

# Prediction of Autoignition Temperatures of Organic Compounds from Molecular Structure

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Received December 31, 1996<sup>®</sup>

A quantitative structure–property relationship study is performed to develop mathematical models that relate the structures of a heterogeneous group of organic compounds to their autoignition temperature values. The molecular structures of the compounds are represented by calculated numerical descriptors which encode their topological, electronic, and geometric features. These descriptors are used to develop several multiple linear regression and computational neural network models to predict the autoignition temperatures of a data set consisting of hydrocarbons, halohydrocarbons, and compounds containing oxygen, sulfur, and nitrogen. Both genetic algorithm and simulated annealing routines are used to select subsets of descriptors based on multiple linear regression and computational neural networks. The models that are developed have predictive ability in the range of the experimental error of autoignition temperature measurements.

## INTRODUCTION

The autoignition temperature (AIT) is defined as the lowest temperature at which a substance in air will ignite in the absence of a spark or flame. The combustible substance reacts with oxygen in the air, leading to exothermic oxidation reactions. Autoignition occurs when the rate of heat evolved by these reactions is just greater than the rate at which heat is lost to the surroundings.

The measurement of AIT is dependent upon many experimental factors, including the test procedure and the apparatus.<sup>1–7</sup> Most methods consist of introducing the sample into the apparatus container and slowly raising the temperature until the appearance of a flame is identified by an observer. Some of the parameters that can vary are the container size, shape, and composition, the air flow into the container, the method of sample introduction, and the rate and duration of heating. Differences in these parameters can lead to changes in the delay time until autoignition, uniform mixing of the sample with air, fuel-to-air ratio, and catalytic effects, all of which can affect the AIT to a certain extent. The measured AIT can vary by hundreds of degrees based on combinations of these factors.

Since autoignition occurs in air without the presence of an ignition source, it is an important safety parameter in many common situations relating to the fire potential of chemicals. Such situations include the manufacture, processing, handling, transport, and storage of combustible materials.<sup>2</sup> Autoignition is also studied because it is related to the performance of combustion engines through the phenomenon of engine knock.<sup>8,9</sup> Many previous studies have shown that the AIT of a compound is very dependent upon its structure,<sup>1,6,10–15</sup> which suggests that further information can be gained through an investigation of this structure–property relationship. The autoignition of organic compounds proceeds by a free radical reaction, where the stability of the free radical intermediates determines the ease of oxidation. The stability of the radicals that are formed relates directly to structure. Not surprisingly, some of the structural features

that affect the mechanism of autoignition are chain length, addition of methyl groups, unsaturation, branching, aromaticity, and strain.<sup>2,11</sup> These studies have also led to a deeper understanding of oxidation and combustion mechanisms.

One method that can be used as an aid to understanding AIT is the area of quantitative structure–property relationships (QSPR). In a QSPR study, a mathematical model is developed which relates the structures of a set of compounds to a physical property such as AIT. The underlying assumption in a QSPR is that there is some sort of relationship between the physical property of interest and the molecular structure of the compounds. Many different physical properties have been studied in this manner, including boiling point,<sup>16,17</sup> aqueous solubility,<sup>18</sup> chromatographic retention indices,<sup>19</sup> and <sup>13</sup>C nuclear magnetic resonance chemical shifts.<sup>20,21</sup> In addition to providing a means to predict a physical property without having to actually measure it, a QSPR also may lead to an understanding of the structural features related to the physical property.

The parametric approach employed involves relating the experimentally determined AIT to structure-based descriptors. Descriptors are numerical representations of structural features of molecules that attempt to encode important information about structures that lead to physical properties. The descriptors can be topological, geometric, electronic, or a combination of these, such as hydrogen bonding and charged partial surface area descriptors which combine geometric and electronic information. Linear and nonlinear models are developed that relate AIT to the structure-based descriptors. The linear models, which will be referred to as type 1 models, are of the form

$$S = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \dots + \beta_n X_n \quad (1)$$

where  $S$  is the experimental AIT,  $\beta_n$  is the linear regression coefficient, and  $X_n$  is the descriptor value.

Improvement of linear models can be achieved with computational neural networks (CNN), which can be considered as a nonlinear mathematical function. The results of these experiments will be referred to as type 2 models.

<sup>®</sup> Abstract published in *Advance ACS Abstracts*, April 1, 1997.

Improvements occur both because of the nonlinear nature and because of the larger number of adjustable parameters. Although the results of neural networks are better, the computational time required is much higher than for linear regression analysis. Regression coefficients for a given subset of descriptors can be calculated in a single step, while the optimization of adjustable parameters in a neural network is an iterative process. The optimization of the neural network in this work is performed using a quasi-Newton BFGS (Broyden–Fletcher–Goldfarb–Shanno)<sup>22–26</sup> algorithm, as opposed to the commonly used back propagation algorithm,<sup>27</sup> because it has proven to give more accurate results and is more computationally efficient. The quasi-Newton BFGS algorithm utilizes second derivative information of the error function to determine the direction of a series of line minimizations.

In addition to improving the results of the model chosen by multiple linear regression analysis, the CNN can also be used as a form of feature selection to select a good subset of descriptors. The subset of descriptors chosen as the best model based on linear criteria will not necessarily be the best subset of descriptors when considering a nonlinear relationship between the descriptors and the AIT. Separate models, type 3 models, are therefore developed using the nonlinear CNN as the determining factor of the quality of a subset.

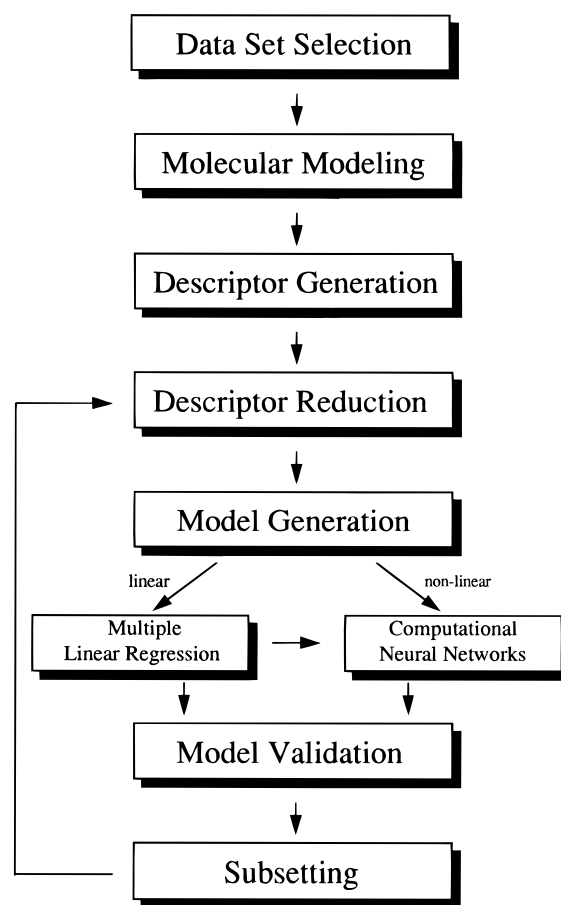
#### EXPERIMENTAL SECTION

The QSPR models in this study were developed using the Automated Data Analysis and Pattern Recognition Toolkit (ADAPT)<sup>28,29</sup> as well as genetic algorithm,<sup>30</sup> simulated annealing,<sup>31,32</sup> and computational neural network<sup>33</sup> routines. All computations were performed on a DEC 3000AXP Model 500 workstation at Penn State University. The flow chart in Figure 1 outlines the procedure used in an ADAPT study.

The selection of the data set was controlled by the availability and quality of data. The data set contained a structurally diverse set of compounds for which a single QSPR model for AIT could not be developed. However, more homogeneous subsets of the compounds had enough common features so that a relationship between structure and AIT could be modeled. There were a large number of compounds with AIT values of similar experimental quality. The data in this study were obtained from the CHEMSAFE Database.<sup>34</sup>

The data set consisted of 327 organic compounds ranging from straight chain hydrocarbons to compounds containing halogens, nitrogen, oxygen, and sulfur. The functional groups represented by this set include alcohol, ether, ester, aldehyde, ketone, carboxylic acid, amine, amide, nitro, nitrile, and thiol, with many of the compounds containing multiple functional groups. The number of non-hydrogen atoms in the compounds varied from two to twenty. The AIT values for these compounds ranged from 140 °C to 705 °C. The experimental error associated with these values is reported to be  $\pm 10$  °C below 300 °C and  $\pm 20$  °C above 300 °C.<sup>34</sup>

The data set was divided randomly into training sets (tssets) and prediction sets (pssets). The tset was used for model development, and the portion of the compounds held aside as an external pset was used for model validation. The initial breakdown of the compounds was into a 300 member tset



**Figure 1.** Flow chart of the ADAPT methodology used to develop autoignition temperature prediction models.

and a 27 member pset. Many different subsets were used to develop models with improved results, and in all cases a pset was chosen that contained approximately 10% of the compounds. For the computational neural networks used in this study, the tset was further divided randomly into a smaller tset and a cross-validation set (cvset). The cvset was used to prevent overtraining of the neural network, as discussed below. The pssets used for linear regression and computational neural networks consisted of the same compounds for comparison purposes. The pssets and cvsets were chosen to be representative of the types of compounds in the data set and to span the range of the AIT values, but the specific compounds were chosen randomly.

The compounds in the data set were entered as two-dimensional sketches into Hyperchem and stored as connection tables. In order to generate accurate three-dimensional structures, the compounds were modeled in a semiempirical molecular orbital modeling routine, MOPAC,<sup>35</sup> and put into their energy minimized conformation. Accurate three-dimensional structures were necessary for the next step of the ADAPT study, descriptor calculation, since many of the descriptors that were generated were dependent upon the geometry of the molecule.

ADAPT routines were used to calculate descriptors to accurately encode the structural features of the compounds. The descriptors were calculated directly from the energy-minimized three-dimensional conformations, with the goal of encoding the structural features that give rise to differences in AIT for different compounds. Topological descriptors

calculated were as simple as counts of certain types of atoms, functional groups, or bond types. Other types of topological descriptors were simple and valence-corrected molecular connectivity indices and path counts to encode the size and degree of branching of the compounds. Geometric descriptors included moments of inertia, molecular surface area, and molecular volume. The electronic environment of the compounds was described by charge descriptors such as the charge on the most positive or negative atom. Charged partial surface area (CPSA) descriptors and hydrogen bonding descriptors were also calculated that incorporated both geometric and electronic structure information. Other descriptors that were not generated by ADAPT programs, such as energy values from the MOPAC minimizations, were included in the descriptor pool based on AIT theory and previous AIT studies.<sup>13</sup> Approximately 160 structure-based descriptors were calculated for each compound.

The resulting descriptor pool was screened to ensure that only descriptors with high information content were used in developing models. The first type of descriptor reduction performed was objective feature selection, where the decisions on which descriptors to retain in the pool were made without use of the dependent variable (AIT). In objective feature selection, descriptors are removed which contain little or redundant information. Pairwise correlations between descriptors were examined so that only one descriptor was retained from a pair contributing similar information (correlation coefficients  $\geq 0.95$ ), and descriptors with greater than 80% identical values were dropped since those descriptors are not encoding the structural differences between the compounds that account for their different AIT values. The reduced descriptor pool of approximately 60 descriptors contained an information-rich subset of the calculated descriptors that was more manageable for model development. One reason for reducing the size of the descriptor pool was to minimize the possibility of developing a model based on chance effects. Such a model could arise from screening too many descriptors relative to the number of observations in the data set. A value of roughly 0.6 for the ratio of screened descriptors to observations was used as a conservative guideline for avoiding chance effects.<sup>36</sup> The use of an external pset was a further check of chance correlations in that a model based on chance effects would be unlikely to have predictive ability. A model that produced a pset error that was not similar to the tset error would have been a flag to investigate the model more closely for chance effects.

The goal of model development was to find a subset of the descriptors that accurately represented the AIT through both linear and nonlinear relationships. Since the AIT values were used, this step was considered subjective feature selection. Because of the large size of the descriptor pool, even after reduction, it was not feasible to investigate all possible combinations of the descriptors. A variety of methods was used to generate linear regression models. A genetic algorithm routine and a simulated annealing routine both investigated a large number of descriptor subsets, with the quality of the model based on root mean square (rms) error and statistical integrity. Good models were further investigated using an interactive regression analysis routine. This routine allowed descriptors to be added or removed and the effect on the model statistics to be determined. A variety of subset sizes was investigated to determine the optimum

number of descriptors in a model. When adding another descriptor did not improve the statistics of a model, it was determined that the optimum subset size had been achieved.

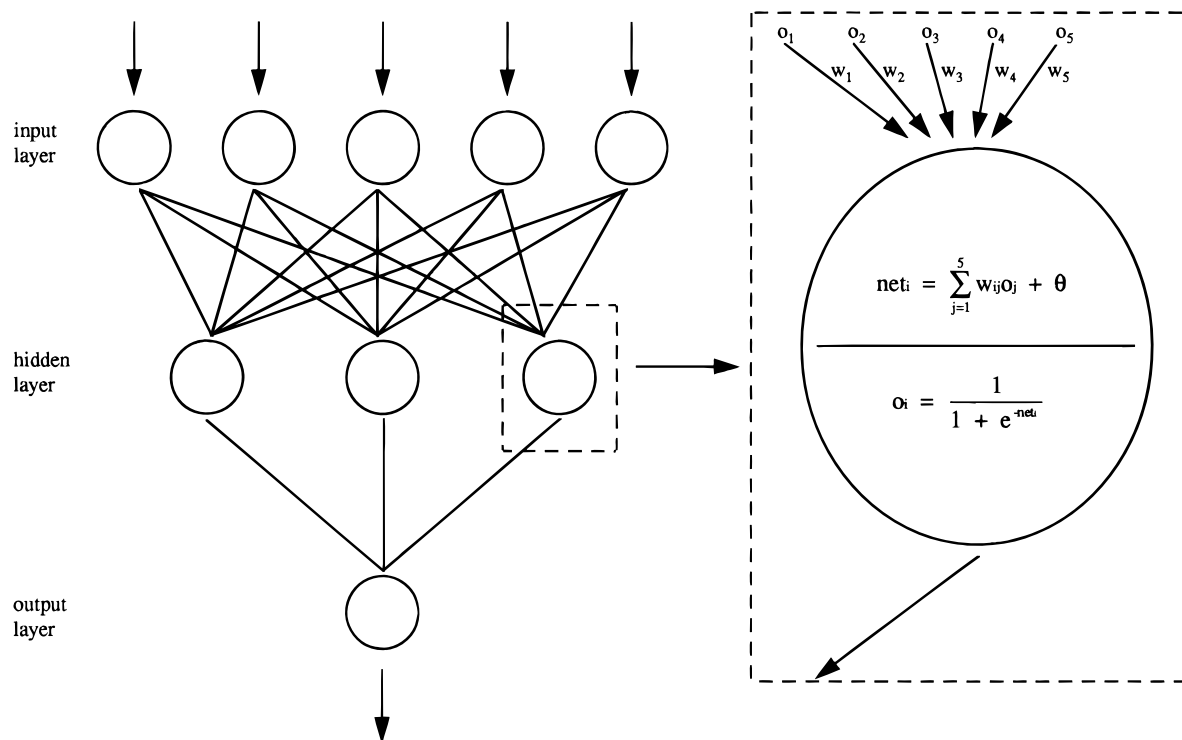
CNN were used in two separate steps of this study. In one step the linear regression model was submitted to a CNN to give improved results. The other step involved choosing the subset of descriptors based on the quality of the CNN results and not assuming a linear relationship between structure and AIT. Figure 2 shows the neural network architecture used in this research, which was a fully-connected, feed-forward, three layer neural network. The input layer consisted of as many neurons as there were descriptors in the linear regression model. The number of neurons in the hidden layer was optimized, and there was one neuron in the output layer to provide the estimated AIT. The number of hidden layer neurons was considered to be optimized when the training set error did not significantly decrease with the addition of another neuron. A linear transformation of the descriptor values restricted them to the interval [0,1], and these values were then used as the input for the network. Each neuron was connected to all of the neurons in the layer above it, and there was a weight associated with each connection. The input value,  $net_i$ , of the hidden layer was the sum of the product of each input layer value and its weight added to a bias term as shown in the enlarged neuron of Figure 2. This value was then converted to the output,  $O_i$ , using the nonlinear sigmoidal function

$$O_i = 1/(1 + e^{-net_i}) \quad (2)$$

The outputs from the hidden layer then became inputs for the output layer and were treated similarly. The result from the output layer was a number on the interval [0,1] which was transformed to obtain the estimated AIT. The network was trained to relate the descriptor values of the input layer to the associated AIT by iteratively adjusting the weights and biases to minimize the sum squared error between the observed and estimated AIT. A cvset was used to prevent overtraining of the network. The cvset was a small subset of compounds, usually 10%, randomly drawn from the tset which was not included during training but was tested periodically during training. When the cvset error was minimized, training was stopped since beyond this point the network was fitting characteristics specific to tset compounds rather than general characteristics of the entire data set which describe the AIT. The use of a cvset increased the confidence with which external predictions could be made using the trained network.

The CNN results were very dependent upon the starting weights and biases, which were randomly selected. Two methods were used to sample a variety of starting points. A generalized simulated annealing algorithm was used to try to optimize the starting weights and biases, and an automated CNN program was run that selected a user-determined number of random starting weights and biases. The results from this large number of trials were then examined to find a good starting point for the weights and biases.

CNN were also used as the basis for subjective feature selection to select a subset of descriptors that accurately represented the AIT. As in the development of the type 1 models, both a genetic algorithm and a generalized simulated annealing routine were used to investigate subsets of descrip-



**Figure 2.** A typical computational neural network architecture.

tors. The quality of the models was based upon

$$\text{quality} = \text{TSET} + 0.4|\text{TSET} - \text{CVSET}| \quad (3)$$

where TSET and CVSET refer to the tset and cvset rms errors.<sup>32</sup> Models chosen with this quality factor that had the lowest tset errors as well as cvset and tset errors that were similar performed better than models chosen with just the tset error as the quality factor. Including the error of the cvset in the quality factor of the CNN gave models with good external predictive ability. The factor of 0.4 in the quality factor was empirically determined. Unlike the development of type 1 models, it was extremely computationally intensive to investigate a large number of different type 3 models. The architecture for the CNN was retained from the type 2 models, providing a basis for comparison. Type 3 models were found that had lower rms errors than the corresponding type 2 models for all of the different breakdowns of the compounds that were tried, proving that the descriptors chosen based on linear criteria were not the best subset that could be found for use with CNN.

All of the models that were developed in the QSPR study were validated with the use of an external pset. The models were able to accurately predict the AIT of these compounds, which had not been used in the development of the models, with pset rms errors of the same magnitude as the tset and cvset errors. The validity of type 1 models was also determined with the use of standard statistical parameters such as the correlation coefficient, the overall *F*-value of the model, and the *T*-values of the individual descriptors. The presence of outliers was detected by looking at regression diagnostics that measured the effect of individual data points on the model, such as standardized and studentized residuals, leverage, and Cook's distance.<sup>37</sup> Compounds were often flagged as outliers if they were not well represented in the data set. An additional method of validation for all

three model types was the visual inspection of both calculated versus observed plots of AIT and plots of residuals.

In cases where satisfactory models were not obtained, further experiments were performed by separating the compounds into more homogeneous subsets and performing the descriptor reduction, model generation, and model validation steps of the study again. The step of descriptor reduction was performed for each of the more homogeneous subsets, leaving a small set of descriptors containing specific information about the structural characteristics of the compounds in the subset from which models were developed. Therefore, the initial reduced pool of about 60 descriptors was further reduced for each of the breakdowns of the data set. One reason for the lack of success in obtaining satisfactory results was the inability of the descriptors to encode the information necessary to relate AIT to structure. Subsetting the compounds in different ways led to models that were able to successfully predict AIT with errors of the magnitude of the experimental error of the measurement technique.

## RESULTS AND DISCUSSION

Initial attempts were made to develop a model for the entire data set, with a tset consisting of 300 compounds used for model development and an external pset of the remaining 27 compounds. These attempts were unsuccessful, with the best type 1 model having 11 descriptors and a tset rms error of 58.5 °C. Dividing the data set into two groups, hydrocarbons and compounds containing heteroatoms, also gave poor results, although the hydrocarbon subset was significantly better than the heteroatom-containing subset. An eight-descriptor model was developed to relate AIT to the structure of the 104 hydrocarbons that had a type 1 model tset rms error of 38.2 °C. The remaining 223 heteroatom-containing compounds were used to develop a 10-descriptor

**Table 1.** Models Developed for the Prediction of AIT Values of Low-Temperature Hydrocarbon Compounds

label	descriptor definition	coeff	SD of coeff	
Type 1 Model Results				
PNSA 2	total charge weighted partial negative surface area	-2.08	±	0.37
NBR	number of basis rings	131	±	16
V6P	valence corrected sixth order path molecular connectivity	248	±	30
WTPT 2	sum of unique path weights/number of atoms	-559	±	86
dHoF	heat of formation	-2010	±	310
	constant	2950	±	400
N = 47, R = 0.872, tset rms error = 19.0 °C, pset rms error = 18.9 °C				
Type 2 Model Results				
tset rms error = 8.99 °C, cvset rms error = 8.78 °C, pset rms error = 13.0 °C				
Type 3 Model Results				
PNSA 2	total charge weighted partial negative surface area			
DPSA 3	difference in atomic charge weighted partial surface areas			
V2	valence corrected second order molecular connectivity			
N4P	count of fourth order paths			
1SP2	count of primary sp <sup>2</sup> carbons			
tset rms error = 8.77 °C, cvset rms error = 6.88 °C, pset rms error = 5.11 °C				

**Table 2.** Low-Temperature Hydrocarbon Compounds with Their Experimental and Calculated AIT Values

compd name	exptl AIT (°C)	calcd AIT (°C)	calcd AIT (°C)	calcd AIT (°C)	compd name	exptl AIT (°C)	calcd AIT (°C)	calcd AIT (°C)	calcd AIT (°C)
		type 1	type 2	type 3			type 1	type 2	type 3
diethylcyclohexane	240	257	252	242	4-ethenylcyclohexene	265	248	271	266
2-methylpentane	300	298	301	301	2,6,6-trimethylbicyclo[3.1.1]heptane	270	255	254	257
dodecane	200	194	210	213	ethylcyclopentane <sup>a</sup>	260	278	264	268
nonane <sup>a</sup>	205	212	214	217	undecane	240	199	212	217
3,4,4-trimethyl-2-pentene	325	305	326	330	4-methyl-1-pentene <sup>b</sup>	300	285	296	291
ethylcyclohexane	260	251	242	259	1-octene	250	237	245	243
2,3-dimethylpentane	330	316	325	324	heptane	215	236	219	219
pentane	265	283	260	257	2,3-dimethyloctane	225	247	240	237
cyclopentane	320	295	304	303	2-methyl-2-butene	290	279	294	304
2-methyl-1-pentene	300	285	314	299	3-methylpentane	300	298	305	301
3-methyloctane <sup>a</sup>	220	231	228	219	cyclohexane	260	287	269	277
2-methyloctane	220	237	223	218	hexadecane	205	201	202	202
1-heptene	260	245	252	253	3-ethyloctane	230	227	232	224
2-methylnonane <sup>b</sup>	210	227	221	210	2,6,6-trimethylbicyclo[3.1.1]hept-2-ene	255	253	254	261
4-ethyloctane	235	239	225	229	3,3-diethylpentane <sup>b</sup>	290	324	312	289
2,4-dimethylpentane <sup>b</sup>	325	316	323	321	decane	205	203	213	217
3,3-dimethylheptane	325	294	310	308	3-methylenepentane <sup>a</sup>	315	276	302	315
1-hexadecene	240	246	240	236	butylcyclohexane	245	229	242	244
1-hexene	265	265	266	271	2,2-dimethylpentane	320	319	323	331
1-decene	235	224	244	239	3,3-dimethylpentane	320	319	327	331
ethyne	305	306	302	306	methylcyclohexane <sup>b</sup>	260	268	246	266
tetradecane	200	191	206	204	1-octyne	225	239	219	228
1-tetradecene	235	233	234	240	hexane	240	276	237	230
ethylcyclobutane <sup>c</sup>	210				1,7-octadiene	230	246	232	226
4-methyloctane	225	258	229	223	1-pentene <sup>a</sup>	290	266	284	296
1,1'-bicyclohexyl	240	261	251	247	2-methyl-1,3-butadiene	220	270	223	226
octane	210	222	215	216					

<sup>a</sup> Cross-validation set compound. <sup>b</sup> Prediction set compound. <sup>c</sup> Outlier compound.

type 1 model with a tset rms error of 61.8 °C.

**Hydrocarbons.** Based on the evidence that there are two distinct autoignition mechanisms for low-temperature and high-temperature regions,<sup>6,9,38,39</sup> the hydrocarbon portion of the data set was further broken down into two subsets, compounds with AIT greater than 350 °C and those with AIT less than or equal to 350 °C. This subsetting choice had proven successful in a previous attempt to model AIT,<sup>13</sup> and it was once again found to be an appropriate way to divide the compounds. Low-temperature and high-temperature models were developed with significantly better results than the model that had been developed for all hydrocarbons.

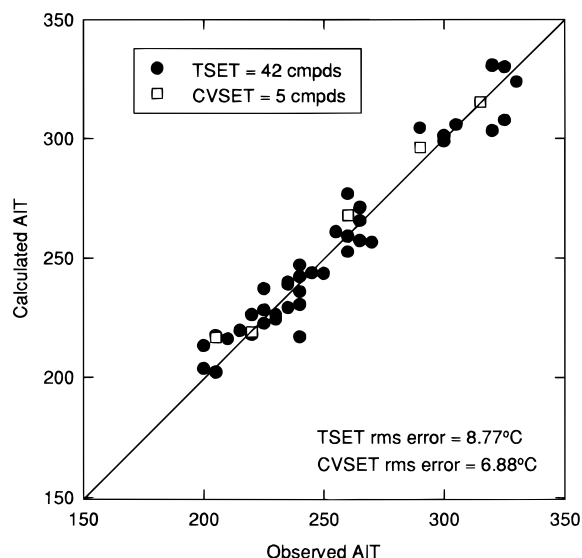
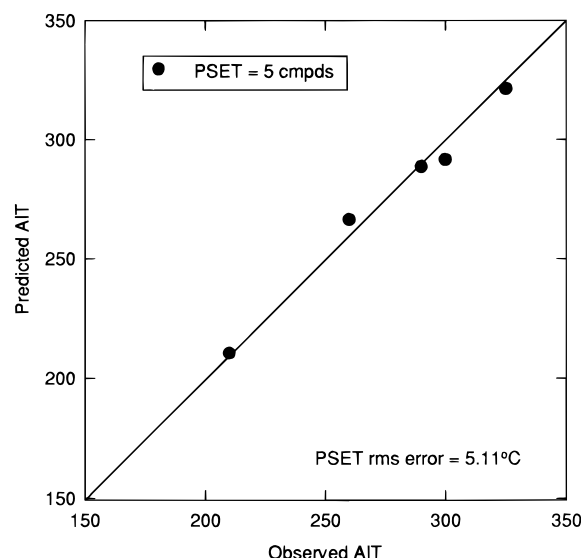
The best models found for the low-temperature hydrocarbons are shown in Table 1. The 53 compounds were divided into a tset of 48 compounds and a pset of five compounds.

The tset was used to choose a subset of five descriptors to map the structures of the compounds to their AIT. Of the five type 1 model descriptors, one was a CPSA descriptor that provided information about the charged partial negative surface areas of the molecules (PNSA 2), three were topological descriptors that contained size and shape information (NBR, V6P, and WTPT 2), and the fifth was the heat of formation value calculated during the MOPAC minimization (dHoF). One compound, ethylcyclobutane, was removed from the training set as an outlier, leaving a tset of 47 compounds with an rms error of 19.0 °C. The five pset compounds had an rms error of 18.9 °C.

Submitting these same five descriptors to a CNN with five input neurons, three hidden neurons, and one output neuron, a 5:3:1 architecture, resulted in a type 2 model with a tset

**Table 3.** Models Developed for the Prediction of AIT Values of High-Temperature Hydrocarbon Compounds

label	descriptor definition	coeff	SD of coeff
Type 1 Model Results			
NSB	number of single bonds	-37.2 ±	3.7
NBR	number of basis rings	111 ±	16
MOLC 8	fourth order path cluster molecular connectivity	71.8 ±	13.7
N4PC	count of fourth order path clusters	-20.1 ±	3.2
V5PC	valence corrected fifth order path cluster molecular connectivity	54.7 ±	9.9
1SP3	count of primary sp <sup>3</sup> carbons	36.7 ±	6.2
	constant	439 ±	15
$N = 46, R = 0.888$ , tset rms error = 23.7 °C, pset rms error = 20.8 °C			
Type 2 Model Results			
tset rms error = 20.6 °C, cvset rms error = 19.7 °C, pset rms error = 8.24 °C			
Type 3 Model Results			
QNEG	charge on the most negative atom		
FPSA 2	fractional total charge weighted partial positive surface area		
NAB	number of aromatic bonds		
N4PC	count of fourth order path clusters		
ALLP 4	total weighted number of paths/number of atoms		
1SP3	count of primary sp <sup>3</sup> carbons		
tset rms error = 18.5 °C, cvset rms error = 17.0 °C, pset rms error = 15.7 °C			


**Figure 3.** Calculated versus observed AIT values for the training set and cross-validation set from the type 3 low-temperature hydrocarbon model.

**Figure 4.** Validation of the type 3 low-temperature hydrocarbon model using the external prediction set.

rms error of 8.99 °C, a cvset rms error of 8.78 °C, and a pset rms error of 13.0 °C. The cvset consisted of five compounds chosen randomly and removed from the tset. The improvement in the results was expected since nonlinear relationships between the descriptors and the AIT were taken into account as well as the fact that a larger number of adjustable parameters was used. The low-temperature hydrocarbon compounds, their experimental AIT, and their calculated AIT from the type 1, 2, and 3 models are shown in Table 2. The cvset and pset compounds and the outlier compound are denoted by superscripts.

A five-descriptor type 3 model was also developed for this subset of 47 hydrocarbons. The descriptors chosen by the nonlinear feature selection are listed in Table 1. The same CPSA descriptor was chosen (PNSA 2) as well as another CPSA descriptor that also provided information about the difference in the partial positive and partial negative surface areas (DPSA 3). The remaining descriptors selected were all topological descriptors (V2, WTPT 1, and 1SP2). The tset rms error was slightly better than the type 2 results

at 8.77 °C, while the cvset and the pset errors showed a much larger improvement to 6.88 °C and 5.11 °C, respectively. Figures 3 and 4 show the calculated and predicted AIT versus observed AIT plots for the type 3 low-temperature hydrocarbon model. Note that the plotting range is from 150 °C to 350 °C, only half of the overall range of the AIT data. Thus, excellent models have been developed that calculate the AIT values for hydrocarbons in the temperature range of 150 °C to 350 °C with great accuracy.

Table 3 shows the models that were developed for the 51 high-temperature hydrocarbon compounds. This subset of 51 compounds, 46 in the tset and five in the pset, required six descriptors to model the AIT. Again, the size and shape of the molecules were very important, as all six descriptors chosen for the type 1 model were topological (NSB, NBR, MOLC 8, N4PC, V5PC, and 1SP3). No electronic or geometric information was necessary to develop a linear model with a tset rms error of 23.7 °C and a pset rms error of 20.8 °C. A CNN with a 6:2:1 architecture improved these results to 20.6 °C, 19.7 °C, and 8.24 °C, respectively, for

**Table 4.** Models Developed for the Prediction of AIT Values of Nitrogen Compounds

label	descriptor definition	coeff	SD of coeff
Type 1 Model Results			
QPOS	charge on the most positive atom	-246	± 49
WNSA 1	surface weighted partial negative surface area	12.0	± 1.5
NC	number of carbons	-34.7	± 7.4
NSB	number of single bonds	-50.4	± 7.8
1SP3	count of primary sp <sup>3</sup> carbons	64.9	± 11.6
2SP3	count of secondary sp <sup>3</sup> carbons	54.0	± 11.8
	constant	499	± 28
$N = 36, R = 0.935$ , tset rms error = 41.1 °C, pset rms error = 37.8 °C			
Type 2 Model Results			
tset rms error = 39.2 °C, cvset rms error = 30.4 °C, pset rms error = 30.9 °C			
Type 3 Model Results			
DPOL	electric dipole moment		
PNSA 1	partial negative surface area		
DPSA 1	difference in charged partial surface areas		
WNSA 1	surface weighted partial negative surface area		
WNSA 3	surface weighted, atomic charge weighted partial negative surface area		
RDTA	ratio of hydrogen bonding donor groups to acceptor groups		
tset rms error = 34.9 °C, cvset rms error = 23.6 °C, pset rms error = 28.2 °C			

the 42-compound tset, 4-compound cvset, and 5-compound pset.

The type 3 model descriptors are also shown in Table 3. Topological descriptors again provided a large portion of the structural information, with four of the six descriptors being topological (NAB, N4PC, ALLP 4, and 1SP3). Two of these descriptors (N4PC and 1SP3) were also chosen in the type 1 model. The other two descriptors of the type 3 model were an electronic descriptor that calculated the charge on the most negative atom in the molecule (QNEG) and a CPSA descriptor that provided information about the partial positive surface areas of the compounds (FPSA 2). The type 3 model showed further improvement over the type 1 and 2 models with tset, cvset, and pset rms errors of 18.5 °C, 17.0 °C, and 15.7 °C. Although these errors were not as low as those for the low-temperature hydrocarbon model, they were still lower than the reported experimental error of +20 °C for AIT greater than 300 °C. Thus, models have been developed that calculate the AIT values for hydrocarbons in the temperature range of 350 °C to 600 °C with accuracy comparable to experiment.

The overall data set contained 31 halogenated hydrocarbon compounds. Various attempts were made to model subsets containing these compounds, including subsets with and without a temperature breakdown. The most successful models resulted from combining the halogenated hydrocarbons with the hydrocarbons in their low-temperature and high-temperature subsets. A low-temperature halohydrocarbon model was developed using 59 compounds from the data set that had five descriptors and a tset rms error of 22.8 °C for the type 1 model. The tset error decreased to 16.6 °C for the type 2 model and 16.2 °C for the type 3 model. There was some overlap in the descriptors chosen between the models with the halogenated compounds included and the models with only hydrocarbon compounds. Four of the 15 unique descriptors appeared in more than one model.

Similarly, a four-descriptor high-temperature halohydrocarbon model was developed from the 79 compounds in the data set. The model had a tset rms error of 42.3 °C for the type 1 model, which was reduced to 34.8 °C and 32.9 °C for the type 2 and 3 models. There was no overlap between the high-temperature halohydrocarbon model and the high-

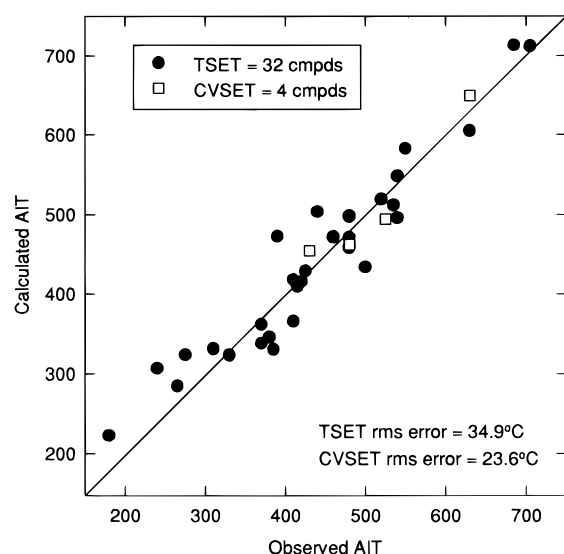
temperature hydrocarbon model in the descriptors chosen, but two of the four descriptors chosen for the type 1 halohydrocarbon model were also chosen for the type 3 halohydrocarbon model. The decrease in the quality of the model upon adding the halogenated compounds was much more significant in the high-temperature region, but this was partially due to the fact that the experimental error was higher in this region and the fact that there were many more compounds added to the high-temperature subset.

**Heteroatom Compounds.** Since the attempt to model all the heteroatomic compounds together was unsuccessful, further subsetting was performed in order to develop improved models. The first subset of compounds that was modeled consisted of the 40 compounds that contained nitrogen. Some of the compounds also included heteroatoms such as oxygen or halogens in addition to nitrogen. The AIT of these compounds range from 150 °C to 750 °C. Table 4 shows the results for this subset. The six-descriptor type 1 model was developed with a tset of 36 compounds and had an error of 41.1 °C. Of the six descriptors, four were simple topological count descriptors (NC, NSB, 1SP3, and 2SP3), one described the electronic environment of the compounds (QPOS), and one was a CPSA descriptor that contained information about the partial negative surface areas of the compounds (WNSA 1). The model had predictive ability on the same order as the tset, with a pset rms error of 37.8 °C. The type 2 model results showed some improvement. The CNN had a 6:2:1 architecture, and the linear tset was divided into a 32-compound tset and a four-compound cvset with rms errors of 39.2 °C and 30.4 °C and a four-compound pset rms error of 30.9 °C.

A six-descriptor type 3 model was developed, and the results are shown in Table 4. As opposed to the type 1 model, no topological descriptors were chosen by the nonlinear feature selection methods. The dipole moment of the molecules (DPOL) was chosen as an important descriptor, with the remaining five descriptors being descriptors that combined electronic and geometric information. Four of the descriptors were CPSA descriptors (PNSA 1, DPSA 1, WNSA 1, and WNSA 3) and the other was a descriptor that contained information on the ability of the compounds to participate in hydrogen bonding (RDTA). This model

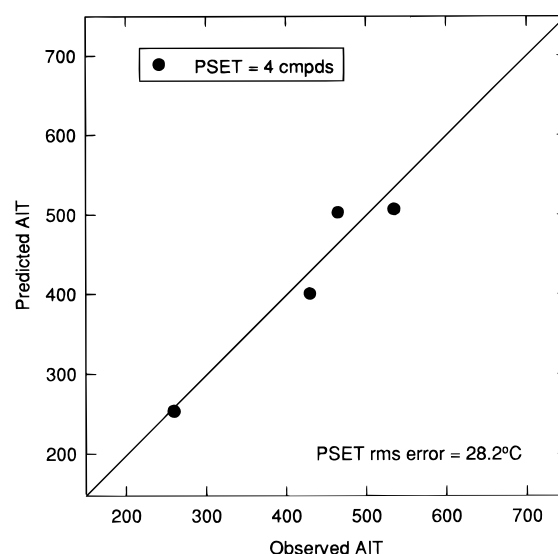
**Table 5.** Models Developed for the Prediction of AIT Values of Oxygen/Sulfur Compounds

label	descriptor definition	coeff	SD of coeff	
Type 1 Model Results				
QPOS	charge on the most positive atom	1430	±	160
QNEG	charge on the most negative atom	1200	±	190
NSB	number of single bonds	−28.6	±	3.1
NDB	number of double bonds	−40.1	±	9.1
N3C	count of third order clusters	36.4	±	4.6
KETO	count of ketone groups	118	±	17
MOMH 1	first moment of inertia	0.0263	±	0.0046
	constant	499	±	35
N = 132, R = 0.824, tset rms error = 55.6 °C, pset rms error = 63.0 °C				
Type 2 Model Results				
tset rms error = 35.2 °C, cvset rms error = 34.6 °C, pset rms error = 32.9 °C				
Type 3 Model Results				
QNEG	charge on the most negative atom			
FNSA 2	fractional charge weighted partial negative surface area			
MOLC 7	third order cluster molecular connectivity			
N2P	count of second order paths			
ALDE	count of aldehyde groups			
MOMH 7	radius of gyration			
dHoF	heat of formation			
tset rms error = 30.8 °C, cvset rms error = 29.7 °C, pset rms error = 32.5 °C				


**Figure 5.** Calculated versus observed AIT values for the training set and cross-validation set from the type 3 nitrogen compound model.

showed further improvement over the type 1 and 2 models. The tset rms error was 34.9 °C, the cvset rms error was 23.6 °C, and the pset rms error was 28.2 °C. Figures 5 and 6 show calculated and predicted AIT versus observed AIT plots for the nitrogen-containing compounds. Note that the plotting range is from 150 °C to 750 °C. Thus, excellent models have been developed for the 40 nitrogen-containing compounds with accuracy comparable to experiment.

The 150 compounds remaining to be modeled contained oxygen or sulfur. Some of these compounds contained halogens and many had multiple functional groups. The seven-descriptor models developed for this subset are shown in Table 5. Both the type 1 and type 3 models contained the three basic types of descriptors: topological, geometric, and electronic. The type 1 model consisted of two descriptors containing electronic information (QPOS and QNEG), four topological descriptors that encode simple features of the compounds like bond types and size and indicate the presence of functional groups (NSB, NDB, N3C, and


**Figure 6.** Validation of the type 3 nitrogen compound model using the external prediction set.

KETO), and the first moment of inertia (MOMH 1) that describes the geometry of the compounds. The tset initially consisted of 135 compounds, but three outliers were flagged and removed, leaving a tset of 132 compounds that had an rms error of 55.6 °C. The 15-compound pset had a slightly higher rms error of 63.0 °C. The type 2 results for this subset showed significant improvement, decreasing to rms errors of 35.2 °C, 34.6 °C, and 32.9 °C for the tset, cvset, and pset. The CNN architecture was 7:5:1, and the 132-compound tset was divided into a tset of 119 compounds and a cvset of 13 compounds.

As was seen with the other subsets, the type 3 model showed further improvement. Only one of the descriptors from the type 1 model appeared in the type 3 model, but many of the other descriptors provided similar information. The electronic environment was described by one of the descriptors from the type 1 model (QNEG) and by the CPSA descriptor (FNSA 2). The topological descriptors encoded the size of the compounds and again had an indicator for a functional group (MOLC 7, N2P, and ALDE). The radius



**Table 6.** Models Developed for the Prediction of AIT Values of Alcohol/Ether Compounds

label	descriptor definition	coeff	SD of coeff	
Type 1 Model Results				
QPOS	charge on the most positive atom	-1700	±	200
RPCG	relative positive charge	820	±	90
SAAA	sum of the surface areas of hydrogen bonding acceptor groups	1.94	±	0.45
RDTA	ratio of hydrogen bonding donor groups to acceptor groups	236	±	31
V4P	valence corrected fourth order path molecular connectivity	-197	±	18
N2P	count of second order paths	43.4	±	3.0
	constant	136	±	24
$N = 67, R = 0.924, \text{tset rms error} = 35.0\text{ }^{\circ}\text{C}, \text{pset rms error} = 30.3\text{ }^{\circ}\text{C}$				
Type 2 Model Results				
$\text{tset rms error} = 31.3\text{ }^{\circ}\text{C}, \text{cvset rms error} = 20.8\text{ }^{\circ}\text{C}, \text{pset rms error} = 29.0\text{ }^{\circ}\text{C}$				
Type 3 Model Results				
RDTA	ratio of hydrogen bonding donor groups to acceptor groups			
MOLC 1	first order path molecular connectivity			
N2P	count of second order paths			
N3C	count of third order clusters			
WTPT 3	sum of all weighted paths starting from heteroatoms			
MOMH 7	radius of gyration			
$\text{tset rms error} = 19.6\text{ }^{\circ}\text{C}, \text{cvset rms error} = 22.0\text{ }^{\circ}\text{C}, \text{pset rms error} = 20.0\text{ }^{\circ}\text{C}$				

of gyration (MOMH 7) contained the geometric information. The final descriptor was the heat of formation (dHoF) calculated during the MOPAC minimization. The combination of these descriptors resulted in a tset rms error of 30.8 °C, a cvset rms error of 29.7 °C, and a pset rms error of 32.5 °C, similar to the errors obtained for the nitrogen subset.

In a final attempt to improve upon the type 1 results of the oxygen/sulfur subset, a further breakdown was made by functional group type. Two subsets were developed: one containing alcohols, ethers, and a combination of these and one containing any type of carboxyl group. The carboxyl group subset had esters, carboxylic acids, aldehydes, ketones, and any combination of these groups. The six-descriptor models developed for the alcohol/ether subset are shown in Table 6. Besides two topological size and shape descriptors (V4P and N2P), the model contained two descriptors with electronic information (QPOS and RPCG) and two hydrogen bonding descriptors (SAAA and RDTA). The type 1 model had a tset rms error of 35.0 °C and a pset rms error of 30.3 °C. A 6:3:1 CNN produced slightly improved type 2 model results of 31.3 °C, 20.8 °C, and 29.0 °C for the tset, cvset, and pset rms errors.

A much larger improvement was seen with the type 3 model. Two of the six descriptors were the same as those chosen for the type 1 model: a hydrogen bonding descriptor (RDTA) and a topological descriptor (N2P). Three other topological descriptors were in the model (MOLC 1, N3C, and WTPT 3), and the final descriptor was the radius of gyration (MOMH 7). The tset, cvset, and pset rms errors for this model dropped to 19.6 °C, 22.0 °C, and 20.0 °C, once again on the order of experimental error for the AIT of the alcohol/ether compounds which ranged from around 200 °C to 600 °C.

The results for the carboxylic group subset were less successful. A five-descriptor type 1 model was developed with the 64 compounds that had a tset rms error of 49.5 °C. The type 2 results improved this to 37.7 °C, and the type 3 tset rms error was 35.1 °C. In all cases the cvset and pset errors were slightly lower than the tset errors. Because these errors showed no improvement over the more robust oxygen/sulfur compound model, there would be no reason to use it for the prediction of AIT of other compounds.

## CONCLUSION

Quantitative structure–property relationships have been developed for structurally congeneric subsets of a diverse set of organic compounds and their autoignition temperatures. Multiple linear regression and computational neural networks are both used successfully in conjunction with simulated annealing and genetic algorithm routines to choose small subsets of descriptors that relate the autoignition temperatures to structural features encoded as descriptors. Subsets of descriptors are chosen based on both linear and nonlinear criteria. Models are reported for low-temperature hydrocarbons, high-temperature hydrocarbons, nitrogen-containing compounds, oxygen- and sulfur-containing compounds, and alcohol and ether compounds which have rms errors near the experimental error of the measuring technique. Many of the models provide the ability to predict autoignition temperatures of compounds with functional groups that have not been modeled before using only structural information, including nitrogen-containing compounds, ethers, aldehydes, ketones, and carboxylic acids. These models can be used to predict the autoignition temperatures of compounds that were not used in their development and to aid in verification of measured values.

## ACKNOWLEDGMENT

This work was supported by the Design Institute for Physical Property Data (DIPPR) Project 931: Data Prediction Methods.

**Supporting Information Available:** Tables SM1–4 of compound names, experimental, and calculated AIT values for the high-temperature hydrocarbon model, nitrogen compound model, oxygen/sulfur compound model, and alcohol/ether compound model, Tables SM5–9 of correlation matrices of descriptors in the low-temperature hydrocarbon model, high-temperature hydrocarbon model, nitrogen compound model, oxygen/sulfur compound model, and alcohol/ether compound model, as well as Figures SM1–6 of calculated and predicted vs observed AIT plots for the type 3 high-temperature hydrocarbon model, oxygen/sulfur compound model, and alcohol/ether model (19 pages). See any current masthead page for ordering and Internet access instructions.

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CI960175L