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1(Heterocyclyl),2,4,5-Tetrasubstituted Benzenes as Protoporphyrinogen-IX Oxidase Inhibiting Herbicides

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1. Introduction

It is well known that agrochemicals have played a important role in agricultural production that provided for about 700 million people during the past 50 years. At the same time, the increasing world population seems to be a major driving force for the need to enhance the output of food production. The agrochemical industry has been very successful in developing new herbicides and other agrochemicals. Herbicides are used widely in the world in protecting crops from undue competition from weeds (Price & Kelton, 2011).

The first commercial inhibitor of protoporphyrinogen oxidase (Protox) is the nitrofen that belongs to diphenyl ether (DPE), which was introduced in 1963 by Rohm & Hass (Now Dow AgroSciences) (Matsunaka, 1976). Some years later, the oxadiazon as the fisrt compound of the 1(heterocyclyl), 2, 4, 5-tetrasubstituted benzene (HTSB) family was introduced in 1968 by Rhone-Poulenc (Metivier et al., 1968). Nitrofen and oxadiazon represent the earliest examples of Protox inhibiting herbicides (Fig. 1). Although their chemical structures are completely different from each other, they share a common mode of action, inhibition of the protoporphyrinogen oxidase enzyme, though this was not known until the late 1980s.

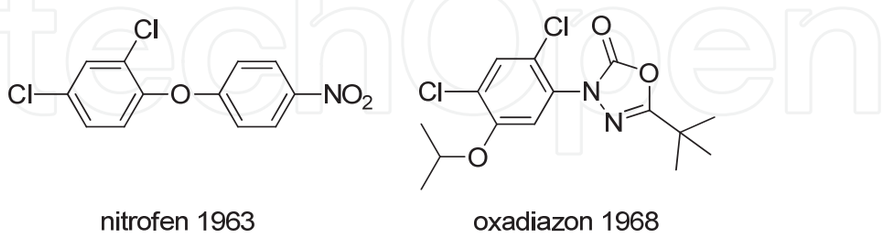


Fig. 1. Chemical structures of two early examples of Protox inhibitors.

Several early inventions of HTSB herbicide in 1960s had a significant impact on our understanding of the structure–activity of this kind herbicides. Rhone-Poulenc first introduced 3-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2(3H)-one in 1965 (Boesch et al., 1965). Further lead optimization at the phenyl ring soon led to the discovery in 1968 of the 2,4-dichloro-5-isopropoxyphenyl substitution pattern of the herbicide oxadiazon

(Boesch et al.,1968). Oxadiazon was the first compound of the cyclic imide family introduced into the markert for the control of annual grasses and broadleaf weeds in pre-emergence or early post-emergence treatment by Rhone-Poulenc in 1969. The second cyclic imide herbicide, chlorophthalim, was introduced by Matsui in 1972. The 2, 4-dihalo-5-substituted pattern at the aromatic ring would become the basis for much of the 2,4,5-trisubstituted phenyl tetrahydrophthalimide research that followed in this area of chemistry.

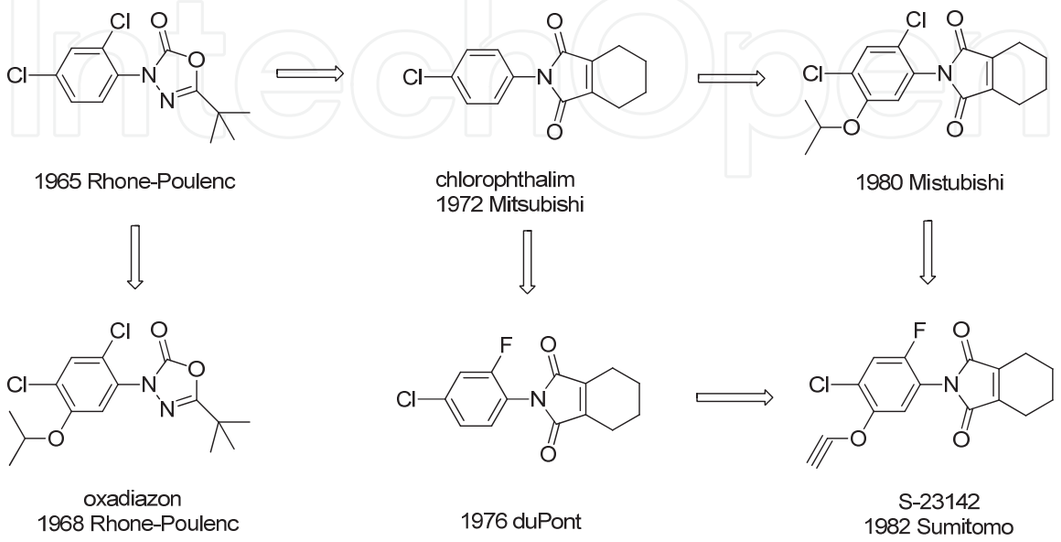


Fig. 2. Incorporation of the 2,4-dihalo-5-alkoxy aromatic pattern of oxadiazon into new phenyl tetrahydrophthalimide ring systems.

A breakthrough discovery was the increasing biological activity caused by the replacement of chlorine by fluorine at the 2-phenyl position. In 1976, DuPont introduced the first example of a 2-fluoro-4-chlorophenyl tetrahydrophthalimide Protox inhibitor (Goddard, 1976) (Fig. 2). The dramatic increase in biological activity caused by the fluorine in the 2 position of the phenyl ring would, in the next decade, the 1980s, influence the lead optimization work in the HTSB area, such as the discovery of the 4-chloro-2-fluorophenyltetrahydrophthalimide herbicide S-23142 (Nagano et al., 1982). Since then, various HTSB derivatives with high herbicidal activity (10-50 g/ha) have been discovered by many companies.

2. Commercialized protoporphyrinogen-IX oxidase inhibiting herbicides

A number of Protox inhibiting compounds have been already commerciallized. Their structures and biological activities are introduced as follows.

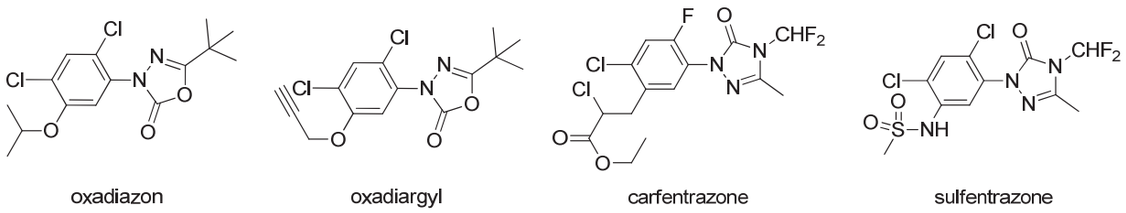
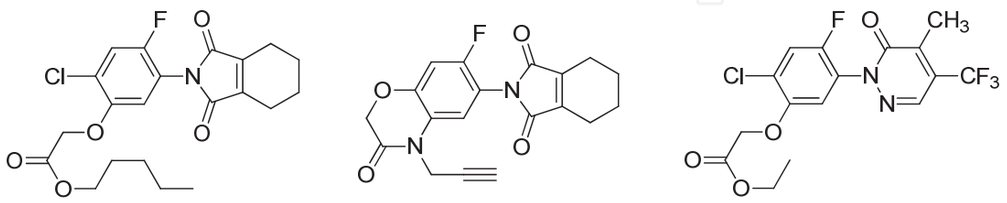


Fig. 3. Chemical structure of oxadiazon, oxadiargyl, carfentrazone, sulfentrazone.

Both oxadiazon and oxdiargyl are developed by Rhone-Poulenc (Fig. 3). Oxadiargyl is a pre-emergence and early post-emergence herbicide in sugarcane and sunflower fields or orchards to control both annual broadleaf and grass weeds. It application rate is rather high at 500-2000 g a. i. /ha. It is also developed as an herbicide for rice and turf.(Oe et al., 1995). FMC developed carfentrazone-ethyl and sulfentrazone. Carfentrazone-ethyl is a post-emergence herbicide in rice, cereals and maize fields. It shows excellent activity against annual broadleaf weeds such as *Gallium*, *Lamium*, and *Veronica* in wheat at 20-35 g a. i./ha. It also controls *Euphorbia*, *Polygogum*, *Abutilon*, *Ipomea*, *Kochia*, *Salsola*, etc. in foliar application (Vansaun et al., 1993; Mize, 1995). Sulfentrazone is a pre-emergence herbicide in soybean and sugarcane fields. It controls *Ipomea*, *Amaranthus*, *Chenopodium*, *Abutilon*, *Polygonum*, *Datura*, etc. at 350-420 g a. i. /ha. (Oliver et al., 1996; Vidrine et al., 1996)



flumiclorac pentyl flumioxazin flufenpyr-ethyl

Fig. 4. Chemical structure of flumiclorac pentyl, flumionazin, flufenpr-ethyl.

The above three herbicides in figure 4 are all developed by Sumitomo. Flumiclorac pentyl was commercialized as the first cyclic imide herbicide in Europe as early as 1993. It controls annual broadleaf weeds such as *Abutilon*, *Euphorbia*, *Chenopodium*, *Datura*, *Ambrosia* and *Xanthium* at 30-60 g a. i. /ha in post- emergence treatment in soybean and maize fields, especilly, it shows excellent activity against *Abutilon at progressed leaf stage at 60* g a. i. /ha (Kurtz & Pawlak, 1992, 1993; Satio et al., 1993). Flumioxazin controls annual broadleaf weeds such as *Abutilon*, *Euphorbia*, *Chenopodium*, *Ipomea* and *Sida* at 50-100 g a. i. /ha in pre-emergence treatment in soybean and peanut fields. But it is less active against annual grass weeds at the same dosage rate.(Yoshida et al., 1991). Flufenpyr-ethyl is commercillized recently as an herbicide in soybean, cotton, corn and sugarcane. It is supposed that it is more selective.

Pentoxazone was discovered by Sagami Chemical Research Center and Kaken Pharmaceutical as a pre-emergence and early post-emergence herbicide in rice (Fig. 5.). It shows excellent activity against both annual and perennial weeds such as *Echinochloa*, *Eleochairs*, *Sagittaria* and *Cyperus* at 145-150 g a. i. /ha (Yoshimura et al., 1992; Hirai et al., 1995). Pyraflufen-ethyl was developed by Nichino, It shows excellent selectivity for winter cereals at the extremely low rates of 6 to 12 g /ha, and also long-term residual activity brought out by chemical and biological stabilities , as a post-emergent contact herbicide active on broadleaf weeds such as cleavers, henbit, clickweeds and wild chamomile; especially provided effective control of 5- to 6-leaf stage of cleavers at the low rate. Azafenidin is developed by Du Pont as a non-selective pre- and post-emergence herbicide for non-cropland and orchard. It has wide herbicidal spectra and controls both annual and perennial weeds at 560 g a. i. /ha (Netzer et al., 1996). Saflufenacil was developed by BASF as an herbicide which is used alone or in mixtures with glyphosate for burn down weed

control, with foliar and residual activity against more than 70 broadleaf weeds, introduced in Nicaragua, Chile, and Argentina as Heat in 2009.

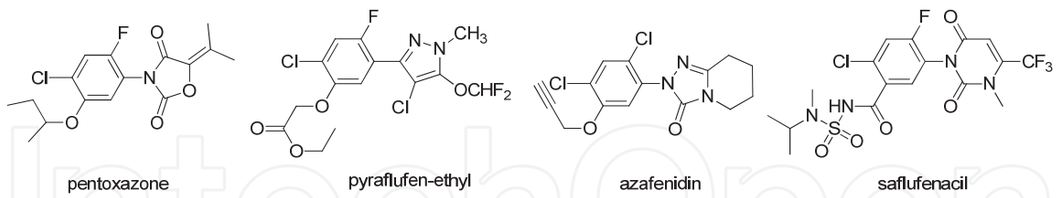


Fig. 5. Chemical structure of pentoxazone, pyraflufen-ethyl, azafenidin, saflufenacil.

3. Mode of action of 1(heterocyclyl),2,4,5-tetrasubstituted benzenes protoporphydrinogen-IX oxidase inhibiting herbicides

The mode of action of 1(heterocyclyl),2,4,5-tetrasubstituted benzenes (HTSB) protoporphyrinogen oxidase (Protox) inhibiting herbicides has been extensively reviewed (Duke et al., 1990). HTSB herbicides inhibit the enzyme Protox in the chlorophyll biosynthesis pathwy (Matringe & Scalla, 1988; Witkowski & Halling, 1988; Lydon & Duke, 1988). The Protox enzyme catalyzes the oxidation of protoporphyrinogen IX to protoporphyrin IX by molecular oxygen. Inhibiting the Protox enzyme, which is located in the chloroplate envelop, results in an accumulation of the enzyme product protoporphyrinogen IX, but not the substrate, via a complex process that has not been entirely elucidated. Enzymatic oxidation of protoporphyrin IX in the cytoplasm yeilds a significant accumulation of protoporphyrin IX from the location of the chlorophll biosynthesis, sequence in choroplasts. In the presence of light, protoporphyrin IX generates large amounts of singlet oxygen ($^1O_2$), which results in the peroxidation of the unsaturated bonds of fatty acids found in cell membranes (Fig. 6). The end result of this peroxidation process is the loss of membrane integrity and leakage, pigment breakdown, and necrosis of the leaf that results in the death of the plant. This is a relatively fast process, with leaf symptoms such as a flaccid wet appearance observed within hours of plant exposure to the Protox herbicides under sunlight.

4. Structure-activity relationships of 1(heterocyclyl),2,4,5-tetrasubstituted benzenes protoporphydrinogen-IX oxidase inhibiting herbicides

4.1 Overviw of structure-activity relationships of 1(heterocyclyl),2,4,5-tetrasubstituted benzenes protoporphydrinogen-IX oxidase inhibiting herbicides

It is very important to analyze structure-activity data accumulated during past trials when formulating ratinonal structure-activity relationships (SARs). The relationships could be utilized as possible guiding principles for further structure transformation leading to novel peroxided herbicides. The information about (sub)molecular mechanisms of biological action may be extracted from the relationship. The structure-activity of Protox herbicides has been extensively reviewed (Fujita & Nakayama, 1999). Figure 6 shows the SARs of 2-fluoro-4-chloro-5-substituted-phenyl heterocycles (Theodoridis, 1997). SAR studies of 2,4,5-trisubstituted-phenyl heterocycles have shown that position 2 of the phenyl ring required a halogen group for optimum biological activity, with fluorine generating the highest overall activity. Introducing a substituent in position 3 of phenyl ring resulted in dramatic decrease

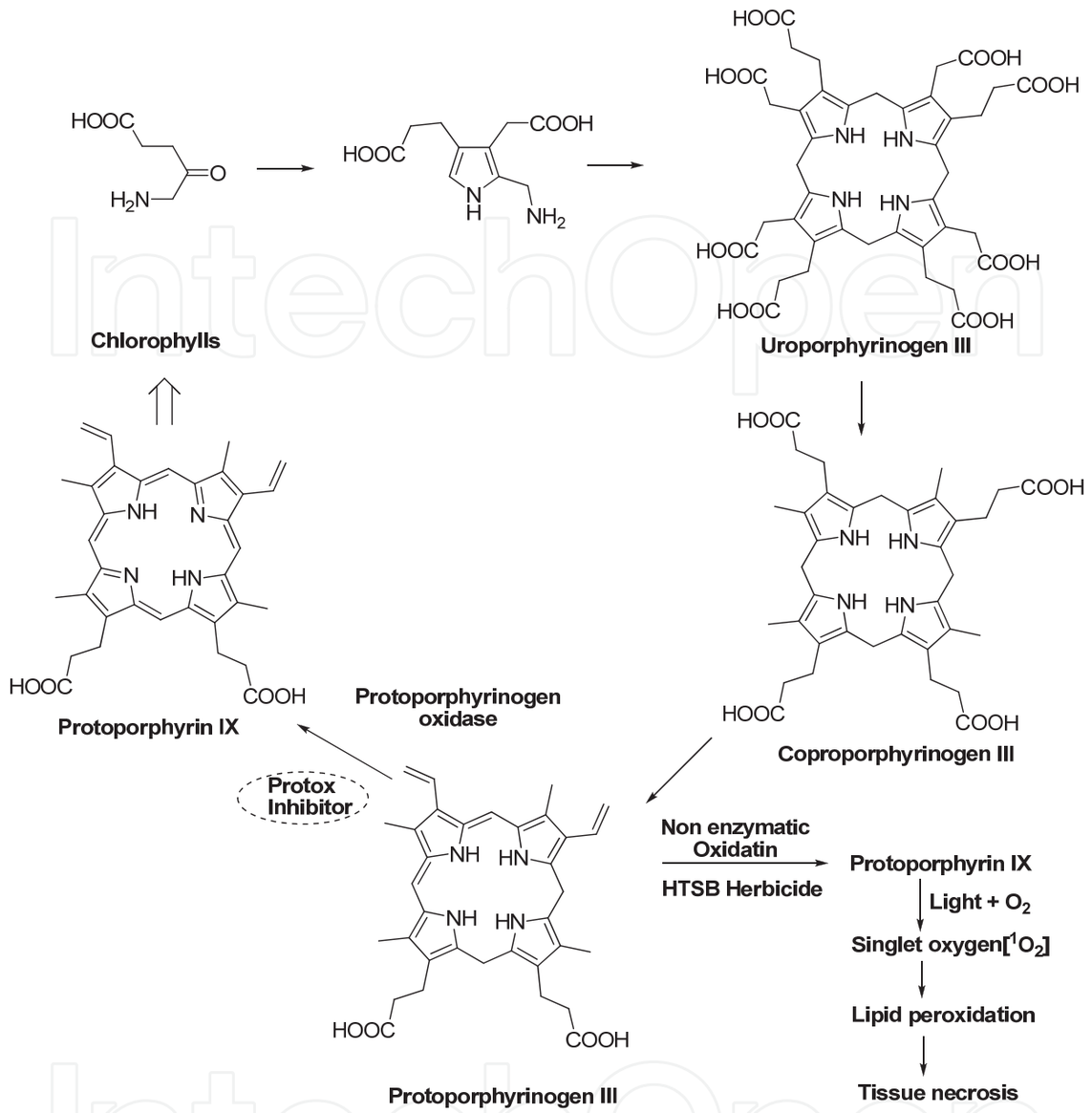


Fig. 6. Chlorophyll biosynthetic pathway.

of herbicidal activity. Position 4 of the phenyl ring required a hydrophobic, electronegative group such as halogen for optimum activity, with chlorine resulting in the best activity. Electron-donating groups such as methoxy resulted in significant loss of biological activity. As shown in Figure 7, the substituent R have a great effect on the bioactivity. Considering herbicidal activity and limited crop selectivity, OCH_2CCH is more favorable than other sunstituents. Considering weed spectrum and multicrop selectivity, R is $NHSO_2Et$ generating the highest overall activity. Many heterocyclic systems, usually attached to aromatic rings via a nitrogen atom, have been introduced in the past fifteen years. Oxadiazolinone (Metivier et al., 1968), oxazolidinedione (Hirai et al., 1989), tetrahydrophthalimide (Matsui et al., 1972), tetrazolinone (Theodoridis et al., 1990), triazolinone (Theodoridis, 1989), pyrimidinedione ring (Wenger, et al., 1988) showed relative higher herbicidal activity than other heterocyclic systems.

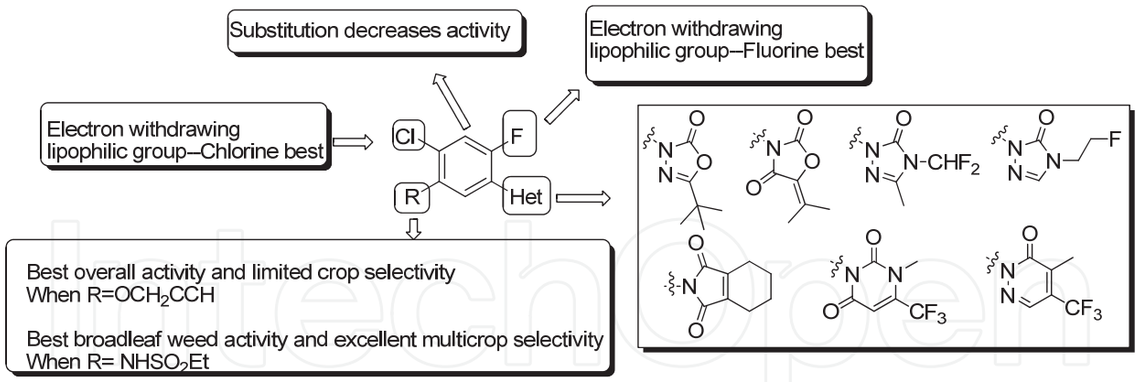


Fig. 7. Structure-activity relationships of the two aromatic rings of 2,4,5-trisubstituted-phenyl heterocyclic systems.

Linking the 4 and 5 positions of phenyl ring to give a new benzoheterocyclic ring, such as benzoxazinone, quinolin-2-one, benzimidazole, resulted in two new classed of Protox herbicides, both increased biological efficacy and new SARs (Fig. 8) (Lyga et al., 1999; , Grawford et al., 1997). As privious studies, position 2 of the phenyl ring required a halogen group for optimum biological activity, with fluorine generating the highest overall activity. The substituent R has a great effect on the herbicidal activity. Introducing propargyl resulted in dramatic increase in the bioactivity.

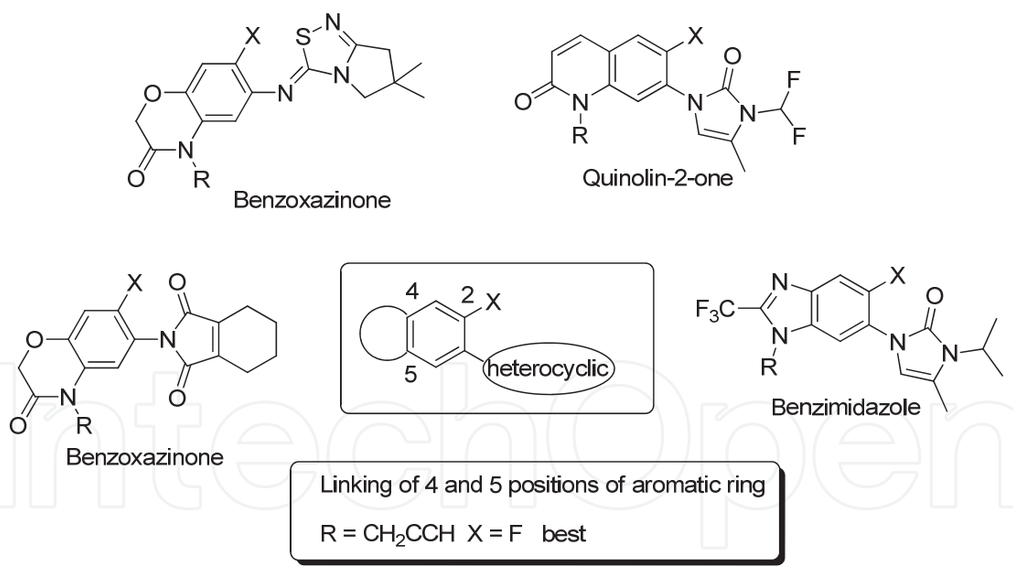


Fig. 8. Structure-activity relationships of benzoheterocycles resulting from linking aromatic positions 4 and 5 of phenyl heterocyclic systerms.

The second class of benzoheteroaryl Protox herbicides are obtained when aromatic positon 5 and 6 are linked togther to form various benzoherocyclic rings, which can be attached to a wide range of heterocycles (Fig. 9). The 6-trifluoromethyl group (R_1=CF_3) in the uracil ring is essential for bioactivity, replacing it with methyl results in complete loss of activity (Thecodoridis et al., 2000 and 1994). Increaseing the size and length of R_2 group resulted in a significant reduction in bioactivity. Substituents X had a dramatic effect on the weed

spectrum and crop selectivity. Compounds with fluoroine and hydrogen resulted in broad-spectrum control of weeds and high herbicidal activity (Lyga et al., 1999).

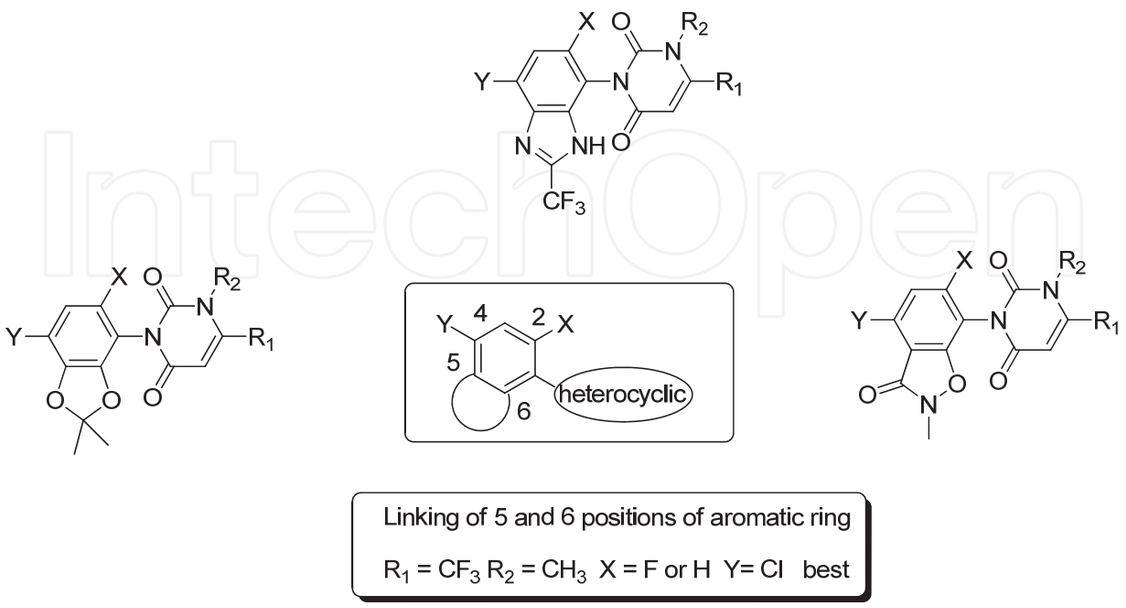


Fig. 9. Structure-activity relationships of benzoheterocycles resulting from linking aromatic positions 5 and 6 of phenyl heterocyclic systerms.

4.2 Pharmacophore analysis

Many molecular modeling studies of ligand binding require some knowledge of the pharmacophore as a starting point. The pharmacophore mode could show the significant structural similarities and identifies the active conformation. The model itself identifies the list of feature classes required and the distances between them. Eight HTSB compounds in table 1 was selected as the testing compounds for the pharmacophore study. A DISCO model of the pharmacophore was developed based on information from X-ray crystal structures of compound I-1 and Sybyl using the Tripos force field. Key pharmacophore elements are a polarizable functionality separated by a fixed distance from two H-bond accepting elements. The compound I-1 was choosed as a reference compound. The crystal data was listed in table 2 and the structure was shown in figure 10. The 3D structures of all the compounds in table 1 were built by SYBYL 6.9/ Sketch, and then optimized using MMFF94 force field, by powell method with energy termination of 0.005 kcal/mol, and a maximum of 1000 iterations. Then, the Gasteiger–Hückel charges were added. Compounds I-1 was selected as the training set and the test set.

As shown in figure 11, the pharmacophore model contains two hydrophobic centers and two acceptor atoms. One hydrophobic center was closed to the 1-heterocyclic ring, which may be interacted with phenylalanine 392 in Protox. Another hydrophobic center, which was in the center of phenyl group, may be interacted with leucine 356 and 372 in Protox. The acceptor atom was oxygen atom located in the carbonyl group and the 5-positon of phenyl group, respectively. The acceptor atom may have interaction with hydrogen atom in target enzyme.

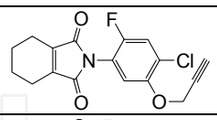
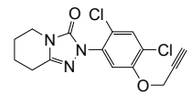
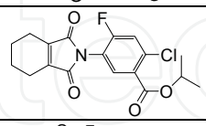
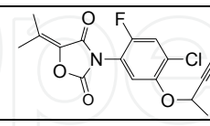
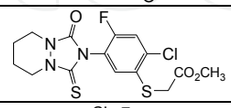
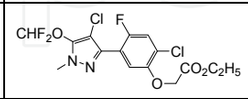
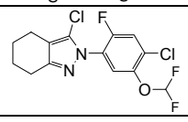
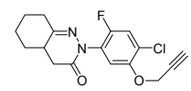
Compound	Structure	PPO pI_{50}	Compound	Structure	PPO pI_{50}
I-1		8.97	I-5		8.49
I-2		8.86	I-6		8.57
I-3		8.92	I-7		8.49
I-4		8.55	I-8		8.96

Table 1. The HTSB compounds for pharmacophore study.

Formula	C17 H13 Cl F N O3
Formula weight	333.73
Color/shape	colorless/prism
Crystal system	Triclinic
Space group	P-1
Unit cell dimensions	a = 9.313(5) Å alpha = 99.663(9) deg. b = 9.380(5) Å beta = 104.263(9) deg. c = 10.485(6) Å gamma = 112.778(8)
Volume	deg.
Z	782.1(8) Å3
Calculated density	2
Absorption coefficient	1.417 g.cm-3
F(000)	0.269 mm-1
Crystal size/mm	344
Temp. /K	0.36 x 0.24 x 0.22
θ ranges/°	293(2)
Limiting indices	2.46 to 25.00 deg.
Reflections collected / unique	-11<=h<=9, -9<=k<=11, -10<=l<=12
Completeness to theta = 25.00	4071 / 2747 [R(int) = 0.0174]
Absorption correction	99.4 %
Max. and min. transmission	Semi-empirical
Refinement method	1.000000 and 0.689808
Data / restraints / parameters	Full-matrix least-squares on F2
Goodness-of-fit on F2	2747 / 1 / 208
Final R indices [I>2sigma(I)]	1.022
R indices (all data)	R1 = 0.0428, wR2 = 0.1095
Largest diff. peak and hole	R1 = 0.0632, wR2 = 0.1228 0.440 and -0.291 e.A-3

Table 2. Crystal data and structure refinement of compound I-1.

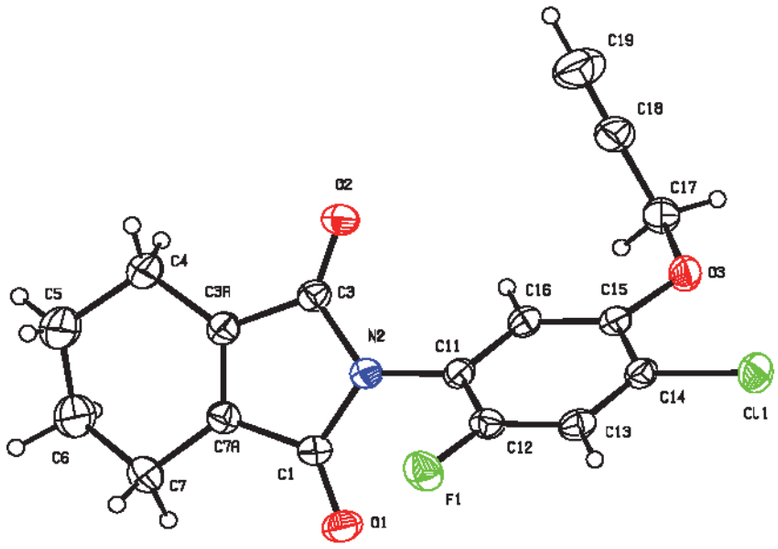
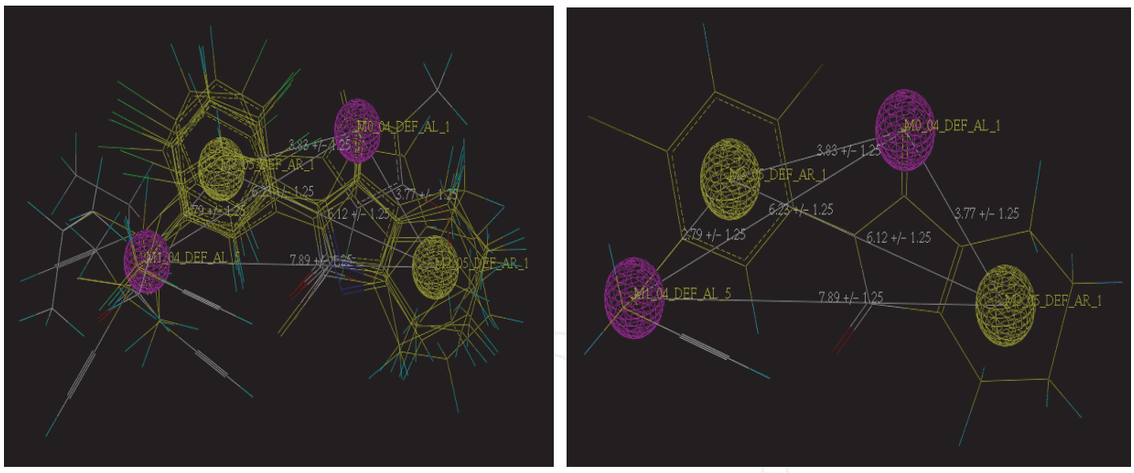


Fig. 10. Molecular structure of crystal compound I-1.



A B

Fig. 11. Pharmacophore A: overlap of all eight compounds; B: model with refererce compound I-1.

4.3 CoMFA analysis

QSAR (quantitative structure-activity relationships) have been reported about the effects on the substituents in phenyl group (Fujita & Nakayama, 1999; Jiang et al., 2010), but little literature about comparative molecular field analysis (CoMFA) on the effect of heterocyclic rings (Zhang et al., 2011). In order to understand the heterocyclic rings and substituents in

phenyl group effects on the PPO inhibition of a series of cyclic imide compounds, the method of CoMFA was applied to understand the quantitative structure–activity relationships. Using the information help us to increase the efficiency of syntheses of new candidate compounds.

37 HTSB compounds in table 3 was selected for the CoMFA study (Fujita & Nakayama, 1999). The 3D structures of all the compounds were built by SYBYL 6.9/ Sketch, and then optimized using MMFF94 force field, by Powell method with energy termination of 0.005 kcal/mol, and a maximum of 1000 iterations. Pharmacophore-based molecule alignment method was applied to superimpose all the compounds by using GALAHAD in SYBYL 6.9. The steric and electrostatic field energies for CoMFA were calculated using the SYBYL default parameters: 2.0 grid points spacing, a sp^3 carbon probe atom with +1 charge and a van der Waals radius of 1.52, and column filtering of 2.0 kcal/mol. The CoMFA descriptors were used as independent variables, and pI_{50} values were used as dependent variables in partial leastsquares (PLS) regression analyses to derive 3D-QSAR models. Leave-one-out (LOO) cross-validated PLS analyses were performed to determine the optimal number of components to be used in the final QSAR models and to check the predictive ability of the models. To visualize the 3D-QSAR results in term of field contributions, isocontour maps were generated using the field type 'stdev * coeff' and the contour levels were set to default values. In CoMFA, compounds II-1 was selected as the training set and the test set.

The alignment of HTSB compounds was shown in figure 12. The molecular modeling studies found good overlap between the 37 HTSB compounds. As listed in Table 3, a predictive CoMFA model was established with the conventional correlation coefficient R^2 = 0.908, the standard error s = 0.319, and F-test value F = 49.5. The contribution of steric and electrostatic fields are 49.5% and 50.5%, respectively. The observed and calculated activity values for all the compounds are given in Table 3, and the plots of the caculated versus the actual activity values for all the compounds are shown in Figure 13.

In Figure 14, the isocontour diagrams of the steric and electrostatic field contributions (''stdev*coeff") obtained from the CoMFA analysis are illustrated together with exemplary ligands. The steric field contour map is plotted in Figure 14A. The green region highlights positions where a bulky group would be favorable for higher PPO inhibition activity. In contrast, yellow indicates positions where a decrease in the bulk of the desired compounds is favored. As shown in Figure 14A, the CoMFA steric contour plots indicated that a big yellow region is located around the group of phenyl in 4, 5-position, while a big green region surrounded the heterocycle group. This map means that the substituents of phenyl in 4, 5-position should be bulky. This steric map explained clearly why compound II-20 and II-21 displayed lower activity than other compounds. The electrostatic contour plot is shown in Figure 14B. The blue contour defines a region where an increase in the positive charge will result in an increase in the activity, whereas the red contour defines a region of space where increasing electron density is favorable. As shown in Figure 14B, the electrostatic contour plot showed that a blue region is around the Z group in the position of 5 of phenyl ring, whereas a red region is around the carbonyl group. The electrostatic contour plot indicated the target compounds bearing an electron-withdrawing group at the position of 5 of phenyl will display higher activity. This contour map indicated that the more electronegative of the oxygen atom of the carbonyl, the higher the activity of inhibitors. This means the carbon atom of one of the carbonyl group played an important role in

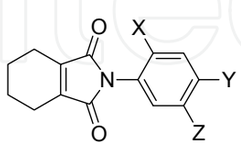
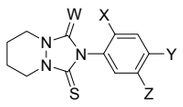
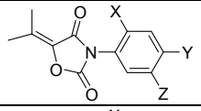
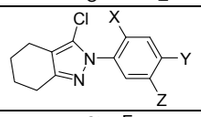
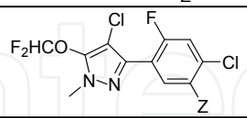
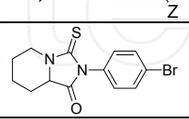
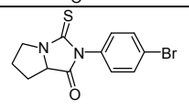
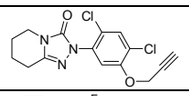
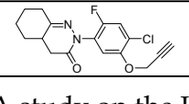
Com-pound	Structure	X, Y, Z	PPO-pI$_{50}$ Obs.	PPO-pI$_{50}$ Cal.	Deviation
II-1		2-F, 4-Cl, 5-OCH(Me)CCH	9	8.69	0.31
II-2		2-F, 4-Cl, 5-OCH$_2$CCH	8.97	9.04	-0.07
II-3		4-Cl, 5-COO-i-Pr	8.9	8.69	0.21
II-4		2-F, 4-Cl, 5-COO-i-Pr	8.86	8.82	0.04
II-5		2-F, 4-Br	8.6	8.51	0.09
II-6		2-F, 4-Cl, 5-OMe	8.52	8.76	-0.24
II-7		2-F, 4-Cl	8.43	8.54	-0.11
II-8		4-Cl, 5-COOEt	8.43	8.17	0.13
II-9		4-Cl, 5-COOCH$_2$COOMe	8.3	8.36	-0.06
II-10		4-Cl, 5-COOMe	8.05	8.12	-0.07
II-11		2-F, 4-Cl, 5-OCHF$_2$	7.96	7.95	0.01
II-12		4-Cl, 5-COO-t-Bu	7.85	8.03	-0.18
II-13		4-Br	7.67	6.80	0.87
II-14		4-Cl	7.6	6.83	0.77
II-15		4-OMe	7	7.11	-0.11
II-16		4-CF$_3$	6.55	6.57	-0.02
II-17		4-NO$_2$	6.4	6.62	-0.22
II-18		4-F	6.37	6.97	-0.60
II-19		4-Me	6.08	6.05	0.03
II-20		H	5.8	6.55	-0.75
II-21		3-Cl	5.6	5.76	-0.16
II-22		W=S; 2-F, 4-Cl, 5-OCH2C*CH	9.05	9.09	-0.04
II-23		W=S; 2-F, 4-Cl, 5-O-i-Pr	8.92	8.88	0.04
II-24		W=S; 4-Cl	8.17	8.32	-0.15
II-25		W=S; 2-F, 4-Cl	8.14	8.12	0.02
II-25		W=S; 4-Br	8.1	8.12	-0.02
II-27		W=O; 2-F, 4-Cl, SCH$_2$COOMe	8.08	8.08	0.0041
II-28		2-F, 4-Cl, 5-OCH(Me)C*CH	8.57	9.02	-0.45
II-29		4-Cl	7.66	7.32	0.34
II-30		2-F, 4-Cl, 5-OCH$_2$C*CH	9.14	9.24	-0.10
II-31		2-F, 4-Cl, 5-OCHF$_2$	8.55	8.46	0.09
II-32		OCH$_2$COOEt	8.49	8.40	0.09
II-33		H	8.49	8.51	-0.02
II-34			8.29	8.17	0.12
II-35			7.77	7.81	-0.04
II-36			8.49	8.42	0.07
II-37			8.96	8.79	0.17

Table 3. CoMFA study on the HTSB compounds.

determining the activity of PPO inhibitors. The stronger the ability of the carbonyl group to accept electrons from receptor, the higher the activity of PPO inhibitor.

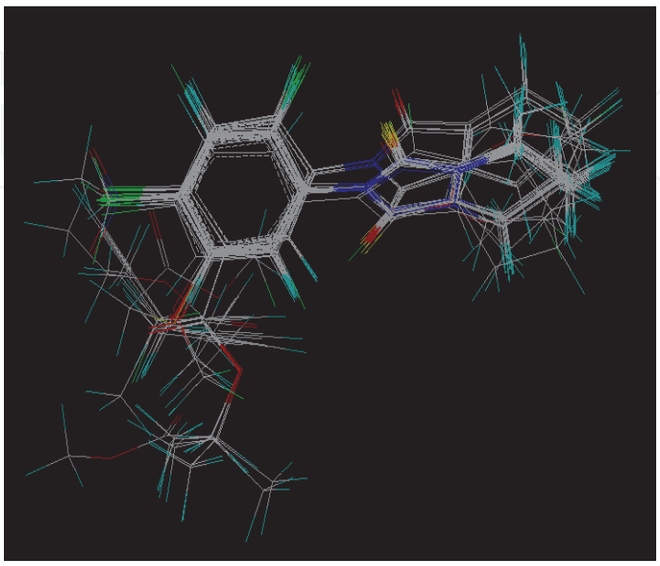


Fig. 12. Alignment of 37 HTSB compounds.

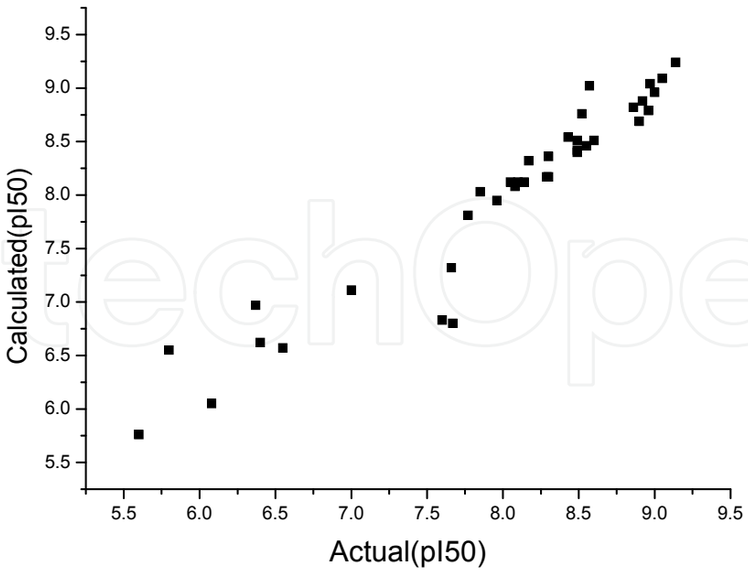
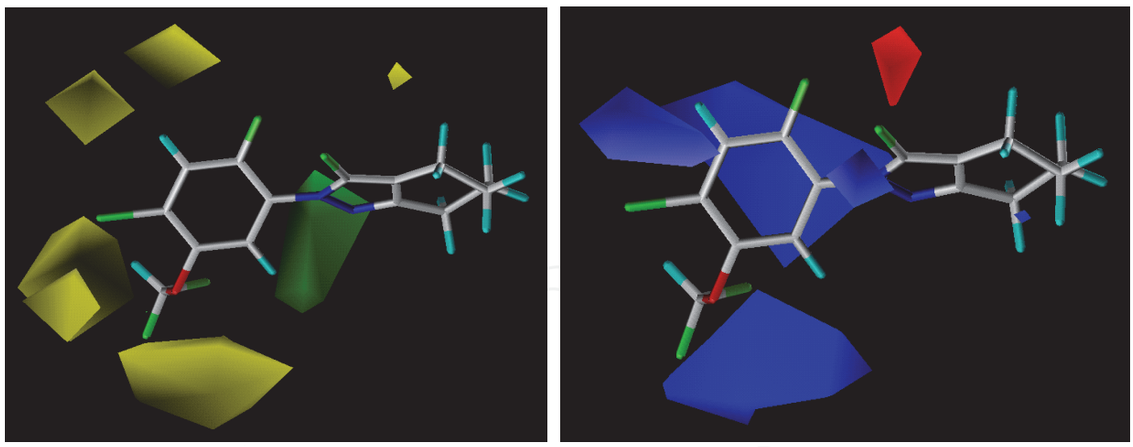


Fig. 13. Calculated pI_{50} (Y-axis) are versus actual pI_{50} (X-axis) values. The dots represent training compounds.



A B

Fig. 14. CoMFA contour maps with compound II-1 as the reference structure. (A) Steric contours. Scattered green areas are regions where bulky substituents are favorable, yellow areas are unfavorable. (B) Electrostatic contours. The red areas are the regions where negative potential is favorable for the activity, blue areas are unfavorable.

5. Conclusions

HTSB herbicides are characterised with their high herbicidal activities, fast acting, and environmentally benign. However, most of them cause short-term damage to the crops applied, which makes them no significant market share in the last 30 years (Qasem, 2011).

In recent years, the development of Protox inhibitor-resistant crops (Li and Nicholl, 2005; Vencill, 2011) began a new era for the use of Protox herbicides. Furthermore, weed shifts observed in genetically modified crops, caused by the development of weed resistance to the widely used glyphosate herbicide, will offer market opportunities for herbicides with other modes of action, such as Protox inhibiting herbicides. So, Protox inhibiting herbicides will continue to be an important area of interest to agrochemical companies, with most efforts focused on fine tuning the 5 position of the phenyl ring. The application of CoMFA approach will seed up the discovery processes.

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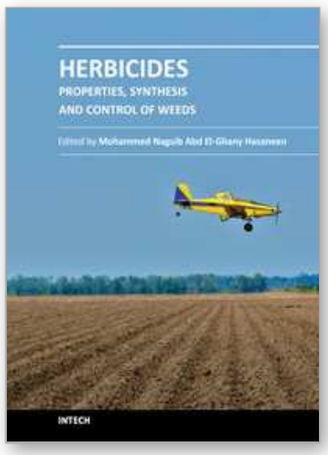

Herbicides - Properties, Synthesis and Control of Weeds
Edited by Dr. Mohammed Nagib Hasaneen

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This book is divided into two sections namely: synthesis and properties of herbicides and herbicidal control of weeds. Chapters 1 to 11 deal with the study of different synthetic pathways of certain herbicides and the physical and chemical properties of other synthesized herbicides. The other 14 chapters (12-25) discussed the different methods by which each herbicide controls specific weed population. The overall purpose of the book, is to show properties and characterization of herbicides, the physical and chemical properties of selected types of herbicides, and the influence of certain herbicides on soil physical and chemical properties on microflora. In addition, an evaluation of the degree of contamination of either soils and/or crops by herbicides is discussed alongside an investigation into the performance and photochemistry of herbicides and the fate of excess herbicides in soils and field crops.

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