Supporting Information

Text S1 Selection reasons of model compounds

The reasons why twenty-nine emerging contaminants included thirteen disinfection byproducts, two pesticides, three pharmaceuticals and personal care products, one perfluoroalkyl and polyfluoroalkyl substance, one endocrine disrupting chemical, one plasticizer and eight tire additives and their derivatives were selected as model compounds were described below.

In recent work, we determined the priority level of 1187 disinfection byproducts (DBPs) by employing 12 endocrine endpoints (Sui et al., 2024). Based on that priority list of 1187 DBPs, we selected 12 high or medium priority DBPs (i.e. 2-hydroxy-3,5-diiodobenzaldehyde, 2,6-Dibromo-1,4-benzoquinone, 2,6-Dichloro-1,4-benzoquinone, Bromochlorophenol Blue, 2-bromo-6-chloro-4-nitrophenol, 2,5-Dibromo-1,4-benzoquinone, 2,6-Diiodo-4-nitrophenol, 4-hydroxy-3,5-diiodobenzaldehyde, Tetrachloro-1,4-benzoquinone, 3,5-dichlorobisphenol A, N,N-diphenylnitrous amide, 4-bromo-2,6-ditert-butylphenol) that do not have data on their potential for disrupting of fish transthyretin (TTR). In addition, we identified 20 DBPs in chlorination of three Iodinated contrast media (iopamidol, iohexol, diatrizoate) (Zhou et al., 2023). Among them, 3-methyl-2-nitrophenol was predicted as a potential TTR binder by the human TTR predictive model developed in our lab (Yang et al., 2023b). In this case, 3-methyl-2-nitrophenol also include in this study. Thus, 13 DBPs in total were selected as model compounds here.

Nonylphenol and butylbenzyl phthalate were listed in the substances of very high concern (SVHC) that were published in accordance with Article 59(10) of the REACH Regulation duo to their endocrine disrupting properties. Nonylphenol is also considered as a priority-controlled chemical in the List of Priority Controlled Chemicals (First Batch) issued by the Ministry of Ecology and Environment of the People's Republic of China (2017). Thus, Nonylphenol and butylbenzyl phthalate were also included here.

Triclocarban (TCC) and triclosan (TCS) have been topical chemicals in recent years. They are commonly used as antimicrobial agents in pharmaceuticals and personal care products, and have been frequently detected in Chinese surface waters (e.g., in the Bohai Rim region, Yangtze River Delta, and Pearl River Delta). They also exhibited high risk to aquatic organisms (Su et al., 2020). Methylparaben (MTP) is the most abundant paraben detected in the environment, with reported concentrations as high as 3,142 ng/L in China and 527 μg/L worldwide (Medkova et al., 2023). Imidacloprid (IMI) and Flupyrifuranone are two different

pesticides of concern. IMI used to be the most widely used neonicotinoid pesticide in China (Liu et al., 2022), and also commonly detected in rivers. Flupyrifuranone is a new butenolide pesticide produced by Bayer which is gaining popularity (Zhong et al., 2021). 6:2 fluorotelomer sulfonic acid (6:2 FTSA) is one of the novel alternatives to perfluorooctane sulfonate (PFOS), which has been widely used in the production of electroplating and firefighting foams in many countries. The 6:2 FTSA has recently been detected for the first time in Laizhou Bay, China (Zhao et al., 2019; Liu et al., 2024). Although it has been observed lower toxicity to aquatic organisms than conventional PFOS, it still poses potential environmental risks (Zhang et al., 2023b).

Tire additives and their derivatives (TADs) are industrial additives of emerging interest, usually released into the aquatic environment from tire wear particles (TWPs) through weathering, photoaging, and natural degradation. TWPs are also one of the major sources of microplastics (Jin et al., 2023; Li et al., 2024). N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine quinone (6PPDQ) is a recently discovered new contaminant capable of causing abnormal mortality in silver salmon with LC_{50} as low as 95ng/L (Tian et al., 2021, 2022). 6PPDQ is mainly derived from the ozone oxidation of N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine (6PPD), which is an antioxidant widely used in tire rubber. 4-hydroxydiphenylamine (4-HDPA) is another major transformation product of 6PPD. 6PPD and its transformation products are widely present in a variety of environmental media, including surface runoff and sediment, and have been shown to have toxic effects on aquatic organisms (Cao et al., 2022; Johannessen and Metcalfe, 2022; Li et al., 2023; Zhang et al., 2023c). In addition, five tire rubber derivatives commonly found in pavement runoff were included, namely 2-Aminobenzothiazole (NHBT), 2-Hydroxybenzothiazole (OHBT), 1,3-Diphenylguanidine (DPG), 1,3-Diphenylurea (DPU), Hexa(methoxymethyl) melamine (HMMM) (Peter et al., 2018; Müller et al., 2022; Jiang et al., 2023; Zhang et al., 2023a). Based on the availability of standards and the above reasons, total 29 emerging contaminants were selected as model compounds to explore their potential binding affinity with CrmTTR.

Text S2 Experimental operation procedures about ANSA-TTR competitive fluorescence displacement assay

The details of experimental operation procedures about ANSA-TTR competitive fluorescence displacement assay had been presented in our previous study (Zhao et al., 2023). Here, the critical steps were listed below. The dissociation constant ($K_{d,probe}$) of 8-anilino-1-naphthalenesulfonate ammonium (ANSA) with recombinant CrmTTR were determined first by direct fluorescent ligand binding assay. 1 μmol/L CrmTTR solution was prepared in buffer (100 m mol/L NaCl/50 mmol/L Tris-HCl, pH 7.40 ± 0.02). Then, 2 ml of 1 μmol/L CrmTTR solution was added into the cuvette, and different volumes of ANSA solution were gradually added into the CrmTTR solution to obtain the desired ANSA concentration. After 15 min incubation at room temperature, the quantitative fluorescence was measured using an INESA 970CRT fluorescence spectrometer (Shanghai Instrument Electric Analytical Instrument Co., Ltd., China). The critical operation parameters included: the excitation wavelength was set at 380 nm; the emission wavelength was set in the range of 400-600 nm; the excitation slit width and emission slit width was 10 nm. The binding ability of THs and model compounds with recombinant CrmTTR were also measured via the similar competitive binding assay. The concentrations of recombinant CrmTTR and ANSA were 0.5 μmol/L and 50 μmol/L. Different volumes of THs and model chemicals solution were gradually added into the CrmTTR and ANSA solution to obtain the desired THs and model chemicals concentration. After 5 min incubation at room temperature, the quantitative fluorescence was measured. After measuring the fluorescence intensity of each chemical, the relative fluorescence intensity (RF_λ) could be derived:

$$RF_\lambda = \frac{F_{\lambda-i}}{F_{\lambda-0}} \quad (1)$$

where $F_{\lambda\text{-}0}$ and $F_{\lambda\text{-}i}$ are the maximum fluorescence intensity without and with *i*-ligand concentration of model compounds, respectively. Then, the average relative fluorescence intensity of three independent repeats for each compound was plotted as a function of ligand concentration. The half maximal inhibitory concentration (IC_{50}) and binding constant (K_d) of ligand were determined using procedures as described in our previous studies. The obtained K_d value of ANSA on CrmTTR was 2924 ± 62 n mol/L (Fig. S2), which was consistent with the value of 2727 ± 277 n mol/L observed by Zhao et al., (2023). To avoid changes in fluorescence values due to solvents, it was ensured that the amount of DMSO added was less than 5% (Zhao et al., 2023). The logarithm of the relative competitive potency (log*RP*) is defined as follows:

$$\log RP(\mathrm{T}_4) = \log \frac{IC_{50,\mathrm{T}_4}}{IC_{50,\mathrm{ligand}}} \quad \text{or} \quad \log RP(\mathrm{T}_3) = \log \frac{IC_{50,\mathrm{T}_3}}{IC_{50,\mathrm{ligand}}} \qquad (2)$$

where $IC_{50,\mathrm{T4}}$/$IC_{50,\mathrm{T3}}$ and $IC_{50,\mathrm{ligand}}$ are the half-maximal inhibitory concentration of T_4/T_3 and competitor, respectively.

Text S3 Validation of classification model

In modeling, the data sets were randomly grouped into a training (75%) and validation set (25%). According to the fish and human TTR binding affinity data, we developed the binary classification models by employing the following machine learning algorithms: k-nearest neighbor (kNN), logistic regression, support vector machine, decision tree, random forest, and gradient boosting decision tree. The machine learning analyses were performed employing the scikit-learn code in Python 3.9 (Pedregosa et al., 2011). The classification model quality was evaluated by using following parameters: sensitivity (S_n), specificity (S_p), predictive accuracy (Q), Matthews Correlation Coefficient (MCC), Receiver Operating Characteristics (ROC) graph (Yang et al., 2021b). The Shapley additive explanation (SHAP) was employed to depict the importance of selected predictive variables in the optimal model (Lundberg and Lee 2017). The applicability domain (AD) of derived binary classification models was defined using Euclidean distance vs leverage-based methods. The Euclidean distance was defined as equation 3 and 4:

$$ED_{\text{Train}} = \sqrt{\sum_{i=1}^{n}\left(\frac{X_i}{\max(X_i)-\min(X_i)} - \left(\frac{X_i}{\max(X_i)-\min(X_i)}\right)_{\text{aver}}\right)^2} \quad (3)$$

$$ED_{\text{Test}} = \sqrt{\sum_{i=1}^{m}\left(\frac{x_i}{\max(X_i)-\min(X_i)} - \left(\frac{X_i}{\max(X_i)-\min(X_i)}\right)_{\text{aver}}\right)^2} \quad (4)$$

where ED_{Train} and ED_{Test} are the Euclidean distance in training and test set, respectively; X_i and x_i are i-descriptor of a compound in training and test set, respectively; $\max(X_i)$ and $\min(X_i)$ are the maximum and minimum values of i-descriptor in training set, respectively; $(X_i/(\max(X_i) - \min(X_i)))_{\text{aver}}$ is the average value of i-descriptor in training set. The leverage was defined as equation 5 and 6 (Wang et al., 2015):

$$H = X(X^{\mathrm{T}}X)X^{T} \quad (5)$$

$$h_j = x_j^{\mathrm{T}}(X^{\mathrm{T}}X)x_j \quad (6)$$

where H and h_j are the leverage value of compounds in training set and jth-compound in set, respectively; X and X^{T} are the descriptor matrix of training set and the transpose of X, respectively; x_j and x_j^{T} are the descriptor vector of the jth-compound and the transpose of x_j, respectively. The threshold values which determined if a given compound in or out the AD of a model depends on two values, i.e. threshold value of Euclidean distance

(*ed**) and threshold value of leverage (*h**). The threshold value of Euclidean distance and leverage were the maximum value of ED_{Train} and H_{i} in training set. Based on the Euclidean distance and leverage of training and test set, a figure can be obtained. And the figure will be divided into four part by threshold value of Euclidean distance (*ed**) and threshold value of leverage (*h**), i.e. within both *ed** and *h**, within *ed** and out of *h**, out of *ed** and within *h**, out of *ed** and out of *h**.

Text S4 Development of TTR profiler

Fig. S3 illustrated the conceptual framework of TTR Profiler. As shown in Fig.S3, the TTR Profiler contained three parts, i.e. the input, calculation and assessment, results report sections.

(1) Input section

TTR profiler supported five input formats: single SMILES code or CAS NO, SMILES code (.csv, .txt, .smi format file) or CAS NO (.csv, .txt format file) in batch mode, structure file mode (.SDF, .mol format file). For CAS NO, the tool will check whether it is in the chemical database or not by comparing the inputted CAS NO and the CAS NO in the chemical database. If the input CAS NO matches one compound in the chemical database, the corresponding basic information such as CAS NO, SMILES code, and experimental data (if available) will be extracted; otherwise, the inputted compound cannot be predicted. When a structure file is the input, the tool will transform it into SMILES code. For input or transformed SMILES code, the tool will check whether it is in the chemical database or not by comparing the input or transformed SMILES code with the SMILES code in the chemical database. If input or transformed SMILES code matches compound in the chemical database, the corresponding basic information such as CAS NO (if available), SMILES code, experimental data (if available) will be extracted; if not, only the input or transformed SMILES code will be used in the next step. The valid input chemical information would be displayed in the compound input interface of the tool.

(2) Calculation and assessment section

The predictive variables required by the SAR models will be calculated for input compound by using the SMEILES code obtained in previous step. Then, the missing data will be filled by employing the model and calculated predictive variables. The tool also evaluates whether the input compound is in the application domain of the predictive model or not by using a Euclidean distance vs leverage-based method.

The reliability of the predicted value of inputted compound was calculated employing Tanimoto similarity index (Yang et al.,2021b; 2023b):

$$T_S = \frac{\sum_{i=1}^{n} Train_{X\text{-}i} \cap Test_{X\text{-}i}}{\sum_{i=1}^{n} Train_{X\text{-}i} + \sum_{i=1}^{n} Test_{X\text{-}i} - \sum_{i=1}^{n} Train_{X\text{-}i} \cap Test_{X\text{-}i}} \quad (7)$$

where $Train_{X\text{-}i}$ and $Test_{X\text{-}i}$ are the i-th descriptor of substance in training and test set, respectively. If the T_S

value of inputted substance is ≥ 0.900, the predicted data for this substance was marked as high reliability; $0.750 \leq T_S < 0.900$, the predicted data was labeled as moderate reliability; otherwise was low reliability.

(3) Results report section

The results will display in the interface of the tool, or be saved as a .csv file. The information in the results will include the basic information of inputted compound (i.e. CAS NO (if available), SMIELS code), experimental value (if available), predicted value, AD assessment result, and reliability assessment result of the predicted value.

Table S1 Comparison of statistical performance for different predictive models of TTR (Yang et al., 2023a)

Method[a]	*Endpoint*[b]	*m*[c]	*n*[d]	Training set[e]	Validation set[f]	AD[g]	Reference
PLS	log*RP*	2	17	n_{Train} = 9, R^2_{Train} = 0.960, Q^2_{LOO} = 0.960, Q^2_{BOOT} = 0.870, $RMSE_{Train}$ = 0.290	n_{EXT} = 8, R^2_{EXT} = 0.930 Q^2_{EXT} = 0.900, $RMSE_{EXT}$ = 0.470	Yes	Papa et al.,2010
MLR	log*K*	1	14	n_{Train} = 14, R^2_{Train} =0.880	-	NO	Cao et al., 2010
CoMSIA	log*RP*	4	28	n_{Train} = 22, Q^2_{LOO} = 0.752	n_{EXT} = 6, Q^2_{EXT} = 0.928	NO	Yang et al., 2011
kNN	Classification	2	29	n_{Train} = 20, Q_{Train} = 0.950, $S_{n\text{-}Train}$ = 1, $S_{p\text{-}Train}$ = 0.870	n_{EXT} = 9, Q_{EXT} = 0.889, $S_{n\text{-}EXT}$ = 0.800, $S_{p\text{-}EXT}$ = 1	Yes	Kovarich et al., 2011
kNN	Classification	2 (3)	19	n_{Train} = 10, Q_{Train} = 0.900 - 1, $S_{n\text{-}Train}$ = 0.830 - 1, $S_{p\text{-}Train}$ = 0.750 - 1	n_{EXT} = 9, Q_{EXT} = 0.900 - 1, $S_{n\text{-}EXT}$ = 1, $S_{p\text{-}EXT}$ = 0.750 - 1	Yes	Kovarich et al., 2012
kNN	Classification	3 (5)	53	n_{Train} = 37, Q_{Train} = 0.840, $S_{n\text{-}Train}$ = 0.910, $S_{p\text{-}Train}$ = 0.790	n_{EXT} = 16, Q_{EXT} = 0.810, $S_{n\text{-}EXT}$ = 0.890, $S_{p\text{-}EXT}$ = 0.860	Yes	Papa et al., 2013
MLR	log*RP*	3	32	n_{Train} = 23, Q^2_{LOO} = 0.810, Q^2_{BOOT} = 0.780	n_{EXT} = 9, *CCC* = 0.940		
PLS	log*RP*	3	47	n_{Train} = 38, R^2_{Train} = 0.860, Q^2_{CUM} = 0.840, $RMSE_{Train}$ = 0.510	n_{EXT} = 9, R^2_{EXT} = 0.950 Q^2_{EXT} = 0.930, $RMSE_{EXT}$ = 0.320	Yes	Yang et al., 2013
kNN	Classification	-(4)	222	n_{Train} = 178, Q_{Train} = 0.880, $S_{n\text{-}Train}$ = 0.890, $S_{p\text{-}Train}$ = 0.870	n_{EXT} = 44, Q_{EXT} = 0.820, $S_{n\text{-}EXT}$ = 0.780, $S_{p\text{-}EXT}$ = 0.850	Yes	Zhang et al., 2015
LIB-SVM	Classification	-	222	n_{Train} = 178, Q_{Train} = 0.820, $S_{n\text{-}Train}$ = 0.950, $S_{p\text{-}Train}$ = 0.780	n_{EXT} = 44, Q_{EXT} = 0.770, $S_{n\text{-}EXT}$ = 0.900, $S_{p\text{-}EXT}$ = 0.730		
PLS-DA	Classification	-	222	n_{Train} = 178, Q_{Train} = 0.800, $S_{n\text{-}Train}$ = 0.930, $S_{p\text{-}Train}$ = 0.720	n_{EXT} = 44, Q_{EXT} = 0.790, $S_{n\text{-}EXT}$ = 0.940, $S_{p\text{-}EXT}$ = 0.690		
PLS	log*RP*	3	29	n_{Train} = 20, R^2_{Train} = 0.934, Q^2_{CUM} = 0.903, $RMSE_{Train}$ = 0.258	n_{EXT} = 9, R^2_{EXT} = 0.674 Q^2_{EXT} = 0.654, $RMSE_{EXT}$ = 0.874	Yes	Yang et al., 2017
PLS	log*RP*	3	29	n_{Train} = 20, R^2_{Train} = 0.922, Q^2_{CUM} = 0.900, $RMSE_{Train}$ = 0.281	n_{EXT} = 9, R^2_{EXT} = 0.670 Q^2_{EXT} = 0.649, $RMSE_{EXT}$ = 0.879		
LDA	Classification	3	24	n_{Train} = 16, Q_{Train} = 0.934, $S_{n\text{-}Train}$ = 1, $S_{p\text{-}Train}$ = 0.833	n_{EXT} = 8, Q_{EXT} = 1, $S_{n\text{-}EXT}$ = 1, $S_{p\text{-}EXT}$ = 1	NO	Kar et al., 2017
GFA-MLR	pIC_{50}	2	15	n_{Train} = 10, R^2_{Train} = 0.860, Q^2_{LOO} = 0.730	n_{EXT} = 5, Q^2_{EXT} = 0.640		

Method[a]	*Endpoint*[b]	*m*[c]	*n*[d]	Training set[e]	Validation set[f]	AD[g]	Reference
MLR	log*RP*	2	23	n_{Train} = 18, R^2_{Train} = 0.828, Q^2_{LOO} = 0.729, Q^2_{BOOT} = 0.776,$RMSE_{Train}$ = 0.418	n_{EXT} = 5, Q^2_{EXT} = 0.902, *CCC* = 0.936, $RMSE_{EXT}$ = 0.316	Yes	Yang et al., 2019
kNN	Classification	3 (3)	94	n_{Train} = 78, Q_{Train} = 0.923, $S_{n\text{-}Train}$ = 0.979, $S_{p\text{-}Train}$ = 0.839	n_{EXT} = 26, Q_{EXT} = 0.923, $S_{n\text{-}EXT}$ = 0.938, $S_{p\text{-}EXT}$ = 0.900	Yes	Xi et al., 2020
MLR	log*RP*	3	29	n_{Train} = 22, R^2_{Train} = 0.850, Q^2_{LOO} = 0.782, Q^2_{BOOT} = 0.736,$RMSE_{Train}$ = 0.376	n_{EXT} = 7, Q^2_{EXT} = 0.795, *CCC* = 0.887, $RMSE_{EXT}$ = 0.399	Yes	Yang et al., 2021a
kNN	Classification	3 (3)	407	n_{Train} = 305, Q_{Train} = 0.856 – 0.872, $S_{n\text{-}Train}$ = 0.854 – 0.888, $S_{p\text{-}Train}$ = 0.854 – 0.859	n_{EXT} = 102, Q_{EXT} = 0.853 – 0.873, $S_{n\text{-}EXT}$ = 0.818 – 0.907, $S_{p\text{-}EXT}$ = 0.833 – 0.930	Yes	Yang et al., 2021b
kNN	log*RP*	4 (3)	88	n_{Train} = 70, R^2_{Train} = 0.886, Q^2_{LOO} = 0.784, Q^2_{BOOT} = 0.639,$RMSE_{Train}$ = 0.442	n_{EXT} = 18, Q^2_{EXT} = 0.897, *CCC* = 0.941, $RMSE_{EXT}$ = 0.466		
MLR	log*RP*	6	88	n_{Train} = 66, R^2_{Train} = 0.812, Q^2_{LOO} = 0.757, Q^2_{BOOT} = 0.755,$RMSE_{Train}$ = 0.567	n_{EXT} = 22, Q^2_{EXT} = 0.852, *CCC* = 0.906, $RMSE_{EXT}$ = 0.561		
kNN	log*RP*	2 (3)	41	n_{Train} = 32, R^2_{Train} = 0.960, Q^2_{LOO} = 0.902, Q^2_{BOOT} = 0.800, $RMSE_{Train}$ = 0.218	n_{EXT} = 9, Q^2_{EXT} = 0.925, *CCC* = 0.963, $RMSE_{EXT}$ = 0.294		
MLR	log*RP*	4	41	n_{Train} = 32, R^2_{Train} = 0.909, Q^2_{LOO} = 0.855, Q^2_{BOOT} = 0.770, $RMSE_{Train}$ = 0.331	n_{EXT} = 9, Q^2_{EXT} = 0.908, *CCC* = 0.959, $RMSE_{EXT}$ = 0.326		
kNN	Classification	3 (3)	445	n_{Train} = 333, Q_{Train} = 0.868, $S_{n\text{-}Train}$ = 0.867, $S_{p\text{-}Train}$ = 0.868	n_{EXT} = 112, Q_{EXT} =0.866, $S_{n\text{-}EXT}$ = 0.841, $S_{p\text{-}EXT}$ = 0.898	Yes	Yang et al., 2023b
kNN	log*RP*	2 (3)	88	n_{Train} = 66, R^2_{Train} = 0.927, Q^2_{LOO} = 0.839, Q^2_{BOOT} = 0.810,$RMSE_{Train}$ = 0.354	n_{EXT} = 18, Q^2_{EXT} = 0.833, *CCC* = 0.910, $RMSE_{EXT}$ = 0.560	Yes	
kNN	log*RP*	2 (3)	41	n_{Train} = 30, R^2_{Train} = 0.910, Q^2_{LOO} = 0.852, Q^2_{BOOT} = 0.760, $RMSE_{Train}$ = 0.336	n_{EXT} = 9, Q^2_{EXT} = 0.870, *CCC* = 0.930, $RMSE_{EXT}$ = 0.390	Yes	
GBDT	Classification	5	445	n_{Train} = 333, Q_{Train} = 0.982, $S_{n\text{-}Train}$ = 0.982, $S_{p\text{-}Train}$ = 0.982	n_{EXT} = 112, Q_{EXT} = 0.902, $S_{n\text{-}EXT}$ = 0.889, $S_{p\text{-}EXT}$ = 0.918	Yes	This study

[a] PLS: Partial-least-squares regression; MLR: Multiple linear regression; CoMSIA: Comparative molecular similarity indices analysis; GBDT: gradient boosting decision tree; kNN: *k*-nearest neighbor; LIB-SVM: Library for support vector machines; PLS-DA: Partial least squares-discriminant analysis; LDA: Linear discriminant analysis; GFA-MLR: genetic function approximation (GFA) - multiple linear regression (MLR).

[b] log*RP*: logarithm of the relative competitive potency; log*K*: logarithm of the binding constant.

[c] m: number of predictive variables; Numbers in parentheses: value of k (number of nearest neighbor); -: number of predictive variables is not available.

[d] n: number of total compounds.

[e] n_{train}: the numbers of model compounds in training set; R^2_{train}: the squared correlation coefficient of observed and predicted values for the training set; Q^2_{LOO}: the leave-one out cross validation Q^2; Q^2_{BOOT}: bootstrapping coefficient; Q^2_{CUM}: the total variation of the dependent variables that can be predicted by all of the extracted PLS components; $RMSE_{train}$: the root mean square errors for the training set; Q_{Train}: predictive accuracy of training set; $S_{n\text{-}Train}$: sensitivity of training set; $S_{p\text{-}Train}$: specificity of training set.

[f] n_{EXT}: the numbers of model compounds in validation set; Q^2_{EXT}: the externally explained variance; CCC: the concordance correlation coefficient; $RMSE_{EXT}$: the root mean square errors for the validation set; Q_{EXT}: predictive accuracy of validation set; $S_{n\text{-}EXT}$: sensitivity of validation set; $S_{p\text{-}EXT}$: sensitivity of validation set; specificity of validation set.

[g] AD: applicability domain.

Table S2 Reagents purchase information of the model chemicals.

Reagents and Chemicals	CAS NO.	Purity	Manufacturer
3,3′,5-tetraiodo-L-thyronine (T_3)	006893-02-3	98%	TCI (Shanghai) Development Co., Ltd. (Shanghai, China)
3,3′,5,5′-tetraiodo-L-thyronine (T_4)	000051-48-9	98%	J&K Scientific Ltd. (Shanghai, China)
Tris-HCl	001185-53-1	99.5%	J&K Scientific Ltd. (Shanghai, China)
8-Anilino-1-naphthalenesulfonate ammonium (ANSA)	028836-03-5	≥ 95%	TCI (Shanghai) Development Co., Ltd. (Shanghai, China)
Dimethyl sulfoxide (DMSO)	000067-68-5	99.8%	J&K Scientific Ltd. (Shanghai, China)
Disinfection byproducts			
3,5-diiodo-2-hydroxybenzaldehyde (2-DIHBA)	002631-77-8	97%	Aladding (Shanghai, China)
2,6-Dibromo-p-benzoquinone (2,6-DBBQ)	019643-45-9	97%	Bide Pharmatech Ltd. (Shanghai, China)
2,6-Dichloro-p-benzoquinone (2,6-DCBQ)	000697-91-6	> 98%	Aladding
Bromochlorophenol Blue (BCPB)	002553-71-1	95%	Aladding (Shanghai, China)
2-bromo-6-chloro-4-nitrophenol (2,6-BCNP)	020294-55-7	97%	Bide Pharmatech Ltd. (Shanghai, China)
2,5-Dibromo-p-benzoquinone (2,5-DBBQ)	001633-14-3	> 98%	Aladding (Shanghai, China)
2,6-Diiodo-4-nitrophenol (2,6-DINP)	000305-85-1	98%	Macklin (Shanghai, China)
3,5-diiodo-4-hydroxybenzaldehyde (4-DIHBA)	001948-40-9	≥ 98%	Macklin (Shanghai, China)
Tetrachloro-1,4-benzoquinone (TCBQ)	000118-75-2	> 98%	TCI (Shanghai) Development Co., Ltd. (Shanghai, China)
3-methyl-2-nitrophenol (3-MNP)	004920-77-8	98%	J&K Scientific Ltd. (Shanghai, China)
3,5-dichlorobisphenol A (3,5-DCBPA)	014151-65-6	98%	Toronto Research Chemicals (North York, ON, Canada)
N,N-diphenylnitrous amide (N-DNA)	000086-30-6	98%	Macklin (Shanghai, China)
4-bromo-2,6-ditert-butylphenol (BDTBP)	001139-52-2	98%	Macklin (Shanghai, China)
Pesticides			
Flupyradifurone (FPFO)	951659-40-8	98%	Bide Pharmatech Ltd. (Shanghai, China)
Imidacloprid (IMI)	105827-78-9	97%	Macklin (Shanghai, China)
Pharmaceuticals and personal care products			
Triclosan (TCS)	003380-34-5	97%	Aladding (Shanghai, China)
Triclocarban (TCC)	000101-20-2	98%	Macklin (Shanghai, China)
Methylparaben (MeP)	000099-76-3	99%	J&K Scientific Ltd. (Shanghai, China)
Alkylphenols			
Nonylphenol (NP)	000104-40-5	98%	Macklin (Shanghai, China)
Perfluoroalkyl and polyfluoroalkyl substances			
6:2 fluorotelomer sulfonic acid (6:2 FTSA)	027619-97-2	98%	Aladding(Shanghai, China)
Plasticizers			
Benzyl butyl phthalate (BBP)	000085-68-7	> 97%	TCI (Shanghai) Development Co., Ltd. (Shanghai, China)
Tire additives and their derivatives			
N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine (6PPD)	000793-24-8	≥ 98%	Macklin (Shanghai, China)

Reagents and Chemicals	CAS NO.	Purity	Manufacturer
N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine quinone(6PPDQ)	2754428-18-5	95%	Yanshen Technology Co., Ltd. (Jilin, China)
2-Aminobenzothiazole (NHBT)	000136-95-8	97%	Aladding (Shanghai, China)
2-Hydroxybenzothiazole (OHBT)	000934-34-9	98%	Macklin (Shanghai, China)
N,N-Diphenylguanidine (DPG)	000102-06-7	97%	Aladding (Shanghai, China)
N,N -Diphenylurea (DPU)	000102-07-8	98%	Aladding (Shanghai, China)
4-hydroxydiphenylamine (4-HDPA)	000122-37-2	98%	Macklin (Shanghai, China)
Hexa(methoxymethyl) melamine (HMMM)	003089-11-0	98%	Aladding (Shanghai, China)

Table S3 Experimental data on the binding affinity of chemicals with *Gobiocypris rarus* TTR from our previous study

NO.	CAS NO.	Chemical name	IC_{50} (nM)	log*RP*(T_4)	Reference
1	000088-06-2	2,4,6-trichlorophenol	1109±96.9	-0.0475±0.0521	Zhao et al., 2023
2	000118-79-6	2,4,6-tribromophenol	567±39.0	0.244±0.0466	
3	000609-23-4	2,4,6-triiodophenol	359±26.5	0.442±0.0480	
4	005324-13-0	4-chloro-2,6-dibromo-phenol	749±48.0	0.123±0.0453	
5	000099-28-5	4-nitro-2,6-dibromophenol	383±0	0.414±0.0358	
6	002973-77-5	3,5-dibromo-4-hydroxybenzaldehyde	1880±105	-0.277±0.0432	
7	000320-72-9	3,5-dichlorosalicylic acid	9330±517	-0.972±0.0431	
8	004068-58-0	3-bromo-5-chlorosalicylic acid	8419±475	-0.928±0.0433	
9	003147-55-5	3,5-dibromosalicylic acid	6276±454	-0.800±0.0476	
10	003337-62-0	3,5-dibromo-4-hydroxybenzoic acid	237268±37091	-2.38±0.0767	
11	002432-14-6	2,6-dibromo-4-methylphenol	3446±184	-0.540±0.0426	
12	002887-72-1	3,5-dibromo-4-hydroxyacetophenone	923±51.7	0.0322±0.0432	
13	001689-84-5	3,5-dibromo-4-hydroxybenzonitrile	732±66.8	0.133±0.0534	
14	000609-21-2	4-amino-2,6-dibromophenol	13409±711	-1.13±0.0425	
15	035852-57-4	3,5-dibromo-4-hydroxybenzotrifluoride	391±23.1	0.405±0.0440	
16	041727-47-3	3,5-dibromo-4-hydroxybenzoic acid methyl ester	512±33.3	0.288±0.0456	
17	000088-82-4	2,3,5-triiodobenzoic acid	51726±5644	-1.72±0.0593	
18	078824-10-9	3,5-dibromosulfanilic acid, sodium salt	261310±23800	-2.42±0.0533	
19	000055-18-5	Nitrosodiethylamine	/	/	
20	003252-43-5	Dibromoacetonitrile	/	/	
21	000079-43-6	Dichloroacetic acid	/	/	
22	000683-57-8	Bromoacetamide	/	/	
23	000075-27-4	Bromodichloromethane	/	/	
24	016086-14-9	Dichloroacetaldehyde hydrate	/	/	
25	000084-66-2	Diethyl phthalate	/	/	
26	000115-96-8	Tris(2-chloroethyl) phosphate	/	/	

Table S4 Selected molecular descriptors in the modeling

NO		Descriptor variables	Selection reasons
1	log$D$[a]	logarithm of the n-octanol/water distribution coefficient	log$D$ could be used to describe the hydrophobic interactions and the distribution ability of ionizable chemical from water to TTR, and was selected as a critical predictive variable in previous modeling related to human TTR (Yang et al., 2019, 2021b)
Chemical form adjusted quantum chemical descriptors [b]			
2	$dipole_{adj}$	the chemical form adjusted dipole moment	Chemical form adjusted quantum chemical descriptors could be employed to characterize the potential hydrogen bonding, the electron donor – acceptor interactions and the ionic pair interactions between ionizable chemical and TTR, and some of chemical form adjusted quantum chemical descriptors had been selected as critical predictive variable in previous modeling related to human TTR (Yang et al., 2019, 2021b), fish TTR (Zhao et al., 2023)
3	$polar_{adj}$	the chemical form adjusted molecular polarizability	
4	$E_{HOMO\text{-}adj}$	the chemical form adjusted energies of highest occupied molecular orbital	
5	$E_{LUMO\text{-}adj}$	the chemical form adjusted energies of lowest unoccupied molecular orbital	
6	μ_{adj}	the chemical form adjusted chemical potential	
7	η_{adj}	the chemical form adjusted chemical hardness	
8	ω_{adj}	the chemical form adjusted electrophilicity index	
9	qO^{-}_{adj}	the chemical form adjusted most negative net atomic charge on an oxygen atom	
10	qX^{-}_{adj}	the chemical form adjusted most negative net atomic charge on a halogen atom (F, Cl, Br, I)	
11	qD^{-}_{adj}	the most negative net atomic charge on an electron donor atom (O, N, X, S, P)	
12	V_{adj}	the chemical form adjusted molecular volume	
13	V_{sadj}	the chemical form adjusted average potentials on the molecular surface	
14	Π_{adj}	the chemical form adjusted average deviation of surface potential	

[a] logD_{OW} were obtained from the Calculator Plugins from MarvinSketch 15.6.29.0, 2015, ChemAxon (http://www.chemaxon.com) at pH = 7.40.

[b] Gaussian 16 was employed to optimize the structures of model substance at the B3LYP/6-31 + G (d,p) level (Frisch et al., 2016). The polarized continuum model (PCM) was used to describe the water solvent effect. Then, the 13 chemical form adjusted quantum chemical descriptors were calculated as following method (Yang et al., 2021b):

$$X_{\mathrm{adj}} = X_{\mathrm{M}} \cdot \delta_{\mathrm{M}} + \sum_{i=1}^{n} X_{\mathrm{I}\text{-}i} \cdot \delta_{\mathrm{I}\text{-}i} \tag{8}$$

where X_{M} and $X_{\mathrm{I}\text{-}i}$ are the neutral and *i*-ionic form descriptors, respectively. The neutral and/or ionic form of *dipole*, *polar*, E_{HOMO}, E_{LUMO}, qO−, qX−, qD−, and volume were extracted directly from the Gaussian 16 output .log file. The neutral and/or ionic form of *V*s and *Π* molecular surface potential descriptors were calculated by GsGrid V1.7 (Lu, 2010) from Gaussian 16 output .cub file. The μ_{adj}, η_{adj}, and ω_{adj} was calculated by following equation:

$$\mu_{\mathrm{adj}} = (E_{\mathrm{HOMO\text{-}adj}} + E_{\mathrm{LUMO\text{-}adj}})/2 \tag{9}$$

$$\eta_{\mathrm{adj}} = (E_{\mathrm{LUMO\text{-}adj}} - E_{\mathrm{HOMO\text{-}adj}})/2 \tag{10}$$

$$\omega_{\mathrm{adj}} = \mu^2_{\mathrm{adj}}/2\eta_{\mathrm{adj}} \tag{11}$$

Table S5 Experimental data on the binding affinity of chemicals with little skate (*Leucoraja erinacea*) TTR (Suzuki et al., 2015)

NO.	Name	CAS NO.	Observed	Predicted		
				CARTSAR	RandomFoSAR	GBDTSAR
1	3,3',5-Triiodo-L-thyronine*	006893-02-3	A	A	A	A
2	L-Thyroxine	000051-48-9	A	A	A	A
3	3,3',5-Triiodo-D-thyronine	066701-15-3	A	A	A	A
4	3,3‘,5’-triiodo-L-thyronine (reverse T3 or rT3)	005817-39-0	A	A	A	A
5	3,3‘,5-triiodothyroacetic acid*	000051-24-1	A	A	A	A
6	3,3’,5,5‘-tetraiodothyroacetic acid	000067-30-1	A	A	A	A
7	3,5-diiodo-L-tyrosine	000300-39-0	I	I	I	I
8	3-iodo-L-tyrosine*	000070-78-0	I	I	I	I
9	pentachlorophenol	000087-86-5	A	A	A	A
10	2,4,6-triiodophenol*	000609-23-4	A	A	A	A
11	2,4,6-tribromophenol	000118-79-6	A	A	A	A
12	2,4,6-trichlorophenol	000088-06-2	A	A	A	A
13	pentabromophenol	000608-71-9	A	A	A	A
14	3,3’,5,5‘-Tetrabromobisphenol A	000079-94-7	A	A	A	A
15	3,3‘,5,5’-tetrachlorobisphenol A	000079-95-8	A	A	A	A
16	3,5-diiodo-L-thyronine	001041-01-6	A	A	A	A
17	Ioxynil (3,5-diiodo-4-hydroxybezonitril) *	001689-83-4	A	A	A	A
18	n-butylbenzyl phthalate*	000085-68-7	I	I	I	I
19	bis(2-ethylhexyl) phthalate*	000117-81-7	I	I	I	I
20	dicyclohexyl phthalate*	000084-61-7	I	I	I	I
21	di-n-butyl phthalate	000084-74-2	I	I	I	I
22	di-2-ethyl phthalate	000084-66-2	I	I	I	I
23	mirex	002385-85-5	I	I	I	I
24	malathion (diethyl 2-dimethoxyphosphinothioylsulfanylbutanedioate	000121-75-5	I	I	I	I
25	dicofol (Kelthane, 2,2,2-trichloro-1,1-bis(4-chloro-phenyl)ethanol	000115-32-2	I	I	I	I
26	2,4-Dichlorophenoxyacetic acid	000094-75-7	I	I	I	I
27	Methoprene (isopropyl (E,E0)-(RS)-11-methoxy-3,7,11-trimethyldodeca-2,4-dienoate)	040596-69-8	I	I	I	I
28	acetochlor (2-chloro-N-(ethoxymethyl)-N-(2-ethyl-6-methylphenyl)acetamide) *	034256-82-1	I	I	I	I
29	benzophenone	000119-61-9	I	I	I	I

NO.	Name	CAS NO.	Observed	Predicted		
				CARTSAR	RandomFoSAR	GBDTSAR
30	bis(2-ethylhexyl) adipate*	000103-23-1	I	I	I	I
31	tributyltin (IV) chloride	001461-22-9	I	I	I	I
32	a-benzoepin (a-endosulfan; 6,7,8,9,10,10-hexachloro-1,5,5a, 6,9,9a-hexahydro-6,9,methane-2,4,3-benzodiathiepine)	000959-98-8	I	I	I	I
33	benzo[a]pyrene	000050-32-8	I	I	I	I
34	Bisphenol A	000080-05-7	I	I	I	I
35	4-nonylphenol	000104-40-5	I	I	I	I
36	o-t-butylphenol	000088-18-6	I	I	I	I
37	2-Isopropylphenol	000088-69-7	I	I	I	I
38	2,4-dinitrophenol	000051-28-5	I	I	I	I

* the compounds in validation set.

Table S6 Experimental data on the binding affinity of chemicals with seabream (*Sparus aurata*) TTR (Morgado et al., 2007; Zhang et al., 2018)

NO.	Chemical Name	CAS NO.	Observed	Predicted		
				CARTSAR	RandomFoSAR	GBDTSAR
1	L-Thyroxine	000051-48-9	A	A	A	A
2	3,3',5-Triiodo-L-thyronine	006893-02-3	A	A	A	A
3	Ioxynil	001689-83-4	A	A	A	A
4	Pentachlorophenol*	000087-86-5	A	A	A	A
5	Diethylstilbestrol	006898-97-1	A	A	A	A
6	4-nonylphenol*	000104-40-5	A	A	A	A
7	2,2',4,5'-tetrabrominated diphenyl ethers	243982-82-3	A	A	A	A
8	3,3',5,5'-Tetrabromobisphenol A	000079-94-7	A	A	A	A
9	2,2',4,4'-tetrabrominated diphenyl ethers	005436-43-1	A	A	A	A
10	2,2',4,4',5-pentabrominated diphenyl ethers*	060348-60-9	A	A	A	A
11	3,4',5-tribrominated diphenyl ethers	407606-57-9	A	A	A	A
12	2,4,4'-tribrominated diphenyl ethers	041318-75-6	A	A	A	A
13	2,4,6-tribromophenol	000118-79-6	A	A	A	A
14	2,2',6-tribrominated diphenyl ethers*	147217-73-0	A	A	A	A
15	2,2',4,4',6-pentabrominated diphenyl ethers	189084-64-8	A	A	A	A
16	3,4,5-tribrominated diphenyl ethers	337513-54-9	A	A	A	A
17	6-HO-2,2',4,4'-tetrabrominated diphenyl ethers	079755-43-4	A	A	A	A
18	bisphenol A	000080-05-7	I	I	I	I
19	2,2',4,4',5,5'-hexabrominated diphenyl ethers	068631-49-2	I	I	I	I
20	3,3',4,5,5'-pentabrominated diphenyl ethers	446254-86-0	I	I	I	I
21	2,2',4,4',6,6'-hexabrominated diphenyl ethers*	035854-94-5	I	I	I	I

NO.	Chemical Name	CAS NO.	Observed	Predicted		
				CARTSAR	RandomFoSAR	GBDTSAR
22	3,3',4,4',5,5'-hexabrominated diphenyl ethers*	446255-18-1	I	I	I	I
23	2,2',3,4,4',5,6-heptabrominated diphenyl ethers	189084-67-1	I	I	I	I
24	2,2',3,4,4',5',6-heptabrominated diphenyl ethers	207122-16-5	I	I	I	I
25	2,2',3,4,5,5',6-heptabrominated diphenyl ethers*	405237-86-7	I	I	I	I
26	2,3,3',4,4',5,6-heptabrominated diphenyl ethers*	189084-68-2	I	I	I	I
27	2,2',3,3',4,4',5,5',6-nonabrominated diphenyl ethers	063387-28-0	I	I	I	I
28	2,2',3,3',4,4',5,5',6,6'-decabrominated diphenyl ethers	001163-19-5	I	I	I	I
29	Benzene, 1,1'-(1-methylethy lidene) bis[3,5-dibromo-4-(2,3-dibromopropoxy)-	021850-44-2	I	I	I	I
30	hexabromocyclododecane alpha	138257-19-9	I	I	I	I
31	hexabromocyclododecane beta	138257-18-8	I	I	I	I
32	hexabromocyclododecane gamma	169102-57-2	I	I	I	I
33	2,2′,4,4′-tetrahydroxybenzophenone	000131-55-5	A	A	A	A
34	2-(3-chloro-2-methylanilino)pyridine-3-carboxylic acid (clonixin)*	017737-65-4	A	A	A	A
35	pentadecafluorooctanoic acid	000335-67-1	A	A	A	A
36	3,5,6-trichloro-2-pyridinol	006515-38-4	A	A	A	A
37	2,4,5-trichlorophenoxyacetic acid	000093-76-5	A	A	A	A

* the compounds in validation set.

Table S7 Experimental data on the binding affinity of chemicals with human TTR (Yang et al., 2021b)

NO	Chemical name	CAS	Observed log*RP*	Predicted log*RP*
1	2,4,6-triiodophenol	000609-23-4	A	A
2	4-bromo-2,6-dichlorophenol*	003217-15-0	A	A
3	4-chloro-2,6-dibromo-phenol*	005324-13-0	A	A
4	4-nitro-2,6-dichlorophenol	000618-80-4	A	A
5	4-nitro-2,6-dibromophenol	000099-28-5	A	A
6	3,5-dichloro-4-hydroxybenzaldehyde	002314-36-5	A	A
7	3,5-dibromo-4-hydroxybenzaldehyde*	002973-77-5	A	A
8	3-bromo-5-chloro-4-hydroxybenzaldehyde*	001849-76-9	A	A
9	5-chlorosalicylic acid*	000321-14-2	A	A
10	5-bromosalicylic acid	000089-55-4	A	A
11	3,5-dichlorosalicylic acid*	000320-72-9	A	A
12	3-bromo-5-chlorosalicylic acid	004068-58-0	A	A
13	3,5-dibromosalicylic acid*	003147-55-5	A	A
14	3,5-dichloro-4-hydroxybenzoic acid*	003336-41-2	A	A
15	3,5-dibromo-4-hydroxybenzoic acid	003337-62-0	A	A
16	2,6-dibromo-4-methylphenol	002432-14-6	A	A
17	3,5-dibromo-4-hydroxyacetophenone	002887-72-1	A	A
18	4-amino-2,6-dibromophenol*	000609-21-2	A	I
19	3,5-dibromo-4-hydroxybenzotrifluoride	035852-57-4	A	A
20	3,5-dibromo-4-hydroxybenzoic acid methyl ester	041727-47-3	A	A
21	Pentachlorophenol	000087-86-5	A	A
22	Hexachlorophene	000070-30-4	A	A
23	2,4,6-Trichlorophenol	000088-06-2	A	A
24	2,4,5-Trichlorophenol*	000095-95-4	A	A
25	2,6-Dichlorophenol*	000087-65-0	A	A

26	2,3-Dichlorophenol	000576-24-9	A	A
27	2-Chlorophenol	000095-57-8	A	A
28	3-Chlorophenol*	000108-43-0	A	I
29	benzene	000071-43-2	I	I
30	1,2-dichlorobenzene	000095-50-1	I	I
31	3,3',4,4'-Tetrachlorobiphenyl*	032598-13-3	I	I
32	phenol	000108-95-2	I	I
33	4-hydroxybiphenyl	000092-69-3	A	A
34	4-chlorophenol	000106-48-9	I	I
35	2,4,5-trichlorophenoxyacetic acid methyl ester	001928-37-6	A	A
36	2,4,5-trichlorophenoxyacefic acid	000093-76-5	A	A
37	2,4-dichlorophenoxyacetic acid*	000094-75-7	A	A
38	2,4-dichlorophenoxybutyric acid*	000094-82-6	A	A
39	2-(2,4-dichlorophenoxy)propionic acid *	000120-36-5	A	A
40	4-(chloro-o-tolyloxy) acetic acid	000094-74-6	A	A
41	4-(4-chloro-2-methylphenoxy)butyric acid	000094-81-5	A	A
42	2-(2,4,5-trichlorophenoxy)propionic acid	000093-72-1	A	A
43	2,4-dinitrophenol	000051-28-5	A	A
44	2,4-dinitro-6-methylphenol	000534-52-1	A	A
45	2,4-dinitro-6-sec-butylphenol	000088-85-7	A	A
46	1,4-Dichlorobenzene	000106-46-7	I	I
47	1,3,5-Trichlorobenzene	000108-70-3	A	A
48	hexachlorobenzene	000118-74-1	A	A
49	methoxychlor*	000072-43-5	I	I
50	p,p'-DDD	000072-54-8	A	A
51	1, l,l-trichloro-2,2-bis(chlorophenyl)ethanol (Dicofol)	000115-32-2	A	A
52	paraoxon	000311-45-5	I	I
53	ethyl-azinphos	002642-71-9	I	I
54	malathion	000121-75-5	A	A

55	ethyl-parathion	000056-38-2	A	A
56	ethyl-bromophos	004824-78-6	A	I
57	2-hydroxybiphenyl	000090-43-7	A	A
58	trichloroethylene	000079-01-6	I	I
59	perchloroethylene	000127-18-4	I	I
60	tetrachloroethane*	000079-34-5	I	I
61	chloroform*	000067-66-3	I	I
62	chloral hydrate*	000302-17-0	I	I
63	hexachloroethane*	000067-72-1	I	I
64	tetrachloromethane	000056-23-5	I	I
65	trichloroacetic acid*	000076-03-9	A	I
66	hexachlorocyclohexane (y-lindane)*	000058-89-9	A	A
67	monuron*	000150-68-5	I	I
68	diuron	000330-54-1	I	I
69	neburon	000555-37-3	I	I
70	linuron*	000330-55-2	A	A
71	chloroxuron	001982-47-4	A	A
72	catechol*	000120-80-9	I	I
73	resorcinol	000108-46-3	I	I
74	o-cresol	000095-48-7	I	I
75	3-aminophenol	000591-27-5	I	I
76	4-tert-butylphenol*	000098-54-4	I	I
77	2,6-di-tert-butyl-4-methylphenol	000128-37-0	I	I
78	pyrogallol	000087-66-1	A	A
79	trimethyltin	001631-73-8	I	I
80	triethyltin*	000997-50-2	I	I
81	endosulfan	000115-29-7	I	I
82	dioctylphtalate	000117-84-0	A	A
83	3,5-bibromo-4-hydroxybenzonitril (Bromoxynil)	001689-84-5	A	A

84	tetrachlorohydroquinone*	000087-87-6	A	A
85	2-HO-1,3,7,8-tetrachlorodibenzo-4-dioxin*	082019-03-2	A	A
86	3-HO-2,6,7,8-tetrachlorodibenzofurans	150975-86-3	A	A
87	4-HO-2',3,3',4',5-Pentachlorobiphenyl	149589-55-9	A	A
88	4-HO-2,2',3,3',4'-Pentachlorobiphenyl	150975-83-0	A	A
89	4-HO-2,3,3',4'-tetrachlorobiphenyl	150975-82-9	A	A
90	4'-HO-3,3',4,5,5'-Pentachlorobiphenyl *	130689-92-8	A	A
91	4-HO-3,3',4'-trichlorobiphenyl	124882-64-0	A	A
92	5'-HO-2,3,3',4,4'-Pentachlorobiphenyl	150975-81-8	A	A
93	5-HO-3,3',4,4'-tetrachlorobiphenyl	042208-08-2	A	A
94	7-HO-2,3,8-trichlorodibenzo-4-dioxin	082019-04-3	A	A
95	2'-HO-2,3,3',4,4'-Pentachlorobiphenyl	150975-80-7	A	A
96	4,4'-(HO)2-2,3,3',5,5'-pentachlorobiphenyl	150975-84-1	A	A
97	4,4'-(HO)2-3,3',5,5'-tetrachlorobiphenyl*	013049-13-3	A	A
98	2-HO-7,8-dichlorodibenzofurans	074423-77-1	I	I
99	8-HO-2,3,4-trichlorodibenzofurans*	103124-63-6	I	A
100	8-HO-2,3-dichlorodibenzo-4-dioxin	097741-80-5	I	I
101	2,3,3',4,4'-Pentachlorobiphenyl	032598-14-4	I	I
102	3'-HO-2,4,6-trichlorobiphenyl	014962-30-2	I	A
103	1,1,1-Trichloro-2-(2-chlorophenyl)-2-(4-chlorophenyl)ethane	000789-02-6	I	I
104	1,1-Dichloro-2,2-bis(p-chlorophenyl)ethylene*	000072-55-9	I	I
105	p,p' -Dichlorodiphenyltrichloroethane	000050-29-3	I	I
106	Acetochlor	034256-82-1	I	I
107	Alachlor	015972-60-8	I	I
108	Methoprene	040596-69-8	I	I
109	4-OH-3,5-dichlorobiphenyl*	001137-59-3	A	A
110	4'-OH-2,3,4,5-tetrachlorobiphenyl	067651-34-7	A	A
111	4'-OH-2,3',4,6-tetrachlorobiphenyl	189578-00-5	A	A
112	4'-OH-2,3',3,4,5-pentachlorobiphenyl	192190-09-3	A	A

113	4'-OH-2,3',4,5',6-pentachlorobiphenyl	190271-92-2	A	A
114	3,3',4,4',5-Pentachlorobiphenyl	057465-28-8	A	A
115	2,2-bis(4-chlorophenyl)ethanol	002642-82-2	A	A
116	Hexabromobenzene	000087-82-1	I	I
117	2,4,6-tribromoaniline	000147-82-0	I	I
118	2,3,5,6-Tetrabromo-p-xylene*	023488-38-2	I	I
119	2,3,4,5,6-Pentabromo-toluene	000087-83-2	I	I
120	Bisphenol A	000080-05-7	I	I
121	Monobromobisphenol A*	006073-11-6	I	I
122	Dibromobisphenol A*	029426-78-6	I	I
123	Bisphenol A diglycidyl ether	001675-54-3	I	I
124	Bisphenol A diglycidyl ether, Brominated	040039-93-8	I	I
125	Bisphenol A bis (2,3-dihydroxypropyl) ether	005581-32-8	I	I
126	Bisphenol A bis (3-chloro-2-hydroxypropyl) ether	004809-35-2	I	I
127	4-Phenoxyphenol	000831-82-3	I	I
128	2'-hydroxy-2,4,4'-trichlorodiphenyl ether	003380-34-5	A	A
129	4'-HO-2,4,6-tribrominated diphenyl ethers	218303-99-2	A	A
130	4'-HO-2,3',4,6-tetrabrominated diphenyl ethers*	218303-98-1	A	A
131	4'-HO-2,3',4,5',6-pentabrominated diphenyl ethers*	091370-78-4	A	A
132	2,4-Dibromophenol	000615-58-7	A	A
133	2,4,6-Tribromophenol	000118-79-6	A	A
134	Pentabromophenol*	000608-71-9	A	A
135	Tribromobisphenol A*	006386-73-8	A	A
136	Tetrabromobisphenol A	000079-94-7	A	A
137	Tetrachlorobisphenol A*	000079-95-8	A	A
138	2,2',6-Trichlorobiphenyl*	038444-73-4	I	I
139	3,5-Dichlorobiphenyl	034883-41-5	I	I
140	3,4,5-Trichlorobiphenyl	053555-66-1	I	I
141	3,3',5,5'-Tetrachlorobiphenyl*	033284-52-5	I	I

142	3,3',4,4',5,5'-Hexachlorobiphenyl	032774-16-6	I	I
143	2,4,4'-Trichlorobiphenyl*	007012-37-5	I	I
144	2',3,5-Trichlorobiphenyl*	037680-68-5	I	I
145	2,2',4,4'-Tetrachlorobiphenyl*	002437-79-8	I	I
146	2,2',5,5'-Tetrachlorobiphenyl	035693-99-3	I	I
147	2,2',3,5',6-Pentachlorobiphenyl*	038379-99-6	I	I
148	2,2',4,4',6-Pentachlorobiphenyl	039485-83-1	I	I
149	2,2',4,5,5'-Pentachlorobiphenyl	037680-73-2	I	I
150	2,3,3',4',6-Pentachlorobiphenyl	038380-03-9	I	I
151	2,3,3',5,5'-Pentachlorobiphenyl*	039635-32-0	I	I
152	2,2',3,4,4',5'-Hexachlorobiphenyl	035065-28-2	I	I
153	2,2',4,4',5,5'-Hexachlorobiphenyl	035065-27-1	A	A
154	2,3,3',4',5,5'-Hexachlorobiphenyl	039635-34-2	I	I
155	2,2',3,4,4',5,5'-Heptachlorobiphenyl	035065-29-3	A	A
156	2,2',4,6,6'-Pentachlorobiphenyl*	056558-16-8	I	I
157	2,3',4,4',5-Pentachlorobiphenyl	031508-00-6	I	I
158	2,2',3,3',4,4'-Hexachlorobiphenyl*	038380-07-3	I	I
159	2,2',3,3',6,6'-Hexachlorobiphenyl	038411-22-2	I	I
160	4-HO-2,3,3',4',5-Pentachlorobiphenyl	152969-11-4	A	A
161	4-HO-2,2',3,4',5,5',6-Heptachlorobiphenyl	158076-68-7	A	A
162	4'-OH-2,2',4,6-tetrachlorobiphenyl*	150304-08-8	A	A
163	4'-HO-2,3,3',5,6-pentachlorobiphenyl	189578-02-7	A	A
164	4'-HO-2,3,3',4,6-Pentachlorobiphenyl*	192190-10-6	A	A
165	4'-OH-2,2',3,5,6-pentachlorobiphenyl	150304-11-3	A	A
166	4'-HO-3,3',4,5'-tetrachlorobiphenyl*	111810-41-4	A	A
167	4'-Hydroxy-2,2',3,3',4,5'-Hexachlorobiphenyl	158076-62-1	A	A
168	4'-Hydroxy-2,2',3,3',4,5,5'-Heptachlorobiphenyl	158076-64-3	A	A
169	3'-Hydroxy-2,2',3,4,4',5,5'-Heptachlorobiphenyl	158076-69-8	A	A
170	3,3',4,5,5'-pentabrominated diphenyl ethers	446254-86-0	A	A

171	2,2',3,4,4',5,6-heptabrominated diphenyl ethers	189084-67-1	A	A
172	2,2',3,4,5,5',6-heptabrominated diphenyl ethers	405237-86-7	A	A
173	2,3,3',4,4',5,6-heptabrominated diphenyl ethers	189084-68-2	A	A
174	6-HO-2,2',4,4'-tetrabrominated diphenyl ethers	079755-43-4	A	A
175	Benzene, 1,1'-(1-methylethylidene)bis[3,5-dibromo-4-(2,3-dibromopropoxy)-	021850-44-2	A	A
176	hexabromocyclododecane alpha	138257-19-9	A	I
177	hexabromocyclododecane beta*	138257-18-8	A	I
178	hexabromocyclododecane gamma	169102-57-2	I	I
179	2,2',6-tribrominated diphenyl ethers	147217-73-0	I	I
180	2,4,4'-tribrominated diphenyl ethers	041318-75-6	I	I
181	3,4,5-tribrominated diphenyl ethers	337513-54-9	A	A
182	3,4',5-tribrominated diphenyl ethers*	407606-57-9	I	I
183	2,2',4,4'-tetrabrominated diphenyl ethers	005436-43-1	A	A
184	2,2',4,5'-tetrabrominated diphenyl ethers	243982-82-3	A	A
185	3,3',4,5'-tetrabrominated diphenyl ethers	446254-48-4	I	I
186	2,2',4,4',5-pentabrominated diphenyl ethers	060348-60-9	I	I
187	2,2',4,4',6-pentabrominated diphenyl ethers	189084-64-8	I	I
188	2,2',4,4',5,5'-hexabrominated diphenyl ethers	068631-49-2	I	I
189	2,2',4,4',6,6'-hexabrominated diphenyl ethers	035854-94-5	I	I
190	3,3',4,4',5,5'-hexabrominated diphenyl ethers*	446255-18-1	A	I
191	2,2',3,4,4',5',6-heptabrominated diphenyl ethers	207122-16-5	I	I
192	2,2',3,3',4,4',5,5',6-nonabrominated diphenyl ethers	063387-28-0	I	I
193	2,2',3,3',4,4',5,5',6,6'-decabrominated diphenyl ethers	001163-19-5	I	I
194	4-HO-2,2',3,4'-tetrabrominated diphenyl ethers*	602326-22-7	A	A
195	3-HO-2,2',4,4'-tetrabrominated diphenyl ethers	024949-31-3	A	A
196	5-HO-2,2',4,4'-tetrabrominated diphenyl ethers	602326-30-7	A	A
197	4'-HO-2,2',4,5'-tetrabrominated diphenyl ethers	602326-23-8	A	A
198	2'-HO-2,3',4,4'-tetrabrominated diphenyl ethers*	184174-87-6	A	A
199	2,3',5',6-Tetrachlorobiphenyl	074338-23-1	I	I

200	2,3',4,5',6-Pentachlorobiphenyl	056558-18-0	I	I
201	2,3,5,6-Tetrafluoro-4-(pentafluorophenyl)phenol	002894-87-3	A	A
202	3'-OH-2,3,4,5-tetrachlorobiphenyl	067651-37-0	I	A
203	4'-HO-2,3',5,5'-tetrachlorobiphenyl*	245084-57-5	A	A
204	2,3',4,5'-tetrabrominated diphenyl ethers	446254-38-2	I	I
205	6'-HO-2,2',4,5'-tetrabrominated diphenyl ethers	497069-16-6	A	A
206	6-HO-2,2',4,4',5-pentabrominated diphenyl ethers	297742-10-0	A	A
207	6-MeO-2,2',4,4'-tetrabrominated diphenyl ethers	102739-99-1	I	I
208	2'-MeO-2,3',4,5'-tetrabrominated diphenyl ethers*	096920-28-4	I	I
209	2,4-difluorophenol	000367-27-1	I	I
210	2,6-difluorophenol	028177-48-2	I	I
211	2,4,6-trifluorophenol*	002268-17-9	I	I
212	Tetraiodothyroacetic acid	000067-30-1	A	A
213	Ibuprofen	015687-27-1	I	I
214	Furosemide	000054-31-9	I	I
215	Sodium diclofenac*	015307-79-6	A	A
216	Mefenamic acid	000061-68-7	A	A
217	Bezafibrate	041859-67-0	I	I
218	Clofibrate	000637-07-0	I	I
219	Clofibric acid	000882-09-7	I	I
220	Diatrizoic acid	000117-96-4	I	I
221	Carbamazepine	000298-46-4	I	I
222	Dichlofluanid	001085-98-9	I	I
223	Trifluoroacetic acid	000076-05-1	I	I
224	2-Fluoro-4-nitrophenol	000403-19-0	I	I
225	2-Nitro-4- (trifluoromethyl) phenol	000400-99-7	I	I
226	Trifluoperazine dihydrochloride*	000440-17-5	I	I
227	l-Cyhalotrin	091465-08-6	I	I
228	Chlorpyrifos	002921-88-2	I	A

229	4-OctylPhenol	001806-26-4	I	I
230	7H-Perfluoroheptanoic acid	001546-95-8	A	A
231	2H-perfluoro-2-octenoic acid	070887-88-6	A	A
232	1-Octanesulfinic acid	000647-29-0	A	A
233	1-Butanesulfonic acid	000375-73-5	A	A
234	Perfluorodecanoic acid	000335-76-2	A	A
235	Perfluorododecanoic acid	000307-55-1	A	A
236	Perfluoroheptanoic acid*	000375-85-9	A	A
237	Perfluorohexanoic acid	000307-24-4	A	A
238	1-Hexanesulfonic acid*	000355-46-4	A	A
239	Perfluorononanoic aci	000375-95-1	A	A
240	Perfluorooctanoic acid*	000335-67-1	A	A
241	Perfluorotetradecanoic acid	000376-06-7	A	A
242	Perfluoroundecanoic acid	002058-94-8	A	A
243	1-Octanesulfonic acid*	001763-23-1	A	A
244	Perfluorooctane sulfonamide	000754-91-6	A	A
245	Hexanoic acid	000142-62-1	I	I
246	Octanoic acid (Caprylic acid)	000124-07-2	I	I
247	Decanoic acid (Capric acid)	000334-48-5	I	I
248	1-Decanesulfonic acid	000335-77-3	I	I
249	2-Perfluorohexyl ethanol	000647-42-7	I	I
250	2-Perfluorooctyl ethanol	000678-39-7	I	I
251	2-(N-methylperfluoro-1-octane sulfonamido) ethanol*	024448-09-7	I	I
252	2-(N-ethylperfluoro-1-octane sulfonamido) ethanol	001691-99-2	I	I
253	N,N-dimethyl perfluorooctane sulfonamide*	213181-78-3	I	I
254	N-methyl perfluorooctane sulfonamide*	031506-32-8	I	I
255	N-ethyl perfluorooctane sulfonamide*	004151-50-2	I	I
256	2'-HO-2,4,4'-tribrominated diphenyl ethers*	004656-58-0	A	A
257	2'-HO-4-monobrominated diphenyl ethers	300560-92-3	A	A

258	2'-HO-2,3',4,5'-tetrabrominated diphenyl ethers	080246-25-9	A	A
259	2'-HO-2,4-dibrominated diphenyl ethers	602326-09-0	A	A
260	3'-HO-2,4,4'-tribrominated diphenyl ethers	024949-30-2	A	A
261	3'-HO-2,4-dibrominated diphenyl ethers	602326-18-1	A	A
262	3'-HO-2,2',4,4',5,6'-hexabrominated diphenyl ethers*	1171030-72-0	A	A
263	4'-HO-2,2',4-tribrominated diphenyl ethers	602326-21-6	A	A
264	6-HO-2,2',3,4,4'-pentabrominated diphenyl ethers	035162-01-7	A	A
265	2,2',4,6'-Tetrachlorobiphenyl	068194-04-7	I	I
266	2,2',5,6'-Tetrachlorobiphenyl	041464-41-9	I	I
267	2,4,4',5-Tetrachlorobiphenyl	032690-93-0	I	I
268	2',3,3',4,5-Pentachlorobiphenyl	076842-07-4	A	A
269	2',3,4,5,6'-Pentachlorobiphenyl	074472-39-2	A	A
270	2,3',4,4',5',6-Hexachlorobiphenyl*	059291-65-5	A	A
271	2,2',3,3',4,4',5-Heptachlorobiphenyl	035065-30-6	A	A
272	2,3,3',4,4',5,6-Heptachlorobiphenyl	041411-64-7	A	A
273	perfluoro-n-pentanoic acid	002706-90-3	A	A
274	perfluorotridecanoic acid	072629-94-8	A	A
275	1-Octanesulfonic acid	027619-97-2	I	I
276	3-HO-2,2',4,4',6-pentabrominated diphenyl ethers	1093168-89-8	A	A
277	4-HO-2,2',3,4',5,5',6-heptabrominated diphenyl ethers	1364619-38-4	A	A
278	Palmitic acid (16:0)	000057-10-3	I	I
279	Linoleic acid (18:2)*	000060-33-3	A	A
280	Oleic acid (18:1)	000112-80-1	A	A
281	Arachidonic acid (20:4)	000506-32-1	A	A
282	Cholesterol	000057-88-5	A	A
283	4-Nonylphenol	000104-40-5	A	A
284	4-(Phenylmethyl)-phenol	000101-53-1	I	I
285	4-(1,1,3,3-Tetramethylbutyl)-phenol	000140-66-9	I	I
286	2-Methyl-4-(1,1,3,3-tetramethylbutyl)-phenol	002219-84-3	I	I

287	4-tert-Pentyl phenol*	000080-46-6	I	I
288	Piperine	000094-62-2	I	I
289	Isosafrole	000120-58-1	I	I
290	Celestolide*	013171-00-1	I	I
291	Galaxolide	001222-05-5	I	I
292	Phantolide	015323-35-0	I	I
293	Tonalide*	021145-77-7	I	I
294	Traseolide	068140-48-7	I	I
295	Musk ambrette	000083-66-9	I	I
296	Musk ketone	000081-14-1	I	I
297	Butylbenzyl phthalate	000085-68-7	I	I
298	Diphenyl sulfone	000127-63-9	I	I
299	Triphenyl phosphate	000115-86-6	I	I
300	Tris(2-chloro-iso-propyl) phosphate	013674-84-5	I	I
301	Perinaphthenone	000548-39-0	I	I
302	(2E)-1,4-Diphenyl-2-butene-1,4-dione*	000959-28-4	I	I
303	7H-Benz[de]anthracen-7-one	000082-05-3	I	I
304	Di-n-butyl phthalate	000084-74-2	I	I
305	Cresyldiphenyl phosphate	026444-49-5	I	I
306	Hexaethyleneglycol monododecyl ether	003055-96-7	I	I
307	Naphthenic acid	001338-24-5	I	I
308	Squalene*	000111-02-4	I	I
309	Tris(2-chloro-ethyl) phosphate	000115-96-8	I	I
310	Tris(2-ethylhexyl) phosphate	000078-42-2	I	I
311	Triclocarban	000101-20-2	I	I
312	Diclofenac*	015307-86-5	A	A
313	perfluoroheptanesulfonic acid (PFHpS)b	000375-92-8	A	A
314	2-(2′-hydroxy-3′-tert-butyl-5′-methylphenyl)-5-chlorobenzotriazole (Tinuvin 326)	003896-11-5	I	I
315	2-(2-hydroxy-3,5-ditert-butylphenyl)-5-chlorobenzotriazole(Tinuvin 327)	003864-99-1	I	I

316	3,5,6-trichloro-2-pyridinol (3,5,6-TC2P)b	006515-38-4	A	A
317	2-tert-butyl-4-(2,4-dichloro-5-isopropoxyphenyl)-5-oxo-1,3,4-oxadiazoline(Oxadiazon)*	019666-30-9	I	I
318	1-[(2,4-dichlorophenyl)aminocarbonyl]-1-cyclopropanecarboxylic acid(cyclanilide)	113136-77-9	I	I
319	3,6-dichloro-2-methoxybenzoic acid (dicamba)	001918-00-9	I	I
320	4-nitrophenol*	000100-02-7	I	I
321	mono-[2-(perfluorohexyl)ethyl] phosphate(6:2 monoPAP)*	057678-01-0	I	I
322	mono[2-(perfluorooctyl)ethyl]phosphate(8:2monoPAP)	057678-03-2	I	I
323	sodium bis(1H,1H,2H,2H-perfluorodecyl)phosphate(6:2PAP)	000678-41-1	I	I
324	sodium bis(1H,1H,2H,2H-perfluorooctyl)phosphate(8:2PAP)*	057677-95-9	I	I
325	perfluorodecyl phosphonic acid (C10-PFPA)	052299-26-0	A	A
326	tris(isobutyl) phosphate(TIBP)	000126-71-6	I	I
327	tris(2-butoxyethyl) phosphate(TBOEP)	000078-51-3	I	I
328	methyl paraben(MP)	000099-76-3	I	I
329	ethyl paraben(EP)	000120-47-8	A	A
330	propyl paraben(PP)	000094-13-3	A	A
331	butyl paraben(BP)	000094-26-8	A	A
332	2-nitro-5-(2-chloro-4-trifluoromethylphenoxy)benzoic acid*	050594-66-6	I	A
333	2,2′-dihydroxy-4,4′-dimethoxybenzophenone	000131-54-4	I	I
334	4,4′-dihydroxydiphenyl sulfone	000080-09-1	A	A
335	2-(3-chloro-2-methylanilino)pyridine-3-carboxylic acid	017737-65-4	A	A
336	2,6-dinitro-p-cresol	000609-93-8	A	A
337	diphenolic acid	000126-00-1	I	I
338	2-[(4-amino-3,5-dichloro-6-fluoro-2-pyridinyl)oxy]acetic acid	069377-81-7	A	A
339	L-γ-glutamyl-p-nitroanilide	067953-08-6	I	I
340	2-[4-(methylsulfonyl)-2-nitrobenzoyl]-1,3-cyclohexanedione*	104206-82-8	A	I
341	3,5,6-trichloro-4-aminopicolinic acid	001918-02-1	A	A
342	1-(4-sulfophenyl)-3-carboxy-5-pyrazolone	000118-47-8	I	I
343	3,5,6-trichloro-2-pyridinyloxyacetic acid	055335-06-3	A	A
344	5-Hydroxy-2,2',3,4,4',6,5'-Heptachlorobiphenyl *	1337921-25-1	A	A

345	3'-Hydroxy-2,2',3,4,4',5,6'-Heptachlorobiphenyl	941713-67-3	A	A
346	4'-Hydroxy-2,2',3,3',4,5,5',6'-OCTACHLOROBIPHENYL	473230-69-2	A	A
347	3'-Hydroxy-2,2',3,4,4',5,5',6-OCTACHLOROBIPHENYL	941713-71-9	A	A
348	4,4'-(OH)2-2,2',3,3',5,5',6,6'-OCTACHLOROBIPHENYL *	021647-18-7	A	A
349	4-Hydroxy-2,2',3,4',5,5'-Hexachlorobiphenyl	145413-90-7	A	A
350	3'-Hydroxy-2,2',3,4,4',5'-HEXACHLOROBIPHENYL *	149589-59-3	A	A
351	4-OH Heptachlorostyrene*	077212-81-8	A	A
352	perfluorohexylphosphonic acid (C6-PFPA)	040143-76-8	I	I
353	3,5-diiodosalicylic acid*	000133-91-5	A	A
354	2'-OH-4-chlorobiphenyl	064181-76-6	A	A
355	2´-sulfooxy-4-chloro-biphenyl	1267806-42-7	A	A
356	3'-OH-4-chlorobiphenyl*	028023-90-7	A	A
357	3´-sulfooxy-4-chlorobiphenyl	1267806-41-6	A	A
358	4'-OH-4-chlorobiphenyl	028034-99-3	A	A
359	4-chloro-4´-sulfooxy-biphenyl	1267806-40-5	A	A
360	4'-OH-3,3'-Dichlorobiphenyl*	053890-78-1	A	A
361	3,3´-dichloro-4´-sulfooxy-biphenyl	1438417-33-4	A	A
362	4'-OH-3,4-Dichlorobiphenyl	053890-77-0	A	A
363	3,4-dichloro-4´-sulfooxy-biphenyl*	1267806-45-0	A	A
364	1,1,2,2-Tetrahydroperfluoro dodecanol	000865-86-1	I	I
365	4"-OH-2,2',2",4-tetrabromo-diphenoxybenzene	1960404-22-1	A	A
366	4"-MeO-2,2',2",4-tetrabromo-diphenoxybenzene	2204277-26-7	I	I
367	2,2',2",4-tetrabromo-diphenoxybenzene*	2210225-95-7	I	I
368	2-chlorothiophenol	0006320-03-2	A	A
369	2-bromothiophenol*	0006320-02-1	A	A
370	2,3-dichlorothiophenol	0017321-95-7	A	A
371	2,4-dichlorothiophenol*	0001122-41-4	A	A
372	2,4,6-trichlorothiophenol*	0024207-66-7	A	A
373	pentachlorothiophenol*	0000133-49-3	A	A

374	pentafluorothiophenol	0000771-62-0	I	I
375	phenylboronic acid*	000098-80-6	I	I
376	2-fluorophenylboronic acid	001993-03-9	I	I
377	2-chlorophenylboronic acid	003900-89-8	I	I
378	2-bromophenylboronic acid	244205-40-1	I	I
379	2,4-difluorophenylboronic acid	144025-03-6	I	I
380	2,4-dichlorophenylboronic acid	068716-47-2	I	I
381	3,5-dibromophenylboronic acid	117695-55-3	I	I
382	2,4,6-trifluorophenylboronic acid	182482-25-3	I	I
383	2,3,5-trichlorophenylboronic acid	212779-19-6	I	I
384	pentafluorophenylboronic acid	001582-24-7	I	I
385	benzoic acid	000065-85-0	I	I
386	2-fluorobenzoic acid	000445-29-4	I	I
387	2-chlorobenzoic acid	000118-91-2	A	A
388	2-bromobenzoic acid	000088-65-3	A	I
389	2-iodobenzoic acid	000088-67-5	I	I
390	2,4-dichlorobenzoic acid	000050-84-0	A	A
391	2,4-dibromobenzoic acid	000611-00-7	A	A
392	2,4,6-trichlorobenzoic acid	000050-43-1	A	A
393	2,4,6-tribromobenzoic acid*	000633-12-5	A	A
394	2,3,5-triiodobenzoic acid	000088-82-4	A	A
395	2,3,4,5,6-pentafluorobenzoic acid	000602-94-8	A	A
396	benzenesulfonic acid	000098-11-3	I	I
397	sodium-2-iodobenzenesulfonate*	062973-69-7	I	I
398	2,5-dichlorobenzene sulfonic acid hydrate	000088-42-6	I	I
399	3,5-dibromosulfanilic acid, sodium salt	078824-10-9	A	A
400	2,4,5-trichlorobenzenesulfonic acid potassium salt	062625-17-6	A	A
401	2-iodo-4-methylbenzoic acid	001829-21-6	I	I
402	1-bromo-2-naphthoic acid	020717-79-7	A	A

403	4-hexylbenzoic acid	021643-38-9	A	A
404	2'-sulfooxy-4-monobrominated diphenyl ether	2248096-31-1	I	I
405	2'-sulfooxy-2,4-dibrominated diphenyl ether	2248096-36-6	A	A
406	3'-sulfooxy-2,4-dibrominated diphenyl ether	2254452-17-8	A	A
407	2'- sulfooxy-2,4,4'-tribrominated diphenyl ether	1788886-79-2	A	A
408	tetrabromobisphenol A-mono(glycidyl ether)	1643949-71-6	A	A
409	tetrabromobisphenol A-mono(allyl ether)	150492-18-5	A	A
410	tetrabromobisphenol A-mono(2,3-dibromopropyl ether)	1400992-49-5	A	A
411	tetrabromobisphenol A-bis(glycidyl ether)	003072-84-2	I	I
412	tetrabromobisphenol A-bis(allyl ether)	025327-89-3	I	I
413	bisphenol AF	001478-61-1	A	A
414	bisphenol TMC	129188-99-4	I	I
415	6:2 Cl-PFAES	763051-92-9	A	A
416	8:2 Cl-PFAES*	756426-58-1	I	A
417	tris(1,3-dichloro-2-propyl) phosphate	013674-87-8	I	I
418	Antiblaze V6*	038051-10-4	I	I
419	diphenyl phosphate	000838-85-7	A	A
420	tris(2-isopropylphenyl) phosphate	064532-95-2	I	I
421	tricresyl phosphate	001330-78-5	A	A
422	2-ethylhexyl diphenyl phosphate	001241-94-7	A	A
423	T2-toxin	021259-20-1	A	A
424	Mono (2-ethylhexyl) phthalate*	004376-20-9	A	A
425	Dimethyl phthalate	000131-11-3	I	I
426	Diethyl phthalate	000084-66-2	I	I
427	Isopropylparaben	004191-73-5	I	I
428	Isobutylparaben	004247-02-3	I	I
429	Benzylparaben *	000094-18-8	A	I

430	Bisphenol B	000077-40-7	A	A
431	Bisphenol Z	000843-55-0	I	I
432	Bisphenol AP	001571-75-1	I	I
433	Naphthalene	000091-20-3	I	I
434	Anthracene	000120-12-7	I	I
435	Pyrene	000129-00-0	I	I
436	Benzo(a)pyrene	000050-32-8	I	I
437	2,4-Dihydroxybenzophenone	000131-56-6	A	A
438	Oxybenzone *	000131-57-7	A	A
439	2,2'-Dihydroxy-4-methoxybenzophenone	000131-53-3	I	I
440	Octabenzone *	001843-05-6	I	A
441	Benzophenone	000119-61-9	I	I
442	Phenyl salicylate	000118-55-8	I	I
443	Methyl 4-aminobenzoate *	000619-45-4	I	I
444	Ethyl 4-aminobenzoate	000094-09-7	I	I
445	Tetrabromobisphenol A bis(2-hydroxyethyl) ether	004162-45-2	I	I

* the compounds in validation set.

Table S8 Information of model compounds and their IC_{50}, K_d and logRP (T_3) values

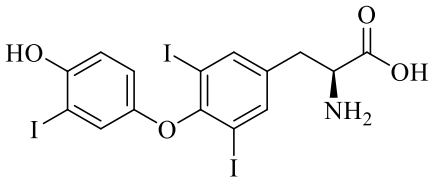
Chemical name	IC_{50} (nM)	Kd	logRP (T_3)
3,3′,5-tetraiodo-L-thyronine	415±64.5	24.3±3.81	0
3,3′,5,5′-tetraiodo-L-thyronine	516±52.2	30.2±3.12	-0.0946±0.0805
3,5-diiodo-2-hydroxybenzaldehyde	1863±117	109±7.27	-0.652±0.0729
2,6-Dibromo-1,4-benzoquinone	994±92.9	58.1±5.57	-0.379±0.0788
2,6-Dichloro-1,4-benzoquinone	1049±102	61.3±6.11	-0.403±0.0796
Bromochlorophenol Blue	75393±44420	4409±2599	-2.26±0.265
2-bromo-6-chloro-4-nitrophenol	206±37.7	12.0±2.22	0.304±0.104
2,5-Dibromo-1,4-benzoquinone	839±56.4	49.1±3.46	0.581±0.204
2,6-Diiodo-4-nitrophenol	109±48.4	6.37±2.83	-0.306±0.0735
3,5-diiodo-4-hydroxybenzaldehyde	542±34.8	31.7±2.14	-0.116±0.073
Tetrachloro-1,4-benzoquinone	276±30.9	16.1±1.84	0.177±0.0832
3-methyl-2-nitrophenol	201281±80521	11771±4715	-2.69±0.186
3,5-dichlorobisphenol A	1006±51.9	58.8±3.28	-0.385±0.0711
N,N-diphenylnitrous amide	>10000		
4-bromo-2,6-ditert-butylphenol	>10000		
Nonylphenol	10980±3974	642±233	-1.42±0.171
6:2 fluorotelomer sulfonic acid	64417±6696	3767±400	-2.19±0.0812
Flupyradifurone	>10000		
Imidacloprid	>10000		
Methylparaben	>10000		
Triclocarban	>10000		
Benzyl butyl phthalate	>10000		
Triclosan	1191±154	69.6±9.11	-0.458±0.0878
N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine	>10000		
N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine quinone	>10000		
2-Aminobenzothiazole	>100000		
2-Hydroxybenzothiazole	>10000		
N,N-Diphenylguanidine	>10000		
N,N -Diphenylurea	>10000		
4-hydroxydiphenylamine	>10000		
Hexa(methoxymethyl) melamine	>100000		

Table S9 Statistical parameters of optimum binary classification models based on Decision tree, Random forest

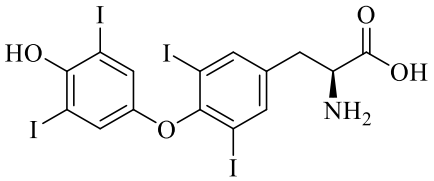
Model	Data set[a]	Descriptor[b]	n	*Sn*	*Sp*	*Q*	*MCC*	*AUC*
Gobiocypris rarus **TTR mechanism-based screening binary classification models**								
Decision tree	T	qD^{-}_{adj}	42	1	1	1	1	1
	V		15	1	1	1	1	1
Random forest	T	qD^{-}_{adj}	42	1	1	1	1	1
	V		15	1	1	1	1	1
Gobiocypris rarus **TTR high throughput screening binary classification models**								
Decision tree	T	*GATS1v*	42	1	1	1	1	1
	V		15	1	1	1	1	1
Random forest	T	*GATS1v*	42	1	1	1	1	1
	V		15	1	1	1	1	1
Little Skate TTR high throughput screening binary classification models								
Decision tree	T	*AMW*	28	1	1	1	1	1
	V		10	1	1	1	1	1
Random forest	T	*AMW*	28	1	1	1	1	1
	V		10	1	1	1	1	1
Seabream high throughput screening binary classification models								
Decision tree	T	*ATS3v*	28	1	1	1	1	1
	V		9	1	1	1	1	1
Random forest	T	*ATS3v*	28	1	1	1	1	1
	V		9	1	1	1	1	1

[a] T and V are training set and validation set, respectively.

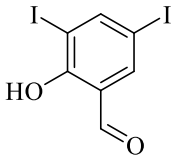
[b] qD^{-}_{adj} is the chemical form adjusted most negative net atomic charge on an electron donor atom; *GATS1v* is Geary autocorrelation - lag 1 / weighted by van der Waals volumes; *AMW* is average molecular weight (Molecular weight / Total number of atoms); *ATS3v* is Broto-Moreau autocorrelation - lag 3 / weighted by van der Waals volumes.



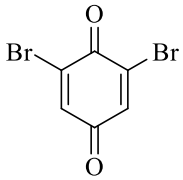
3,3′,5-tetraiodo-L-thyronine



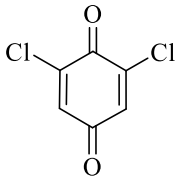
3,3′,5,5′-tetraiodo-L-thyronine



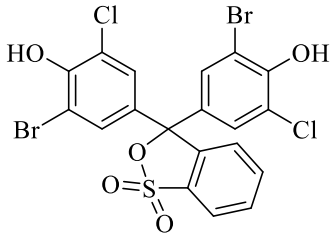
3,5-diiodo-2-hydroxybenzaldehyde



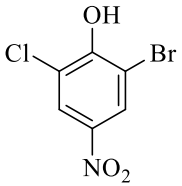
2,6-Dibromo-p-benzoquinone



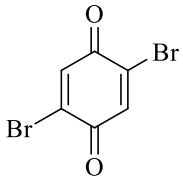
2,6-Dichloro-p-benzoquinone



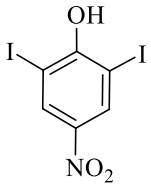
Bromochlorophenol Blue



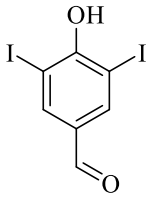
2-bromo-6-chloro-4-nitrophenol



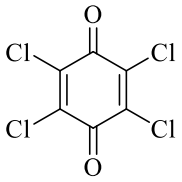
2,5-Dibromo-p-benzoquinone



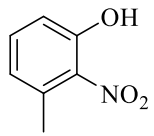
2,6-Diiodo-4-nitrophenol



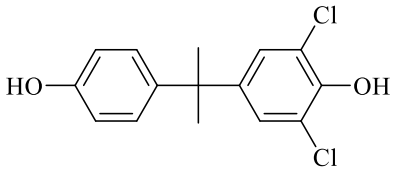
3,5-diiodo-4-hydroxybenzaldehyde



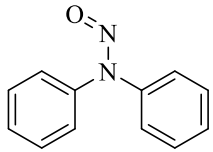
Tetrachloro-1,4-benzoquinone



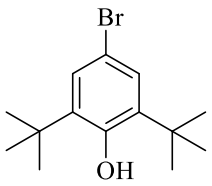
3-methyl-2-nitrophenol



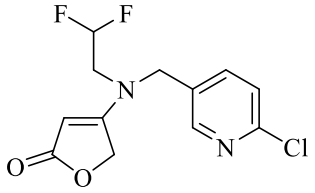
3,5-dichlorobisphenol A



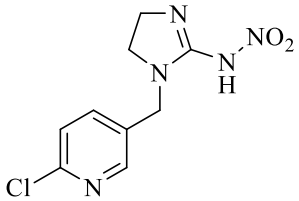
N,N-diphenylnitrous amide



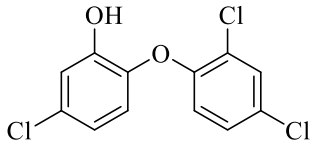
4-bromo-2,6-ditert-butylphenol



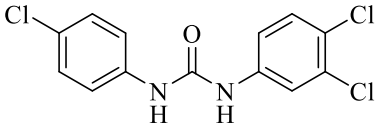
Flupyradifurone



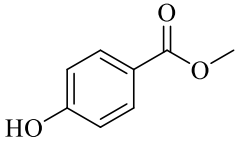
Imidacloprid



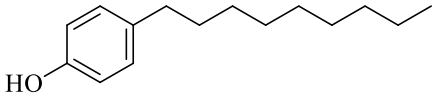
Triclosan



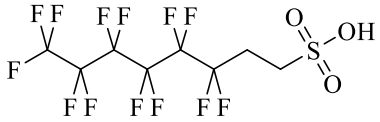
Triclocarban



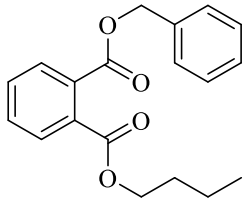
Methylparaben



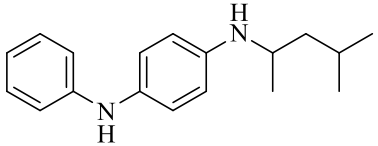
Nonylphenol



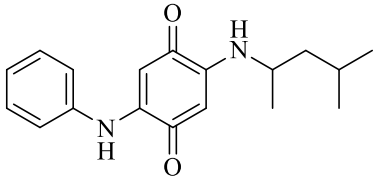
6:2 fluorotelomer sulfonic acid



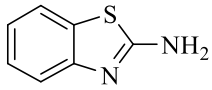
Benzyl butyl phthalate



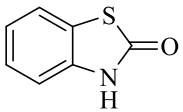
N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine



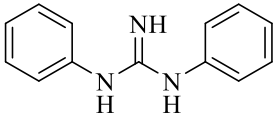
N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine quinone



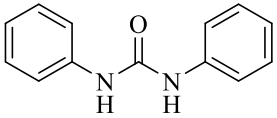
2-Aminobenzothiazole



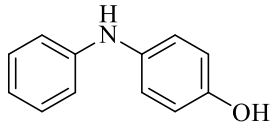
2-Hydroxybenzothiazole



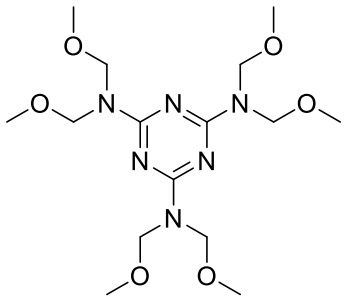
N,N-Diphenylguanidine



N,N-Diphenylurea



4-hydroxydiphenylamine



Hexa(methoxymethyl) melamine

Fig. S1 Chemical structures of THs and 29 chemicals used in this study.

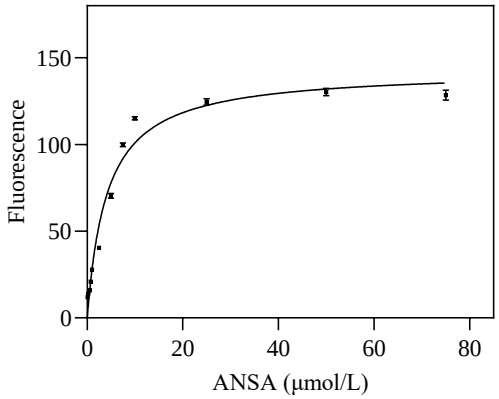


Fig. S2 Plots of ANSA binding to recombinant CrmTTR. The error bars represent the standard deviation of triplicate independent determinations

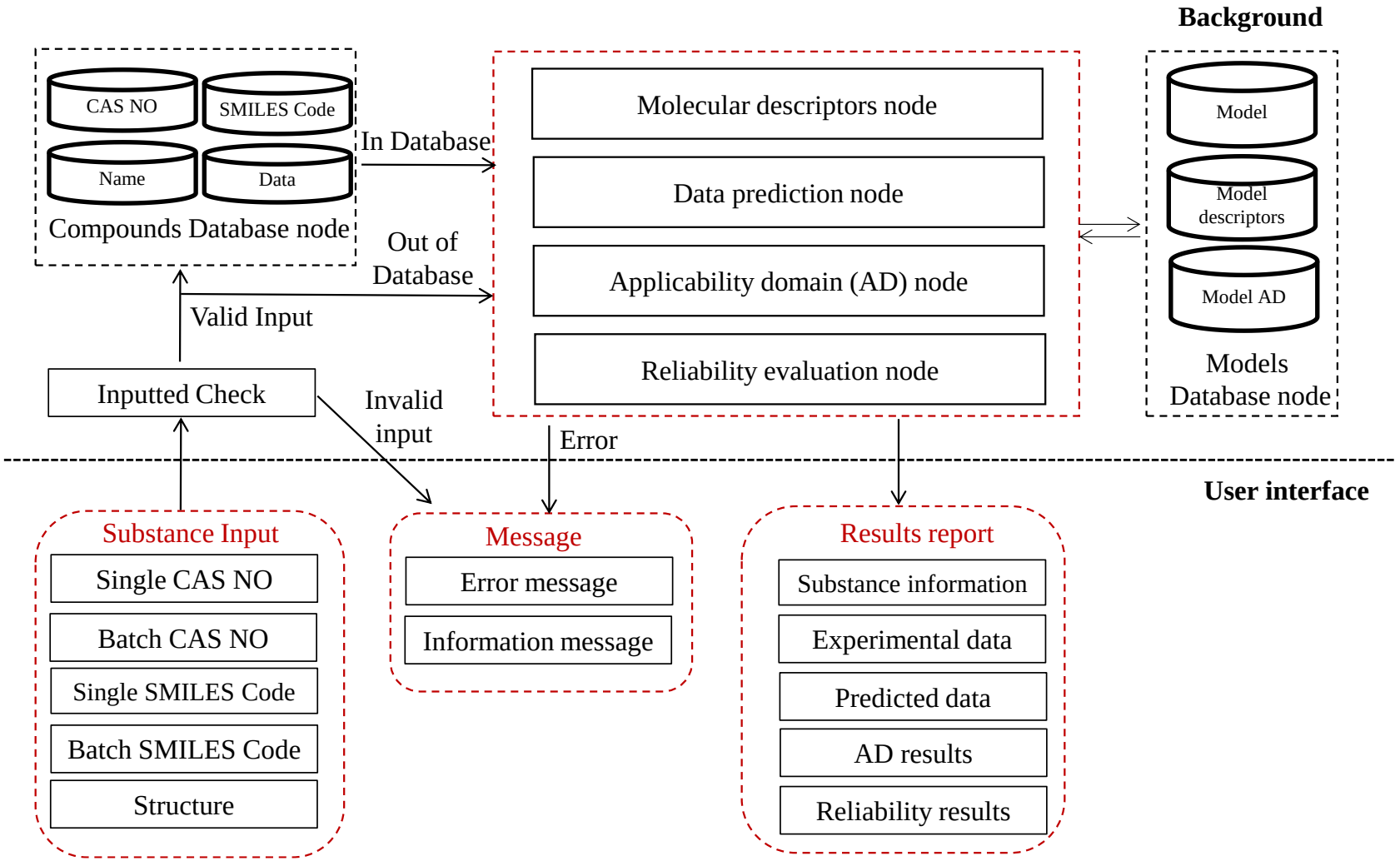


Fig. S3 Conceptual framework of TTR Profiler

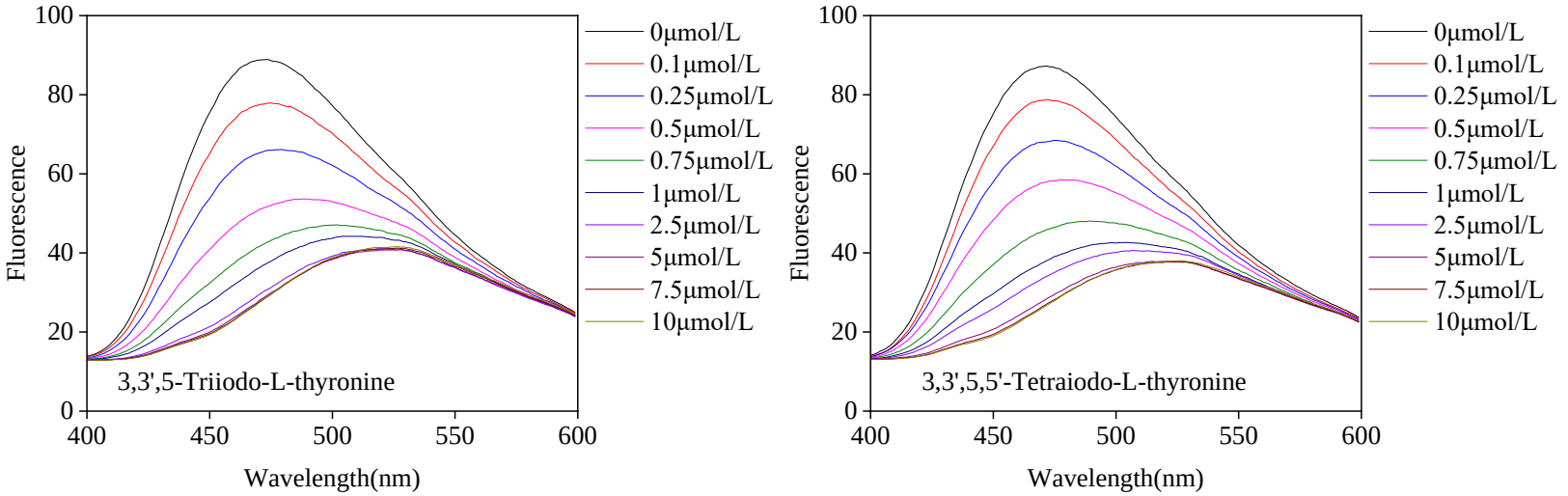
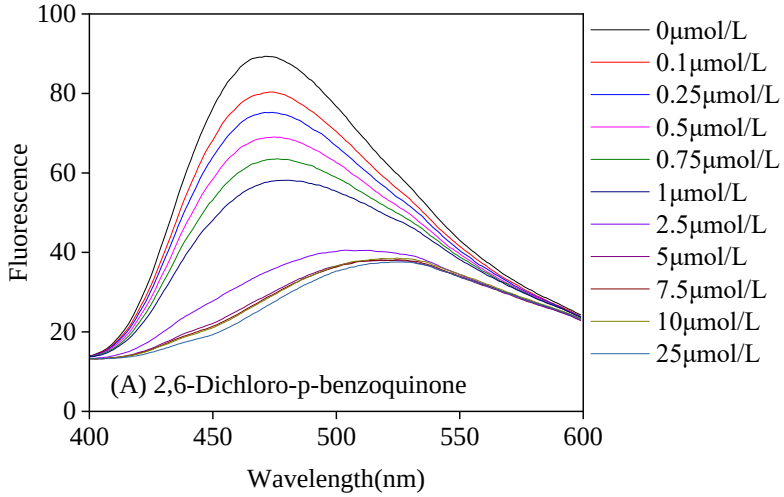
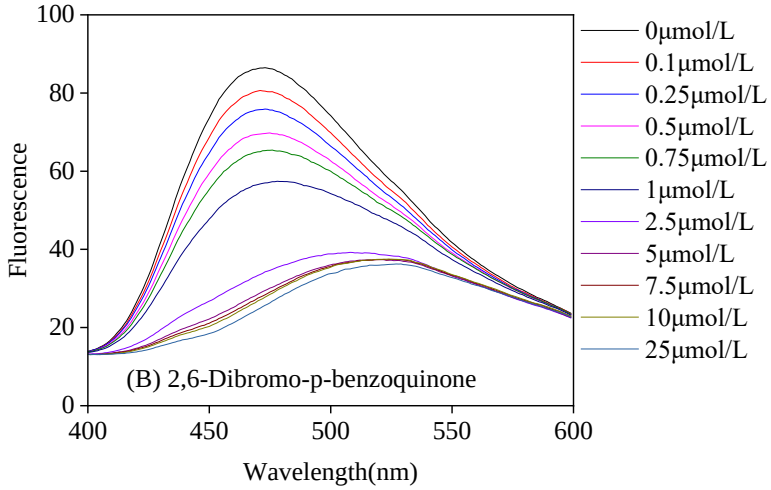
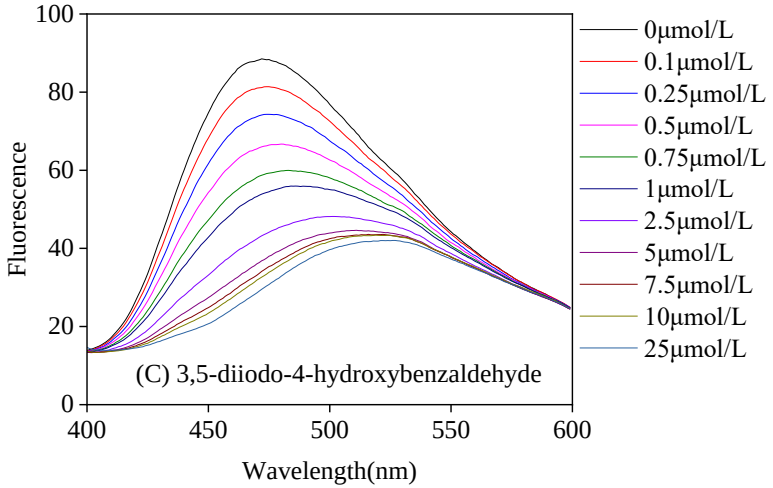
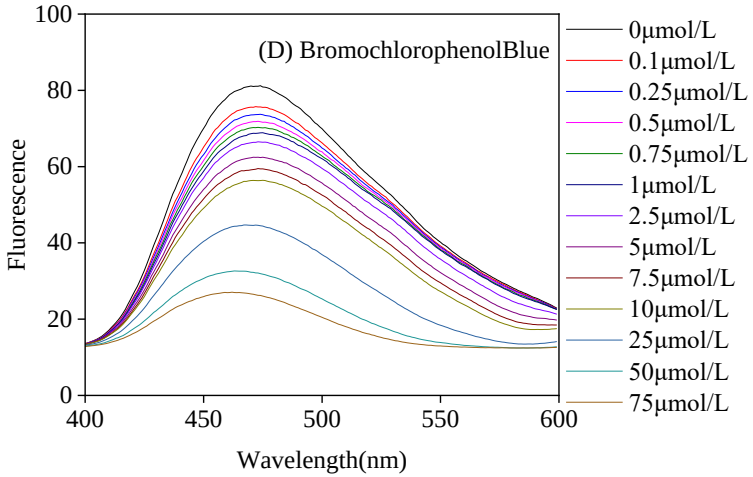


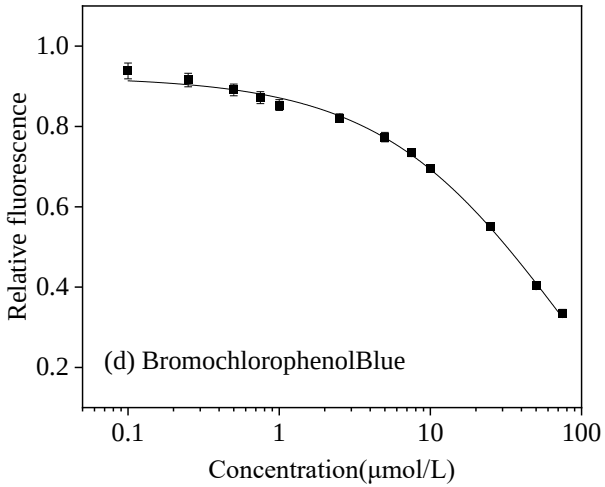
Fig. S4 Fluorescence spectra of 3,3′,5-tetraiodo-L-thyronine (T3) and 3,3′,5,5′-tetraiodo-L-thyronine (T4) titrated into the solution of 0.5 μmol/L recombinant CrmTTR and 50 μmol/L ANSA.

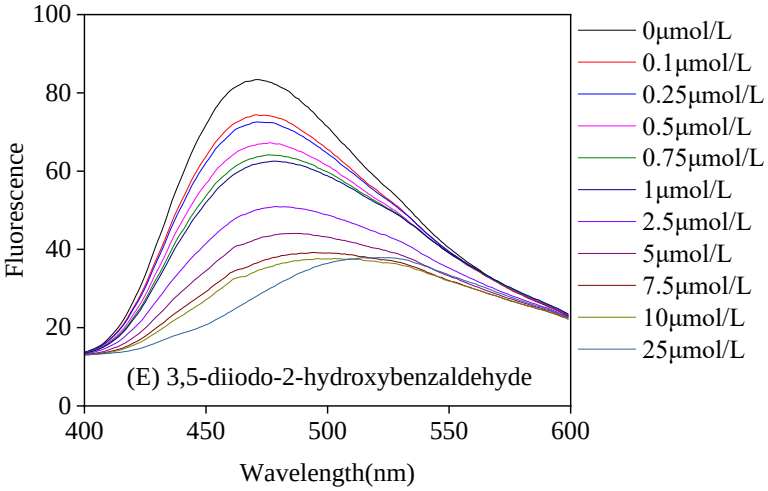

Fluorescence
Wavelength(nm)
(A) 2,6-Dichloro-p-benzoquinone
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

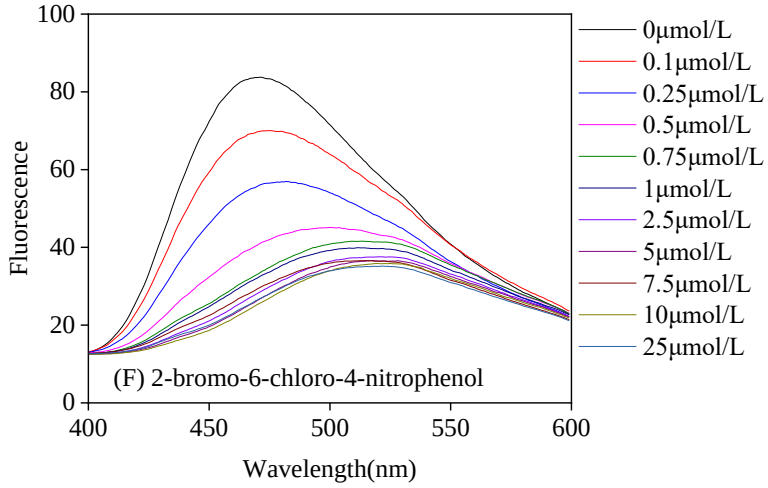

Fluorescence
Wavelength(nm)
(B) 2,6-Dibromo-p-benzoquinone
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

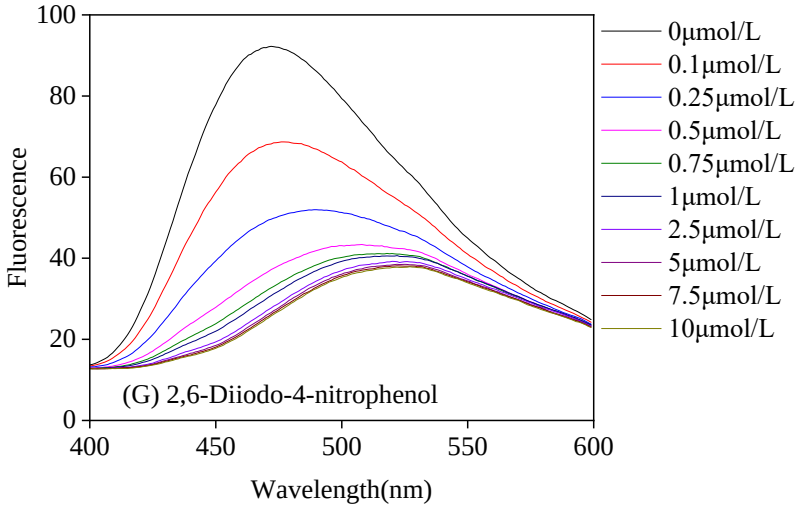

Fluorescence
Wavelength(nm)
(C) 3,5-diiodo-4-hydroxybenzaldehyde
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

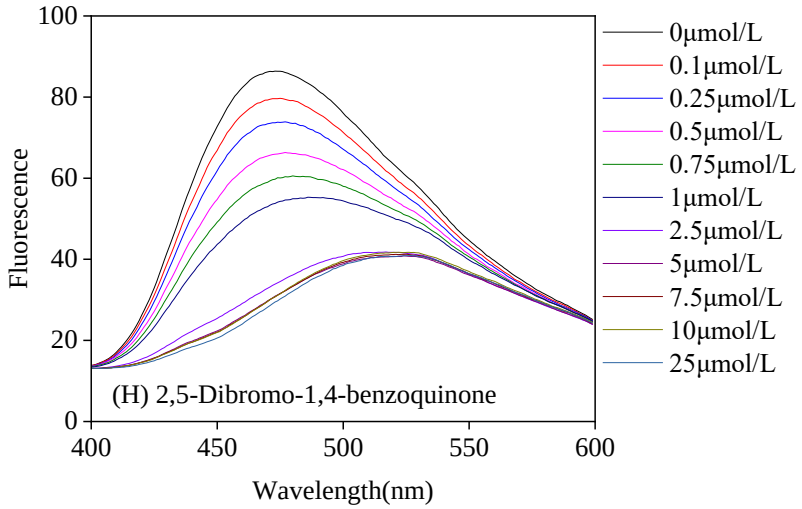

Fluorescence
Wavelength(nm)
(D) BromochlorophenolBlue
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L

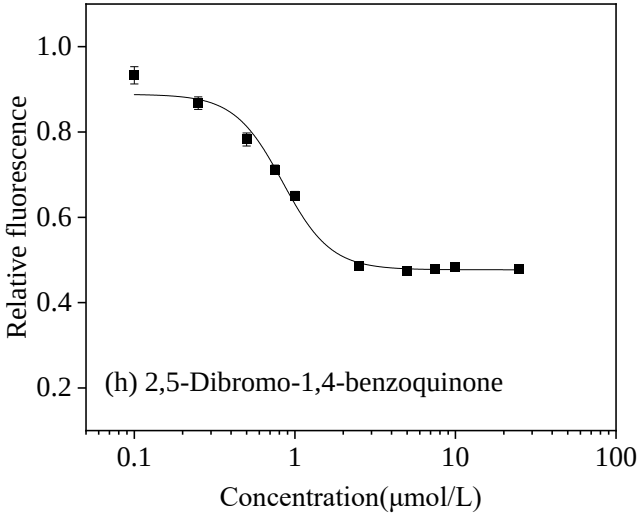

Relative fluorescence
Concentration(μmol/L)
(d) BromochlorophenolBlue

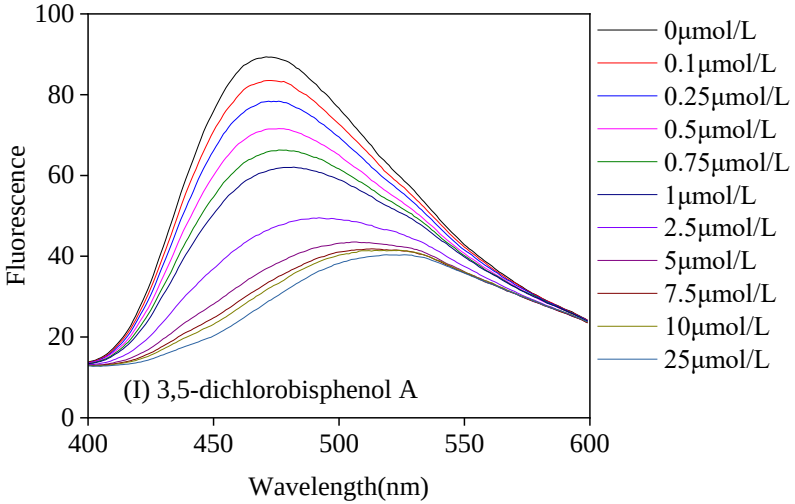

Fluorescence
Wavelength(nm)
(E) 3,5-diiodo-2-hydroxybenzaldehyde
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

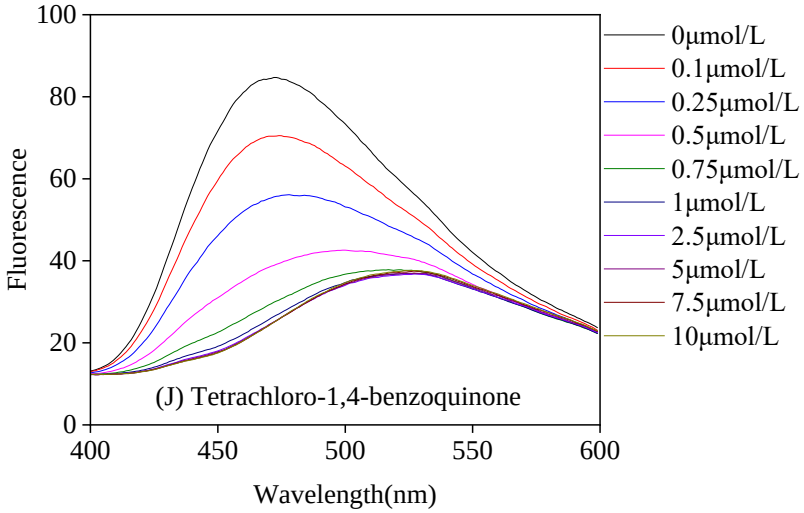

Fluorescence
Wavelength(nm)
(F) 2-bromo-6-chloro-4-nitrophenol
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

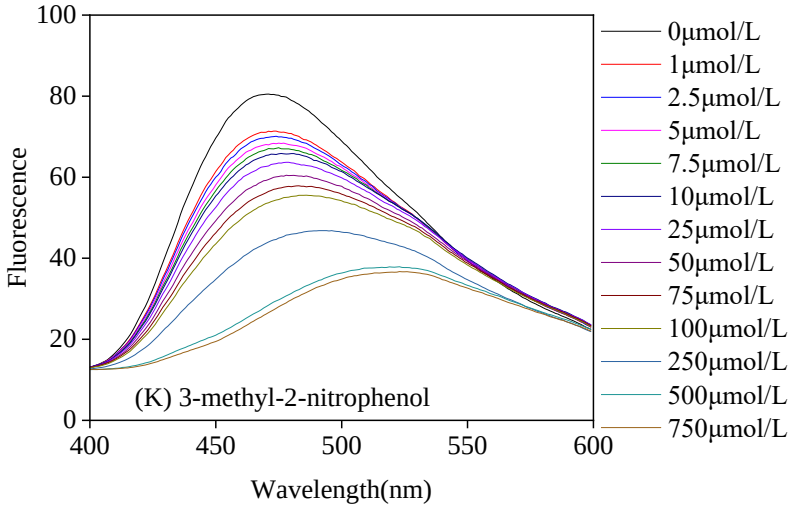

Fluorescence
Wavelength(nm)
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
(G) 2,6-Diiodo-4-nitrophenol

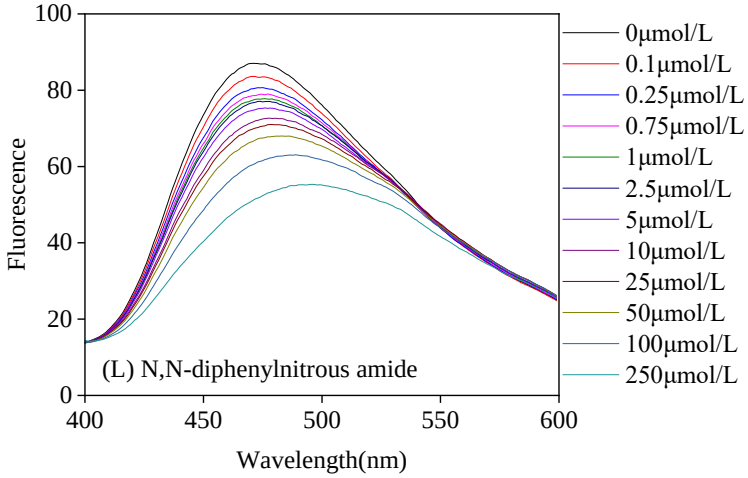

Fluorescence
Wavelength(nm)
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
(H) 2,5-Dibromo-1,4-benzoquinone

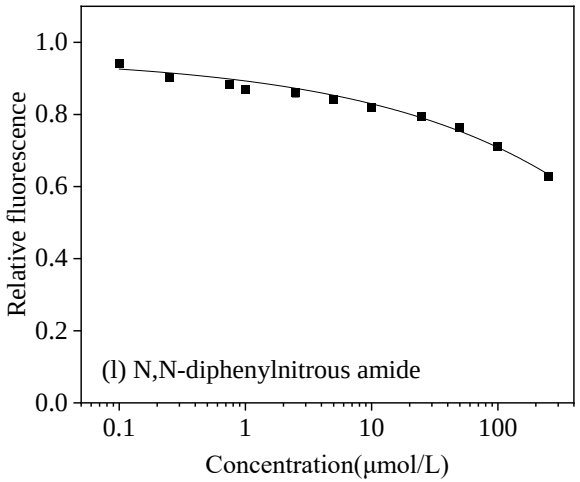

Relative fluorescence
Concentration(μmol/L)
(h) 2,5-Dibromo-1,4-benzoquinone

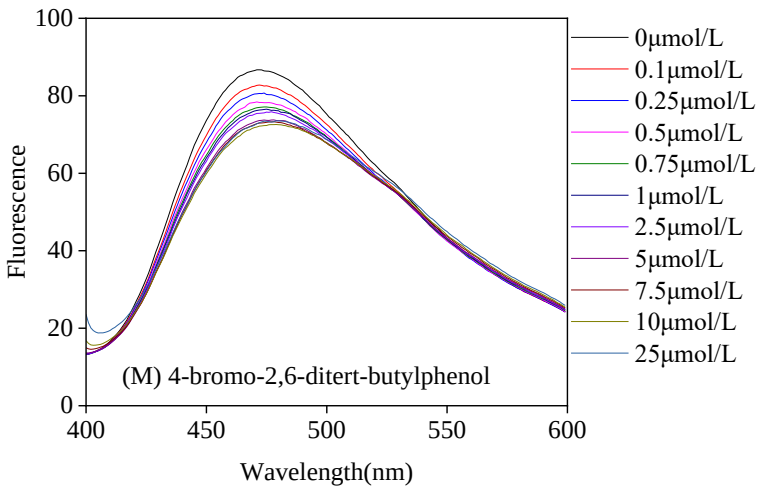

100
80
60
40
20
0
Fluorescence
400
450
500
550
600
Wavelength(nm)
(I) 3,5-dichlorobisphenol A
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

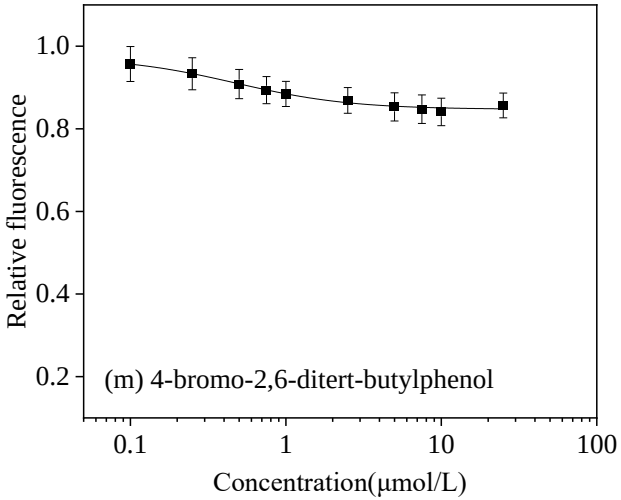

100
80
60
40
20
0
Fluorescence
400
450
500
550
600
Wavelength(nm)
(J) Tetrachloro-1,4-benzoquinone
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L

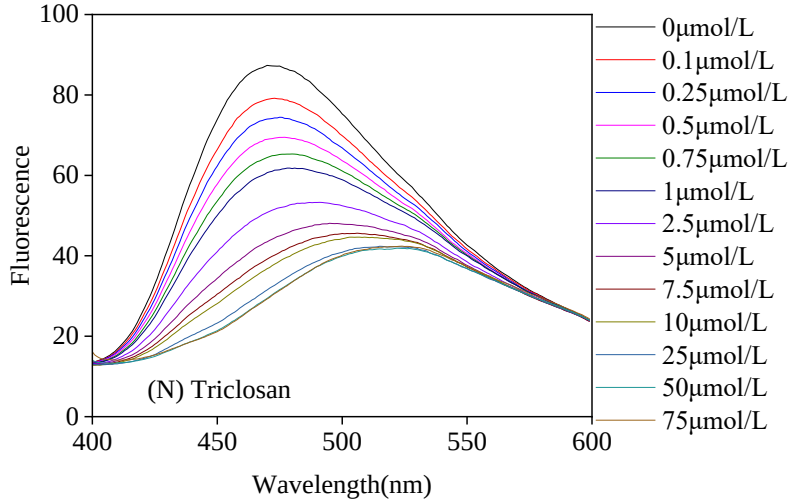

Fluorescence
Wavelength(nm)
(K) 3-methyl-2-nitrophenol
0μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L
250μmol/L
500μmol/L
750μmol/L

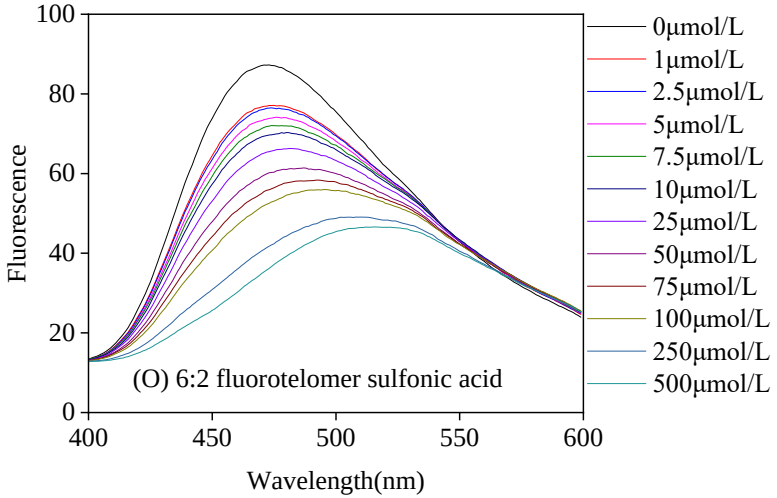

Fluorescence
Wavelength(nm)
(L) N,N-diphenylnitrous amide
0μmol/L
0.1μmol/L
0.25μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
10μmol/L
25μmol/L
50μmol/L
100μmol/L
250μmol/L

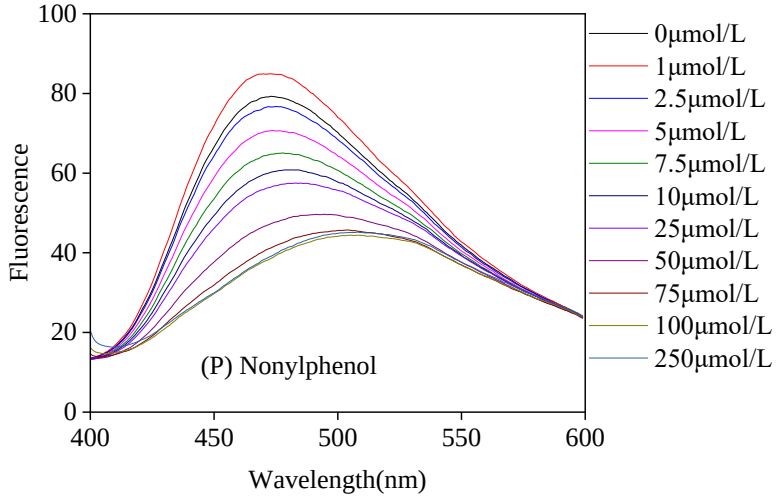

Relative fluorescence
Concentration(μmol/L)
(l) N,N-diphenylnitrous amide

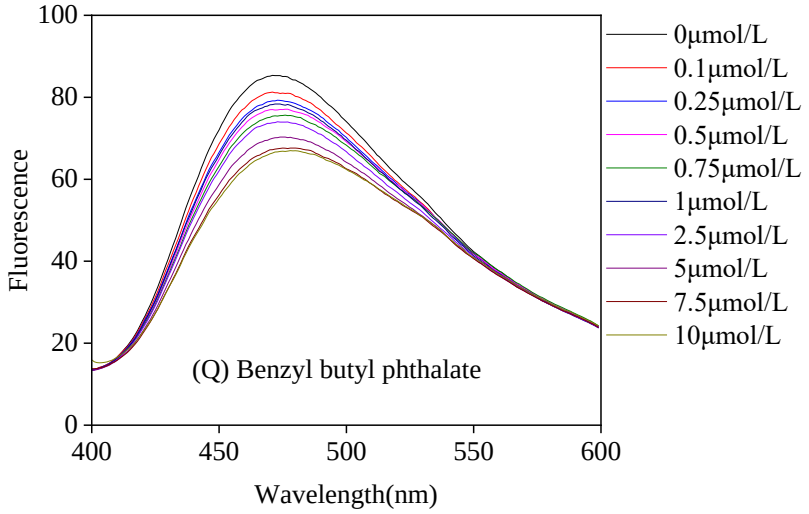

Fluorescence
Wavelength(nm)
(M) 4-bromo-2,6-ditert-butylphenol
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

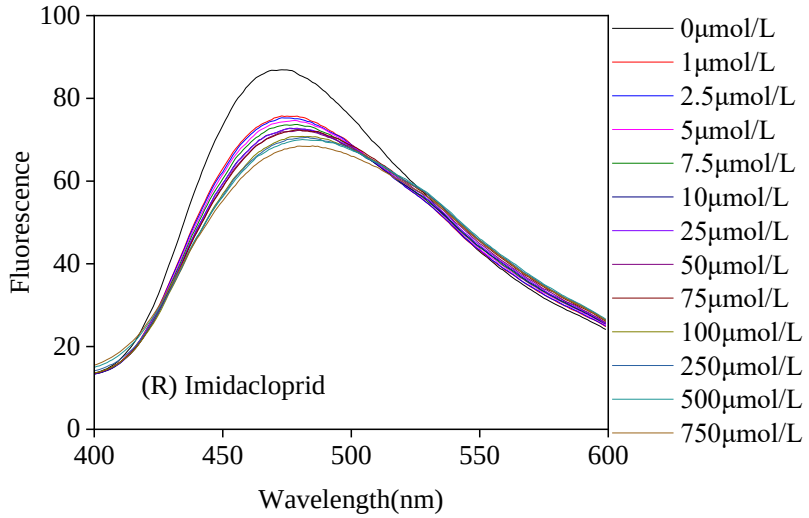

Relative fluorescence
Concentration(μmol/L)
(m) 4-bromo-2,6-ditert-butylphenol

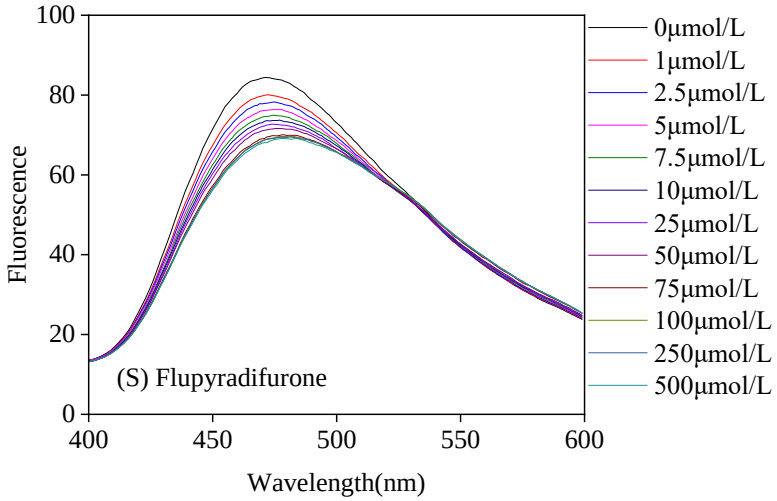

Fluorescence
Wavelength(nm)
(N) Triclosan
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L

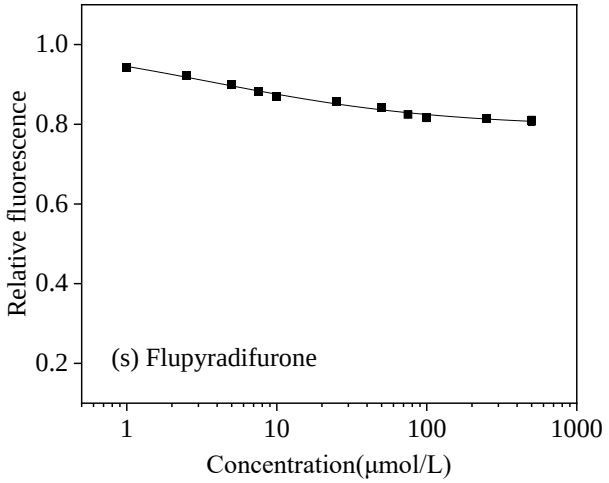

Fluorescence
Wavelength(nm)
(O) 6:2 fluorotelomer sulfonic acid
0μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L
250μmol/L
500μmol/L

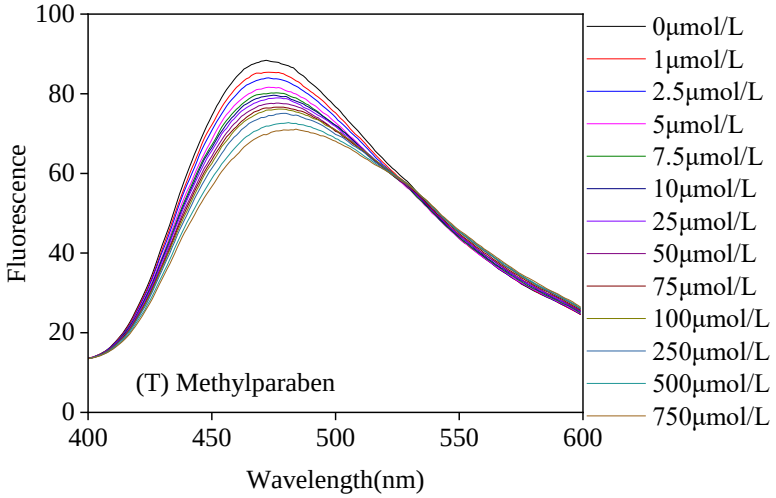

Fluorescence
Wavelength(nm)
(P) Nonylphenol
0μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L
250μmol/L

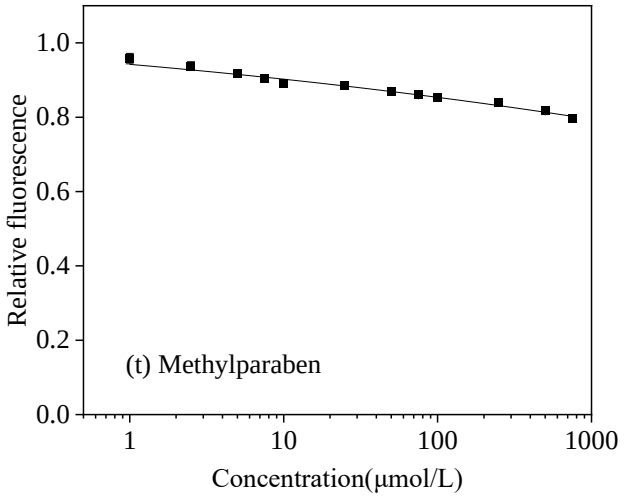

100
80
60
40
20
0
Fluorescence
400
450
500
550
600
Wavelength(nm)
(Q) Benzyl butyl phthalate
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L

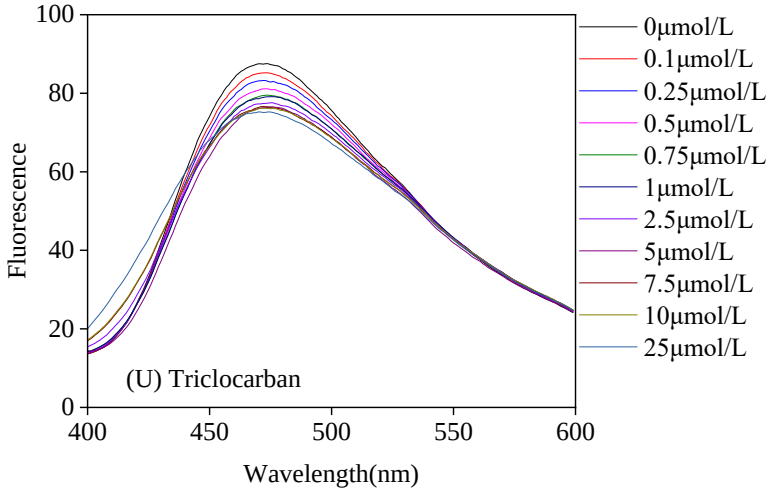

100
80
60
40
20
0
Fluorescence
400
450
500
550
600
Wavelength(nm)
(R) Imidacloprid
0μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L
250μmol/L
500μmol/L
750μmol/L

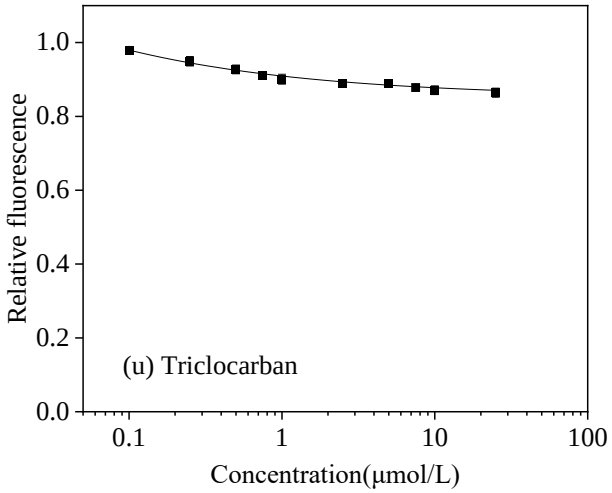

Fluorescence
Wavelength(nm)
(S) Flupyradifurone
0μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L
250μmol/L
500μmol/L

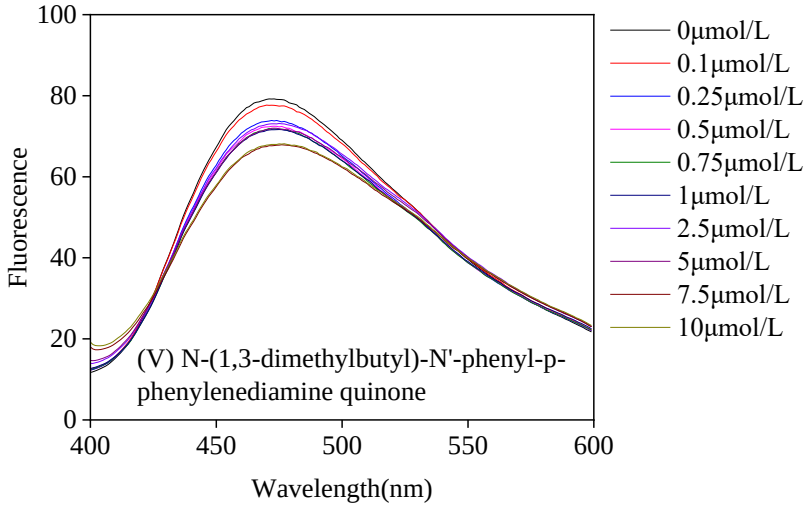

Relative fluorescence
Concentration(μmol/L)
(s) Flupyradifurone

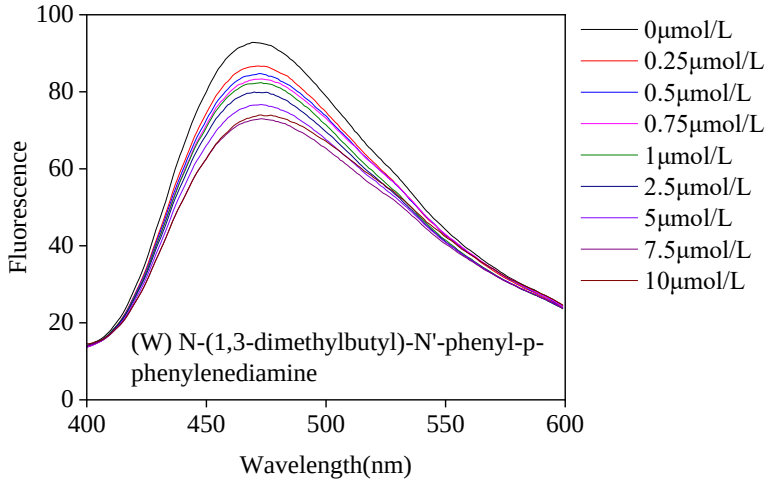

Fluorescence
Wavelength(nm)
(T) Methylparaben
0μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L
250μmol/L
500μmol/L
750μmol/L

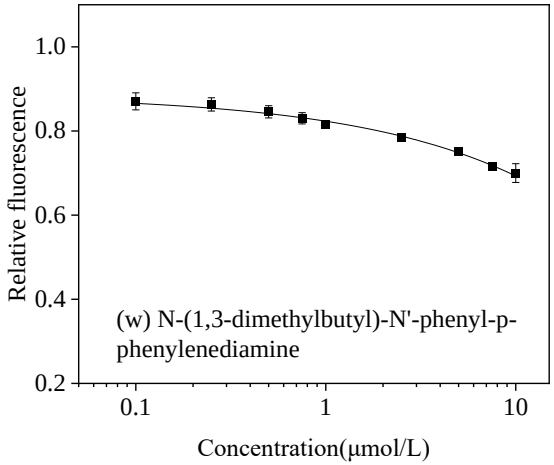

Relative fluorescence
Concentration(μmol/L)
(t) Methylparaben

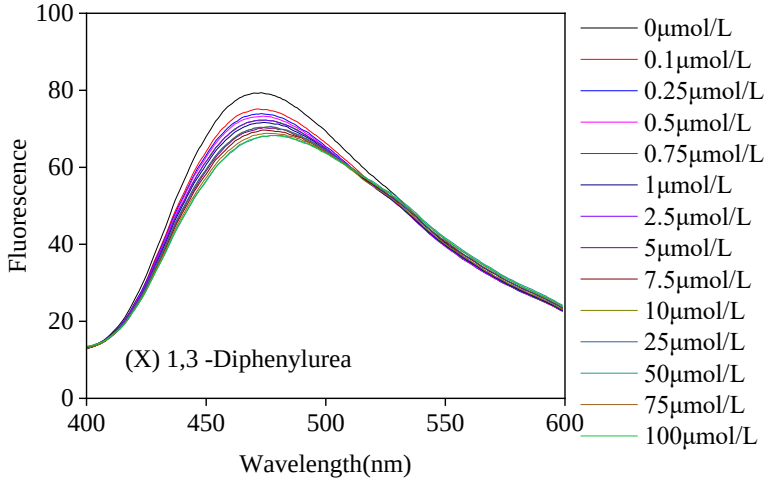

Fluorescence
Wavelength(nm)
(U) Triclocarban
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

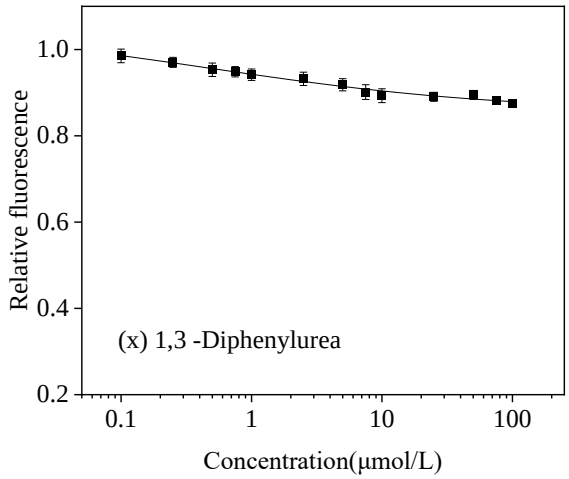

Relative fluorescence
Concentration(μmol/L)
(u) Triclocarban

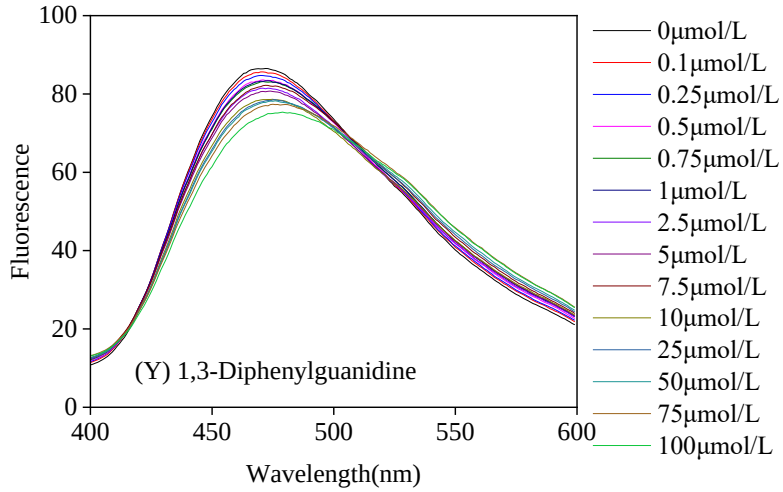

Fluorescence
Wavelength(nm)
(V) N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine quinone
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L

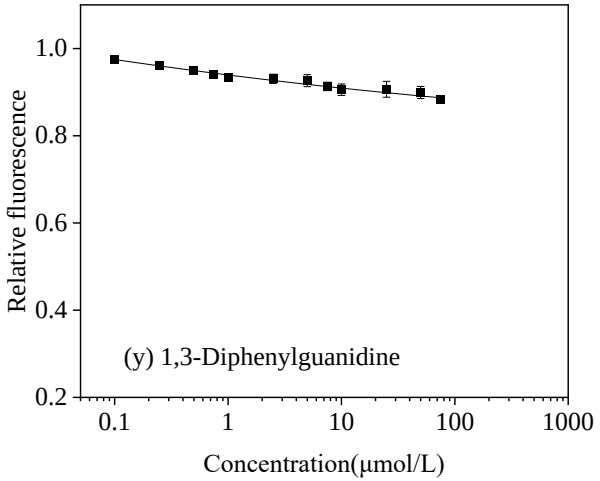

Fluorescence
Wavelength(nm)
(W) N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine
0μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L

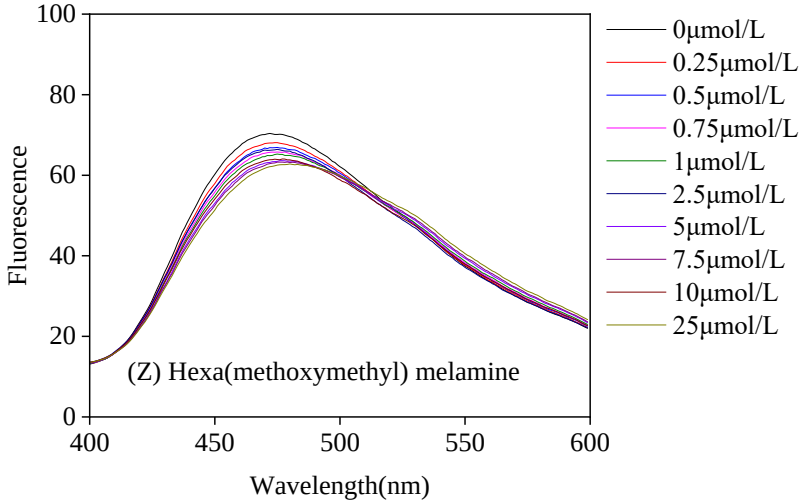

Relative fluorescence
Concentration(μmol/L)
(w) N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine

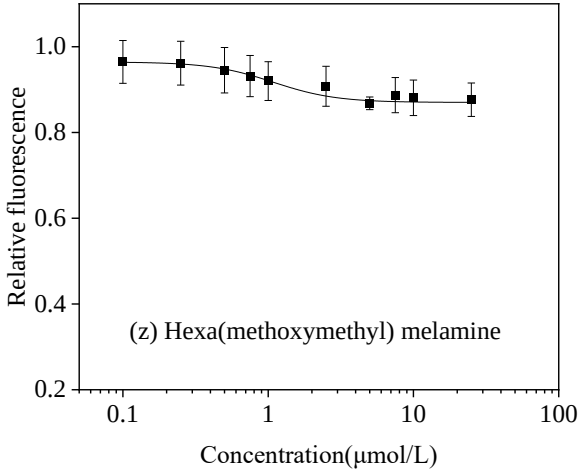

Fluorescence
Wavelength(nm)
(X) 1,3 -Diphenylurea
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L

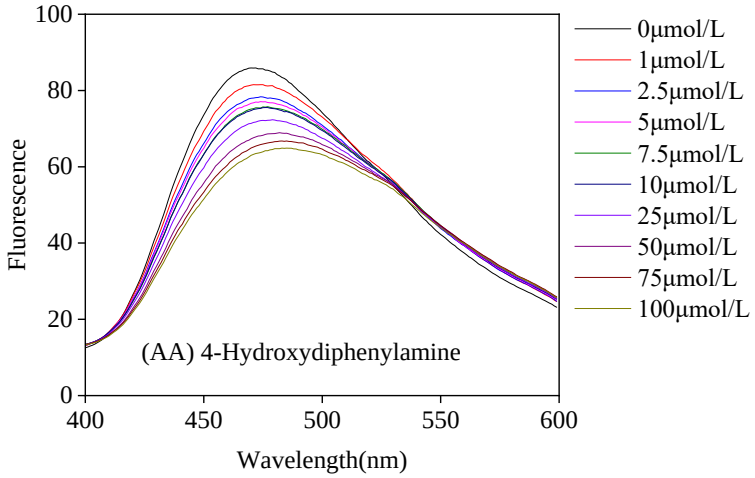

Relative fluorescence
Concentration(μmol/L)
(x) 1,3 -Diphenylurea

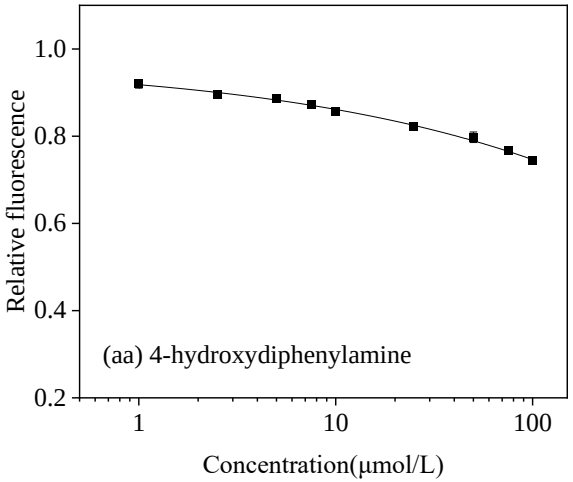

Fluorescence
Wavelength(nm)
(Y) 1,3-Diphenylguanidine
0μmol/L
0.1μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L

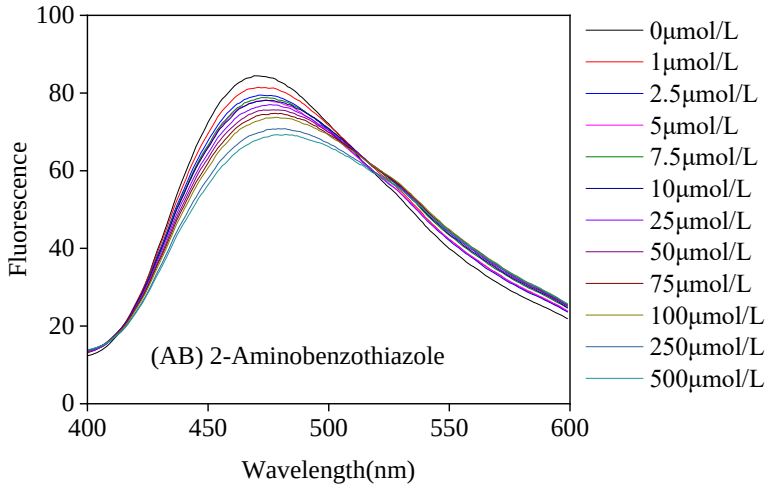

Relative fluorescence
Concentration(μmol/L)
(y) 1,3-Diphenylguanidine

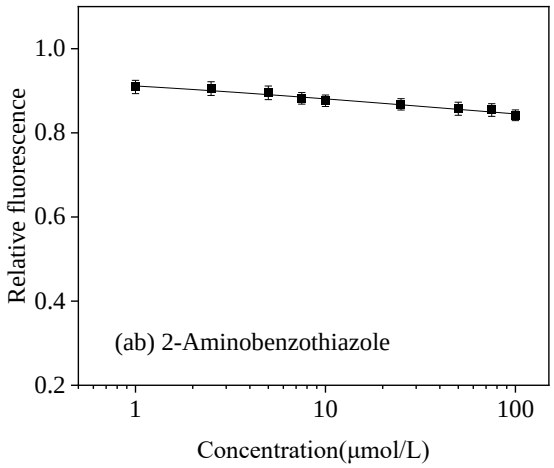

Fluorescence
Wavelength(nm)
(Z) Hexa(methoxymethyl) melamine
0μmol/L
0.25μmol/L
0.5μmol/L
0.75μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L

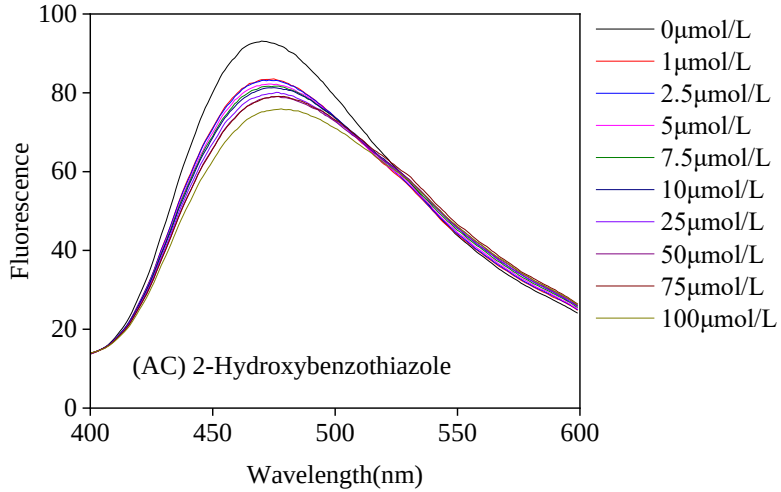

Relative fluorescence
Concentration(μmol/L)
(z) Hexa(methoxymethyl) melamine


Fluorescence
Wavelength(nm)
(AA) 4-Hydroxydiphenylamine
0μmol/L
1μmol/L
2.5μmol/L
5μmol/L
7.5μmol/L
10μmol/L
25μmol/L
50μmol/L
75μmol/L
100μmol/L


Relative fluorescence
Concentration(μmol/L)
(aa) 4-hydroxydiphenylamine







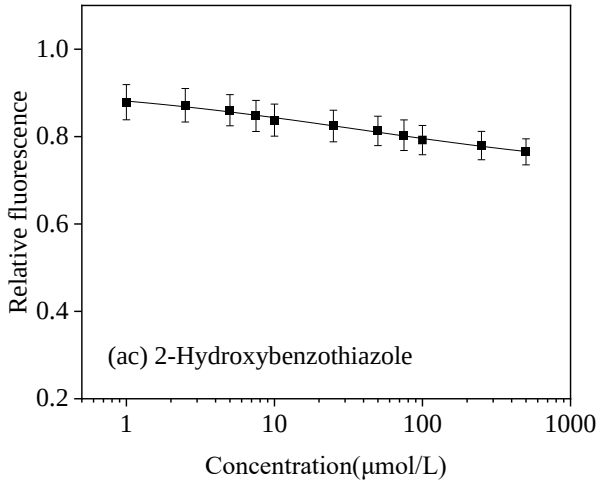


Fig. S5 Fluorescence spectra (A-AC) and fluorescence displacement curve (a-ac) of 29 chemicals titrated into the solution of 0.5 μmol/L recombinant CrmTTR and 50 μmol/L ANSA. The error

bars represent the standard deviation of triplicate independent determinations. The missing fluorescence displacement curves of 2,6-Diiodo-4-nitrophenol (2,6-DINP), 2-bromo-6-chloro-4-nitrophenol (2,6-BCNP), 3,5-diiodo-4-hydroxybenzaldehyde (4-DIHBA), 2,6-Dichloro-p-benzoquinone (2,6-DCBQ), 2,6-Dibromo-p-benzoquinone (2,6-DBBQ), 3-methyl-2-nitrophenol (3-MNP), 3,5-dichlorobisphenol A (3,5-DCBPA), Tetrachloro-p-benzoquinone (TCBQ), Triclosan (TCS), Nonylphenol (NP), 6:2 fluorotelomer sulfonic acid (6:2-FTSA), 3,5-diiodo-2-hydroxybenzaldehyde (2-DIHBA), Imidacloprid (IMI), Benzyl butyl phthalate (BBP) and N-(1,3-dimethylbutyl)-N'-phenyl-p-phenylenediamine quinone (6PPDQ) were presented in Figure 1 of the main text.

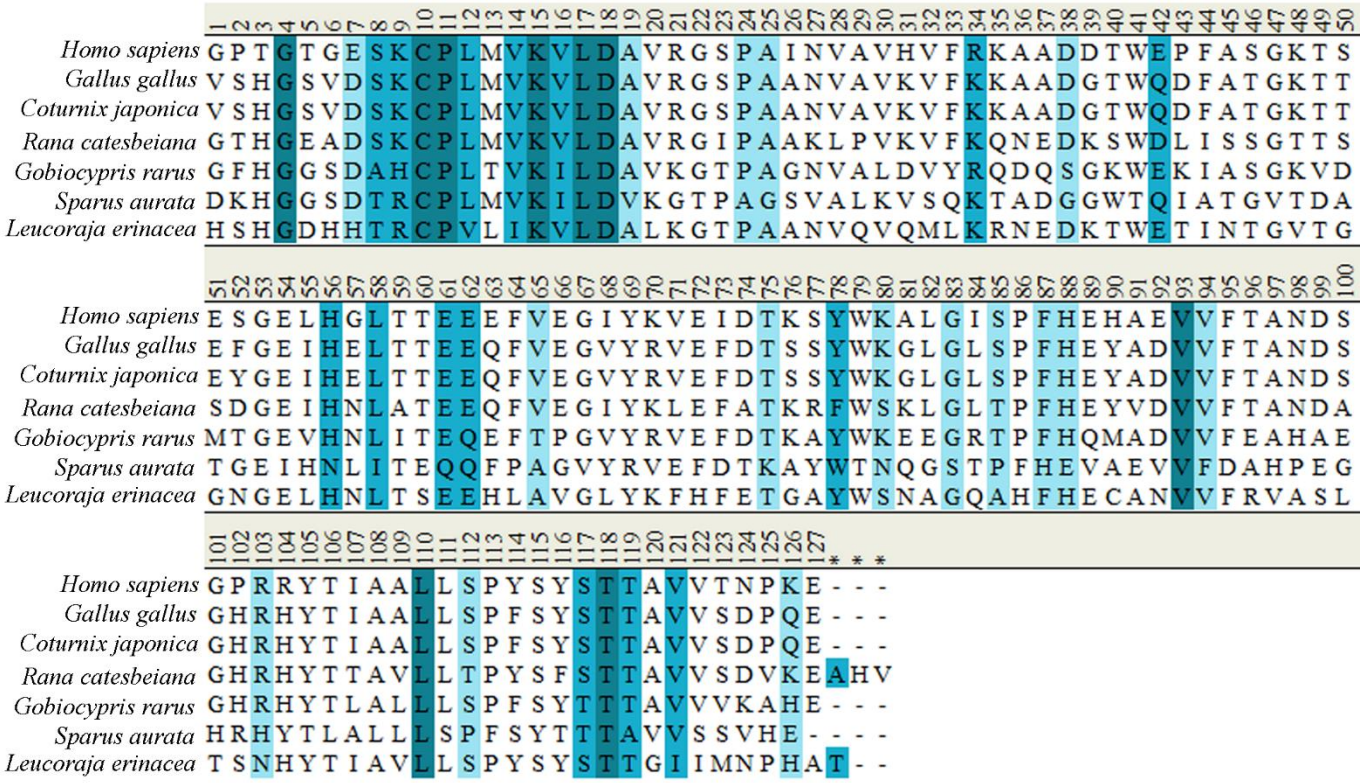


Fig. S6 Multiple amino acid sequence alignment of *Homo sapiens* (NP_000362.1, https://www.ncbi.nlm.nih.gov/protein/NP_000362.1), *Gallus gallus* (NP_990666.1, https://www.ncbi.nlm.nih.gov/protein/NP_990666.1), *Coturnix japonica* (XP_015710943.1, https://www.ncbi.nlm.nih.gov/protein/XP_015710943.1), *Rana catesbeiana* (BAA33456.1, https://www.ncbi.nlm.nih.gov/protein/BAA33456.1), *Gobiocypris rarus* (QKX44762.1, https://www.ncbi.nlm.nih.gov/protein/QKX44762.1), *Sparus aurata* (XP_030288250.1, https://www.ncbi.nlm.nih.gov/protein/XP_030288250.1) and *Leucoraja erinacea* (*XP_055490285.1*, https://www.ncbi.nlm.nih.gov/protein/XP_055490285.1). Sequence was aligned at Discovery

Studio Visualizer v17.2.0.16349 (Dassault Syste`mes Biovia Co.).

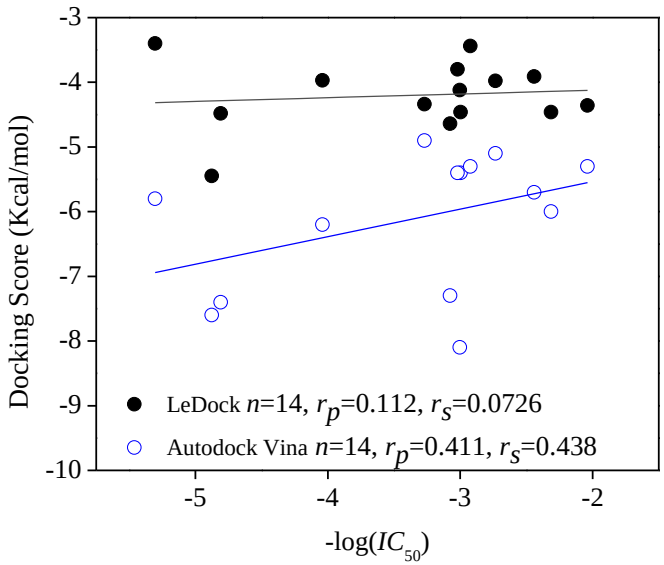
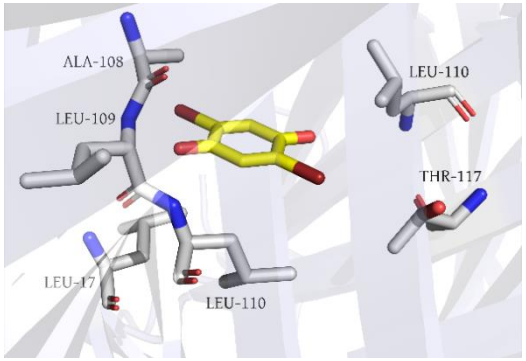
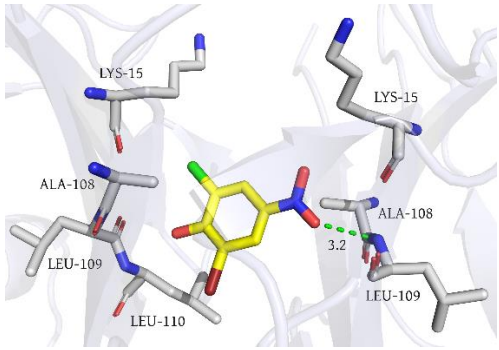


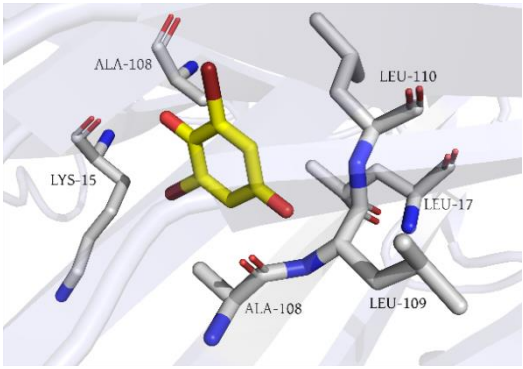
Fig. S7 Correlation of docking scores and experimental values of two docking programs for 14 active CrmTTR binders. (Docking score takes the minimum binding energy of all poses.)



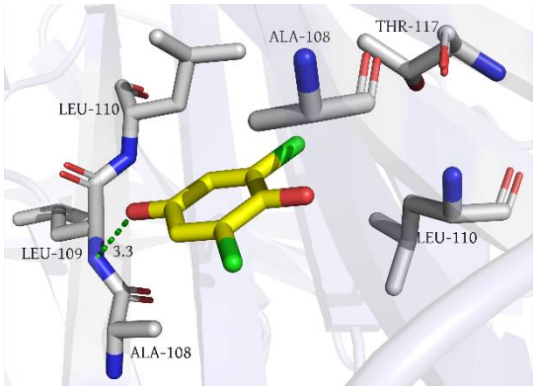
2,5-Dibromo-p-benzoquinone



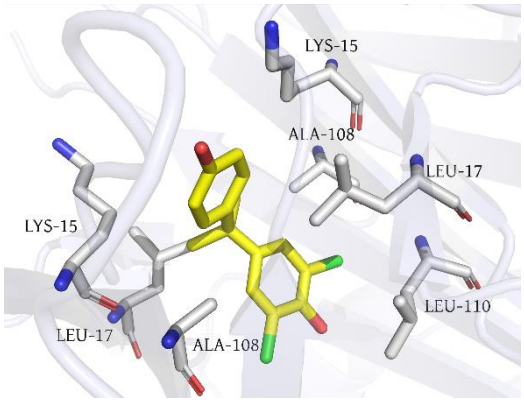
2-bromo-6-chloro-4-nitrophenol



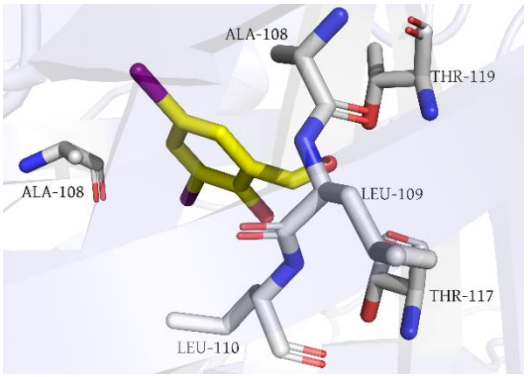
2,6-Dibromo-p-benzoquinone



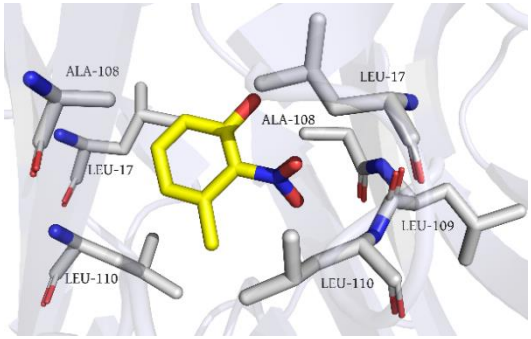
2,6-Dichloro-p-benzoquinone



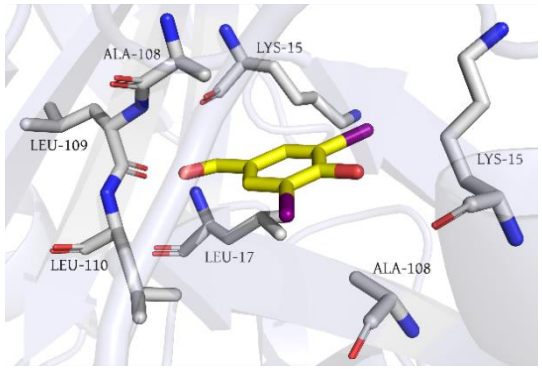
3,5-dichlorobisphenol A



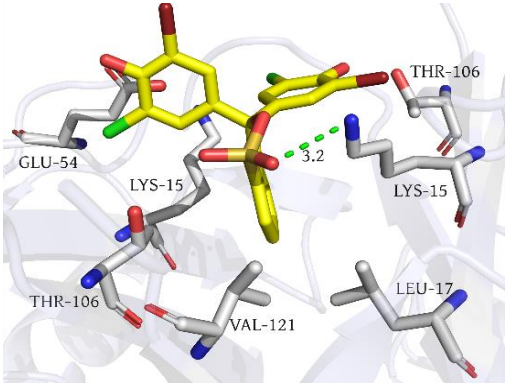
3,5-diiodo-2-hydroxybenzaldehyde



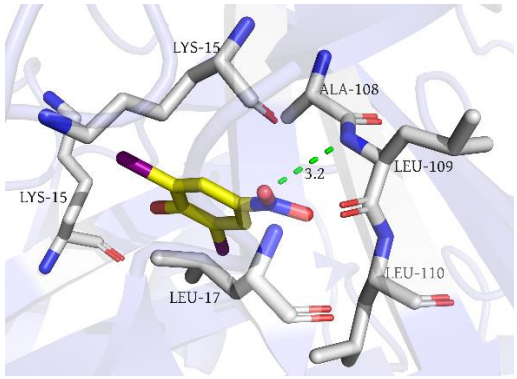
3-methyl-2-nitrophenol



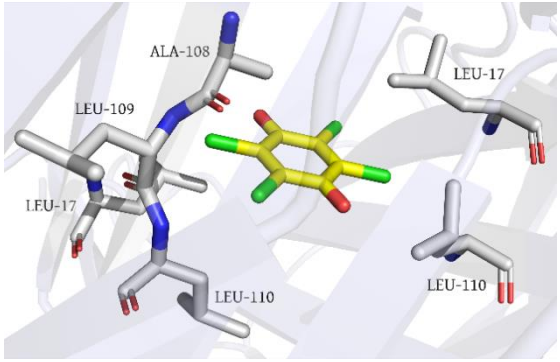
3,5-diiodo-4-hydroxybenzaldehyde



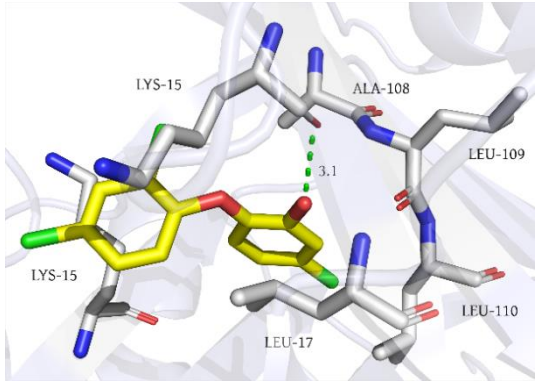
Bromochlorophenol Blue



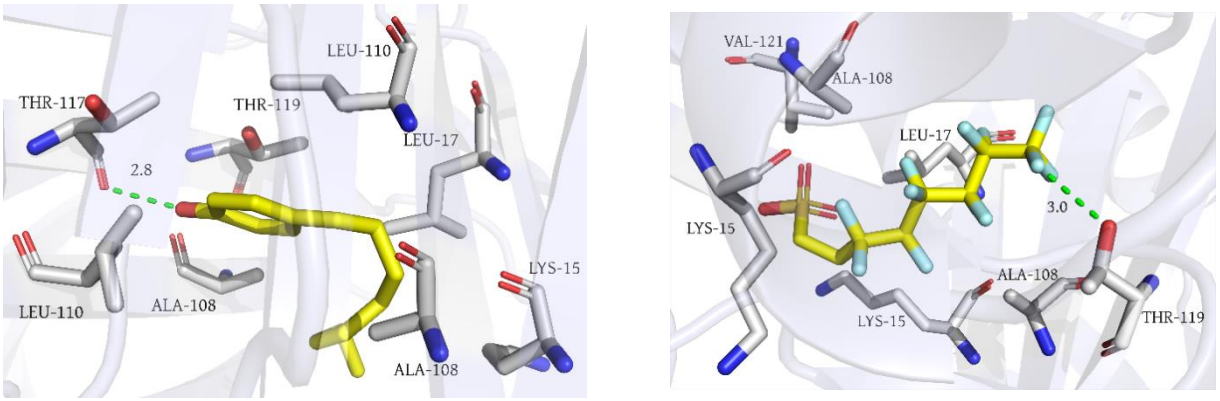
2,6-Diiodo-4-nitrophenol



Tetrachloro-1,4-benzoquinone

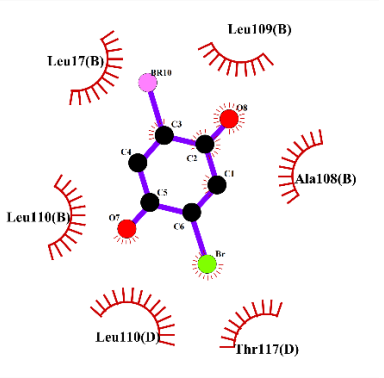


Triclosan

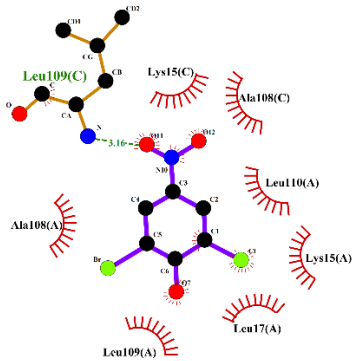


Nonylphenol 6:2 fluorotelomer sulfonic acid

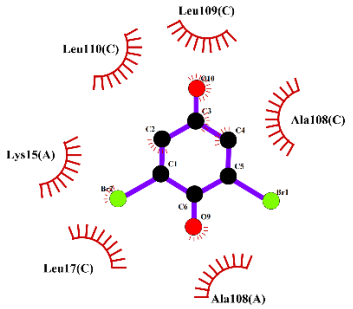
Fig. S8 Binding mode of model compounds in CrmTTR. The green dashed lines represent hydrogen bonds. Binding mode was illustrated at Pymol v2.6.0 software (The PyMOL Molecular Graphics System 2024)



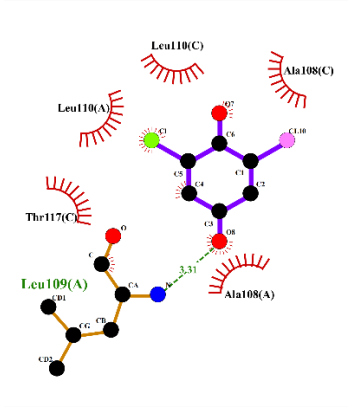
2,5-Dibromo-p-benzoquinone



2-bromo-6-chloro-4-nitrophenol



2,6-Dibromo-p-benzoquinone



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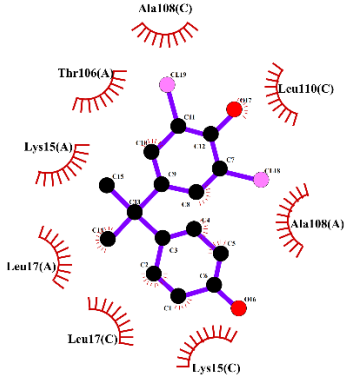
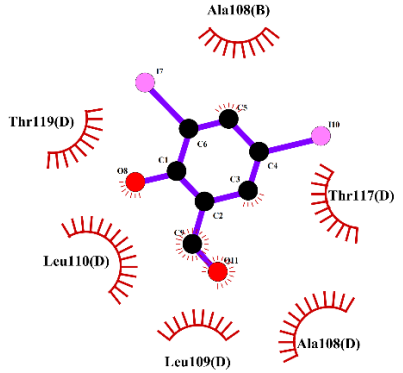
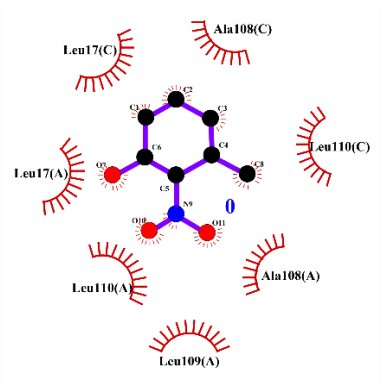


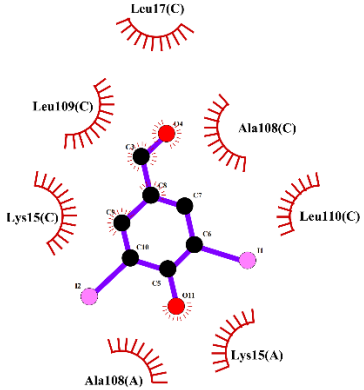
3,5-dichlorobisphenol A



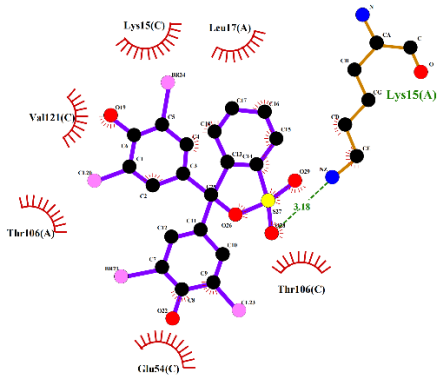
3,5-diiodo-2-hydroxybenzaldehyde



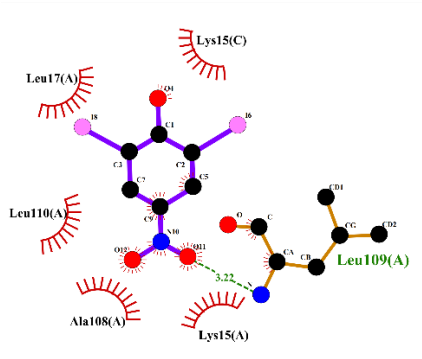
3-methyl-2-nitrophenol



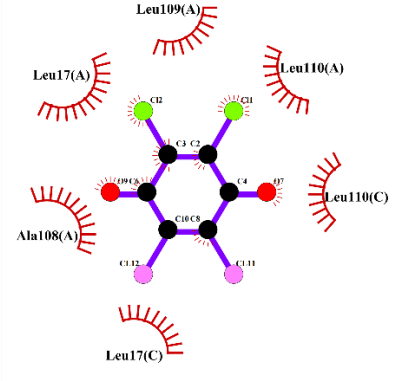
3,5-diiodo-4-hydroxybenzaldehyde



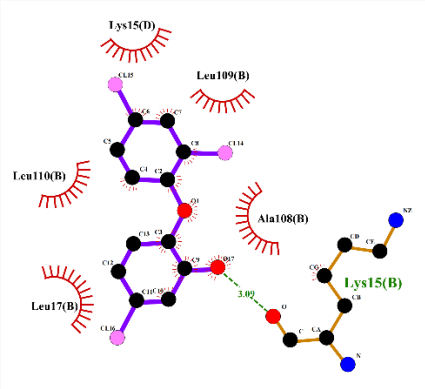
Bromochlorophenol Blue



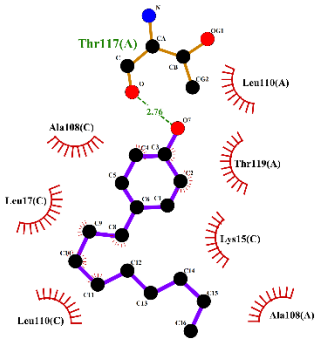
2,6-Diiodo-4-nitrophenol

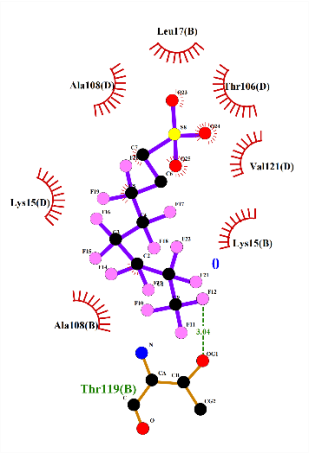


Tetrachloro-1,4-benzoquinone



Triclosan





Nonylphenol

6:2 fluorotelomer sulfonic acid

Fig. S9 Hydrophobic interaction of chemicals with CrmTTR in the binding site (ligand bond, non-ligand bond, hydrogen bond and its length, non-ligand residues involved in hydrophobic contacts, Corresponding atoms involved in hydrophobic contacts)

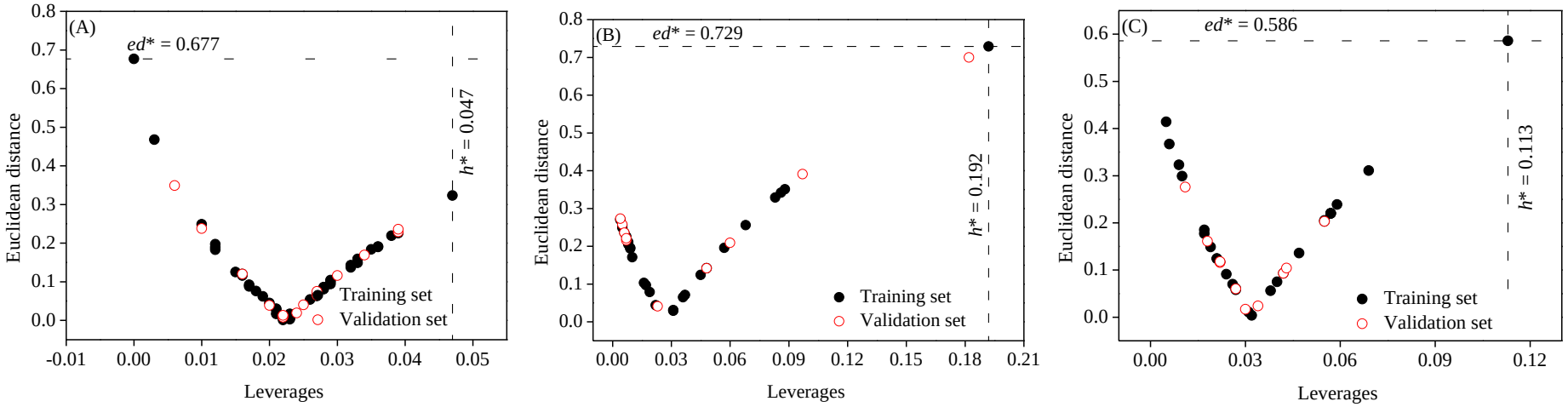


Fig. S10 Application domain of gradient boosting decision tree models for *Gobiocypris rarus* TTR mechanism-based model (A), Little Skate TTR high throughput model (B), Seabream high throughput model (C) defined by using Euclidean distance vs leverage-based methods

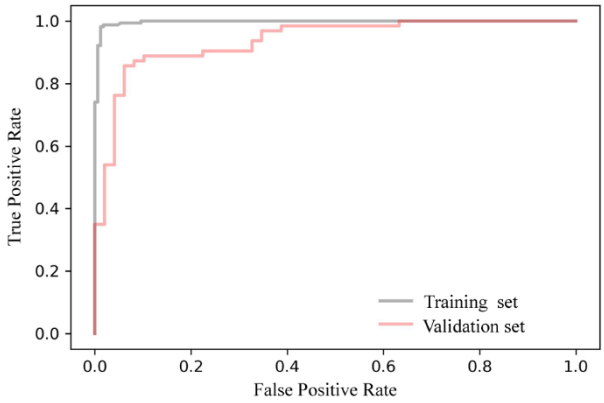


Fig. S11 ROC graph of the human TTR classification model based on gradient boosting decision tree (GBDT) method

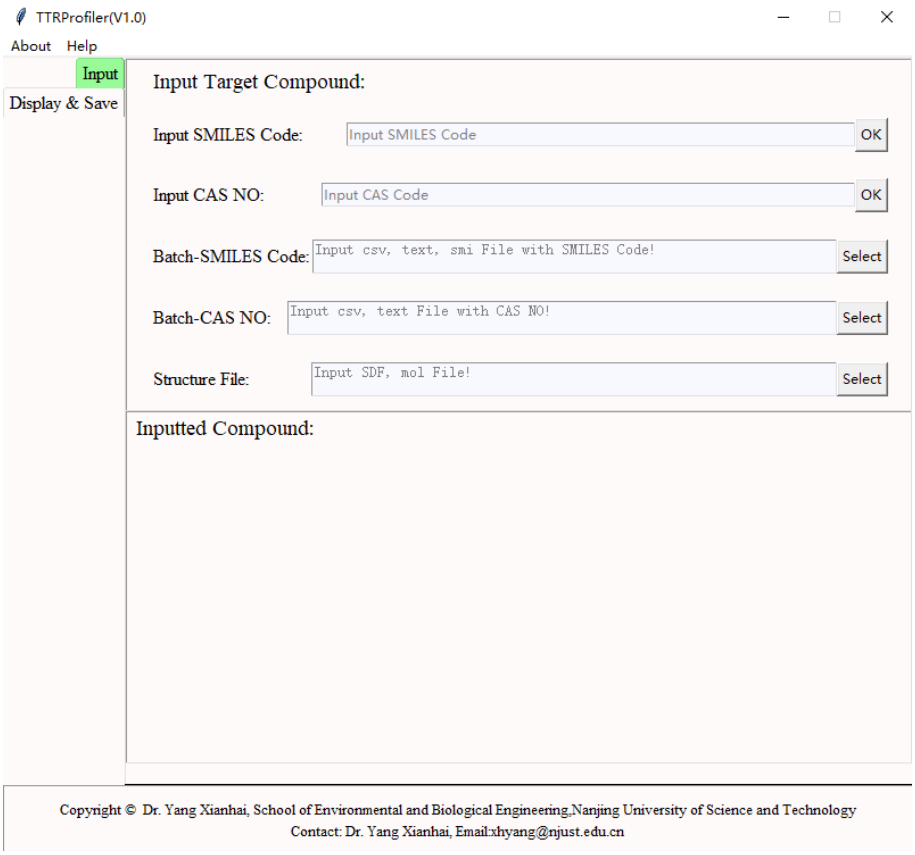


Fig. 12 The input interface of TTR profiler

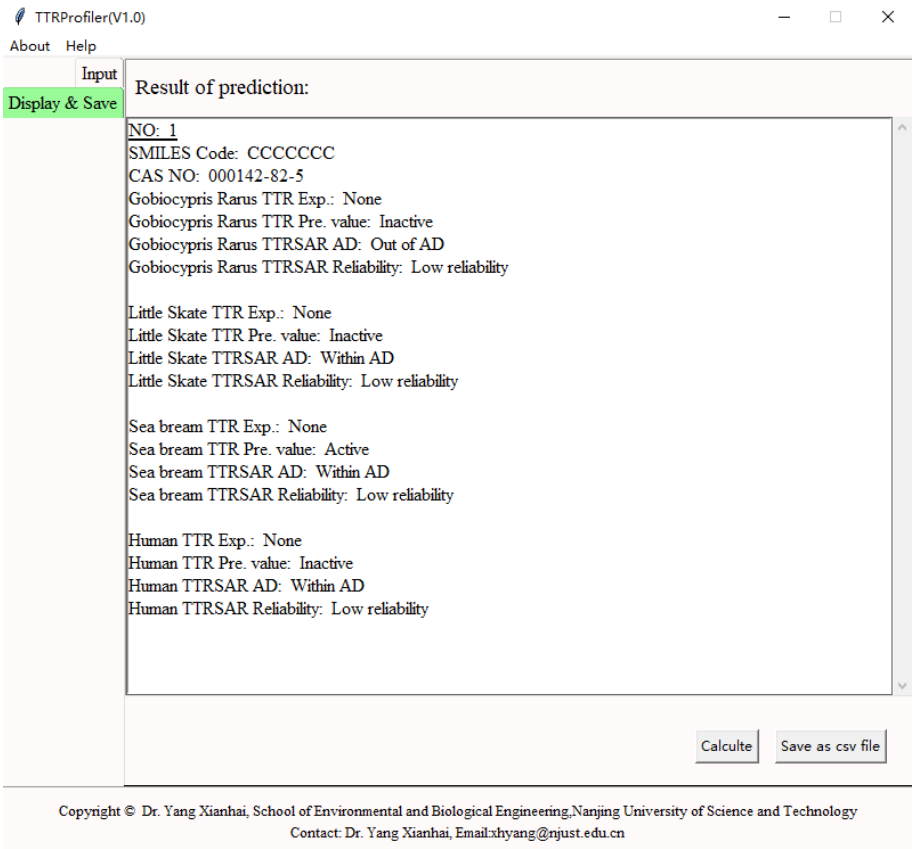


Fig. S13 The display and save interface of TTR profiler

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