Actes Inst. Agron. Vet. (Maroc) 1998, Vol. 18 (1) : 61-65

Structure-sulfur odor relationships for some organic compounds

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(Reçu le 14/03/1997 ; Accepté le 27/05/1997)

العلاقة بين البنية والرائحة الكبريتية

يتمحور هذا المقال حول دراسة وبحث عن العوامل الرئيسية والمسؤولة عن وجود رائحة الكبريت في الجزيئات العضوية، يتبين من خلال الدراسة أن وجود ذرة الكبريت مهم، ولكن عدد هذه الذرات لايؤثر على رائحة الماء. يمكننا من خلال ماسبق أن نستنتج أن هناك حلول لتغطية رائحة الكبريت التي تعتبر من بين الروائح الكريهة.

الكلمات المفتاحية : شبكة الأعصاب – رائحة الكبريت – ت – ف – م – ت – ذ

Relations structure-odeur soufrée pour une série de composés organiques

Les relations structure-odeur soufrée sont établies en choisisant les fragments de molécules comme descripteurs selon les principes de la méthode GESDEM (Genération et Sélection de Descripteurs et Elaboration de Motifs). La série étudiée comporte 48 molécules soufrées et 34 non-soufrées. 96 % des molécules ont été classées en tant que telles par un modèle obtenu en utilisant un réseau neuronal (RN) de configuration 8-5-1.

Mots clés : Réseaux neuronaux - Odeur soufrée - GESDEM- Relations quantitatives structure-odeur (QSOR)

Structure-sulfur odour relationships for some organic compounds

Structure-sulfur odour relationships were established using molecular fragments as descriptors generated by GESDEM methodology (Generation and Selection of Descriptors and Elaboration of Patterns). The studied sample included 48 sulfuraceous and 34 non-sulfuraceous molecules. 96 % of good classification was obtained using a neural network (NN) model having a 8-5-1 configuration.

Key words : Neural networks- Sulfur odour- GESDEM- Quantitative structure-odour relationships (QSOR)

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INTRODUCTION

The sulfur odor is one of the most extensively problem in the environment. It is generally well admitted that the presence of this odor is closely associated with the presence of the sulfur atom.

One noticed that structure-odor relationships were not sufficiently studied for sulfur. Thus, we try, in this preliminary work, to establish structure-sulfur odor relationships for a set of compounds using the neural network approach. Descriptors used were generated using GESDEM method (Zakarya, 1989). Evaluation of the contribution of relevent descriptors to the sulfur odor, were given and discussed.

MATERIALS & METHODS

The set studied included 82 compounds (48 molecules having the sulfur odor and 34 non-sulfuraceous odorants) (Table 1).

Table 1. List of the compounds studied

N° Compound	Observed odour (s(1) and n.s(0)	Calculated odour (by NN)	Reference
1. 1-propyl disulfide	1	0.811	(Dravnieks, 1961)
2. 1-Propyl trisulfide	1	0.809	(Dravnieks, 1961)
3. 2-Propenyl-2-propenthiosulfinate	1	0.811	((Dravnieks, 1961)
4. 2-Thienyl mercaptans	1	1.000	(Dravnieks, 1961)
5. 3-Methyl thiopropyl alcohol	0	0.216	(Dravnieks, 1961)
6. 4-Methyl mercaptobutylamine	0	0.416	(Dravnieks, 1961)
7. 4-Nitrophenyl-iso-thiocyanate	0	0.091	(Dravnieks, 1961)
8. Allyl-iso-thiocyanate	0	0.091	(Dravnieks, 1961)
9. Allyl mercaptan	1	1.000	(Dravnieks, 1961)
10. Allyl propyl disulfide	1	0.886	(Dravnieks, 1961)
11. Amyl mercaptan	0	0.091	(Dravnieks, 1961)
12. Benzyl disulfide	1	0.887	(Dravnieks, 1961)
13. Benzyl mercaptan	0	0.188	(Dravnieks, 1961)
14. Benzyl-iso-thiocyanate	0	0.091	(Dravnieks, 1961)
15. Carbon disulfide	0	0.811	(Dravnieks, 1961)
16. Diallyl disulfide	1	0.895	((Dravnieks, 1961)
17. Diallyl sulfide	1	0.811	(Dravnieks, 1961)
18. Dibutyl sulfide	0	0.441	(Dravnieks, 1961)
19. Dicrotyl sulfide	1	0.872	(Dravnieks, 1961)
20. Dimethyl disulfide	1	0.894	(Dravnieks, 1961)
21. Dodecyl mercaptan	0	0.091	(Dravnieks, 1961)
22. Ethyl thioglycolate	1	1.000	(Dravnieks, 1961)
23. Ethylene glycol monoallyl ether	0	0.091	(Dravnieks, 1961)
24. Hexane methylthional	0	0.103	(Dravnieks, 1961)
25. iso-Butyl-iso-thiocyanate	1	1.000	(Dravnieks, 1961)
26. Methyl-1-propyl disulfide	1	1.000	(Dravnieks, 1961)
27. Methyl-ß-methylthiolpropionate	1	0.814	(Dravnieks, 1961)
28. n-Butyl mercaptan	0	0.099	(Dravnieks, 1961)
29. n-Butyl-iso-thiocyanate	0	0.091	(Dravnieks, 1961)
30. n-Hexyl mercaptan	0	0.091	(Dravnieks, 1961)
31. Phenylethyl-iso-thiocyanate	0	0.091	(Dravnieks, 1961)
32. Sulfur dioxyde	0	0.091	(Dravnieks, 1961)
33. Thioguaiacol	1	0.564	(Dravnieks, 1961)
34. Mercaptan-2-ethanoic acid	1	0.532	(Dravnieks, 1961)
35. 1,4 Dithiane2,5 diol 2,5 dimethyl	1	1.000	(Arctander, 1969)
36. Tetrahydro-thiophene	0	0.103	(Arctander, 1969)
37. Thioglycolic acid	1	0.835	(Arctander, 1969)
38. Butanthoic acid	1	0.874	(Arctander, 1969)
39. Methyl thiobutyrate	0	0.103	(Arctander, 1969)

Table 1. List of the compounds studied (continued)

N° Compound	Observed odour (s(1) and n.s(0)	Calculated odour (by NN)	Reference
40. Butyl sulfide	1	0.899	(Arctander, 1969)
41. Hydrogen sulfide	0	0.091	(Windholz *etal.* ,1983)
42. Thiophenol	1	1.000	(Morton &MacLeod, 1990)
43. Vinyl sulfide	1	1.000	(Othmer, 198)
44. Methanethiol	1	1.000	(Grignard *etal.* ,1971)
45. Etanthiol	1	1.000	(Grignard *etal.* ,1971)
46. 1-Propanethiol	1	0.798	(Grignard *etal.* ,1971)
47. 1-Methyl-2-propanethiol	1	1.000	(Grignard *etal.* ,1971)
48. 1-Butanethiol	0	0.091	(Grignard *etal.* ,1971)
49. Dichlorosulfur carbone	0	0.114	(Foucher, 1974)
50. Tetrachloro sulfur carbone	0	0.091	(Foucher, 1974)
51. Ethyl thiocarbonic acid	0	0.115	(Foucher, 1974)
52. Thiocarbonate diethylic	0	0.094	(Foucher, 1974)
53. Ethyl thiocarbonate phenyl	0	0.130	(Foucher, 1974)
54. Chlorothiocarbonate phenyl	0	0.091	(Foucher, 1974)
55. Thionecarbonate diethylic	0	0.403	(Foucher, 1974)
56. 3-Mercapto-2-butanone	0	0.090	(Mottram & Madruga, 1995)
57. 3-Mercapto-2-pentanone	0	0.162	(Mottram & Madruga, 1995)
58. 2-Mercapto-2-pentanone	1	1.000	(Mottram & Madruga, 1995)
59. bis (1-Methyl-2-oxopropyl) sulfide	1	1.000	(Mottram & Madruga, 1995)
60. bis (1-Ethyl-2-oxopropyl) sulfide	1	0.868	(Mottram & Madruga, 1995)
61. 2-[(1-methyl-2-oxopropyl)-thio]-3-pentanone	1	0.868	(Mottram & Madruga, 1995)
62. bis (1-methyl-2-oxopropyl) disulfide	1	0.809	(Mottram & Madruga, 1995)
63. bis (1-ethyl-2-oxopropyl) disulfide	1	0.809	(Mottram & Madruga, 1995)
64. bis (1-methyl-2-oxobutyl) disulfide	1	0.809	(Mottram & Madruga, 1995)
67. 2-[(methyl-2-oxopropyl)-dithio]-3-pentanone	1	0.809	(Mottram & Madruga, 1995)
65. 3-[(methyl-2-oxobutyl)-dithio]-2-pentanone	0	0.809	(Mottram & Madruga, 1995)
66. 3-[(methyl-2-oxopropyl)-dithio]-2-pentanone	1	0.809	(Mottram & Madruga, 1995)
68. bis (methyl-2-oxopropyl) trisulfide	1	0.809	(Mottram & Madruga, 1995)
69. bis (1-ethyl-2-oxopropyl) trisulfide	1	0.809	(Mottram & Madruga, 1995)
70. bis (1-ethyl-2-oxobutpyl) trisulfide	1	0.809	(Mottram & Madruga, 1995)
71. 3-[(1-methyl-2-oxobutyl)-trithio]-2-pentanone	1	0.809	(Mottram & Madruga, 1995)
72. 3-[(1-methyl-2-oxopropyl)-trithio]-2-pentanone	1	0.809	(Mottram & Madruga, 1995)
73. 2-[(1-methyl-2-oxopropyl)-trithio]-3-pentanone	1	0.809	(Mottram & Madruga, 1995)
74. bis[(2-methyl-3-furyl)-dithio]-2-pentanone	0	0.809	(Mottram & Madruga, 1995)
75. 3-[(2-methyl-3-furyl)-dithio]-2-pentanone	1	0.809	(Mottram & Madruga, 1995)
76. bis(2-furylmethyl) sulfide	0	0.091	(Mottram & Madruga, 1995)
77. bis (2-furylmethyl) disulfide	1	0.814	(Mottram & Madruga, 1995)
78. bis (2-furylmethyl) trisulfide	1	0.809	(Mottram & Madruga, 1995)
79. 3-[(2-furylmethyl) dithio]-2-butanone	1	0.809	(Mottram & Madruga, 1995)
80. 3-[(2-furylmethyl) dithio]-2-pentanone	1	0.809	(Mottram & Madruga, 1995)
81. 2-[(furylmethyl) dithio]-3-pentanone	1	0.809	(Mottram & Madruga, 1995)
82. 2-Methyl-3-[(2-furylmethyl) dithio]-2-furan	0	0.091	(Mottram & Madruga, 1995)

- Molecules not classified by the model ; - s(1) : sulfuraceous ; - ns(0) : non-sulfuraceous

In this study, the odor is coded using a binary variable which takes value 1 for compounds described as strong to extremely strong sulfuraceous, and 0 for the others.

GESDEM methodology (Zakaria, 1989) was used to generate different sets of fragments of different sizes. Descriptors are groups of atoms held together by bonds as constituting specific subgraphs. All

descriptors generated can not be useful. So, the total number of descriptors increase with the order. In general, the descriptors of order one (^1D_i) are the different types of atoms in the studied sample (not including hydrogen atoms). Descriptors of order two (^2D_i) were elaborated by adding an atom , in all possible ways, to descriptors of order one, etc.

Structure-odor relationships were established using Neural Network (NN) approach.

Each neuron of the input layer is fully interconnected with each neuron of the hidden layer which in turn is fully interconnected with the output neuron. There are no connections between the neurons within a layer nor any direct connection between those of the input and output layers. The sigmoidal transfer function used is given by eq.i where O_i and O_j are the outputs of neuron i and j, respectively, and W_{ij} is the weight connecting neuron i to neuron j.

$O_j = (1+\exp(-\Sigma W_{ij.xi}))^{-1}$ Eq.i

x_i : value of the neuron i

$O_k = (1+\exp(-\Sigma W_{jk}.O_j))^{-1}$ Eq.ii

The back-propagation algorithm (Chastrette *et al.*, 1994) was used to adjust the weights (MacClelland *et al.*,1988).

The NN used has three layers : the input one representing descriptors, a hidden layer and the output representing the calculated odor. Optimization of the configuration of NN lead to five neurons in the hidden layer. All the trials were stopped for 3000 epochs.

RESULTS & DISCUSSIONS

96 % of the molecules were correctly classified by the NN with descriptors of order 1 to 3. These results show that it is possible to predict efficiently the sulfur odor.

The prédiciton ability of the NN for each class of compounds is shown in table 2.

Table 2. Influence of the order of descriptors on the classification

Order of descriptors	Classification of sulfur	Classification of non-sulfur	Average
1	34	28	75.6%
2 (+ pertinent from order 1)	48	28	92.7 %
3 (+ pertinent from lower orders)	48	31	96.3 %

The final weight of connections between all the neurons are given in Table 3.

Table 3.Weights matrix for the connection between neurons

Neurons	H_1	H_2	H_3	H_4	H_5
I_1	3.946	-13.206	-7.321	-6.190	-0.792
I_2	-35.879	42.019	-6.939	6.704	-35.799
I_3	2.035	-7.589	9.996	17.168	21.486
I_4	-5.480	-6.143	3.285	12.279	17.597
I_5	2.007	-5.008	10.519	4.114	8.876
I_6	0.597	-6.484	8.235	0.392	-1.373
I_7	-5.170	-0.009	0.477	7.265	-3.701
I_8	12.243	-3.080	-17.710	5.512	-1.940
I_9	-0.458	1.747	-10.487	-16.461	10.725
O	-22.284	-23.590	-16.136	-17.384	22.570

I_1...I_8 : input neurons representing descriptors; I_9: bias H_1...H_5 : hidden neurons. O: output neuron.

In order to explicit the rules found by the NN model, the contribution of each descriptors according to the method developped by Zakarya *et al.* (1996) was calculated.

Cc = (+)2.32 %, Cs = (+)54.16 %,
$C_{C\text{-}S}$ = (+)20.81 %, $C_{C=O}$ = (+)7.74 %, C_{CCS} = (+)10.43 %,
C_{CSH} = (+)1.29 %, C_{CSC} = (+)1.25 %, C_{SCO} = (-)1.96 %

C_X : Contribution of functional group X (10), the sign of the contribution is evaluated by a method recently introduced by Zakarya *et al.* (1996).

Except for C=O, all pertinent descriptors included sulfur atoms.

Odor prediction

In order to test the prediction ability of the neural network, we remove in 10 times 10% of compounds of the global sample and trained the neural network on the remained compounds. The obtained results were not far from those calculated using the global model. In table 4, we give the classification for all trials.

According to the established model S-S and S-S-S fragments are not involved in the discrimination between sulfur and non-sulfur molecules, while the fragments including S atom only contribute with approximately 89%.

Analysis of all statistical parameters shows that the model presented is efficient, significant and suggest the possibility to derive relations between sulfur odor and various chemical structures.

Table 4. Correlation between predicted and observed values

Test	1	2	3	4	5	6	7	8	9
r^2 (%)	80.39	80.57	80.95	84.46	81.11	79.19	79.75	78.48	80.15
σ	0.249	0.248	0.246	0.229	0.245	0.242	0.254	0.251	0.257

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Déjà paru

Actes Inst. Agron. Vet. (Maroc) 1997, Vol. 17 (4)

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