

Additional File 2

To build the QSAR model for the activity of free radical scavenging, a library of 70 di(hetero)aryl compounds, belonging to 3 different families (A, B and C), which differ in terms of the constitution of their linker, was used. Family A (Figure S1, Figure S2, Figure S3, Table S1, Table S2 and Table S3) has a linker made up of an amine group (NH), family B (Figure S4, Figure S5 and Table S4) has a linker made up of a methanimine group (CH₂NH) and family C (Figure S6, Figure S7, Figure S8, Figure S9, Figure S10, Table S5 and Table S6) the compounds have a linker made up of an amide group (CONH). Within each family previously mentioned, the compounds were grouped into classes according to the similarity in their base structure for a better perception of the results. The Classes obtained were:

- **Family A** – consisting of 26 compounds divided into 3 classes A-I (6 compounds), A-II (14 compounds) and A-III (6 compounds) as represented in Figure S1, S2 and S3, respectively. Tables S1, S2 and S3 show the constituents of the various R groups that make up each compound in each class.

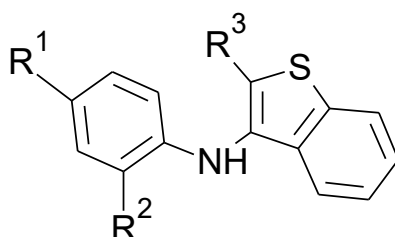


Figure S1. Base structure of compounds belonging to Class A-I.

Table S1. R groups of each compound belonging to Class A-I.

COMPOUND	R ¹	R ²	R ³
A1 ^[25]	OCH ₃	OCH ₃	H
A2 ^[25]	OCH ₃	OCH ₃	COOH
A3 ^[25]	OCH ₃	OCH ₃	COOCH ₂ CH ₃
A4 ^[25]	OH	OH	COOCH ₂ CH ₃
A5 ^[25]	H	OH	COOCH ₂ CH ₃
A6 ^[25]	H	F	H

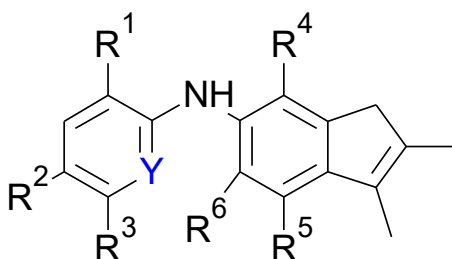


Figure S2. Base structure of compounds belonging to Class A-II.

Table S2. R groups of each compound belonging to Class A-II.

COMPOUND	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	Y
A7 ^[25]	OCH ₃	OCH ₃	H	H	H	CH ₃	C
A8 ^[25]	H	OCH ₃	OCH ₃	H	H	CH ₃	C
A9 ^[25]	H	OCH ₃	H	CH ₃	CH ₃	H	C
A10 ^[25]	H	OCH ₃	H	H	H	CH ₃	C
A11 ^[25]	H	H	OCH ₃	H	H	CH ₃	C
A12 ^[25]	H	CH=O	H	H	H	CH ₃	C
A13 ^[25]	H	C≡N	H	CH ₃	CH ₃	H	C

A14 ^[25]	Br	OCH ₃	OCH ₃	H	H	CH ₃	C
A15 ^[25]	Br	OCH ₃	H	CH ₃	CH ₃	H	C
A16 ^[25]	Br	OCH ₃	H	H	H	CH ₃	C
A17 ^[25]	Br	H	H	H	H	CH ₃	C
A18 ^[25]	Br	H	H	CH ₃	CH ₃	H	C
A19 ^[25]	I	H	H	H	H	CH ₃	C
A20 ^[25]	H	H	H	CH ₃	CH ₃	H	N

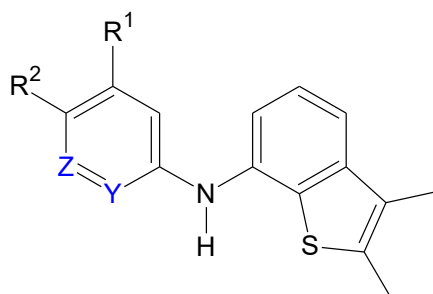


Figure S3. Base structure of compounds belonging to Class A-III.

Table S3. R groups of each compound belonging to Class A-III.

COMPOUND	R ¹	R ²	Z	Y
A21 ^[25]	OCH ₃	OCH ₃	CH	CH
A22 ^[25]	OCH ₃	H	CH	CH
A23 ^[25]	H	OCH ₃	CH	CH
A24 ^[25]	C≡N	H	CH	CH
A25 ^[25]	H	H	N	CH
A26 ^[25]	H	H	CH	N

- Family B** – consisting of 24 compounds divided into 3 classes B-I (22 compounds), B-II (1 compound) and B-III (1 compound) as represented in Figure S4 and S5. Table S4 shows the constituents of the various R groups that make up each compound in class B-I. Classes B-II and B-III are made up of only 1 compound so there are no different R groups.

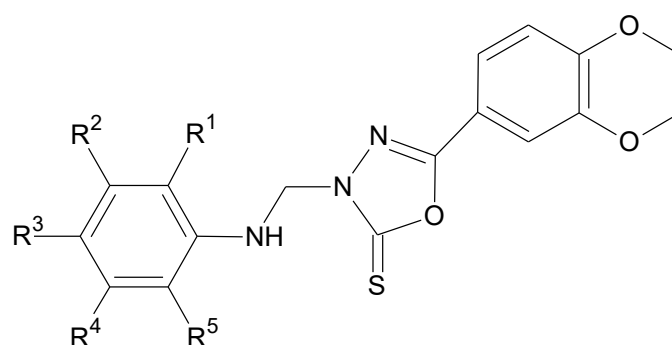


Figure S4. Base structure of compounds belonging to Class B-I.

Table S4. R groups of each compound belonging to Class B-I.

COMPOUND	R ¹	R ²	R ³	R ⁴	R ⁵	COMPOUND	R ¹	R ²	R ³	R ⁴	R ⁵
B1 ^[36]	H	F	F	F	H	B12 ^[36]	H	Cl	Cl	H	H
B2 ^[36]	H	H	H	H	H	B13 ^[36]	H	H	H	H	Br
B3 ^[36]	H	H	H	H	F	B14 ^[36]	H	H	Br	H	H
B4 ^[36]	H	H	F	H	H	B15 ^[36]	Br	H	Br	H	H
B5 ^[36]	F	H	H	H	F	B16 ^[36]	H	H	H	H	NO ₂
B6 ^[36]	H	H	H	H	CF ₃	B17 ^[36]	H	NO ₂	H	H	H

B7 ^[36]	H	H	H	CF ₃	H	B18 ^[36]	Cl	H	NO ₂	H	H
B8 ^[36]	H	CF ₃	H	CF ₃	H	B19 ^[36]	CH ₃	H	H	H	H
B9 ^[36]	H	H	H	H	Cl	B20 ^[36]	H	H	CH ₃	H	H
B10 ^[36]	Cl	H	Cl	H	H	B21 ^[36]	H	H	OCH ₃	H	H
B11 ^[36]	Cl	H	H	Cl	H	B22 ^[36]	CH ₃ CH ₂ O	H	H	H	H

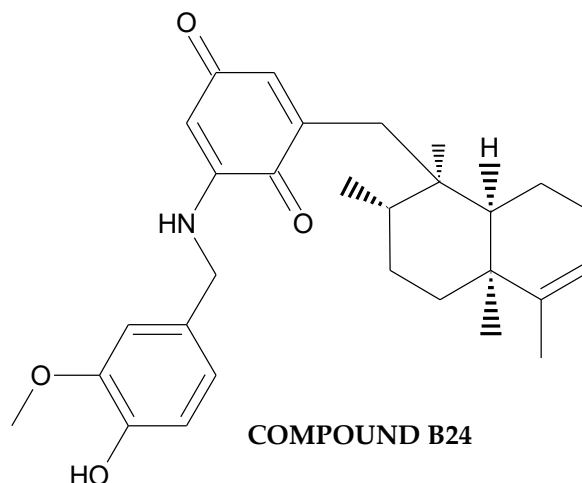
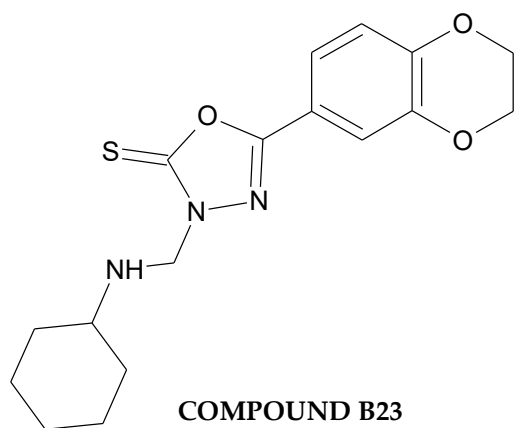


Figure S5. Structure of compound B23^[36] (only Class B-II compound) and B24^[37] (only Class B-III compound).

- Family C** – consisting of 20 compounds divided into 10 classes C-I (1 compound), C-II (7 compounds), C-III (1 compound), C-IV (1 compound), C-V (1 compound), C-VI (1 compound), C-VII (2 compounds), C-VIII (1 compound), C-IX (3 compounds) and C-X (2 compounds) as shown in Figure S6, S7, S8, S9 and S10. Tables S5 and S6 show the constituents of the various R groups that make up each compound from class C-II to C-VII. Table S7 shows the constituents of the various R groups that make up each compound from classes C-IX and C-X. Classes C-I, C-III, C-IV, C-V, C-VI, and C-VIII are made up of only 1 compound so there are no different R groups.

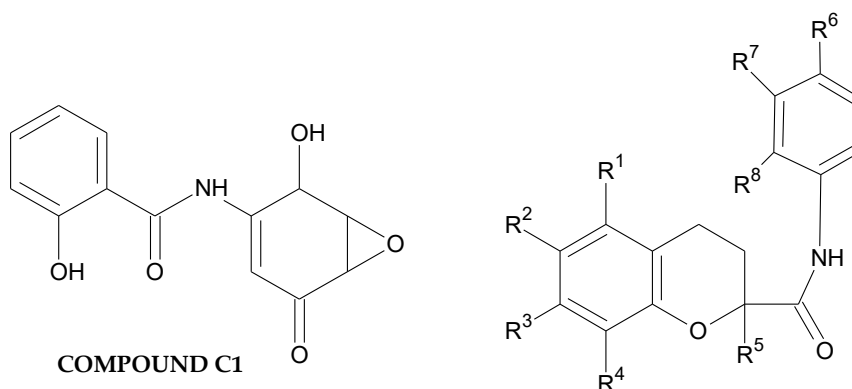
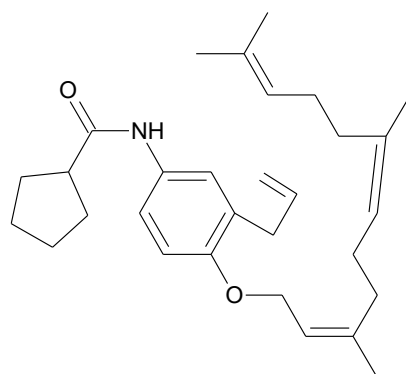


Figure S6. Base structure of compound C1^[38] (only compound belonging to Class C-I) and base structure of compounds belonging to Class C-II.

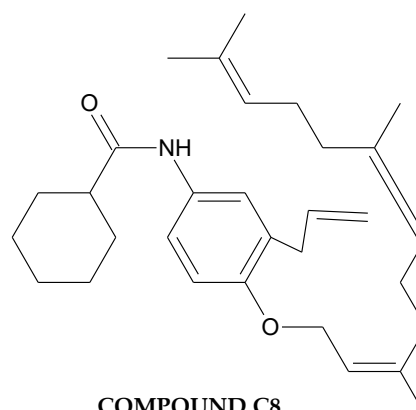
Table S5. R groups of each compound belonging to Class C-II.
W – NHCO(CH₂)₄CHC₃H₅S₂; **X** – NHCO(CH₂)₄CHSH₂(CH₂)SH;
Y – OC₆H₄NHCO(CH₂)₄C₃H₅S₂; **Z** – NHCO(CH₂)₂C₃H₅S₂

COMPOUND	R ¹	R ²	R ³	R ⁴	R ⁵	R ⁶	R ⁷	R ⁸
C2 ^[39]	CH ₃	OH	CH ₃	CH ₃	CH ₃	H	H	W
C3 ^[39]	CH ₃	OH	CH ₃	CH ₃	CH ₃	NH ₂	H	H
C4 ^[39]	CH ₃	OH	CH ₃	CH ₃	CH ₃	H	H	X
C5 ^[39]	CH ₃	OH	CH ₃	CH ₃	CH ₃	Y	H	H

C6 ^[39]	CH ₃	OH	CH ₃	CH ₃	CH ₃	Z	H	H
C14 ^[42]	H	OCH ₃	OH	H	H	H	H	H
C15 ^[42]	H	OCH ₃	OH	H	H	NO ₂	H	H

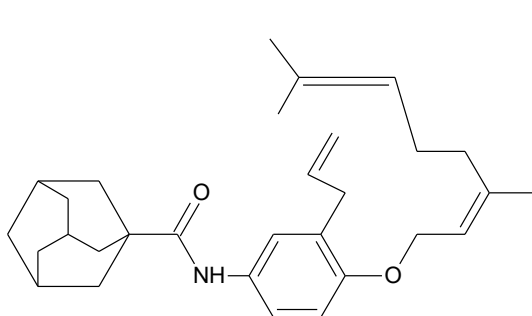


COMPOUND C7

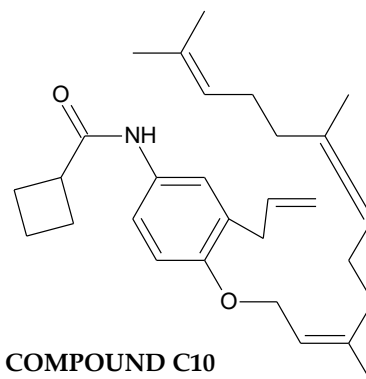


COMPOUND C8

Figure S7. Base structure of compound C7^[40] (only compound belonging to Class C-III) and C8^[40] (only compound belonging to Class C-IV).

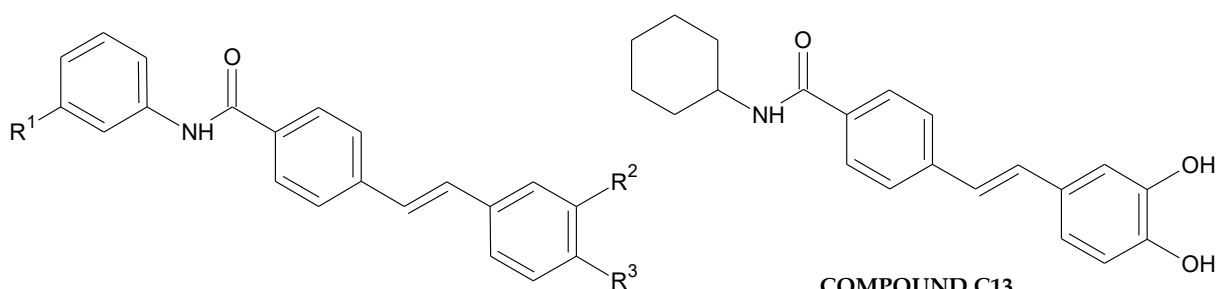


COMPOUND C9



COMPOUND C10

Figure S8. Base structure of compound C9^[40] (only compound belonging to Class C-V) and C10^[40] (only compound belonging to Class C-VI).



COMPOUND C13

Figure S9. Base structure of compounds belonging to Class C-VII and base structure of compound C13^[38] (only compound belonging to Class C-VIII).

Table S6. R groups of each compound belonging to Class C-VII

COMPOUND	R1	R2	R3
C11 ^[41]	COOCH ₂ CH ₃	OH	OH
C12 ^[41]	H	OH	OH

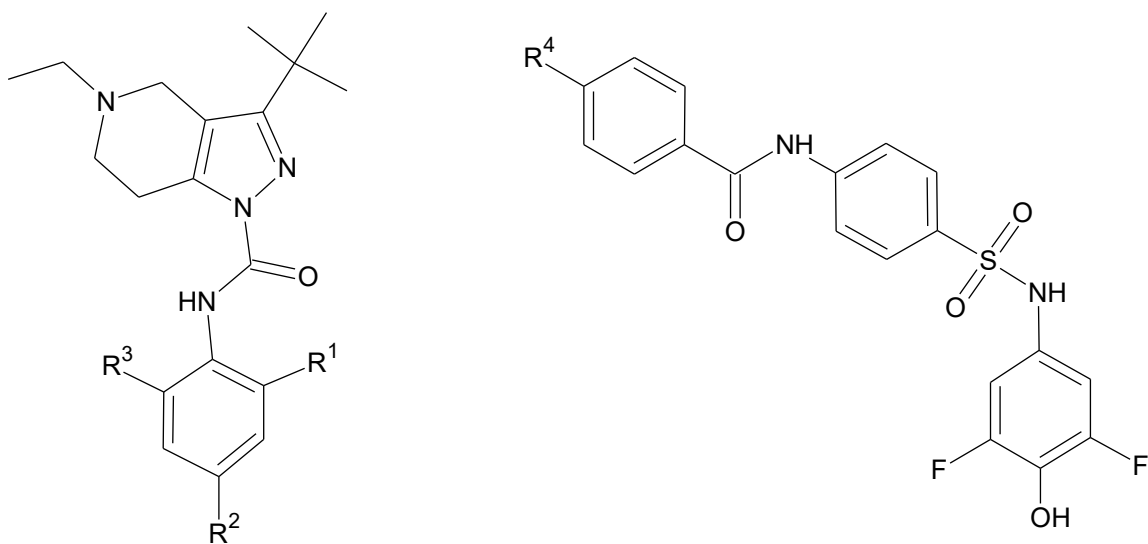


Figure S10. Base structure of compounds belonging to Class C-IX and C-X

Table S7. R groups of each compound belonging to Class C-IX and C-X.

COMPOUND	R1	R2	R3	R4
C16 ^[43]	H	Br	H	-
C17 ^[43]	CH ₃	CH ₃	H	-
C18 ^[43]	CH ₃	H	CH ₃	-
C19 ^[44]	-	-	-	H
C20 ^[44]	-	-	-	OCH