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Synthesis, Characterization and Prediction of Biological Activity of Anthrone Schiff Bases Using Pass

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Abstract

The computer system PASS provides simultaneous prediction of several hundreds of biological activity types of any drug like compounds. In this study the PASS (Prediction of activity spectra for substances) computer program, which is able to simultaneously predict more than one thousand biological and toxicological activities from only the structural formulae of the chemicals, was used to predict the biological activity of schiff base of anthrone were synthesized using p-aminobenzoic acid, o-phenylenediamine, p-phenylenediamine, 3-nitroaniline and 4-nitroaniline with Anthrone. The characterization and nature of bonding have been deduced from UV-Visible, FT-IR and ^{1}H-NMR spectral studies.

Keywords: Anthrone, schiff bases, Marvin Sketch, PASS.

Contents

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1. Introduction

Schiff bases are also known to have biological activities such as antimicrobial, antifungal, antitumor, and as herbicides (1). It was well known that many compounds containing anthraquinone skeleton have good bioactivities. Some of them are good antitumor medicines such as daunorubicin, doxorubicin, mitoxantrone, bisantrene and so on. 10-substituted benzylidene anthrone and the schiff base of anthrone with substituted anilines also have good antitumor activities **(**2). 5-[1-(anthracen-9(10H)-ylideneamino)-2-(1H-imidazol-5-yl) ethyl]-1,3,4-thiadiazol-2-amine has good activity to *Gibberela*, *Cercospora arachidicola*, *Physolospora piricola* and *Fusarium oxysporum* (3). Schiff base of anthrone have antimicrobial activity against one strain of Gram +ve bacteria *Staphylococcus aureus*, Gram –ve bacteria *Escherichia coli* and a fungus *Candida albicans*(4). Aminobenzanthrone schiff base has been utilized as a fluorescent carrier in the preparation of an optical sensor for iodine (5). We are interested to synthesis five different schiff bases of anthrone and predict biological activity using an online software PASS. PASS is a software product designed as a tool for evaluating the general biological potential of an organic drug-like molecule. PASS provides simultaneous predictions of many types of biological activity based on the structure of organic compounds. It can predict more than 1500 pharmacological effects, molecular mechanism of action, and toxicities on basis of structural descriptors of compounds. Thus, PASS can be used to estimate the biological activity profiles for virtual molecules, prior to their chemical synthesis and biological testing.

Pa (probability to be active) estimates the chance that the studied compound is belonging to the sub-class of active compounds resembles the structures of molecules, which are the most typical in a sub-set of actives in PASS training set. **Pi** (probability to be inactive) estimates the chance that the studied compound is belonging to the sub-class of inactive compounds resembles the structures of molecules, which are the most typical in a sub-set of inactive in PASS training set(6). If Pa>0.7, the substance is very likely to exhibit the activity in experiment, but the change of the substance being the analogue of a known pharmaceutical agent is also high. If 0.5<Pa<0.7, the substance is likely to exhibit the activity in experiment, but the probability is less, and the substance is unlike known pharmaceutical agents. If Pa<0.5, the substance is unlikely to exhibit the activity in experiment. However, if the presence of this activity is confirmed in the experiment the substance might be a new chemical entity (7)

2. Materials and Methods

All chemicals used in the present work were of analytical reagent (A.R.) grade. The melting points were determined by open capillary tube method. The electronic spectra of schiff base in methanol were recorded in the range of 200nm-800nm on the Shimadzu spectrophotometer. FT-IR spectra of schiff bases were recorded using KBr discs in the range of 400-4000cm^{-1} on a Shimadzu spectrophotometer. ^{1}H-NMR spectra of schiff bases were recorded in the range of 400MHz on a Shimadzu spectrophotometer.

Synthesis of Ligand

A mixture of anthrone (0.001mol) and active amines (p-aminobenzoicacid, o-phenylenediamine, 3-nitroaniline, 4-nitroaniline and p-phenylenediamine) (0.001mol) were dissolved in an absolute ethanol, to which 2-3 drops of glacial acetic acid were added and the mixture was refluxed for 2 hours. After evaporating the solvent to one third of its volume a solid product was obtained. The product was filtered off and recrystallized from ethanol.

PASS Prediction

The possible bioactivities of all the molecules were predicted with PASS software (V. Poroikov et al, version 1.917). Opening the PASS online software the window appeared as given in Fig.1.

Fig.1. PASS Prediction Window

The bioactivity result of the synthesized compound appears on the new window as given in Fig.2.

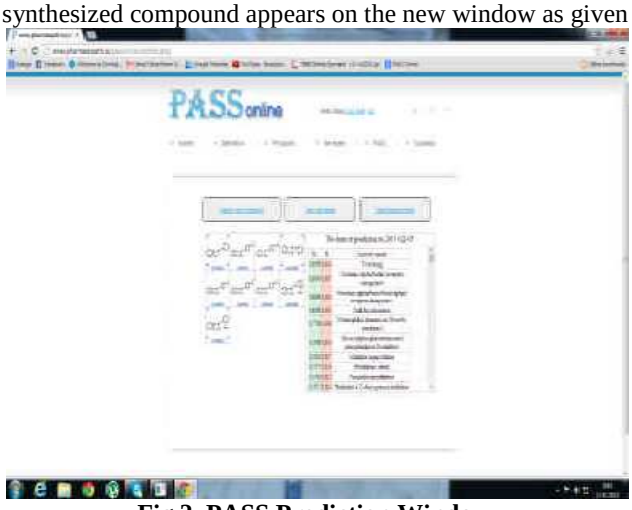


Fig.2. PASS Prediction Window

3. Result and Discussion

Table 1. Physical characteristics of the schiff Bases

S.No.	Ligand	Molecular Formula	Colour	%Yield	Melting Point(◦C)
1.	A	$C_{21}H_{15}NO_2$	Yellow	85	210-215
2.	B	$C_{20}H_{16}N_2$	Brown	65	215
3.	C	$C_{20}H_{14}N_2O_2$	Yellow	55	170
4.	D	$C_{20}H_{14}N_2O_2$	Yellow	70	180
5.	E	$C_{20}H_{16}N_2$	Purple	80	200

Table 2. Important IR Spectral frequencies of Anthrone schiff bases

S.No	Ligand	ν_{-OH} (cm^{-1})	$\nu_{-C=N}$ (cm^{-1})	$\nu_{-C=O}$ (cm^{-1})	ν_{-NH2} (cm^{-1})
1.	A	3350	1600	1670	-
2.	B	3350	1620	1616	3325
3.	C	3350	1615	1624	-
4.	D	3350	1581	1636	-
5.	E	3350	1604	1642	3370

Table 3. Important ^{1}H-NMR values of Anthrone schiff bases

S.No.	Ligand	1H-NMR(δ,ppm)
1.	A	Anthrone nucleus signals at 7.83, 7.48, 7.44, 7.23and 4.29. Aromatic nucleus at 7.83,6.96,6.96 and 7.83
2.	B	Anthrone nucleus signals at 7.83, 7.48, 7.44, 7.23and 4.29. Aromatic nucleus at 7.11,6.98,6.81 and 7.27
3.	C	Anthrone nucleus signals at 7.83, 7.48, 7.44, 7.23and 4.29. Aromatic nucleus at 7.72,7.41,6.65 and 7.69
4.	D	Anthrone nucleus signals at 7.83, 7.48, 7.44, 7.23and 4.29. Aromatic nucleus at 8.09,6.95,6.95 and 8.09
5.	E	Anthrone nucleus signals at 7.83, 7.48, 7.44, 7.23and 4.29. Aromatic nucleus at 6.85,6.85,6.98 and 6.98

Table 4. PASS prediction activities for 4-[(9, 10-dihydroanthracen-9-ylidene) amino]benzoic Acid

Pa	Pi	Activity
0,900	0,003	Pullulanase inhibitor
0,888	0,002	Arylalkyl acylamidase inhibitor
0,888	0,002	Sulfite oxidase inhibitor
0,887	0,004	Dehydro-L-gulonate decarboxylase inhibitor
0,886	0,008	Testosterone 17beta-dehydrogenase (NADP+) inhibitor
0,882	0,004	Glucan endo-1,6-beta-glucosidase inhibitor
0,880	0,003	Creatininase inhibitor
0,881	0,004	Prolyl aminopeptidase inhibitor
0,879	0,004	Taurine dehydrogenase inhibitor
0,876	0,003	3-Hydroxybenzoate 6-monooxygenase inhibitor
0,872	0,004	Glutathione thiolesterase inhibitor
0,864	0,003	L-glutamate oxidase inhibitor
0,858	0,003	Corticosteroid side-chain-isomerase inhibitor
0,858	0,004	5-O-(4-coumaroyl)-D-quinate 3'-monooxygenase inhibitor
0,863	0,010	Methylenetetrahydrofolate reductase (NADPH) inhibitor

0,856	0,003	Aldehyde dehydrogenase (pyrroloquinoline-quinone) inhibitor
0,860	0,008	Sugar-phosphatase inhibitor
0,850	0,004	Ribulose-phosphate 3-epimerase inhibitor
0,849	0,005	Glutamyl endopeptidase II inhibitor
0,848	0,003	Aspartate-phenylpyruvate transaminase inhibitor
0,846	0,004	N-benzyloxycarbonylglycine hydrolase inhibitor

Table 5. PASS prediction activities for 1-N-(9,10-dihydroanthracen-9-ylidene)benzene-1,2-Diamine

Pa	Pi	Activity
0,761	0,004	General pump inhibitor
0,725	0,019	Lysase inhibitor
0,703	0,004	Albendazole monooxygenase inhibitor
0,740	0,058	Phobic disorders treatment
0,702	0,024	Glucose oxidase inhibitor
0,709	0,032	Nicotinic alpha6beta3beta4alpha5 receptor antagonist

Table 6. PASS prediction activities for N-(3-nitrophenyl)-9,10-dihydroanthracen-9-imine

Pa	Pi	Activity
0,885	0,008	Ubiquinol-cytochrome-c reductase inhibitor
0,849	0,005	Glucan endo-1,6-beta-glucosidase inhibitor
0,819	0,005	Bisphosphoglycerate phosphatase inhibitor
0,812	0,006	Superoxide dismutase inhibitor
0,820	0,016	Acrocylindropepsin inhibitor
0,820	0,016	Chymosin inhibitor
0,820	0,016	Saccharopepsin inhibitor
0,802	0,004	Arylalkyl acylamidase inhibitor
0,782	0,005	L-glutamate oxidase inhibitor
0,784	0,009	Fusarinine-C ornithinesterase inhibitor
0,772	0,005	Poly(alpha-L-guluronate) lyase inhibitor
0,770	0,004	(R)-6-hydroxynicotine oxidase inhibitor
0,767	0,004	N-hydroxyarylamine O-acetyltransferase inhibitor
0,763	0,003	Salicylate 1-monooxygenase inhibitor
0,748	0,004	UGT2B12 substrate
0,755	0,015	GST A substrate
0,747	0,008	Cutinase inhibitor
0,727	0,004	Hyponitrite reductase inhibitor
0,737	0,017	Lysase inhibitor
0,747	0,029	Polyporopepsin inhibitor
0,719	0,005	Alkylglycerone-phosphate synthase inhibitor
0,723	0,009	Phosphatidylserine decarboxylase inhibitor
0,720	0,011	Phospholipid-translocating ATPase inhibitor

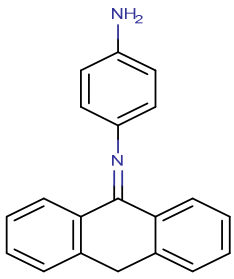
Table 7. PASS prediction activities for N (4nitrophenyl) 9, 10dihydroanthracen 9 imine

Pa	Pi	Activity
0,869	0,004	Glucan endo-1,6-beta-glucosidase inhibitor
0,870	0,011	Ubiquinol-cytochrome-c reductase inhibitor
0,840	0,013	Acrocylindropepsin inhibitor
0,840	0,013	Chymosin inhibitor
0,840	0,013	Saccharopepsin inhibitor
0,830	0,004	Arylalkyl acylamidase inhibitor
0,805	0,003	N-hydroxyarylamine O-acetyltransferase inhibitor
0,805	0,004	L-glutamate oxidase inhibitor
0,805	0,007	Fusarinine-C ornithinesterase inhibitor
0,794	0,007	Bisphosphoglycerate phosphatase inhibitor
0,790	0,004	(R)-6-hydroxynicotine oxidase inhibitor
0,782	0,006	Cutinase inhibitor
0,769	0,004	UGT2B12 substrate
0,767	0,009	Superoxide dismutase inhibitor
0,769	0,013	Lysase inhibitor
0,777	0,024	Polyporopepsin inhibitor
0,757	0,004	Hyponitrite reductase inhibitor
0,748	0,008	Phospholipid-translocating ATPase inhibitor
0,739	0,003	Salicylate 1-monooxygenase inhibitor
0,737	0,007	Poly(alpha-L-guluronate) lyase inhibitor
0,730	0,007	Spermidine dehydrogenase inhibitor
0,726	0,004	Bothrolysin inhibitor
0,725	0,005	Aldehyde dehydrogenase (pyrroloquinoline-quinone) inhibitor

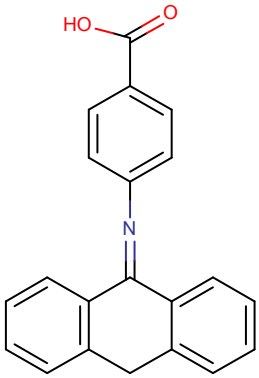
Table 8. PASS prediction activities for 1- N (9, 10-dihydroanthracen 9 ylidene)benzene -1,4 diamine

Pa	Pi	Activity
0,784	0,011	Lysase inhibitor
0,732	0,004	N-hydroxyarylamine O-acetyltransferase inhibitor
0,703	0,004	Albendazole monooxygenase inhibitor
0,703	0,007	Cholestanetriol 26-monooxygenase inhibitor
0,740	0,058	Phobic disorders treatment
0,702	0,024	Glucose oxidase inhibitor
0,709	0,032	Nicotinic alpha6beta3beta4alpha5 receptor antagonist

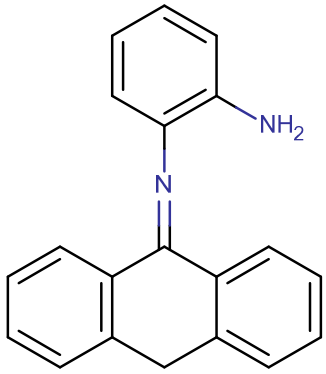
Discussion:



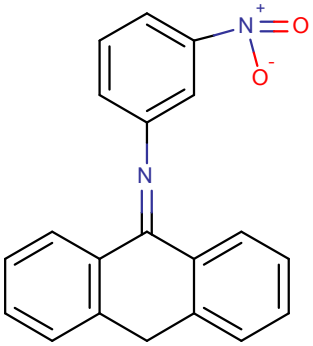
1-N(9,10 dihydroanthracen 9 ylidene)benzene1,4 diamine



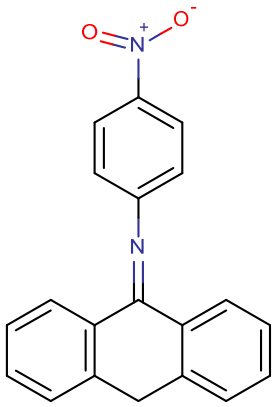
4[(9,10-dihydroanthracen-9-ylidene) Diamine



1N(9,10dihydroanthracen-9-ylidene)benzene1,2amino]benzoicAcid



N-(3-nitrophenyl)-9,10-dihydro



N(4-nitrophenyl)-9,10-dihydroanthracen-9-imineanthracen-9-imine

Table 1, 2 and 3 shows the UV-Visible, IR and NMR spectral values of the newly synthesized Anthrone schiff bases. From those spectral studies the schiff bases may have the following structures.Table 4, 5,6,7,8 shows the activities of Anthrone schiff bases having Pa> 0.7. From that the following activity is common to all schiff bases, Lysase inhibitor, Albendazole monooxygenase inhibitor, cholestanetriol 26-monooxygenase inhibitor, Phobic disorders treatment, Glucose oxidase inhibitor, Pullulanase inhibitor, General pump inhibitor, Glucan endo-1,6-beta-glucosidase inhibitor, Ubiquinol-cytochrome-c reductase inhibitor and Superoxide dismutase inhibitor.

4. Conclusion

From the literature, Anthrone moiety has more biological activity. UV, IR, NMR spectral studies revealed the structure of the schiff bases.4-[(9,10-dihydroanthracen-9-ylidene)amino]benzoicacid has shown 90% of Pullulanase inhibitor, 1 -N-(9, 10-dihydroanthracen-9-ylidene) benzene -1,2-Diamine shows 76% of General pump inhibitor, N-(3-nitrophenyl) -9,10-dihydroanthracen-9-imine has 88.5% of Ubiquinol-cytochrome-c reductase inhibitor, N-(4□nitrophenyl)-9, 10-dihydroanthracen-9-imine shows 86.9% of Glucan endo-1,6-beta-glucosidase inhibitor, 1-N-(9,10-dihydroanthracen -9-ylidene) benzene-1,4-diamine exhibit 78.4% of Lysase inhibitor.

5. References

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