ALKYL 1-[2-(OXIDO ANION)-, 3-, 4-, 5-ALKYL SUBSTITUTED] PHENYL KETYL RADICALS*

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Reactions of R^2,R^3-alkyl substituted 2-hydroxybenzenecarboxylic acids 2-HO—$C_6H_2R_2$——COOH with Grignard reagents R^1MgBr in the presence of nickel give stable aryl alkyl ketyl radicals 2-O^-—R^2—, R^3—C_6H_2—$CO^{\cdot+}$-R^1 where $R^1 = CH_3, C_2H_5, C_2D_5$, n-$C_3H_7$ and $R^2, R^3 =$ $= CH_3$, C_2H_5, i-C_3H_7, t-C_4H_9. The β protons of ketyl group are equivalent (splitting constant 1·25 mT) and non-equivalent (splitting constants within 0·5 to 1·5 mT) for R^1 = methyl and other alkyl groups, respectively. Interaction of the γ protons with the unpaired electron was only observed in the case of R^1 = n-propyl (splitting constants about 0·07 mT). The substituents R^1 have but slight effect on values of splitting constants of the protons in R^2,R^3 and *vice versa*. Also splitting constants of the benzene nucleus ($a_4^H = 0{\cdot}55$ mT, $a_6^H = 0{\cdot}44$ mT) are only slightly affected by the substituents R^1,R^2,R^3, which indicates dominant electron-donor effect of the oxido-anion group eliminating the relatively smaller contributions of the alkyl substituents.

In previous reports[1-3] it was stated that reaction of nickel(II) 3,5-diisopropyl--2-hydroxybenzenecarboxylate [Ni(DIPS)$_2$] with Grignard reagents results in reduction of the carboxylic to carbonyl group with formation of the respective aryl alkyl ketone. The transition metal present in such system enables the electron-transfer from alkyl of the Grignard reagent to the formed ketone, which results in formation of ketyl radicals. The reports[2,3] also gave mechanism of formation of radicals in reaction of Ni(DIPS)$_2$ with various hydrides and Grignard reagents. Systematical variation of reducing agents enabled (with the use of ESR) structure determination of the formed radicals and assignment of their splitting constants. The present communication extends the previous studies to radicals with various substituents in benzene nucleus of 2-hydroxybenzenecarboxylate. The aim is to investigate redistribution change of spin density of the unpaired electron with respect to type and number of the ring substituents and confirm the presumed assignement of the proton splitting constants of these structures. For this purpose we investigated reactions of the fol-

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lowing alkyl substituted carboxylic acids: 2-hydroxybenzenecarboxylic acid (*I*) and its substituted homologues 5-tert-butyl (*II*), 3,5-ditert-butyl (*III*), 3,5-di-isopropyl (*IV*), 4-methyl (*V*), 4-ethyl (*VI*), 4-isopropyl (*VII*), 4-tert-butyl (*VIII*) with the following Grignard reagents: CH_3MgBr (*a*), C_2H_5MgBr (*b*), C_2D_5MgBr (*c*) and n-C_3H_7MgBr (*d*).

These reactions give aryl alkyl ketyl radicals, the alkyl and the aryl being derived from the Grignard reagent and the carboxylic acid, respectively. Choice of the alkyls enabled unambiguous assignement of the splitting constants and evaluation of effect of the alkyls on spin density redistribution of the unpaired electron. As in ref.[4] in this case, too, the whole series of the generated radicals exhibited interactions of the ketyl γ protons with the unpaired electron, if n-C_3H_7MgBr was used.

EXPERIMENTAL

The experimental technique used was similar to that in refs[2,5]. All the measurements were carried out with elimination of traces of humidity under argon atmosphere at 20°C. Solutions of the 2-hydroxybenzenecarboxylic acids (1·0M) in diethyl ether were used in contrast to the previous works where the respective nickel(II) salts were dissolved in benzene. Nickel(II) acetylacetonete or dried nickel(II) chloride or cobalt(II) bromide was added to the solutions to make the final Ni or Co concentration in the reaction mixture 10^{-4}M. Then 2M solution of Grignard reagent in diethyl ether was added, the ratio acid to RMgX being 1 : 4. Application of the carboxylic acids instead of their nickel(II) salts proved to be useful, as preparation of most nickel(II) salts of the acids *I* to *VIII* has not yet been satisfactorily mastered (the respective carboxylates have undefined composition and low solubilities). In cases when it was possible to prepare these carboxylates, their reduction gave identical spectra of radicals as those obtained from pure acids with added $NiCl_2$.

The used acids *V*, *VI* were obtained from Pharmaceutical Faculty, Comenius University, Bratislava; the acid *I* is from Reanal, Budapest; the acids *II* to *IV*, *VII* and *VIII* were prepared according to refs[6-10]. Preparation of the Grignard reagents is described in refs[2,3]. The spectra were measured and simulated with a Varian E-3 spectrometer equipped with a spectral computer Varian Spectra System 100.

RESULTS AND DISCUSSION

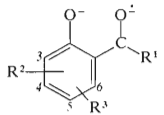
The experimental spectra obtained for the reactions of the acids *I* to *VIII* with the Grignard reagents *a* to *d* are given in Fig. 1 along with the respective simulated spectra. The simulated and the experimental spectra agree relatively well. On the basis of variation of individual parameters it could be estimated that accuracy

FIG. 1

The Experimental and Simulated Spectra Obtained in Reactions of Alkyl Substituted 2-Hydroxybenzenecarboxylic Acids *I* to *VIII* with *a*) CH_3MgBr, *b*) C_2H_5MgBr, *c*) C_2D_5MgBr and *d*) n-C_3H_7MgBr

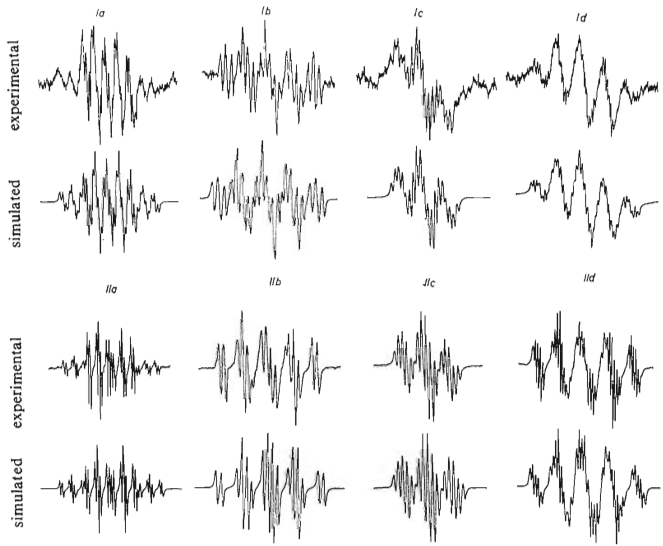
in determination of the splitting constants was $\pm 0{\cdot}01$ mT or, in some cases, even better.

In the previous reports[2,3] course of the reaction between 2-hydroxybenzenecarboxylic acid and Grignard reagents was analyzed in detail. Also the substituted acids *I* to *VIII* studied here confirm the expected reduction course; hydrogen of phenoxy group is eliminated to give oxido-anion, and carboxylic group is reduced to carbonyl. The product formed from the various reagents is given in the following structure:



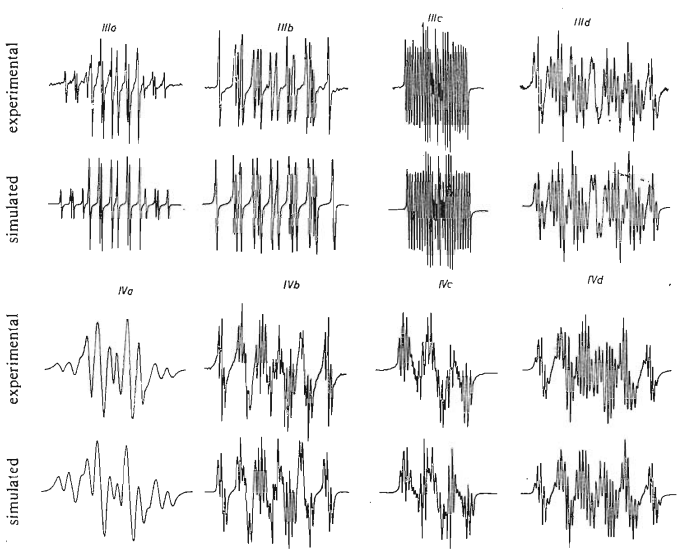
$R^1 = CH_3, C_2H_5, C_2D_5, n\text{-}C_3H_7$

$R^2, R^3 = CH_3, C_2H_5, i\text{-}C_3H_7, t\text{-}C_4H_9$

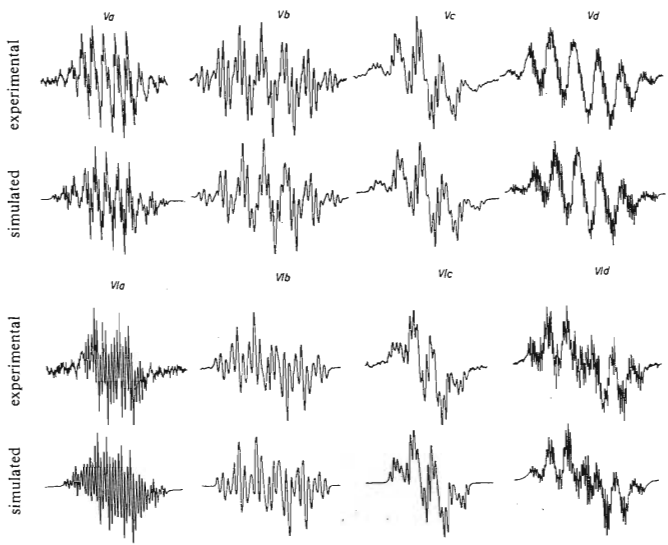


On the basis of this structure it is possible to interpret the spectra of all the formed radicals *I–VIII* (*a*,*b*,*c*,*d*). Table I gives these structures of ketyl radicals derived from individual alkyl-substituted carboxylic acids, and the splitting constants are assigned to the individual protons. Scope of the studied series and systematic variation of substituents enable unambiguous assignement of the splitting constants.

Assignement of splitting constants. Variation of alkyl (CH_3, C_2H_5, C_2D_5 and n-C_3H_7) of the Grignard reagent used in the reactions enabled, on basis of ESR spectra, to assign the splitting constants to the protons coming from the Grignard reagents and to those of aromatic ring of the acids. Thus *e.g.* from the structure *Ia*,*b*,*c*,*d* (Table I) it is obvious that variation of the alkyl R^1 (*a* CH_3, *b* C_2H_5, *c* C_2H_5, and *d* n-C_3H_7) does not change values of the splitting constants a_3, a_4, a_5, a_6, whereas $a_{1'}$, $a_{1''}$, $a_{2'}$ take various values depending on the alkyl type. On the basis of this fact it can be presumed that a_3, a_4, a_5, a_6 constants are due to the protons of the aromatic ring, whereas $a_{1'}$, $a_{1''}$, $a_{2'}$ belong to the protons of the alkyl R^1.



This presumption is in accordance with analysis of the splitting constants of the alkyl protons. In case of methyl, *i.e.* structure *Ia*, a relatively high value of the splitting constant ($a_{1'} = 1{\cdot}24$ mT) was found for the three equivalent protons. Methylene protons in ethyl group of the structure *Ib* exhibit markedly lower splitting constants for the two non-equivalent protons, *viz.* $a_{1'} = 0{\cdot}676$ mT, $a_{1''} = 0{\cdot}598$ mT. Unambiguity of the assignement of two splitting constants to the ethyl protons is confirmed by the structure *Ic*, where ethyl group is substituted by its deuterated analogue, the respective spectra reflecting the presumed changes in nuclear spin number ($I_H = \frac{1}{2}$ to $I_D = 1$) and in the splitting constant values ($a^H_{1'} = 0{\cdot}676$ mT $\rightarrow a^D_{1'} = 0{\cdot}098$ mT and $a^H_{1''} = 0{\cdot}598$ mT $\rightarrow a^D_{1''} = 0{\cdot}0865$ mT). The splitting constants of the structure *Id*, where the respective alkyl is n-propyl, also agree with the above assignement. For the β protons of the ketyl radical *Id* similar values of the constants are obtained as those of the β protons of the structure *Ib*. In addition, in the structure *Id* there is interaction of two more protons with the splitting constant 0·062 mT. These inter-



actions can only be due to the protons in n-propyl, and, in accord with ref.[4], we assigned them to γ protons of the ketyl radical. Analogous consideration of assignement of the alkyl protons applies for the structures *II* to *VIII*, too. There remains to assign the splitting constants of the structures *I* to *VIII* with the average values $\bar{a}_3 = 0{\cdot}125$ mT, $\bar{a}_4 = 0{\cdot}53$ mT, $\bar{a}_5 = 0{\cdot}16$ mT and $\bar{a}_6 = 0{\cdot}45$ mT to the individual protons of the benzene ring. In accord with known distribution of spin density of the unpaired electron in aryl ketyl radical it can be presumed that the highest splitting constant a_4 is due to the *para*-proton, the second highest a_6 is due to the *ortho*-proton, and the remaining a_3 and a_5 are due to the *meta*-protons in ketyl radical. Such assignement of the splitting constant a_4 also follows from the structure *VIII*, where substitution of the *para*-proton by tert-butyl group causes the interaction corresponding to $\bar{a}_4 = 0{\cdot}53$ mT to be absent in the spectrum, whereas the other constants have approximately the original values. Assignement of the *meta*-protons was explained similarly with the structure *II* in which the 5-proton is replaced by tert-butyl group, and,

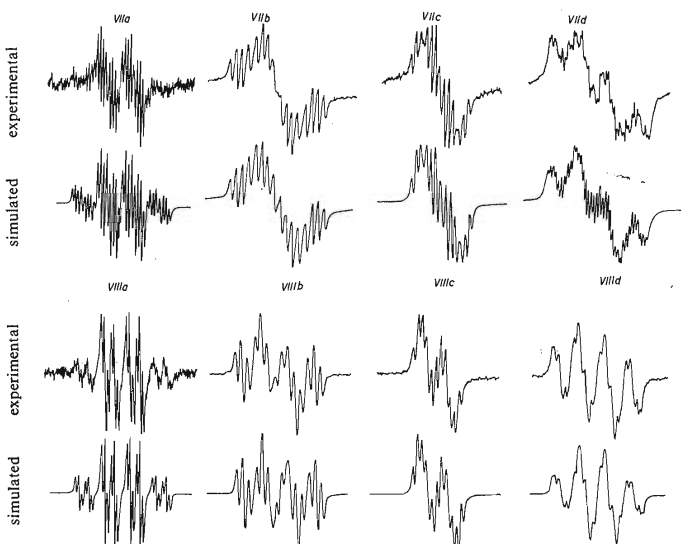
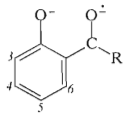


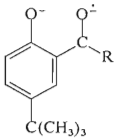
TABLE I

Structures and Assignement of Splitting Constants of the Ketyl Radicals Generated by Reactions of Alkyl Substituted 2-Hydroxybenzenecarboxylic Acid with Alkylmagnesium Halogenides

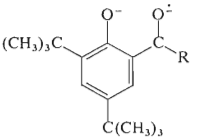
Structure		Splitting constants, mT						
		a_3	$a_{4(\alpha)}$	a_5	a_6	a_1'	a_1''	a_2'
	a	0·12	0·571	0·16	0·469	1·24	—	—
I	*b*	0·12	0·571	0·16	0·469	0·676	0·598	—
	c	0·12	0·571	0·16	0·469	0·098	0·0865	—
	d	0·125	0·561	0·155	0·469	0·686	0·598	0·062
	a	0·117	0·568	—	0·459	1·24	—	—
II	*b*	0·117	0·568	—	0·459	0·658	0·568	—
	c	0·117	0·568	—	0·459	0·1005	0·0875	—
	d	0·117	0·568	—	0·459	0·658	0·568	0·058
	a	—	0·532	—	0·435	1·235	—	—
III	*b*	—	0·53	—	0·43	1·205	0·38	—
	c	—	0·532	—	0·4315	0·1815	0·0565	—
	d	—	0·519	—	0·439	1·228	0·303	0·073
	a	0·069	0·52	0·069	0·42	1·265	—	—
IV	*b*	0·057	0·5215	0·071	0·425	0·818	0·5465	—
	c	0·057	0·5215	0·071	0·425	0·1256	0·0836	—
	d	0·064	0·525	0·064	0·428	0·828	0·575	0·064
	a	0·125	0·591	0·154	0·484	1·25	—	—
V	*b*	0·134	0·591	0·154	0·484	0·684	0·617	—
	c	0·123	0·591	0·154	0·484	0·1073	0·089	—
	d	0·116	0·60	0·153	0·493	0·652	0·63	0·06
	a	0·13	0·46	0·16	0·491	1·26	—	—
VI	*b*	0·13	0·452	0·16	0·491	0·68	0·60	—
	c	0·13	0·452	0·16	0·491	0·1025	0·0905	—
	d	0·122	0·457	0·158	0·477	0·77	0·535	0·055
	a	0·13	0·285	0·155	0·495	1·25	—	—
VII	*b*	0·13	0·287	0·155	0·492	0·685	0·607	—
	c	0·132	0·27	0·157	0·480	0·107	0·093	—
	d	0·13	0·287	0·155	0·492	0·685	0·607	0·064
	a	0·13	—	0·16	0·48	1·27	—	—
VIII	*b*	0·13	—	0·155	0·492	0·685	0·607	—
	c	0·13	—	0·155	0·50	0·106	0·09	—
	d	0·122	—	0·165	0·484	0·664	0·632	0·063



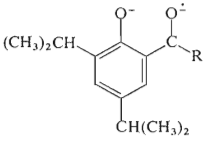
Ia, b, c, d



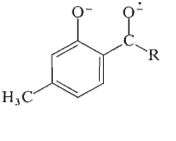
IIa, b, c, d,



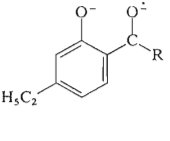
IIIa, b, c, d



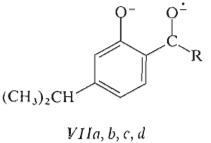
IVa, b, c, d



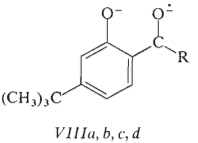
Va, b, c, d



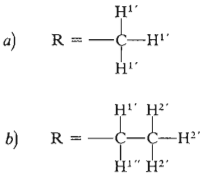
VIa, b, c, d

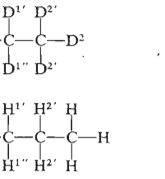


VIIa, b, c, d



VIIIa, b, c, d





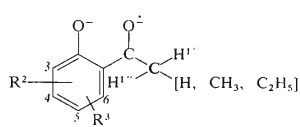
consequently, the spectrum lacks the splitting constant a_5. Changes of splitting constants of the remaining structures agree with this assignement. Thus *e.g.* substitution of the 4-proton by CH_3, C_2H_5, i-C_3H_7, t-C_4H_9 (structures *V* to *VIII*) causes gradual lowering (in case of t-C_4H_9 disappearance) of the splitting constant of the proton at 4 position. Similarly, substitution of the 3,5-protons by t-C_4H_9 (structure *III*) causes the splitting constants a_3 and a_5 to be absent in the spectrum.

Influence of substituents on redistribution of spin density of the unpaired electron. Comparison of the splitting constants a_3, a_4, a_5, a_6 of the benzene ring protons for a single acid (*e.g.* the structures *Ia,b,c,d*) in Table I indicates that their values are practically independent of the alkyls in the Grignard reagents $a-d$. Therefore, for further discussion Table II gives average values of the splitting constants $\bar{a}_4$, $\bar{a}_6$ of the structures *a,b,c,d* for the respective structures *I* to *VIII*. Effect of the alkyl substituents will be obtained from comparison of the non-substituted structure *I* with the splitting constants of *II* to *VIII*.

From data of Table II it follows that gradual alkyl substitution of benzene ring at 3,5 positions (structures *I* to *IV*) results in decrease of values of splitting constants at positions 4 and 6. This decrease is relatively small but, within the experimental error, statistically significant. Small increase of the splitting constant a_6 is encountered with the structures *V* to *VIII* as compared with *I* due to alkyl substitution at 4-position. This increase is, however, insignificant. Also effect of alkyl substituents R^2, R^3 in benzene ring on the splitting constants $a_{1'}$ and $a_{1''}$ of the alkyl protons in β position of the ketyl is insignificant. The constants $a_{1'}$ and $a_{1''}$ of the structures *V*, *VI* are

TABLE II

Experimental Values of Splitting Constants of Protons Found for Various Substituents of Benzene Ring of Ketyl Radical



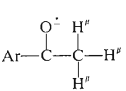
Compound	Substituents R^2, R^3	Splitting constants, mT			
		$\bar{a}_4$ [a]	$\bar{a}_6$ [a]	$a_{1'}$ [b]	$a_{1''}$ [b]
I	unsubstituted	0·569	0·469	0·681	0·598
II	5-t-C_4H_9	0·568	0·459	0·658	0·568
III	3,5-di-t-C_4H_9	0·528	0·434	1·216	0·341
IV	3,5-di-i-C_3H_7	0·522	0·424	0·823	0·567
V	4-CH_3	—	0·486	0·668	0·624
VI	4-C_2H_5	—	0·488	0·725	0·567
VII	4-i-C_3H_7	—	0·490	0·685	0·607
VIII	4-t-C_4H_9	—	0·489	0·675	0·619

[a] Average values of the splitting constants of the structures *a,b,c,d*; [b] average values of the splitting constants of the structures *b,d*.

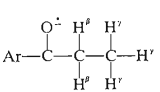
very close to those of *I*. Substitution in the structures *III*, *IV* causes an increase of non-equivalency of the protons 1′ and 1″, but their overall spin density is not markedly increased, if it is compared with the respective protons of *I*.

Generally alkyl substituents in benzene ring and in ketyl group of the discussed radical type do not affect the spin density distribution of the unpaired electron. This remarkable fact can be logically explained, if the oxido-anion group at 2-position and its strong electron-donor effect are taken into account. It can be expected that the push-effect of this group is so marked that relative contributions of alkyl groups are small and practically non-detectable in spectrum. This explanation is supported by further experiments which are now being carried out: similar structures but without the oxido-anion group are investigated, and electron-donor effect of alkyl substituents is observed in this type of radicals.

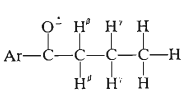
Interaction of γ-protons of ketyl groups with unpaired electron. The investigated series of the radicals *I* – *VIIIa,b,d* can, with respect to *β*- and *γ*-protons of the ketyl group, be characterized generally by the following structures:



i)



ii)



iii)

where Ar represents aromatic ring of the acids *I* to *VIII*. It is noteworthy to compare interactions of the individual protons at *β* and *γ* positions of the ketyl group with the unpaired electron. If there is a methyl group at position (type *i*), its protons are equivalent with the splitting constant 1·25 mT. On the contrary, if there are methylene protons at position of ethyl group (type *ii*), their non-equivalency is manifested in the values of the splitting constants 0·6 mT and 0·7 mT, which indicates limited rotation of methylene group. Interaction of the *γ*-protons (*i.e.* methyl protons) of the ethyl group does not make itself felt in the spectrum. In the third case (type *iii*) the respective alkyl is n-propyl. The *β* protons usually have the same values of the splitting constants as those in ethyl group. At *γ* position there are not methyl but methylene protons (in contrast to the type *ii*). It is remarkable that the substitution

of methyl by methylene protons at γ position makes itself felt by interaction of the methylene protons with the unpaired electron, the splitting constant being 0·07 mT. Analogous phenomenon was observed for longer n-alkyl group, too.

Interactions of γ protons are rare, and their mechanism of transfer of spin density of the unpaired electron is not clear. Furthermore, in the studied system different behaviour of methyl and methylene protons at γ position is observed. Obviously the methyl group rotates freely in contrast to the methylene group the rotation of which will probably be limited, its sterical orientation towards the ketyl group being possible. The observed splitting of the γ protons could be explained by hyperconjugation mechanism.

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