PREDICTION OF BIOLOGICAL ACTIVITY AND TOXICITY OF 2-DIALKOXYPHOSPHORYL-1,4-DIHYDROBENZODIAZINES

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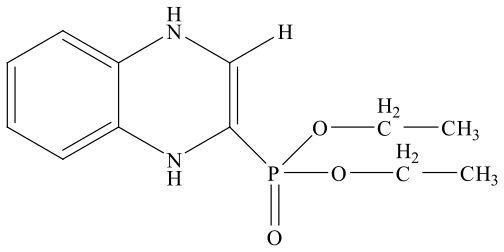
The biological activity of 2-dialkoxyphosphoryl-1,4-dihydrobenzodiazines was analyzed by PASS (Prediction of Activity Spectra for Substances) and toxicity by GUSAR (General Unrestricted Structure-Activity Relationships)

Getting these compounds:

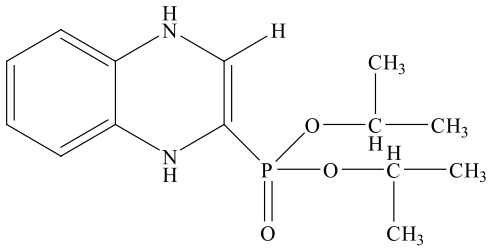
2-Diethoxyphosphoryl-1,4-dihydrobenzodiazine Hydrochloride 1(a). A solution of aldehyde 1a (0.86 g, 4 mmol) in ether (5 ml) was added with stirring to a solution of o-phenylenediamine (0.43 g, 4 mmol) in ether (20 ml) at 0 °C. The reaction mixture was stirred with cooling for 1 h and at room temperature for 2 h. The precipitate of 1(a) was filtered off and recrystallized from ethanol- acetonitrile to give 1.03 g (84%).

2-Diisopropoxyphosphoryl-1,4-dihydrobenzodiazine Hydrochloride 1(b) was obtained analogously in 87%.

To determine the potential biological activity, the PASS program was chosen, which is based on an analysis of the structure-activity dependencies. The forecast results are presented to the user in the form of a list of names of probable types of activity with calculated estimates of the probabilities of presence (Pa) and absence of each type of activity (Pi), which have values from 0 to 1. Pa and Pi are presented as estimates of the measure of membership of the substance in the classes of active and inactive compounds respectively. The larger the Pa value for a specific activity and the smaller the Pi value, the greater the chance of detecting this activity in the experiment. Predictions of the biological activity of the compounds are shown in table 1.



1(a)



1(b)

Table 1

Prediction of biological activity according to the results of the PASS program

1(a)

№	Pa	Pi	Activity
1	0,877	0,004	Antihypertensive
2	0,772	0,018	2-Alpha-N-acetylglucosaminyl transferase inhibitor
3	0,714	0,009	Cutinase Inhibitor
4	0,742	0,051	Aspulvinone Dimethylallyl Transferase Inhibitor
5	0,695	0,012	Acetyl esterase inhibitor
6	0,681	0,023	Pseudolysin Inhibitor
7	0,671	0,039	Sugar phosphatase inhibitor
8	0,662	0,031	5-O- (4-coumaroyl) -D-quinate 3'-monooxygenase inhibitor
9	0,655	0,029	Dehydro-L-Gulonate Decarboxylase Inhibitor
10	0,633	0,022	Thioredoxin Inhibitor

1(b)

№	Pa	Pi	Activity
1	0,918	0,004	Antihypertensive
2	0,866	0,004	Dehydro-L-Gulonate Decarboxylase Inhibitor
3	0,824	0,005	Supplement Factor D Inhibitor
4	0,822	0,007	Glutamyl Endopeptidase II Inhibitor
5	0,804	0,005	IgA-specific serine endopeptidase inhibitor
6	0,798	0,012	Feruloyl Esterase Inhibitor
7	0,764	0,004	Endopeptidase So Inhibitor
8	0,760	0,004	General pump inhibitor
9	0,746	0,010	2-hydroxy-muconate-semi-aldehyde hydrolase inhibitor
10	0,741	0,009	Acetyl esterase inhibitor

Table 2

Prediction of acute toxicity in rats using the GUSAR software product

1(a)

Rat IP LD50 Log10(mmol/kg)	Rat IV LD50 log10(mmol/kg)	Rat Oral LD50 log10(mmol/kg)	Rat SC LD50 log10(mmol/kg)
0,010 in AD	-0,886 in AD	0,185 in AD	0,037 in AD
Rat IP LD50 (mg/kg)	Rat IV LD50 (mg/kg)	Rat Oral LD50 (mg/kg)	Rat SC LD50 (mg/kg)
274,600 in AD	34,850 in AD	411,200 in AD	292,100 in AD

1(b)

Rat IP LD50 Log10(mmol/kg)	Rat IV LD50 log10(mmol/kg)	Rat Oral LD50 log10(mmol/kg)	Rat SC LD50 log10(mmol/kg)
-0,075 in AD	-0,967 in AD	0,450 in AD	-0,032 in AD
Rat IP LD50 (mg/kg)	Rat IV LD50 (mg/kg)	Rat Oral LD50 (mg/kg)	Rat SC LD50 (mg/kg)
249,300 in AD	31,960 in AD	834,300 in AD	275,200 in AD

Table 3

Acute classification of rodent toxicity by chemicals under the OECD project using the GUSAR software product

1(a)

Rat IP LD50 Classification	Rat IV LD50 Classification	Rat Oral LD50 Classification	Rat SC LD50 Classification
Class 4 in AD	Class 3 in AD	Class 4 in AD	Class 4 in AD

1(b)

Rat IP LD50 Classification	Rat IV LD50 Classification	Rat Oral LD50 Classification	Rat SC LD50 Classification
Class 4 in AD	Class 3 in AD	Class 4 in AD	Class 4 in AD

As can be seen from table 1, we can say that both compounds exhibit different inhibitory ability.

Next, a forecast of acute toxicity of the test compound was carried out using the software product GUSAR (General Unrestricted Structure-Activity Relationships) presented in tables 2 and 3.

From table 3 we can conclude that the toxicity of both compounds is low, 3-4 hazard class.

Thus, the results obtained in predicting biological activity using the PASS program and the toxicity of the studied compounds using the GUSAR software product allow us to conclude that compound 1 (b) is more active than 1 (a), and the toxicity of both compounds is equal. Therefore, compound 1 (b) has a higher potential activity, and this compound can be prospectively used for further laboratory studies.

References

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2. Huseynov F.I., Asadov H.A., Burangulova R.N. Moscow, Chemistry of Heterocyclic Compounds, 2001, Volume 37, No. 8, p. 1044.

МЕТОДЫ ЗАЩИТЫ ПОЛИМЕРНЫХ МАТЕРИАЛОВ ОТ СТАРЕНИЯ

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Конструкции на основе полимерных материалов стали неотъемлемой частью современной промышленности. Химические и физические свойства высокомолекулярных соединений способствуют их повсеместному использованию [1]. В рамках эксплуатации полимерных материалов требуемый срок службы может составлять несколько десятков лет. Потому исследование способов защиты полимерных материалов от старения является актуальным направлением химической науки.

Цель работы: знакомство с различными методами защиты полимерных материалов от старения.

Старение полимеров – это совокупность физических и химических превращений, происходящих при переработке, хранении и эксплуатации полимерного материала и приводящих к потере им комплекса необходимых свойств. Данный процесс сопровождается нарушением структуры и строения макромолекул. Деструкция – процесс разрушения полимера с разрывом связей макромолекул. Структурирование – процесс образования макромолекул из образовавшихся в результате деструкции осколков [2].

Основные причины, влияющие на разрушение полимерных материалов, – это окисление и биологическое воздействие.

Окисление и биологическое старение полимеров. Химическое взаимодействие полимера с кислородом, приводящее к его окислению, играет большую роль в процессе старения полимерного материала. Важнейшими факторами, влияющими на скорость окисления, являются