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# Partial Order Ranking of Organophosphates with Special Emphasis on Nerve Agents

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**Abstract**

Organophosphates, especially the so-called nerve agents including G-agent like Sarin, Tabun, Soman, and V-agents like VX are in general highly toxic substances. Data on the latter compounds are typically classified material and thus only scarcely available. However, a wide variety of structurally related compounds are well known and well characterized, i.e., organophosphor insecticides.

Partial order ranking appears as an obvious possibility to remedy the lack of availability of data. Through the partial ordering it is possible to give the nerve agents an identity by comparing them to structurally related organophosphor insecticides and hereby obtain data necessary in order to perform a risk assessment in relation to the demilitarisation activities.

The paper describes the development of a partial order based ranking of organophosphates with focus on selected nerve agents. Descriptors applied to rank these substances are "noise-deficient" QSAR generated data, i.e., data not being hampered by random fluctuations as they are forced to obey a first order equation. Potential substitutes for nerve agents to be applied in, e.g., experimental studies are disclosed based on an analysis of average ranks.

## 1 Introduction

Organophosphates are in general rather highly toxic substances that exert their toxic effect by inhibition of acetylcholine esterase. Among these compounds we find the so-called nerve agents including G-agent like Sarin, Tabun, Soman, and V-agents like VX, Amiton etc. These compounds have received considerable interest due to their potential use as weapons of mass destruction.

According to the 'Convention for the Prohibition of the Development, Production [CWC], Stockpiling and Use of Chemical Weapons and their Destruction' major emphasis is given on declaration and destruction of existing stockpiles of chemical weapons as well as of chemical weapons production facilities. The Convention covers the destruction of both chemical weapons stockpiles and destruction or conversion of chemical weapons production facilities. In both cases risk to the environment as well to human health prevails. However, due to the fact that these compounds have been developed for military purposes data on these compounds are typically classified material and thus only scarcely available.

Even though the data on some of these substances in practice are unavailable a wide variety of structurally related compounds are well known and well characterized, i.e., organophosphor insecticides such as parathion, malation, diazinon, etc. with respect to physico-chemical and toxicological characteristics [FADINAP] (Figure 1).


Figure 1. Generalized formula for the Nerve agents and for organophophor insecticides

The lack of data can to a certain extent be remedied through QSAR modelling. Thus, in the present study physico-chemical properties of nerve agents have been generated using QSAR models based on the EPI Suite [EPI 2000]. In the case of toxicity data are not as easily derived as general QSAR models as e.g. ECOSAR does not take into account compound class

specific action as in the present case the acetylcholine esterase inhibiting effect. Various studies have been devoted to models to remedy this problem [de Bruijn and Hermens, 1933;Verhaar et al., 1994; Eldred and Jurs1999; Singh, 2001]. The present study primarily focuses on the environmental aspects and only to a minor extent to toxicological aspects, as the extreme toxicity of the nerve agents is obvious. It should be emphasized that the environmental processes of these substances are not different from other substances. However, the high toxicity must obviously be considered.

Chemical weapons, as the nerve agents, have been developed to kill or pacify humans. Halabja constitutes a scaring example [Halabja, 1988]. However, obviously the environmental aspects of these substances are of major interest. The substances will typically be spread as a mixture of gas and droplets that eventually will be deposited on surfaces such as soil, plant, buildings etc. Thus, the exposure may be due to a direct action of the primary cloud or through action of a secondary cloud resulting from evaporation from contaminated surfaces [FOI 2002].

The possible contamination of territories may constitute a significant strategic element in chemical warfare. Thus, the advance of troops through possible contaminated territory may be done only under full personal protection that will severely hamper the mobility and action capability. Obviously, environmental characteristics such as solubility, sorption, vapor pressure and persistence are of major importance in order to evaluate when it will be safe to send in troops without personal protection equipment. In this connection it should be mentioned that the relatively high number of casualties during the terrorist attack in the Tokyo subway March 20$^{th}$, 1995 [Tokyo, 1995] can be attributed to the use of Sarin, exhibiting a relatively high vapor pressure. Had VX, exhibiting a much lower vapor pressure, been used, the direct consequences would probably have been less pronounced even though the toxicity of VX is significantly higher than that of Sarin. On the other hand the subsequent decontamination of the station, the train etc. would have been much more demanding.

The present study paper emphasizes the development of a partial order based ranking of organophosphates with focus on selected nerve agents. The main objective is to disclose experimentally well-characterized compounds that can be used experimentally to study the

environmental behaviour without exhibiting the extreme toxicity of the nerve agents, however, still from an overall viewpoint exhibit analogous environmental characteristics as the nerve agents. Further, through the partial ordering it appears possible to give the single nerve agent an identity by comparing to structurally related organophosphor insecticides, hereby obtaining data necessary in order to perform a risk assessment in relation to the demilitarisation activities.

## 2 Method

The partial order ranking of the organophosphor compounds is done by an application of the WHasse software [Brüggemann et al, 1995] using solubility (log *Sol*), octanol-water partitioning coefficients (log $K_{OW}$), organic carbon-water partitioning coefficients (log $K_{OC}$), bioconcentration factors (log *BCF*), biodegradation potentials for ultimate degradation (*BDP3*), vapour pressures (log *VP*) and Henry Law constants as generated by the EPI Suite, (log *HLCe*), and by the bond contribution method, (log *HLCb*), respectively, as descriptors. The theory of partial order ranking is presented elsewhere [e.g. in Davey and Priestley, 1990] and application in relation to QSAR is presented previously [Carlsen et al., 2001; Brüggemann et al., 2001; Carlsen and Walker, 2003, Carlsen et. al., 2003] and shall not be repeated here. The visualization of the ranking is made through the Hasse Diagrams.

The generation of the average rank of the single compounds in the Hasse diagram can be obtained through deriving a large number of randomly generated linear extensions [Sørensen et al., 2001; Lerche et al., 2002; Lerche et al., 2003]. Alternatively, the average rank of a specific compounds, $\boldsymbol{q}$, can be obtained applying the simple empirical relation

$$\boldsymbol{Rk_{av} = (N+1) - (S+1)\cdot(N+1)/(N+1-U)} \qquad \text{(Eq. 1)}$$

Where N is the number of elements in the diagram, *S* the number of successors to $\boldsymbol{q}$ and *U* the number of elements being incomparable to $\boldsymbol{q}$ [Brüggemann et al., 2004].

Descriptors applied to rank these substances are based on QSAR modelling, the test set being experimental data for up to 65 organophosphor pesticides [Carlsen, subm]. Data are known for a few of the nerve agents, the latter being adopted as validation set [Carlsen, subm].

In the present study the descriptors are generated through QSAR modelling, the EPI Suite being the primary tool [Carlsen, subm; EPI 2000]. Thus, log $K_{OC}$ and *BDP3* data are used as estimated by the appropriate modules in the EPI Suite, whereas the EPI generated values for log $K_{OW}$, log *VP* and log *HLC* are further treated, i.e., new linear QSAR models are build by estimating the relationships between the EPI generated data and available experimental data for up to 65 organophosphor insecticides, the general formula for the descriptors, $D_i$, to be used being

$$\boldsymbol{D_i = a_i \cdot D_{EPI} + b_i} \qquad \text{(Eq. 2)}$$

$D_{EPI}$ being the EPI generated descriptor value and $a_i$ and $b_i$ being constants. The log $K_{OW}$ values generated in this way are subsequently used to generate log *BCF* values according to the Connell formula [Connell and Hawker, 1988]

$$\log BCF = 6.9 \cdot 10^{-3} \cdot (\log K_{ow})^4 - 1.85 \cdot 10^{-1} \cdot (\log K_{ow})^3 + 1.55 \cdot (\log K_{ow})^2 - 4.18 \cdot \log K_{ow} + 4.72 \qquad \text{(Eq. 3)}$$

The model was somewhat modified. Thus, a linear decrease of log *BCF* with log $K_{OW}$ was assumed in the range $1 < \log K_{OW} < 2.33$, the log $BCF = 0.5$ for $\log K_{OW} \leq 1$, the latter value being in accordance with BCFWin [EPI 2000].

Subsequently data for missing organophosphor insecticides and the nerve agents are calculated based on these formula and the appropriate EPI generated data. The descriptors generated this way are denoted “noise-deficient” as they are not hampered by random fluctuations as they are forced to obey a first order equation. For details on the QSAR modelling [Carlsen, subm)] should be consulted.

In Table 1 the single descriptor combinations, denoted ‘cases’, are visualized. In the single cases one or more of the descriptors are multiplied by -1 (marked by *) to secure identical ranking order by all used descriptors. Thus, in all cases the compounds exhibiting the environmentally more problematic characteristic are associated with the lowest rank.

Consequently, the environmentally most hazardous compounds are found in the top of the Hasse diagrams.

Table 1. Descriptor combinations applied (for example: in case 5 the descriptors log *Sol* and - log *Kow* were applied to get a partial order)

| Case | log *Sol* | log *Kow* | log *Koc* | log *BCF* | *BDP3* | log *VP* | log *HLCe* | log *HLCb* |
|---|---|---|---|---|---|---|---|---|
| **0** | | | | **X** | **X*** | | | |
| **1** | | | | **X** | **X*** | **X*** | | |
| **2** | | | | | **X*** | **X*** | | |
| **3** | | | | | **X*** | | **X*** | |
| **4** | | | | | **X*** | | | **X*** |
| **5** | **X** | **X*** | | | | | | |
| **6** | **X** | | **X*** | | | | | |
| **7** | | **X** | | | | | **X*** | |
| **8** | | **X** | | | | | | **X*** |
| **9** | **X** | | | | **X*** | | **X*** | |
| **10** | **X** | | | | **X*** | | | **X*** |

The single descriptor combinations are chosen in order to focus on PB characteristics (persistence and bioaccumulation) (case 0), PB characteristics including evaporation from surfaces (case 1), environmental persistence including evaporation from surfaces (case 2) and from aqueous solutions (case 3 - 4) and the environmental availability expressed as the ability to wash out (case 5 - 6), persistence in aqueous solutions (case7 - 8) and persistence in aqueous solutions taking degradation into account (case 9 - 10), respectively.

## 3 Results and Discussion

Both experimental as well as EPI Suite generated data are obviously defective. Thus, the basic idea of using the above mentioned type of QSAR modelling, is to eliminate the noise associated with the data in order to secure that the subsequent rankings are not hampered by incidental variations neither in experimental data nor in the EPI generated data. The applied QSAR modelling is illustrated in Fig. 2, visualizing the modelling of log $K_{OW}$ (eqn. 5) based on a test set including 53 organophosphor insecticides.

$$\log K_{OW} = 0.894 \cdot \log K_{OW(EPI)} + 0.487; \qquad r^2 = 0.947 \qquad \text{(Eq. 5)}$$

The EPI-based modified QSAR models for the single descriptors described above are subsequently used to generate the values for organophosphor insecticides possibly not included in the test set due to the non-availability of experimental data as well as for the 16 know or potential nerve agents. As 81 compounds are included in the ranking, the resulting Hasse diagrams being rather confusing. In Fig. 3 the Hasse diagram disclosing the PB characteristics of the 81 compounds, i.e. corresponding to Case 0, (cf. Table 1) is displayed.

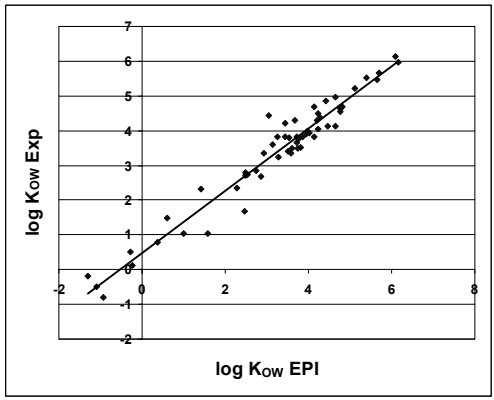


Figure 2. Visualization of the EPI-based modified QSAR modeling of **log $K_{OW}$** based on 53 organophosphor insecticides

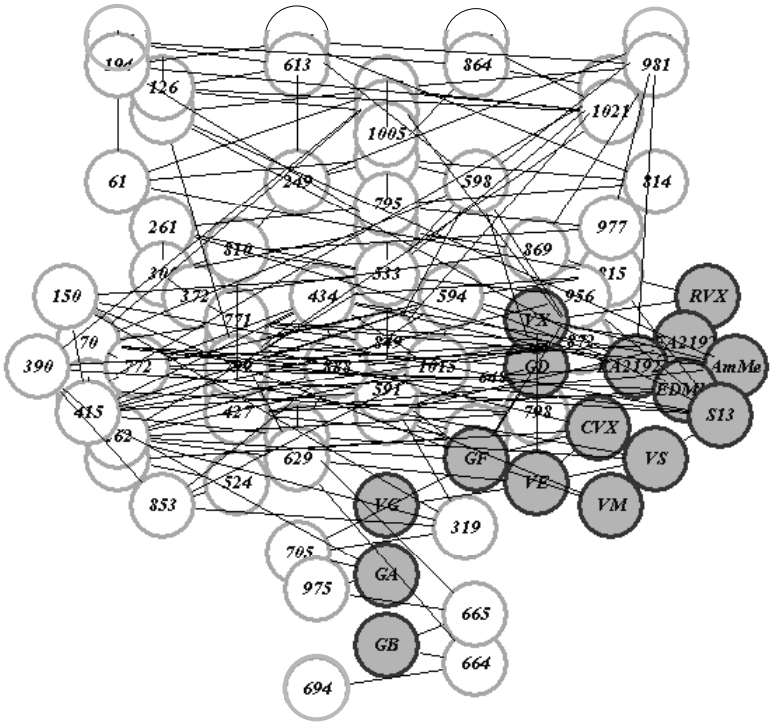


Figure 3. Hasse diagram displaying the PB characteristics of the 65 organophosphor insecticides and 16 nerve agent (hatched), The numbers corresponds to the numbering of the organophosphor insecticides in the FADINAP database

As mentioned in the introduction specific, e.g., highly toxic compounds as the nerve agents may obtain an identity by comparison to significant less toxic organophosphor insecticides. Thus, this comparison may lead to the disclosure of compounds, which from an overall viewpoint exhibit analogous environmental characteristics as the nerve agents. However, these compounds are experimentally well characterized, however, without necessarily exhibiting the extreme toxicity of the nerve agents. Thus, these compounds may be used experimentally to study the environmental behaviour of the nerve agents.

A priori compounds located on the same level in the Hasse diagram are assumed to be close in their overall characteristics based on the set of descriptors used. On this basis, in the above example (Fig. 3) the highly toxic EDMM ($LD_{50}$ (rats, acute, oral) = 0.121 mg/kg) may be substituted by, e.g., compounds No. 71 (Azinphos Methyl; $LC_{50}$ = 4 mg/kg), 312 (Dichlorvos; $LC_{50}$ = 56 mg/kg), 591 (Iprobenfos; $LC_{50}$ = 490 mg/kg) or 648 (Mephosfolan; $LC_{50}$ = 8.9 mg/kg).

However, a further analysis is necessary to disclose how close these compounds actually are. For this analysis we have chosen the concept of average rank [Lerche et al., 2002; Brüggemann et al., 2004]. Thus, it is assumed that if the average ranks, $Rk_{av}$, of two compounds are close, the two compounds will on an average basis display similar characteristics as being determined by the set of descriptors applied. In Table 2 the average ranks for the four compounds are compared.

Table 2. Average ranks for the PB characteristics as determined by log *BCF* and the biodegradation potential for EDMM, Azinphos Methyl, Dichlorvos, Iprobenfos and Mephosfolan

| Compound | $LC_{50}$ (mg/kg) Rat, acute, oral | $RK_{av}$ Linear Extensions[a] | $RK_{av}$ eqn. 1 |
|---|---|---|---|
| EDMM | 0.121 | 55.6 | 55.9 |
| Azinphos Methyl | 4 | 46.6 | 51.1 |
| Dichlorvos | 56 | 52.7 | 55.9 |
| Iprobenfos | 490 | 48.5 | 50.6 |
| Mephosfolan | 8.9 | 53.6 | 57.9 |

[a] based on 20.000 randomly selected linear extensions.

It is immediately seen that the four possible substitutes for EDMM located on the same level in the Hasse diagram based on average ranks apparently can be regarded as being rather close. Thus, taking the actual toxicities, as expressed through the $LC_{50}$ values into account Dichlorvos appear as the optimal choice as substitute for EDMM in studies where the PB characteristics of the compounds is important, the toxicity associated with the experiments being decreased by a factor close to 500.

Similar analyses are obviously immediately practicable for the other descriptor combinations focusing at other characteristics being determined by two or more descriptors. In the follow-

ing only one more illustrative example shall be given. Thus, looking at the persistence in water, taking the biodegradation into account, i.e., using the descriptors log *Sol*, log *HLCe* and the biodegradation potential (cf. Table 1: Case 9), we generate the Hasse diagram depicted in Fig. 4.

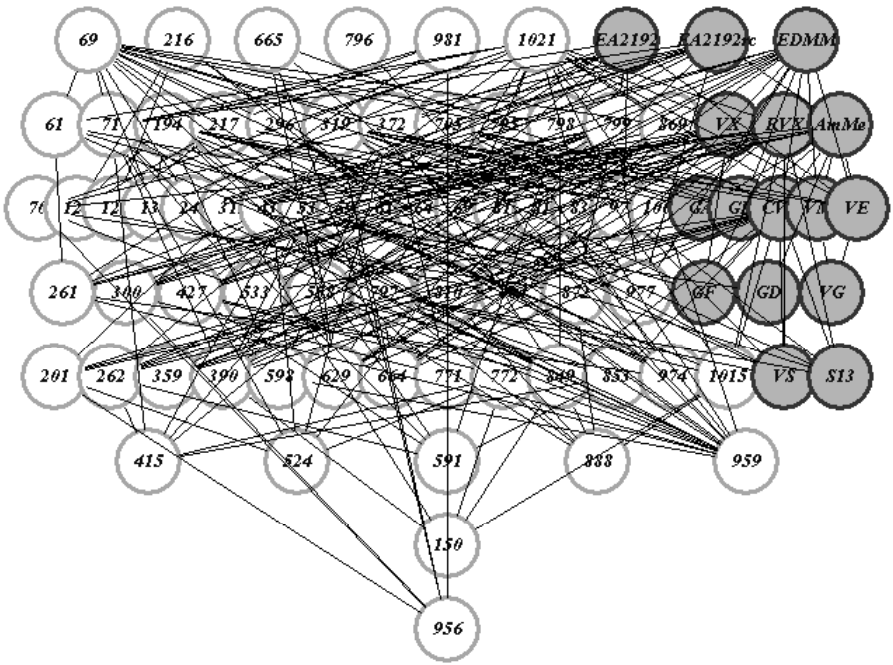


Figure 4. Hasse diagram displaying the persistence in water, taking degradation into account, of the 65 organophosphor insecticides and 16 nerve agent (hatched), The numbers corresponds to the numbering of the organophosphor insecticides in the FADINAP database

In this case we may be interested in the acute percutaneous toxicity of the nerve agent GA (Tabun) in relation to its persistence in water. It is disclosed that GA, exhibiting a $LC_{50}$ = 12.6 mg/kg, is found on the same level as Butamifos, the latter exhibiting a $LC_{50}$ = 5000 mg/kg. However, with reference to the above argument, a further analysis of the average ranks of the two compounds should be performed. The results are displayed in Table 3.

Table 3. Average ranks for the persistence in water as determined by log *Sol, log HLCe* and the biodegradation potential for GA (Tabun) and Butamifos

| Compound | $LC_{50}$ (mg/kg) Rat, acute, percutaneous | $RK_{av}$ Linear Extensions[a] | $RK_{av}$ eqn. 1 |
|---|---|---|---|
| GA (Tabun) | 12.6 | 46.5 | 58.6 |
| Butamifos | 5000 | 44.2 | 61.5 |

[a] based on 20.000 randomly selected linear extensions.

The data displayed in Table 3 strongly support Butamifos as a proper substitute for GA in studies focusing on the persistence in water. Obviously, the substitution of GA with Butamifos will decrease the toxicity by a factor of approx. 400.

It should be noted that some deviations between the average ranks determined based on randomly selected linear extensions and based on the empirical formula eqn. 1 apparently prevail in this case. For a discussion on this matter Brüggemann et al [2004] should be consulted. However, what is important in the present case is that based on both methods of deriving average ranks, a close agreement between the rank of the nerve agent and that of the potential substitute can be observed.

## 4 Conclusions

The present study has demonstrated that partial order ranking using “noise-deficient” QSAR generated descriptors is an effective tool to give compounds where experimental data are not available an identity by comparing to a test set of experimentally well characterized, structurally similar compounds.

It has further been elucidated how experimentally well-characterized compounds that can be selected as substitutes for highly toxic compounds, as the nerve agent, in order experimentally to study the environmental behaviour of the latter, however, without exhibiting the extreme toxicity, but nevertheless, from an overall viewpoint exhibit analogous environmental characteristics.

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Appendix 1. Descriptor values as produced by the respective QSAR models (cf. Carlsen, subm.) for OP insecticides

| *FADINAD* | *CAS No.* | *Name* | *log Sol* | *log $K_{OW}$* | *log VP* | *log HLCe* | *log HLCb* | *log BCF* | *BDP3* |
|---|---|---|---|---|---|---|---|---|---|
| 61 | 64249-01-0 | Anilofos | 1.05 | 3.57 | -1.23 | -7.82 | -8.77 | 2.26 | 2.28 |
| 69 | 35575-96-3 | Azamethiphos | 3.62 | 1.38 | -6.77 | -11.00 | -10.54 | 0.71 | 2.17 |
| 70 | 2642-71-9 | Azinphos ethyl | 1.53 | 3.62 | -6.99 | -9.23 | -8.36 | 2.31 | 2.59 |
| 71 | 86-50-0 | Azinphos methyl | 2.24 | 2.75 | -6.68 | -9.58 | -8.54 | 1.49 | 2.65 |
| 126 | 2104-96-3 | Bromophos | -0.11 | 5.06 | -4.72 | -4.92 | -5.15 | 3.81 | 2.00 |
| 127 | 4824-78-6 | Bromophos ethyl | -1.07 | 5.93 | -1.23 | -4.77 | -4.97 | 4.39 | 1.93 |
| 139 | 36335-67-8 | Butamifos | 0.19 | 4.74 | -5.43 | -6.11 | -7.45 | 3.52 | 2.22 |
| 150 | 95465-99-9 | Cadusapfos | 1.54 | 4.03 | -3.98 | -5.76 | -6.08 | 2.76 | 2.76 |
| 194 | 470-90-6 | Chlorfenvinphos | 1.10 | 4.20 | -5.21 | -6.68 | -6.85 | 2.94 | 1.97 |
| 201 | 24934-91-6 | Chlormephos | 2.45 | 0.49 | -3.15 | -5.70 | -4.68 | 0.50 | 2.66 |
| 216 | 2921-88-2 | Chlorpyriphos | 0.19 | 4.65 | -4.95 | -5.50 | -5.58 | 3.43 | 1.74 |
| 217 | 5598-13-0 | Chlorpyriphos methyl | 0.90 | 3.78 | -4.51 | -5.70 | -5.76 | 2.48 | 1.81 |
| 249 | 56-72-4 | Coumaphos | 0.81 | 4.48 | -6.84 | -8.34 | -6.60 | 3.25 | 2.52 |
| 261 | 13067-93-1 | Cyanofenphos | 0.76 | 4.24 | -1.23 | -7.27 | -6.75 | 2.99 | 2.47 |
| 262 | 2636-26-2 | Cyanophos | 2.43 | 2.70 | -4.11 | -6.80 | -6.17 | 1.46 | 2.73 |
| 296 | 10311-84-9 | Dialifos | 0.15 | 4.19 | -7.15 | -8.04 | -7.48 | 2.93 | 2.31 |
| 300 | 333-41-5 | Diazinon | 1.42 | 3.94 | -4.61 | -6.34 | -6.67 | 2.66 | 2.53 |
| 312 | 62-73-7 | Dichlorvos | 3.85 | 1.02 | -2.18 | -5.91 | -5.93 | 0.51 | 2.52 |
| 319 | 141-66-2 | Dicrotophos | 5.41 | -0.50 | -4.07 | -9.64 | -10.33 | 0.50 | 2.78 |
| 359 | 3811-49-2 | Dioxabenzofos | 2.86 | 3.05 | -1.23 | -6.35 | -4.98 | 1.74 | 2.88 |
| 372 | 5131-24-8 | Ditalimfos | 1.73 | 3.83 | -1.23 | -9.82 | -7.70 | 2.54 | 2.54 |
| 390 | 17109-49-8 | Edifenphos | 1.66 | 3.71 | -5.70 | -7.86 | -7.68 | 2.41 | 2.71 |
| 415 | 13194-48-4 | Ethoprophos | 1.95 | 3.29 | -3.79 | -5.97 | -6.26 | 1.97 | 2.82 |
| 427 | 38260-54-7 | Etrimfos | 2.22 | 0.49 | -4.53 | -7.03 | -7.09 | 0.50 | 2.57 |
| 434 | 22224-92-6 | Fenamiphos | 1.91 | 3.43 | -5.24 | -7.57 | -8.90 | 2.11 | 2.45 |
| 524 | 66767-39-3 | Fonofos | 1.64 | 0.49 | -3.81 | -5.69 | -4.34 | 0.50 | 2.68 |
| 533 | 83733-82-8 | Fosmethilan | 0.63 | 4.08 | -1.23 | -8.54 | -6.76 | 2.82 | 2.73 |
| 534 | 98886-44-3 | Fosthiazate | 3.33 | 2.70 | -5.38 | -9.13 | -8.31 | 1.46 | 2.57 |
| 558 | 23560-59-0 | Heptonophos | 2.97 | 1.75 | -3.63 | -6.75 | -5.83 | 0.92 | 2.63 |
| 591 | 26087-47-8 | Iprobenfos | 1.91 | 3.68 | -4.52 | -6.73 | -6.98 | 2.37 | 2.74 |
| 594 | 42509-80-8 | Isazofos | 1.36 | 3.40 | -4.57 | -6.22 | -6.05 | 2.08 | 2.45 |

| | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| 598 | 25311-71-1 | Isofenphos | 0.92 | 4.64 | -5.18 | -6.48 | -7.23 | 3.42 | 2.58 |
| 613 | 18181-70-9 | Jodfenphos | -0.65 | 5.31 | -5.21 | -4.93 | -5.33 | 4.01 | 1.98 |
| 629 | 121-75-5 | Malathion | 2.49 | 2.53 | -4.33 | -7.00 | -8.19 | 1.36 | 2.90 |
| 648 | 950-10-7 | Mephosfolan | 3.95 | 1.90 | -1.23 | -9.04 | -8.83 | 1.01 | 2.60 |
| 664 | 62610-77-9 | Methacrifos | 3.70 | 0.49 | -3.09 | -6.81 | -5.69 | 0.50 | 2.96 |
| 665 | 10265-92-6 | Methamidophos | 6.13 | -0.34 | -2.15 | -8.26 | -8.18 | 0.50 | 2.89 |
| 694 | 7786-34-7 | Mevinphos | 4.95 | 0.27 | -3.17 | -8.15 | -7.69 | 0.50 | 3.00 |
| 705 | 6923-22-4 | Monocrotophos | 5.24 | -0.68 | -4.84 | -10.41 | -10.58 | 0.50 | 2.81 |
| 771 | 56-38-2 | Parathion | 1.10 | 3.82 | -4.78 | -6.25 | -6.28 | 2.53 | 2.54 |
| 772 | 298-00-0 | Parathion methyl | 2.07 | 2.95 | -4.35 | -6.71 | -6.46 | 1.65 | 2.60 |
| 795 | 2310-17-0 | Phosalone | 0.57 | 4.32 | -1.23 | -7.96 | -6.18 | 3.08 | 2.29 |
| 796 | 36519-00-3 | Phosdiphen | -1.09 | 0.49 | -1.23 | -6.43 | -7.28 | 0.50 | 1.61 |
| 797 | 947-02-4 | Phosfolan | 3.92 | 0.49 | -1.23 | -8.42 | -8.92 | 0.50 | 2.64 |
| 798 | 732-11-6 | Phosmet | 2.21 | 2.70 | -7.18 | -10.15 | -7.42 | 1.46 | 2.65 |
| 799 | 13171-21-6 | Phosphamidon | 3.98 | 0.83 | -4.78 | -9.02 | -10.25 | 0.50 | 2.46 |
| 810 | 24151-93-7 | Piperophos | 0.94 | 4.27 | -5.82 | -7.26 | -8.66 | 3.02 | 2.52 |
| 814 | 23505-41-1 | Pirimiphos ethyl | 0.38 | 4.44 | -5.18 | -5.98 | -5.39 | 3.20 | 2.29 |
| 815 | 29232-93-7 | Pirimiphos methyl | 1.09 | 3.56 | -4.74 | -6.17 | -5.58 | 2.25 | 2.35 |
| 836 | 41198-08-7 | Profenofos | 0.28 | 4.80 | -5.29 | -5.97 | -6.97 | 3.57 | 2.19 |
| 849 | 7292-16-2 | Propafos | 1.54 | 3.82 | -5.02 | -6.94 | -7.44 | 2.53 | 2.68 |
| 853 | 31218-83-4 | Propetamphos | 2.65 | 0.49 | -3.93 | -6.74 | -6.80 | 0.50 | 2.72 |
| 864 | 34643-46-4 | Prothiofos | -0.28 | 5.57 | -1.23 | -4.64 | -4.57 | 4.20 | 2.21 |
| 869 | 77458-01-6 | Pyraclofos | 1.12 | 3.85 | -6.39 | -8.11 | -10.88 | 2.56 | 2.35 |
| 872 | 13457-18-6 | Pyrazophos | 1.02 | 3.64 | -1.23 | -8.13 | -10.32 | 2.33 | 2.59 |
| 888 | 13593-03-8 | Quinolphos | 0.93 | 3.20 | -5.26 | -6.65 | -7.68 | 1.88 | 2.69 |
| 956 | 3689-24-5 | Sulfotep | 1.17 | 4.05 | -4.29 | -5.69 | -5.81 | 2.78 | 2.79 |
| 959 | 35400-43-2 | Sulphofos | -0.08 | 5.54 | -5.13 | -5.49 | -5.73 | 4.18 | 2.64 |
| 974 | 3383-96-8 | Temephos | -1.36 | 6.00 | -1.23 | -6.17 | -7.91 | 4.42 | 2.48 |
| 975 | 107-49-3 | TEPP | 4.32 | 0.49 | -1.23 | -9.46 | -8.62 | 0.50 | 2.87 |
| 977 | 13071-79-9 | Terbufos | 0.95 | 4.28 | -3.97 | -5.15 | -5.55 | 3.03 | 2.50 |
| 981 | 22248-79-9 | Tetrachlorvinphos | 1.29 | 3.89 | -5.67 | -7.41 | -7.13 | 2.61 | 1.75 |
| 1005 | 57018-04-9 | Tolclofos methyl | 0.81 | 4.75 | -4.56 | -5.69 | -4.82 | 3.52 | 2.20 |
| 1015 | 24017-47-8 | Triazophos | 1.76 | 3.10 | -5.43 | -7.63 | -8.97 | 1.78 | 2.68 |
| 1021 | 52-68-6 | Trichlorfon /Chlorophos | 4.96 | 0.24 | -4.53 | -9.71 | -10.07 | 0.50 | 2.06 |

Appendix 2. Descriptor values as produced by the respective QSAR models (cf. Carlsen, subm.) for Nerve agents

| *Type* | *CAS No.* | *Name* | *log Sol* | *log $K_{OW}$* | *log VP* | *log HLCe* | *log HLCb* | *log BCF* | *BDP3* |
|---|---|---|---|---|---|---|---|---|---|
| CWA | 77-81-6 | Tabun (GA) | 5.05 | 0.74 | -2.29 | -6.37 | -7.23 | 0.50 | 2.84 |
| CWA | 107-44-8 | Sarin (GB) | 5.21 | 0.70 | -0.70 | -5.65 | -5.16 | 0.50 | 2.89 |
| CWA | 329-99-7 | Cyclosarin (GF) | 3.94 | 1.92 | -1.99 | -5.86 | -5.15 | 1.02 | 2.80 |
| CWA | 96-64-0 | Soman (GD) | 3.78 | 1.92 | -1.54 | -5.17 | -4.88 | 1.02 | 2.58 |
| CWA | 50782-69-9 | VX | 4.07 | 2.33 | -3.38 | -7.47 | -7.93 | 1.25 | 2.35 |
| CWA | 159939-87-4 | R-VX | 4.03 | 2.40 | -4.14 | -8.34 | -7.93 | 1.29 | 2.35 |
| CWA | | C-VX | 3.96 | 2.46 | -4.41 | -8.61 | -7.93 | 1.32 | 2.65 |
| "CWA" | | EA2192 | 4.70 | 1.85 | -5.42 | -10.57 | -9.90 | 0.98 | 2.42 |
| "CWA" | | R/C "EA2192" | 5.55 | 1.09 | -5.28 | -11.26 | -10.09 | 0.55 | 2.48 |
| Possible V | 78-53-5 | VG (Amiton) | 4.38 | 2.01 | -4.06 | -8.58 | -8.55 | 1.07 | 3.64 |
| Possible V | | Amiton methyl | 5.36 | 1.13 | -3.83 | -9.30 | -8.73 | 0.57 | 2.57 |
| Possible V | | Vx (EDMM) | 5.91 | 0.71 | -3.03 | -8.93 | -8.30 | 0.50 | 2.48 |
| Possible V | | VM | 4.94 | 1.59 | -3.78 | -8.84 | -8.11 | 0.83 | 3.22 |
| Possible V | | VE | 4.45 | 2.02 | -4.11 | -8.73 | -8.02 | 1.08 | 3.19 |
| Possible V | | VS | 3.60 | 2.77 | -4.22 | -8.00 | -7.84 | 1.51 | 3.15 |
| Possible V | | S12 | 2.78 | 3.48 | -3.41 | -8.10 | -7.92 | 2.16 | 3.12 |