

Application of the Log k pair linearity rule and Proportionality rule to the RPP mobile phase scales estimation on diol-silica column

TOMISLAV J. JANJIĆ[#], GORDANA VUČKOVIĆ^{*,#} and MILENKO B. ČELAP[#]

Faculty of Chemistry, University of Belgrade, P. O. Box 158, YU-11001 Belgrade, Yugoslavia

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By the application of the Log k pair linearity rule and the Proportionality rule to the previously published log k values for 27 compounds, obtained on diol-silica columns with acetonitrile, methanol and tetrahydrofuran as modifiers, the existence of common RPP scales was established. The obtained correlation coefficients of the linear function $\log k = f(\text{RPP})$ were better than 0.9900 for 26 compounds in the first, 21 in the second and 20 in the third case. In addition, in the case of the two first modifiers a linear correlation between the obtained RPP values and mol % of modifier in the mobile phase was found. On the basis of this, the following simple linear function: $\log k = f(\text{mol \% of modifier})$ was proposed as a criterion for log k values judgement in practical work. A linear correlation was also established between intercept and slope of the function, in spite of the fact that the investigated compounds essentially differ in their descriptors.

Keywords: column chromatography, diol-silica sorbent, log k pair linearity rule, proportionality rule, RPP scale.

INTRODUCTION

On the basis of the previously described R_M (or log k) pair linearity rule and Proportionality rule,^{1–3} in our latest paper⁴ a new variant of these methods was proposed by which, on the basis of the average log k values, it is possible to establish if there is a common RPP scale of solvents for one group of the examined compounds being separated by the same series of solvents; if it is established by this method it can also be estimated. The method was illustrated by literature data obtained on C_{18} columns by means of solvents containing methanol or acetonitrile as modifiers and various aqueous phases. In most cases a good linear dependence was established between the experimentally determined log k values of the examined substances and the obtained RPP values [correlation coefficients (r) were 0.9980–0.9990]. Continuing these investigations, we wanted to ascertain if this method could also be

[#] Author for correspondence (E-mails: gordanav@helix.chem.bg.ac.yu or evuckogo@ubbg.etf.bg.ac.yu).

* Serbian Chemical Society active member.

applied to $\log k$ values obtained on other sorbents, which, in the case of a positive result, would prove the wider applicability of the described method. In addition, we wanted to examine if the Log k pair linearity rule and the Proportionality rule could be used for a simpler estimation of $\log k$ values, compared to the procedure based on the Solvation parameter model.⁵

RESULTS AND DISCUSSION

As the first successive sorbent, diol-silica sorbent ($\equiv\text{Si}(\text{CH}_2)_3\text{OCH}_2\text{CH}(\text{OH})\text{CH}_2\text{OH}$) was chosen. In the examinations, capacity factors data of 27 compounds (Table I) given in the literature⁵ were used and the corresponding modifiers were acetonitrile (ACN), methanol (MeOH), tetrahydrofuran (THF) and propane-2-ol (IPA), the content of which in water was in the range from 1–50 % v/v. In the course of the examinations, the capacity factors were obtained the purpose of which was to prove the validity of the Solvation parameter model in interpreting the retention processes in reverse-phase (RP) liquid chromatography by means of the following equation:

$$\log k = c + mV_x/100 + rR_2 + s\pi_2^H + a\alpha_2^H + b\beta_2^H \quad (1)$$

In the above equation V_x , R_2 , π_2^H , α_2^H and β_2^H represent solute descriptors, the values c , m , r , s , a and b represent the corresponding system constants that depend on the sorbent used, the nature of the modifier and its concentration (% v/v). The main significance of this model is that it provides an interpretation of the retention properties under RP chromatographic conditions, which would not be possible by other means. However, its great disadvantage is the great number of solute descriptors and system constants necessary for the calculation of the $\log k$ values using Eq. (1). While the solute descriptors for a great number of compounds can be found in the literature, the system constants must be determined from the experi-

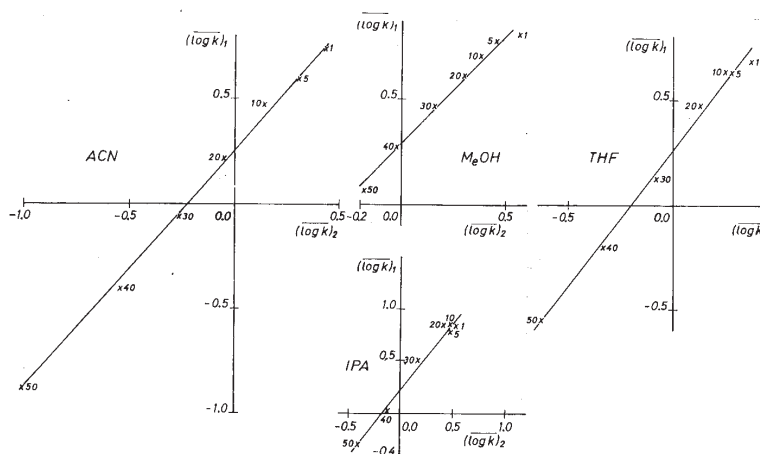


Fig. 1. The straight lines obtained by the Log k pair linearity rule used on the basis of the Proportionality rule for the estimation of the corresponding RPP scale.

mentally obtained log *k* values of the examined substances with different known solute descriptors, obtained on a given sorbent for various contents of each modifier in the solvent mixture, using multiple linear regression analysis.

TABLE I. List of compounds used

I group	II group	Control group
1. Naphthalene	10. Anisole	19. <i>p</i> -Cresol
2. Benzene	11. Acetophenone	20. 2-Chlorophenol
3. Propylbenzene	12. Nitrobenzene	21. 1-Naphthol
4. Chlorobenzene	13. Ethyl phenyl ketone	22. 4-Phenylphenol
5. Bromobenzene	14. Methyl benzoate	23. Benzyl alcohol
6. 1,2-Dichlorobenzene	15. Hexane-2-one	24. 2-Phenylethanol
7. 1,2-Dibromobenzene	16. Octane-2-one	25. 2-Nitroaniline
8. Benzaldehyde	17. Phenol	26. Benzamide
9. Benzonitrile	18. <i>m</i> -Cresol	27. Acetanilide

The previously mentioned 27 compound with various solute descriptors considered in the Solvation parameter model were divided into 3 groups (Table I), regardless of these parameters. On the basis of the first and second group, the mean values $(\log k)_1$ and $(\log k)_2$, respectively, were calculated, to check the validity of Log *k* pair linearity rule and to estimate the RPP parameters. The third group of the compounds was used to see if the obtained RPP parameters were applicable to some other compoundst as well.

TABLE II. Parameters of the linear equation $(\log k)_1 = f(\log k)_2$, as well as the estimated mobile phase RPP parameters. $(\log k)_1$ are average log *k* values of the first and $(\log k)_2$ of the second group of compounds from Table I

Modi- fier	Inter.	Slope	Cor. coef. (<i>r</i>)	RPP* for vol % of modifier in water						
				50	40	30	20	10	5	1
ACN	0.2537	1.1599	0.9985	0.00	0.32	0.52	0.69	0.83	0.92	1.00
MeOH	0.2872	1.0025	0.9928	0.00	0.25	0.49	0.68	0.80	0.90	1.00
THF	0.2547	1.3135	0.9963	0.00	0.29	0.55	0.82	0.93	0.95	1.00
IPA	0.2573	1.2301	0.9938							

*In the system modifier/water. RPP values are the relative point position on the given regression straight line (Fig. 1). **Because of the fact that the average log *k* values for 20, 10, 5 and 1 % v/v of modifier only slightly differ (Fig. 1)

Figure 1 shows that the Log *k* pair linearity rule is also valid in this case. Due to the fact that in the case of IPA the mean log *k* values for 20, 10, 5 and 1 % v/v of the modifiers differ slightly, the corresponding RPP scale was not determined. The corresponding regression data and the calculated RPP scales for the other modifiers are shown in Table II. It can be seen from this Table that considerably lower *r* values were obtained than in the case of the earlier examined C₁₈ column,⁴ when better than 0.9980 values were obtained, but nevertheless good enough for an RPP scale to be satisfactorily calculated.

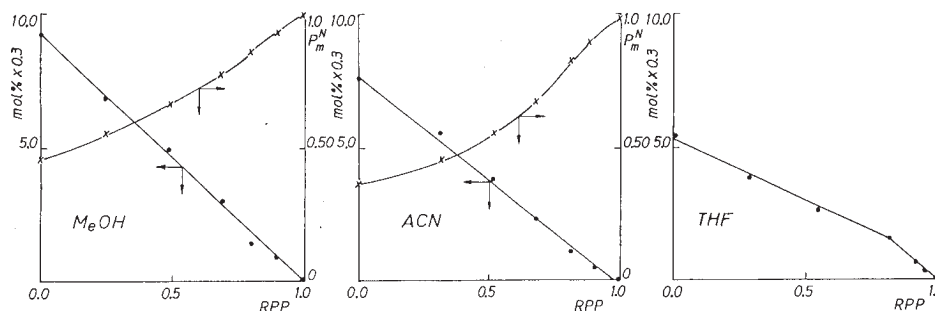


Fig. 2. Functional dependence between mol % of modifier in the mobile phase and RPP values found for all the modifiers examined, as well as the dependence of the RPP values and mobile phase polarity parameter P_m^N for MeOH and ACN.

The r values of the linear function $\log k = f(\text{RPP})$ obtained for all 27 compounds with all three above mentioned modifiers are shown in Table III. The best results are obtained with ACN, where in 26 cases the obtained r was better than 0.9900. Worse results were obtained with MeOH, when in only 21 cases was r better than 0.9900. There are various reasons for the lower r values of 6 compounds (footnote of Table III), which indicates that in these cases the error is not systematic. Finally, when THF was used in only 20 cases was r better than 0.9900, so these results may be considered as the poorest, because in 4 cases with 20 % v/v of modifier there was an upwards deviation from the straight line, which indicates that these compounds have another, much better RPP scale (r was better than 0.9978). It is important to point out that in spite of the fact that only group I and II group compounds (*i.e.*, the first 18 compounds) were used for the determination of the RPP scales, these scales led to no worse results in the control group of the compounds (Nos. 19–27), although the solute descriptors of all 27 compounds differ considerably among themselves.

Since in similar investigations on C_{18} columns with ACN and MeOH as modifiers a very good correlation between the obtained RPP values and Bosch's mobile phase polarity parameters P_m^N was found,⁶ this dependence was also investigated for the diol-silica column and the obtained results are shown in Fig. 2. It can be seen that this correlation is not linear but that in the cases with ACN and MeOH as modifiers there is a comparatively good linear correlation between RPP values and mol % of modifier in the mobile phase, the r values being -0.9970 and -0.9981 , respectively. Only in the case of THF is a clear discontinuity from the obtained straight line visible at the point corresponding to 20 % v/v of THF.

As RPP values have to be determined, and the mol % of modifier is easy to calculate, the correlation data of the linear function:

$$\log k = p(\text{mol \% of modifier}) + q \quad (2)$$

for ACN and MeOH are presented in Tables IV and V, respectively, for all 27 compounds. The slope of the straight line in Eq. (2) can be defined as the change in the log *k* value which is brought about by a unit change of the mol % of modifier and the intercept is equal to the log *k* value that would be obtained with pure water.

TABLE III. Correlation coefficients (*r*) of the linear function: $\log k = f(\text{RPP})^+$. Ordinal numbers designate the compounds in Table I

No.	ACN	MeOH	THF
1	0.9974	0.9967	0.9945
2	0.9930	0.9789**	0.9693**
3	0.9985	0.9940	0.9952
4	0.9991	0.9921	0.9957
5	0.9987	0.9880**	0.9978
6	0.9987	0.9918	0.9970
7	0.9953	0.9977	0.9949
8	0.9977	0.9977	0.9953
9	0.9987	0.9829***	0.9973
10	0.9986	0.9982	0.9993
11	0.9941	0.9940	0.9830*
12	0.9986	0.9881*	0.9968
13	0.9958	0.9937	0.9855*
14	0.9988	0.9992	0.9954
15	0.9951	0.9657***	0.9753****
16	0.9984	0.9914	0.9987
17	0.9971	0.9893 [#]	0.9861 [#]
18	0.9975	0.9956	0.9968
19	0.9988	0.9944	0.9968
20	0.9998	0.9958	0.9992
21	0.9961	0.9981	0.9949
22	0.9949	0.9989	0.9888*
23	0.9917	0.9955	0.9929
24	0.9971	0.9939	0.9961
25	0.9989	0.9978	0.9999
26	0.9889*	0.9983	0.9781*
27	0.9981	0.9971	0.9931

⁺In the case when *r* values are worse than 0.9900 the examined function was graphically presented to establish the cause of low correlation, the following was found: *The straight line breaks at the fourth point with increasing slope; **The dependence is not linear; ***The first point (50 % v/v) is very high; ****The last point (1 % v/v) is very high; [#]The points are irregularly dispersed around the regression line

As can be seen from Table IV, out of the 27 examined compounds, in 23 cases *r* values (for *n* = 7) better than 0.9900 were obtained. Leaving out the experimental

point which deviates mostly from the regression straight line, r values better than 0.9900 were also obtained with the compounds Nos. 2, 15, 23 and 26.

TABLE IV. Regression data of the linear function: $\log k = p(\text{mol \% ACN}) + q$. Sorbent: diol-silica $n = 7$ if it is not differently cited

Compound No. from Table I	q	$-p$	$-r$
1	1.0974	0.0779	0.9978
2	0.2697	0.0422	0.9890
	0.2382	0.0361	0.9947 (without 50 % v/v, $n = 6$)
3	0.9240	0.0723	0.9986
4	0.6433	0.0583	0.9976
5	0.7294	0.0625	0.9990
6	0.9647	0.0707	0.9995
7	1.2193	0.0805	0.9967
8	0.3320	0.0504	0.9923
9	0.3528	0.0510	0.9943
10	0.4140	0.0529	0.9949
11	0.4299	0.0560	0.9901
12	0.4400	0.0546	0.9941
13	0.6007	0.0629	0.9924
14	0.5317	0.0629	0.9959
15	0.1353	0.0431	0.9886
	0.0922	0.0406	0.9921 (without 1 % v/v, $n = 6$)
16	0.4784	0.0579	0.9950
17	0.1315	0.0403	0.9931
18	0.3311	0.0509	0.9929
19	0.3229	0.0495	0.9952
20	0.4840	0.0564	0.9970
21	1.0103	0.0787	0.9957
22	1.1997	0.0905	0.9953
23	0.0421	0.0359	0.9840
	0.0090	0.0295	0.9933 (without 50 % v/v, $n = 6$)
24	0.1324	0.0403	0.9929
25	0.5000	0.0554	0.9968
26	0.1379	0.0367	0.9862
	0.0869	0.0339	0.9962 (without 1 % v/v, $n = 6$)
27	0.1973	0.0420	0.9948

As can be seen from Table V, out of the 27 examined compounds, in 21 cases r values (for $n = 7$) better than 0.9900 were obtained. Leaving out the point which mostly deviates from the regression straight line, the r values for the compounds

Nos. 5, 9 and 15 were also better than 0.9900, while this value was almost reached for compound number 12. The remaining two compounds (Nos. 2 and 17), in spite of a comparatively low dispersion of points around the regression straight line, have considerably lower *r* values (*n* = 7), probably due to the small slope of the regression lines. Namely, it is known that in such cases low *r* values are obtained, which has been discussed by some other authors as well.^{6,7}

TABLE V. Regression data of the linear function: $\log k = p(\text{mol \% MeOH}) + q$. Sorbent: diol-silica *n* = 7 if it is not differently cited

Compound No. from Table I	<i>q</i>	<i>-p</i>	<i>-r</i>
1	1.2952	0.0342	0.9980
2	0.2944	0.0128	0.9758
3	0.9531	0.0242	0.9941
4	0.6986	0.0192	0.9931
5	0.7973	0.0211	0.9894
	0.8177	0.0220	0.9916 (without 1 % v/v, <i>n</i> = 6)
6	1.0910	0.0273	0.9937
7	1.3842	0.0346	0.9987
8	0.4681	0.0228	0.9934
9	0.4551	0.0175	0.9799
	0.4765	0.0207	0.9937 (without 50 % v/v, <i>n</i> = 6)
10	0.4963	0.0190	0.9940
11	0.6433	0.0285	0.9907
12	0.6340	0.0236	0.9817
	0.5915	0.0216	0.9898 (without 1 % v/v, <i>n</i> = 6)
13	0.8392	0.0324	0.9912
14	0.7173	0.0260	0.9990
15	0.3002	0.0247	0.9584
	0.2284	0.0209	0.9942 (without 1 % v/v, <i>n</i> = 6)
16	0.5867	0.0235	0.9940
17	0.1779	0.0144	0.9879
18	0.4081	0.0190	0.9944
19	0.4044	0.0187	0.9912
20	0.6162	0.0240	0.9954
21	1.1962	0.0342	0.9965
22	1.4535	0.0410	0.9990
23	0.0749	0.0137	0.9904
24	0.1934	0.0151	0.9912
25	0.6624	0.0234	0.9937
26	0.2929	0.0240	0.9991
27	0.3339	0.0222	0.9952

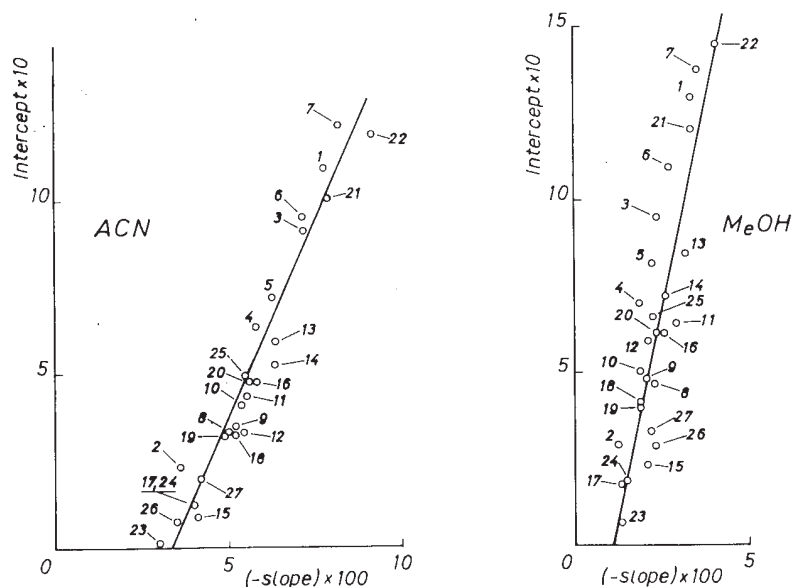


Fig. 3. Dependence between the intercept and the slope of the linear function: $\log k = f(\text{mol \% of modifier})$. The data are taken from Tables IV and V. In the cases when r values for $n = 7$ were lower than 0.9900 the values for $n = 6$ were taken.

Although Eq. (1) characterizes the retention ($\log k$ values) on the basis of the Solvation parameter model, and Eq. (2) is empirical, both equations are of practical interest, because in some cases the obtained experimental capacity factors are in better agreement with those calculated by Eq. (1), and in the other cases with those obtained by Eq. (2) (Table VI).

TABLE VI. A comparative review of the experimental and calculated capacity factors for some compounds: 1) Experimentally found values; 2) The values calculated by Equation (1) (system constants for 50 % v/v for ACN are unknown); 3) The values calculated by Equation (2) with the parameters p and q from Tables IV and V. Mol % of modifiers were calculated according to the Equation: $(\text{mol \%})^{-1} = A(\% \text{ v/v})^{-1} + 0.01(1-A)$, where A in the case of MeOH is 2.2475 and of ACN 2.9352

Compound	% v/v of modifier in the mobile phase								
	50	40	30	20	10	5	1		
Benzyl alcohol	MeOH	1)	0.44	0.58	0.76	0.88	0.93	1.12	1.19
		2)	0.42	0.57	0.79	0.99	1.18	1.51	1.91
		3)	0.45	0.58	0.72	0.87	1.02	1.11	1.17
	ACN	1)	0.11	0.29	0.44	0.60	0.74	0.87	1.09
		2)	-	0.28	0.41	0.59	0.76	0.94	1.43
		3)	-	0.29	0.43	0.60	0.80	0.91	1.02
1-Naphthol	MeOH	1)	1.31	2.70	4.73	7.33	9.49	13.48	14.97
		2)	1.23	2.34	3.89	6.21	7.97	10.56	12.67
		3)	1.39	2.59	4.45	7.14	10.84	13.12	15.17

Compound			% v/v of modifier in the mobile phase						
			50	40	30	20	10	5	1
1,2-Dichloro- benzene	ACN	1)	0.11	0.39	0.92	1.99	4.63	7.89	12.25
		2)	-	0.39	0.88	1.90	3.96	6.55	9.05
		3)	0.10	0.35	1.02	2.47	5.29	7.44	9.62
	MeOH	1)	1.66	2.85	4.97	7.30	9.36	9.94	10.83
		2)	1.64	2.87	4.41	6.35	7.30	8.51	9.09
		3)	1.78	2.93	4.50	6.57	9.17	10.68	11.99
	ACN	1)	0.15	0.46	1.14	2.50	4.71	7.00	9.46
		2)	-	0.43	1.11	2.34	4.27	5.83	7.73
		3)	0.15	0.45	1.16	2.57	5.09	6.92	8.72
Cresol	MeOH	1)	0.64	0.93	1.34	1.79	1.97	2.29	2.40
		2)	0.62	0.92	1.35	1.69	1.83	2.19	2.29
		3)	0.67	0.94	1.27	1.65	2.08	2.32	2.51
	ACN	1)	0.09	0.30	0.54	0.86	1.30	1.61	2.10
		2)	-	0.31	0.56	0.92	1.31	1.62	2.07
		3)	0.11	0.24	0.48	0.85	1.40	1.74	2.06
Anisol	MeOH	1)	0.80	1.14	1.64	2.14	2.31	2.74	3.18
		2)	0.81	1.22	1.74	2.31	2.70	3.26	3.87
		3)	0.82	1.15	1.56	2.02	2.55	2.84	3.08
	ACN	1)	0.10	0.32	0.61	1.02	1.55	1.90	2.59
		2)	-	0.35	0.66	1.13	1.67	2.03	3.07
		3)	0.12	0.27	0.54	1.00	1.66	2.09	2.49
Acetanilide	MeOH	1)	0.47	0.65	0.93	1.24	1.58	1.89	2.31
		2)	0.46	0.67	1.02	1.43	1.71	2.35	2.94
		3)	0.45	0.67	0.95	1.29	1.70	1.92	2.11
	ACN	1)	0.13	0.29	0.46	0.68	1.00	1.28	1.77
		2)	-	0.27	0.44	0.71	1.05	1.36	2.20
		3)	0.13	0.26	0.46	0.74	1.11	1.33	1.52

In spite of the fact that the 27 examined compounds differ considerably in their solute descriptors, most of these compounds with both modifiers (MeOH and ACN) surprisingly exhibit an approximate congenerity, because the functional dependence (intercept $\times 10$) = $f(-\text{slope} \times 100)$ does not deviate much from linearity (Fig. 3). Thus, the following regression parameters were obtained:

For ACN ($n = 27$) $r = 0.9740$, $s = 0.785$, inter. = -7.8079 and slope 2.3003 , and for MeOH ($n = 27$) $r = 0.8859$, $s = 1.765$, inter. = -5.0887 and slope = 4.8637 .

In order to illustrate the mentioned linearity the fact that the r_{test} value for $n = 27$ with a certainty of 99.9 % amounts to 0.597 could be cited.

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ИЗВОД

ПРИМЕНА ПРАВИЛА ЛИНЕАРНОСТИ $\log k$ ПАРОВА И ПРАВИЛА ПРОПОРЦИОНАЛНОСТИ ЗА ОДРЕЂИВАЊЕ RPP СКАЛА МОБИЛНИХ ФАЗА У ХРОМАТОГРАФИЈИ НА КОЛОНИ ДИОЛ-СИЛИКА ГЕЛА

ТОМИСЛАВ Ј. ЈАЊИЋ, ГОРДАНА ВУЧКОВИЋ* и МИЛЕНКО Б. ЋЕЛАП

Хемијски факултет, Универзитет у Београду, б. бр. 158, 11001 Београд

Применом Правила линеарности $\log k$ парова и Правила пропорционалности на литературне $\log k$ вредности добијене за 27 једињења у колони диол-силика гела утврђено је постојање заједничких RPP скала у случају мобилних фаза које су поред воде садржавале као модификаторе ацетонитрил, метанол или терахидрофуран. Добијени корелациони коефицијенти линеарне функције $\log k = f(\text{RPP})$ били су бољи од 0.9900 у првом случају код 26, у другом код 21, а у трећем код 20 једињења. Поред тога, код прва два модификатора утврђена је линеарна зависност између нађених RPP вредности и мол % модификатора. Из тога је произашла линеарна функција: $\log k = f(\text{мол \% модификатора})$ предложена за процену $\log k$ вредности у практичном раду. Између одсечка и нагиба ове функције нађена је линеарна корелација за већину испитиваних једињења, иако се изучавана једињења битно разликују по својим параметрима који карактеришу њихову способност за остваривање различитих интеракција са стационарном фазом.

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