DOI: 10.6060/ivkkt.20206307.6253

УДК: 544.18

СРАВНИТЕЛЬНЫЕ ОСОБЕННОСТИ СТРУКТУРЫ И СВОЙСТВ БИОМАРКЕРОВ НАФТАЛАНСКОЙ НЕФТИ

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Представлены результаты исследований структурных особенностей биомаркеров Нафталанской нефти (в частности, R, S-холестанов и гопанов с C_{28}-C_{31}) методом гибридного функционала плотности в приближении 6-311G+(d,p). Показано, что исследуемые вещества имеют четырехъядерную циклопентанопергидрофенантреновую систему, которая присуща смолам и асфальтенам тяжелых нефтей, а также характеризуется трехмерной пространственной конфигурацией. Соединения, содержащие такую кольцевую систему, имеют большое значение для организма, в том числе при воздействии антимикробных реагентов. Строение и положение примыкающих к основному циклу боковых групп и атомов, положение двойных связей в молекуле, пространственная конфигурация оказывают определенное влияние на биологическую активность биомаркеров Нафталанской нефти. Рассчитанные геометрические параметры исследуемых соединений показывают, что молекулы устойчивы, и устойчивость определяется конформацией колец (циклогексановые кольца имеют конформацию кресла, а циклопентановые — полукресла), характером соединения между собой и пространственным расположением атомов водорода, радикалов и функциональных групп. Из рассчитанных значений торсионных углов холестанов и гопанов показано, что сочленение циклов A/B, B/C и C/D находится в транс-конфигурации (118,37º - 129,94º). Исследуемые молекулы обладают транс-сочленением колец при 5,10-, 8,9-, и 13,14-положениях (в случае гопанов 5-10 также при 17,18-положении). Связи в молекулах, образующих кольца, незначительно искажены, а сами кольца не являются плоскими. Выявлена зависимость между биологической активностью тритерпенов и их значениями потенциалов ионизации и сродства к электрону. Исследуемые биомаркеры по геометрическим и энергетическим параметрам сходны с производными бетулина и могут проявлять биологическую активность.

Ключевые слова: биомаркеры, Нафталанская нефть, холестаны, гопаны, бетулин, метод гибридного функционала плотности, структура

COMPARATIVE FEATURES OF STRUCTURE AND PROPERTIES OF BIOMARKERS OF NAPHTHALAN PETROLEUM

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The results of studies of the structural features of the biomarkers of Naphthalan petroleum (in particular, R, S-cholestanes and hopanes with C_{28}-C_{31}) by the hybrid density functional in the approximation 6-311G+(d,p) are presented. It was shown that the studied substances have a quad-cyclopentanoperhydrophenanthrene system, which is inherent in resins and asphaltenes of heavy oils, and is also characterized by a three-dimensional spatial configuration. Compounds containing such a ring system are of great importance both for the body, including when exposed to antimicrobial reagents. The structure and position of the side groups and atoms adjacent to the main cycle, the position of double bonds in the molecule, and the spatial configuration have a definite effect on the biological activity of the biomarkers of Naphthalan petroleum. The calculated geometric parameters of the studied compounds show that the molecules are stable, and the stability is determined by the conformation of the rings (cyclohexane rings have the chair conformation, and cyclopentane rings have half-chairs), the nature of the connection between each other and the spatial arrangement of hydrogen atoms, radicals and functional groups. From the calculated values of the torsion angles of cholestanes and hopanes, it was shown that the junction of the A/B, B/C and C/D cycles is in the trans configuration (118.37° - 129.94°). The studied molecules possess a trans-articulation of the rings at the 5,10-, 8,9-, and 13,14-positions (in the case of 5-10 hopanes, also at the 17,18-position). The bonds in the molecules that form the rings are slightly distorted, and the rings themselves are not flat. A relationship was found between the biological activity of triterpenes and their values of ionization potentials and electron affinity. The studied biomarkers are similar in geometry and energy parameters to betulin derivatives and can exhibit biological activity.

Key words: biomarkers, Naphthalan petroleum, cholestans, hopanes, betulin, density functional hybrid method, structure

Для цитирования:
Колчина Г.Ю., Мовсумзаде Э.М. Сравнительные особенности структуры и свойств биомаркеров Нафталанской нефти. *Изв. вузов. Химия и хим. технология*. 2020. Т. 63. Вып. 7. С. 82–87

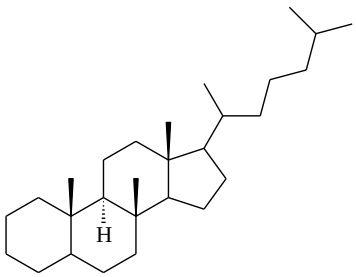
For citation:
Kolchina G.Yu., Movsumzade E.M. Comparative features of structure and properties of biomarkers of Naphthalan petroleum. *Izv. Vyssh. Uchebn. Zaved. Khim. Khim. Tekhnol*. [Russ. J. Chem. & Chem. Tech.]. 2020. V. 63. N 7. P. 82–87

INTRODUCTION

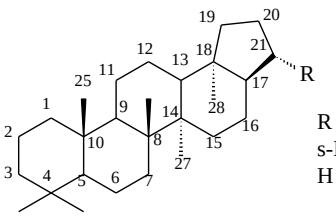
The composition of hydrocarbons and their ratio in oils are directly related to the conditions of their formation, namely: temperature and pressure (catagenesis), the effect of microorganisms (biodegradation), the composition and structure of the original organic matter [1-6].

Biomarkers (chemofossilia) are peculiar organic compounds and have a complex-built carbon skeleton of biogenic nature, inherited in whole, or in the form of fragments from the precursor molecules of the original organisms. A large number of biomarkers in petroleum are polycyclic hydrocarbons (steranes and triterpans), which are found in all living organisms [7-10].

Naphthalan oil its individual fractions obtained by distillation under vacuum or by the percolation method, as well as some organic compounds of non-hydrocarbon nature isolated from this oil, have significant biological activity [11-16].



14α-17α-cholestan-20R(S)(**1**,**2**)
14β-17β-cholestan-20R(S) (**3**,**4**)



R = i-Pr (**5**), Et (**6**), s-Bu (**7**,**8**), s-Pe (**9**), H (**10**)

Fig. 1. Structures of the studied Naphthalan biomarker molecules
Рис. 1. Структуры исследуемых молекул биомаркеров Нафталанской нефти

EXPERIMENTAL TECHNIQUE

The geometry of the molecules is fully optimized within the framework of the method of the hybrid density functional B3LYP/6-311+G(d,p). All calculations were performed using the FireFly program [16].

RESULTS AND DISCUSSION

The compounds contained in Naphthalan petroleum have a quad-cyclopentanoperhydrophenanthrene system and are characterized by a three-dimensional spatial configuration (Fig. 1). The structure and position of the side groups and atoms adjacent to the main cycle, the position of double bonds in the molecule, the spatial configuration, etc., have a definite effect on the biological activity of these compounds.

The geometrical shape of the studied biomarkers is stable and is determined by the conformation of the rings (cyclohexane rings have the chair conformation, cyclopentane rings have half-chairs), the nature of their interconnection, and also the arrangement of hydrogen atoms, radicals and functional groups that are attached to the nucleus (Tables 1, 2).

Table 1

The geometric characteristics of cholestanes calculated by the B3LYP/6-311+G(d,p) method

Таблица 1. **Геометрические характеристики холестанов, рассчитанные методом B3LYP/6-311+G(d,p)**

Parameters	Compounds			
	1	**2**	**3**	**4**
l(C_1–C_2), Å	1.539	1.538	1.538	1.538
C_2–C_3	1.535	1.534	1.535	1.534
C_3–C_4	1.535	1.535	1.535	1.535
C_4–C_5	1.538	1.538	1.539	1.539
C_5–C_6	1.525	1.534	1.534	1.534
C_6–C_7	1.532	1.533	1.532	1.532
C_7–C_8	1.538	1.539	1.539	1.539
C_8–C_9	1.557	1.556	1.551	1.551
C_9–C_{10}	1.579	1.547	1.571	1.571
C_{10}–C_1	1.555	1.554	1.555	1.554
C_9–C_{11}	1.545	1.545	1.542	1.542
C_{11}–C_{12}	1.644	1.543	1.537	1.538
C_{12}–C_{13}	1.543	1.549	1.549	1.548
C_{13}–C_{14}	1.557	1.558	1.558	1.558
C_{14}–C_{15}	1.537	1.535	1.555	1.555
C_{15}–C_{16}	1.553	1.552	1.553	1.553
C_{16}–C_{17}	1.563	1.567	1.548	1.548
C_{13}–C_{17}	1.569	1.570	1.564	1.564
∠($C_1C_{10}C_9$), °	110.25	110.08	109.86	109.85
∠$C_4C_5C_6$	112.64	112.88	112.72	112.78
∠$C_{10}C_9C_{11}$	114.60	114.51	114.37	114.49
∠$C_{12}C_{13}C_{17}$	116.97	116.62	113.14	113.69
∠$C_7C_8C_{14}$	111.71	111.75	111.20	111.18
∠$C_8C_{14}C_{15}$	18.97	119.21	116.30	116.23
∠$C_{13}C_{17}C_{20}$	120.61	120.34	118.67	119.18
∠($C_1C_{10}C_9C_{19}$), °	120.85	120.81	120.62	120.58
∠$C_1C_{10}C_9C_5$	-116.51	-116.57	-116.63	-116.64
∠$C_4C_5C_6C_{10}$	-129.3	-129.45	-129.27	-129.33
∠$C_9C_8C_{14}C_7$	-123.21	-123.09	-127.46	-112.88
∠$C_{10}C_9C_8C_{11}$	-130.31	-130.32	-128.51	-128.66
∠$C_{12}C_{13}C_{17}C_{18}$	127.10	127.12	124.91	125.16
∠$C_{12}C_{13}C_{17}C_{14}$	-114.10	-114.21	-116.48	-116.43
∠$C_8C_{14}C_{15}C_{13}$	-129.94	-129.89	128.30	128.33
∠$C_{13}C_{17}C_{16}C_{20}$	-131.40	-130.95	133.19	134.13
∠$C_{17}C_{20}C_{22}C_{21}$	125.89	-124.07	128.07	124.99

Angular ("angular") methyl groups at C_{10} and C_{13} atoms and a side chain at C_{17} consisting of eight carbon atoms are attached to the ring system of cholestanes **1**–**4**. The side chain and two angular methyl groups are located above the plane in the molecules of cholestanes, and β-orientation is attributed to them. The hydrogen atom at C_8 also has a β orientation. Hydrogen atoms at C_9 and C_{14} are α-oriented. In cyclohexane rings, hydrogen atoms attached to adjacent carbon atoms are removed from each other at a distance of 2.46-2.48 Å, which indicates the stable position of cyclohexane rings in the chair conformation.

As can be seen, from the calculated values of the torsion angles of cholestanes **1**–**4** and hopanes **5**–**10**, the junction of the A/B, B/C and C/D cycles is in the trans configuration (118.37°-129.94°). Eight carbon atoms form a zigzag chain, the hydrogen atoms of the individual units are maximally distant from each other, the methyl group at the C_{20} atom is removed from the angular methyl group at C_{13}, and it follows that repulsions between the hydrogen atoms are minimized. This conformation is the most stable (Fig. 2).

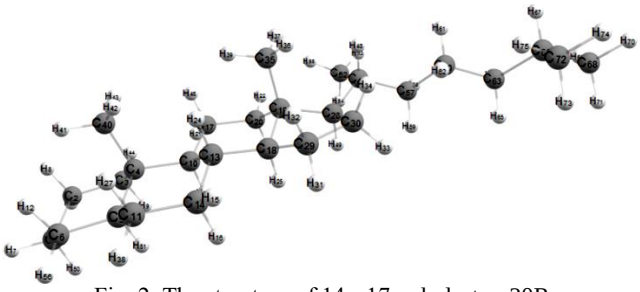


Fig. 2. The structure of 14α-17α-cholestan-20R
Рис. 2. Структура 14α-17α-холестана-20R

The studied molecules possess a transarticulation of the rings at the 5,10-, 8,9-, and 13,14-positions (in the case of hopanes **5-10**, also at the 17,18-position). The bonds in the molecules that form the rings are slightly distorted, and the rings themselves are not flat. The bonds C_9-C_{10} and C_8-C_{14} (and C_{13}-C_{18} in the case of hopanes) connecting the two cycles have an anti-configuration. It has been shown that pairs of carbon atoms C_2 and C_3, C_{10} and C_5, C_8 and C_7 are in the same plane, and carbon atoms C_1, C_9, C_{14}, C_{13} and C_{11} are located in another plane parallel to the first and 0.84 away from it Å. In hopanes (**5-10**), the bond lengths between the carbons in the cycles remain unchanged, in addition to the E ring, where the radical fragment at the C_{21} atom affects the bond lengths and energies. In cholestanes, the bond

lengths are distorted depending on the location relative to the plane of the hydrogen atoms at C_{14} and C_{17}, as well as the influence of the position of the radical fragment. For example, in the case of the α-position of hydrogen atoms at C_{14} and C_{17}, the C_{14}-C_{15} bond is significantly shortened to 1.535-1.537 Å and a significant increase in the C_{11}-C_{12} bond to 1.543-1.644 is observed.

Table 2

The geometric characteristics of hopanes calculated by the B3LYP/6-311+G(d,p) method

***Таблица 2.* Геометрические характеристики гопанов, рассчитанные методом B3LYP/6-311+G(d,p)**

Parameters	Compounds					
	5	***6***	***7***	***8***	***9***	***10***
C_1–C_2	1.535	1.535	1.535	1.535	1.535	1.535
C_2–C_3	1.530	1.530	1.530	1.530	1.530	1.530
C_3–C_4	1.550	1.550	1.550	1.549	1.550	1.550
C_4–C_5	1.571	1.570	1.570	1.570	1.570	1.570
C_4–C_{23}	1.545	1.544	1.544	1.545	1.544	1.544
C_4–C_{24}	1.547	1.547	1.547	1.547	1.547	1.547
C_5–C_6	1.537	1.537	1.537	1.537	1.537	1.537
C_6–C_7	1.536	1.536	1.536	1.536	1.536	1.536
C_7–C_8	1.553	1.554	1.554	1.553	1.554	1.554
C_8–C_9	1.576	1.577	1.576	1.577	1.576	1.577
C_8–C_{26}	1.555	1.555	1.555	1.555	1.555	1.556
C_8–C_{14}	1.618	1.618	1.618	1.617	1.617	1.618
C_9–C_{10}	1.585	1.586	1.585	1.585	1.585	1.585
C_{10}–C_1	1.556	1.556	1.556	1.556	1.556	1.556
C_{10}–C_{25}	1.551	1.551	1.551	1.550	1.551	1.551
C_9–C_{11}	1.546	1.546	1.546	1.546	1.546	1.546
C_{11}–C_{12}	1.540	1.539	1.540	1.540	1.540	1.539
C_{12}–C_{13}	1.539	1.538	1.539	1.539	1.539	1.538
C_{13}–C_{18}	1.561	1.560	1.560	1.560	1.560	1.557
C_{13}–C_{14}	1.574	1.578	1.575	1.575	1.575	1.578
C_{14}–C_{15}	1.559	1.562	1.558	1.559	1.558	1.563
C_{14}–C_{27}	1.557	1.557	1.558	1.555	1.558	1.558
C_{15}–C_{16}	1.545	1.545	1.545	1.545	1.545	1.545
C_{16}–C_{17}	1.529	1.525	1.530	1.529	1.530	1.523
C_{17}–C_{18}	1.554	1.551	-	1.554	1.547	1.551
C_{17}–C_{21}	1.567	1.554	1.570	1.569	1.571	1.534
C_{18}–C_{19}	1.549	1.552	1.549	1.549	1.549	1.553
C_{19}–C_{20}	1.548	1.554	1.547	1.548	1.546	1.561
$\angle C_1C_{10}C_9$	108.06	108.16	108.12	108.16	108.08	108.18
$\angle C_4C_5C_6$	114.72	114.65	114.65	114.66	114.68	114.63
$\angle C_{10}C_9C_{11}$	113.97	113.87	113.98	114.04	114.04	113.88
$\angle C_{12}C_{13}C_{18}$	114.41	114.70	114.49	114.43	114.52	114.64
$\angle C_7C_8C_{14}$	110.65	110.71	110.64	110.60	110.59	110.63
$\angle C_8C_{14}C_{15}$	110.84	110.66	110.79	110.81	110.78	110.76
$\angle C_{13}C_{18}C_{17}$	107.89	106.97	107.81	107.90	107.86	107.60
$\angle C_{17}C_{16}C_{15}$	109.34	108.82	109.29	109.27	109.31	109.05
$\angle C_{19}C_{18}C_{17}$	99.37	99.30	99.42	99.34	99.45	99.69
$\angle C_{18}C_{17}C_{21}$	107.16	107.07	107.20	107.17	107.05	104.57
$\angle C_{20}C_{21}C_{17}$	101.99	102.89	102.15	101.98	102.23	103.46
$\angle C_1C_{10}C_9C_{25}$	118.79	118.80	118.80	118.75	118.75	118.77
$\angle C_1C_{10}C_9C_5$	-115.61	-115.65	-115.61	-115.62	-115.65	-115.69
$\angle C_4C_5C_6C_{10}$	-135.41	-135.29	-135.35	-135.50	-135.35	-135.30
$\angle C_9C_8C_{14}C_{15}$	-175.50	-175.41	-175.69	-175.56	-175.83	-175.34
$\angle C_{10}C_9C_8C_{11}$	-132.68	-132.58	-132.70	-132.80	-132.78	-132.58
$\angle C_{12}C_{13}C_{18}C_{14}$	-130.98	-130.91	-130.95	-131.01	-130.98	-130.96
$\angle C_8C_{14}C_{15}C_{13}$	-118.37	-118.62	-118.47	-118.38	-118.49	-118.50
$\angle C_9C_8C_{14}C_{26}$	122.12	122.12	122.17	122.18	-122.16	122.18
$\angle C_9C_8C_{14}C_7$	-120.31	-120.25	-120.27	-120.31	-120.32	-120.23
$\angle C_8C_{14}C_{15}C_{13}$	-118.37	-118.62	-118.47	-118.38	-118.49	-118.50
$\angle C_8C_{14}C_{15}C_{27}$	120.53	120.25	120.42	120.47	120.37	120.28
$\angle C_{13}C_{18}C_{17}C_{28}$	127.46	127.06	127.34	127.41	127.24	127.31
$\angle C_{13}C_{18}C_{19}C_{17}$	114.11	113.41	114.10	114.12	114.25	114.42

The studied structures are similar in structure with steroid hormones [18] and betulin (betulin derivatives) (Fig. 3), which also belong to the lupane series triterpenes [19-24].

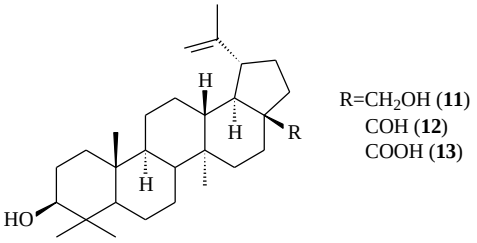


Fig. 3. The structure of betulin and its derivatives
Рис. 3. Структура бетулина и его производных

Table 3 shows the energy characteristics of the studied structures in comparison with the values of betulin and its derivatives. It has been established that betulin and its derivatives have a number of antibacterial and antimicrobial activities [19, 20].

The dependence of antimicrobial and antibacterial activity on the energy of the boundary molecular orbitals of betulin molecules and its derivatives **11-13** was studied. The dependence of the biological activity of betulin and its derivatives on their values of ionization potentials and electron affinity has been established.

Based on the results and comparing the values of the boundary orbitals with the orbits of the biomarkers, it can be assumed that the biomarkers of Naftalan oil, which have a similar structure with betulin derivatives, are also able to exhibit biological activity.

Table 3.
Energy parameters of the studied molecules and betulin derivatives calculated by the B3LYP/6-311+G(d,p) method
***Таблица 3.* Энергетические параметры исследуемых молекул и производных бетулина, рассчитанные методом B3LYP/6-311+G(d,p)**

Compound	$-E_{HOMO}$, eV	E_{LUMO}, eV	Δε, eV
1	7.094	-0.024	7.070
2	7.102	-0.046	7.56
3	7.151	-0.060	7.91
4	7.151	-0.063	7.88
5	6.961	-0.101	6.86
6	6.969	-0.101	6.868
7	6.955	-0.112	6.843
8	6.955	-0.106	6.849
9	6.953	-0.117	6.836
10	6.982	-0.095	6.887
11	6.550	-0.294	6.256
12	6.759	-0.909	5.85
13	6.651	-0.261	6.39

CONCLUSIONS

Quantum-chemical studies have made it possible to establish the structure of the biomarkers of Naftalan oil containing quad-cyclopentanoperhydrophenanthrene systems. It was found that the geometric shape of the studied biomarkers is stable and is determined by the conformation of the rings that are located in the trans-conformation. The compounds under study are similar in structure to betulin derivatives and may possibly exhibit biological activity.

The reported study was funded by RFBR according to the research project № 19-29-074071/19.

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Поступила в редакцию (Received) 05.02.2020
Принята к опубликованию (Accepted) 07.05.2020