a somewhat weaker odor than **7**, whereas the odor of **9** is more like that of phenol, rather unpleasant, and definitely not Sandalwood-like [20].

3. Method of Calculations. – The method of calculation and the comparison of molecular surfaces was described in detail previously [1]. Molecular surfaces can only be estimated and compared after an accurate determination of the geometries of the compounds under investigation. Therefore, conformational analysis *e.g.* using a molecular-calculation program based on the MM2 force field of *Allinger* [21] (MOLBMEC [22]), was an important prerequisite of these determinations. As a result of these calculations, the thermodynamically most stable conformations were stored in a data base for further use.

For accurate surface comparisons, the different conformations had to be superimposed to the rigid standard **4**. For the matching routine itself, a set of comparable atoms was selected in both molecules, *e.g.* the atoms of the OH group and the centers of the hydrophobic part of the molecules. As such an atom matching is highly dependent on the selection of the corresponding atoms, a volume matching had to be applied in continuation of the matching procedure of Sandalwood-odor molecules [1]. The volume in common of both structures was optimized by gradual rotation and translation of the molecule with respect to the standard.

For the description of molecular surfaces, which can be used for a comparison of different molecules, lines through the midpoint of the standard molecule **4** were defined, and the intersection points with the *Van der Waals* surfaces of the molecules under investigation were calculated. The differences between the intersection points on each line can be taken as a measure of the agreement of the molecular surfaces.

In the present study, a 'mean surface' out of five Sandalwood-odor molecules was computed. The standard molecule (*tert*-butyl)perhydronaphthalenol (**4**), β-santalol (**7**), the two active *exo*-isocamphanylcyclohexanols 3a- and 5a-**1** as well as 5a-**2** were used for the calculation of the mean surface which should describe the steric properties of an ideal molecule with the distinct biological activity. All interesting molecular surfaces were then compared to this mean surface.

Additionally, we compared also special parts of the whole surface. The molecular surfaces were divided into eight parts according to the axes of the *Cartesian* space and the molecular comparisons performed for each part separatedly. This should allow the recognition of surface parts which are essential for odor activity. In such important regions, the surfaces of active molecules are rather close together, whereas inactive compounds should have a distinctly different surface. As such a calculation of partial surfaces depends much on the orientation of the molecules in the *Cartesian* space, another feature was developed: having chosen one point in space, a cube of a certain size was defined around it, and only the molecular surfaces within this cube were then considered for comparison.

The results of these surface comparisons can be shown either as graphical representations or as tables which contain the deviations of the different surfaces or surface parts from the mean surface. A very useful approach furnishes three values for each molecule: The size of the surface part (in % of the entire surface) which is rather close to the mean surface (surface differences less than ± 0.3 Å) and two values for the surface parts showing larger deviations (surface differences $> +0.7$ Å and < -0.7 Å) which take into account the number of the surface dots that are more than 0.7 Å apart from the mean surface and their absolute distance value. These latter two values are obtained by multiplying the % value for each deviation with the squared distance from the mean surface; there are two values for discerning between negative and positive deviations. Those parts which are smaller than the average molecule can be easily distinguished from the larger ones.

4. Results. – The mean surface was compared with the molecular surface of the five Sandalwood odorants used for its calculation *i.e.* **4**, **7**, 3a- and 5a-**1**, and 5a-**2**, of all other *exo*-isocamphanylcyclohexanols *i.e.* 2a-, 2e-, 3e-, 4a-, 5e-, 6a-, and 6e-**1**, the two isobornylcyclohexanols **5** and **6**, of 5e-**2**. Thus, only the first five compounds are definitely Sandalwood-odor molecules, 4a- and 5e-**1** are considered to be reminiscent of the

Table 1. *Comparison of the Individual Molecular Surfaces with the Mean Surface*

	(Surface deviation [%] < –0.7 Å)·d^2a)	Surface agreement [%] –0.3 to 0.3 Å	(Surface deviation [%] > 0.7 Å)·d^2a)
4b)	*11.73*	**47.50**	*7.23*
7b)	32.71	**34.22**	*14.10*
2a-**1**	34.89	25.78	39.69
2e-**1**	63.72	19.38	53.14
3a-**1**b)	*17.24*	**38.81**	*26.53*
3e-**1**	42.77	22.97	36.67
4a-1	*20.30*	23.66	*19.14*
5a-**1**b)	*12.41*	**37.19**	*13.51*
5e-**1**	40.91	23.44	39.36
6a-**1**	56.92	20.32	49.88
6e-**1**	41.52	23.75	42.06
5a-**2**b)	*21.20*	**30.59**	*8.07*
5e-**2**	58.07	25.79	38.13
6	68.24	19.99	58.83
5	38.16	24.07	33.18

a) d = Distance from the mean surface in Å. b) Sandalwood-odor compounds.

odor, and the fragrance of **6** is not proven. *Table 1* shows that for the five Sandalwood compounds, more than 30% of their total molecular surface is rather close to the mean surface, with a deviation of less than 0.3 Å in either direction. For these compounds, also the values characterizing deviations from the mean surface are not especially high. Only β-santalol (**7**) has a rather large surface part with a negative deviation of more than 0.7 Å from the mean surface. Some surface parts are, therefore, a little bit too small in comparison to the ideal molecular shape of Sandalwood-odor molecules.

For the other compounds listed in *Table 1*, substances without a Sandalwood scent, the agreement of the total molecular surface with the mean surface is below 30%. In addition, the positive or negative deviations from the mean surface are enhanced, which might lead to steric hindrance or a diminished affinity at a convenient receptor site.

It has to be emphasized that such a general consideration of the molecular surface gives no information about the importance of surface parts for an association; but nevertheless, a good agreement value or less good deviation values elucidate the similarities of the molecular surface and the surface of an ideal Sandalwood-odor molecule.

Visual Representation. The mean surface as well as the comparisons of the molecular surfaces of an odor molecule and of a non-odorant molecule are given in *Fig. 1*. The pictures are drawn on a graphical screen of a workstation *Iris 3115* using the molecular modeling program package MOLCAD [23] which interpolates the calculated surface points by triangulation. In the case of the mean surface (*Fig. 1*, top), the coloring of the surface represents the standard deviation of the corresponding surface parts calculated from the five Sandalwood-odor compounds. Green areas are parts with a small standard deviation, blue spots indicate surface parts with less agreement between the five different molecules. The other pictures show comparisons of the surface of the Sandalwood-odor molecule **4** (bottom, left) and the non-odorous compound 5e-**1** (bottom, right) with the mean surface. Again, the properties of a good agreement with the mean

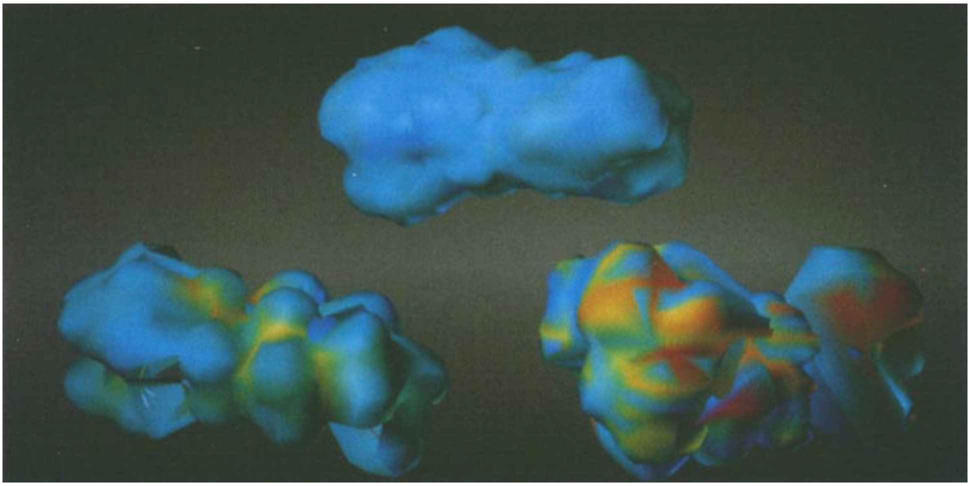

Fig. 1. *Graphical presentation of the mean surface* (top) *and comparison of the molecular surface of* **4** (bottom, left) *and of* 5e-**1** (bottom, right) *with the mean surface.* See text.

surface (green or blue) or more or less strong deviations (yellow or red) are projected onto the molecular surfaces. Mainly green or blue colors indicate a rather good coincidence of the molecule with the ideal Sandalwood-fragrance molecule, whereas in the case of the substance without Sandalwood scent, large parts of the surface appear in yellow or even in red color.

The Search for Relevant Surface Parts. The method of the comparison of molecular surfaces used here makes it possible to search for surface parts which could be important for the fragrance of the compounds. As the total mean surface can be divided in different octants, each octant can be analyzed in a comparable manner as the total surface. In octants where the differences between Sandalwood-odor molecules are small and the differences between fragrance compounds and non-odorous compounds are significant, a surface part important for an association may be located. Octants which show no significant differences between the two groups of molecules are probably of no importance for an interaction between the molecules and the receptor site. Nevertheless, it has to be pointed out that up to now, no selective matching of the molecular surfaces in the various octants was performed. In *Fig. 2,* the central projections for compound **4** are

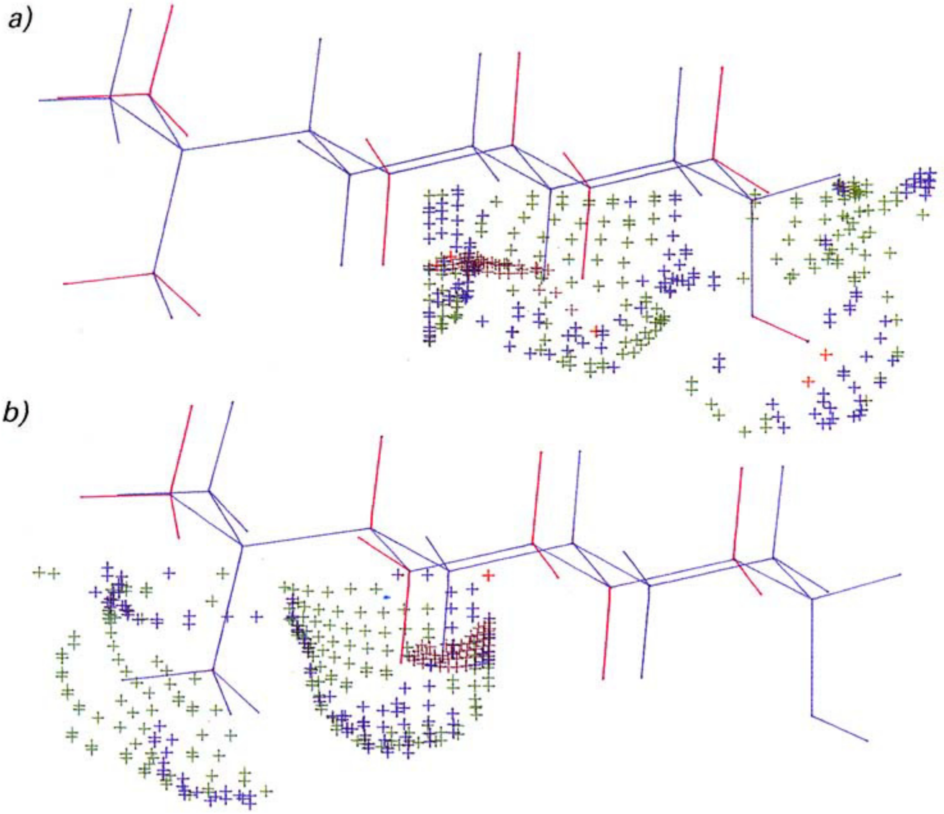

Fig. 2. *Molecular surface of* **4** *in* a) *octant* 1 *and* b) *octant* 6. The coloring represents the deviation of the individual surface from the mean surface: green 0–0.30 Å, blue 0.30–0.90 Å, black 0.90–1.70 Å, and red 1.70 Å and more.

shown for the octants *1* and *6*. The coloring indicates the deviation of each point of the molecular surface from the corresponding point of the calculated mean surface.

In *Table 2*, the deviations of the individual surface from the mean surface in octants *6* are given for the compounds already mentioned in *Table 1*. In this octant, the surface agreement of the Sandalwood-scent molecules is usually as high as in *Table 1*. Only 4a-**1** and 5e-**2** as non-Sandalwood-odor compounds show a similarly good agreement, but 5e-**2** has also large deviations in octant *6*, and 4a-**1** gives rather bad results in octant *3*. The octants *1*, *3*, and *4* behave similarly as octant *6*, important surface parts are postulated to exist in these octants.

Table 2. *Deviation of the Individual Surfaces from the Mean Surface within Octant* 6

	(Surface deviation [%] < −0.7 Å)·d^2[a])	Surface agreement [%] −0.3 to 0.3 Å	(Surface deviation [%] > 0.7 Å)·d^2[a])
4[b])	*29.77*	**52.24**	*0.19*
7[b])	*6.45*	**34.33**	*12.68*
2a-**1**	55.13	19.40	38.26
2e-**1**	30.31	24.47	31.29
3a-**1**[b])	*3.82*	**37.90**	*16.06*
3e-**1**	106.60	11.04	*3.92*
4a-**1**	*19.23*	**44.18**	*15.85*
5a-**1**[b])	*21.84*	**33.73**	*3.84*
5e-**1**	32.85	24.18	*20.38*
6a-**1**	*27.72*	28.36	*14.62*
6e-**1**	*18.32*	24.18	*21.30*
5a-**2**[b])	*10.65*	**32.24**	*13.60*
5e-**2**	*15.17*	**31.34**	32.56
6	*8.31*	17.91	84.92
5	*20.23*	22.09	33.86

[a])[b]) See *Table 1*.

Table 3. *Deviation of the Individual Surfaces from the Mean Surface within Octant* 8

	(Surface deviation [%] < −0.7 Å)·d^2[a])	Surface agreement [%] −0.3 to 0.3 Å	(Surface deviation [%] > 0.7 Å)·d^2[a])
4[b])	*2.88*	25.40	*20.26*
7[b])	112.32	24.77	*4.46*
2a-**1**	*15.87*	22.89	49.05
2e-**1**	*5.17*	7.20	210.73
3a-**1**[b])	*11.76*	18.18	86.96
3e-**1**	48.45	18.18	*17.85*
4a-**1**	*14.10*	29.78	*25.14*
5a-**1**[b])	32.18	**39.50**	*4.30*
5e-**1**	*18.27*	11.92	149.23
6a-**1**	*2.59*	20.07	136.02
6e-**1**	*21.22*	**30.10**	80.79
5a-**2**[b])	*2.61*	29.47	*5.89*
5e-**2**	52.10	15.99	104.65
6	53.31	25.39	37.49
5	99.14	13.80	33.95

[a])[b]) See *Table 1*.

In the octants *2, 5, 7,* and *8,* no significant differences between odorous and non-odorous compounds can be observed; this is exemplified by the statistics given for octant *8* in *Table 3*. In octant *8*, *e.g.*, the Sandalwood-odor molecule 3a-**1** shows only a very poor agreement with the mean surface, and the positive deviation value is rather large. We can assume, therefore, that this part of the molecular surface is not important for a common structural unit of all Sandalwood-odor molecules.

This result can be verified by calculating also other molecules *i.e.* 2a-, 2e-, 3e-, 4a-, 4e-, 6a-, and 6e-**2**, 2a-, 2e-, 5a-, 5e-, 6a-, and 6e-**3**, **8**, and **9** in the same way (see *Table 4*): only **8** possesses Sandalwood odor, but about six compounds show a rather big surface part with a deviation of less than 0.3 Å (more than 30%). However, only **8** has at the same time small values for the big deviations (< 30% in both directions), whereas **9** which resembles *β*-santalol (**7**) shows a definitely larger value for 'positive' deviations, although quite a big part of its surface is very close to the mean surface, too. A graphical representation of the comparison of the molecular surface of **9** with the mean surface is given in *Fig. 3*.

Table 4. *Deviation of the Individual Surfaces from the Mean Surface within Octant* 6

	(Surface deviation [%] < -0.7 Å)·d^2[a])	Surface agreement [%] -0.3 to 0.3 Å	(Surface deviation [%] > 0.7 Å)·d^2[a])
2a-**2**	56.11	22.39	*15.85*
2e-**2**	34.95	29.25	*15.20*
3e-**2**	287.00	6.00	*0.00*
4a-**2**	121.62	14.03	*16.29*
4e-**2**	*12.45*	24.19	47.37
6a-**2**	77.38	25.07	*7.05*
6e-**2**	62.61	24.47	*2.43*
2a-**3**	*26.17*	**35.23**	*11.80*
2e-**3**	38.11	29.85	*23.21*
5a-**3**	34.66	**39.70**	64.39
5e-**3**	45.22	10.14	63.55
6a-**3**	35.96	**34.93**	*17.59*
6e-**3**	66.34	**38.21**	*6.20*
8[b])	*21.17*	**42.39**	*6.31*
9	*14.00*	**37.61**	*34.84*

[a])[b]) See *Table 1*.

Specific Surface Areas. As octant *6* shows some distinct differences, a more specific study of this region seemed appropriate. Therefore, a special feature of the program was developed allowing the definition of a specific point in space and a cube containing the whole octant *6* and a bit of octant *3* around it. Only the surface area within this cube was taken into consideration. Several such cubes were tested, one significant result is shown in *Table 5*. This surface part shows the similarities and the differences of Sandalwood-odor molecules and non-odorous analoga within the bulky aliphatic residue, especially on the same side where the OH group is located. The values in *Table 5* show similarly or even better significant high values for the surface agreement of Sandalwood-fragrance compounds, comparable to the results of *Tables 1–3*. Again some substances have good agreement values (higher than 30%), *e.g.* 4a-**1** or 6a-**3**, but they show either large deviation values in the same surface part, or they fit very badly in another significant surface region.

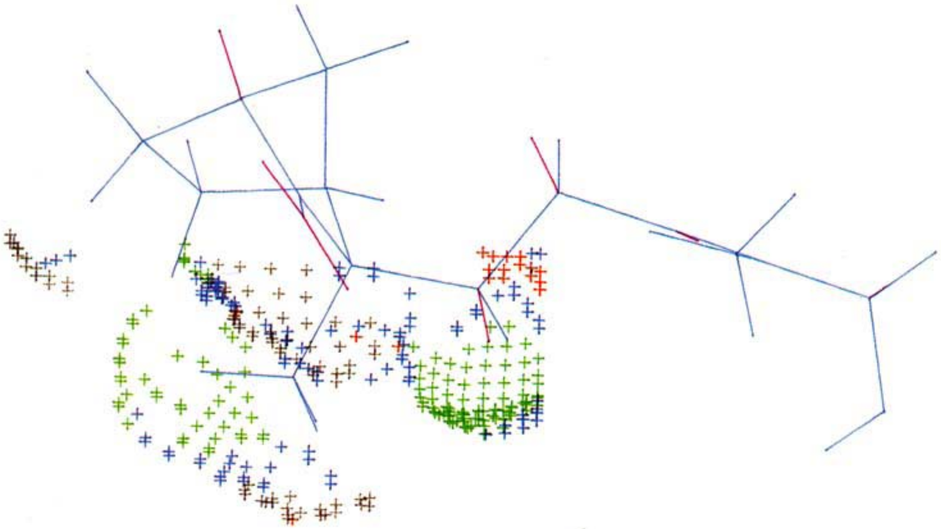

Fig. 3. *Comparison of the molecular surface of* **9** *with the mean surface in octant* 6. The coloring is the same as in *Fig. 2*.

Table 5. *Deviation of the Individual Surfaces from the Mean Surface within a Cube Around Point (–5|–4|5)* (side length 10 Å)

	(Surface deviation [%] < –0.7 Å)·d^2a)	Surface agreement [%] –0.3 to 0.3 Å	(Surface deviation [%] > 0.7 Å)·d^2a)
4b)	*24.69*	**52.40**	*0.15*
7b)	*12.41*	**32.80**	*11.59*
2a-**1**	55.93	20.00	32.41
2e-**1**	47.39	21.32	*24.67*
3a-**1**b)	*5.82*	**41.77**	*12.48*
3e-**1**	84.99	12.76	*6.86*
4a-**1**	*22.49*	**41.10**	*14.33*
5a-**1**b)	*21.69*	**31.64**	*5.16*
5e-**1**	*26.12*	28.40	*20.52*
6a-**1**	69.88	25.49	*11.40*
6e-**1**	*20.54*	22.84	*17.38*
2a-**2**	45.68	**53.57**	*19.37*
2e-**2**	73.69	29.73	*10.58*
3e-**2**	261.76	0.00	*0.00*
4a-**2**	98.26	15.39	*23.79*
4e-**2**	56.20	20.04	33.08
5a-**2**b)	*16.27*	**34.51**	*11.07*
5e-**2**	44.61	23.51	*28.51*
6a-**2**	63.68	25.48	*9.50*
6e-**2**	92.82	21.95	*3.63*
2a-**3**	40.07	***32.56***	*9.70*
3a-**3**	30.69	28.61	34.99
5a-**3**	*28.29*	**41.32**	58.05
5e-**3**	36.83	10.68	69.14
6a-**3**	40.00	**37.33**	*13.54*
6e-**3**	66.13	**34.82**	*7.77*

Table 5 (cont.)

	(Surface deviation [%] < –0.7 Å)·d^2[a])	Surface agreement [%] –0.3 to 0.3 Å	(Surface deviation [%] > 0.7 Å)·d^2[a])
8[b])	*20.73*	**42.66**	*7.10*
9	*19.07*	**31.94**	33.70
6	67.52	18.66	59.36
5	30.44	25.81	*26.71*

[a])[b]) See *Table 1*.

5. Discussion. – Sandalwood odorants show a high structural sensitivity of the scent, since only slight structural changes within an odor molecule lead to the complete loss of the fragrance. The shape of the molecules is, therefore, responsible for the possibility of the association of such molecules at the corresponding receptor. The special surface comparison of the present study demonstrates the differences of the molecular surfaces of odorant and non-odorant compounds and enables additionally the finding of relevant parts of the molecular surfaces. A surface part close to the functional group (octant *6*) as well as a larger part of the hydrophobic residue seem to be important for an association at the receptor site. Nevertheless, for a more detailed analysis or even a receptor modeling, it is necessary to estimate the stereospecifity of a larger number of Sandalwood odorants and to take them into account for the surface comparisons described above.

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REFERENCES

[1] G. Buchbauer, S. Winiwarter, P. Wolschann, *J. Comp. Aided Mol. Design* **1992,** *5,* in press.
[2] A. Becker, G. Buchbauer, S. Winiwarter, P. Wolschann, *Monatsh. Chem.* **1992,** *123,* in press.
[3] A. Becker, G. Buchbauer, S. Winiwarter, P. Wolschann, *J. Ess. Oil Res.* **1990,** *2,* 221.
[4] J. E. Amoorc, in 'Fragrance Chemistry. The Science of the Sense of Smell', Ed. E. T. Theimer, Academic Press, New York, 1982, p. 27.
[5] T. Engen, The Perception of Odours', Academic Press, New York, 1982.
[6] G. Ohloff, *Experientia* **1986,** *42,* 271.
[7] G. Ohloff, 'Riechstoffe und Geruchssinn', Springer-Verlag, Berlin–Heidelberg, 1990.
[8] E. J. Brunke, E. Klein, in 'Fragrance Chemistry. The Science of the Sense of Smell', Ed. E. T. Theimer, Academic Press, New York, 1982, p. 397.
[9] R. E. Naipawer, in 'Dev. Food Science, Flavors and Fragrances; A World Perspective', Eds. B. M. Lawrencc, B. D. Mookherjee, and B. J. Willis, Elsevier, Amsterdam–Oxford–New York, 1988, Chapt. 18, p. 805.
[10] R. S. Marmor, *Perfum. Flavor.* **1983,** *8,* 37.
[11] R. E. Naipawer, K. L. Purzycki, G. W. Shaffer, R. E. Erickson, in 'Essential Oils', Eds. B. D. Mookherjee and C. S. Mussinan, Allured Publ. Corp., Wheaton, Illinois, 1981, p. 105.
[12] M. Chastrette, D. Zakarya, C. Pierre, *Eur. J. Med. Chem.* **1990,** *25,* 433.
[13] E. Demole, *Helv. Chim. Acta* **1964,** *44,* 1766.
[14] E. J. Brunke, E. Klein, Dtsch. Offenlegungsschrift 1979, 2935683.
[15] J. G. Witteveen, A. J. A. Van der Weerdt, *Recl. Trav. Chim. Pays-Bas* **1987,** *106,* 29.
[16] E. Demole, *Helv. Chim. Acta* **1969,** *52,* 2065.
[17] W. I. Fanta, W. F. Erman, *J. Org. Chem.* **1972,** *37,* 1624.
[18] A. Nikiforov, J. Jirovetz, G. Buchbauer, V. Raverdino, *Spectrosc. Int. J.* **1988,** *6,* 283.
[19] E. J. Brunke, A. Böhme, H. Struwe, *Liebigs Ann. Chem.* **1982,** 1105.
[20] E. J. Brunke, *Dragoco-Reports* **1983,** *30,* 27.
[21] N. L. Allinger, *J. Am. Chem. Soc.* **1977,** *99,* 8127.
[22] A. Beyer, P. Wolschann, A. Becker, G. Buchbauer, *J. Mol. Struct.* **1989,** *196,* 371.
[23] J. Brickmann, M. Waldherr-Teschner, M. Knoblauch, Technische Universität Darmstadt.