The dependence of the 1,2-disubstituted propanes $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3H^3_3$ methyl protons ($C^3H^3_3$) chemical shifts on the nature of substituents X in the ^1H NMR spectra. An anomeric effect action?

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November 2015

Abstract. The chemical shifts values δ^H_{CH3} in the PMR spectra of 97 disubstituted propanes of general formula $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3H^3_3$ were analyzed. All 97 compounds divided on 12 series, wherein the row number determined by substituent **Y**. All substituents **X** and **Y** divided into four groups depending on the electronegativity of the atom in the substituent that is bound to a propane skeleton of molecule. The rule of the electronegativity additive effect of both substituents **X** and **Y** on the chemical shift δ^H_{CH3} is suggested. In 15 of 16 cases we observed the predicted changes of parameter δ^H_{CH3}. The only exception is the case when both substituents **X** and **Y** are the heteroatoms of the second period - atoms **N** and **O**. In this case, instead of the expected downfield shift of δ^H_{CH3} occurs it upfield shift. To explain this phenomenon, we hypothesized the certain action of the well-known vic-anomeric effect, apparently occurring also for parameters of ^1H NMR spectra.

Key words: 1,2-disubstituted propanes, chemical shift of methyl protons δ^H_{CH3}, substituents **X** and **Y**, four groups of substituents.

1. Introduction

Earlier [1] we have observed that in the ^1H NMR spectra of 1,2-disubstituted arylpropanes of general formula $\mathbf{Ar}\text{-}C^1H^1(X)\text{-}C^2H^2(Y)\text{-}C^3H^3_3$ the presence of such electron withdrawing substituents **X** as **X = -OR**, and **X = -NR₂** at the carbon atom C^1 leads to a **up field** shift of the methyl protons signals in the fragment $\text{-}C^3H^3_3$, which we studied compared to the signal of $\text{-}C^3H^3_3$ in the unsubstituted analog $Ar\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3H^3_3$ (where **X** = H). Such shift can not be considered something extraordinary, because it is known that the magnitude of the chemical shifts of protons in organic compounds may be influenced by other factors except electronegativity of functional substituents present in the molecule under consideration.

In order to establish the causes of this phenomenon, we have undertaken the study ^1H NMR spectra of the simpler objects – the series of 1-**X**,2-**Y**-disubstituted propanes of general formula $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3H^3_3$. This class of compounds, not contain the 1-aryl moiety **Ar** in the unaltered propyl skeleton of the molecule ($\mathbf{C^1\text{-}C^2\text{-}C^3}$). This should simplify the explanation of the observed phenomenon.

2. Objects of research

As stated above we choose as objects of study the simplest compounds of this class **1- X,2-Y -propanes** of the general formula $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3H^3_3$, in which we are studying the **changes in the chemical shift of the methyl protons**, depending on the structure of the substituents **X** and **Y**. We unite compounds with the same substituents **Y** at **C-2** in an appropriate series (rows), where their number is equal to the number of investigated substituents **Y**. The substances included in every of these rows differ from each other only in the structure of the substituents **X**. Let us denote each of these series with bold Arabic numeral, which will corresponds the substituents **Y**; and the substituents **X** indicated in bold lowercase Latin letters. Then each of the compounds discussed below is designated two-valued symbol «**Nn**»: numeral **N** and letter **n**, indicating the structure of the substituents, respectively, **Y** and **X**. For example, the compound with the designation «**2d**» includes a series of substances containing substituent **Y**, indicated by the numeral **2**, and also contains a substituent **X**, denoted by the letter **d**.

Unfortunately, the most reliable (in our opinion) sources of information about the NMR spectra of organic compounds [2, 3] we use give much less spectral data than we would like to comprehensive review of the problem studied. So we necessitate choose to review a fairly limited number of functional substituents **X** and **Y**. The numbering of the series **N**, we started with the most electron-donating substituents **Y** - alkyl groups - and the gradual transition to a more electron-withdrawing substituents **Y** - halogen atoms. We numbered substituents **X** by the same principle. Note that the number of substituents **Y** (12) is smaller than the number of substituents **X** (16).

Thus, the **12** series of substances **Nn**, which are defined by the structure of substituents **Y** at **C-2** are designated by such numerals: **$-C_3H_7^i$ (1)**, **$-C_2H_5$ (2)**, **$-CH_3$ (3)**, **-H (4)**, **$-C_6H_5$ (5)**, **$-C(O)-CH_3$ (6)**, **$-C(O)O-CH_2-CH_3$ (7)**, **$-NH_2$ (8)**, **-OH (9)**, **-SH (10)**, **-Cl (11)**, **-Br (12)**. Each row can include up to **16** members - the maximum possible number of substituents **X** (including hydrogen atom), which designated by Latin letters. We show in round brackets the letter designated of substituent **X**; in some cases can be given the abbreviated Latin letters of definable designation: **$-t-C_4H_9$ (a, Bu^t)**, **$-i-C_3H_7$ (b, Pr^i)**, **$-C_2H_5$ (c, Et)**, **$-CH_3$ (d, Me)**, **-H (e, -)**, **$-CH{=}CH_2$ (f, Vin)**, **$-C_6H_5$ (g, Ph)**, **$-C(O)CH_3$ (h, Ac)**, **$-C(O)OCH_2CH_3$ (j, COOEt)**, **$-NH_2$ (k, -)**, **-OH (L, -)**, **$-OCH_3$ (m, OMe)**, **-SH (p, -)**, **-Cl (r, -)**, **-Br (s, -)**, **-I (t, -)**. To avoid confusion, we are not attracted to the designation of substituents **X** those letters, which are commonly used for some common symbols or abbreviations (**i**, **n**, **o**), as well as signs, graphics of which are not very different from other graphics of letters or numerals (for example, we used a capital letter «**L**» instead of lowercase letter «**l**», whose graphic is not very different from the graphic of numeral "**1**").

The values of the discussed base spectral parameters **δ^{H}_{CH3}** - the chemical shifts of the three methyl protons in each compound **Nn** - designated as **δ^{H}_{Nn}** (for the compounds of a row **Y** = **N** with substituent **X** = **n**). In addition to absolute values of chemical shifts - parameters **δ^{H}_{Nn}** - for the convenience of discussion for each compound **Nn** are introduced the **calculated** relative value – the **differential parameter** **$\Delta\delta^{H}_{Nn}$**. It corresponds to the **difference** between the parameters **δ^{H}_{Nn}** considered in compound **Nn** and parameter **δ^{H}_{Ne}** in monosubstituted isopropane **Ne** of general formula $\mathbf{H}\text{-}C^1H^1_2\text{-}C^2H^2(\mathbf{Y})\text{-}C^3\boldsymbol{H}^3_3$, wherein the substituent **X** is designated by the letter "**e**" is hydrogen atom, ie, **$\Delta\delta^{H}_{Nn} = \delta^{H}_{Nn} - \delta^{H}_{Ne}$**. Since we consider **only** the chemical shifts of the methyl protons **δ^{H}_{CH3}**, we introduced abbreviations «**ΔNn**» of differential parameter **$\Delta\delta^{H}_{Nn}$**. Differential parameter **ΔNn**, being the result of subtracting of two chemical shifts, can have both positive and negative sign, so is necessarily accompanied by a symbols: "+" or "-".

3. Experimental

The choice of literature sources we grounded on the observation of their reliability and compatibility. We try to use only **δ^{H}_{Nn}** values obtained in deuterochloroform as a solvent and described in the reference books [2, 3]. Spectra obtained in other solvent, *e.g.* DMSO-d6, we do not examine here. But Table 1 shows the spectral data of n-propane **4e** obtained in CCl_4. This exception is made in respect of the importance of the substance **4e**, because without parameter **δ^{H}_{4e}**, it is impossible to calculate all the differential parameters **Δ4n** for a **4n** series (**N = 4**, where **Y** = **H**)]. The parameters **δ^{H}_{Nn}** given in [2] were obtained using instruments with different frequency: low-frequency (90 MHz) and high-frequency (300 or 400 MHz). "Low-frequency" parameters were used only in the absence of “high-frequency” values. The authors of data represented in [2] give their own attribution of spectra signals; the authors of data represented in [3] do not give their own attribution of spectra signals; so we do this by ourselves. The signals of studied methyl protons in the spectra of compounds **Nn** are easy to interpret. Typically, this is doublet of 3H intensity, which is usually located in the strongest field (0.8 to 1.7 ppm).

In order to increase the quantity of discussed parameters **ΔNn** in five occasions we went to the minor (in our opinion) changes in the structure of substituents **X** and/or **Y**. «Changed substituents» are marked by the introduction of dash and call "dashed substituents." These changes are shown in the notes to Table 1. Thus, in the first case, instead of parameter δ^{H}_{2h} of 4-methyl-2-hexanone **2h** we gave proton chemical shift value of 5-methyl group in 5-methyl-3-heptanone, which was designated as **2h'**. I.e., we have replaced the acetyl group [$CH_3C(O)$-] as a substituent **X** onto a propionyl group [$CH_3CH_2C(O)$-]. In the second case, instead of the parameter δ^{H}_{2j} of ethyl 3-methylvalerate **2j** we have given the magnitude of the methyl protons chemical shift of the 3-methylvaleric acids itself, that we have designated as **2j'**. In the third case, instead of the parameter δ^{H}_{5j} of ethyl 3-phenylbutyrate **5j** we also brought the methyl protons chemical shift of the 3-phenylbutiric acids itself, which we have designated as **5j'**. In the fourth case instead of the parameter δ^{H}_{6j} of ethyl 3-methyl-4-ketovalerate **6j** also we show the magnitude of the methyl protons chemical shift of the 3-methy-4-ketolvaleric acids itself, denoted as **6j'**. And, in the last fifth case, instead of the parameter δ^{H}_{7j} of the diethyl 2-methylsuccinate **7j** we brought the value of the methyl protons chemical shift of the dimethyl-2-methylsuccinate which we have designated as **7j'**.

We estimate the inaccuracy of measurements of the parameters δ^{H}_{Nn} (and hence the calculated differential parameters **ΔNn**) as ± 0.02 ppm [20 **mlrd**, **mlrd** - is part per billion (**milliard**)]. In our opinion this is a very small value indicates a greater accuracy of measurements. Unfortunately, the most of the parameters **ΔNn** are comparable with it. "Absolute" (δ^{H}_{Nn}) and differential **ΔNn** ($\Delta\delta^{H}_{Nn}$) parameters of all 97 propane derivatives **Nn** are summarized in Table 1, which, for convenience divided into two parts. In the second part is re-introduced column of parameters "e", where substituent **X** is a hydrogen atom (δ^{H}_{Ne} and **ΔNe**). All parameters δ^{H}_{Nn} (but three of the buyout discussed below) are given from our "main sources" [2 and 3]. The values δ^{H}_{Nn} given in [2] is not specifically allocated; whereas all figures given in [3] in the table enclosed in yellow boxes. Furthermore, it is for this study were recruited missing in [2, 3] δ^{H}_{Nn} spectral data for the three compounds: isobutane **3e**, isobutylamine **3k** and n-butane **4d**, taken from the "additional" sources [4, 5]. Note that without the parameter δ^{H}_{3e} for isobutane **3e** it is impossible to calculate all differential parameters **Δ3n** for a **3n** serie (**N = 3**). Parameter δ^{H}_{3e} which is taken from the textbook of Prëtcsh [4], signed in purple rectangle, and the parameters δ^{H}_{3k} and δ^{H}_{4d} taken from the textbook of Abraham [5] - in the gray rectangles.

Each compound **Nn**, located in Table 1, placed in its own "cell". The top row of this cell shows the values of the "absolute" parameters δ^{H}_{Nn} expressed in parts per million (ppm), and in its bottom row shows the value of the differential parameters **ΔNn**, expressed in billionths parts (**mlrd**).

In two cases (compound **4L** and **9L**) at our disposal there are two experimental parameter for each substance, taken from both sources [2 and 3], whose values differ by more than 20 **mlrd**. Since we were not able to reasonably choose the preferred spectral value, in these cells of the Table we give both parameter δ^{H}_{Nn} (and, accordingly, both differential parameters **ΔNn**). Both alternatives values δ^{H}_{Nn} for substance **4L** and substance **9L** give differential parameters **ΔNn** the same in sign in each case (positive in the case of **4L** and negative in the case of **9L**), so when we discuss the results, we do not focus our attention on the difference in their numerical values.

Table 1

Spectral parameters δ^H_{Nn} (δ^H_{CH3}) and ΔNn of 1-X,2-Y-propanes Nn of general formula $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3\underline{H}^3_3$.

The first part of Table 1

№ of row	substituent Y is equal to:	The values δ^H_{Nn} and ΔNn when in $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3\underline{H}^3_3$, substituent X is equal to:								
		-Bu^t (a)	-Pr^i (b)	-Et (c)	-Me (d)	-H (e)	-Vin (f)	-Ph (g)	Ac (h)	-COOEt (j)
1	-CH(CH$_3$)$_2$	-	-	0.781	0.788	0.843	-	-	-	-
		-	-	-62	-55	0	-	-	-	-
2	-CH$_2$-CH$_3$	0.896	0.827	0.841	0.86	0.869	0.865	-	0.88[1]	0.969[2]
		+27	-42	-28	-9	0	-4		+11	+100
3	-CH$_3$	0.907	0.853	0.864	0.869	0.89	0.900	0.901	0.926	0.958
		+17	-37	-26	-21	0	+10	+11	+36	+68
4	-H	0.880	0.880	0.884	0.89	0.899	0.910	0.94	0.930	0.96
		-19	-19	-15	-9	0	+11	+41	+31	+61
5	-Ph	-	-	-	1.237	1.253	-	-	-	1.115[3]
					-16	0				-138
6	-C(O)-CH$_3$	-	-	1.079	1.081	1.111	-	-	-	1.179[4]
				-32	-30	0				+68
7	-C(O)-O-C$_2$H$_5$	-	-	1.137	1.151	1.165	1.155	-	-	1.226[5]
				-28	-14	0	-10			+61
8	-NH$_2$	-	1.05	1.053	1.05	1.070	-	-	-	1.125
			-20	-17	-20	0				+55
9	-OH	1.192	1.180	1.172	1.184	1.200	1.209	-	-	1.229
		-8	-20	-28	-16	0	+9			+29
10	-SH	-	-	-	1.322	1.336	-	-	-	-
					-14	0				
11	-Cl	-	-	-	1.502	1.52	-	-	-	-
					-18	0				
12	-Br	-	-		1.703	1.71	-	1.665	-	-
					-7	0		-45		

1) Data for 5-methyl-3-heptanone (**2h'**) instead of 4-methyl-2-hexanone (**2h**).

2) Data for 3-methylvaleric acid (**2j'**) instead of its ethyl ester (**2j**).

3) Data for 3-phenyl-butyric acid (**5j'**) instead of its ethyl ester (**5j**).

4) Data for 3-methyl-4-ketovaleric acid (**6j'**) instead of its ethyl ester (**6j**).

5) The data for dimethyl ether MeO-C(O)-CH(CH$_3$)-CH$_2$-C(O)-O-Me, instead of diethyl ether Et-O-C(O)-CH(CH$_3$)-CH$_2$-C(O)-O-Et.

The second part of Table 1

№ of row	substituent Y is equal to:	The values δ^H_{Nn} and ΔNn when in $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3\underline{H}^3_3$, substituent X is equal to:							
		-H (e)	-NH$_2$ (k)	-OH (L)	-O-Me (m)	-SH (p)	-Cl (r)	-Br (s)	-I (t)
1	-CH(CH$_3$)$_2$	0.843	-	-	-	-	-	-	-
		0							
2	-CH$_2$-CH$_3$	0.869	0.891	0.904	-	-	-	-	0.977
		0	+22	+35					+108
3	-CH$_3$	0.890	0.900	0.922	-	0.983	1.013	1.028	1.020
		0	+10	+32		+93	+123	+138	+130
4	-H	0.899	0.92	0.941 0.92	0.930	0.986	1.020	1.030	0.990
		0	+21	+42 +21	+31	+87	+121	+131	+91
5	-Ph	1.253	1.254	1.255	-	-	-	-	-
		0	+1	+2	-	-	-	-	-
6	-C(O)-CH$_3$	1.111	-	1.134	-	-	-	-	-
		0		+23					
7	-C(O)-O-C$_2$H$_5$	1.165	-	1.18	-	-	-	1.30	-
		0		+15				+135	

8	**-NH$_2$**	**1.070**	**1.050**	**1.048**	**1.030**	-	-	-	-
		0	**-20**	**-22**	**-40**				
9	**-OH**	**1.200**	**1.147**	**1.154; 1.13**	**1.145**	**1.250**	**1.272**	**1.30**	-
		0	**-53**	**-46 -70**	**-55**	**+50**	**+72**	**+100**	
10	**-SH**	**1.336**	-	**1.250**	-	**1.400**	-	-	-
		0		**-86**		**+64**			
11	**-Cl**	**1.52**	-	**1.50**	-	-	**1.615**	**1.649**	-
		0		**-20**			**+95**	**+129**	
12	**-Br**	**1.71**	-	-	-	-	**1.79**	**1.825**	-
		0					**+80**	**+115**	

4. Results and Discussion

Below we discuss the spectral parameters and δ^{H}_{Nn} and **ΔNn** for 97 (out of 192 possible, 50.5%) of 1,2-disubstituted propanes of general formula X-$C^{1}H^{1}_{2}$-$C^{2}H^{2}(Y)$-$C^{3}\underline{H^{3}}_{3}$ (**Nn**), summarized in 12 rows. In each row (depending on the means at our disposal spectral data) contains a different number of compounds. As mentioned above, the maximum possible number of terms - 16, so on average, each row filled with a number of slightly more than half. There is only one completely filled row with a number of 16 members - a row number **4n** (**Y** = **H**). "Filling" a few more rows [**3n** (**Y** = **Me**) – 15 members, **9n** (**Y** = **OH**) - 13 members, **2n** (**Y** = **Et**) - 11 members] close to the maximum.

These 12 rows are expedient to divide into two large groups, depending on the structure of substituent **Y**. The first group includes rows №№ **1 - 7**, in which the atom, linking substituent **Y** with atom **C^2** of the propane molecule skeleton is either carbon atom (rows №№ **1 - 3** and №№ **5 - 7**) or a hydrogen atom (row № **4**). The second group includes rows №№ **8 - 12**, in which the atom linking the substituent **Y** with **C^2** of the propane molecule skeleton is a **heteroatom** (**N** in row № **8**, **O** in row № **9**, **S** in row № **10**, **Cl** in row № **11**, and **Br** in row № **12**).

Each of these two groups is expedient to divide into two subgroups. The first subgroup of the first group combine rows №№ **1 - 4**, wherein the substituent **Y** is either an alkyl group (rows №№ **1 - 3**) or hydrogen atom (row № **4**). In the 2nd subgroup of Group 1 we unite the rows №№ **5 - 7**, in which the carbon atom connecting substituent **Y** with atom **C^2** of the propane molecule skeleton, bonded with other moiety of substituent **Y** with multiple bonds (**C = C** in the row № **5**) (or **C = O** in rows №№ **6, 7**).

The 1-st subgroup of group № 2 unit the rows № **8** and № **9** in which a heteroatom in the substituent **Y** is an element of the second period (**N** or **O**). The 2-nd subgroup of group № 2 combine rows №№ **10 - 12**, in which the heteroatom in the substituent **Y** is an element of the third period (**S** or **Cl**) or fourth period (**Br**).

Thus, all 12 rows are *divided into **four types***: the first type – the rows №№ **1 - 4**; the second type – the rows №№ **5 - 7**; the third type - the rows №№ **8** and **9**; the fourth type – the rows №№ **10 - 12**.

4. 1. The spectral parameters δ^{H}_{Nn} in monosubstituted propanes Ne $C^{1}\underline{H^{1}_{3}}$-$C^{2}H^{2}(Y)$-$C^{3}\underline{H^{3}}_{3}$.

Let's consider chemical shifts δ^{H}_{Ne} of symmetric monosubstituted 2-propanes $C^{1}\underline{H^{1}_{3}}$-$C^{2}H^{2}(Y)$-$C^{3}\underline{H^{3}}_{3}$ in all 12 rows of the compounds of general formula **Ne** [wherein the substituent **X** = **H (e)**]. We give these parameters with regard to their division into 4 types: Type 1 - **0.843 (1e), 0.869 (2nd), 0.890 (3rd), 0.899 (4th)**; Type 2 - **1.253 (5th), 1.111 (6th), 1.165 (7th)**; 3 type - **1.070 (8th), 1200 (9th)**; Type 4 - **1.336 (10e), 1.52 (11e), 1.71 (12e)**.

Let's consider individually the δ^{H}_{Ne} values for each type of rows. All the values δ^{H}_{Ne} for 4 compounds of type 1 (**N = 1 ÷ 4**) are in the range of ~ **0.85 ÷ 0.9** ppm. For compounds of type 2 (**N = 5 ÷ 7**) they are in the range of ~ **1.1 ÷ 1.25** ppm. Both values of compounds of type 3 (**N = 8, 9**) fall into approximately at the same interval, whereas the δ^{H}_{Ne} values for compounds of type 4 (**N = 10 ÷ 12**) are the most downfield (~ **1.3 ÷ 1.7** ppm).

4.2. Spectral parameters and δ^{H}_{Nn} and ΔN in disubstituted propanes $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3\underline{\mathit{H}}^3_3$

The fruitfulness of the above approach, dividing the substituents **Y** onto 4 types were confirmed in the similar division of substituents **X**. On the same principle all 16 substituents **X** are divided onto 4 types. The structure of the first type substituents include 4 alkyl groups (**a, b, c, d**) and hydrogen atom (**e**). The composition of the substituents **X** of the second type includes four substituents containing multiple bonds **C = C** or **C = O** (**f, g, h, j**). The composition of the third type of substituents **X** include 3 substituents containing heteroatoms of the 2nd period (**k, L, m**). Finally, a fourth type of composition of substituents **X** are four remaining substituents containing heteroatoms of 3rd and 4th periods (**p, r, s, t**).

4. 2. 1. The dependence of the differential parameters ΔNn on structure of alkyl groups for substituents X of the first type (columns «a - d» in the rows 1 – 12).

Let's consider the differential parameters **ΔNn** for all disubstituted **1-X,2-Y**-propanes **X**-$C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3\underline{\mathit{H}}^3_3$ in all 12 rows of the compounds with substituents **X** of the first type (**X = Alk, H**). We stress that in the above 12 monosubstituted substances **Ne [X = H (e)]**, by definition **ΔNn** = 0. For convenience of the discussion the values of the considered differential parameters **ΔNn** we are interested re shown in Table 2, which is a simplified part of Table 1.

Table 2

Number of row	Substituent Y	The $\Delta\delta^{H}_{CH3}$ values for substituent X in X-$C^1H^1_2$-$C^2H^2(Y)\text{-}C^3\underline{\mathit{H}}^3_3$ (in mlrd.)				
		-Bu^t (a)	-Pr^i (b)	-Et (c)	-Me (d)	-H (e)
1	-CH(CH$_3$)$_2$			-62	-55	0
2	-CH$_2$-CH$_3$	+27	-42	-28	-9	0
3	-CH$_3$	+17	-37	-26	-21	0
4	-H	-19	-19	-15	-9	0
5	-Ph				-16	0
6	-C(O)-CH$_3$			-32	-30	0
7	-C(O)-O-C$_2$H$_5$			-28	-14	0
8	-NH$_2$		-20	-17	-20	0
9	-OH	-8	-20	-28	-16	0
10	-SH				-14	0
11	-Cl				-18	0
12	-Br				-7	0

We have a 41 (out of 60 possible, 68.3%) **ΔNn** parameters of all 12 discussed rows (**N = 1 - 12, n = «a" - "e"**). Both for hydrogen atom as substituent **X** (column «**n = e**") and for methyl group as substituent **X** (column «**n = d**»), there are data for all 12 rows. For ethyl group as substituent **X** (column «**n = c**») there are parameters for the 8 rows; for the isopropyl group as substituent **X** (column «**n = b**») - for 5 rows, and for tert-butyl group as substituent **X** (column «**n = a**") - only for 4 rows. Only for 4 rows (**N = 2, 3, 4, 9**) we have the experimental data for all five possible substituents **X** (columns **n = «a» - «e»**). These rows we named "complete rows". More one row (**N = 8**), there is data for the four substituents **X** (no data for **n = «a»**); and for three rows (**N = 1, 6, 7**) – the data available for the three substituents **X** (except **n = «a», «b»**). In the remaining four rows the needed data are available for only two of five possible substituents (**X = «d» and «e»**). Thus, the most comprehensive data available for the first (rows **1 - 4**) and third (rows **8 and 9**) types of the substituents **Y**, which allows us to do for these series most reasonable conclusions. The data for second and fourth types of substituents **Y** do not contradict these findings.

We suggest the rule of the electronegativity (electropositivity) additive effect for located in the **adjacent (vicinal) position** relative to each other **substituents X and Y** on the **chemical shift** δ^{H}_{CH3}. So, for the **alkyl substituents of first group** it supposed the presence of **electropositive effect**, which led to a **upfield shift** of studied parameter δ^{H}_{CH3} (ie, the **negative value of differential parameter ΔNd,** blue colour).

Taking into account the structure of the alkyl substituents **X**, one would expect a gradual reduction of electron-donating ability of the substituent at the transition from t-butyl group (**n = «a»**) to a methyl group (**n = «d»**), and then to the hydrogen atom (**n = «e»**). This suggests that: a) all values of differential parameters **ΔNn** (**n = «a» - «d»**) must have a negative value (or zero if **n = «e»**); b) it is expected that the greatest absolute magnitude of **ΔNn** negative value should be **ΔNa** parameter; slightly smaller **ΔNb** parameter; even fewer - **ΔNc** parameter. And the smallest in absolute negative value should be **ΔNd** parameter. In general, both of these assumptions are confirmed*.

An exception is the ratio of the absolute values of the parameters and **ΔNa** and **ΔNb**. In all four available to us "complete" rows (**N = 2, 3, 4, 9**) the **negative ΔNa parameter is not the largest in absolute value**. While the absolute value of the negative parameter **Δ9a** (**-8 mlrd.**) is less than the absolute value of the respective parameter **Δ9b (-40 mlrd.**), for the parameters **Δ4a** and **Δ4b** the values of these parameters have equal (at **-19 mlrd.**). And the **Δ3a** and **Δ2a** parameters are not negative at all, but have the **positive** values.

We assume that the decrease in the absolute value of the negative parameter **ΔNa** and even their transition in the region of positive values in the rows of compounds with alkyl substituents **Y** (**N = 2** and **3**) may be **associated with the action of steric factors**. This effect should manifest itself clearly, in our opinion, in cases where both substituents (**X** and **Y**), are expected to have increased space requirements. Its consequence is (by our assumption) the downfield shift of the studied methyl protons absorption (or an increase in the positive value of the parameter **ΔNn**). That is, the stronger will be the spatial interaction, the more positive will be the parameter **ΔNn**. And if the spatial interaction is sufficiently large, the parameter **ΔNn** can go from an expected negative values to positive values.

Let us consider as an example the spatial aspect of interaction between substituents **X** and **Y** in the three compounds **2a, 3a** and **4a**, which contain tert-butyl group as substituent **X**. For a start let us compare the spatial requirements of ethyl (row № **2**) and methyl (row № **3**) groups as a substituent **Y**. It is obvious that for ethyl group, these space requirements will be higher due to its higher branching. Therefore, a stronger interaction with t-butyl group (the substituent **X**, **n = a**) is assumed for more branched and more voluminous ethyl group (substituent **Y**) in the compound **2a**

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* From 41 parameters **ΔNn** available at our disposal in the discussed rows (**N = 1 - 12**, **n** = «**a**» - «**e**») positive in magnitude are only two parameters. Alleged reasons for increasing values of the parameters **Δ2a** and **Δ3a** and moving them out of the area of negative values in the field of positive values are discussed below.

Several cases of failure of the expected parameters **Nb**, **Nc** and **Nd** ratio are observed. In the tetranomial row **8n** the absolute value of the parameter **8c** less than parameter **8d** (ie $|\Delta\delta^{H}_{8c}| < |\Delta\delta^{H}_{8d}|$), although it was expected inverse relationship (ie $|\Delta\delta^{H}_{8d}| < |\Delta\delta^{H}_{8c}|$). In a five-membered row **9n** the absolute value of the parameter **9b** less than **9c** (ie $|\Delta\delta^{H}_{9b}| < |\Delta\delta^{H}_{9c}|$), although it was expected inverse relationship (ie $|\Delta\delta^{H}_{9c}| < |\Delta\delta^{H}_{9b}|$), what is said below.

as compared to the less voluminous methyl group as a substituent **Y** in the compound **3a**. For the hydrogen atom as a substituent **Y** (**Y = H, N = 4**), by definition, there are absent whatever space requirements. Therefore, the compound **4a** (**Y = H, N = 4**) we expected minimum of three considered here spatial interactions, part of which is constant in all three cases - the contribution of the substituent **X** (**-Bu^t, n = a**), with variable contribution of the substituent **Y**.

We emphasize that the parameters **ΔNa** decreased in same direction**:** (**Δ2a = +27 mlrd.**) > (**3a = +17 mlrd.**) > (**4a = -19 mlrd.**). Note that at the transition from the row № **3** (**Y = Me, N = 3**) to the row № **4** (**Y = H, N = 4**) there is a transition from positive to the expected negative value of the parameter **ΔNa**. However, the absolute value of the parameter **Δ4a** not exceed, as might be expected, the absolute value of the parameter **Δ4b**.

And for a row № **9**, wherein the substituent **Y** is a hydroxyl group (also with minimum space requirements), again there is the exceeding of the absolute value of the negative parameter **Δ9b** over the absolute value of negative parameter **Δ9a**.

4. 2. 2. The dependence of the differential parameters ΔNn on structure of second type of substituents X (columns «f - j» in the rows 1 – 12).

We assume that all 4 substituents **X** of the second type [**CH_2=CH- (f)**, **C_6H_5- (g)**, **$CH_3C(O)$- (h)**, **$C_2H_5OC(O)$- (j)**] showing more great electron accepting properties than hydrogen atom as a substituent **X** [**X = H (e)**]. Therefore, according to our assumption, it **can be expected** that all **parameters ΔNn** for the **second type of substituents X (n = f ÷ j)** will be **positive in magnitude**. For convenience of the discussion the values of the considered differential parameters **ΔNn** we are interested re shown in Table 3, which is a simplified part of Table 1.

Table 3

Number of row	Substituent Y	The $\Delta\delta^{H}_{CH3}$ values for substituent X in X-$C^1H^1_2$-C^2H^2(Y)-$C^3\underline{H^3}_3$ (in mlrd.)				
		-H (e)	-Vin (f)	-Ph (g)	-C(O)R (h or h’)	-COOR (j or j’)
2	-CH_2-CH_3	0	-4		+11	+100
3	-CH_3	0	+10	+11	+36	+68
4	-H	0	+11	+41	+31	+61
5	-Ph	0				-138
6	-C(O)-O-C_2H_5	0				+68
7	-C(O)-O-C_2H_5	0	-10			+61
8	-NH_2	0				+55
9	-OH	0	+9			+29
12	-Br	0		-45		

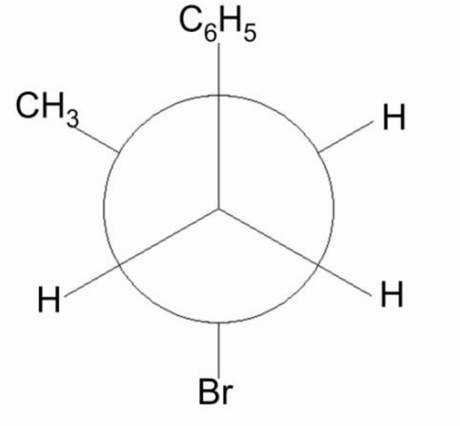
We have only 19 (out of possible 48, 39.6%) parameters **ΔNn** in 9 of 12 discussed rows (rows **N = 1 - 12**, columns **n** = «**f**» - «**j**»). For vinyl substituent «**n = f**», we have at our disposal the data for five rows. For the phenyl substituent «**n = g**» there are parameters only for 3 rows; for the acetyl substituent «**n = h**» - for even less - two rows. But most data is available for carbetoxyl substituent «**n = j**» (or for « replacing» its carboxyl substituent «**n = j’**») – for 8 rows.

Only for two «full» rows (**N = 3** and **4**) the experimental data available for all four substituents **X** (**n** = «**f**» - «**j**»). For three rows (**N = 2, 7** and **9**) available data only for two substituents **X** (for **n** = «**f**» and «**j**»); and for four rows (**N = 5, 6, 8** and **12**) - available data only for one substituent **X**. Thus, the most comprehensive data available for the first (rows **1 - 4**) of the substituents **Y**, which allows us to make the most reasoned conclusions for them. The rest of the data because of their fragmentation do not represent, in our view, of interest to general conclusions, although some interesting observations we still do.

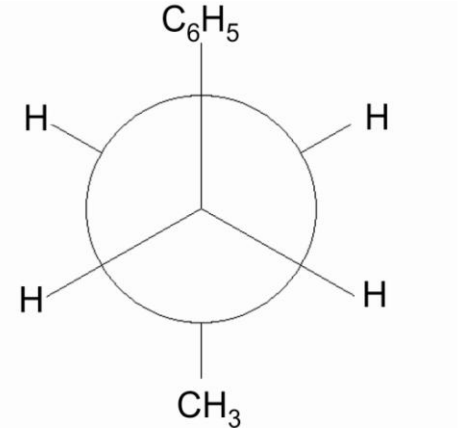
Note that **all** the values of the parameters **Δ3n** and **Δ4n** of both «full» rows have a **positive sign**. This is consistent with our assumptions above expressed on more electron accepting (than a hydrogen atom) properties of the second type substituent **X** (**n = «f» - «j»**), which cause the **downfield shift** of δ^{H}_{Nn} parameters studied in comparison with the corresponding parameters δ^{H}_{Ne} of monosubstituted compounds **Ne** of general formula **X**-$C^1H^1_2$-$C^2H^2_2$-$C^3H^3_3$, [where **Y** = **H** (**e**)].

However, **not all** of 19 parameters **ΔNn** in discussed rows (**N = 1 - 12**, **n** = «**f**» - «**j**») have positive values. The values of the four parameters (**Δ2f**, **Δ5j'**, **Δ7f** and **Δ12g**) are less than zero. We emphasize that the first two parameters belong to vinyl-containing compounds of general formula **Nf** [substituent **X**: **CH_2=CH- (f)**] and have a very small absolute value (**Δ2f** = - 4 **mlrd**; **Δ7f** = - 10 **mlrd.**). The three remaining parameters of compounds **Nf**, also have a very small absolute value, although with the sign «+» (**Δ3f** = +10 **mlrd**; **Δ4f** = +11 **mlrd**; **Δ9f** = +9 **mlrd**). Therefore, we can say that all five parameters **ΔNf**, being very small in absolute value, can have both positive or negative signs. That is, the values of all 5 parameters **ΔNf** are stacked in a small interval in a width of about **20 mlrd.**, which corresponds to the value of adopted by us experimental error. Therefore, the negative values of parameters and **Δ2f** and **Δ7f** are not represented, by our opinion, the considerable interest in terms of finding the general laws of the second type of substituents **X** influence on the value of the studied parameter **ΔNn** (where **n = «f» - «j»**).

Much more interesting to discuss seems to us the third negative by sign parameter **Δ12g**. It has a rather large absolute value (| 45 **mlrd.** |). This parameter we discussed previously [1], attributing the highfield shift of methyl absorption we are studying to the effect of six π-electrons of the phenyl ring. In support of this thesis, we consider here the most stable (in our opinion) conformation of the 2-bromphenylpropane (**12g**). This conformation depicted in the picture on the left side, where the molecule of **12g** is considering along the axis coinciding with the connection of atoms C-1 and C-2.



Stable conformation of **12g**.



Stable conformation of **4g**.

The large and heavy substituent **Y** at the **C-2** – the **bromine atom** - makes the most voluminous substituent **X** at the C-1 – the **phenyl group** - take transoidal position relatively of bromine atoms (both groups of top and bottom in the left figure). While the methyl group $C^3H^3_3$ (the second "of voluminousity" substituent at **C-2**, which is located in the left side of vertical line in the left picture) - takes "scewed" position relative to the phenyl group, ie, dihedral angle Ph-C^1-C^2-C^3 is equal to ~ 60^0. This enables the methyl group $C^3H^3_3$ fall in maximal degree within the scope of the cone magnetic anisotropy of six π-electrons of phenyl ring - the substituent **X** at **C-1**. It is just this influence we have previously [1] explained the highfield shift of three protons singlet signal due to absorption of the methyl group in the spectrum of compound **12g**.

Thus, it appears that the **phenyl group as the substituent X at C-1**, has <u>two opposite in sign effects</u> on the chemical shift of the methyl group $C^3\mathbf{H}^3{}_3$: 1) the assumed above electronegativity, causing downfield shift; 2) the effect of 6 π-electrons causing upfield shift. Possibly, the second effect overbalanced the first one, so that the total effect of the phenyl group results in an overall **upfield shift** of parameter $\boldsymbol{\delta^{H}{}_{12g}}$ in 2-bromphenylpropane **12g** compared with the absorption of methyl group (parameter $\boldsymbol{\delta^{H}{}_{4g}}$) in 1-phenylpropane **4g**.

Let us consider now the most stable conformation of 1-phenylpropane **4g** , which depicts in the picture on the right side. In **4g** the big and heavy bromine atom, which is a substituent **Y** at **C-2** in the 2-bromphenylpropane **12g** is absent. Therefore in 1-phenylpropane **4g** the most voluminous substituent **X** at the **C-1** - phenyl group - forces take the transoid position with respect to the most voluminous substituent at **C-2** – the methyl group $C^3\mathbf{H}^3{}_3$. As a result, it <u>minimizes the effect of magnetic anisotropy of six π-electrons on phenyl ring cone on protons of the $C^3\mathbf{H}^3{}_3$ methyl group</u>, so this is not observed upfield shift of their signal, which occurs in the above example of 2-bromphenylpropane **12g** (left side of the picture).

It seems to us, that the fourth negative parameter **Δ5j'**, obtained for compound **5j'** with «hatching substituent»- carboxyl group - is not less interesting for the discussion. Its absolute value is the largest of all 97 parameters **ΔNn** (| -138 **mlrd**. |). However, at the present time we do not have any reasonable assumptions about the reasons, that have caused upfield shift of absorption signal of the methyl group ($\boldsymbol{\delta^{H}{}_{Nn}}$ = 1.115 ppm) in 3-phenylbutyric acid **5j'** compared with the absorption of methyl groups in cumene **5e** ($\boldsymbol{\delta^{H}{}_{Nn}}$ = 1.253 ppm).

4. 2. 3. The dependence of the differential parameters ΔNn on structure of third type of substituents X (columns «k - m» in the rows 1 – 12).

We assume that all 3 substituents **X** of the third type [**NH_2- (k)**, **OH- (L)**, **CH_3O- (m)**], includes in its membership the most electronegative oxygen and nitrogen atoms, according to our assumption should **demonstrate the greatest electron accepting properties**, which are much larger, than for substituents of second type **[X = f, g, h, j]**. Therefore, **one would expect** that all **parameters ΔNn** for the **third type of substituents X** (**n = k ÷ m**) will be **<u>positive in sign and large in magnitude</u>**. For convenience of the discussion the values of the considered differential parameters **ΔNn** we are interested re shown in Table 4, which is a simplified part of Table 1.

Table 4

Num-ber of row	**Substituent Y**	**The $\Delta\delta^{H}{}_{CH3}$ values for substituent X in X-$C^1H^1{}_2$-C^2H^2(Y)-$C^3\underline{H}^3{}_3$ (in mlrd.)**			
		-H (e)	**-NH_2 (k)**	**-OH (L)**	**-O-Me (m)**
2	**-CH_2-CH_3**	**0**	**+22**	**+35**	
3	**-CH_3**	**0**	**+10**	**+32**	
4	**-H**	**0**	**+21**	**+42 +21**	**+31**
5	**-Ph**	**0**	**+1**	**+2**	
6	**-C(O)-CH_3**	**0**		**+23**	
7	**-C(O)-O-C_2H_5**	**0**		**+15**	
8	**-NH_2**	**0**	**-20**	**-22**	**-40**
9	**-OH**	**0**	**-53**	**-46 -70**	**-55**
10	**-SH**	**0**		**-86**	
11	**-Cl**	**0**		**-20**	

We have only 19 (out of possible 36, 52.8%) parameters **ΔNn** in 10 of 12 discussed rows (rows **N = 1 - 12**, columns **n = «k» - «m»**) for substituents **X** of the third type [**NH_2- (k)**, **OH- (L)**, **CH_3O- (m)**]. For amino group substituent «**n = k**», we have at our disposal the data for 6 rows; 13 remaining parameters **ΔNn** are calculated for the two oxygen-containing substituents («**n = L**» and «**n = m**»). The largest amount of data available for the first of them - the hydroxyl group («**n = L**»): for it there are parameters for 10 rows. A minimum amount of data available for the second oxygen-containing substituent - methoxyl group «**n = m**» - parameters for 3 rows.

Only three «full» rows (**N = 4, 8** and **9**) contain the experimental data for all three substituents **X** of the third type (**n = «k»** ÷ **«m»**). More for three rows (**N = 2, 3** and **5**) contain data for only two substituents **X** (for **n = «k»** and **«L»**); and four rows (**N = 6, 7, 10** and **11**) - only for one substituents **X**. Thus, the most comprehensive data available for the first (row **4**) and third (row **8** and **9**) types of the substituents **Y**. It allows us to make the most reasonable conclusions for these rows. The data for second and fourth types of substituents **Y** do not contradict these findings. For convenience of the discussion the data of Table 4 divided into two tables - № 5 and № 6.

4.2.4. The substances with substituents Y of first and second types (rows 2 – 7)

Here is a table 5, which is the upper part of Table 4.

Table 5

The data for substances with substituents Y of first and second types (rows 2 – 7).

Number of row	**Substituent Y**	**The $\Delta\delta^{H}_{CH3}$ values for substituent X in X-$C^1H^1_2$-C^2H^2(Y)-$C^3H^3_3$ (in mlrd.)**			
		-H (e)	**-NH_2 (k)**	**-OH (L)**	**-O-Me (m)**
2	**-CH_2-CH_3**	**0**	**+22**	**+35**	
3	**-CH_3**	**0**	**+10**	**+32**	
4	**-H**	**0**	**+21**	**+42** **+21**	**+31**
5	**-Ph**	**0**	**+1**	**+2**	
6	**-C(O)-CH_3**	**0**		**+23**	
7	**-C(O)-O-C_2H_5**	**0**		**+15**	

Let us consider first rows (**N** = **2** ÷ **4**) with alkyl substituents **Y** of the first type. Note that **all** the values of the parameters **ΔNn** of the full row **Δ4n** have the **positive sign**. This is consistent with our assumptions expressed above about larger electron accepting (than a hydrogen atom) properties of substituents **X** of the third type (columns **n = «k»** ÷ **«m»**), which cause the downfield shift of studied δ^{H}_{Nn} parameters in comparison with the corresponding parameters δ^{H}_{Ne} for monosubstituted compounds of general formula **Ne**: **X**-$C^1H^1_2$-$C^2H^2_2$-$C^3H^3_3$, [where **Y** = **H (e)**]. The same applies to the binomial rows **Δ2n** and **Δ3n**. However, based on the above considerations, we expected more significant values of positive in sign parameters **ΔNn**, than the observed values (**10** ÷ **40 mlrd.**).

What has been said for the rows of the first type (**N** = **1** ÷ **4**) fully applies to the rows (**N** = **5** ÷ **7**) of the second type, in which a carbon atom of substituent **Y** contains multiple (double) **C = C** or **C = O** bonds. For 4 compounds of this type, we are also seeing the presence of expected us positive by sign parameters **ΔNn**, but somewhat smaller in value than the above-considered (0 ÷ 30 **mlrd.** versus 10 ÷ 40 **mlrd.**).

Thus, the experimental values of the parameters **ΔNn** for 11 (out of 21 possible, 52.4%) of the considered compounds correspond to the above assumption about expected larger (than that of the hydrogen atom) the electron accepting properties of the substituents **X** of third-type (**n = «k»** - **«m»**) for compounds containing the substituents **Y** of first and second types. This provide a relatively small downfield shift of studied parameters $\boldsymbol{\delta^{H}_{Nn}}$ of considered compounds in comparison with the corresponding parameters $\boldsymbol{\delta^{H}_{Ne}}$ of monosubstituted compounds **Ne** of general formula **X**-$C^1H^1_2$-$C^2H^2_2$-$C^3\underline{H^3}_3$, [where **Y = H (e)**].

4.2.5. The substances with substituents Y of third and fourth types (rows 8 – 12)

Completely different behavior of the **ΔNn** parameter holds for compounds where **both substituents - and X, and Y are substituents of third type [NH_2- (k), OH- (L), CH_3O- (m)].** Actually, for the sake of compounds of this type we are considering whole class of 1,2-disubstituted propanes **Nn**.

Here is a table 6, which is the bottom part of Table 4.

Table 6

The data for substances with substituents Y of third and forth types (rows 8 – 12).

Number of row	**Substituent Y**	**The $\Delta\delta^{H}_{CH3}$ values for substituent X in X-$C^1H^1_2$-C^2H^2(Y)-$C^3\underline{H^3}_3$ (in mlrd.)**			
		-H (e)	**-NH_2 (k)**	**-OH (L)**	**-O-Me (m)**
8	**-NH_2**	**0**	**-20**	**-22**	**-40**
9	**-OH**	**0**	**-53**	**-46 -70**	**-55**
10	**-SH**	**0**		**-86**	
11	**-Cl**	**0**		**-20**	

The parameters ΔNn of all 6 available to us compounds, which are forming two complete rows **8n** and **9n**, are **negative in sign**, and quite large in absolute values (-20 ÷ -70 **mlrd.**).

What has been said for the series **8n** and **9n** (which contain substituents **Y** of the third type) fully applies to the remaining two compounds **10L** and **11L**, where substituents **Y** are substituents of the fourth type [**X** = **Cl** (row №**10**), and **X** = **Br** (row №**11**)]. For these 2 compounds are also observed the presence of negative parameter **ΔNn** values: a relatively small in absolute value (**Δ11L = -20 mlrd.**), and the second much more larger (**Δ10L = -86 mlrd.**). The last parameter has the greatest absolute value among the 36 negative parameters **ΔNn**, calculated for all the 93 we reviewed the 1-**X**,2-**Y**-disubstituted propanes **Nn** (except for the inexplicable value of «the hatched» parameter **Δ5j'**, of which mentioned above).

Thus, the experimental values of the parameters **ΔNn** for **all** 8 (out of 15, 53.3%) considered compounds in this section correspond to the previous idea of an unexpected behavior of the more electron accepting (than that of the hydrogen atom) **substituents X of third-type** (**n = «k» - «m»**) - heteroatoms of 2nd period - when substituents **Y** are also heteroatoms (as a third or fourth type of substituents **Y**). The simultaneous presence in the molecule of propane, two such substituents does not lead to the expected significant largest ***downfield shift***, but to a unique and quite large in size **upfield shift** of studied parameters $\boldsymbol{\delta^{H}_{Nn}}$ (rows **N = 8 - 12**, columns **n = «k» - «m»**) compared to respective parameters $\boldsymbol{\delta^{H}_{Ne}}$ of monosubstituted propanes of general formula $C^1H^1_3$-C^2H^2**Y**-$C^3\underline{H^3}_3$, [where **X = H (e)**].

Another important confirmation of the presence of anomalous effect of oxygen and/or nitrogen-containing substituents **X** in disubstituted propane molecules of the general formula **X**-$C^1H^1_2$-C^2H^2**Y**-$C^3\underline{H^3}_3$, which contain, as substituent **Y** one more fragment with **O** or **N** atom, bonded with the **C-2**, is the binomial row of **1-X,2**-nitropropanes **X**-$C^1H^1_2$-C^2H^2(**NO_2**)-$C^3\underline{H^3}_3$,which is denoted as **17n**. Due to the short length of this serie, which consists of only two compounds: 2-nitropropane (**17e**) and 2-nitropropanol (**17L**), we did not enter it into the overall review. For 2-

nitropropane **17e** in an additional source [4] the chemical shift of 6 methyl protons is equal: $\boldsymbol{\delta^{H}_{17e}}$ = 1.530 ppm [4]; and for 2-nitropropanol **17L** the value of the chemical shift of 3 methyl protons is equal: $\boldsymbol{\delta^{H}_{17L}}$ = 1.525 ppm [3]. The calculated differential parameter **Δ17L** is equal to: **Δ17L** = 1.525 - 1.530 = - 0.005 ppm = **- 5 mlrd.** It is **<u>negative in sign</u>**, though small in absolute value. Therefore, the calculated value **Δ17L** also **<u>confirms the above conclusion</u>**.

4. 2. 6. The dependence of the differential parameters ΔNn on structure of forth type of substituents X (columns «r - t» in the rows 1 – 12).

We assume that all 3 substituents X of the forth type [**SH-** (**r**), **Cl-** (**s**), **Br-** (**t**)], includes in its membership the electronegative atoms of third and forth periods – sulphur, chlorine and bromine, according to our assumption should **demonstrate the greatest electron accepting properties**. Therefore, **one would expect** that all **parameters ΔNn** for the **forth type of substituents X (n = r ÷ t)** will be **<u>positive in sign and very large in magnitude</u>**. For convenience of the discussion the values of the considered differential parameters **ΔNn** we are interested re shown in Table 7, which is a simplified part of Table 1.

Table 7

Num-ber of row	**Substituent Y**	**The $\Delta\delta^{H}_{CH3}$ values for substituent X in X-**$C^1H^1_2$-C^2H^2(**Y**)-$C^3\underline{H^3}_3$ (in **mlrd.**)				
		-H (e)	**-SH (p)**	**-Cl (r)**	**-Br (s)**	**-I (t)**
2	**$-CH_2-CH_3$**	**0**				**+108**
3	**$-CH_3$**	**0**	**+93**	**+123**	**+138**	**+130**
4	**-H**	**0**	**+87**	**+121**	**+131**	**+91**
7	**$-C(O)-O-C_2H_5$**	**0**			**+135**	
9	**-OH**	**0**	**+50**	**+72**	**+100**	
10	**-SH**	**0**	**+64**			
11	**-Cl**	**0**		**+95**	**+129**	
12	**-Br**	**0**		**+80**	**+115**	

We have only 18 (out of possible 48, 37.5%) parameters **ΔNn** in 8 of 12 discussed rows (rows **N = 2** ÷ **4, 7, 9** ÷**12**, columns **n = «k» - «m»**) for substituents X of the forth type [**SH-** (**r**), **Cl-** (**s**), **Br-** (**t**)]. For Br-atom as substituent X (column **n = s**), at our disposal are data for six rows; for Cl-atom as substituent X (column **n = r**) - data for five rows; for thiol group (**-SH**, column **n = p**) – for 4 rows and for iodine atom (column **n = t**) – the parameters **ΔNn** of only 3 rows.

Only for two full rows (№ **3** and № **4**) there are experimental data for all four substituents X of the fourth type (**n = «p»** ÷ **«t»**). More for a row № **9** we have data for three substituents X (**n = «p», «r»** and **«s»**); and another one of a row № **12** - only for two substituents X (**n = «r»** and **«s»**). Each of the two remaining parameters **ΔNn** (**Δ2t** and **Δ11r**) is the only parameter in the appropriate row. Thus, the most complete data are available for two rows (№№ **3** and **4**) and a little less for a third row (**9n**) of hydroxyl group as substituent Y, which allows us to do for these series most reasonable conclusions. Data for the remaining four rows do not contradict these findings.

So **<u>all ΔNn parameters</u>** of ***all 18 available to us compounds*** (both these forming two complete rows **3n** and **4n**, and a little less than the full row, trinomial row **9n**, and 5 others) have, as predicted, large in absolute magnitude (**+ 50** ÷ **+135 mlrd.**) positive values.

It is interesting to mark next. In both complete rows (**3n** and **4n**), as well as in a trinomial row **9n**, we mark the consistent growth of **ΔNn** values on the left side of row (**ΔNp** → **ΔNr** → **ΔNs**). In both full tetranomial rows we observe subsequent decrease of parameter **ΔNn** when going from parameter **ΔNs** (with **Br**-atom as substituent X) to the parameter **ΔNt** with an iodine atom as a substituent X (**n** = «**t**») in the right part of row (**ΔNs** → **ΔNt**).

Thus, the **positive values** of all without exception 17 **ΔNn** parameters for compounds with the substituents X of fourth type (**n** = «**r**» ÷ «**t**»), which do not depend on the structure of the substituents Y, **confirm above conclusions**.

* * *

So, when analyzing the series of 97 compounds $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3H^3_3$ becomes apparent that the **rule of additive effect of heteroatoms electronegativity** of located in the **adjacent (vicinal) position** relative to each other **substituents** X and Y on the **chemical shift** δ^{H}_{CH3} is **not performed in all cases**. Therefore it is possible to put forward the following proposition:

The heteroatoms of second period - N, O - in the **substituents** X and Y located **in vicinal position** in the 1-X,2-Y-disubstituted propanes $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3H^3_3$ **can interact with each other**. The **result** of this interaction is the **reduction of their summary electronegativity**. This effect **resembles (or is) well-known vic-anomeric effect** in its broadest interpretation.

As a **result** of this **effect** is **decrease** of methyl protons **signals** δ^{H}_{CH3} **downfield shift compared with the expected value (ie, its upfield shift).**

5. General conclusions

1. We have analyzed the protons chemical shifts values δ^{H}_{CH3} in the PMR spectra of 97 (of 192 possible, 50.5%) 1-X,2-Y-disubstituted propanes of general formula $X\text{-}C^1H^1_2\text{-}C^2H^2(Y)\text{-}C^3H^3_3$. We considered 12 series of these compounds, wherein the row number is determined by substituent Y. Each of these twelve series includes from 3 to 16 compounds with different substituents X. All substituents X and Y divided into four groups depending on the nature of the atom in the substituent that is bound to a propane skeleton of molecule. In the first two groups such atom is a carbon atom; in a first group it included in the saturated alkyl moiety (**Alk**); in the second group it is bonded with a double bond with one of the remaining atoms of the substituent. In the third and fourth groups such atom is heteroatom: in the third group - this is the atom of the second period - nitrogen or oxygen; in a fourth group – it is an atom of third (or fourth) periods: sulfur, chlorine, bromine, iodine.

2. We suggest the rule of the electronegativity (electropositivity) additive effect for located in the adjacent (vicinal) position relative to each other substituents X and Y on the chemical shift δ^{H}_{CH3}.

3. In 15 of 16 cases we observed the predicted changes of parameter δ^{H}_{CH3}, depending on the nature of the substituents X with any type of substituent Y.

4. The only exception is the case when *both substituents* X and Y are the heteroatoms of the second period - atoms **N** and **O**. In this case, instead of the expected downfield shift of δ^{H}_{CH3} **occurs upfield shift** of the parameter δ^{H}_{CH3} in all six studied examples.

5. To explain this phenomenon, we hypothesized the certain action of the well-known **vic-anomeric effect**, apparently occurring also for **parameters of ^{1}H NMR spectra**.

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Acknowledgements

We acknowledge the National Institute of Advanced Science and Technology (SDBS Web://:riodb 01.ibase.aist.go.jp/sdbs) for the given in the article data for ^{13}C NMR spectra.

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