Interaction between unbound fragments of molecule in esters of ω-arylaliphatic acids.

Volodymyr Mizyuk and Volodymyr Shibanov

Ukrainian Academy of Printing, Lviv, Ukraine, e-mail: *vlm46@mail.ru*

Abstract. The analysis of chemical shifts in ^{1}H NMR spectra of the ω-aryl fatty acids by general formula: $Ar\text{-}(CR^1R^2)_m\text{-}X\text{-}(CR^3R^4)_n\text{-}COOAlk$, where Alk = Me or Et, and X = N or O methyl and ethyl esters was made. The presence or absence of the aryl fragment influence on the alkoxy group was judged on the value of the basic spectral parameters - the chemical shifts of methyl protons ($\delta_{CH3}{}^H$) as well as ($\delta_{CH2}{}^H$ and $\delta_{CH3}{}^H$) in ethyl groups. There were developed and validated specific criteria for identifying such effect. We make the overall conclusion about high probability of the studied effect existence in esters of arylacetic and 3-arylpropionic acids.

Keywords: NMR ^{1}H spectra, ω-aryl fatty acids methyl and ethyl esters, basic spectral parameters, mean and additional experimental differential parameters, virtual differential parameters.

I. Introduction

While analyzing the peculiarities of NMR ^{1}H and ^{13}C spectra of different classes of organic compounds we suppose that under recording spectra conditions the intramolecular interactions between unbound fragments of molecule may take place through the space. The existence of mentioned interactions leads, to our mind, to the observed changes in spectra compared with anticipated (expected) values.

The schematic drawing of investigated molecule containing fragments "K-L-M" is represented in Fig. 1. The arbitrary division into the fragments is in accordance with functional principle and depends upon the formulated aim. The aim is the investigation of NMR spectral parameters of the fragment "M" depending upon the structure of the fragment "K". The absence of chemical bonds between atoms of the fragments "K" and "M" is an indispensable condition. Both fragments are bound by chemical bonds only with "medium" fragment "L", with its opposite sides.
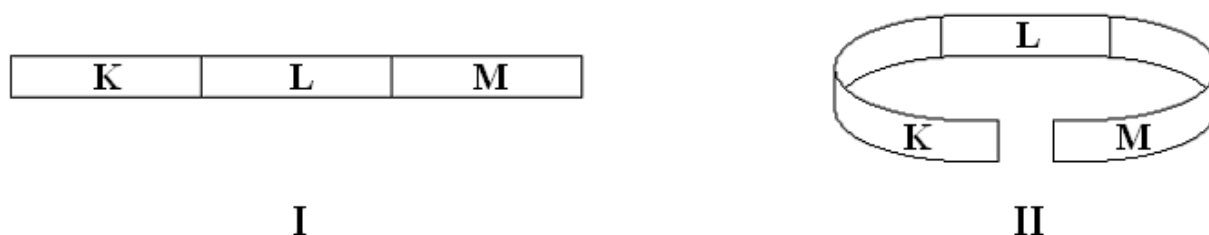

Fig.1

In the linear conformation **I** the interaction of unbound fragments "K" and "M" is absent. It is possible in the curved conformation **II**. To our mind, the deviation of spectral parameters of the fragment "M" from the anticipated values reveals about this.

The transition states with curved conformations, the same as **II**, are well-known in the synthetic chemistry, e.g. in the reactions of electrophylic cyclization or in substitution reactions proceeding with the transfer of reactive centre. Similar transition state was given in an article [1] describing NMR ^{17}O spectra of crowded alcohols, where authors had postulated through-space interaction in CH_3---O.

We suppose the following explanation of the observed phenomenon in accordance with the postulate: "*The possible interaction between two energy states* **occurs always** *under the given conditions if it* **leads to the decrease of the system total energy**". The changes of energy levels of two-component system taking place during their interaction are represented in Fig. 2. At the initial state "A" the interaction between energy levels of its components (A^1 and A^2) does not occur. The result is the system transition to its new state "B". In this connection two new energy levels (B^1 and B^2) are formed and new system occupies a lower energy level (state B^1).
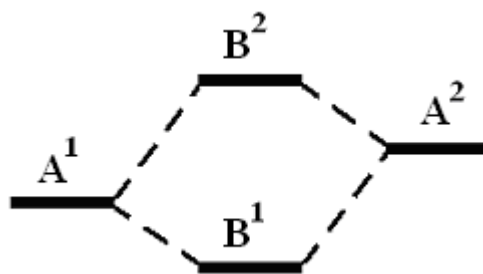

Fig. 2

It is logically to suppose that intramolecular interaction of unbound fragments of the molecule through the space in the conformation **II** leads to some energy gain (the decrease of the total energy of the system). It is the reason the interaction occurs.

The supposed interaction in the structures "K-L-M" is expressed in the change of expected values of the "M" fragment spectral parameters. It was postulated by us earlier [2, 3] for *para*-substituted alkylbenzenes by the general formula **III** (including monoalkylbenzenes, where X=H [2]). In the molecules of mentioned compounds the fragment "K" is the alkyl group (Alk) and the fragment "M" includes nuclei of atoms H-2 (H-6), H-3 (H-5), C-2 (C-6) and C-3 (C-5) of the phenyl ring.

In the second example – phenylsulfones **IV** – functional groups X are the fragments "K" and protons H-2, H-3 and H-4 [4, 5] are the fragments "M". One more example shows aryl-containing methyl and ethyl ethers **V**, where protons of alkoxyl groups are the fragments "M" and aryl groups (Ar) are the fragments "K" [6].

III   IV   V
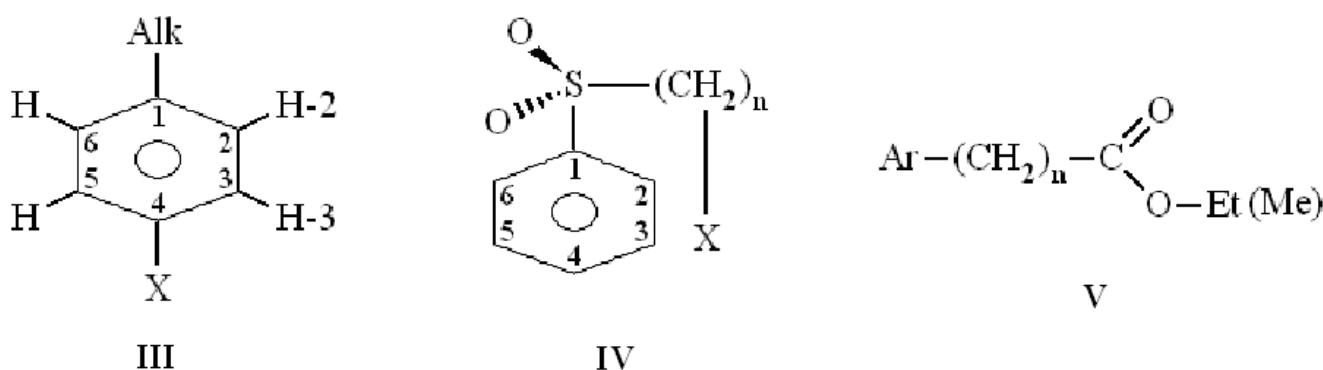
The same but not described earlier deviations from the anticipated values of δ^H parameters in the NMR ^{1}H spectra we also observed for ethers, acetales, alcohols, saturated alkanes, etc. The variety of compounds for which the described phenomenon takes place allows us to assume that **the observed results are widely spread** and **may be general for all classes of compounds**.

The present paper is the "comprehensive variant" of our previous report [6]. We examine spectral data of methyl and ethyl ethers of ω-aryl-containing aliphatic acids of the general formula Ar-$(CR^1R^2)_n$-COOAlk which allow to suppose (to our mind) the hypothetic interaction of unbound fragments "K" and "M" in these molecules.

II. Experimental

We used the data of **basic spectral parameters δ^H** taken from two comparable [7, 8] literature sources [9, 10]. The values of δ^H parameters are given there with the accuracy of 0.01 ppm and coincide with each other with the accuracy of 0.02 ppm. Such value was accepted by us as the measurements error. It means if the calculated absolute value of differential parameter $\Delta\delta^H$ (see below) is equal to 0.01 ppm, it will not be interpreted as a reliable result. So only parameters $\Delta\delta^H$ equal to 0.02 ppm by their absolute values or exceeding this value will be interpreted as reliable results and will be discussed.

III. Results and Discussion

The spectral parameters δ^H_{OAlk} of alkoxyl groups OCH_3 and OCH_2CH_3 were compared in two ways. The first one using virtual values is more obvious but less strict. The second one using only experimental data is more strict but less obvious.

We consider **some systematic deviations of experimental values (δ_{exp}^H) from anticipated values W (δ_{ant}^H = W; see below) are the most obvious criterion of the presence of supposed interaction between unbound fragments "K" and "M" in the molecules** of investigated esters. The **virtual differential parameters ΔW ($\Delta W = \delta_{exp}^H - \delta_{ant}^H$, i.e. δ_{exp}^H-W)** are introduced for the **quantitative comparison of deviations**.

The second set of **experimental differential spectral parameters** is stricter to our mind. They are denoted as $\Delta\delta_{OAlk}^{H,N}$ and calculated as a difference between experimental values: $\Delta\delta^H = \delta_{OAlk}^{H,№} - \delta_{OAlk}^{H,stand}$. The last value is the corresponding basic spectral parameter $\delta_{OAlk}^{H,stand}$ of the compound taken by us as a standard. **The advantage** of this set of differential parameters is using of **only experimental values** for the calculations. The main **disadvantage** is the **absence of evident physical meaning.**

"Anticipated values" of the basic spectral parameters are estimated virtual values and denoted by capital Roman letters, e.g. $W^{№}$. The numerical values of W parameters are approximate and open to question. They are equal to those supposed values of the chemical shifts of alkoxyl group protons which would take place in the case of absence of interaction between unbound fragments "K" and "M" in the molecules of investigated compounds. We consider them as "virtual" values because under the "anticipated value" term we mean logically founded virtual value of the basic spectral parameter "W", i.e. non-existing value of the signal interesting for us which we would expect to see in NMR ^{1}H spectrum.

**Introduced symbols.** The investigated compounds are enumerated by bold Arabic numerals. If the general formulas of the row of related compounds are denoted by mentioned numerals, we add bold Roman letters to denote the specific compound, e.g. **12c**. To prevent confusion we denoted methyl and ethyl ethers of the same acid by different numerals. The substituents in the phenyl ring are denoted as "S".

Basic spectral parameters. Chemical shifts of protons of methyl and methylene groups are taken from [9, 10] and denoted as $\delta_{OAlk}^{H,№}$. The superscript includes letter indicating the proton spectrum "H", number of compound denoted by bold and literature source in square brackets. The subscript includes group to which protons (CH$_2$ or CH$_3$) belong, e.g. $\delta_{CH2}^{H12c[10]}$.

Differential "**experimental**" spectral parameters are denoted by the symbol "$\Delta\delta_{OAlk}^{H,№}$" It is the difference between two experimental basic parameters: e.g. $\Delta\delta_{CH2}^{H12c} = \delta_{CH2}^{H12c} - \delta_{CH2}^{HN}$. The subtrahend is the parameter of the standard compound **N**. Such parameters are denoted as "$\Delta\delta_{CH3}^{H}$" and "$\Delta\delta_{CH2}^{H}$" and named as the "**main experimental differential parameters**".

Sometimes it is advisable to use "an additional standard compound" **N1** which may vary in every individual case. Then calculated "additional differential spectral parameters" are denoted as $\Delta^1\delta^H$, e.g. $\Delta^1\delta_{CH2}^{H12c} = \delta_{CH2}^{H12c} - \delta_{CH2}^{HN1}$. If it is necessary, one more additional parameter $\Delta^2\delta^H$ may be used.

"Anticipated values" of differential spectral parameters, which we also call as virtual parameters, are calculated evaluation values. They are denoted by symbol "ΔW", e.g. ΔW_{CH2}^{12c}. It is the difference between experimental basic parameter δ_{OAlk}^H and virtual anticipated parameter W: $\Delta W_{CH2}^{12c} = \delta_{CH2}^{H12c} - W_{CH2}^{12c}$.

III.1. Criteria of the presence of supposed interaction between unbound fragments "K" and "M" in the molecules of investigated esters.

On the basis of previous reasoning [4, 5] we chose the following criteria for the cases when "K" fragment is aryl group:

1. **Negative values of virtual differential parameters** ΔW. The greater values mean the stronger interaction.

2. If **the absolute values** of ΔW parameters, i.e. $|\Delta W|$, **are close to zero**, the founded assumptions about the presence or absence of mentioned interaction is maid with difficulty. To our mind, in this cases the interaction is absent. The examples may be $|\Delta W|$ parameters which are close to zero in a case of α-ketoacids esters **14b** and **15** (see below).

3. **The negative values of the main "experimental" differential parameters $\Delta\delta^H_{OAlk}$**. The greater absolute value of the negative parameter means the stronger supposed interaction. However we don't exclude the cases when supposed interaction may take place at the positive value of $\Delta\delta^H_{OAlk}$ parameter.

4. **The negative values of additionnal "experimental" differential parameters $\Delta^1\delta^H_{OAlk}$**, because these parameters are introduced for the compounds similar by structure.

III.2. The division of investigated compounds into classes accordingly to their structural peculiarities.

For uniformity purposes let us consider all investigated esters as substituted acetates. Then depending on the amount of substituents X, Y and Z introduced into acyl group we present three types of compounds of the general formulas 1-3:

CH₂X-COO-Alk	CHXY-COO-Alk	CXYZ-COO-Alk
1	**2**	**3**
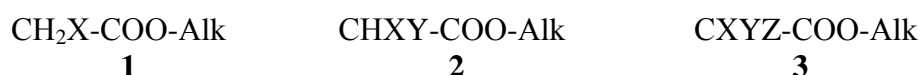
One of the substituent in the fragment "K" must necessarily present an aryl group (for example, "X" in the formula **1** or "X", "Y", "Z" in the formulas **2-3**). The middle part of the molecule is the fragment "L" (for example, $-CH_2COO-$ fragment in the formula **1**). The alkyl group "Alk" (methyl or ethyl) is the fragment "M" for all three compounds.

To calculate the experimental differential prameters $\Delta\delta^H_{OAlk}$ we chose the following compounds as **standards**: methylacetate **4a** ($\delta^H_{CH3}{}^{4a}$ = 3.66 ppm [9,10]; $\Delta\delta^H_{CH3}$ = 0) for methyl ethers and ethylacetate **5a** ($\delta^H_{CH2}{}^{5a}$ = 4.12 ppm, $\Delta\delta^H$ = 0 and $\Delta\delta^H_{CH3}{}^{5a}$ = 1.26 ppm [9,10]; $\Delta\delta^H$ = 0) for ethyl ethers. The reasons of such choice are given below.

| **CH₃-COO-CH₃**	**CH₃-COO-CH₂-CH₃**
4a	**5a**
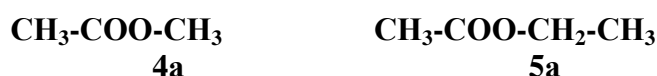
We assumed the following order of examination for the esters of ω-arylsubstituted acids of the general formula Ar-(CR¹R²)ₙ-COOAlk. At first we examine the compounds in which the fragments "K" and "M" are maximally close. Obviously in such a case the fragment "L" should be the shortest (at n=0), so it turn into fragment "–COO-". The esters of aromatic acids belong to such compounds and carboxyl group is the fragment "L". Then we lengthen the fragment "L" step-by-step. We introduce unsubstituted (or substituted) methylene groups of the general formula $-(CR^1R^2)-$ into the fragment "L": at first at n=1, then at n=2, etc. Since some necessary data are absent in the Refs. [9, 10] we decide to examine also the esters of ω-substituted acids in which one of the methylene groups CR^1R^2 is substituted for heteroatom N or O. The general formula of all investigated compounds is Ar-$(CR^1R^2)_p$-Het-$(CR^1R^2)_r$-COOAlk, where p + r = n-1.

III.3. Alkyl esters of aromatic acids Ar-COO-Alk (benzoates and α-naphthoates).

Benzoates (including those substituted into a ring, i.e. containing substituted phenyl group - C_6H_4-S) should be refered to the **triple-substituted acetates**, i.e. compounds of type 3. The fragment of phenyl ring C_6H_5 (or C_6H_4-S¹) is considered as three substituents (X+Y+Z). The "virtual" parameters W and ΔW for the compounds **6-8** are not examined because we could not find criteria for their logical evaluation.

III.3.1. Methyl ethers of aromatic acids: benzoates 6 and 1-naphthoate 7.

$$S^1S^2C_6H_3\text{-COO-CH}_3 \qquad \alpha\text{-C}_{10}H_7\text{-COO-CH}_3$$
$$\textbf{6} \qquad\qquad \textbf{7}$$
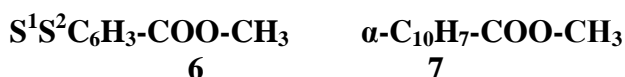
III.3.1.1. Methyl benzoates 6.

The following values of basic spectral parameters are given in the literature for unsubstituted (S=H) methylbenzoate Ph-COOCH$_3$ **6a** (S=H): $\delta^H_{CH3}{}^{6a[9]}$ = **3.90ppm** and $\delta^H_{CH3}{}^{6a[10]}$ = **3.886 ppm.** For the calculations we assume the averaged value $\delta^H_{CH3}{}^{6a}$ = 3.89 ppm. Then the calculated "experimental" differential spectral parameter is equal to $\underline{\Delta\delta^H_{CH3}{}^{6a}}$ = **3.89 – 3.66 = +0.23 ppm.**

For methylbenzoates **6** substituted into a phenyl ring the values of differential parameters $\Delta\delta^H_{CH3}$ depend upon the nature of substituent S and its position in the phenyl ring. However almost for all types of substituents S the differential parameter $\Delta\delta^H_{CH3}$ is positive and has value of 0.25±0.10 ppm. For example, for methyl para-anisate with metoxy-group **6b** (S=4-OCH$_3$), the value $\underline{\boldsymbol{\delta^H_{CH3}{}^{6b[10]}}\textbf{ is}}$ **equal to 3.845 ppm** (rounded to 3.85 ppm); hence the parameter $\underline{\Delta\delta^H_{CH3}}$ = **3.85 – 3.66 = +0.19 ppm.** Let us also calculate the additional differential spectral parameter $\Delta^1\delta^H$. The methyl benzoate **6a** unsubstituted into the phenyl ring is chosen as auxiliary standard compound **N1**. The value of additional differential parameter $\Delta^1\delta^H$ is equal to: $\Delta^1\delta^H_{CH3}{}^{6b[10]}$ = 3.85 – 3.89 = **-0.040 ppm.**

For methyl para-nitrobenzoate **6c** with electron-acceptor nitrogroup (S=4-NO$_2$) ($\delta^H_{CH3}{}^{6c[10]}$ = **3.987** ppm, rounded to 3.99 ppm) we calculated the "experimental" parameter $\underline{\Delta\delta^H_{CH3}\textbf{ = +0.33 ppm}}$ which is more greater than parameter $\Delta\delta^H_{CH3}{}^{6a}$ =**+0.23 ppm** but it is also in the declared interval. The value of additional differential parameter $\Delta^1\delta^H$ is equal to: $\Delta^1\delta^H_{CH3}{}^{6c[10]}$ = 3.99 – 3.89 = **+0.10 ppm.**

Taking as an example three isomeric methyl brombenzoates (S = Br, **6d, 6e** and **6f**) we examine the effect of substitutent position in the phenyl ring on the spectral parameters of methyl group. The values of all three parameters are approximately equal: for ortho-isomer $\underline{\boldsymbol{\delta^H_{CH3}{}^{6d[10]}\textbf{ = 3.914ppm,}}}$ for meta-isomer $\underline{\boldsymbol{\delta^H_{CH3}{}^{6e[10]}\textbf{ = 3.918 ppm}}}$, for para-isomer $\underline{\boldsymbol{\delta^H_{CH3}{}^{6f[10]}\textbf{ = 3.909 ppm}}}$. The values of corresponding differential parameters $\Delta^1\delta^H$ are equal to: $\Delta^1\delta^H_{CH3}{}^{6d[10]}$ = 3.914 – 3.89 = **+0.024ppm**, $\Delta^1\delta^H_{CH3}{}^{6e[10]}$ = 3.918 – 3.89 = **+0.028ppm**, $\Delta^1\delta^H_{CH3}{}^{6f[10]}$ = 3.909 – 3.89 = **+0.019 ppm**. While analyzing these three examples we conclude that the main factor affecting the chemical shift of metoxy group in the substituted methylbenzoates **6** is the substituent nature. The position of ubstituent in the ring has less influence.

III.3.1.2. Methyl ethers of naphthoic acids: methyl 1-naphthoate (7).

In methyl 1-naphthoate **7** ($\underline{\boldsymbol{\delta^H_{CH3}{}^{7[10]}\textbf{ = 3.93 ppm}}}$) the value of "experimental" parameter $\underline{\Delta\delta^H_{CH3}{}^{7}}$ is even greater than that in methyl benzoate **6a** an equal to **+0.27 ppm**.

Hence, **instead of expected decrease** of "experimental" **parameter** $\Delta\delta^H_{CH3}$ down to its negative values (which should take place in the existence of intramolecular interaction with aryl fragment, as it was said above) in the most cases we found the **essential increase** of the parameter up to the values $\Delta\delta^H_{CH3}$ = 0.2 ÷ 0.35 ppm. It is logically to suppose that **the intramolecular interaction** thruogh the space of aryl and methyl groups **is absent** for methyl ethers of aromatic acids.

III.3.1.3. Methyl ethers of substituted aromatic acids in which aryl group is a substituent: methyl 2-tolylbenzoate (6g).

$$\text{Ortho-(4-CH}_3\text{-C}_6H_4)\text{-C}_6H_4\text{-COO-CH}_3$$

Spectral data of the esters of substituted benzoic acids in which aryl groups are substituents "S" are in a great contrast with the parameters of above-mentioned substituted benzoates **6a-6f.** The typical example is methyl 2-(para-tolyl)benzoate **6g** ($\underline{\boldsymbol{\delta^H_{CH3}{}^{6g[10]}\textbf{ = 3.653 ppm}}}$). Its calculated "experimental"

differential parameter **is negative** and equal to $\underline{\Delta\delta^H_{CH3}}^{6g}$ = 3.653 − 3.66 = **-0.007 ppm**. As it was mentioned above, the **negative value** of **calculated main differential parameter** indicates the **presence** of required **interaction**. The additional differential spectral parameter $\Delta^1\delta^H$ relatively to methyl benzoate **6a** is equal to: $\Delta^1\delta^H_{CH3}{}^{6g[10]}$ = 3.653 − 3.89 = **-0.237** ppm. The order of this value differs from the value of above-mentioned additional differential parameters of substituted benzoates **6b-6f** which are in the interval from -0.050 to +0.100 ppm.

We presume that **phenyl group located in ortho-position to esteric fragment in 6g** is situated in the space in a position **convenient for the effect on investigated metoxy** group. As a result we observe the **great shift** to the **high field** of the signal of methyl group protons of metoxyl fragment.

III.3.2. Ethyl ethers of aromatic acids.

$$S^1S^2C_6H_3\text{-COO-CH}_2\text{-CH}_3$$
8
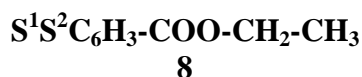
In oxyethyl fragment of ethyl ethers of aromatic acids **8** the methyl group is situated farther from aryl fragment (by one methylene group) than that in methyl benzoates **6**. Therefore we consider it as "**outlying**" group (in contrast to "**nearby**" methylene group). It is the reason we expect the decrease of aryl fragment effect on the methyl group in etoxyl fragment of ethylbenzoates **8** compared with the effect on methylene group.

In unsubstituted ethylbenzoate **8a** (S=H, $\delta^H_{CH2}{}^{8a[9]}$ = **4.37 ppm**, $\delta^H_{CH3}{}^{8a[9]}$ = **1.38 ppm**) the value of experimental differential parameter of "nearby" methylene group $\underline{\Delta\delta^H_{CH2}}^{8a}$ is even greater than that in methyl benzoate **6a** and equal to **4.37 − 4.12 = +0.25 ppm**. For ethyl anisate **8b** (S=4-OCH$_3$) we calculate the following "experimental" parameters $\Delta\delta^H_{OAlk}{}^{8b}$: $\underline{\Delta\delta^H_{CH2}}^{8b[10]}$ = **+0.22ppm** and $\underline{\Delta\delta^H_{CH3}}^{8b[10]}$ = **+0.11ppm**. For ethyl para-nitrobenzoate **8c** (S=4-NO$_2$): $\underline{\Delta\delta^H_{CH2}}^{8c[10]}$ = **+0. 32 ppm** and $\underline{\Delta\delta^H_{CH2}}^{8c[10]}$ = **+0.18 ppm**.

In accordance with above-mentioned criteria due to the ***great positive values of "experimental" differential spectral parameters*** $\Delta\delta^H_{Alk}$ we may conclude that ***in unsubstituted methyl benzoate 6a, in unsubstituted ethyl benzoate 8a and in their analogues substituted in phenyl ring (except those cases when S=Ar), as well as in methyl 1-naphthoate 7 the intramolecular interaction of unbound aryl and alkoxyl fragments through the space is absent. Probably the small length of the fragment "L" (–COO– group) does not allow to molecule parts to come close in the space with the aim of effective interaction.***

In those cases when aryl group is the substituent in ortho-position, the mutual location of aryl groups with the alkyl group of alkoxyl fragment in the space allows to realize the interaction which causes the considerable shift of $\delta^H_{Alk.}$***signal to the high field.***

III.4. Alkyl arylacetates.

Here we consider the compounds of the general formula Ar-$(CR^1R^2)_n$-COO-Alk (where n = 1). The aryl and carboxyl groups are separated in them by one unsubstituted (or substituted) methylene group CR^1R^2 (i.e. -CR^1R^2-COO- is the fragment "L"). The anticipated basic spectral parameters W may be evaluated for the mentioned compounds. Let us introduce the evaluation criteria for W values.

III.4.1. Evaluation of anticipated (virtual) basic spectral parameters W.

To evaluate the anticipated values of basic parameters W let us consider three main rules describing the influence of substituents X, Y and Z in substituted acetates of the general formulas **1-3** on the chemical shifts of alkyl groups protons. These rules are partially confirmed by the results for benzoates **6-8**.

1. Electron-dononating substituents X, Y, Z, e.g. alkyl groups, in the compounds **1-3** slightly shift the signals of alkoxyl protons δ^H_{OAlk} to the high field. It leads to the appearance of small by value

and negative by sign "experimental" parameters $\Delta\delta^H_{OAlk}$. For example, basic parameters of methyl and ethyl ethers of trimethylacetic acid are equal to: $\delta^H_{CH3}{}^{[9]}$ = **3.65 ppm**; $\delta^H_{CH2}{}^{[9]}$ = **4.11ppm**; $\delta^H_{CH3}{}^{[9]}$ = **1.25 ppm**. All three **main differential parameters $\Delta\delta^H_{OAlk}$** are equal to **-0.01 ppm**.

On the contrary, electron-accepting substituents X, Y and Z considerably shift the δ^H_{OAlk} signal to the low field. It leads to the considerable positive values of "experimental" differential parameters $\Delta\delta^H_{OAlk}$. It was shown in the case of benzoates **6** that the stronger electron-acceptor properties of the substituent X, the higher values of the parameter $\Delta\delta^H_{OAlk}$. Usually the increase of parameter $\Delta\delta^H_{Oalk}$ correlates with the increase of electronegativity by Poling of the substituents X, Y and Z. For example, in the row of monohaloidsubstituted ethylacetates $X-CH_2-COOCH_2CH_3$ (X = Hal) we calculated values of the main differential parameters $\Delta\delta^H_{CH2}$ for different substituents using data from [9]: **+0.08 (I), +0.12 (Br), +0.14 (Cl), +0.16 (F)**. Parameters $\Delta\delta^H_{CH3}$ are equal to: **+0.02 (I), +0.05 (Br), +0.05 (Cl), +0.06 (F).**

2. **The increase of $\Delta\delta^H$ parameters also takes place while hydrogen atoms are successively substituted for several electron-acceptor substituents X, Y and Z, i.e. while accumulation of electron-acceptor substituents. For example, in the row** $CH_3COOAlk \rightarrow CH_2XCOOAlk \rightarrow CHXYCOOAlk \rightarrow CXYZCOOAlk$**, values of $\Delta\delta^H_{CH3}$ in the row of chlorsubstituted methyl acetates (X=Y=Z=Cl) and calculated using data from [9] are**: CH_3COOCH_3 ($\Delta\delta^H$ = 0) $\rightarrow CH_2ClCOOCH_3$ ($\Delta\delta^H$ = +0.15 ppm) $\rightarrow$ $CHCl_2COOCH_3$ ($\Delta\delta^H$ = +0.24 ppm) $\rightarrow CCl_3COOCH_3$ ($\Delta\delta^H$ = +0.35 ppm).

3. If there are several methylene groups between the substituent X and carbaloxyl group (in the case of substituted acetates $XCH_2COOAlk$ there is one group), the influence of the sunstituent X on the differential parameters $\Delta\delta^H_{OAlk}$ decreases as far as amount of methylene groups increases. Thus, it would be more correctly to such esters perhaps not as acetates, but as propionates, butyrates, etc. On the other hand, such esters as methyl 3-nitropropionate $O_2NCH_2CH_2COOCH_3$ and methyl 4-nitrobutyrate $O_2NCH_2CH_2CH_2COOCH_3$ may be also considered as substituted acetates $XCH_2COOAlk$, where the substituents X are not nitrogroups but the fragments O_2NCH_2- and $O_2NCH_2CH_2$-. Then the influence of NO_2 functional group on the value of differential parameters $\Delta\delta^H$ decreases proportionally to the amount of methylene groups between the functional group and carbaloxyl group: $O_2NCH_2COOCH_3$ **($\Delta\delta^H_{CH3}{}^{[9]}$ = +0.21 ppm)** $\rightarrow$ $O_2NCH_2CH_2COOCH_3$ **($\Delta\delta^H_{CH3}{}^{[9]}$ = +0.09 ppm)** $\rightarrow$ $O_2NCH_2CH_2CH_2COOCH_3$ **($\Delta\delta^H_{CH3}{}^{[9]}$ = +0.04 ppm**). We evaluate the value of "attenuation factor" as 2÷3 (average value is 2.5) per one introduced methylene group. Therefore in the further calculations we assumed that "**attenuation factor" is 2.5 per one methylene** group.

The same situation is in the above-mentioned examples for ethyl benzoates **8**. The values of "experimental" parameter of "outlying" methyl group $\Delta\delta^H_{CH3}$ are smaller in few times compared with the parameter of "nearby" methylene group $\Delta\delta^H_{CH2}$. The latter is comparable with the parameter $\Delta\delta^H_{CH3}$ of methyl ethers **6** which is also "nearby" parameter.

III.4.2. Possible additivity of increments of the substituents X, Y and Z in the compounds of the general formulas 2 and 3.

To calculate the anticipated values of the basic parameter W of polysubstituted compounds of the general formulas 2 and 3 it is advisable to use the simplest approach assuming the existance of approximate additivity of the influence of every three substituents X, Y and Z on the value of alkyl group chemical shifts. It is calculated by the formula (1):

$$W = \delta^H_{Alk}{}^N + i_X + i_Y + i_Z \tag{1}$$

For example, to calculate every from two "virtual" anticipated values W (W_{CH2} и W_{CH3}) in triple-substituted ethyl acetate **3 (R=Et)** we add three increments i_X, i_Y и i_Z to the basic spectral parameter δ^H_{Alk} in standard ethyl acetate **5a** (δ^H_{CH2} = 4.12 ppm, δ^H_{CH3} = 1.26 ppm). The increments are defined by the nature of substituents X, Y and Z and characterize their influence on the spectral parameter δ^H_{Alk}. These sets of increments are different for the calculations of every W_{CH2} and W_{CH3} parameters. For the "nearby" parameter W_{CH2} they are considerably greater than those for "outlying" W_{CH3} parameter. The obtained sum should be approximately the same as anticipated value of the virtual parameter W.

We tried to confirm the adaptability of such approach by the experiments. Since we could not find in the literature sources [9, 10] NMR ^{1}H spectra for ethylacetate **3** with three different substituents X, Y and Z, we decided to examine the approach taking as an example disubstituted ester of the general formula **2**, namely ethyl 2,3-dibrompropionate **5b** (X = Br и Y = CH$_2$Br, Z = H):

<div align="center">

Br-CH$_2$-CHBr-COO-CH$_2$-CH$_3$
5b

</div>
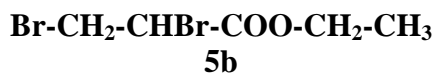
To calculate the both increments i$_X$ and i$_Y$ we compare basic parameters δ^H_{Alk} in pairs containing monosubstituted and unsubstituted acetates. In the first pair ethyl bromacetate **5c** (X = Br, Y = Z = H) is chosen as monosubstituted acetate and ethyl acetate **5a** − as unsubstituted one. The second pair consists of ethyl 3-brompropionate **5d** (X = H, Y = CH$_2$Br, Z = H) and ethyl acetate **5a**. The following values are represented in [9, 10]: for **5c** $\boldsymbol{\delta^H_{CH2}}^{\textbf{5c[9]}} = \textbf{4.24ppm}$ and $\boldsymbol{\delta^H_{CH2}}^{\textbf{5c[10]}} = \textbf{4.237ppm}$; $\boldsymbol{\delta^H_{CH3}}^{\textbf{5c[9]}} = \textbf{1.31 ppm}$ and $\boldsymbol{\delta^H_{CH3}}^{\textbf{5c[10]}} = \textbf{1.305ppm.}$ For **5d**: $\boldsymbol{\delta^H_{CH2}}^{\textbf{5d [9]}} = \textbf{4.19 ppm}$ and $\boldsymbol{\delta^H_{CH2}}^{\textbf{5d [10]}} = \textbf{4.192 ppm}$; $\boldsymbol{\delta^H_{CH3}}^{\textbf{5d [9]}} = \textbf{1.28 ppm}$ and $\boldsymbol{\delta^H_{CH3}}^{\textbf{5d[10]}} = \textbf{1.286 ppm.}$ For the calculations we assume averaged values of basic spectral parameters: $\delta^H_{CH2}{}^{5c} = 4.24$ ppm, $\delta^H_{CH3}{}^{5c} = 1.30$ ppm; $\delta^H_{CH2}{}^{5d} = 4.19$ ppm, $\delta^H_{CH3}{}^{5d} = 1.28$ ppm.

The values of increments $\mathbf{i_X^{Br}}$ (X = Br) and $\mathbf{i_Y^{CH2Br}}$ (Y = CH$_2$Br) are calculated in accordance with formula (1): for methylene group $\mathbf{i_X^{Br}}_{CH2} = 4.24 − 4.12 = \textbf{+0.12 ppm}$, $\mathbf{i_Y^{CH2Br}}_{CH2} = 4.19 − 4.12 = \textbf{+0.07 ppm}$; for methyl group $\mathbf{i_X^{Br}}_{CH3} = 1.31 − 1.26 = \textbf{+ 0.05 ppm}$, $\mathbf{i_Y^{CH2Br}}_{CH3} = 1.28 − 1.26 = \textbf{+ 0.02 ppm}$.
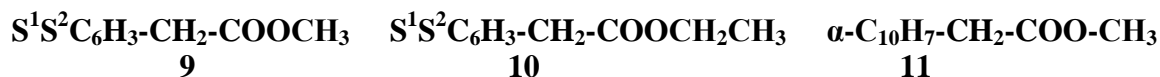
Using calculated increments and formula (1) we calculate the virtual anticipated basic parameters W^{5b} for ethyl 2,3-dibrompropionate **5b**. For methylene group W$^{5b}_{CH2}$ = 4.12 + 0.12 + 0.07 = 4.31 ppm; for methyl group W$^{5b}_{CH3}$ = 1.26 + 0.05 + 0.02 = 1.33 ppm.

In the sources [9, 10] the experimental values of basic spectral parameters for the compound **5b** are represented: $\boldsymbol{\delta^H_{CH2}}^{\textbf{5b [9]}} = \textbf{4.30 ppm}$ and $\boldsymbol{\delta^H_{CH2}}^{\textbf{5b [10]}} = \textbf{4.298 ppm}$, $\boldsymbol{\delta^H_{CH3}}^{\textbf{5b[9]}} = \textbf{1.33 ppm}$ and $\boldsymbol{\delta^H_{CH3}}^{\textbf{5b[10]}} = \textbf{1.33 ppm}$. The calculated average values are: $\delta^H_{CH2}{}^{5b}$ = 4.30 ppm and $\delta^H_{CH3}{}^{5b}$ =1.33 ppm. Comparing calculated virtual (W) and experimental ($\delta^H_{Alk}{}^{5b}$) parameters, we observe their very good agreement: the coincidence of W$^{5b}_{CH3}$ and $\delta^H_{CH3}{}^{5b}$ parameters is complete; parameters W$^{5b}_{CH2}$ and $\delta^H_{CH2}{}^{5b}$ differ by only 0.01 ppm.

Hence, we may conclude that the method of increments additivity is suitable for calculations of **anticipated parameters W in polysubstituted compounds of the general formulas 2 and 3.**

III.4.3. Alkyl arylacetates Ar-CH$_2$COOAlk without other substituents (Y=Z=H), except aryl group (X = Ar)

In the formulas **9-11** the aryl group is considered as the substituent X and both hydrogen atoms of CH$_2$ group may be considered as the substituents Y and Z, i.e. Y=Z=H. In the compounds **9, 10** the aryl group is monosubstituted fragment [S^1-C$_6$H$_4$-], and (S^2=H); or disubstituted fragment [S^{1}S^{2}C$_6$H$_3$-].

<div align="center">

S^{1}S^{2}C$_6$H$_3$-CH$_2$-COOCH$_3$ **S^{1}S^{2}C$_6$H$_3$-CH$_2$-COOCH$_2$CH$_3$** **α-C$_{10}$H$_7$-CH$_2$-COO-CH$_3$**
9 **10** **11**

</div>

III.4.3.1. Evaluation of anticipated increments i$_X^{Ph}$ of phenyl group in 9a, 10a.

It is known that aryl groups are weakly or middle electron-acceptor ones. They do not exceed iodine atom by their electron-accepting strength. Therefore, taking into account the first item in Section 1.2 we may expect such aryl groups as phenyl, substituted phenyl and α- and β-naphthyl grousp lead to the relatively small positive increment **i$_X^{Ph}$**. Its value we evaluate within the range of +0.07÷+0.10 ppm.

The same conclusion may be done using the other approach. Taking into account the values of "nearby" parameters $\Delta\delta^H_{CH3}{}^{6a} \approx \Delta\delta^H_{CH2}{}^{8a} \approx$ +0.20÷0.25 ppm in unsubstituted benzoates **6a** and **8a** and assuming the "attenuation factor" equal to 2.5 we may evaluate the value of "outlying" parameter

$\Delta\delta^H_{CH3}$[8a] of ethyl group and compare the calculated and experimental values. After the division of the first value ($\approx$ +0.20÷0.25 ppm) by the second one (2.5) we obtain the value $\Delta\delta^H_{CH3}$[8a] equal to +0.08÷+0.10 ppm. This value is within the interval (+0.07÷+0.10 ppm). Therefore, **for phenyl group C_6H_5** we assume the **increment value for "nearby" parameter equal to 0.08 ppm** and will use it for the further calculations accordingly to the formula (1).

The values of i_X increment for "outlying" methyl groups of etoxyl fragment in ethyl ethers taking into account the "attenuation factor" are equal to: $\mathbf{i_X^{Ph}{}_{CH3} = \Delta W_{CH3} = 0.08 / 2.5 \approx +0.03\ ppm.}$

III.4.3.2. Methyl arylacetates Ar-CH₂COOCH₃.

III.4.3.2.1. Methyl phenylacetate 9a.
C_6H_5-CH₂-COOCH₃
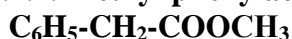
<u>Experimental data:</u> $\boldsymbol{\delta^H_{CH3}{}^{9a[9]} = 3.64\ ppm}$ and $\boldsymbol{\delta^H_{CH3}{}^{9a[10]} = 3.653\ ppm.}$ For the calculations we use averaged value of $\boldsymbol{\delta^H_{CH3}{}^{9a} = 3.65\ ppm}$.

<u>Calculated parameters.</u> The main experimental differential parameter $\boldsymbol{\underline{\Delta\delta^H_{CH3}{}^{9a}} = 3.65 - 3.66 = \underline{-0.01\ ppm.}}$

<u>Virtual parameters.</u> Using $\mathbf{i_X^{Ph}} = 0.08$ ppm for phenyl group in methyl esters, the value of <u>anticipated basic parameter $W_{CH3}{}^{9a}$</u>, calculated by formula (1) is equal to the sum of experimental basic parameter $\delta^H_{CH3}{}^{4a}$ of methylacetate **4a** and increment $\mathbf{i_X^{Ph}}$, i.e.: $\mathbf{W^H_{CH3}{}^{9a} = 3.66 + 0.08 = 3.74\ ppm.}$

Then <u>the virtual differential parameter ΔW_{CH3}</u> is equal to: $\underline{\Delta W_{CH3} = 3.65 - 3.74 = \mathbf{-0.09\ ppm.}}$

III.4.3.2.2. Methyl 1 naphthylacetate 11.
α-$C_{10}H_7$-CH₂-COO-CH₃.
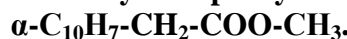
<u>Experimental data:</u> $\boldsymbol{\delta^H_{CH3}{}^{11[9]} = 3.63\ ppm}$ and $\boldsymbol{\delta^H_{CH3}{}^{11[10]} = 3.59\ ppm.}$ The averaged value is $\delta^H_{CH3}{}^{11} = 3.61$ ppm.

<u>Calculated parameters.</u> Main "experimental" differential parameter $\boldsymbol{\Delta\delta^H_{CH3}{}^{11} = 3.61 - 3.66 = -0.05\ ppm.}$

<u>Virtual parameters.</u> 1-Naphthyl group has more electron-accepting properties than phenyl group. The values of $\boldsymbol{\delta^H_{CH3}{}^{6a[10]} = 3.89\ ppm}$ and $\boldsymbol{\delta^H_{CH3}{}^{7[10]} = 3.93\ ppm}$ reveal about this fact. Therefore we assume that for 1-naphthyl group 1-$C_{10}H_7$ the value i_X is no less (greater or equal) than the same parameter of phenyl group, i.e. $\mathbf{i_X^{1\text{-}Naft} \geq 0.08\ ppm}$. Then the value $\underline{\mathbf{W^H_{CH3}{}^{11}}}$ is no less than $\mathbf{3.66 + 0.08}$ $= \underline{\mathbf{3.74\ ppm}}$.

<u>Virtual differential parameter ΔW_{CH3}</u> is no less than: $\underline{\boldsymbol{\Delta W_{CH3} = 3.61 - 3.74 = \text{-}0.13\ ppm.}}$

Let us stress that "experimental" differential parameter $\Delta\delta^H_{CH3}{}^{11}$ in methyl 1-naphthylacetate **11** (-0.05 ppm) is greater by absolute value than the same parameter $\Delta\delta^H_{CH3}{}^{9a}$ in methyl phenylacetate **9a** (-0.01 ppm).

Thus, **small by absolute value** (till 0.05 ppm) **"experimental" differential parameters $\Delta\delta^H_{CH3}$** in unsubstituted methyl arylacetates **9a** and **11** have **negative sign**, i.e. experimental signals of methyl protons δ^H_{CH3} are shifted to the high field compared even with methylacetate **4a**! In comparison with **anticipated "virtual" position in the spectrum they are shifted to the high field by** $\approx$ **0.10÷0.15 ppm**.

As it was mentioned above such ***ratio between ΔW_{CH3} and $\Delta\delta^H_{CH3}$ values in unsubstituted methyl arylacetates*** indicates the presence of considerable ***interaction in the space between aryl fragment and methoxyl group unbound with each other.***

III.4.3.2.3. Phenylacetates 9b-9g substituted in pnehyl ring
$S^1S^2C_6H_3$-CH₂-COOCH₃.

The spectral parameters (experimental and calculated) of phenylacetates substituted in pnenyl ring are represented in Table 1. We could not find the reliable evaluation criteria of increments i_X^{Ar} for

every phenyl groups substituted in a ring in esters **9a-9g** therefore we used the same value of phenyl group increment (i_X = 0.08 ppm) to calculate virtual basic spectral parameters W^H_{CH3} for all esters. Pro tanto, the anticipated parameter W_{CH3} in every case is equal to 3.66 + 0.08 = 3.74 ppm.

Table 1

Spectral parameters of the compounds **9b-9g**

Number of compound	Substituent S^1	Experimental spectral parameters		Virtual differential spectral parameters $\Delta W_{CH3}{}^{\mathbf{9}}$
		Basic $\delta^H{}_{CH3}{}^{\mathbf{9}}$	Differential $\Delta\delta^H{}_{CH3}{}^{\mathbf{9}}$	
9b	p-Bu^t	3.67	+0.01	-0.07
9c	p-Cl	3.69	+0.03	-0.05
9d	o-Cl	3.71	+0.05	-0.03
9e	p-OH	3.69	+0.03	-0.05
9f	p-OMe	3.66	0.00	-0.08
9g	p-OBu	3.66	0.00	-0.08

In the methyl arylacetates **9b-9g** substituted in phenyl ring the small (from 0.00 to +0.05 ppm) "experimental" parameters $\Delta\delta^H{}_{CH3}{}^{\mathbf{9}}$ have positive values, in contrast to the same parameters of unsubstituted in phenyl ring compounds **9a** and **11**, where they are negative. All virtual differential parameters $\Delta W^H{}_{CH3}{}^{\mathbf{9b-g}}$, the same as $\Delta W^H{}_{CH3}{}^{\mathbf{9a}}$ parameter, have negative sign but by absolute value they are smaller than above-mentioned parameters $\Delta W^H{}_{CH3}{}^{\mathbf{9a}}$ and $\Delta W^H{}_{CH3}{}^{\mathbf{11}}$. Possibly, the positive values of "experimental" parameters $\Delta\delta^H{}_{CH3}$ in esters **9b-9g** substituted in phenyl ring (as well as in esters **10b-e,** see below) are explained by the creation of steric barriers to the interaction with metoxyl fragments by the substituent S.

The observed ***ratio between*** ΔW_{CH3} ***and*** $\Delta\delta^H_{CH3}$ in methyl arylacetates **9b-9g** substituted in phenyl ring also presumes the presence of ***interaction in the space between aryl fragment and methoxyl group unbound with each other*** in spite of the positive values of "experimental" parameters $\Delta\delta^H{}_{CH3}$.

III.4.3.3. Ethyl phenylacetates Ar-CH$_2$-COO-CH$_2$-CH$_3$ (10).

III.4.3.3.1. Ethyl phenylacetate C$_6$H$_5$-CH$_2$-COO-CH$_2$-CH$_3$ (10a).

<u>Experimental data:</u> $\delta^H{}_{CH2}{}^{\mathbf{10a[9]}}$ = **4.135 ppm**, $\delta^H{}_{CH3}{}^{\mathbf{10a[9]}}$ = **1.23 ppm.** For the calculations $\delta^H{}_{CH2}{}^{\mathbf{10a}}$ is rounded to 4.14 ppm.

<u>Calculated parameters.</u> Main experimental differential parameters: $\underline{\Delta\delta^H{}_{CH2}{}^{\mathbf{10a}}}$ = **4.14 − 4.12 = + 0.02 ppm**; $\underline{\Delta\delta^H{}_{CH3}{}^{\mathbf{10a}}}$ = **1.23 − 1.26 = - 0.03 ppm**.

<u>Virtual basic parameters W.</u> We use increments of phenyl group for ethyl ethers: : $i_X{}^{Ph}{}_{CH2}$ = 0.08 ppm and $i_X{}^{Ph}{}_{CH3}$ = 0.03 ppm. Then $\underline{\mathbf{W^H{}_{CH2}{}^{10a}}}$ = **4.12 + 0.08 = 4.20 ppm**; $\underline{W^H{}_{CH3}{}^{\mathbf{10a}}}$ = **1.26 + 0.03 = 1.29 ppm**.

<u>Virtual differential parameters:</u> : $\Delta W_{CH2}{}^{\mathbf{10a}}$ = **4.14 − 4.20 = -0.06 ppm**; $\Delta W_{CH3}{}^{\mathbf{10a}}$ = **1.23 − 1.29 = -0.06 ppm.**

Main experimental differential parameter of methylene group $\Delta\delta^H{}_{CH2}{}^{\mathbf{10a}}$ (the same as above-mentioned «main experimental" parameters $\Delta\delta^H{}_{CH3}{}^{\mathbf{9b}} \div \Delta\delta^H{}_{CH3}{}^{\mathbf{9f}}$) is small positive value (+0.02 ppm). The parameter of "outlying" methyl group $\Delta\delta^H{}_{CH3}{}^{\mathbf{10a}}$ has the negative value equal to -0.03 ppm. Its absolute value may be evaluated as considerable one for "outlying" parameters.

Both virtual differential parameters $\Delta W_{CH2}{}^{\mathbf{10a}}$ and $\Delta W_{CH3}{}^{\mathbf{10a}}$ are equal to -0.06 ppm. The parameter of "nearby" methylene group $\Delta W_{CH2}{}^{\mathbf{10a}}$ is almost twice less by its absolute value than

absolute values of the same parameters of "nearby" methyl groups in methyl ethers ΔW_{CH3}^{9a} and ΔW_{CH3}^{11} ($\approx$ to -0.10 ppm). On the contrary, the value of virtual parameter ΔW_{CH3}^{10a} (-0.06 ppm) may be considered as considerable one taking into account the great "outlying" of methyl group from phenyl fragment of the molecule. Let us note that both differential parameters (virtual ΔW_{CH3}^{10a} and "experimental $\Delta \delta^{H}_{CH3}^{10a}$) have negative sign.

The same as in the case of unsubstituted methyl ethers **9a** and **11**, *the ratio between ΔW_{CH3} and $\Delta \delta^{H}_{CH3}$ in unsubstituted ethyl arylacetate 10a* presumes the presence of *interaction in the space between phenyl fragment and "outlying" etoxyl group unbound with each other.* At the same time taking into account the ratio between differential parameters ΔW_{CH2} and $\Delta \delta^{H}_{CH2}$, **the interaction with "nearby" methylene group** of etoxyl fragment (if it exists) should be **considerably less than the interaction with "outlying" methyl group**. The possible explanation is the insufficient length of middle fragment "L" in arylacetate molecules allowing to realize the effective interaction only with "outlying" methyl group.

III.4.3.3.2. Ethyl phenylacetates substituted in phenyl ring 10b-10e.

For all ethyl ethers **10b-10e**, the same as for substituted methyl ethers **9b-9f,** we use the same values of phenyl group increments to calculate the virtual basic spectral parameters W_{CH3} : for "nearby" methylene group $i_X^{Ph}_{CH2} = \Delta W_{CH2} = +0.08$ ppm; for "outlying" methyl group $i_X^{Ph}_{CH3} = \Delta W_{CH3} = +0.03$ ppm. Then the anticipated virtual basic spectral parameters W_{CH2} and W_{CH3} for every compound **10b-10e** are equal to: : $\underline{W_{CH2}^{10b-e}} = 4.12 + 0.08 = \underline{\textbf{4.20 ppm}}$; $\underline{W_{CH3}^{10b-e}} = 1.26 + 0.03 = \underline{\textbf{1.29 ppm.}}$ The other spectral parameters of ethyl phenylacetates substituted in phenyl ring are represented in Table 2.

Table 2

Spectral parameters of compounds **10b-10e**

| Number of compounds	Substituent S^1 (or substituents S^1 and S^2)	Experimental spectral parameters of methylene group		Virtual differential spectral parameters ΔW_{CH2}^{10}, ppm	Experimental spectral parameters of methyl group		Virtual differential spectral parameters ΔW_{CH3}^{10}, ppm
		Basic $\delta^{H}_{CH2}^{[9]}$, ppm	Differential $\Delta \delta^{H}_{CH2}^{[9]}$, ppm		Basic $\delta^{H}_{CH3}^{[9]}$, ppm	Differential $\Delta \delta^{H}_{CH3}^{[9]}$, ppm	
10b	o-OMe	4.14	+0.02	-0.06	1.23	-0.03	-0.06
10c	p-Me	4.13	+0.01	-0.07	1.23	-0.03	-0.06
10d*	m-OMe	4.146	+0.03	-0.05	1.252	-0.01	-0.04
10e	S^1= 4-OH, S^2= 3-OMe	4.14	+0.02	-0.06	1.23	-0.03	-0.06

* Experimental data are taken from [10].

In ethyl arylacetates (**10b-10e**) substituted in the nucleus, the same as in unsubstituted ethyl phenylacetate **10a,** the values of "experimental" parameters of methylene group $\Delta \delta^{H}_{CH2}$ have small ($\leq$ 0.05 ppm) positive values. In contrast to them, the "experimental" differential parameters $\Delta \delta^{H}_{CH3}^{10}$ for "outlying" methyl protons in **10a-10e** have negative values (-0.01÷-0.03 ppm).

The general conclusion may be done that *in arylacetates 9,10 and 11 the length of fragment "L" already allows the interaction in the space of unbound fragments "K" and "M". Obviously due to the farther outlying of methyl groups from "K" aryl fragment the interaction in ethyl arylacetates with "outlying" methyl group is greater than that with "nearby" methylene group.*
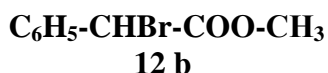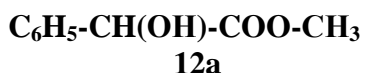
III.4.4. Alkyl arylacetates 12-15 containing functional substituents instead of hydrogen atoms in methylene group (Y, Z≠H).

The interesting examples for investigation of interaction in the space of unbound fragments "K" and "M" are di- (**12, 13**) and triple-substituted (**14, 15**) compounds of the general formula **2** and **3**, respectively, in which the first substitutent (X) is phenyl group and alkyl group is methyl (**12, 14**) or ethyl (**13, 15**) group.

$$C_6H_5\text{-CHY-COO-Alk} \qquad C_6H_5\text{-CYZ-COO-Alk}$$
$$\textbf{12, 13} \qquad\qquad \textbf{14, 15}$$
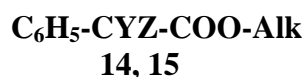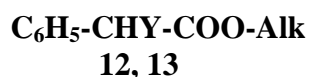
III.4.4.1. Monosubstituted alkyl phenylacetates 12 and 13.

III.4.4.1.1. Monosubstituted methyl phenylacetates 12.

$$C_6H_5\text{-CH(OH)-COO-CH}_3 \quad C_6H_5\text{-CHBr-COO-CH}_3 \quad (C_6H_5)_2\text{CH-COO-CH}_3$$
$$\textbf{12a} \qquad\qquad\qquad \textbf{12 b} \qquad\qquad\qquad \textbf{12c}$$

Spectra of three methyl ethers of the general formula **12** are represented in [9]: methyl phenyl(α-oxy)acetate **12a** (X = Ph, Y=OH), methyl phenyl(α-brom)acetate **12b** (X = Ph, Y=Br) and methyl diphenylacetate **12c** (X = Y= Ph).

<u>Experimental data:</u> $\boldsymbol{\delta^H_{CH3}{}^{12a[9]} = 3.72}$ **ppm;** $\boldsymbol{\delta^H_{CH3}{}^{12b[9]} = 3.76}$ **ppm;** $\boldsymbol{\delta^H_{CH3}{}^{12c[9]} = 3.72}$ **ppm.**

<u>Calculated parameters.</u> Main experimental differential parameters $\underline{\Delta\boldsymbol{\delta^H_{CH3}}}$ are equal to: $\underline{\Delta\boldsymbol{\delta^H_{CH3}}{}^{12a}}$ **= 3.72 – 3.66 = $\underline{+\,0.06}$ ppm;** $\underline{\Delta\boldsymbol{\delta^H_{CH3}}{}^{12b}}$ **= 3.76 – 3.66 = $\underline{+\,0.10}$ ppm;** $\underline{\Delta\boldsymbol{\delta^H_{CH3}}{}^{12c}}$ **= 3.72 – 3.66 = $\underline{+\,0.06}$ ppm.**

It is also advisable to choose as auxiliary standard compounds the following substances: oxyester **4b** (HOCH$_2$-COO-CH$_3$) for oxyester **12a** and bromester **4c** (BrCH$_2$-COO-CH$_3$) for bromester **12b**. In such a case the transition from standard compounds **4b and 4c** to the corresponding compounds **12** takes place while changing of one hydrogen atoms of methylene group in **4** for substituent Y (i.e. hydroxyl group in the case of compound **12a** or bromine atom for **12b**).

<u>Experimental data:</u> $\boldsymbol{\delta^H_{CH3}{}^{4b[9]} = 3.78}$ **ppm and** $\boldsymbol{\delta^H_{CH3}{}^{4c[9]} = 3.79}$ **ppm.**

<u>Calculated data.</u> Additional experimental differential parameters are equal to: $\underline{\Delta^1\boldsymbol{\delta^H_{CH3}}{}^{12a}}$ **= 3.72 – 3.78 = $\underline{-\,0.06}$ ppm**; $\underline{\Delta^1\boldsymbol{\delta^H_{CH3}}{}^{12b}}$ **= 3.76 – 3.79 = $\underline{-\,0.03}$ ppm.** Calculated **auxiliary parameters** $\Delta^1\boldsymbol{\delta^H_{CH3}}{}^{12}$ **are in agreement** by their value and sign with above-mentioned **main** experimental differential **parameters** for the compounds unsubstituted **9** and **11**, where $\Delta\boldsymbol{\delta^H_{CH3}} \approx -\,0.01 \div -0.07$ ppm.

<u>Virtual parameters of the compounds **12**.</u> To calculate the virtual basic parameter of oxyester **12a** we calculate the increment of hydroxyl group $\mathbf{i_Y^{OH}}$ (as second substituent in the compound of the general formula **2**). The same as ethyl 2,3-dibrompropionate **5b**, the increment $\mathbf{i_Y}$ is calculated by the formula: $\mathbf{i_Y^{OH}} = \delta^H_{CH3}{}^{4b} - \delta^H_{CH3}{}^{4a} = 3.78 - 3.66 = \underline{\mathbf{+0.12}}$ **ppm.** Analogously we calculate the increment $\mathbf{i_Y^{Br}} = 3.79 - 3.66 = \underline{\mathbf{+0.13}}$ **ppm.** Let us note that the latter value (+0.13 ppm) practically coinsides with the value of $\mathbf{i_X^{Br}}_{CH2} = 0.12$ ppm calculated earlier from the spectral data of ethyl bromacetate **5c**.

Using the increment $\mathbf{i_X^{Ph}} = 0.08$ ppm for phenyl group in methyl ethers, we calculate the anticipated basic spectral parameters $\mathbf{W_{CH3}}{}^{12}$ by the formula (1): $\underline{\mathbf{W^H_{CH3}}{}^{12a} = 3.66 + 0.08 + 0.12 = \mathbf{3.86}}$ **ppm** and $\underline{\mathbf{W^H_{CH3}}{}^{12b}} = 3.66 + 0.08 + 0.13 = \underline{\mathbf{3.87}}$ **ppm;** $\underline{\mathbf{W^H_{CH3}}{}^{12c}} = 3.66 + 0.08 + 0.08 = \underline{\mathbf{3.82}}$ **ppm.**

<u>Virtual differential parameters</u> $\Delta W_{CH3}{}^{12}$ are equal to: $\underline{\Delta W_{CH3}{}^{12a}} = 3.72 - 3.86 = \underline{\textbf{-0.14 ppm;}}$ $\underline{\Delta W_{CH3}{}^{12b}} = 3.76 - 3.87 = \underline{\textbf{-0.11 ppm;}}$ $\underline{\Delta W_{CH3}{}^{12c}} = 3.72 - 3.82 = \underline{\textbf{-0.10 ppm.}}$

These values are in agreement with the values of analogous virtual differential parameters $\Delta W_{CH3}{}^9$ and $\Delta W_{CH3}{}^{10}$ (see above) within the interval from **-0.006 to -0.014 ppm (-0.10±0.04 ppm).**

III.4.4.1.2. Ethyl phenyl(α-oxy)acetate C$_6$H$_5$-CH(OH)-COO-CH$_3$ (13).

<u>Experimental data</u> of ethyl phenyl(α-oxy)acetate **13** (X = Ph, Y=OH): $\boldsymbol{\delta^H_{CH2}{}^{13[9]} = 4.20}$ **ppm** ("centr of gravity" of the multiplet signal of magnetic non-equivalent protons)**,** $\boldsymbol{\delta^H_{CH3}{}^{13[9]} = 1.20}$ **ppm;**

$\delta^H_{CH2}{}^{13[10]} = $ **4.184 ppm**, $\delta^H_{CH3}{}^{13[10]} = $ **1.193 ppm.** For calculations we rounded $\delta^H_{CH2}{}^{13}$ to 4.19 ppm and $\delta^H_{CH3}{}^{13}$ – to 1.20 ppm.

Calculated parameters. Main experimental differnetial parameters are equal to: $\underline{\Delta\boldsymbol{\delta}^H_{CH2}{}^{13}} = $ **4.19 – 4.12 = + 0.07 ppm;** $\underline{\Delta\boldsymbol{\delta}^H_{CH3}{}^{13}} = $ **1.20 – 1.26 = - 0.06 ppm**.

Ethyl glycolate **5e** (HO-CH$_2$COOC$_2$H$_5$) is chosen as auxiliary standard compound: $\boldsymbol{\delta}^H_{CH2}{}^{5e[9]} = $ **4.25 ppm**, $\boldsymbol{\delta}^H_{CH3}{}^{5e[9]} = $ **1.30 ppm;** $\boldsymbol{\delta}^H_{CH2}{}^{5e[10]} = $ **4.24 ppm**, $\boldsymbol{\delta}^H_{CH3}{}^{5e[10]} = $ **1.30 ppm.** For the calculation we assume: $\delta^H_{CH2}{}^{5e} = 4.25$ ppm and $\delta^H_{CH3}{}^{5e} = 1.30$ ppm. Auxiliary experimental differnetial parameters are equal to: $\underline{\Delta\boldsymbol{\delta}^H_{CH2}{}^{13}} = $ **4.19 – 4.25 = - $\underline{0.06}$ ppm;** $\underline{\Delta\boldsymbol{\delta}^H_{CH3}{}^{13}} = $ **1.20 – 1.30 = - 0.10 ppm**.

Virtual basic parameters W. The same as previous calculations of the virtual parameter $W^H_{CH3}{}^{12a}$ we calculate $W^H_{CH2}{}^{13}$ and $W^H_{CH3}{}^{13}$. $\underline{W^H_{CH2}{}^{13}} = $ **4.12 + 0.08 + 0.12 = $\underline{4.32}$ ppm;** $\underline{W^H_{CH3}{}^{13}} = $ **1.26 + 0.03 + (1.30 – 1.26) = $\underline{1.33}$ ppm**.

Virtual differential parameters are equal to: $\underline{\Delta W_{CH2}{}^{13}} = $ **4.19 – 4.32 = $\underline{-0.13}$ ppm;** $\underline{\Delta W_{CH3}{}^{13}} = $ **1.20 – 1.32 = $\underline{-0.12}$ ppm**.

Both types of "experimental" differential parameters of methyl group $\Delta\delta^H_{CH3}$ in ethyl phenyl(α-oxy)acetate **13** – main and auxiliary – have negative sign (-0.06 and -0.10 ppm, relatively). The analogous parameters of methylene group $\Delta\delta^H_{CH2}$ are practically equal by their absolute values but have opposite signs (+0.07 and -0.06 ppm, relatively). At the same time both virtual differential parameters have negative value greater in two times ($\approx$-0.13 ppm).

The ratio between ΔW_{CH3}**,** $\Delta\delta^H_{CH3}$ ***and*** $\Delta^1\delta^H_{CH3}$ ***values in the investigated methyl- (12) and ethyl- (13) acetates*** presumes the ***presence of interaction in the space between aryl fragment and alkoxyl group unbound with each other***. Taking into account the ratio between differential parameters ΔW_{CH2} and $\Delta\delta^H_{CH2}$, **the interaction with "nearby" methylene group** of etoxyl fragment in **13** is **considerably less than the interaction with "outlying" methyl group**. Taking into consideration the values of corresponding parameters $\Delta\delta^H_{CH2}{}^{10a}$ and $\Delta\delta^H_{CH2}{}^{13}$, the latter interaction in hydroxysubstituted ester **13** is more considerable than that in unsubstituted ethyl phenylacetate **10a.** Perhaps the introduction of hydroxyl group in α-position favors the mentioned phenomenon.

III.4.4.2. Methyl disubstituted phenylacetates 14.

We found spectra of only two compounds of the general formula **14** in [9, 10]: methyl benzylate **14a** and methyl benzoylformate **14b**.

III.4.4.2.1. Methyl diphenyloxyacetate (methyl benzylate) 14a.
(C$_6$H$_5$)$_2$C(OH)-COO-CH$_3$.

Experimental data of methyl diphenyloxyacetate **14a** (X=Y=Ph, Z=OH): $\delta^H_{CH3}{}^{14a[9]} = $ **3.82 ppm.**

Calculated parameters. Main experimental differential parameter $\Delta\boldsymbol{\delta}^H_{CH3}$ is equal to: $\underline{\Delta\boldsymbol{\delta}^H_{CH3}{}^{14a}} = $ **3.82 – 3.66 = + 0.16 ppm**

Methyl glycolate **4c** for which $\underline{\boldsymbol{\delta}^H_{CH3}{}^{4a[9]}} = \underline{3.78\ ppm}$ is chosen as auxiliary standard compound. The additional "experimental" differential parameter $\Delta^1\delta^H_{CH3}{}^{14a} = $ **3.82 – 3.78 = + 0.04 ppm**.

Virtual parameters of ethyl benzylate **14a**. To calculate virtual basic parameter of oxyester **14a** we use above-mentioned increments of phenyl ($i_X{}^{Ph} = i_Y{}^{Ph} = 0.08$ ppm) and hydroxyl ($i_Z{}^{OH} = 0.12$ ppm) groups. Then the virtual value of anticipated basic spectral parameter is equal to: $\underline{W^H_{CH3}{}^{14a}} = $ **3.66 + 0.08 + 0.08 + 0.12 = $\underline{3.94}$ ppm.**

Virtual differential parameter $\Delta W_{CH3}{}^{14a} = $ **3.82 – 3.94 = $\underline{-0.12}$ ppm.** Its value is approximately the same as value of analogous virtual differential parameters $\Delta W_{CH3}{}^{9}$, $\Delta W_{CH3}{}^{10}$ and $\Delta W_{CH3}{}^{12}$ (see above) which are equal to +0.10±0.04 ppm.

The ratio between ΔW_{CH3} ***and*** $\Delta\delta^H_{CH3}$ ***in ethyl diphenyl(α-oxy)acetate 14a presumes the presence of interaction in the space between one or two phenyl groups and methyl group in spite of the positive sign of the parameter*** $\Delta\delta^H_{CH3}$***.***

III.4.4.2.2. Methyl benzoylformate 14b.
C_6H_5-C(O)-COO-CH_3.
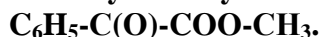
Let us examine together methyl **14b** and ethyl **15a** esters of benzoylformic acid.

Experimental data of methyl benzoylformate **14b** (X=Ph, Y+Z=O): $\delta^H_{CH3}{}^{14b[10]}$ = **3.94 ppm** (in CD_2Cl_2) [11].

Calculated parameters. Main experimental differential parameter: $\Delta\delta^H_{CH3}$ = **3.94 – 3.66 = + 0.28 ppm**

Oxoester **3b** (CH_3-CO-COO-CH_3), where X = CH_3, and Y+Z=O is chosen as auxiliary standard compound for methyl benzoylformate **14b**. $\delta^H_{CH3}{}^{3b[10]}$ = **3.881 ppm.** Then the additional experimental differential parameter is $\Delta^1\delta^H_{CH3}{}^{14b}$ = 3.94 – 3.88 **= + 0.06 ppm.**

Virtual parameters of benzoylformate **14b**. To calculate the virtual basic parameter we use increment of phenyl ($i_X{}^{Ph}$ = 0.08 ppm) and calculate increment ($i_Z{}^O$) of ketone function (Y+Z=O).

We assume the value ($i_Z{}^O$) as a difference between basic parameters δ^H_{CH3} of ketoester **3b** and standard ester **4a**: $i_Z{}^O$ = **3.88 – 3.66 = +0.22 ppm.** Then the virtual value of anticipated basic spectral parameter $W_{CH3}{}^{14b}$ = 3.66 + 0.08 +0.22 = **3.96 ppm.**

Virtual differential parameter $\Delta W_{CH3}{}^{14a}$ is equal to: $\Delta W_{CH3}{}^{14b}$ = **3.94 – 3.96 = -0.02 ppm**. The absolute value of the parameter is essentially less than absolute value of analogous virtual differential parameters $\Delta W_{CH3}{}^9$, $\Delta W_{CH3}{}^{10}$ and $\Delta W_{CH3}{}^{12}$ (see above), which are approximately equal to **0.10±0.04 ppm.**

III.4.4.2.3. Ethyl benzoylformate 15.
C_6H_5-C(O)-COO-CH_2-CH_3

Experimental data of ethyl benzoylformate **15** (X=Ph, Y+Z=O): $\delta^H_{CH2}{}^{15[9]}$ = **4.45 ppm**, $\delta^H_{CH2}{}^{15[10]}$ = **4.449 ppm**, $\delta^H_{CH3}{}^{15[9]}$ = **1.42 ppm**, $\delta^H_{CH3}{}^{15[10]}$ = **1.465 ppm**. For the calculations we assume averaged values: $\delta^H_{CH2}{}^{15}$ = 4.45 ppm, $\delta^H_{CH3}{}^{15}$ = 1.44 ppm.

Calculated values. Main experimental differential parameters are equal to: $\Delta\delta^H_{CH2}{}^{15}$ = **4.45 – 4.12 = + 0.33 ppm;** $\Delta\delta^H_{CH3}{}^{15}$ = **1.44 – 1.26 = + 0.18 ppm**

Oxoester **3c** (CH_3-CO-COO-CH_2-CH_3) is chosen as auxiliary standard compound (the same as for methyl benzoylformate **14b**).). $\delta^H_{CH2}{}^{3c[10]}$ = **4.332 ppm;** $\delta^H_{CH3}{}^{3c[10]}$ = **1.376 ppm** For the calculations we assume rounded values: $\delta^H_{CH2}{}^{3c}$ = 4.33 ppm, $\delta^H_{CH3}{}^{3c}$ = 1.38 ppm

Then additional experimental differential parameters $\Delta^1\delta^H_{CH2}{}^{15}$ = **4.45 – 4.33 = + 0.11 ppm** и $\Delta^1\delta^H_{CH3}{}^{15}$ = **1.44 – 1.38 = + 0.06 ppm**

Virtual parameters of ethyl benzoylformate **15**. To calculate virtual basic parameter of oxyester **15** we use increments of phenyl ($i_X{}^{Ph}$ = 0.08 ppm) and ketone (for methylene group $i_Z{}^O_{CH2}$ = +0.22 ppm) fragments. To evaluate the increment of "oulying" methyl group of ketone fragment we divide the increment of "nearby" methylene group ($i_Z{}^O_{CH2}$ = +0.22 ppm) by "attenuation factor" equal to 2.5: $i_Z{}^O$ = +0.22 ppm / 2.5 ≈ 0.09 ppm

Virtual values of anticipated basic parameters: $W^H_{CH2}{}^{15}$ = **4.12 + 0.08 +0.22 = 4.42 ppm, and** $W^H_{CH3}{}^{15}$ = **1.26 + 0.03 +0.09 = 1.38 ppm**

Virtual differential parameters are equal to: $\Delta W_{CH2}{}^{15}$ = **4.45 – 4.42 = + 0.03 ppm and** $\Delta W_{CH3}{}^{15}$ = **1.44 – 1.38 = +0.06 ppm** Let us note that both virtual differential parameters have **positive sign**, i.e. anticipated values of chemical shifts $\delta^H_{Alk}{}^{15}$ **are even lower than experimental ones.**

It is the main difference of virtual parameters $\Delta W_{CH3}{}^{14b}$, $\Delta W_{CH2}{}^{15}$ **and** $\Delta W_{CH3}{}^{15}$ **on the one hand** and analogous virtual differential parameters $\Delta W_{CH3}{}^9$, $\Delta W_{CH3}{}^{10}$ and $\Delta W_{CH3}{}^{12}$ on the other hand.

Therefore we may conclude that in the esters of ketoacids **14b and 15** *in contrast to the above-mentioned phenylacetates 9-13 and 14a the interaction between unbound fragments "K" (phenyl) and "M" (alkoxyl) groups is absent because of the peculiarities of fragment "L" (-COCOO-) structure.*

III.5. β-Arylsubstituted propionates.

In this Section we examine the compounds of **1** and **2** types in which aryl and carbaloxyl groups are separated by two unsubstituted (or substituted) methylene groups CR^1R^2. As it was mentioned above, the β-arylsubstituted propionates may be considered here as α-benzylsubstituted acetates with benzyl group $C_6H_5CH_2$- as a substituent X.

III.5.1. Methyl β-arylpropionates Ar-CH₂-CH₂-COOCH₃ (16), free of other substituents (Y, Z), except benzyl group (X = CH₂Ar).

The phenyl fragment is the fragment "K" in methyl 3-phenylpropionate (**16a**) and 4-hydroxyphenyl group – in methyl ether **16b.** The fragment "L" is the middle part of the molecule (fragment –CH₂-CH₂-COO–) containing two methylene groups. The fragment "M" is methyl group.

$$C_6H_5\text{-}CH_2\text{-}CH_2\text{-}COO\text{-}CH_3 \qquad HO\text{-}C_6H_4\text{-}CH_2\text{-}CH_2\text{-}COO\text{-}CH_3$$
$$\textbf{16a} \qquad\qquad\qquad \textbf{16b}$$

III.5.1.1. Methyl 3-phenylpropionate (16a).

Experimental data of methyl 3-phenylpropionate **16a** (X= CH₂Ph): $\delta^H{}_{CH3}{}^{16a[9]}$ = **3.65 ppm**
Calculated parameters. Main experimental differential parameter is equal to: $\Delta\delta^H{}_{CH3}{}^{16a}$ = **3.65 – 3.66 = - 0.01 ppm**

Virtual parameters of methyl 3-phenylpropionate **16a.** To calculate the virtual basic parameter of methyl 3-phenylpropionate **16a** we calculate increment of benzyl group ($i_X{}^{PhCH2}$). We divide the value of phenyl increment ($i_X{}^{Ph}$ = +0.08 ppm) by "attenuation factor" equal to 2.5: +0.08/2.5=+0.03 ppm. Then the virtual value of anticipated basic spectral parameters is: $\underline{W^H{}_{CH3}{}^{16a}}$ = **3.66 + 0.03 = 3.69 ppm**

Virtual differential parameter $\Delta W_{CH3}{}^{16a}$ = 3.65 – 3.69 = **-0.04 ppm**, is some lower than analogous differential parameters $\Delta W_{CH3}{}^{9a}$ и $\Delta W_{CH3}{}^{11}$ (-0.10±0.03 ppm), calculated for unsubstituted in phenyl ring methyl arylacetates **9a** and **11**. However, the ratio of this difference ($\Delta W_{CH3}{}^{16a}$ = -0.04 ppm) and main experimental differential parameter ($\Delta\delta^H{}_{CH3}{}^{16a}$ = **- 0.01 ppm**) shows the ***possibility of interaction between molecule fragments "K" (phenyl) and "M" (methyl) groups.***

III.5.1.2. Methyl 3-(4-oxyphenyl)propionate HO-C₆H₄-CH₂-CH₂-COO-CH₃ (16b).
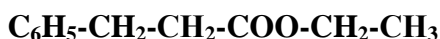
Experimental data: $\delta^H{}_{CH3}{}^{16b[9]}$ = **3.67 ppm**
Calculated data. Main experimental differential parameters is equal to: $\underline{\Delta\delta^H{}_{CH3}{}^{16b}}$ = **3.67 – 3.66 = + 0.01 ppm**

Virtual parameters of methyl 3-(4-oxyphenyl)propionate **16b**. To calculate the virtual basic parameter of methyl 3-(4-oxyphenyl)propionate $W^H{}_{CH3}{}^{16b}$ we assume the increment of p-oxybenzyl groups equal to the increment of benzyl group ($i_X{}^{p\text{-}HO\text{-}C6H4\text{-}CH2}$ = $i_X{}^{PhCH2}$ = **+0.03 ppm**). Then the value of anticipated parameter $\underline{W^H{}_{CH3}{}^{16b}}$ = **3.66 + 0.03 = 3.69 ppm**

Virtual differential parameter is equal to: $\Delta W_{CH3}{}^{16b}$ = **3.67 – 3.69 = -0.02 ppm,** what is more less than analogous parameter $\Delta W_{CH3}{}^{16a}$.

Since absolute values of both differential parameters $\Delta W_{CH3}{}^{16b}$ и $\Delta\delta^H{}_{CH3}{}^{16b}$ *slightly differ from zero, the reliable evaluation criterion of possible interaction between molecule fragments "K" (phenyl) and "M" (methyl) groups in 3-(4-oxyphenyl)propionate 16b is absent. We may suppose that only small interaction takes place.*

III.5.2. Ethyl 3-phenylpropionate (17).

$$C_6H_5\text{-}CH_2\text{-}CH_2\text{-}COO\text{-}CH_2\text{-}CH_3$$

Experimental data: $\delta^H_{CH2}{}^{17[9]}$ = **4.11 ppm**, $\delta^H_{CH3}{}^{17[9]}$ = **1.22 ppm**; $\delta^H_{CH2}{}^{17[10]}$ = **4.109 ppm**, $\delta^H_{CH3}{}^{17[10]}$ = **1.212 ppm.** For the calculations we rounded the parameter: $\delta^H_{CH3}{}^{17}$ = 1.22 ppm

Calculated parameters. Main experimental differential parameters are equal to: $\underline{\Delta\delta^H_{CH2}{}^{17}}$ = **4.11 – 4.12 = - 0.01 ppm;** $\underline{\Delta\delta^H_{CH3}{}^{17}}$ = **1.22 – 1.26 = - 0.04 ppm**
Let us note that absolute value of negative "outlying" methyl parameter of ethyl group ($\Delta\delta^H_{CH3}{}^{17}$ = -0.04 ppm) is considerably greater than that of "neraby" methylene parameter $\Delta\delta^H_{CH2}{}^{17}$ (-0.01 ppm).

Virtual basic parameters: $\underline{W^H_{CH2}{}^{17}}$ = **4.12 + 0.03 = 4.15 ppm.** To calculate the second virtual basic parameter $\underline{W^H_{CH3}{}^{17}}$ of ethyl 3-phenylpropionate **17** we have to calculate increment of benzyl group ($i_X{}^{PhCH2}$) for outlying metyl group of ethoxyl fragment. For this purpose we divide the value of benzyl increment ($i_X{}^{PhCH2}$ = +0.03 ppm) by "attenuation factor" equal to 2.5: $+0.03/2.5=\underline{+0.01\ ppm.}$ So, $\underline{W^H_{CH3}{}^{17}}$ = **1.26 + 0.01 = 1.27 ppm**

Virtual differential parameters: $\underline{\Delta W_{CH2}{}^{17}}$ = **4.11 – 4.15 = -0.04 ppm;** $\underline{\Delta W_{CH3}{}^{17}}$ = **1.22 – 1.27 = - 0.05 ppm**

Both virtual differential parameters $\Delta W_{CH2}{}^{17}$ and $\Delta W_{CH3}{}^{17}$ are approximately equal by value and by a negligible margin less than zero. ***Ratio between values of parameters ΔW and $\Delta\delta^H$ for ethyl 3-phenylpropionate 17*** probably reveals the present of ***interaction in the space between phenyl fragment and etoxy group unbound with each other.***

At the same time (accordingly to the ratio between values of differential parameters ΔW_{CH2} and $\Delta\delta^H_{CH2}$) the ***interaction with "nearby" methylene group of etoxyl fragment is considerably less than interaction with "outlying" methyl group***. The latter is more considerable compared with that in ethyl phenylacetate **10a** taking into account values of $\Delta\delta^H_{CH2}$ and $\Delta\delta^H_{CH3}$. ***Perhaps the introduction of two methylene groups between phenyl ("K") and carbalkoxyl fragments is sufficient to realize such interaction.***

III.5.3. Alkyl β-arylpropionates of the general formula Ar-CR^{1}R^2-CYZ-COOAlk, containing benzyl group (X = -CR^{1}R^{2}Ar) as well as substituents differ from hydrogen (Y≠H and/or Z≠H)

Above-mentioned methyl 2-tolylbenzoate **6g** may be examined as derivative of **β-arylpropionates** of the general formula **Ar-CR^{1}R^2-CYZ-COOAlk,** in which substituents ($R^1 + R^2$) and ($Y + Z$) are fragment of benzene ring =CH-CH=CH-CH=.

The interesting example for investigations of interaction in the space of unbound fragments "K" and "M" is disubstituted ethyl ether **18** related to the compounds of the general formula **2**. The substituent X in it is benzyl group (X = C_6H_5-CH$_2$-), and substituent Y – benzoyl group (Y = C_6H_5-CO-).

III.3.1. Ethyl 2-benzylbenzoylacetate (18).

C$_6$H$_5$-CH$_2$-CH(C$_6$H$_5$-CO)-COO-CH$_2$-CH$_3$

Experimental data: $\delta^H_{CH2}{}^{18[9]}$ = **4.08 ppm** ("centr of gravity" of the multiplete signal of magnetic non-equivalent protons), $\delta^H_{CH3}{}^{18[9]}$ = **1.09 ppm.**

Calculated parameters. Main experimental differential parameters are equal to: $\underline{\Delta\delta^H_{CH2}{}^{18}}$ = **4.08 – 4.12 = - 0.04 ppm;** $\underline{\Delta\delta^H_{CH3}{}^{18}}$ = **1.09 – 1.26 = - 0.17 ppm.** Let us note that both parameters have negative signs. The large absolute value of methyl parameter ($\Delta\delta^H_{CH3}{}^{17}$ = **-0.17 ppm**) is greater by order than analogous parameter of "unsubstituted" compound **17**. The absolute value of methylene parameter ($\Delta\delta^H_{CH2}{}^{18}$ = **-0.04 ppm**) is also considerable compared with the parameter $\Delta\delta^H_{CH2}{}^{17}$ = **-0.01 ppm** and analogous positive by sign parameters of ethyl ethers of phenylacetic acids **10 and 13** containing less methylene groups (by one) in the acid fragment.
The auxiliary standard compound is ketonic form of ethyl benzoylacetate **2c** (C_6H_5-CO-CH$_2$-COO-CH$_2$-CH$_3$). $\delta^H_{CH2}{}^{2c[10]}$ = **4.205 ppm** $\delta^H_{CH3}{}^{2c[10]}$ = **1.251 ppm** For the calculations we assume: $\delta^H_{CH2}{}^{3c}$ = 4.21 ppm, $\delta^H_{CH3}{}^{3c}$ = 1.25 ppm

Then <u>additional experimental differential parameters are:</u> : $\underline{\Delta^1\delta^H{}_{CH2}{}^{18}}$ = **4.08 – 4.21 = - 0.13 ppm** и $\underline{\Delta^1\delta^H{}_{CH3}{}^{18}}$ = **1.21 – 1.25 = – 0.04 ppm**

<u>Virtual parameters</u> of ethyl 2-benzylbenzoylacetate **18**. To calculate the virtual basic parameter of ester **18** we use above-mentioned basic parameters of ethyl benzoylacetate **2c** and earlier used increments of benzyl fragment: for methylene group $i_X{}^{PhCH2}{}_{CH2}$ = +0.03 ppm, and for methyl group $i_X{}^{PhCH2}{}_{CH3}$ = +0.01 ppm.The values of <u>anticipated basic spectral parameters</u> are equal to: $\underline{W^H{}_{CH2}{}^{18}}$ = 4.21 + 0.03 = **4.24 ppm**, а $\underline{W^H{}_{CH3}{}^{15}}$ = 1.25 + 0.01 = <u>1.26 ppm</u>

<u>Virtual differential parameters:</u> $\underline{\Delta W_{CH2}{}^{18}}$ = 4.08 – 4.24 = **- 0.16 ppm** ; $\underline{\Delta W_{CH3}{}^{18}}$ = 1.09 – 1.26 = **- 0.17 ppm.**

Let us note that **all 4 negative "experimental" differential parameters** $\Delta\delta^H{}_{CH2}$, $\Delta\delta^H{}_{CH3}$, $\Delta^1\delta^H{}_{CH2}$ и $\Delta^1\delta^H{}_{CH3}$ in ethyl 2-benzylbenzoylacetate **18** have **very large absolute values** (to 0.20 ppm). The shift of signal of "outlying" methyl protons $\delta^H{}_{CH3}$ to the high field is of special interest compared with its anticipated absorption (the difference is almost 0.20 ppm).

The observed *ratio between* ΔW_{CH3} *and* $\Delta\delta^H{}_{CH3}$ *values in ethyl 2-benzylbenzoylacetate 18 indicates the presense of strong interaction in the space between phenyl fragment of benzyl and/or benzoyl group, i.e. fragment "K" and etoxyl group (fragment "M") unbound with each other.*

III.6. Aryloxysubstituted acetates.

Methyl (**19**) and ethyl (**20**) aryloxyacetates are representatives of above-mentioned compounds of the general formula Ar-$(CR^1R^2)_p$-Het-$(CR^1R^2)_r$-COOAlk, where Het = O, p = 0, r = 1. In this paper we consider them as derivatives of 3-arylpropionates (or rather as benzylacetates derivatives), in which one of methylene groups is substituted by oxygen atom.

$$S^1\text{-}C_6H_4\text{-}O\text{-}CH_2\text{-}COO\text{-}CH_3 \qquad S^1\text{-}C_6H_4\text{-}O\text{-}CH_2\text{-}COO\text{-}CH_2\text{-}CH_3$$
$$\textbf{19} \qquad\qquad\qquad \textbf{20}$$
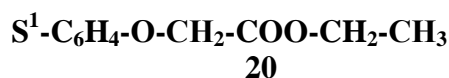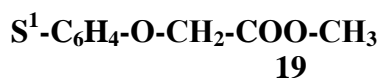
III. 6. 1. Methyl phenoxyacetate C_6H_5-O-CH_2-COO-CH_3 (19a).

<u>Experimental data</u> **19a** (X = -O-Ph, S^1=H): $\underline{\delta^H{}_{CH3}{}^{19a[9]} = \delta^H{}_{CH3}{}^{19a[10]}}$ = **3.78 ppm.**

<u>Calculated data. Main experimental differential parameters</u> is equal to: $\Delta\delta^H{}_{CH3}{}^{19a}$ = 3.78 – 3.66 = **+ 0.12 ppm.**

Methyl glycolate **4c** is chosen as auxiliary standard compound for which $\delta^H{}_{CH3}{}^{4a[9]}$ = **3.78 ppm** (see above). Then <u>additional experimental differential parameter</u> $\Delta^1\delta^H{}_{CH3}{}^{19a}$ = 3.78 – 3.78 = **0.00 ppm.**

<u>Virtual parameters</u> of methyl phenoxyacetate **19a**. To evaluate the virtual basic parameter of phenoxyester **19a** we use the increment of benzyl group ($i_X{}^{PhCH2}$ = 0.03 ppm). The increment of oxygen atom is added. In phenoxyl fragment we asusme it equal to the abovementioned increment of hydroxyl group ($i_Z{}^{O-}$ = $i_Z{}^{OH}$ = 0.12 ppm). Then the value of <u>anticipated basic parameter is</u> $\underline{W^H{}_{CH3}{}^{19a}}$ = 3.66 + 0.03 + 0.12 = **3.81 ppm**

<u>Virtual differential parameter</u> is equal to: $\Delta W_{CH3}{}^{19a}$ = 3.78 – 3.81 = **-0.03 ppm.**

III. 6. 2. Methyl (p-tolyloxy)acetate (19b).
4-CH_3-C_6H_4-O-CH_2-COO-CH_3

<u>Experimental data</u> **19b** (X = O-Ph, S^1=CH_3): $\delta^H{}_{CH3}{}^{19b[9]}$ = **3.77 ppm**

<u>Calculated parameters. Main experimental differential parameters</u> is equal to: $\underline{\Delta\delta^H{}_{CH3}{}^{19b}}$ = **3.77 – 3.66 = + 0.11 ppm**

Methyl glycolate **4c** is chosen as auxiliary standard compound (see above). Then <u>additional experimental differential parameter</u> $\underline{\Delta^1\delta^H{}_{CH3}{}^{19b}}$ = 3.77 – 3.78 = **- 0.01 ppm**

Virtual parameters of methyl (p-tolyloxy)acetate **19b**. To calculate the virtual basic parameter of aryloxyester **19b** we assume the increment of phenoxyl fragment substituted in a ring equal to the increment of unsaturated compound, i.e. $i_X^{p-MeC6H4-CH2-O} = i_X^{PhCH2-O} = +0.15$ ppm. Then the value of anticipated basic parameter is $W^H_{CH3}{}^{19a} = 3.66 + 0.15 = \underline{\textbf{3.81 ppm.}}$

Virtual differential parameter is equal to: $\underline{\Delta W_{CH3}{}^{19b}} = 3.77 - 3.81 = \underline{\textbf{-0.04 ppm.}}$ This value is practically equal to $\Delta W_{CH3}{}^{19a}$ value.

The absolute values of both parameters ($\underline{\Delta W_{CH3}{}^{19a}}$ and $\underline{\Delta W_{CH3}{}^{19b}}$) are essentially less than the absolute values of analogous virtual differential parameters $\Delta W_{CH3}{}^9$, $\Delta W_{CH3}{}^{11}$, $\Delta W_{CH3}{}^{12}$ and $\Delta W_{CH3}{}^{14}$ (see above), which are equal to -0.10±0.04 ppm

The ratio between values of ΔW_{CH3} and $\Delta\delta^H_{CH3}$ in aryloxyacetates 19a and 19b, the same as for above-mentioned compounds **16** does not allow to assert undoubtly that ***interaction between aryl groups and ester methyl group takes place, but it assumes such possibility.***

III.6.3. Ethyl (p-tolyloxy)acetate (20a).
4-CH$_3$-C$_6$H$_4$-O-CH$_2$-COO-CH$_2$CH$_3$

Experimental data of **20a** (X = O-Ph, S^1= p-CH$_3$): $\delta^H_{CH2}{}^{20a[9]} = \textbf{4.245 ppm}$, $\delta^H_{CH3}{}^{20a[9]} = \textbf{1.28 ppm.}$

Calculated parameters. Main experimental differential parameters are equal to: $\underline{\Delta\delta^H_{CH2}{}^{20a}} = \textbf{4.25} - \textbf{4.12} = \underline{\textbf{+ 0.13 ppm}}$; $\underline{\Delta\delta^H_{CH3}{}^{20a}} = \textbf{1.28} - \textbf{1.26} = \underline{\textbf{+ 0.02 ppm}}$

Ethyl glycolate **5e** (see above) is chosen as auxiliary standard compound. Then additional experimental differential paramters are euqal to: $\underline{\Delta^1\delta^H_{CH2}{}^{13}} = \textbf{4.25} - \textbf{4.25} = \underline{\textbf{0.00 ppm}}$; $\underline{\Delta^1\delta^H_{CH3}{}^{13}} = \textbf{1.28} - \textbf{1.30} = \underline{\textbf{-0.02 ppm}}$

Virtual basic parameters W. Similar to the above-mentioned calculation of virtual parameter $W^H_{CH3}{}^{19a}$ we calculate the virtual basic parameters $\underline{W^H_{CH2}{}^{20a}} = \textbf{4.12} + \textbf{0.15} = \underline{\textbf{4.27 ppm}}$; $\underline{W^H_{CH3}{}^{20a}} = \textbf{1.26} + \textbf{0.01} + (\textbf{0.12} / \textbf{2.5}) = \underline{\textbf{1.32 ppm}}$

Virtual differential parameters: $\underline{\Delta W_{CH2}{}^{20a}} = 4.25 - 4.27 = -0.02$ ppm; $\Delta W_{CH3}{}^{20a} = 1.28 - 1.32 = -0.04$ ppm.

III.4.4. Ethyl 2-(4-chlorphenoxy)-2-methylpropionate (20b).
p-Cl-C$_6$H$_4$-O-C(CH$_3$)$_2$-COO-CH$_2$-CH$_3$
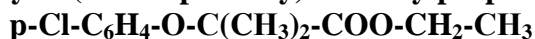
Experimental data of **20b**: $\delta^H_{CH2}{}^{20b[9]} = \textbf{4.225 ppm}$, $\delta^H_{CH3}{}^{20b[9]} = \textbf{1.25 ppm.}$

Calculated parameters. Main experimental differential parameters are equal to: $\underline{\Delta\delta^H_{CH2}{}^{20b}} = \textbf{4.23} - \textbf{4.12} = \underline{\textbf{+ 0.11 ppm}}$; $\underline{\Delta\delta^H_{CH3}{}^{20b}} = \textbf{1.25} - \textbf{1.26} = \underline{\textbf{- 0.01 ppm}}$

Virtual basic parameters W. Owing to the absence of suitable criteria for calculations of corresponding inctrements we assume virtual basic parameters $W^{H,20b}$ equal to analogous parameters of ester **20a**: $\underline{W^H_{CH2}{}^{20b} = \textbf{4.27 ppm}}$; $\underline{W^H_{CH3}{}^{20b} = \textbf{1.32 ppm}}$

Virtual differential parameters: $\underline{\Delta W_{CH2}{}^{20b}} = \textbf{4.23} - \textbf{4.27} = \underline{\textbf{-0.04 ppm}}$; $\underline{\Delta W_{CH3}{}^{20b}} = \textbf{1.25} - \textbf{1.32} = \underline{\textbf{-0.07 ppm.}}$

Owing to the exchange of methylene group for oxygen atom in the acid chain of esters **19** and **20**, the above-mentioned criteria of the presence (or absence) of interaction between unbound fragments "K" and "M" of the molecule became indefinite. Therefore, in contrast to esters **16** and **17,** there are no sufficient reasons to suppose the presence or absence of ***interaction in the space between aryl groups and esteric alkyl group***.

If such interaction takes place in ethyl ethers **20**, it is ***weaker with "nearby" methylene group than with "outlying" methyl group taking into consideration the ratio between values of differential parameters ΔW_{CH2}, $\Delta\delta^H_{CH2}$, ΔW_{CH3} and $\Delta\delta^H_{CH3}$.***

# III.7. Arylaminosubstituted acetates.

Ethyl arylaminoacetates are particular cases of the compounds of general formula $Ar-(CR^1R^2)_p-Het-(CR^1R^2)_r-COOAlk$, where $Het = NR$, $p = 0$, $r = 1$. In this paper we consider them as derivatives of 3-arylpropionates (or rather as benzylacetate derivatives) in which 3-methylene group is substituted for nitrogen atom.

III.5.1. Compound of general formula $S^1S^2-C_6H_3-NR-CH_2-COO-CH_3$.

We found in [9] PMR spectra of the only one representative of arylamoniacetates – compound **21** – symmetric dimeric diester.

III.5.1.1. Tetraethyl 1,2-bis(2-amino-5-methylphenoxy)ethane-N,N,N^1,N^1-tetraacetate (21).
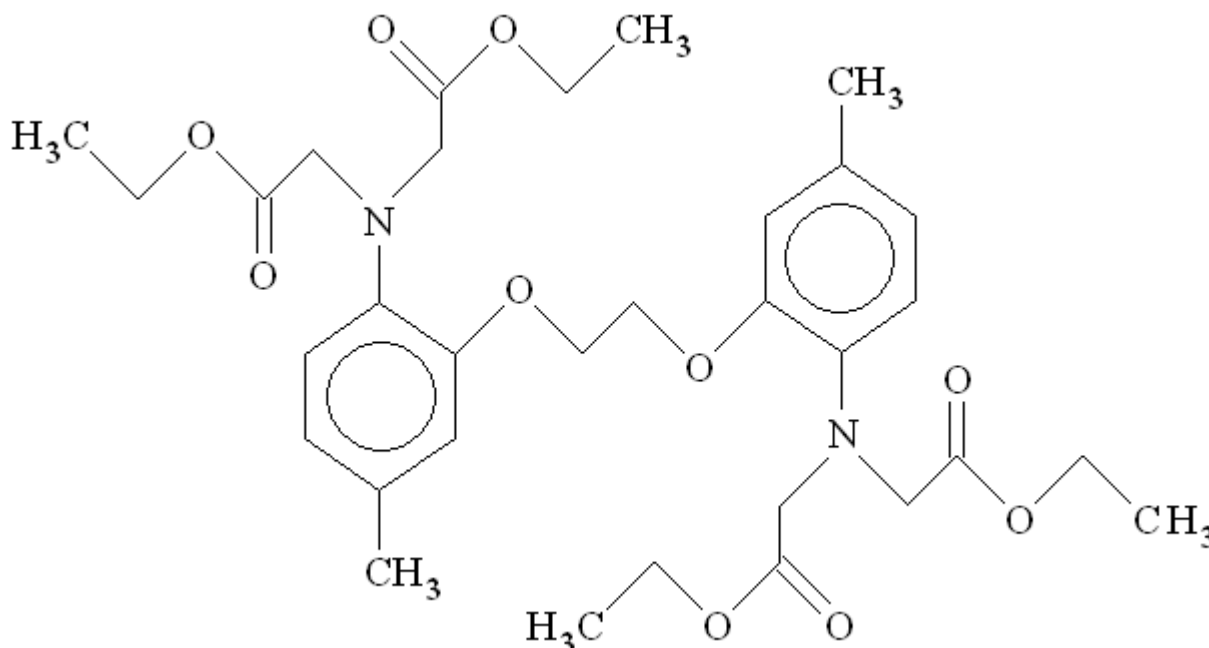
Experimental data of tetraethyl tetraacetate **21** ($X = N-Ar$, $S^1=m-CH_3$, $S^2 = o-O-CH_2-$): $\delta^H_{CH2}{}^{21[9]}$ = 4.05 ppm, $\delta^H_{CH3}{}^{21[9]}$ = 1.15 ppm.

Calculated parameters. Main experimental differential parameters are equal to: $\underline{\Delta\delta^H_{CH2}{}^{21}}$ = 4.05 – 4.12 = $\underline{\text{- 0.07 ppm}}$; $\underline{\Delta\delta^H_{CH3}{}^{21}}$ = 1.15 – 1.26 = $\underline{\text{- 0.11 ppm.}}$

Ethyl ether of dimethylglycine **5f** $(H_3C)_2N-CH_2-COO-CH_2-CH_3$ is chosen as auxiliary standard compound. Its experimental basic parameters are equal to: $\delta^H_{CH2}{}^{5f[9]}$ = **4.20 ppm**, $\delta^H_{CH3}{}^{5f[9]}$ = **1.29 ppm.**

Then additional experimental differential parameters: $\underline{\Delta^1\delta^H_{CH2}{}^{21}}$ = 4.05 – 4.20 = $\underline{\text{-0.15 ppm}}$; $\underline{\Delta^1\delta^H_{CH3}{}^{21}}$ = 1.15 – 1.29 = $\underline{\text{-0.14 ppm.}}$

Virtual basic parameters W. Owing to the absence of suitable evaluation criteria for corresponding increments we assume the increment of disubstituted nitrogen atom in arylamine fragment equal to half of the increment of hydroxyl group: for methylene fragment ($i_Z{}^{-N-}_{CH2}$ =1/2 $i_Z{}^{OH}_{CH2}$ = 0.06 ppm) and for methyl fragment ($i_Z{}^{-N-}_{CH3}$ =1/2 $i_Z{}^{OH}_{CH3}$ = 0.02 ppm). Then the values of virtual basic parameters are: $\underline{W^H_{CH2}{}^{21}}$ = 4.12 + 0.06 = $\underline{\text{4.18 ppm}}$; $\underline{W^H_{CH3}{}^{21}}$ = 1.26 + 0.02 = $\underline{\text{1.28 ppm.}}$

Virtual differential parameters: $\underline{\Delta W_{CH2}{}^{21}}$ = 4.05 – 4.18 = $\underline{\text{-0.13 ppm}}$; $\underline{\Delta W_{CH3}{}^{13}}$ = 1.15 – 1.28 = $\underline{\text{- 0.13 ppm.}}$

Thus, all 4 "experimental" differential parameters $\Delta\delta^H_{CH2}$, $\Delta\delta^H_{CH3}$, $\Delta^1\delta^H_{CH2}$ and $\Delta^1\delta^H_{CH3}$) **are very large** by their avsolute values in tetraethyl tetraacetate **21** and have **negative signs**. Moreover,

experimentally found signals of methyl protons δ^H_{CH3} in them are shifted to the high field compared with their expected positions in spectra PMR by the value equal to the absolute value of parameters $\underline{\Delta W_{CH2}}^{21}$ and $\underline{\Delta W_{CH3}}^{21}$, i.e. approximately by 0.150 ppm. In this case tetraester **21** is like ester **18**.

The ratio between ΔW_{CH3} and $\Delta\delta^H_{CH3}$ values in tetraacetate 21 indicates the **presence** of *interaction in the space between aryl fragments "K" and etoxyl group (fragment "M") unbound with each other.*

III.8. γ-Arylsubstituted butyrates.

For these compounds we found in [9, 10] only spectrum of ethyl 2-oxy-4-phenylbutyrate (**22**). Moreover, spectra of two compounds, in which β-methylene group of ester acid fragment is substituted for nitrogen atom, are represented in [9]. There are compounds of benzylaminoacetates class – **22b** and **22c**.

III.8.1. Ethyl ether of 2-hydroxy-4-phenyl-butyric acid (22a).
C₆H₅-CH₂- CH₂-CH(OH)-COO-CH₂-CH₃.

Ether **22a** may be considered as a variant of substituted ethylacetate of the general formula **2**, in which phenetyl group (C₆H₅-CH₂-CH₂-) is the substituent X and hydroxyl group is the substituent Y. The phenyl group in the compound **22a**, on the contrary to similar ether **13**, is situated farther from carbetoxyl group by not one, but by three methylene fragments.

Experimental data of **22a**: $\delta^H_{CH2}{}^{22a[9]}$ = **4.188 ppm**, $\delta^H_{CH3}{}^{22a[9]}$ = **1.269 ppm.**

Calculated parameters. Main experimental differential parameters are equal to: $\underline{\Delta\delta^H_{CH2}{}^{22a}}$ = **4.19 – 4.12 = + 0.07 ppm**; $\underline{\Delta\delta^H_{CH3}{}^{22a}}$ = 1.27 – 1.26 = **+0.01 ppm**

Ethyl glycolate **5e** HO-CH₂COOC₂H₅ is chosen as auxiliary standard compound: $\delta^H_{CH2}{}^{5e}$= 4.25 ppm и $\delta^H_{CH3}{}^{5e}$ =1.30 ppm. Then additional experimental differential parameters are: $\underline{\Delta^1\delta^H_{CH2}{}^{22a}}$ = **4.19 – 4.25 = - 0.06 ppm**; $\underline{\Delta^1\delta^H_{CH3}{}^{22a}}$ = 1.27 – 1.30 = **-0.03 ppm.**

The second auxiliary standard compound is phenyl(α-oxy)acetate **13**, in which phenyl substituent is at α-position (not at γ-position, as in **22a**): $\delta^H_{CH2}{}^{13}$ = 4.19 ppm и $\delta^H_{CH3}{}^{13}$ = 1.20 ppm Then additional "experimental" differential parameters are equal to: $\underline{\Delta^2\delta^H_{CH2}{}^{22a}}$ = 4.19 – 4.19 = **0.00 ppm**; $\underline{\Delta^2\delta^H_{CH3}{}^{22a}}$ = 1.27 – 1.20 = **+0.07 ppm**

Virtual basic parameters W. To evaluate virtual basic parameters of oxyester **22a** we use increments of hydroxyl group ($i_Z^{OH}{}_{CH2}$ = 0.12 ppm for methylene and $i_Z^{OH}{}_{CH3}$ = 0.04 ppm for methyl groups) given for **13a**. The increment of phenetyl group (for "nearby" methylene fragment) is calculated as increment of phenyl group twice divided (by the number of methylene groups in C₆H₅-CH₂- CH₂-) by factor 2.5, i.e. $i_X^{PhCH2CH2}{}_{CH2}$ = ($i_Y^{Ph}{}_{CH2}$ / 2.5) : 2.5 ≈ 0.01 ppm And increment $i_X^{PhCH2CH2}{}_{CH3}$ for methyl group is assumed to be equal to zero.

The values of anticipated basic spectral parameters: $\underline{W^H_{CH2}{}^{22a}}$ = 4.12 + 0.12 + 0.01 = **4.25 ppm,** $\underline{W^H_{CH3}{}^{22a}}$ = 1.26 + 0.04 + 0.00= **1.30 ppm.**

Virtual differential parameters: $\underline{\Delta W_{CH2}{}^{22a}}$ = 4.19 – 4.25 = -**0.06 ppm**; $\Delta W_{CH3}{}^{22a}$ = 1.27 – 1.30 = -**0.03 ppm.**

The ratio between ΔW_{CH3} and $\Delta\delta^H_{CH3}$ values in ethyl 2-oxy-4-phenylbutyrate 22a indicates the **presence** of *interaction in the space between aryl fragment and etoxyl group unbound with each other.* In accordance with the ratio between values of differential parameters ΔW_{CH2} and $\Delta\delta^H_{CH2}$ *the interaction with "nearby" methylene group of etoxyl fragment is stronger than that with "outlying" methyl group.* We suppose that outlying by two methylene groups of the phenyl substituent in **22a** compared with **13** weakens the influence on methyl fragment (perhaps because of too far position).

III.8.2. Ethyl ether of N-benzylglycine (22b).
C₆H₅-CH₂-NH-CH₂-COO- CH₂-CH₃.

Ester **22** is one compounds of the general formula Ar-$(CR^1R^2)_p$-Het-$(CR^1R^2)_r$-COOAlk, where Het = NH, p = 1, r = 1. In this paper we consider it as derivative of 4-arylbutyrate (rather as phenylacetate derivatives) in which 3-methylene group of the acid residual is substituted for nitrogen atom (NH group).

<u>Experimental data of **22b**</u>: $\delta^H_{CH2}{}^{22b[9]}$ = 4.18 ppm, $\delta^H_{CH3}{}^{22b[9]}$ = 1.26 ppm.

<u>Calculated parameters. Main experimental differential parameters</u> are equal to: $\underline{\Delta\delta^H_{CH2}{}^{22b}}$ = **4.18 – 4.12 = + 0.06 ppm**; $\underline{\Delta\delta^H_{CH3}{}^{22b}}$ = **1.26 – 1.26 = 0.00 ppm.**

Ethyl ether of dimethylglycine **5f** $(H_3C)_2N$-CH_2-COO-CH_2-CH_3 is chosen as auxiliary standard compound: $\delta^H_{CH2}{}^{5f[9]}$ = **4.20 ppm**, $\delta^H_{CH3}{}^{5f[9]}$ = **1.29 ppm.**

Then <u>additional experimental differential parameters</u> are: $\underline{\Delta^1\delta^H_{CH2}{}^{22b}}$ = 4.18 – 4.20 = **-0.02 ppm**; $\underline{\Delta^1\delta^H_{CH3}{}^{22b}}$ = **1.26 – 1.29 = -0.03 ppm**

<u>Virtual basic parameters W</u>. Owing to the absence of suitable criteria for calculations of corresponding increments we assume (the same as for the compound **21**) the increment of benzylamine fragment equal to half of the increment of hydroxyl group: $[1/2(i_Z^{OH}{}_{CH2})$ = 0.06 ppm and $1|2 (i_Z^{OH}{}_{CH3})$ = 0.02 ppm]. We evaluate the values of virtual basic parameters $\underline{W^H_{CH2}{}^{22b}}$ =**4.12 + 0.06 = 4.18 ppm**; $\underline{W^H_{CH3}{}^{22b}}$= 1.26 + 0.02 = <u>1.28 ppm.</u>

<u>Virtual differential parameters</u>: $\underline{\Delta W_{CH2}{}^{22b}}$ = 4.18 – 4.18 = **0.00 ppm**; $\underline{\Delta W_{CH3}{}^{22b}}$ = 1.26 – 1.28 = **-0.02 ppm.**

All absolute values of differential parameters are close to zero. ***The ratio between ΔW_{CH3} and $\Delta\delta^H_{CH3}$ values in 22a** cannot exactly indicates the presence or absence of **interaction in the space between phenyl "K" and etoxyl "M" fragments unbound with each other. But to our mind such interaction (may be very small by value) exists.***

III.8.3. Ethyl ether of N-benzyl-D-proline (22c).
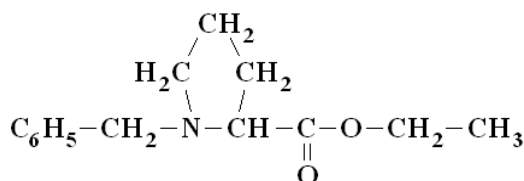
<u>Experimental data of **22c**</u>: $\delta^H_{CH2}{}^{22c[9]}$ = **4.12 ppm**, $\delta^H_{CH3}{}^{22c[9]}$ = **1.24 ppm.**

<u>Calculated parameters. Main experimental differential parameters</u> are equal to: $\underline{\Delta\delta^H_{CH2}{}^{22c}}$ = **4.12 – 4.12 = 0.00 ppm**; $\Delta\delta^H_{CH3}{}^{22c}$ = 1.24 – 1.26 = **- 0.02 ppm**

Ethyl ether of methypipecoline acid **5g** is chosen as auxiliary standard compound. Its experimental basic parameters are equal to: $\delta^H_{CH2}{}^{5g[9]}$ = **4.22 ppm**, $\delta^H_{CH3}{}^{5g[9]}$ = **1.29 ppm.**

<u>Additional experimental differential parameters</u>: $\underline{\Delta^1\delta^H_{CH2}{}^{22c}}$ = 4.12 – 4.22 = **-0.10 ppm**; $\underline{\Delta^1\delta^H_{CH3}{}^{22c}}$ = 1.24 – 1.29 = **-0.05 ppm.**

<u>Viertual basic parameters</u>. Owing to the absence of suitable criteria for calculations of corresponding increments we assume (the same as for the compounds **21 and 22b**) the increment of benzylamine fragment equal to half of the increment of hydroxyl group. We evaluate the values of virtual basic parameters are: $\underline{W^H_{CH2}{}^{22c}}$ =4.12 + 0.06 = **4.18 ppm**; $W^H_{CH3}{}^{22c}$= 1.26 + 0.02 = **1.28 ppm.**

<u>Virtual differential parameters</u>: $\underline{\Delta W_{CH2}{}^{22c}}$ = 4.12 – 4.18 = **-0.06 ppm**; $\underline{\Delta W_{CH3}{}^{22c}}$ = 1.24 – 1.28 = **-0.04 ppm.**

The ratio between ΔW_{CH3} and $\Delta\delta^H_{CH3}$ values in ethyl ether of N-benzyl-D-proline (22c)** confirms the presence of small **interaction in the space between aryl fragment and etoxyl group unbound with each other. According to the ratio between differential parameters ΔW_{CH2} and $\Delta\delta^H_{CH2}$ (compared with the ratio between ΔW_{CH3} and $\Delta\delta^H_{CH3}$) the interaction with "nearby" methylene and "outlying" methyl groups are approximately the same.

III.9. ε-Arylsubstituted caproates.

The most long-chain ester of ω-arylalkane acids, PMR spectra of which we found in [9, 10] is diester **23.** Aryl fragment in it is separated from carbetoxyl fragment by five methylene groups. Diester **23** is one of the compounds of the general formula $Ar\text{-}(CR^1R^2)_p\text{-}Het\text{-}(CR^1R^2)_r\text{-}COOAlk$, where Het = NR, p = 2, r = 2. We consider it as N-substituted derivative of 6-phenylcaproic acid in which methylene group C-4 is substituted for R-N= fragment.

III.9.1. Diethyl 3,3'-(phenylimino)dipropionate (23).

$C_6H_5\text{-}CH_2\text{-}CH_2\text{-}N(CH_2\text{-}CH_2\text{-}CO\text{-}O\text{-}CH_2\text{-}CH_3)_2$
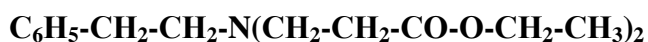
Experimental data of diester **23**: $\delta^H{}_{CH2}{}^{23[9]}$ = 4.12 ppm, $\delta^H{}_{CH3}{}^{23[9]}$ = 1.25 ppm
Calculated parameters. Main experimental differential parameters are equal to: $\Delta\delta^H{}_{CH2}{}^{23}$ = 4.12 − **4.12 = 0.00 ppm**; $\Delta\delta^H{}_{CH3}{}^{23}$ = 1.25 − 1.26 = **- 0.01 ppm**
Ethyl ether of caproic acid **5h** is chosen as auxiliary standard compound. Its experimental basic parameters are equal to: $\delta^H{}_{CH2}{}^{5h[9]}$ = **4.125 ppm**, $\delta^H{}_{CH3}{}^{5h[9]}$ = **1.25 ppm** Additional experimental differential parameters: $\Delta^1\delta^H{}_{CH2}{}^{23}$ = 4.12 − 4.13 = **-0.01 ppm**; $\Delta^1\delta^H{}_{CH3}{}^{23}$ = 1.25 − 1.25 = **0.00 ppm**
Virtual basic parameters. We take into consideration only increment of ethylamine fragment ($R^1R^2N\text{-}CH_2\text{-}CH_2\text{-}$), because increments of other "outlying" substituents bound with C-6 atom (phenyl group) and C-6^1 atom (carbetoxyl group) are very difficult to account. We assume that increments of so "outlying" groups should have very small absolute values, therefore we neglect them. We assume the increment of ethylamine fragment ($R^1R^2N\text{-}CH_2\text{-}CH_2\text{-}$) in **23** equal to the increment of ethylamine fragment $(CH_2)_5N\text{-}CH_2\text{-}CH_2\text{-}$ in ethyl 1-piperidinopropionate $(CH_2)_5N\text{-}CH_2\text{-}CH_2\text{-}COO\text{-}CH_2\text{-}CH_3$ (**5i**) for which $\delta^H{}_{CH2}{}^{5i[9]}$ = **4.135 ppm**, $\delta^H{}_{CH3}{}^{5i[9]}$ = **1.26 ppm** Then calculated increments $i_Z{}^{-(CH2)5N\text{-}CH2\text{-}CH2\text{-}}$ are following: for methylene ($i_Z{}^{-N=}{}_{CH2}$ = 4.14 − 4.12 = +0.02 ppm) and for methyl fragment ($i_Z{}^{-N=}{}_{CH3}$ = 1.26 − 1.26 = 0.00 ppm). Values of virtual basic parameters are: $\underline{W^H{}_{CH2}{}^{23}}$ =**4.12 + 0.02 = 4.14 ppm**; $\underline{W^H{}_{CH3}{}^{23}}$ = **1.26 + 0.00 = 1.26 ppm.**
Virtual differential parameters: $\Delta W_{CH2}{}^{23}$ = 4.12 − 4.13 = **-0.01 ppm**; $\Delta W_{CH3}{}^{23}$ = 1.25 − 1.26 = **- 0.01 ppm.**

The absolute values of all differential parameters ΔW_{CH2}, $\Delta\delta^H{}_{CH2}$, ΔW_{CH3} *u* $\Delta\delta^H{}_{CH3}$ in diester (**23**) are very small and do not exceed stipulated threshold of measurements accuracy. Therefore for this compound *it is impossible to make conclusions about the presence or absence of the interaction between phenyl fragment and etoxyl group unbound with each other.*

IV. Conclusion.

In conclusion we compare values of differential spectral parameters (experimental and virtual) of all investigated methyl and ethyl ethers of ω-arylacetic acids (**9-23**). Depending upon the absolute value these parameters are united in several groups. Those parameters, the absolute values of which do not exceed the measurements error (±0.02 ppm) we include to the first group. We denote it by symbols "+" or "-" depending upon the parameter sign. The second group involves middle by absolute value parameters within the interval of 0.03÷0.10 ppm (for "nearby" alkyl groups) and within the interval of 0.03÷0.05 ppm (for "outlying" methyl groups). We denote them as "++" and "--". The third group involves greater by size parameters, absolute values of which are more than 0.10 ppm (for "nearby") and more than 0.05 ppm "outlying" alkyl groups. We denote them as "+++" and "---". Table 3 represents all differential parameters of the compounds **9-23** in a view of mentioned symbols. The negative values are green and positive values are red.

Table 3.

Classification of differential parameters of esters **9-23** of the general formula
Ar-(CR^{1}R^2)$_n$-COO-Alk.

Number of compound	Value n	Parameters of "nearby" alkyl groups			Parameters of "outlying" methyl groups		
		$\Delta\delta^H$	$\Delta^1\delta^H$ (and $\Delta^2\delta^H$)	ΔW^H	$\Delta\delta^H$	$\Delta^1\delta^H$ (and $\Delta^2\delta^H$)	ΔW^H
9a	1	+	absent	++			
9b-9g		+	absent	++			
10a		+	absent	++	++	absent	+++
10b-10e		+	absent	++	+	absent	++
11		++	absent	+++			
12a		++	++	+++			
12b		++	++	+++			
12c		++	absent	++			
13		++	++	+++	++	++	+++
14a		+++	+	+++			
14b		+++	++	+			
15		+++	+++	+	+++	++	+
16a	2	+	absent	++			
16b		+	absent	+			
17		+	absent	++	++	absent	++
18		++	+++	+++	+++	++	+++
19a		+++	0	++			
19b		+++	+	++			
20a		+++	0	+	+	+	++
20b		+++	absent	++	+	absent	+++
21		++	+++	+++	+++	+++	+++
22a	3	++	++	++	+	++	+++
22a		++	$\Delta^2\delta^H = 0$	++	$\Delta^2\delta^H$: +	+++	++
22b		++	+	0	0	++	+
22c		0	+++	++	+	++	++
23	5	0	+	+	+	0	+

Two types of differential parameters ("experimental" and "virtual") are represented in Table 3. To calculate the "main experimental" parameters $\Delta\delta^H_{OAlk}$ we use the main standard compounds methyl (**4a**) and ethyl (**5a**) acetates without electron-acceptor substituents. The chemical shifts of alkoxyl groups δ^H_{OAlk} in them belong to the most high-field shifts among the compounds of such type. Therefore we expect that the "main experimental" parameters $\Delta\delta^H_{OAlk}$ in the compounds of the general formula **1-3** in which the substituents X,Y and Z are usually electron-acceptor groups, shift the signals of alkoxyl groups toward low field. So it is more probably that the "main experimental" parameters

$\Delta\delta^H_{OAlk}$ (relatively to acetates **4a or 5a**) would have a positive sign. However for three methyl ethers (**9a, 11, 16a**) the $\Delta\delta^H_{CH3}$ parameters have the negative signs and denoted in the table by green color. Moreover, ester of 1-naphthylacetic acid **11** has category "++". Similarly, the parameters of "nearby" methylene groups $\Delta\delta^H_{CH2}$ of three ethyl esters (**17, 18, 21**) have negative (green) values.

The most of parameters $\Delta\delta^H_{CH3}$ of "outlying" methyl groups of etoxyl fragment are negative (green) and involved in the category "++". Two compounds (**18 and 21**) belong to the category "+++". Therefore, the negative by sign "main experimental" parameters $\Delta\delta^H_{OAlk}$ have the maximum value while determination of interaction between unbound fragments of the molecule during recording of NMR^{1}H spectra.

The majority of "auxiliary experimental" differential parameters $\Delta^1\delta^H_{OAlk}$ are also negative by sign. It is no wonder, because esters with al least one electron-acceptor group Y are used as standard compounds. The exclusions are esters of ketone acids **14b and 15**. The positive sign of their parameters $\Delta^1\delta^H_{OAlk}$ is the main argument in favour of absence in them the interaction between unbound fragments during recording of NMR^{1}H spectra.

All above-mentioned refer mostly to the "virtual" differential parameters ΔW^H_{OAlk}. They take into account the increments i_Y and i_Z of electron-acceptor groups Y and Z present in the molecules of compounds **2 and 3** as well as aryl group (in the substituent X). In accordance with all mentioned criteria we consider that **interaction betwen unbound phenyl and alkoxyl fragments is absent only in esters of ketone acids 14b and 15 during recording of NMR^{1}H spectra.**

Taking into account the relative importance of every three differential parameters (Table 3) we suppose that the greatest probability of metioned interaction is present in the compounds **21, 18, 11, 16a, 10a** and **13** (in decreasing order). **The greatest probability of the interaction was found for ethyl esters of β-arylpropionic acids (especially for "outlying" methyl groups), methyl esters of the same acids and for methyl and ethyl esters of arylacetic acids.**

While analysing the dependence between probability of intramolecular interaction and remoteness of interactive groups it seems to us that optimal interaction takes place at n=2 in the formula Ar-(CH$_2$)$_n$-COO-Alk. The numbers n=1 and n=3 are less favourable for the interaction. With the further increase of the number n (i.e. with the increase of aryl fragment remoteness from alkoxyl fragment) the probability of their interaction decreases, seemingly.

General conclusions.

1. The influence of aryl group position in the alkyl chain of the acidic fragment of methyl and ethyl esters of linear ω-arylcarbonic acids of the general formulas Ar-(CH$_2$)$_n$-COO-Alk and Ar-(CR^{1}R^2)$_p$-Het-(CR^{1}R^2)$_r$-COOAlk (where p + r = n-1) on the values of chemical shifts of alkoxyl groups δ^H_{Alk} (δ^H_{CH2} and δ^H_{CH3}) has been determined.

2. The greatest shifts (to 0.2 ppm) of the basic spectral parameters δ^H_{CH2} and δ^H_{CH3} toward high field have been found for esters of 3-arylpropionic and arylacetic acids (n=2 or 1).

3. The notion of "virtual anticipated value of chemical shift" has been introduced and method of its evaluation has been proposed. The comparison of experimental and anticipated values δ^H_{Alk} allows to suppose the presence of aryl group effect on the chemical shifs of alkoxyl fragments during spectrum recording. The value of difference between experimental (δ^H_{Alk}) and anticipated (W) values of basic spectral parameters δ^H indicates the presence or absence of the interaction.

4. Basic spectral parameters δ^H_{OAlk} found by the experiments have been compared with the same parameters of the compounds chosen as primary and secondary standards. The difference between these parameters (so called "experimental" differential parameters) is the important criterion to determine the possibility of aryl fragment effect on alkoxyl group in the investigated compounds.

5. It has been supposed that probability of aryl fragment ("K") effect on alkoxyl group (fragment "M") depends upon the amount of methylene groups in the "middle" fragment "L" of esteric molecule "K-L-M".

6. The effect of aryl group of the fragment "K" on the methylene and methyl groups of etoxyl fragment "M" is supposed to be different by value.

7. Esters of 2-arylbenzoic acid, methyl 2-para-tolylbenzoat **6g** is a special case. Its differential parameters suppose the presence of strong interaction between phenyl and methyl groups. Aryl (para-tolyl) group is ortho-position may be considered as rigidly oriented in the space additional substituent in β-position of α,β-polysubstituted propionic acid. Probably, the rigid of carbonic skeleton in ester **6g** causes the greatest influence of para-tolyl group on metoxyl one owing to favourable conformation of the molecule. The result is the greatest by the absolute value (among all calculated) corresponding differential parameter $\Delta^1\delta^H_{CH3}{}^{6g[10)} =$ **-0.237 ppm.**

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