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QUANTITATIVE DESCRIPTION OF STRUCTURAL EFFECTS ON MELTING POINTS OF SUBSTITUTED ALKANES

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Structural effects on the melting points of substituted alkanes, both branched and unbranched, ranging in length from 1 to 19 carbon atoms, were successfully correlated with a variant of the intermolecular force equation which included a variable capable of accounting for the packing energy contribution of the alkyl group. The final data set had 366 data points. The regression equation obtained accounted for 91·85% of the variance of the data with a standard error of 17·9 K. Twenty-nine data points could not be included in the correlation; nine of these are carboxamides. The contributions of the polar variables are slightly larger than those of the nonpolar variables while the contribution of structural variation in the substituent is greater than that in the alkyl group. It will be necessary to determine appropriate values of the packing parameter if compounds with chains longer than 20 carbon atoms are to be included in the model.

INTRODUCTION

There are many properties which are a function of the difference in intermolecular forces (imf) between substrates in an initial (i) and a final (f) phase. The change in the free energy associated with the property is given by the expression

$$\Delta G = f(\text{imf}_\text{f} - \text{imf}_\text{i}) = f(\Delta \text{ imf}) \qquad (1)$$

We are interested in the quantitative description of the variation of the property with structure. A relationship which is capable of this is termed a structure–property quantitative relationship (SPQR).

In order to model the effect of structure on the property of interest, we must parameterize the intermolecular forces involved. They include hydrogen bonding (hb), van der Waals [dipole–dipole (dd), dipole–induced dipole (di) and induced dipole–induced dipole (ii)] interactions, charge-transfer (ct) interactions and ion–neutral [ion–dipole (Id) and ion–induced dipole (Ii)] interactions. Our best present model of these is the intermolecular force (imf) equation.[1–6] This can be written in its most general form as

$$Q_\text{X} = L\sigma_{l\text{X}} + D\sigma_{d\text{X}} + R\sigma_{e\text{X}} + A\alpha_\text{X} + H_1 n_\text{HX} + H_2 n_{n\text{X}} + Ii_\text{X} + B_\text{DX} n_\text{DX} + B_\text{AX} n_\text{AX} + S\psi_\text{X} + B^0 \qquad (2)$$

where the paramaterizations of the imf are shown in Table 1. The term $S\psi$, also present in equation (2), is there to account for steric effects; ψ is an appropriate steric effect parameterization.[9] It may be monoparametric using the υ steric parameters, polyparametric, using the simple branching model:

$$S\psi = B_1 n_1 + B_2 n_2 + B_3 n_3 + \cdots \qquad (3)$$

the expanded branching model:

$$S\psi = B_{11} n_{11} + B_{12} n_{12} + B_{13} n_{13} + B_{21} n_{21} + B_{22} n_{22} + B_{23} n_{23} + B_{31} n_{31} + \cdots \qquad (4)$$

the segmental model:

$$S\psi = S_1 \upsilon_1 + S_2 \upsilon_2 + S_3 \upsilon_3 + \cdots \qquad (5)$$

or a composite model using a combination of the υ parameter and the branching model. It may or may not include the n_b parameter, which is a measure of group length.[7] The imf model has been applied to the modeling of transport parameters,[1–4] including partition coefficients chromatographic properties and amino acid hydrophobicities, of amino acid peptide and protein bioactivities,[4] of protein conformational parameters,[4] of substrate binding to abiotic polymers[5] and of solvent effects on enzyme reactivity.[6]

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Table 1. Parameterization of intermolecular forces

Imf type	Parameterization
hb	n_H: equal to the number of OH and/or NH and/or C^{sp}—H bonds[a] n_n: equal to the number of O and/or N lone pairs and/or $C\equiv C$ bonds[a] σ_l: localized (field and/or inductive) electrical effect parameter[b] σ_d: delocalized (resonance) electrical effect parameter[b] σ_e: electronic demand sensitivity parameter[b]
dd	μ: bond moment of the C^{sp^3}—X bond or the C^{sp^2}—X bond, depending on the substrate structure.[c] Also σ_l, σ_d, σ_e
di	μ, σ_l, σ_d, σ_e and α: polarizability parameters defined from group molar refractivites[a]
ct	n_D: equals 1 where X is capable of acting as a charge transfer acceptor, otherwise 0[a] n_A: equals 1 when X is capable of acting as a charge transfer donor, otherwise 0[a] Also σ_l, σ_d, σ_e, n_n
Id	i: equals 1 for ionic X, otherwise 0[a] Also μ, σ_l, σ_d, σ_e
Ii	i, α

[a] Ref: 4.
[b] Ref: 7.
[c] Ref: 8.

The melting point, T_m, is a property of some environmental significance. We have previously studied melting point variation with structure by applying the imf model[10] to data sets with certain constraints. Dearden[11] has correlated melting points of substituted anilines with a QSAR model. The two basic assumptions made in the application of the imf model to the structural dependence of melting points were that T_m obeys equation (1), that is, depends on the difference in imf between the solid and liquid states, and that it is also dependent on the way in which the substrate packs in the crystal lattice. Other attempts to estimate T_m have been made by Yalkowsky and co-workers.[12,13]

As the melting point represents the temperature at which solid and liquid phases are in equilibrium, it follows that

$$\Delta G_m = \Delta H_m - T_m \, \Delta S_m \tag{6}$$

As ΔG_m must equal zero:

$$T_m = \Delta H_m / \Delta S_m \tag{7}$$

There are two possibilities: (1) ΔS_m is variable and proportional to ΔH_m, or (2) ΔS_m is approximately constant, in which case

$$T_m = a \, \Delta H_m \tag{8}$$

Evidence has been reported which shows that the first case actually obtains.[14]

In order to establish the validity of the imf model for melting points, we have considered substrates of the type XG, where either X or G or both may vary in structure. Both X and G will contribute to the intermolecular forces in the two phases. With regard to the effects of packing however there are three possible cases: (1) the packing is determined largely or entirely by G with X making a negligible contribution; (2) the packing is determined largely or entirely by X with G making a negligible contribution; or (3) both X and G make major contributions to the packing.

We have previously shown that if we restrict the study to compounds for which G is alkyl (Ak), we can derive from the imf equation linear structure–enthalpy relationships of the form

$$T_{m,XAk} = a_1 T_{m,XAk^0} + a_0 \tag{9}$$

In applying equation (9) the reference alkyl group, Ak^0 and the alkyl group of interest, Ak, are held constant and X is varied. By choosing long unbranched alkyl groups for both Ak and Ak^0, the packing energy was held approximately constant. Sets with G equal to Ar were also successfully correlated with equation (9). Sets with constant X and G equal to unbranched Ak with two or more C atoms were successfully correlated with an equation of the form

$$T_m = B_C n_C + B_{ev} n_{ev} + B^0 \tag{10}$$

where n_C is the number of C atoms in the Ak group and n_{ev} is a parameter which accounts for the difference in packing between unbranched Ak groups with odd or even numbers of C atoms, taking the value 1 when the number is even. Data sets in which X was held constant and Ak allowed to vary in both length and branching were successfully correlated with an equation of the form

$$T_m = B_C n_C + B_{sym} n_{sym} + B_1 n_1 + B_2 n_2 + B_3 n_3 \tag{11}$$

where n_{sym} is a parameter which accounts for the symmetry of the Ak group.

In all of the previous work the nature of the variation of T_m with changing structure of X was not considered. Here we commence a study of this problem. For this purpose, we have begun by considering three types of data set: (1) G is even-numbered unbranched alkyl with n_C not less than 4 (set 1); (2) G is odd-numbered

Table 2. T_m values used in the correlations[a,b]

AK	X, T_m(K)[c]
Me	F, 131·15; Cl, 175·45; Br, 189·15; I, 206·65; SH, 150·15; CO$_2$Et, 189·55; CO$_2$Me, 175·05; CN, 229·35; C$_2$H, 170·35; Ac, 177·80; CHO, 149·65; OAc, 175·05; OH, 179·25; NH$_2$, 179·65; Ph, 178·15; OMe, 134·65; SMe, 174·85; SEt, 167·25; COCl, 160·25; Me, 89·85; Et, 85·45; Vi, 87·95; NO$_2$, 256·15; CONH$_2$, 353·25; CO$_2$H, 289·78; CH$_2$OH, 158·65
Et	H, 89·85; F, 129·95; Cl, 136·15; Br, 154·55; I, 162·25; SH, 125·25; CO$_2$Et, 199·25; CO$_2$Me, 185·15; CN, 180·35; C$_2$H, 147·45; Ac, 186·45; Me, 85·45; Et, 134·75; CHO, 192·15; OAc, 189·15; CO$_2$H, 252·35; OH, 158·65; NH$_2$, 192·15; Ph, 178·15; OEt, 156·85; SMe, 167·25; COCl, 179·15; NO$_2$, 183·15; Vi, 87·85; Bz, 291·75; CONH$_2$, 352·15; CH$_2$OH, 146·65
Pr	H, 85·45; Me, 134·75; Et, 143·45; F, 114·15; Cl, 150·35; Br, 163·05; I, 172·15; SH, 160·05; CO$_2$Et, 175·15; CO$_2$Me, 188·35; CN, 161·25; C$_2$H, 141·25; Vi, 107·95; Ac, 195·35; CHO, 176·75; OAc, 181·15; OH, 146·65; CH$_2$OH, 184·55; NH$_2$ 190·15; Ph, 173·55; SMe, 160·15; COCl, 184·15; NO$_2$, 181·85; CONH$_2$, 389·15; CO$_2$H, 268·15
iPr	H, 85·45; Me, 113·75; Cl, 155·95; Br, 184·15; I, 183·05; SH, 142·65; CO$_2$Me, 188·45; CN, 201·65; C$_2$H, 183·45; Vi, 104·65; Ac, 181·15; OAc, 199·75; CO$_2$H, 243·85; OH, 183·65; NH$_2$, 177·95; CONH$_2$, 401·15; Ph, 249·95; NO$_2$, 180·15
Bu	H, 134·75; Me, 143·45; Et, 177·75; F, 139·15; Cl, 150·05; Br, 160·75; I, 169·65; SH, 157·45; CO$_2$Et, 181·85; CN, 176·35; C$_2$H, 167·45; Vi, 133·35; Ac, 216·25; CHO, 181·15; CO$_2$H, 239·45; OH, 184·55; CH$_2$OH, 194·25; NH$_2$, 190·15; Ph, 173·55; COCl, 163·15; OAc, 199·65, OMe, 157·65; OEt, 170·15; NO$_2$, 191·85; CONH$_2$, 387·15
iBu	H, 113,75, Cl, 142·85; Br, 155·75; CN, 172·35; CO$_2$Et, 183·65; CHO, 222·15; Ac, 188·45; C$_2$H, 168·05; Vi, 119·55; CONH$_2$, 410·15; OAc, 174·57; SCN, 214·15
tBu	H, 113·75; Me, 256·65; Cl, 247·75; Br, 256·95; I, 234·95; SH, 274·26; CO$_2$Et, 183·65; CN, 288·65; C$_2$H, 191·95; Vi, 157·95; Ac, 223·35; CO$_2$H, 308·15; OH, 247·65; NH$_2$, 205·65; CHO, 279·15; OMe, 164·15; OEt, 179·15; SEt, 182·15; SMe, 175·35; SCN, 283·65; Ph, 215·35
Pe	H, 143·45; Me, 177·75; Et, 182·55; Cl, 174·15; Br, 185·15; I, 187·15; SH, 197·45; CO$_2$Et, 206·15; CO$_2$Me, 202·15; CN, 192·85; C$_2$H, 192·15; Vi, 154·25; Ac, 238·15; CHO, 217·15; CO$_2$H, 269·15; OH, 194·25; CH$_2$OH, 221·55; NH$_2$, 218·15; Ph, 194·85; OAc, 202·35; COCl, 186·15; CONH$_2$, 389·15
neoPe	H, 256·65; Cl, 253·15; C$_2$H, 197·45; CONH$_2$, 407·15; OH, 325·65
Hx	H, 177·75; Me, 182·55; Et, 216·35; Br, 188·15; SH, 192·65; CO$_2$Et, 207·15; C$_2$H, 193·85; Vi, 171·45; Ac, 257·15; CHO, 230·15; CO$_2$H, 265·65; OH, 221·55; CH$_2$OH, 238·55; NH$_2$, 250·15; OAc 192·25
Hp	H, 182·55; Me, 216·35; Et, 219·65; Cl, 204·15; Br, 215·15; I, 224·95; SH, 229·95; CO$_2$Et, 226·15; CO$_2$Me; 233·15; CN, 227·55; C$_2$H, 223·15; Vi, 191·75; Ac, 265·65; CO$_2$H, 289·75; OH, 238·55; CH$_2$OH, 258·15; NH$_2$, 250·15; OAc, 222·95; COCl, 210·15; CONH$_2$, 381·15
Oc	H, 216·35; Me, 219·65; Et, 243·45; Cl, 212·15; Br, 218·15; I, 227·25; SH, 223·95; CN, 238·95; Vi, 206·85; CO$_2$H, 285·65; OH, 258·15; CH$_2$OH, 267·15; NH$_2$, 270·15; OAc, 258·10; COCl, 212·65
No	H, 219·65; Me, 243·45; Et, 247·55; Cl, 233·75; CO$_2$Et, 253·15; CO$_2$Me, 255·15; CN, 255·25; C$_2$H, 248·15; Vi, 223·95; Ac, 284·65; CHO, 268·15; CO$_2$H, 304·55; OH, 267·65; CH$_2$OH, 280·05; NH$_2$, 272·15; COCl, 238·65; CONH$_2$, 381·15
Dc	H, 243·45; Me, 247·56; Et, 263·55; Pr, 267·65; F, 238·15; Cl, 241·85; Br, 243·95; I, 257·85; SH, 247·15; CO$_2$Et, 258·15; C$_2$H, 254·15; Vi, 237·92; Ac, 294·15; CHO, 269·15; CO$_2$H, 301·75; OH, 280·15; CH$_2$OH, 289·15; NH$_2$, 288·15; CH$_2$CN, 277·15; OAc, 258·10
Udc	H, 247·95; Me, 263·55; Et, 267·75; CO$_2$Et, 271·35; CO$_2$Me, 278·35; CN, 277·15; Vi, 250·05; Ac, 303·65; CO$_2$H, 317·75; OH, 289·05; CH$_2$OH, 296·95; NH$_2$, 290·15; CONH$_2$ 383·15; COCl, 256·15
Ddc	H, 263·55; Me, 267·75; Et, 279·05; Cl, 263·85; Br, 263·65; I, 273·45; CO$_2$Me, 279·65; CN, 282·85; C$_2$H, 279·65; Vi, 260·25; CO$_2$H, 317·65; OH, 296·95; CH$_2$OH, 305·65; NH$_2$, 301·45; CONH$_2$, 373·15
Trd	H, 267·75; Me, 279·05; Et, 283·05; Cl, 279·35; CN, 292·35; C$_2$H, 283·15; Vi, 278·15; Ac, 312·65; CO$_2$H, 331·65; OH, 305·65; CH$_2$OH, 310·95; NH$_2$ 300·55; CO$_2$Et, 285·45; CO$_2$Me, 292·15; CONH$_2$, 379·15; COCl, 272·15; CHO, 303·15
Ted	H, 279·05; Me, 283·05; Et, 291·35; Cl, 278·75; C$_2$H, 288·15; Vi, 277·25; OH, 310·95; NH$_2$, 314·15
Pdc	H, 283·05; Me, 291·35; Et, 295·15; Br, 292·15; CN, 304·15; Vi, 284·35; Ac, 321·15; CO$_2$H, 336·65; CH$_2$OH, 323·15; NH$_2$ 310·45; CO$_2$Et, 297·15; CO$_2$Me, 303·15; CONH$_2$, 380·15; COCl, 285·15; CHO, 307·15
Hxd	H, 291·32; Me, 295·15; Et, 301·33; F, 291·15; Cl, 291·05; Br, 291·15; I, 297·85, SH, 292·15; CO$_2$Et, 301·15; CO$_2$Me, 303·15; CN, 307·15; C$_2$H, 300·15; Vi, 290·65; Ac, 297·35; CHO, 309·15; CH$_2$Br, 305·15; CO$_2$H, 334·35; OH, 322·42; CH$_2$OH, 327·15; NH$_2$, 319·92; CONH$_2$, 381·35; Ph, 289·25
Hpd	H, 295·15; Me, 301·35; Et, 305·05; Cl, 305·15; CN, 314·15; Vi, 310·65; Ac, 330·15; CO$_2$H, 344·35; CH$_2$OH, 331·05; NH$_2$, 322·15; CO$_2$Et, 305·15; CO$_2$Me, 312·15; CONH$_2$ 381·65; COCl, 296·15
Ocd	H, 301·33; Me, 305·05; Et, 309·95; Cl, 301·75; Br, 301·35; I, 307·15; SH, 301·15; CN, 316·15; C$_2$H, 309·15; Vi, 301·65; Ac, 331·15; CO$_2$H, 342·55; OH, 332·75; CH$_2$OH, 335·65; NH$_2$, 326·01; OAc, 307·65; NMe$_2$, 296·04
Nde	H, 305·05; Me, 309·55; CO$_2$H, 350·15; CO$_2$Et, 323·15; CO$_2$Me, 327·65; OH, 335·65

[a] Non-standard abbreviations: Hx, hexyl; Hp, heptyl; Oc, octyl; No, nonyl; Dc, decyl; Udc, undecyl; Ddc, dodecyl; Trd, tridecyl; Ted, tetradecyl; Pdc, pentadecyl; Hxd, hexadecyl; Hpd, heptadecyl; Ocd, octadecyl; Ndc, nonadecyl; Vi, vinyl.

[b] Sets studied: 1, even-numbered unbranched alkyl groups with n_C equal to 4–18; 2, odd-numbered unbranched alkyl groups with n_C equal to 5–19; 3, Me, Et, Pr, iPr, iBu, tBu, iPe, tPe, neoPe; 11, unbranched alkyl groups with n_C equal to 4–19; 21, set 11 + Et, Pr; 22, unbranched alkyl groups with n_C equal to 1–19; 23, set 22 + iPr, tBu; 24, set 23 + iBu, neoPe.

[c] Melting points (T_m) were taken from Refs 15 and 16.

unbranched alkyl with n_C not less than 5 (set 2); and (3) G is branched or unbranched alkyl with n_C not more than 5 for the former or 3 for the latter (set 3).

METHOD

The data sets studied are presented in Table 2. They were correlated with equations derived from equation (2) by means of multiple linear regression analysis. The parameter values used are reported in Table 3.

It is helpful in discussing our results to use C_i, the percentage contribution of each independent variable in the regression equation. This quantity is given by

$$C_i = \frac{100 a_i x_i}{\sum_{1}^{m} a_i x_i} \tag{12}$$

where a_i is the regression coefficient of the ith independent variable and x_i is its value for some reference group. We have defined a hypothetical reference group for which $\sigma_l = \sigma_d = \mu = n_H = n_n = v_1 = v_2 = v_3 = n_{ev} = 1$, $\sigma_e = 0{\cdot}1$, $\alpha = 0{\cdot}2$, $n_C = 10$ and $p_{Ak} = 1$. The C_i values are particularly useful in comparing the relative importance of the contribution of the different independent

Table 3. Parameter values used in the correlations[a]

X	σ_l	σ_d	σ_e	μ	α	n_H	n_n	v_1	v_2	v_3
H	0	0	0	0	0	0	0	0	0	0
Me	−0·01	−0·14	−0·030	0	0·046	0	0	0·52	0	0
Et	−0·01	−0·12	−0·036	0	0·093	0	0	0·52	0·52	0
Pr	−0·01	−0·15	−0·036	0	0·139	0	0	0·52	0·52	0·52
CH_2Br	0·20	−0·08	−0·026	2·069	0·124	0	0	0·52	0·65	0
CH_2CN	0·20	−0·01	−0·011	3·53	0·099	0	1	0·52	0·40	0·40
CH_2OH	0·11	−0·10	−0·025	1·58	0·062	1	2	0·52	0·32	0
CF_3	0·40	0·13	−0·026	2·321	0·040	0	0	0·90	0·27	0
CCl_3	0·36	0·10	−0·018	1·755	0·191	0	0	1·38	0·55	0
Vi	0·11	−0·08	−0·12	0·364	0·100	0	0	0·57	0·57	0
Ph	0·12	−0·12	−0·12	0·37	0·243	0	0	0·57	0·57	0·57
C_2H	0·29	−0·02	−0·10	0·75	0·085	1	1	0·58	0·58	0
F	0·54	−0·48	0·41	1·8549	−0·001	0	0	0·27	0	0
Cl	0·47	−0·28	−0·011	1·895	0·050	0	0	0·55	0	0
Br	0·47	−0·27	−0·018	1·84	0·079	0	0	0·65	0	0
I	0·40	−0·20	−0·057	1·618	0·129	0	0	0·78	0	0
CHO	0·30	0·27	−0·10	2·69	0·059	0	2	0·50	0	0
Ac	0·30	0·25	−0·095	2·89	0·114	0	2	0·50	0·32	0
COCl	0·44	0·31	−0·060	*2·71*	0·116	0	2	0·50	0·32	0
CO_2H	0·30	0·17	−0·051	1·70	0·059	1	4	0·50	0·32	0
CO_2Me	0·32	0·16	−0·070	1·706	0·118	0	4	0·50	0·32	0
CO_2Et	0·30	0·18	−0·064	1·84	0·164	0	4	0·50	0·32	0
$CONH_2$	0·28	0·12	−0·055	3·72	0·088	2	3	0·50	0·32	0
Bz	0·30	0·22	−0·11	2·96	0·293	0	2	0·50	0·32	0
CN	0·57	0·12	−0·055	3·9185	0·053	0	1	0·40	0·40	0
OH	0·35	−0·57	−0·044	1·77	0·018	1	2	0·32	0	0
OMe	0·30	−0·55	−0·064	1·31	0·068	0	2	0·32	0·52	0
OEt	0·28	−0·55	−0·070	1·22	0·114	0	2	0·32	0·52	0·52
OAc	0·38	−0·24	−0·005	1·706	0·114	0	4	0·32	0·50	0·32
SH	0·27	−0·40	−0·098	*1·52*	0·082	0	0	0·60	0	0
SMe	0·30	−0·38	−0·13	*1·06*	0·128	0	0	0·60	0·52	0
SEt	0·26	−0·39	−0·12	*1·06*	0·174	0	0	0·60	0·52	0·52
SCN	0·56	−0·15	−0·040	*4·13*	0·124	0	0	0·60	0·40	0·40
SPh	0·31	−0·34	−0·17	1·50	0·333	0	0	0·60	0·57	0·57
SSMe	0·41	−0·45	−0·17	1·985	0·210	0	0	0·60	0·60	0·52
NH_2	0·17	−0·68	−0·13	1·296	0·044	2	1	0·35	0	0
NMe_2	0·17	−0·66	−0·24	0·612	0·145	0	1	0·63	0·52	0
$NHNH_2$	0·11	−0·64	−0·11	*1·75*	0·074	3	2	0·35	0·35	0
NO_2	0·67	0·18	−0·077	3·56	0·063	0	4	0·35	0·32	0

[a] Parameter values were taken from Refs 9 and 17–22, or estimated as discribed therein; estamated values of μ given in italics.

variables to the regression equation both within a given data set and between data sets.

RESULTS

Unbranched alkyl groups

The correlation equation used for sets 1 and 2 is

$$\begin{aligned} T_{\mathrm{mXAk}} = {} & L\sigma_{\mathrm{lX}} + D\sigma_{\mathrm{dX}} + R\sigma_{\mathrm{eX}} + M\mu_{\mathrm{X}} + A\alpha_{\mathrm{X}} \\ & + H_1 n_{\mathrm{HX}} + H_2 n_{n\mathrm{X}} + S_1\upsilon_{1\mathrm{X}} + S_2\upsilon_{2\mathrm{X}} \\ & + S_3\upsilon_{3\mathrm{X}} + B_{\mathrm{C}} n_{\mathrm{CAk}} + B^0 \end{aligned} \qquad (13)$$

No term in i was considered necessary as none of the compounds studied should be ionized in the solid state. The alkyl groups require no parameterization other than polarizability, which in this case is represented by n_{C}. The steric effects of unbranched alkyl groups with three or more carbon atoms are constant. The electrical effects of all alkyl groups are constant.[9] We have chosen to represent the steric effect of the X group by the segmental method. In set 1 the T_{m} value for $\mathrm{BuCONH_2}$ deviated strongly while the values for BuH, BuMe, $\mathrm{BuCH{=}CH_2}$, and DcAc deviated somewhat (abbreviations for alkyl groups are reported in the footnotes to Table 2). On exclusion of the values for these compounds the best regression obtained was

$$\begin{aligned} T_{\mathrm{mXAk}} = {} & -77{\cdot}6(\pm 18{\cdot}3)\sigma_{\mathrm{lX}} + 119(\pm 32{\cdot}9)\sigma_{\mathrm{eX}} \\ & +12{\cdot}2(\pm 2{\cdot}16)\mu_{\mathrm{X}} + 20{\cdot}0(\pm 2{\cdot}33)n_{\mathrm{HX}} \\ & +5{\cdot}24(\pm 1{\cdot}06)n_{n\mathrm{X}} + 27{\cdot}7(\pm 9{\cdot}04)\upsilon_{1\mathrm{X}} \\ & +9{\cdot}64(\pm 0{\cdot}266)n_{\mathrm{CAk}} + 136(\pm 5{\cdot}37) \end{aligned} \qquad (14)$$

with $100R^2$, 92·75; $A100R^2$, 92·41; F, 226·7; S_{est}, 14·5; S^0, 0·278; n, 132; $C_{\sigma\mathrm{l}}$, 30·9; $C_{\sigma\mathrm{e}}$, 4·43; C_{μ}, 4·87; $C_{n\mathrm{H}}$, 7·98; C_{nn}, 2·09; $C_{\upsilon 1}$, 11·0; $C_{n\mathrm{C}}$, 38.4. The $100R^2$ statistic represents the percentage of the variance of the data accounted for by the regression equation; the $A100R^2$ statistic is the adjusted value of $100R^2$, and takes into account the number of independent variables in the regression equation; the F statistic is a measure of the significance of the correlation and its confidence level is given in parentheses; the S_{est} statistic is the standard error of the estimate and is useful in detecting outliers, but it is of no use as a measure of the goodness of fit of different data sets to a model if they involve different types of data as it depends on the nature of the data correlated; the S^0 statistic may be thought of as a standard error of the estimate which has been corrected for the nature of the data and is a useful measure of the goodness of fit of the data to the regression equation.

As four of the five deviant compounds in set 1 were butyl derivatives, correlation with equation (13) was repeated after the exclusion of those compounds for which the alkyl group was butyl (set 1.1). The best regression equation obtained was

$$\begin{aligned} T_{\mathrm{mXAk}} = {} & -70{\cdot}7(\pm 11{\cdot}4)\sigma_{\mathrm{lX}} + 105(\pm 30{\cdot}5)\sigma_{\mathrm{eX}} \\ & +13{\cdot}2(\pm 1{\cdot}97)\mu_{\mathrm{X}} + 20{\cdot}2(\pm 2{\cdot}17)n_{\mathrm{HX}} \\ & +4{\cdot}34(\pm 1{\cdot}01)n_{n\mathrm{X}} + 23{\cdot}6(\pm 8{\cdot}33)\upsilon_{1\mathrm{X}} \\ & +8{\cdot}41(\pm 0{\cdot}290)n_{\mathrm{CAk}} + 153(\pm 5{\cdot}25) \end{aligned} \qquad (15)$$

with $100R^2$, 91·46; $A100R^2$, 90·97; F, 159·1; S_{est}, 12·5; S^0, 0·303; n, 112; $C_{\sigma\mathrm{l}}$, 31·2; $C_{\sigma\mathrm{e}}$, 4·62; C_{μ}, 5·81; $C_{n\mathrm{H}}$, 8·92; C_{nn}, 1·92; $C_{\upsilon 1}$, 10·4; $C_{n\mathrm{C}}$, 37·1.

The agreement between both the coefficients and the C_i values obtained for sets 1 and 1.1 shows clearly that exclusion of the values for BuX has not altered the results. Further, the statistics obtained for set 1 are better than those for set 1.1. There is then no justification for the exclusion of the butyl derivatives.

Correlation of set 2 with equation (13) also resulted in the deviation of five compounds, PeH, $\mathrm{PeCH{=}CH_2}$, $\mathrm{PeCH_2OH}$, $\mathrm{PeCONH_2}$ and $\mathrm{HpCONH_2}$. On exclusion of these compounds, the best regression obtained was

$$\begin{aligned} T_{\mathrm{mXAk}} = {} & -93{\cdot}0(\pm 19{\cdot}7)\sigma_{\mathrm{lX}} + 23{\cdot}7(\pm 10{\cdot}0)\sigma_{\mathrm{dX}} \\ & +15{\cdot}7(\pm 3{\cdot}12)\mu_{\mathrm{X}} - 189(\pm 54{\cdot}7)\alpha_{\mathrm{X}} \\ & +23{\cdot}1(\pm 4{\cdot}16)n_{\mathrm{HX}} + 5{\cdot}18(\pm 1{\cdot}56)n_{n\mathrm{X}} \\ & +66{\cdot}1(\pm 13{\cdot}0)\upsilon_{1\mathrm{X}} + 56{\cdot}6(\pm 24{\cdot}3)\upsilon_{3\mathrm{X}} \\ & +8{\cdot}52(\pm 0{\cdot}320)n_{\mathrm{CAk}} + 142(\pm 6{\cdot}55) \end{aligned} \qquad (16)$$

with $100R^2$, 92·32; $A100R^2$, 91·77; F, 147·0; S_{est}, 14·2; S^0, 0·289; n, 120; $C_{\sigma\mathrm{l}}$, 22·9; $C_{\sigma\mathrm{d}}$, 5·82; C_{μ}, 3·86; C_{α}, 9·30; $C_{n\mathrm{H}}$, 5·68; C_{nn}, 1·28; $C_{\upsilon 1}$, 16·3; $C_{\upsilon 3}$, 13·9; $C_{n\mathrm{C}}$, 21·0.

Based on our previous work and our experience with set 1 we have assumed that pentyl derivatives belong in set 2.

Although there are many similarities between equations (15) and (16) there are also some important differences. Thus, set 1 shows no dependence on σ_{d}, α or υ_3, whereas set 2 does. Set 2 shows no dependence on σ_{e} whereas set 1 does. The dependence on υ_1 for set 2 is much smaller than it is for set 1. The C_i values further illustrate the differences between the two sets. Presumably, these differences are due to a difference in packing between the even- and odd-numbered alkyl groups.

We examined the possibility of combining sets 1 and 2 into a single data set (set 11) by the introduction of the parameter p_{ev}, which is intended to account for the difference in packing between odd- and even-numbered unbranched alkyl groups; it takes the value 0 for the former and 1 for the latter. The best results were obtained on exclusion of the values for the amides with Ak equal to Bu, Pe, Hp and No. The best regression equation was

$$\begin{aligned}T_{\mathrm{mXAk}} = {} & -86\cdot4(\pm10\cdot2)\sigma_{\mathrm{lX}} + 68\cdot1(\pm29\cdot7\sigma_{\mathrm{eX}} \\ & +15\cdot6(\pm1\cdot64)\mu_{\mathrm{X}} - 107(\pm44\cdot3)\alpha_{\mathrm{X}} \\ & +17\cdot8(\pm2\cdot09)n_{\mathrm{HX}} + 6\cdot28(\pm0\cdot914)n_{n\mathrm{X}} \\ & +53\cdot0(\pm9\cdot38)\upsilon_{1\mathrm{X}} + 29\cdot4(\pm13\cdot2)\upsilon_{3\mathrm{X}} \\ & +9\cdot52(\pm0\cdot211)n_{\mathrm{CAk}} - 5\cdot76(\pm1\cdot97)p_{\mathrm{ev}} \\ & +132(\pm4\cdot25) \qquad (17)\end{aligned}$$

with $100R^2$, 91·91; $A100R^2$, 91·61; F, 280·5; S_{est}, 15·4; S^0, 0·291; n, 258; $C_{\sigma1}$, 25·6; $C_{\sigma\mathrm{e}}$, 2·02; C_{μ}, 4·61; C_{α}, 6·33; $C_{n\mathrm{H}}$, 5·28; C_{nn}, 1·86; $C_{\upsilon1}$, 15·7; $C_{\upsilon3}$, 8·71; $C_{n\mathrm{C}}$, 28·2; $C_{p\mathrm{ev}}$, 1·70.

The fit of the data to the model for the combined set is not very much different from that obtained for sets 1 and 2. It is interesting that many of the compounds which deviated from sets 1 and 2 could be included in set 11. Surprisingly, no major dependence on p_{ev} was observed.

We next considered the possibility of including EtX and PrX in the data set (set 21). The best results were obtained on the exclusion of T_{m} values for $\mathrm{AkCONH_2}$ with Ak equal to Et, Pr, Bu, Pe, Hp and No; EtX with X equal to $\mathrm{CH{=}CH_2}$, $\mathrm{CH_2OH}$ and Bz; and PrH. The regression equation obtained was

$$\begin{aligned}T_{\mathrm{mXAk}} = {} & -69\cdot3(\pm12\cdot1)\sigma_{\mathrm{lX}} + 15\cdot8(\pm6\cdot06)\sigma_{\mathrm{dX}} \\ & +57\cdot2(\pm30\cdot0)\sigma_{\mathrm{eX}} + 15\cdot8(\pm1\cdot99)\mu_{\mathrm{X}} \\ & -93\cdot4(\pm44\cdot7)\alpha_{\mathrm{X}} + 22\cdot4(\pm2\cdot67)n_{\mathrm{HX}} \\ & +5\cdot96(\pm1\cdot03)n_{n\mathrm{X}} + 53\cdot2(\pm9\cdot69)\upsilon_{1\mathrm{X}} \\ & +40\cdot5(\pm13\cdot1)\upsilon_{3\mathrm{X}} \\ & +9\cdot91(\pm0\cdot194)n_{\mathrm{CAk}} + 121(\pm4\cdot24) \qquad (18)\end{aligned}$$

with $100R^2$, 92·46; $A100R^2$, 92·23; F, 358·0; S_{est}, 16·9; S^0, 0·280; n, 303; $C_{\sigma1}$, 20·2; $C_{\sigma\mathrm{d}}$, 4·59; $C_{\sigma\mathrm{e}}$, 1·67; C_{μ}, 3·74; C_{α}, 5·44; $C_{n\mathrm{H}}$, 6·51; C_{nn}, 1·74; $C_{\upsilon1}$, 15·5; $C_{\upsilon3}$, 11·8; $C_{n\mathrm{C}}$, 28·9.

Overall, the fit of set 21 to the model is comparable to that of set 11, although the standard error of the estimate is larger. The coefficients L, R, M, A, H_2, S_1 and S_3 of set 21 are not significantly different from those of set 11 and the differences in the coefficients H_1 and B_{C} are barely significant. The major differences between the two sets is that there is no dependence of set 21 on p_{ev} and no dependence of set 11 on σ_{d}.

We next considered the possibility that unbranched chains longer than propyl differ significantly in packing from those which are shorter. To account for this difference we introduced the packing parameters n_{Et} and n_{Pr}, which take the value 1 when Ak is Et for the former or Pr for the latter and 0 otherwise. The correlation equation is then

$$\begin{aligned}T_{\mathrm{mXAk}} = {} & L\sigma_{\mathrm{lX}} + D\sigma_{\mathrm{dX}} + R\sigma_{\mathrm{eX}} + M\mu_{\mathrm{X}} + A\alpha_{\mathrm{X}} \\ & + H_1 n_{\mathrm{HX}} + H_2 n_{n\mathrm{X}} + S_1\upsilon_{1\mathrm{X}} + S_2\upsilon_{2\mathrm{X}} \\ & + S_3\upsilon_{3\mathrm{X}} + B_{\mathrm{C}} n_{\mathrm{CAk}} + p_{\mathrm{Et}} n_{\mathrm{Et}} \\ & + p_{\mathrm{Pr}} n_{\mathrm{Pr}} + B^0 \qquad (19)\end{aligned}$$

Correlation of set 21 with equation (19) (set 21.1) gave the best results on exclusion of the data points for $\mathrm{AkCONH_2}$, with Ak equal to Et, Pr, Bu, Pe, Hp and No; EtX with X equal to Me, $\mathrm{CH{=}CH_2}$, $\mathrm{CH_2OH}$ and Bz; and $\mathrm{PrCO_2H}$. The groups excluded are almost the same as those excluded from set 21. The regression equation obtained was

$$\begin{aligned}T_{\mathrm{mXAk}} = {} & -71\cdot1(\pm11\cdot8)\sigma_{\mathrm{lX}} + 12\cdot2(\pm5\cdot88)\sigma_{\mathrm{dX}} \\ & +53\cdot3(\pm29\cdot6)\sigma_{\mathrm{eX}} + 13\cdot6(\pm1\cdot93)\mu_{\mathrm{X}} \\ & -80\cdot2(\pm43\cdot4)\alpha_{\mathrm{X}} + 21\cdot3(\pm2\cdot59)n_{\mathrm{HX}} \\ & +5\cdot92(\pm0\cdot994)n_{n\mathrm{X}} + 54\cdot7(\pm9\cdot32)\upsilon_{1\mathrm{X}} \\ & +37\cdot8(\pm12\cdot7)\upsilon_{3\mathrm{X}} + 9\cdot66(\pm0\cdot200)n_{\mathrm{CAk}} \\ & -19\cdot7(\pm3\cdot82)n_{\mathrm{Pr}} + 122(\pm4\cdot12) \qquad (20)\end{aligned}$$

with $100R^2$, 93·12; $A100R^2$, 92·88; F, 357·8; S_{est}, 16·4; S^0, 0·268; n, 303; $C_{\sigma1}$, 20·1; $C_{\sigma\mathrm{d}}$, 3·44; $C_{\sigma\mathrm{e}}$, 1·50; C_{μ}, 3·85; C_{α}, 4·53; C_{nH}, 6·02; C_{nn}, 1·67; $C_{\upsilon1}$, 15·4; $C_{\upsilon3}$, 10·7; $C_{n\mathrm{C}}$, 27·3; $C_{n\mathrm{Pr}}$, 5·55.

The results are comparable to but somewhat better than those obtained for set 21. The values of the coefficients in equation (20) do not differ significantly from those in equation (18). Although there is no dependence on n_{Et} there is a highly significant dependence on n_{Pr}.

We then considered the possibility of including MeX in the data set (set 22) by introducing the packing parameter n_{Me} into the correlation equation. Correlation of set 22 with a variant of equation (19) including n_{Me} gave the best results on exclusion of T_{m} values for $\mathrm{AkCONH_2}$ with Ak equal to Me, Et, Pr, Bu, Pe, Hp and No; EtX with X equal to Me, $\mathrm{CH{=}CH_2}$, $\mathrm{CH_2OH}$ and Bz; PrX with X equal to $\mathrm{CO_2H}$ and H; and MeX with X equal to Me, Et, $\mathrm{CH{=}CH_2}$, $\mathrm{CH_2OH}$, $\mathrm{CO_2H}$ and $\mathrm{NO_2}$. The regression equation obtained was

$$\begin{aligned}T_{\mathrm{mXAk}} = {} & -63\cdot5(\pm1\cdot7)\sigma_{\mathrm{lX}} + 13\cdot9(\pm5\cdot72)\sigma_{\mathrm{dX}} \\ & +85\cdot8(\pm25\cdot6)\sigma_{\mathrm{eX}} + 13\cdot0(\pm1\cdot92)\mu_{\mathrm{X}} \\ & +23\cdot9(\pm2\cdot42)n_{\mathrm{HX}} + 4\cdot45(\pm0\cdot894)n_{n\mathrm{X}} \\ & +42\cdot6(\pm7\cdot02)\upsilon_{1\mathrm{X}} + 24\cdot4(\pm9\cdot01)\upsilon_{3\mathrm{X}} \\ & +9\cdot65(\pm0\cdot203)n_{\mathrm{CAk}} - 17\cdot7(\pm3\cdot97)n_{\mathrm{Pr}} \\ & +13\cdot8(\pm4\cdot38)n_{\mathrm{Me}} + 124(\pm4\cdot21) \qquad (21)\end{aligned}$$

with $100R^2$, 92·93; $A100R^2$, 92·70; F, 369·2; S_{est}, 16·7; S^0, 0·271; n, 321; $C_{\sigma1}$, 19·7; $C_{\sigma\mathrm{d}}$, 4·30; $C_{\sigma\mathrm{e}}$, 2·66; C_{μ}, 4·03; $C_{n\mathrm{H}}$, 7·91; C_{nn}, 1·38; $C_{\upsilon1}$, 13·2; $C_{\upsilon3}$, 7·56, $C_{n\mathrm{C}}$, 29·9; $C_{n\mathrm{Me}}$, 4·27; $C_{n\mathrm{Pr}}$, 5·50.

There is indeed a dependence on n_{Me}. The results obtained are comparable to those for set 21.1. Again, the coefficients of equation (21) are generally not significantly different from those of equations (19) and (20). The major difference is that no dependence on the polarizability of X is observed for set 22.

The packing parameterization we introduced for individual alkyl groups has the form $p_{\mathrm{Ak},i}n_{\mathrm{Ak},i}$, where $n_{\mathrm{Ak},i}$ is 1 when Ak is Ak,i and 0 when it is not, the value of $p_{\mathrm{Ak},i}$ being obtained from the regression equation. In this parameterization the variation of the packing with alkyl *group structure* is accounted for by p_{Ak}. Then, setting the sum of the packing terms in the regression equal to $B_P p_{Ak}$, we have

$$B_P p_{Ak} = \sum_{i=1}^{n} p_{Ak,i} n_{Ak,i} = n_{Ak,i} \sum_{i=1}^{n} p_{Ak,i} \qquad (22)$$

As $n_{Ak,i}$ is 1 we can conclude on equating coefficients that the p_{Ak} values obtained from equation (21) can be used as parameters which represent the packing effect of individual alkyl groups while the coefficient B_p should have a value of 1. The correlation equation then becomes

$$\begin{aligned} T_{mXAk} = {} & L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + M\mu_X + A\alpha_X \\ & + H_1 n_{HX} + H_2 n_{nX} + S_1 \upsilon_{1X} + S_2 \upsilon_{2X} \\ & + S_3 \upsilon_{3X} + B_C n_{CAk} + B_P p_{AK} + B^0 \qquad (23) \end{aligned}$$

Correlation of set 22 with equation (23) after excluding the same T_m values (set 22.1) gave as the best regression equation

$$\begin{aligned} T_{mXAk} = {} & -62{\cdot}8(\pm 11{\cdot}7)\sigma_{lX} + 13{\cdot}8(\pm 5{\cdot}69)\sigma_{dX} \\ & + 87{\cdot}8(\pm 25{\cdot}5)\sigma_{eX} + 12{\cdot}9(\pm 1{\cdot}92)\mu_X \\ & + 23{\cdot}9(\pm 2{\cdot}41)n_{HX} + 4{\cdot}42(\pm 0{\cdot}892)n_{nX} \\ & + 42{\cdot}3(\pm 6{\cdot}99)\upsilon_{1X} + 24{\cdot}2(\pm 8{\cdot}99)\upsilon_{3X} \\ & + 9{\cdot}64(\pm 0{\cdot}179)n_{CAk} \\ & + 1{\cdot}02(\pm 0{\cdot}165)p_{Ak} + 125(\pm 4{\cdot}07) \qquad (24) \end{aligned}$$

with $100R^2$, 92·95; $A100R^2$, 92·74; F, 408·6; S_{est}, 16·6; S^0, 0·270; n, 321; $C_{\sigma l}$, 21·6; $C_{\sigma d}$, 4·75; $C_{\sigma e}$, 3·02; C_μ, 4·45; C_{nH}, 8·24; C_{nn}, 1·52; $C_{\upsilon 1}$, 14·6; $C_{\upsilon 3}$, 8·32; C_{nC}, 33·2; C_{pAk}, 0·352.

Branched and short alkyl groups

We have noted above some success in correlating T_m values of AkX (in which Ak varies and X is constant) with equation (11). Set 3 was therefore initially correlated with the imf equation in the form

$$\begin{aligned} T_{mXAk} = {} & L\sigma_{lX} + D\sigma_{dX} + R\sigma_{eX} + M\mu_X + A\alpha_X \\ & + H_1 n_{HX} + H_2 n_{nX} + S_1 \upsilon_{1X} + S_2 \upsilon_{2X} + S_3 \upsilon_{3X} \\ & + B_C n_{CAk} + B_1 n_{1AK} + B_2 n_{2Ak} + B_3 n_{3Ak} + B^0 \qquad (25) \end{aligned}$$

in which steric effects of the alkyl group have been parameterized by the simple branching equation. The results were poor, accounting for only about 65% of the variance of the data. We considered the use of a symmetry parameter based on the number of planes of symmetry including the longest chain of the hydrogen suppressed alkyl group, and a shape parameter given by

$$p_{sh} = n_C/(n_C - n_{C'}) \qquad (26)$$

where $n_{C'}$ is the number of C atoms in branches. The best results were obtained, however, by introducing the parameter p_q, which takes the value 1 when a 'quasi-quarternary' C atom (one which is bonded to four atoms other than hydrogen) is present in the compound. The compounds $EtCH_2OH$, iPrPh, tBuI, tBuMe, neoPeH, and $neoPeCH_2OH$ deviated significantly. On excluding these compounds, the regression equation obtained was

$$\begin{aligned} T_{mXAk} = {} & 58{\cdot}2(\pm 30{\cdot}0)\sigma_{lX} + 69{\cdot}1(\pm 11{\cdot}8)\sigma_{dX} \\ & + 340(\pm 64{\cdot}9)\sigma_{eX} + 14{\cdot}0(\pm 4{\cdot}78)\mu_X \\ & - 385(\pm 56{\cdot}6)\alpha_X + 72{\cdot}3(\pm 5{\cdot}37)n_{HX} \\ & + 44{\cdot}9(\pm 18{\cdot}2)\upsilon_{1X} + 58{\cdot}8(\pm 6{\cdot}37)p_{qAk} \\ & + 88{\cdot}6(\pm 8{\cdot}63) \qquad (27) \end{aligned}$$

with $100R^2$, 84·22; $A100R^2$, 83·35; F, 84·05; S_{est}, 25·8; S^0, 0·411; n, 135; $C_{\sigma l}$, 13·6; $C_{\sigma d}$, 16·1; $C_{\sigma e}$, 7·93; C_μ, 3·28; C_α, 18·0; C_{nH}, 16·9; $C_{\upsilon 1}$, 10·5; C_{pq}, 23·7.

In order to determine whether compounds with branched alkyl groups and with unbranched alkyl groups can be included in the same data set, we correlated the compounds of set 3 which have unbranched alkyl groups (those with Ak equal to Me, Et or Pr) (set 3.1) with the imf equation. The best regression equation was

$$\begin{aligned} T_{mXAk} = {} & 95{\cdot}5(\pm 38{\cdot}9)\sigma_{lX} + 56{\cdot}9(\pm 16{\cdot}2)\sigma_{dX} \\ & + 166(\pm 84{\cdot}1)\sigma_{eX} + 9{\cdot}62(\pm 6{\cdot}93)\mu_X \\ & - 474(\pm 68{\cdot}1)\alpha_X + 72{\cdot}0(\pm 7{\cdot}53)n_{HX} \\ & + 83{\cdot}7(\pm 10{\cdot}0) \qquad (28) \end{aligned}$$

with $100R^2$, 79·95; $A100R^2$, 78·57; F, 56·74; S_{est}, 26·5; S^0, 0·469; n, 78; $C_{\sigma l}$, 27·6; $C_{\sigma d}$, 16·5; $C_{\sigma e}$, 4·82; C_μ, 2·78; C_α, 27·5; C_{nH}, 20·8.

A comparison of the results for set 3 with those for set 3.1 shows that the coefficients of most variables are in rough agreement. The difference between the sets is that set 3 is dependent on υ_1 whereas set 3.1 is not. As the branched alkyl groups in set 3 generally exhibit a larger steric effect than the unbranched alkyl groups, the lack of dependence on υ_1 is not surprising.

All alkyl groups

In view of the mediocre results obtained for set 3, we considered the possibility of including XAk with branched alkyl groups in set 22. Unbranched alkyl groups were included with iPrX and tBuX in set 23 and this set was then correlated with a variant of equation (22) which included the parameters n_{iPr} and n_{tBu}. The best results were obtained on the exclusion of the points excluded from set 22; the T_m values for iPrX with X equal to H, Me, $CH{=}CH_2$, Ph and $CONH_2$; those for tBuX with X equal to H, SH and CN; and EtH. The regression equation obtained was

$$\begin{aligned} T_{\mathrm{mXAk}} = {} & -60{\cdot}8(\pm12{\cdot}2)\sigma_{\mathrm{lX}} + 23{\cdot}2(\pm5{\cdot}91)\sigma_{\mathrm{dX}} \\ & + 99{\cdot}3(\pm29{\cdot}6)\sigma_{\mathrm{eX}} + 12{\cdot}3(\pm1{\cdot}97)\mu_{\mathrm{X}} \\ & - 97{\cdot}2(\pm43{\cdot}7)\alpha_{\mathrm{X}} + 24{\cdot}4(\pm2{\cdot}63)n_{\mathrm{HX}} \\ & + 4{\cdot}47(\pm0{\cdot}994)n_{n\mathrm{X}} + 60{\cdot}1(\pm9{\cdot}85)\upsilon_{1\mathrm{X}} \\ & + 43{\cdot}2(\pm11{\cdot}3)\upsilon_{3\mathrm{X}} + 9{\cdot}56(\pm0{\cdot}189)n_{\mathrm{CAk}} \\ & + 1{\cdot}04(\pm0{\cdot}177)p_{\mathrm{AK}} \\ & + 29{\cdot}7(\pm4{\cdot}36)n_{\mathrm{tBu}} + 126(\pm4{\cdot}48) \qquad (29) \end{aligned}$$

with $100R^2$, 91·59; $A100R^2$, 91·32; F, 306·8; S_{est}, 17·9; S^0, 0·296; n, 351; $C_{\sigma1}$, 15·9; $C_{\sigma\mathrm{d}}$, 6·04; $C_{\sigma\mathrm{e}}$, 2·58; C_{μ}, 3·20; C_{α}, 5·06; $C_{n\mathrm{H}}$, 6·35; C_{nn}, 1·6, $C_{\upsilon1}$, 15·6; $C_{\upsilon3}$, 11·3; $C_{n\mathrm{C}}$, 24·9; C_{pAk}, 0·271; $C_{n\mathrm{tBu}}$, 7·73.

The results are not as good as those obtained for set 22 although the coefficients are generally in good agreement. Like sets 21 and 21.1 but unlike set 22, there is some dependence on polarizability. No dependence on n_{iPr} was observed. Correlation of set 23 with equation (23) using p_{Ak} values of 0 and 29·7 for iPr and tBu, respectively [obtained from equation (29)] on exclusion of the same T_{m} values as in set 23 gave the regression equation (set 23.1)

$$\begin{aligned} T_{\mathrm{mXAk}} = {} & -59{\cdot}9(\pm12{\cdot}1)\sigma_{\mathrm{lX}} + 23{\cdot}7(\pm5{\cdot}88)\sigma_{\mathrm{dX}} \\ & + 110(\pm29{\cdot}4)\sigma_{\mathrm{eX}} + 12{\cdot}6(\pm1{\cdot}96)\mu_{\mathrm{X}} \\ & + 85{\cdot}6(\pm43{\cdot}4)\alpha_{\mathrm{X}} + 25{\cdot}5(\pm2{\cdot}61)n_{\mathrm{HX}} \\ & + 4{\cdot}21(\pm0{\cdot}990)n_{n\mathrm{X}} + 58{\cdot}0(\pm9{\cdot}80)\upsilon_{1\mathrm{X}} \\ & + 41{\cdot}5(\pm11{\cdot}8)\upsilon_{3\mathrm{X}} + 9{\cdot}57(\pm0{\cdot}186)n_{\mathrm{CAk}} \\ & + 1{\cdot}06(\pm0{\cdot}113)p_{\mathrm{Ak}} + 127(\pm4{\cdot}44) \qquad (30) \end{aligned}$$

with $100R^2$, 91·67; $A100R^2$, 91·43; F, 339·2; S_{est}, 17·8; S^0, 0·294; n, 351; $C_{\sigma1}$, 17·1; $C_{\sigma\mathrm{d}}$, 6·78; $C_{\sigma\mathrm{e}}$, 3·14; C_{μ}, 3·59; C_{α}, 4·89; $C_{n\mathrm{H}}$, 7·27; C_{nn}, 1·20; $C_{\upsilon1}$, 16·6; $C_{\upsilon3}$, 11·9; $C_{n\mathrm{C}}$, 27·3; C_{pAk}, 0·302.

The results for set 23.1 are comparable to those for set 23. We next included the T_{m} values for iBuX and neoPeX with set 23 (set 24). All of the T_{m} values excluded from set 23 and the values for iBuCONH$_2$ and neoPeC$_2$H were excluded from set 24. The best regression equation obtained was

$$\begin{aligned} T_{\mathrm{mXAk}} = {} & -64{\cdot}4(\pm12{\cdot}0)\sigma_{\mathrm{lX}} + 22{\cdot}9(\pm5{\cdot}85)\sigma_{\mathrm{dX}} \\ & + 106(\pm29{\cdot}1)\sigma_{\mathrm{eX}} + 13{\cdot}6(\pm1{\cdot}93)\mu_{\mathrm{X}} \\ & - 93{\cdot}9(\pm42{\cdot}9)\alpha_{\mathrm{X}} + 25{\cdot}4(\pm2{\cdot}60)n_{\mathrm{HX}} \\ & + 4{\cdot}51(\pm0{\cdot}977)n_{n\mathrm{X}} + 61{\cdot}9(\pm9{\cdot}63)\upsilon_{1\mathrm{X}} \\ & + 45{\cdot}1(\pm11{\cdot}6)\upsilon_{3\mathrm{X}} + 9{\cdot}57(\pm0{\cdot}187)n_{\mathrm{CAk}} \\ & + 1{\cdot}05(\pm0{\cdot}114)p_{\mathrm{Ak}} - 22{\cdot}4(\pm5{\cdot}60)n_{\mathrm{iBu}} \\ & + 96{\cdot}2(\pm9{\cdot}17)n_{\mathrm{neoPe}} + 124(\pm4{\cdot}31) \qquad (31) \end{aligned}$$

with $100R^2$, 91·85; $A100R^2$, 91·58; F, 305·3; S_{est}, 17·9; S^0, 0·291; n, 366; $C_{\sigma1}$, 13·4; $C_{\sigma\mathrm{d}}$, 4·75; $C_{\sigma\mathrm{e}}$, 2·21; C_{μ}, 2·81; C_{α}, 3·89; $C_{n\mathrm{H}}$, 5·26; C_{nn} 0·935; $C_{\upsilon1}$, 12·8; $C_{\upsilon3}$, 9·35; $C_{n\mathrm{C}}$, 19·8; C_{pAk}, 0·218; $C_{n\mathrm{iBu}}$, 4·63; $C_{n\mathrm{neoPe}}$, 19·9.

Correlation of set 24 with equation (23) after excluding the same T_{m} values excluded from set 24 gave the regression equation (set 24.1)

$$\begin{aligned} T_{\mathrm{mXAk}} = {} & -64{\cdot}4(\pm12{\cdot}0)\sigma_{\mathrm{lX}} + 22{\cdot}9(\pm5{\cdot}82)\sigma_{\mathrm{dX}} \\ & + 105(\pm28{\cdot}9)\sigma_{\mathrm{eX}} + 13{\cdot}6(\pm1{\cdot}92)\mu_{\mathrm{X}} \\ & - 94{\cdot}5(\pm42{\cdot}8)\alpha_{\mathrm{X}} + 25{\cdot}3(\pm2{\cdot}59)n_{\mathrm{HX}} \\ & + 4{\cdot}52(\pm0{\cdot}973)n_{n\mathrm{X}} + 62{\cdot}1(\pm9{\cdot}59)\upsilon_{1\mathrm{X}} \\ & + 45{\cdot}5(\pm11{\cdot}5)\upsilon_{3\mathrm{X}} + 9{\cdot}57(\pm0{\cdot}184)n_{\mathrm{CAk}} \\ & + 1{\cdot}02(\pm0{\cdot}0693)p_{\mathrm{Ak}} + 124(\pm4{\cdot}24) \qquad (32) \end{aligned}$$

with $100R^2$, 91·85; $A100R^2$, 91·62; F, 362·7; S_{est}, 17·9; S^0, 0·290; n, 366; $C_{\sigma1}$, 17·7; $C_{\sigma\mathrm{d}}$, 6·28; $C_{\sigma\mathrm{e}}$, 2·89; C_{μ}, 3·72; C_{α}, 5·19; $C_{n\mathrm{H}}$, 6·95; C_{nn}, 1·24; $C_{\upsilon1}$, 17·0; $C_{\upsilon3}$, 12·5; $C_{n\mathrm{C}}$, 26·3; C_{pAk}, 0·280. The correlation matrix for this equation is given in Table 4.

It seems that all types of alkyl groups can be included in the correlation by determining p_{Ak} values for them.

Table 4. Correlation matrix for set 24.1

σ_{l}	σ_{d}	σ_{e}	μ	α	n_{H}	n_n	υ_1	υ_2	υ_3	n_{C}	p_{Ak}	
1	0·071	0·106	0·788	0·056	0·127	0·255	0·198	0·082	0·026	0·187	0·009	σ_{l}
	1	0·006	0·321	0·310	0·381	0·411	0·119	0·387	0·129	0·073	0·076	σ_{d}
		1	0·021	0·397	0·223	0·040	0·308	0·316	0·034	0·050	0·003	σ_{e}
			1	0·053	0·073	0·414	0·102	0·019	0·078	0·081	0·003	μ
				1	0·318	0·204	0·558	0·552	0·493	0·108	0·021	α
					1	0·232	0·178	0·181	0·144	0·130	0·071	n_{H}
						1	0·118	0·243	0·015	0·005	0·018	n_n
							1	0·183	0·029	0·198	0·038	υ_1
								1	0·343	0·027	0·040	υ_2
									1	0·170	0·050	υ_3
										1	0·087	n_{C}
											1	p_{Ak}

DISCUSSION

Prediction of T_{m}

In order to determine the predictive capability of the model, we calculated values of T_{m} for 45 compounds which were not included in the correlations from equation (32). The calculated and observed values of T_{m}, the differences between calculated and observed values, Δ, and the ratio of Δ to the standard error of the estimate are presented in Table 5. The T_{m} values examined fall into three groups: (1) those with X and Ak groups used to establish the regression equation; (2) those with X groups not included in the data sets correlated; and (3) those with Ak groups not included in the data sets studied.

The unbranched compounds in the first group (TedCHO, $TedCO_2H$, $TedCO_2Me$, OcdPh, OcdAc) all show good agreement between calculated and observed T_{m} values. Of the compounds with branched alkyl groups, iPrSMe, tBuF and iBuX with X equal to I, OH, NH_2 and CO_2H show good agreement, iBuSH deviates slightly and iBuPh deviates strongly. The neopentyl derivatives studied all show very large deviations. Of the ten neoPeX values available, four (X = H, Cl, OH, $CONH_2$) seem to require $p_{\mathrm{AK}} = 96{\cdot}2$ and the remainder (X = Me, Et, Vi, C_2H, CH_2OH and CO_2H) seem to require $p_{\mathrm{AK}} \approx -14$.

The five compounds in the second group are MeX with X = SSMe, $NHNH_2$, CCl_3, CF_3 and SPh. The first three compounds show good agreement between observed and calculated T_{m} values, the fourth shows some deviation and the last deviates severely.

The third group consists of 22 compounds with unbranched alkyl groups from 20 to 30 carbon atoms in length. The results show good agreement with the EcX, the quality of the fit to equation (32) decreasing with increasing chain length. It will be necessary to determine p_{Ak} values for the longer chains if they are to be included in the model.

Composition of the structural effects

In interpreting our results it is important to recall that electrical and steric effects, bond moments and charge-transfer interactions of unbranched alkyl group with four or more carbon atoms are either constant or zero. We may expect to observe only polarizabilily effects for these groups. For the other alkyl groups any other variation in the alkyl group is accounted for by p_{Ak}. The

Table 5. Calculated and observed values of T_{m} (K)[a]

AkX	$T_{\mathrm{m,obs}}$	$T_{\mathrm{m,calc}}$	Δ	NSD	AkX	$T_{\mathrm{m,obs}}$	$T_{\mathrm{m,calc}}$	Δ	NSD
$MeCCl_3$	240·15	216·38	23·77	1·328	$MeCF_3$	161·85	205·81	−43·96	2·456
MeSSMe	188·45	161·16	27·29	1·525	MeSPh	258·15	154·17	103·98	5·809
$MeNHNH_2$	220·75	240·84	−20·09	1·122					
iPrSMe	171·65	150·6	21·03	1·175					
iBuI	179·65	161·36	18·29	1·022	iBuOH	165·15	176·80	−11·65	0·651
iBuSH	194·15	152·78	41·37	2·311	iBuPh	221·65	159·76	61·89	3·458
$iBuNH_2$	188·55	191·58	−3·03	0·170	$iBuCO_2H$	235·55	211·62	23·93	1·337
tBuF	196·15	193·20	2·95	0·165					
$neoPeCO_2H$	279·65	342·17	−62·52	3·493	neoPeVi	136·65	279·36	−142·71	7·972
neoPeEt	149·35	287·59	−138·24	7·723	$neoPeCH_2OH$	213·15	341·24	−128·09	7·156
neoPeMe	173·25	292·21	−118·96	6·646					
TedCHO	297·65	305·44	−7·79	0·435	$TedCO_2H$	326·65	330·17	−3·52	0·197
$TedCO_2Me$	292·65	294·87	−2·22	0·124					
OcdPh	309·15	316·58	−7·43	0·415	OcdAc	307·65	330·71	−23·06	1·288
EcH	309·55	315·40	−5·85	0·327	EcOH	345·65	352·77	−7·12	0·398
$EcCO_2H$	355·15	387·59	−32·44	1·812	EcMe	313·15	337·63	−24·48	1·368
UncH	313·15	324·97	−11·82	0·660	UncMe	317·55	347·20	−29·65	1·656
$UncCO_2H$	353·15	397·16	−44·01	2·459	$UncCO_2Me$	326·65	361·86	−35·21	1·967
$UncCO_2Et$	322·15	361·71	−39·56	2·210					
DocH	317·25	334·54	−17·29	0·966	DocOH	344·15	371·91	−27·76	1·551
DocMe	320·45	356·77	−36·32	2·029					
TrcH	320·45	344·11	−23·66	1·322					
TecH	324·15	353·68	−29·53	1·650					
HpcH	332·15	382·39	−50·24	2·807	$HpcCO_2H$	363·55	454·58	−91·03	5·086
OccH	334·65	391·96	−57·31	3·202	OccOH	356·45	429·33	−72·88	4·072
NocH	337·65	401·53	−63·88	3·569	NocOH	355·65	438·90	−83·25	4·651
TcH	341·15	411·1	−69·95	3·908	$TcCO_2H$	365·15	489·29	−118·14	6·600

[a] T_{m} values are from the same sources as those in Table 2. Further abbreviations: Ec, eicosanyl; Unc, uncosanyl; Doc, docosanyl; Trc, tricosanyl; Tec, tetracosanyl; Hpc, heptacosanyl; Occ, octacosanyl; Noc, nonacosanyl; Tc, triacontanyl.

overall effect of the alkyl group, C_{Ak}, is therefore given by the sum of C_{nC}, C_{nev} and $C_{p\mathrm{Ak}}$ in all sets which do not have terms in n_{Ak}. The values for C_{Ak} for sets 11, 22.1, 23.1 and 24.1 are 28·9, 33·6, 27·6 and 26·6, respectively. It follows then that the structural effects of the substituent X are predominant in determining the value of the melting point. The effect of the alkyl group is due largely to its polarizability. Owing to collinearities between variables it is most convenient to group the parameters of the imf model into two categories: (1) polar parameters, including σ_1, σ_d, σ_e, μ, n_H, n_n and i; and (2) non-polar parameters, including α, υ_1, υ_2 and υ_3. The polar and non-polar contributions, C_P and C_{NP}, respectively, are given by the equations

$$C_P = C_{\sigma 1} + C_{\sigma d} + C_{\sigma e} + C_\mu + C_{nH} + C_{nn} + C_i \quad (33)$$

$$C_{NP} = C_\alpha + C_{\upsilon 1} + C_{\upsilon 2} + C_{\upsilon 3} \quad (34)$$

For sets 11, 22.1, 23.1 and 24.1 the values of C_P and C_{NP} are 38·5, 32·7, 43·6, 22·9; 39·1, 32·8; and 38·8, 34·7. The contributions are roughly comparable.

Packing in monosubstituted alkanes

In the solid state, the molecule presumably adopts the conformation which maximizes intermolecular attractions between molecules. In the liquid state, the molecule should have a different conformation resulting in a different degree of intermolecular attraction. There are therefore two different contributions to the energy change resulting from the change in state: (1) the difference in imf between the liquid and the solid states; and (2) the difference in energy between the conformations in the liquid and solid states. This is what we mean by packing energy.

One of the major assumptions in this work is that the entropy is either constant or proportional to the enthalpy. This must be the case in order to fit the data to the imf model. The packing contribution to the melting point must be dependent in some manner on ΔS. It seems reasonable then that the packing parameter p_{Ak} should be a function of ΔS. Thus we may separate ΔG_m into two components, ΔG_{imf}, which accounts for the effect of intermolecular forces, and ΔG_{pk}, which accounts for the effect of packing:

$$\Delta G_m = \Delta G_{\mathrm{imf}} + \Delta G_{\mathrm{pk}} \quad (35)$$

If ΔS_{pk} depends only on packing and is constant for a given type of packing while ΔS_{imf} is constant, then we may rewrite equation (36) as equation (37).

$$T_m = \frac{\Delta H_{\mathrm{imf}}}{\Delta S_{\mathrm{imf}}} + \frac{\Delta H_{\mathrm{pk}}}{\Delta S_{\mathrm{pk}}} \quad (36)$$

$$= f(\mathrm{imf}) + B_{\mathrm{Ak}} p_{\mathrm{Ak}} \quad (37)$$

It is convenient to separate packing effects into those due to the alkyl group and those due to the substituent.

Alkyl group effects.

As the length of the alkyl group increases, both the magnitude of the dispersion force and the number of possible conformations increase. These two quantities should have opposite effects on the melting point. It seems not unreasonable, then, that a plot of melting point versus p_{Ak} should pass through a minimum. Structural features which increase the rotational barrier should decrease ΔS_{Ak} and therefore increase p_{Ak}, resulting in an increase in melting point. Quaternary carbon atoms are an example of such a structural feature.

Our results are in agreement with our assumption that packing effects in compounds with unbranched alkyl groups having four or more carbon atoms are constant, and that in such compounds the packing is determined by the alkyl groups. It is well known that for many straight-chain substituted alkanes the T_m values when plotted against n_C lie on two different curves. The two curves become closer as n_C increases, converging on a constant T_m value when n_C becomes very large. In the range of n_C studied in this work, no such convergence was observed. For X = H, CHO and CO_2H the even-n_C compounds melt higher whereas for X = Cl or Br the odd-n_c compounds melt higher. This is understood if we compare the size (υ value) and polarizability (α value) of the Me, Cl and Br groups. The values of X, υ and α are Me, 0·52, 0·046; Cl, 0·55, 0·050; and Br, 0·65, 0·079. Hence the Me and Cl groups are comparable in size and polarizability, and the Br group is not much different. Then, to a first approximation a straight-chain chloro- or bromoalkane should be equivalent to the even-n_C alkane with one more carbon atom. They may therefore be expected to behave in packing like alkanes with even N_C. The fact that 1-alkanoic acids crystallize as hydrogen-bonded dimers should make no difference with regard to the odd–even alternation in melting point, as our evidence suggests that the alkyl group is the major factor in packing.

We were surprised, therefore, to find that in sets containing all types of alkyl groups there is no observable dependence on whether the chain is odd or even in the number of carbon atoms. In discussing the effects of other types of alkyl groups we make use of the p_{Ak} values, for which the reference alkyl group, Ak^0, is unbranched with four or more carbon atoms. For Ak^0 the value of of p_{Ak} is 0, for other alkyl groups the values are Me 13·8, Et 0, Pr −17·7, iPr 0, iBu −22·4, tBu 29·7 and neoPe 96·2 or −14. The values for Et and iPr, both of which have a longest chain of two carbon atoms, are the same. The values for the Pr and iBu groups, both of which have a longest chain of three carbon atoms, are not significantly different. The presence of a quaternary carbon atom in tBu, which has a longest chain of two carbon atoms, or in some neoPe derivatives where the neoPe group has a longest chain of three seems to cause an increase in p_{Ak} as expected.

Before we can generalize further it will be necessary to determine p_{Ak} values for many more alkyl groups.

Substituent effects

The packing of alkylamides with less than ten carbon atoms in the longest chain of alkyl group tends to be dominated by the carboxamido group. This is shown by the deviation of the carboxamides with Ak equal to Me, Et, Pr, iPr, Bu, iBu, Pe, Hp and No. While there are eight deviant T_m values for alkanes (MeEt, EtMe, PrH, iPrH, MeMe, EtH, iPrMe, tBuH), only three compounds with very low melting points are involved (EtH, 89·85; PrH, 85·45; tBuH, 113·75). If these melting points are reliable then the model breaks down at very low melting points. There may be a tendency for compounds with alkyl groups having a longest chain shorter than four carbon atoms and no quaternary carbon atom to deviate when the substituent is a planar π-bonded group. $AkCH{=}CH_2$, with Ak equal to Me, Et or iPr, MeX with X equal to CO_2H or NO_2, EtBz, $PrCO_2H$, and iPrPh show deviations from the model, but it should be noted that many other compounds in this category do not. Many more functional groups must be studied before conclusions can be drawn.

CONCLUSIONS

Our results clearly demonstrate the applicability of the imf equation to the quantitative description of the variation of melting points with structure. The model we have developed here, although indeed useful for the estimation of melting point for compounds whose X and Ak groups have been studied, should be regarded as a starting point. We must determine p_{Ak} values for many additional alkyl groups. Once this has been achieved we may be able to determine the variation of p_{Ak} with alkyl group structure. It may also be necessary to determine packing parameters p_X for substituents which dominate the packing contribution.

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