Boiling Points of Halogenated Ethanes: An Explanatory Model Implicating Weak Intermolecular Hydrogen−Halogen Bonding

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This study explores via structural clues the influence of weak intermolecular hydrogen−halogen bonds on the boiling point of halogenated ethanes. The plot of boiling points of 86 halogenated ethanes versus the molar refraction (linked to polarizability) reveals a series of straight lines, each corresponding to one of nine possible arrangements of hydrogen and halogen atoms on the two-carbon skeleton. A multiple linear regression model of the boiling points could be designed based on molar refraction and subgroup structure as independent variables ($R^2 = 0.995$, standard error of boiling point 4.2 °C). The model is discussed in view of the fact that molar refraction can account for approximately 83.0% of the observed variation in boiling point, while 16.5% could be ascribed to weak C−X···H−C intermolecular interactions. The difference in the observed boiling point of molecules having similar molar refraction values but differing in hydrogen−halogen intermolecular bonds can reach as much as 90 °C.

1. Introduction

Investigation into the variation of boiling points of halogenated alkanes has been the subject of several studies in the last two decades for environmental, toxicological, and practical reasons.[1−3] On a molecular level, a number of physical parameters have been explored to elucidate differences in boiling points: relative molecular mass, polarizability, molecular polarity, density, or size.[2,4,5] Textbook explanations of observed discrepancies in boiling points of organic molecules have abundantly drawn upon these parameters. Although molecular mass has shown interesting features, it has not been able to consistently explain boiling point variations in halogenated alkanes, particularly when considering interchanged hydrogen and fluorine atoms.[6] Polarity has also fallen short as a predictor, notably with molecules H_3C-CX_3 where its higher value is at odds with the observed lower boiling point. Furthermore, compelling evidence from previous research has demonstrated that a permanent dipole had no significant influence on the boiling points of halogenated methanes.[7,8]

Other researchers have investigated halogenated alkane boiling points via group contribution, neural networks, topological indices, or structural features (QSPR) with the aim of evaluating models and predicting the physical properties of this important group of molecules.[9−12] These works apply a variety of multivariate statistical techniques required to validate a group of variables that can satisfactorily explain the boiling point variation.

Another line of study could explore intermolecular links other than conventional van der Waals cohesive forces. It is acknowledged that C−H groups can act as weak hydrogen donors.[13] More specifically, a study based on electrostatic potentials of molecules has given a clear indication of the hydrogen atom as a Lewis acid or proton donor in halogenated ethanes.[14] "Organic" halogens have been generally considered as weak proton acceptors, but recent studies have demonstrated that halogens in halomethanes can engage in weak bonding to a hydrogen donor.[15,16] Examination of supramolecular structures has definitely identified weak C−H···X−C hydrogen bonds of donor−acceptor complexes in organic molecules with directional interactions.[17,18] The specific geometrical characteristics of this bond are the following: the observed H···X distances increase from fluorine to the iodine acceptor, and the C−X···H bond angle appears to be larger for fluorine than the heavier halogens (110−180° vs 90−130°). The study of dimers may give an indication as to how molecules interact at close range in the liquid phase. Quantum mechanical calculations of minimum intermolecular potential energy of halogenated methane dimers point toward the formation of one predominantly stable isomer where a hydrogen atom from each molecule interacts with the halogen atom on the counterpart molecule.[19−22] The spectral analyses of all four methyl halide dimers generated by supersonic-jet expansion are consistent with the theoretically predicted isomer.[19−21] In all four cases, the intermolecular H···X bond distances were smaller than those based on van der Waals radii. In another experimental study, based on cluster formation and dissociation, the presence of the stable methyl fluoride dimer was also observed.[22] Another important aspect of the work done in the area of dimer studies relates to the specific stabilization energy either calculated or measured for the chloromethane series.[23,24] Molecules $CHCl_3$, CH_2Cl_2, and CH_3Cl had significantly higher stabilization energies relative to that of the CCl_4 molecule. This observation suggests that intermolecular bonds in the perhalogenated alkanes are weaker than those in halogenated alkanes containing hydrogen atoms. If very weak bonds of this nature are of major structural, synthetic, and pharmacological significance,[1] then it might be suspected that these interactions may play an important role in physical properties such as the boiling point of haloethane derivatives.

It is also well recognized that intermolecular noncovalent interactions between covalently bonded halogen atoms may occur in halogenated alkanes. The basis for the halogen bonding system is the region of positive potential found on the outer surface of iodine and bromine atoms along the extension of the

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covalent bond. This region exists simultaneously with a negative region on the lateral portions of the halogen surface.[25,26] Thus, there can be attractive interactions between the negative portion of a halogen in one molecule and the positive portion of another halogen on a neighboring molecule to form halogen bonding.

The main purpose of the current study is to explore via a multiple linear regression model (MLR) the variation in boiling point of halogenated ethanes. Selected independent variables are (a) the molar refraction (MR, linked to the molecule's polarizability) and (b) intermolecular hydrogen−halogen bonding (via the structural features displayed by this group of molecules relative to the various arrangements of hydrogen atoms on the two-carbon skeleton). A secondary objective is to briefly discuss how halogen bonding may be implicated in the boiling point variation in this series of molecules. Finally, the boiling point model will be explained in terms of the weak −CH···XC− intermolecular interactions that characterize and influence the observed boiling points in this set of molecules.

2. Computational Methods

The normal boiling point values of the 86 molecules used in this study were taken from several sources.[3,4,10,11,27] Two molecules were excluded on account of large discrepancies in independent reports of boiling point determinations (FH_2C-CH_2F:[6] 10.5, 24.0, and 30.7 °C; $BrCl_2C-CH_2Br$: [3,27]161.5 and 178.3 °C). Other molecules were excluded from the analysis for various reasons such as a reduced pressure determination ($Br_2HC-CBr_3$[27]), a triple point value (Cl_3C-CCl_3[27]), or decomposition before attaining the boiling point (Br_3C-CBr_3; BrH_2C-CBr_3[27]). All calculations were performed with version 9 of the SAS statistical software.

MLR analysis is a statistical technique that can be a powerful tool for building a mathematical model when two or more independent variables are simultaneously investigated to explain the variance of the dependent variable (here the boiling point). We thus obtain an algebraic equation of the type

$$\text{Boiling Point} = B_0 + B_1X_1 + B_2X_2 \ldots + \varepsilon \qquad (1)$$

When applied to the data of interest, B_0 is the intercept; B_1 and B_2 correspond to the partial regression coefficients of the independent variables X_1 and X_2 tested; and ε is the error term. Boiling Point is the predicted value of the boiling point for the individual compounds. MLR specifically quantifies (as % of total) each explanatory variable's impact on the dependent variable.

In addition to validating (or not) predictor variables of continuous type, the flexibility of MLR allows that independent variables of categorical nature, such as structure grouping factors, be inserted into the analysis. For this particular procedure, if a dichotomy is tested, for example, as in the case of a molecule having or not at least one hydrogen atom, then orthogonal contrast values −1 and +1 are assigned to the independent variable used for distinguishing group membership (see Table 1).

The goals in using MLR analysis are:

(1) To reduce the number of explanatory variables by discarding those that, when added to the other variables already in the model, are not statistically associated with the boiling point (p value superior to 0.05);

2) To include the greatest number of molecules from the sample population to obtain a unified solution instead of a number of part solutions.

3. Results and Discussion

Analysis of the different combinations and arrangements of hydrogen atoms (H) and unspecified halogen atoms (X) on the two-carbon skeleton of ethane provides nine separate structures shown in Figure 1. For the present work, each structure is also given a relative "Head-Tail" orientation along the C−C bond axis. Then, by plotting the boiling points of individual molecules as a function of its MR value (calculated as the sum of C−C, C−H, and C−X bond refraction values[28]), Figure 2 is obtained. As can be seen, a series of essentially straight lines emerge, each related to a distinct structure subgroup. The relative boiling point order of the structures in Figure 1 was established by taking an MR = 15 value in Figure 2 and drawing a vertical line parallel to the y axis. As different plots are encountered, the specific structures were displayed in an orderly fashion in Figure 1.

By examining Figures 1 and 2, the following set of rules concerning the boiling point order can be put forward:

1) In each structure subgroup, the boiling point increases proportionally with the MR value (Figure 2). The interpretation of this rule can now be supported on a molecular level. Rule 1 states that the more polarizable a molecule the higher its boiling point. Although this was expected, the fact that a highly linear relationship within structure subgroups is observed is an interesting result which warrants further investigation as to the relationship between different structures.

Subsequent rules are directly related to the existence of weak intermolecular hydrogen−halogen bonds. The perhalogenated ethane molecules have the lowest boiling points of all nine groups. Addition of one or several hydrogen atoms significantly increases the boiling point of molecules at similar MR (by as much as 90 °C). This observation is congruent with the dimer studies cited in the Introduction and implies that as hydrogen atoms are added stronger links in the form of C−H···X−C replace weaker C−X···X−C bonds and can lead to a more stable arrangement in the liquid phase thus requiring a higher boiling temperature. At equal MR.

2) Compounds containing on or more H atoms (structures 2 through 9) have a higher boiling point than the perhalogenated ethanes (structure 1).

The eight structures depicted in Figure 1 that contain hydrogen can be sorted into three groups (Figure 1) according to the presence of both atom types (H and X) on both carbon atoms (group A), one carbon atom only (group B), and neither carbon atom (group C). It is reasonable to suppose that structures able to engage in weak halogen−hydrogen bonds at both extremities of the molecule (head and tail) and in greater number may produce more stronger links with neighboring molecules in the liquid phase. Following this, within structures having at least one hydrogen atom.

3) On average, compounds of group A have higher boiling points than all other compounds. On average, compounds of group B have higher boiling points than compounds of group C. Taken globally, rule 3 argues that the boiling point will be the highest where there are more opportunities of hydrogen−halogen intermolecular linking (see examples in Figure 3). Group C molecules can only form head-to-tail links, while group B molecules can form head-to-tail and head-to-head links. Finally, group A molecules can form head-to-head, head-to-tail, and tail-to-tail links in the liquid phase.

Within group B molecules, structures (6) and (5) have three H atoms on the tail carbon atom. Between these structures, the molecule having the most halogen atoms on the head carbon has a higher boiling point since it can engage in more

TABLE 1: Physical Properties, Intermolecular Hydrogen−Halogen Categorical Factors, and Predicted Boiling Point of Halogenated Ethanes

				rule							
				1	2	3		4		5	
				F1	F2	F3	F4	F5	F6	F7	
	compound	subg.	[a]exp. BP/°C	[b]MR	[c]weak intermolecular C−H···X−C bonding						[d]pred. BP/°C
1	F_3C-CF_3	1	−78.1	10.8	−1	0	0	0	0	0	−78.9
2	F_3C-CF_2Cl	1	−37.9	15.8	−1	0	0	0	0	0	−37.2
3	F_3C-CF_2Br	1	−21.0	18.7	−1	0	0	0	0	0	−13.0
4	ClF_2C-CF_2Cl	1	3.8	20.8	−1	0	0	0	0	0	4.5
5	$F_3C-CFCl_2$	1	4.0	20.8	−1	0	0	0	0	0	4.5
6	$F_3C-CFClBr$	1	26.0	23.7	−1	0	0	0	0	0	28.6
7	$ClF_2C-CFCl_2$	1	47.7	25.7	−1	0	0	0	0	0	45.3
8	F_3C-CCl_3	1	46.1	25.7	−1	0	0	0	0	0	45.3
9	BrF_2C-CF_2Br	1	47.3	26.6	−1	0	0	0	0	0	52.8
10	$F_3C-CFBr_2$	1	47.4	26.6	−1	0	0	0	0	0	52.8
11	$BrF_2C-CFCl_2$	1	74.0	28.6	−1	0	0	0	0	0	69.5
12	F_3C-CCl_2Br	1	69.5	28.6	−1	0	0	0	0	0	69.5
13	$ClF_2C-CFClBr$	1	72.0	28.6	−1	0	0	0	0	0	69.5
14	$Cl_3C-CClF_2$	1	91.5	30.7	−1	0	0	0	0	0	87.0
15	$Cl_2FC-CFCl_2$	1	93.0	30.7	−1	0	0	0	0	0	87.0
16	$BrF_2C-CFClBr$	1	93.0	31.5	−1	0	0	0	0	0	93.7
17	F_3C-CBr_3	1	114.0	34.4	−1	0	0	0	0	0	117.8
18	$Cl_3C-CFCl_2$	1	135.0	35.7	−1	0	0	0	0	0	128.7
19	F_3C-CHF_2	2	−50.0	10.9	1	1	1	0	0	−1	−53.8
20	$F_3C-CHFCl$	2	−9.5	15.9	1	1	1	0	0	−1	−12.2
21	ClF_2C-CHF_2	2	−10.0	15.9	1	1	1	0	0	−1	−12.2
22	$F_3C-CHFBr$	2	9.0	18.8	1	1	1	0	0	−1	12.0
23	BrF_2C-CHF_2	2	−3.0	18.8	1	1	1	0	0	−1	12.0
24	$ClF_2-CHFCl$	2	28.0	20.9	1	1	1	0	0	−1	29.5
25	$F_3C-CHCl_2$	2	27.8	20.9	1	1	1	0	0	−1	29.5
26	$Cl_2FC-CHF_2$	2	30.0	20.9	1	1	1	0	0	−1	29.5
27	$BrF_2C-CHFCl$	2	52.5	23.8	1	1	1	0	0	−1	53.7
28	$F_3C-CHClBr$	2	50.2	23.8	1	1	1	0	0	−1	53.7
29	$ClF_2C-CHFBr$	2	52.0	23.8	1	1	1	0	0	−1	53.7
30	Cl_3C-CHF_2	2	73.0	25.8	1	1	1	0	0	−1	70.4
31	$Cl_2FC-CHFCl$	2	72.5	25.8	1	1	1	0	0	−1	70.4
32	$ClF_2C-CHCl_2$	2	71.9	25.8	1	1	1	0	0	−1	70.4
33	$F_3C-CHBr_2$	2	73.0	26.7	1	1	1	0	0	−1	77.9
34	$BrF_2C-CHFBr$	2	76.0	26.7	1	1	1	0	0	−1	77.9
35	$ClF_2C-CHClBr$	2	94.7	28.7	1	1	1	0	0	−1	94.5
36	$Cl_3C-CHFCl$	2	116.5	30.8	1	1	1	0	0	−1	112.1
37	$Cl_2FC-CHCl_2$	2	116.0	30.8	1	1	1	0	0	−1	112.1
38	$BrClFC-CHFBr$	2	120.0	31.6	1	1	1	0	0	−1	118.7
39	$BrF_2C-CHClBr$	2	116.0	31.6	1	1	1	0	0	−1	118.7
40	$Cl_3C-CHCl_2$	2	159.8	35.8	1	1	1	0	0	−1	153.7
41	F_3C-CH_2F	3	−26.1	11.0	1	1	1	0	0	0	−36.9
42	F_3C-CH_2Cl	3	6.1	16.0	1	1	1	0	0	0	4.8
43	ClF_2C-CH_2F	3	12.0	16.0	1	1	1	0	0	0	4.8
44	F_3C-CH_2Br	3	26.0	18.9	1	1	1	0	0	0	29.0
45	BrF_2C-CH_2F	3	30.0	18.9	1	1	1	0	0	0	29.0
46	ClF_2C-CH_2Cl	3	46.8	21.0	1	1	1	0	0	0	46.5
47	FCl_2C-CH_2F	3	48.4	21.0	1	1	1	0	0	0	46.5
48	BrF_2C-CH_2Cl	3	70.5	23.9	1	1	1	0	0	0	70.6
49	ClF_2C-CH_2Br	3	68.0	23.9	1	1	1	0	0	0	70.6
50	Cl_2FC-CH_2Cl	3	88.6	25.9	1	1	1	0	0	0	87.3
51	BrF_2C-CH_2Br	3	92.5	26.8	1	1	1	0	0	0	94.8
52	Cl_3C-CH_2Cl	3	130.5	30.9	1	1	1	0	0	0	129.0
53	F_3C-CH_3	4	−47.5	11.1	1	−1	1	0	0	0	−50.8
54	ClF_2C-CH_3	4	−9.7	16.1	1	−1	1	0	0	0	−9.2
55	BrF_2C-CH_3	4	13.0	19.0	1	−1	1	0	0	0	15.0
56	Cl_2FC-CH_3	4	32.0	21.1	1	−1	1	0	0	0	32.5
57	Cl_3C-CH_3	4	74.0	26.1	1	−1	1	0	0	0	74.2
58	H_3C-CH_2F	5	−37.6	11.4	1	1	1	1	0	1	−29.0
59	H_3C-CH_2Cl	5	12.3	16.3	1	1	1	1	0	1	11.9
60	H_3C-CH_2Br	5	38.5	19.2	1	1	1	1	0	1	36.1
61	H_3C-CHF_2	6	−24.9	11.3	1	1	1	−1	0	0	−22.9
62	$H_3C-CHFCl$	6	16.2	16.2	1	1	1	−1	0	0	17.9
63	$H_3C-CHCl_2$	6	57.4	21.2	1	1	1	−1	0	0	59.6
64	$H_3C-CHClBr$	6	83.0	24.1	1	1	1	−1	0	0	83.8
65	$H_3C-CHBr_2$	6	109.0	27.0	1	1	1	−1	0	0	108.0

TABLE 1: Continued

				rule							
				1	2	3		4		5	
				F1	F2	F3	F4	F5	F6	F7	
	compound	subg.	[a]exp. BP/°C	[b]MR		[c]weak intermolecular C−H···X−C bonding					[d]pred. BP/°C
66	$\mathrm{F_2HC{-}CHF_2}$	7	−19.9	11.0	1	0	−1	0	1	0	−20.9
67	$\mathrm{ClFHC{-}CHF_2}$	7	17.0	16.0	1	0	−1	0	1	0	20.8
68	$\mathrm{Cl_2HC{-}CHF_2}$	7	59.5	21.0	1	0	−1	0	1	0	62.5
69	$\mathrm{ClFHC{-}CHFCl}$	7	59.6	21.0	1	0	−1	0	1	0	62.5
70	$\mathrm{Cl_2HC{-}CHFCl}$	7	102.0	25.9	1	0	−1	0	1	0	103.3
71	$\mathrm{Cl_2HC{-}CHCl_2}$	7	146.5	30.9	1	0	−1	0	1	0	145.0
72	$\mathrm{BrClHC{-}CHClBr}$	7	195.0	36.7	1	0	−1	0	1	0	193.4
73	$\mathrm{Br_2HC{-}CHBr_2}$	7	243.5	42.5	1	0	−1	0	1	0	241.7
74	$\mathrm{FH_2C{-}CHF_2}$	8	5.0	11.1	1	0	−1	0	0	0	−8.3
75	$\mathrm{FH_2C{-}CHFCl}$	8	35.5	16.1	1	0	−1	0	0	0	33.4
76	$\mathrm{ClH_2C{-}CHF_2}$	8	35.1	16.1	1	0	−1	0	0	0	33.4
77	$\mathrm{BrH_2C{-}CHF_2}$	8	57.0	19.0	1	0	−1	0	0	0	57.5
78	$\mathrm{ClH_2C{-}CHFCl}$	8	73.7	21.1	1	0	−1	0	0	0	75.1
79	$\mathrm{ClH_2C{-}CHCl_2}$	8	113.8	26.1	1	0	−1	0	0	0	116.7
80	$\mathrm{BrH_2C{-}CHClBr}$	8	163.0	31.9	1	0	−1	0	0	0	165.1
81	$\mathrm{BrH_2C{-}CHBr_2}$	8	188.9	34.8	1	0	−1	0	0	0	189.3
82	$\mathrm{FH_2C{-}CH_2Cl}$	9	53.0	16.2	1	0	−1	0	−1	0	46.0
83	$\mathrm{FH_2C{-}CH_2Br}$	9	71.5	19.1	1	0	−1	0	−1	0	70.1
84	$\mathrm{ClH_2C{-}CH_2Cl}$	9	83.5	21.2	1	0	−1	0	−1	0	87.6
85	$\mathrm{ClH_2C{-}CH_2Br}$	9	107.0	24.1	1	0	−1	0	−1	0	111.8
86	$\mathrm{BrH_2C{-}CH_2Br}$	9	131.6	27.0	1	0	−1	0	−1	0	136.0

[a] Experimental boiling points were taken from refs 3, 4, 10, 11, and 27. [b] Values of atomic bond refractions were taken from ref 28: C−C is 1.21; C−H is 1.71; C−F is 1.60; C−Cl is 6.57; and C−Br is 9.47. [c] Categorical factors F2 to F7 are variables that relate to the comparison of subgroups. [d] The predicted boiling point was calculated with eq 2.

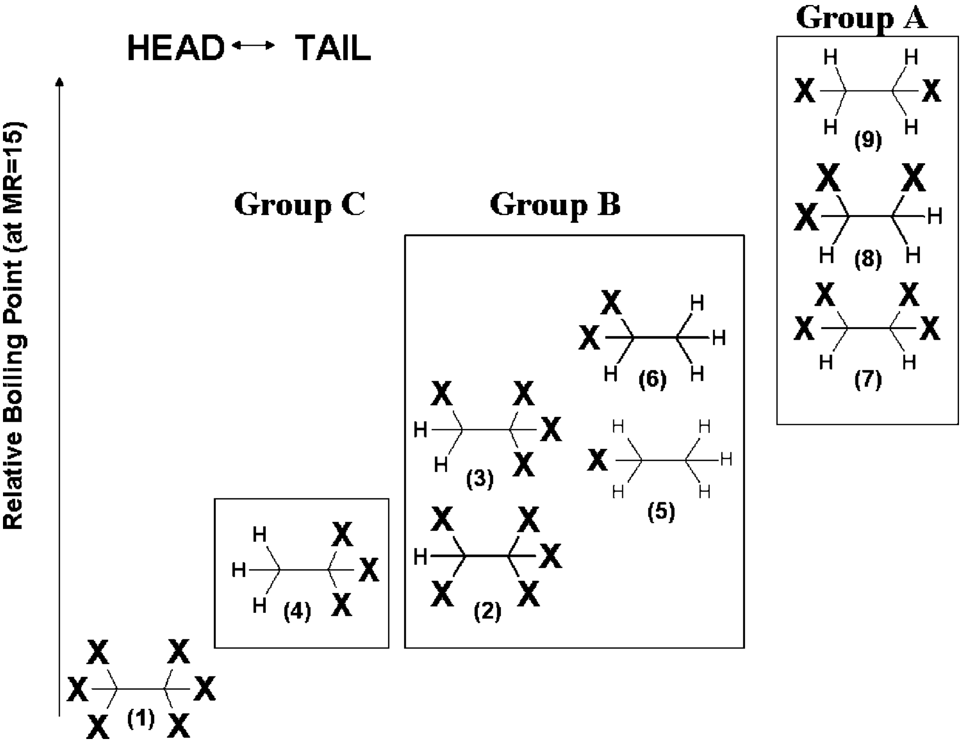

Figure 1. Relative boiling points of the nine different structures characterized by distinct arrangements of hydrogen atoms (H) and halogen atoms (X) of halogenated ethane derivatives at a similar molar refraction (MR) value.

C−H···X−C bonding (see Figure 3b and 3c). By analogy, structure (3) has a higher boiling point than structure (2) since the former has more hydrogens on its head carbon that can link to neighboring halogens. Consequently,

4) Within group B, structure (3) molecules have a higher boiling point than structure (2) molecules, and structure (6) molecules have a higher boiling point than structure (5) molecules. In each of these sets, the compound having the highest number of atoms on the head carbon able to participate in hydrogen−halogen bonds with the atoms on the tail carbon has the greater boiling point.

The data presented a unique opportunity to study the combined effect of geminal halogen and hydrogen atoms on the boiling point of halogenated ethanes. This could be

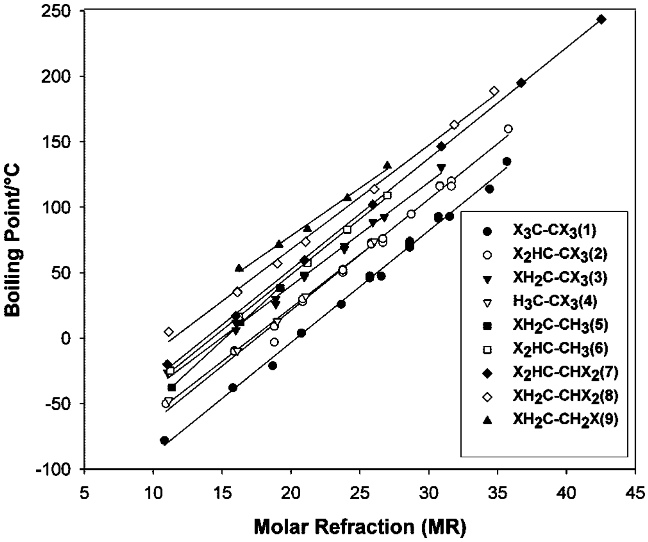

Figure 2. Plot of boiling point versus molar refraction (MR) for the halogenated ethanes included in the study.

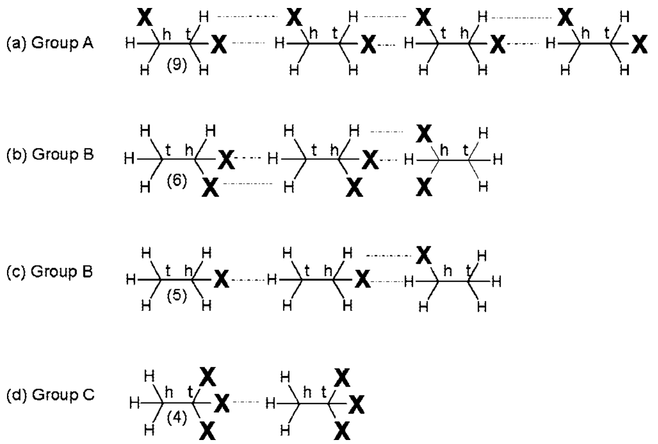

Figure 3. Potential weak H···X bonding of different structure groups. "h" is the head carbon, and "t" is the tail carbon atom. In (a), structure (9) can form head-to-head, head-to-tail, and tail-to-tail hydrogen−halogen bonds. In (b), structure (6) can form head-to-head and head-to-tail hydrogen−halogen bonds. In (c), structure (5) can form head-to-head and head-to-tail hydrogen−halogen bonds but fewer total bonds than structure (6). Finally in (d), structure (4) can only form head-to-tail hydrogen−halogen bonds.

investigated since there are 15 pairs of positional isomers in subgroups (2) and (3) (identical MR), where each pair is related by simply switching distinct vicinal halogens (see Figure 4). If all halogen atoms were the same size, symmetry dictates that the boiling points of these isomer pairs would be the same. However, it can be seen in Figure 4 that 13 of the 15 isomer pairs show a reduction in boiling point as a result of having a larger halogen on the carbon bearing the hydrogen atom(s). The net effect observed is that the more sterically hindered a hydrogen atom is by (a) halogen(s) on the same carbon atom the less this hydrogen can engage in a C−X···H−C bond and the lower the molecule's boiling point will be. On account of the skewed distribution of differences in boiling point due to the outlying pair F_3C−CHFBr and BrF_2C−CHF_2, a nonparametric Sign test was used to test differences in boiling points of the more hindered and less hindered isomers. The difference is statistically significant ($M = 5.5$, $p = 0.007$). Two other pairs of isomers do exist in subgroups 7 and 8, respectively, but the boiling points of the isomers do not differ. By switching halogens, the reduction in hydrogen atom accessibility at one carbon is compensated by greater hydrogen atom accessibility at the other carbon atom, and the effects balance out. The general consequence of the current demonstration is that the more halogens there are in a structure the less accessible the H atoms will be for intermolecular bonding. Following this,

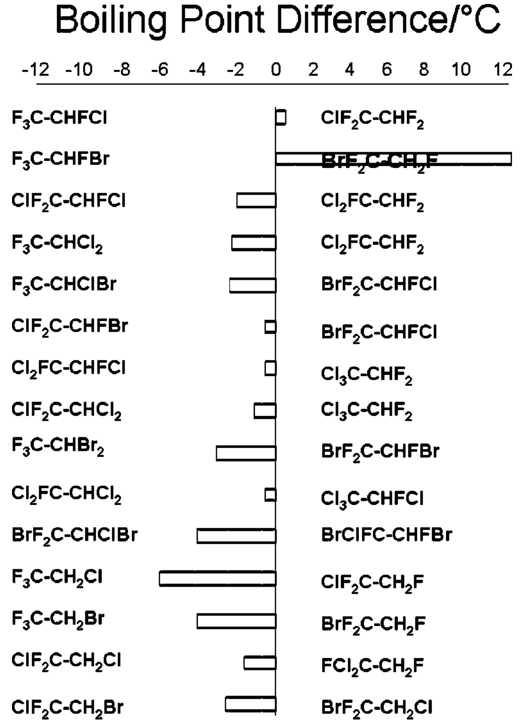

Figure 4. Difference in boiling point of positional isomers with the more hindered hydrogen(s) (left column) relative to the isomer having the less hindered hydrogen(s) (right column).

5) In group A, structure (9) has a greater boiling point than structure (7). In group B, structure (6) has a greater boiling point than structure (3), and structure (5) has a greater boiling point than structure (2). In each of these three sets, the compound having the least number of X atoms has a higher boiling point.

From this set of rules, it is possible to code categorical variables for each molecule directly as one or more factors (F2 through F7) in the form of contrast values −1 and +1 (or 0 if the molecule is not in the contrasted structure subgroups). More explicitly, following rule 2, F2 values for the perhalogenated ethanes (subgroup 1) are −1 and +1 for other molecules (subgroups 2 through 9). From rule 3, F3 opposes subgroup 4 (value = −1) to combined subgroups 2, 3, 5, and 6 (value = +1), and F4 contrasts combined subgroups 2, 3, 4, 5, and 6 (value = +1) with combined subgroups 7, 8, and 9 (value = −1). From rule 4, only one comparison was statistically significant: F5 as subgroup 6 was contrasted to subgroup 5. Finally, for rule 5, the three sets of comparison (9 vs 7, 6 vs 3, and 5 vs 2) generated three factors, from which only two were found to be statistically significant, i.e., F6 (9 vs 7) and F7 (5 vs 2). Together, with the continuous variable MR, they give rise to a total of seven independent factors, identified in Table 1.

By inserting each predictor variable sequentially in the MLR model, a clear indication of the importance of each rule appears in terms of % of variance or model explanation (R^2, Table 2). Furthermore, an algebraic equation results from this modeling, permitting the estimation of boiling points

$$\text{Boiling Point} = 8.3\text{MR} + 25.3\text{F2} + 7.4\text{F3} - 17.6\text{F4} + 11.5\text{F5} - 11.8\text{F6} - 16.1\text{F7} - 143.7 \quad (2)$$

Thus, based on MLR of the boiling points by seven factors, it was possible to construct a model that can explain 99.5% of

TABLE 2: Analysis of Variance for a Linear Model ($R^2 = 0.995$)

source							
rule	factors	SS[a]	DF[b]	MS[c]	F[d]	R^2 (adjusted)	p[e]
1	MR	240277.07	1	240277.07	13926.12	0.8300	<0.0001
2	F2	24894.30	1	24894.30	1442.84	0.0860	<0.0001
3	F3	3611.17	1	3611.17	209.30	0.0125	<0.0001
3	F4	13495.77	1	13495.77	782.20	0.0466	<0.0001
4	F5	455.92	1	455.92	26.42	0.0016	<0.0001
5	F6	1542.98	1	1542.98	89.43	0.0053	<0.0001
5	F7	3845.59	1	3845.59	222.89	0.0133	<0.0001
residual		1345.80	78	17.25			
total		289468.60	85			0.9953	

[a] Sum of squares. [b] Degrees of freedom. [c] Mean square. [d] Ratio of mean squares. [e] Probability in relation to the F distribution.

TABLE 3: Predicted Boiling Point of Molecules Not in the Model

		predicted boiling point (°C)		
compound	exists	this model	ref 4	ref 12
FH_2C-CH_2F	yes	5.1	–	–
$BrCl_2C-CH_2Br$	yes	177.4		
FH_2C-CCl_3	no	87.3	86.0	88.8
$FH_2C-CHCl_2$	no	75.1	76.8	74.4

the variability in boiling points. The calculated standard error of the boiling point was 4.2 °C.

The polarizability is thus an outstanding predictor of the boiling point (partial $R^2 = 0.83$). In this paradigm, the molecular polarity of halogenated ethanes was not considered as an independent variable since previous studies on the boiling points of halogenated methane analogues concluded that the dipole moment values of molecules were not a significant predictor of the boiling point variation beyond that explained by the MR.[7,8]

The results of this work resolve a previously exposed divergence of the boiling point of geminally and vicinally substituted dihaloethanes where the latter is always more elevated.[10] It can be readily seen that they originate from completely different hydrogen atom-based structure subgroups and therefore differ in boiling point. In the same train of thought, it was shown that there is a difference between boiling points of positional isomers with switching of halogen atoms only since the larger halogens reduce the access to the geminal hydrogen atom. Furthermore, this work based on polarizability and weak hydrogen–halogen interactions presents an interesting resolution to the previously observed downward variation of boiling points of fluorinated ethanes as a function of molecular weight.[29]

The regressional model reveals that MR (polarizability) is the most important predictor of the boiling points of halogenated ethanes (F1, 83.0%). Although weak intermolecular $C-H\cdots X-C$ bonding had less importance (F2–F7, 16.5%), it is nonetheless critical in clarifying the understanding of the boiling point variation of these molecules. On the basis of eq 2, it was also possible to estimate the boiling point of molecules not included in the model building or yet to be synthesized (Table 3).

Although the mathematical model was robust in quantifying the importance of the different explanatory variables, some compounds can be considered as outliers in this group of 86 molecules. The greatest deviations occurred for the following three molecules: BrF_2C-CHF_2 (**23**), F_3C-CH_2F (**41**), and FH_2C-CHF_2 (**74**). The important discrepancy for these molecules from their respective subgroup plot is readily apparent in Figure 2. It can be also observed from Figure 2 that the subgroup 5 slope is greater than those of the other subgroups. The physical interpretation of this observation is not clear. It can be speculated that an increased halogen size appears to better facilitate the formation of weak intermolecular bonds in this subgroup. Could it be an enhanced protrusion of the single halogen atom that, as its size increases, renders the atom more accessible? It cannot be excluded that halogen bonding may come into view more evidently within the monohalogenated ethanes since a recent review of halogen acceptors reported the simultaneous intermolecular binding of heavier halogens to another halogen and hydrogen in dimers of halogenated methanes.[30] An answer to this question could possibly be found by analysis of halogenated propane and butane boiling points in relation to their structure.

With respect to the secondary objective of this study, i.e., to examine the possible role of halogen bonding on the boiling points in halogenated ethanes, it is essential to describe what has been observed in halogenated alkanes.[31] In bromomethane, a positive potential exists on the surface of the halogen, and in bromoethane, the positive potential is smaller. If hydrogens in bromomethane are replaced by fluorine atoms, then there is a greater positive potential. In the case of chloromethane, a positive potential exists on the halogen only in the presence of an electron-withdrawing group. Clearly, in the case of the halogenated ethanes in this study, it may be difficult to select molecules exhibiting a strong positive potential and compare their boiling points with those of other molecules devoid of a surface positive potential. Halogen bonding may be, to a certain extent, confounded in the MR value. In another respect, halogen bonding is also known to compete with hydrogen bonding in some circumstances.[32] Perhaps a study that included iodine compounds could better examine possible effects of halogen bonding on boiling points.

4. Conclusions

In this study, the influence of MR and weak hydrogen–halogen bonds on the boiling point of halogenated ethanes was investigated. The results are consistent with weak hydrogen–halogen interactions playing a critical role in clarifying the different boiling points. More specifically, the layout of hydrogen and halogen atoms on the two-carbon skeleton dictates the extent of this weak bonding. The mathematical model described was able to explain 99.5% of the variance of the boiling points in this series of compounds.

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