

## QSRR Correlation of Free-Radical Polymerization Chain-Transfer Constants for Styrene

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Received June 5, 2000

Quantitative structure–reactivity relationships (QSRR) are deduced for kinetic chain-transfer constants for 90 agents on styrene polymerization at 60 °C. Three- and five-parameter correlations were obtained with  $R^2$  of 0.725 and 0.818, respectively. The descriptors involved in the correlations are consistent with the proposed mechanism of the chain-transfer reactions.

### INTRODUCTION

Quantitative structure–activity relationships (QSAR) are now universally applied in considerations of biological activity. Quantitative structure–property relationships (QSPR) are making considerable headway as outlined in a recent perspective.<sup>1</sup> By contrast, quantitative structure–reactivity relationships (QSRR) have not progressed beyond relatively simplistic models involving sets of highly cognate structures.<sup>2</sup> We now demonstrate with an example of considerable importance that QSRR may have great potential from both a practical and a theoretical point of view.

Kinetic chain-transfer constants play an important role in polymer chemistry. Understanding chain transfer clarifies our understanding of the microkinetic processes in polymerization reactions.<sup>3</sup> During the last 15 years, considerable interest has arisen in the use of chain-transfer agents to produce “living polymers”.<sup>4,5</sup> In general, chain-transfer reactions modulate molecular weight and broaden the molecular weight distribution during synthesis. Molecular weight and molecular weight distributions determine polymer processability. Thus, control of these macromolecular features is required when high molecular weight polymers are not suitable for a given application. Knowledge of chain-transfer constants assists the industrial scale-up of polymerization processes using kinetic modeling techniques and reduces the number of iterative adjustments required to achieve optimum (co-) polymerization.<sup>6,7</sup> This article relates theoretically calculated molecular descriptors with experimentally determined kinetic transfer constants providing a quantitative structure reactivity model. The model allows the prediction of transfer constants for a variety of additives (transfer agents) and helps in the theoretical understanding of free-radical polymerization kinetics.

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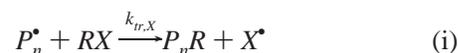
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### BACKGROUND

The following equations describe the chain-transfer process during radical polymerization. The first reaction depicts the formation of the unreactive (dead) polymer. The second reaction represents propagation. The third reaction is the initiation of a new polymer chain by a radical formed from the chain-transfer agent in eq i<sup>8</sup>



where  $P_n$  is a polymer molecule of chain length  $n$ ,  $RX$  is a transfer agent, and  $M$  is a monomer molecule.

The transfer constant is defined as dimensionless quantity given by the following ratio

$$C_X = \frac{k_{tr,X}}{k_p} \quad (\text{iv})$$

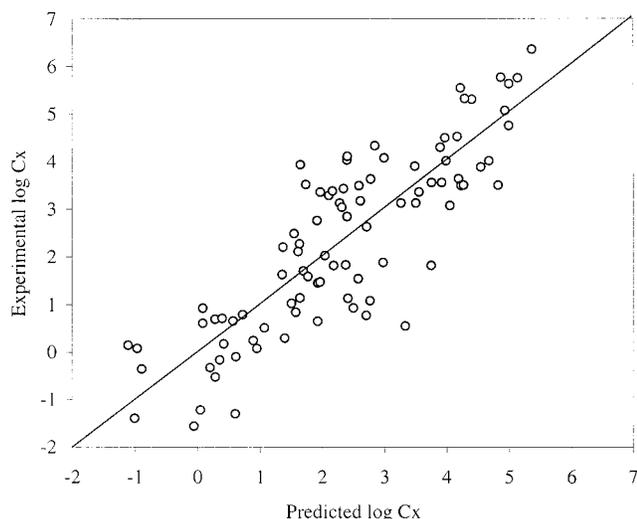
where  $k_p$  is the rate constant of free-radical polymerization propagation.

The amount of polymer,  $P_n$ , with length  $n$ , is accordingly given as follows

$$\frac{1}{P_n} = \frac{1}{P_{n0}} + \sum C_X \frac{[X]}{[M]} \quad (\text{v})$$

where  $P_{n0}$  is the amount of polymer with chain length  $n$  formed in the absence of any transfer agent, and  $[X]$  and  $[M]$  are the concentrations of monomer and transfer agent, respectively.

Equation v is only valid when<sup>8</sup> (a) all new radicals react only to initiate new growing polymer radicals; (b) all polymer radicals have equal reactivity regardless of their size; (c) all rate constants are independent of solvent; (d) the consumption



**Figure 1.** The plot of experimental kinetic transfer constants vs calculated  $\log C_X$  by three-parameter correlation (eq 1) for whole set.

of monomer by initiation and transfer is negligible compared with propagation; and (e) a steady-state concentration of polymer radical is quickly established  $d[P\cdot]/dt = 0$ .

#### METHOD

This study employed a random set of additives selected from ref 8. All data relate to radical polymerization of styrene at 60 °C (Table 1). To develop the molecular descriptors for QSPR, the geometry of each transfer agent molecule was optimized using the AM1 parametrization.<sup>9</sup> The resulting output files of the MOPAC program<sup>10</sup> were then used as input for the CODESSA software package<sup>11</sup> that includes the following: (a) a calculation engine for more than 500 constitutional, geometrical, electrostatic and charge distribution related, quantum chemical, and thermodynamic descriptors and (b) an engine for the development of the statistically most important linear and nonlinear QSPR regression models.

#### RESULTS AND DISCUSSION

The treatment of data on  $\log C_X$  using the stepwise selection of descriptor scales resulted in the following three-parameter linear correlation (cf. Figure 1):

$$\log C_X = (-1.19 \pm 0.10)\epsilon_{LUMO} + (0.292 \pm 0.033)HA + (0.403 \pm 0.059)^1KH - (0.201 \pm 0.285)$$

$$R^2 = 0.7249, \quad F = 75.5234, \quad n = 90, \quad R_{CV}^2 = 0.7025, \quad s^2 = 1.0048 \quad (1)$$

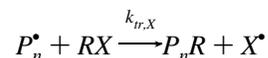
where  $\epsilon_{LUMO}$  denotes the energy of the lowest unoccupied molecular orbital (LUMO) of the transfer agent,  $HA$  is the hydrogen-bonding dependent hydrogen donor charged area (HA dependent HDCA-1 [Semi-MO PC]),<sup>12</sup> and  $^1KH$  is the first-order Kier and Hall index.<sup>12</sup>

The HA dependent HDCA-1 [Semi-MO PC] is defined as  $\sum_{i \in HA} |q_i| S_i$ , where  $q_i$  is the partial charge of the hydrogen acceptor atom and  $S_i$  is the solvent-accessible surface area of this atom. The notation [Semi-MO PC] indicates that the charge distribution in the molecule has been obtained using the Mulliken population analysis of semiempirical AM1

LCAO MO calculated molecular wave functions. The solvent-accessible surface was calculated as  $4\pi(r_{i,VDW} + 1.5)^2$  where  $r_{i,VDW}$  is the van der Waals atomic radius of the H-bond acceptor atom. Hydrogen bond acceptors were defined as functional groups containing heteroatoms with lone pairs, including amino, cyano, hydroxy, carbonyl, carboxyl groups, and di- and tricoordinated nitrogen atoms.

The  $\epsilon_{LUMO}$  of the transfer agents were calculated using AM1 semiempirical theory and extracted from the MOPAC output files using CODESSA software package.

Notably, each of the descriptors of eq 1 is consistent with the assumed mechanism of the chain transfer. Thus, the  $\epsilon_{LUMO}$  can be directly related to the reactivity of the additive in the transfer reaction



The negative sign of the corresponding regression coefficient indicates that, as expected, additives with lower LUMO energies are more reactive. The HA dependent HDCA-1 descriptor reflects the importance of the polarity and hydrogen-bonding ability of the transfer agents in facilitating the transfer reaction. The first-order Kier and Hall index reflects the influence of the steric factor on the reactivity of the transfer agents.

The three-parameter correlation 1 can be further refined by adding two more descriptors:

$$\log C_X = (-1.06 \pm 0.27)\epsilon_{LUMO} + (-1.26 \pm 0.08)\#HD + (319 \pm 44)HA' + (0.448 \pm 0.049)^1KH + (1.01 \pm 0.22)BO_{C,min} - (1.057 \pm 0.275)$$

$$R^2 = 0.8181, \quad R_{CV}^2 = 0.7951, \quad n = 90, \quad F = 75.56, \quad s^2 = 0.6801 \quad (2)$$

In eq 2,  $\#HD$  denotes the count of the H-donor sites in the transfer agents and  $BO_{C,min}$  is the minimum bond order of a C atom. In this second correlation, the HA dependent HDCA-1 [Semi-MO PC] has been replaced by the closely related HA dependent HDCA-2/TMSA [Semi-MO PC] ( $HA'$ ).<sup>2</sup> Whereas the  $\#HD$  descriptor gives a further adjustment for the influence of hydrogen bonding and/or adjustment for additives having multiple reactive sites (multiple H $\cdot$  donors), the  $BO_{C,min}$  describes the reactivity of the weakest bond at the carbon atom. This last descriptor is directly related to the probability of formation of the carbon-centered radical  $X^{\bullet}$  that is the presumed intermediate in the chain-transfer reaction.

The absolute error chart was prepared (cf. Figure 3) on the basis of eq 2. Only four structures are outliers according to 95% statistical reliability level ( $\pm 1.649$ , 1-(1,2-dibromoethyl)benzene, hydroquinone, 2,2,2-trichloroacetic acid, acetyl bromide).

#### CROSS-VALIDATION

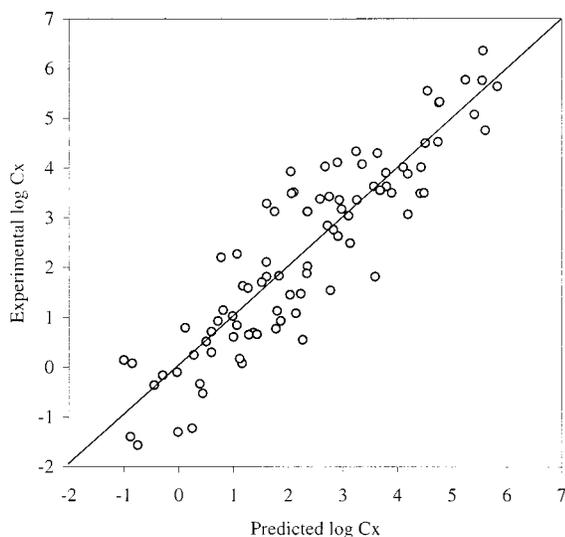
For the validation of the results the following procedure was used. Cross-validation of the five-parameter correlation (eq 2) for the whole set was performed in the following manner. The whole set of 90 compounds was randomly divided into three equal size groups (Table 1, A, B, C). Three

**Table 1.** Results of Predicting of Transfer Constant Logarithm Using Four Correlation Equations

no.	transfer agent name	set	exp. log $C_x$	corr log $C_x$		diff log $C_x$	
				(1)	(2)	(1)	(2)
1	benzene	C	-1.56	-0.06	-0.74	1.51	0.82
2	1-chlorobutane	A	-1.40	-1.01	-0.88	0.39	0.52
3	( <i>tert</i> -butyl)benzene	B	-1.30	0.61	-0.01	1.91	1.29
4	1-bromobutane	A	-1.22	0.05	0.25	1.27	1.47
5	methyl 2-chloroacetate	B	-0.52	0.29	0.44	0.81	0.96
6	acetonitrile	A	-0.36	-0.89	-0.45	-0.54	-0.09
7	diethyl malonate	A	-0.33	0.20	0.39	0.53	0.72
8	1-ethylbenzene	A	-0.16	0.36	-0.29	0.52	-0.13
9	1-chlorobenzene	B	-0.10	0.61	-0.03	0.71	0.07
10	2-chlorobutane	C	0.08	-0.96	-0.84	-1.04	-0.92
11	trichloromethane	A	0.08	0.95	1.16	0.87	1.08
12	1-chloro-2-methylpropane	C	0.15	-1.11	-1.00	-1.25	-1.14
13	2-propen-1-ol	B	0.18	0.42	1.11	0.24	0.94
14	1-bromobenzene	C	0.25	0.89	0.28	0.64	0.03
15	phenylamine	C	0.30	1.40	0.60	1.10	0.30
16	1,4-diisopropylbenzene	A	0.52	1.07	0.50	0.55	-0.02
17	1,4-hydroxybenzene	C	0.56	3.33	2.27	2.78	1.71
18	dimethyl ketone	A	0.61	0.09	1.00	-0.53	0.39
19	benzaldehyde	B	0.66	1.93	1.28	1.27	0.62
20	<i>N,N</i> -dimethylacetamide	C	0.66	0.57	1.43	-0.09	0.77
21	2-butanone	C	0.70	0.28	1.36	-0.42	0.67
22	di(2-propenyl)propanedioate	B	0.72	0.39	0.60	-0.32	-0.12
23	2-phenylacetic acid	B	0.78	2.71	1.78	1.93	1.00
24	( <i>sec</i> -butyl)benzene	C	0.79	0.72	0.12	-0.07	-0.67
25	1,4-dibutylbenzene	C	0.85	1.58	1.06	0.73	0.22
26	acetaldehyde	A	0.93	0.09	0.71	-0.84	-0.22
27	4-chlorobenzaldehyde	A	0.94	2.50	1.86	1.57	0.93
28	1,4-di( <i>sec</i> -butyl)benzene	A	1.03	1.51	0.99	0.48	-0.04
29	4-bromobenzaldehyde	C	1.08	2.77	2.14	1.68	1.06
30	3-chlorobenzaldehyde	B	1.14	2.41	1.80	1.28	0.66
31	phenol	B	1.15	1.64	0.81	0.50	-0.33
32	chloroacetic acid	B	1.46	1.93	2.03	0.47	0.58
33	diethyl-2,2-dichloropropanedioate	B	1.48	1.97	2.23	0.49	0.75
34	dichloroacetic acid	A	1.54	2.58	2.77	1.03	1.23
35	4-methylphenol	A	1.59	1.77	1.26	0.18	-0.33
36	2-methylphenol	C	1.63	1.36	1.17	-0.28	-0.46
37	(4-methoxyphenyl)acetonitrile	C	1.71	1.70	1.52	-0.01	-0.19
38	(4-chlorophenyl)acetonitrile	A	1.82	2.18	1.60	0.37	-0.22
39	trichloroacetic acid	C	1.82	3.75	3.59	1.93	1.77
40	(3-bromophenyl)acetonitrile	B	1.84	2.38	1.83	0.54	-0.00
41	4-formylbenzoinitrile	B	1.88	2.98	2.34	1.09	0.46
42	tetrachloromethane	A	2.03	2.04	2.35	0.01	0.32
43	<i>N,N</i> -diethenylphenylamine	A	2.11	1.61	1.60	-0.50	-0.51
44	1-chloro-4-ethynylbenzene	C	2.21	1.37	0.78	-0.84	-1.43
45	1-bromo-4-ethynylbenzene	A	2.28	1.64	1.07	-0.64	-1.21
46	2,6-di(2-propyl)phenol	C	2.49	1.55	3.14	-0.94	0.64
47	2-bromoacetic acid	C	2.63	2.71	2.91	0.08	0.28
48	2,3,5,6-tetramethylphenol	B	2.76	1.92	2.83	-0.85	0.07
49	diethyl-2-bromopropanedioate	B	2.85	2.40	2.72	-0.45	-0.13
50	3-methyl-3-buten-2-one oxime	C	3.04	2.31	3.10	-0.73	0.06
51	methanesulfonyl chloride	C	3.07	4.05	4.19	0.98	1.12
52	1,2-dibenzenediol (conf. 1)	A	3.13	3.27	2.35	0.14	-0.78
53	1,2-dibenzenediol (conf. 2)	A	3.13	3.51	2.36	0.38	-0.77
54	1,2-dibenzenediol (conf. 3)	C	3.13	2.28	1.75	-0.85	-1.38
55	( <i>E</i> )-2-butenal oxime	B	3.18	2.61	2.98	-0.56	-0.20
56	(1,2-dibromoethyl)benzene	B	3.29	2.11	1.61	-1.18	-1.68
57	4-methyl-2-pentanone oxime	A	3.36	1.97	2.93	-1.39	-0.43
58	triphenylgermane	C	3.36	3.56	3.26	0.20	-0.10
59	triethylgermane	C	3.38	2.16	2.58	-1.22	-0.80
60	3-buten-2-one oxime	B	3.43	2.34	2.75	-1.09	-0.68
61	4-methoxybenzenesulfonyl chloride	A	3.49	4.23	4.42	0.74	0.93
62	1-ethynyl-4-nitrobenzene	A	3.50	2.59	2.06	-0.91	-1.43
63	4-methylbenzenesulfonyl chloride	B	3.50	4.27	3.89	0.77	0.39
64	phenylmethanesulfonyl chloride	A	3.50	4.82	4.49	1.32	0.98
65	2-chloroacetyl chloride	C	3.52	1.74	2.10	-1.78	-1.42
66	4-( <i>tert</i> -butyl)-1,2-benzenediol (conf. 1)	A	3.56	3.76	3.69	0.20	0.13
67	4-( <i>tert</i> -butyl)-1,2-benzenediol (conf. 2)	B	3.57	3.92	3.68	0.36	0.12
68	2-methyl-1-penten-3-one oxime	B	3.63	2.78	3.57	-0.86	-0.07
69	benzenesulfonyl chloride	C	3.64	4.19	3.80	0.56	0.16
70	4-chlorobenzenesulfonyl chloride	A	3.88	4.55	4.19	0.66	0.30

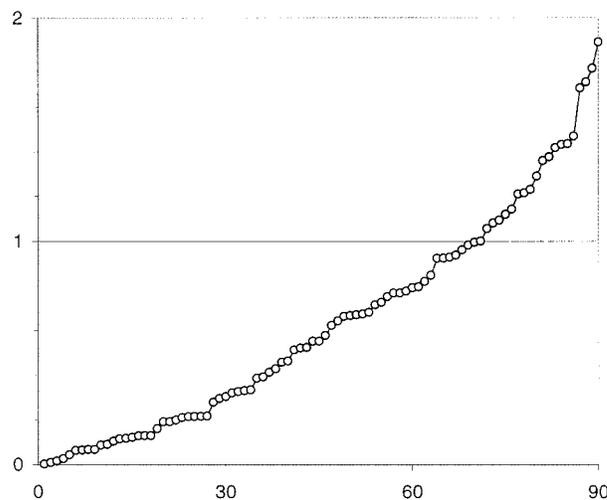
Table 1 (Continued)

no.	transfer agent name	set	exp. log $C_X$	corr log $C_X$		diff log $C_X$	
				(1)	(2)	(1)	(2)
71	iodoacetic acid	C	3.90	3.49	3.79	-0.41	-0.12
72	acetyl bromide	C	3.93	1.65	2.05	-2.28	-1.89
73	1,2,3-benzenetriol (conf. 1)	C	4.02	3.99	4.10	-0.03	0.09
74	1,2,3-benzenetriol (conf. 2)	A	4.02	4.67	4.43	0.66	0.41
75	1-propenaloxime	B	4.03	2.40	2.67	-1.64	-1.36
76	diethyl 2,2-dibromopropanedioate	B	4.08	3.00	3.35	-1.08	-0.73
77	2-methyl-2-propenal oxime	B	4.11	2.40	2.90	-1.71	-1.21
78	(1,1,2,2-tetraphenylethyl)benzene	B	4.30	3.90	3.63	-0.41	-0.67
79	tetrabromomethane	B	4.33	2.85	3.24	-1.49	-1.09
80	chloro(diethyl)germane	A	4.50	3.97	4.51	-0.53	0.01
81	chloro(dimethyl)germane	B	4.52	4.17	4.74	-0.36	0.21
82	dichloro(ethyl)germane	B	4.76	4.99	5.60	0.24	0.85
83	2,4,6-trinitrophenylamine	C	5.07	4.93	5.40	-0.14	0.33
84	2-methoxy-1,3,5-trinitrobenzene	B	5.31	4.40	4.76	-0.91	-0.55
85	2,4,6-trinitrophenol	A	5.32	4.29	4.77	-1.04	-0.55
86	1,3,5-trinitrobenzene	A	5.55	4.22	4.55	-1.33	-1.00
87	2,5-dimethyl-2,5-cyclohexadiene-1,4-dione	C	5.63	4.99	5.83	-0.64	0.19
88	ethyl 2,4,6-trinitrobenzoate	B	5.76	5.13	5.55	-0.62	-0.21
89	2-bromo-1,3,5-trinitrobenzene	C	5.76	4.87	5.24	-0.90	-0.52
90	2,5-cyclohexadiene-1,4-dione	A	6.36	5.36	5.56	-0.99	-0.79

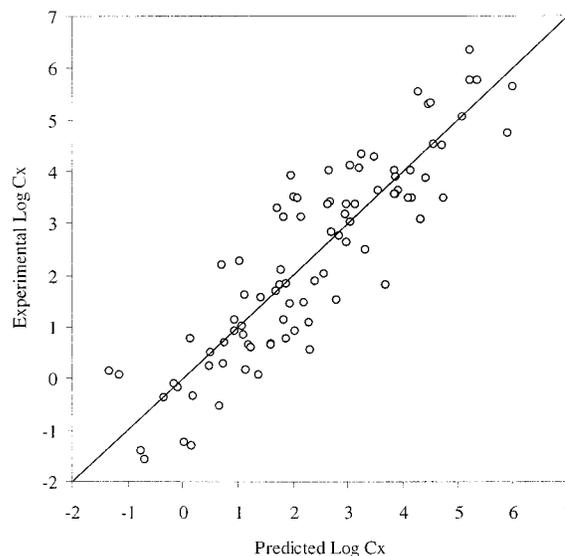


**Figure 2.** The plot of experimental kinetic transfer constants vs calculated log  $C_X$  by five-parameter correlation (eq 2) for whole set.

subsets, A + B, A + C and B + C, were formed from these groups by combining the groups A and B, A and C, and B and C, respectively. The descriptors that were obtained in the best five-parameter correlation (eq 2) for the whole set were selected. With these descriptors, the transfer constant of subsets A + B, A + C, and B + C were predicted and correlated with their experimental transfer constant which afforded  $R^2$  values of 0.857, 0.834, and 0.750, respectively. The coefficients of the descriptors for subsets A + B, A + C, and B + C were recorded. The logarithms of the transfer constant for group C were then predicted using the descriptor partition coefficients from subset A + B. Similarly, group B and group A logarithms of the transfer constant were predicted using the partition coefficients from subsets A + C and B + C, respectively. Next, the predicted logarithms of the transfer constant were correlated with experimental values. The resulted  $R^2$  0.739, 0.708, and 0.901 were obtained for subsets C, B, and A, respectively. All the predicted logarithms of the transfer constant for groups A, B, and C were combined and correlated with the experimental logarithms of the transfer constant of the whole set. This afforded



**Figure 3.** The absolute value of the error distribution for individual compounds, sorted by  $|\epsilon|$  value (along X-axis).



**Figure 4.** The combined plot of experimental kinetic transfer constants vs calculated log  $C_X$  by three five-parameter correlations for subsets A, B, and C.

a squared correlation coefficient of 0.787 compared to that found in the original five-parameter correlation (eq 2, 0.818).

The successful prediction of  $\log C_X$  for the validation subsets using these correlations is depicted in Figure 4. The predictions are impressive considering the approximation involved in the five assumptions required in the generation of eq 2. In addition, the constants themselves, having been culled from the literature, contain considerable variance since several experimental methodologies were employed for the measurement of molecular weight in the determination of  $C_X$ .

### CONCLUSIONS

The development of highly significant QSAR or QSPR equations by extraction of molecular descriptors from large descriptor spaces has been successful for the prediction of many physical properties and biological activity of chemical compounds.<sup>1</sup> The present work clearly demonstrates that analogous QSRR equations can be developed for the description of complex chemical processes such as the chain-transfer reaction in the polymerization. Importantly, the descriptors employed in the best correlation equations are indicative for the elucidation of the details of physical interactions determining the reaction mechanism and the reactivity of compounds.

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