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INVESTIGATIONS TO CHARGE DEPENDENCE OF $^{13}C^{13}C$ SPIN-SPIN COUPLING CONSTANTS - AMINOBENZOIC ACIDS AND THEIR IONIC SPECIES

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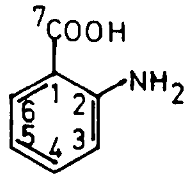
Abstract - The $^{13}C^{13}C$ spin-spin coupling constants of ortho-, meta- and para-aminobenzoic acids, benzoic acid and aniline have been measured for the neutral compounds and both for the corresponding anions and cations. The results are compared with the behaviour of the ^{13}C chemical shifts and discussed with respect to MO calculations.

$^{13}C^{13}C$ spin-spin coupling constants can give a detailed insight into the electron distribution in a molecule. In hydrocarbons they provide a direct measure of carbon hybridization.[1,2] Recently, we have observed[3] a remarkable pH dependence of $^{13}C^{13}C$ spin-spin coupling constants in vitamin C, which was interpreted in terms of ground state contribution of different mesomeric forms of the molecule. During this work it occurred to us, that no systematic study of the effect of charge on $^{13}C^{13}C$ spin-spin coupling constants has been given in the literature, with the exception of one study of aspartic and glutamic acid[4]. Two reports deal with proline[5] and histidine[6] and very recently two papers by Olah[7,8] describe some oxonium ions under stable ion conditions.

We have initiated a study to measure the $^{13}C^{13}C$ spin-spin coupling constants in ortho-, meta- and para-aminobenzoic acid (1), (2), and (3), both for the neutral compounds and the corresponding cations 1a, 2a, 3a and anions 1b, 2b and 3b respectively.

We wanted to compare these results with the behaviour of the ^{13}C chemical shifts in order to see if there is a correlation between chemical shift changes and spin coupling constant variation on protonation or deprotonation. Furthermore it was of interest to determine, whether the ortho- and para-series differ from the meta series by possible resonance effects. In order to detect substituent effects on spin-spin coupling constants the results of benzoic acid (4), its anion 4b, aniline (5) and anilinium hydrochloride (5a) are included.



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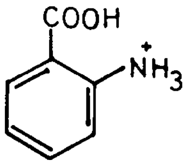

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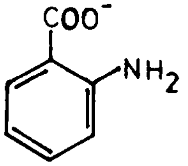

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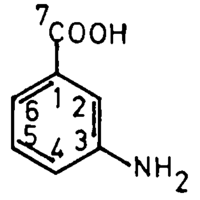

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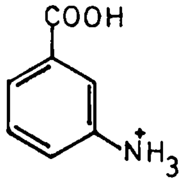

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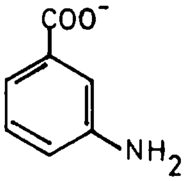

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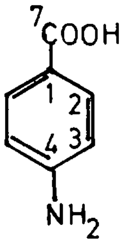

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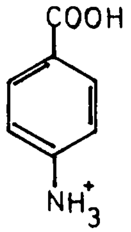

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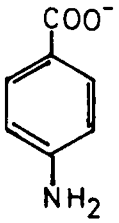

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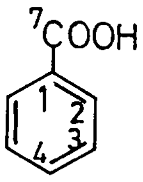

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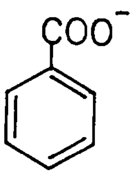

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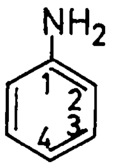

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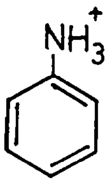
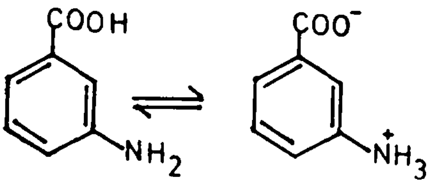


5a

Results and Discussion

1. ^{13}C Chemical Shifts

The ^{13}C chemical shifts of the aminobenzoic acids have been given earlier.[9,10] Recently, a detailed study was published, where the tautomer partitioning within the meta- and para-series was investigated,[11] and it was found that in diluted D_2O solution 3 exists mainly as the molecular form, whereas 2 is a 41%/59% mixture of molecular and zwitterionic form 6. Similar data for 1 unfortunately are not available, however, it was shown from calorimetric and ionization data,[12] that 1 behaves similar to 3.



2 6

For this work saturated DMSO-d_6 solutions were necessary in order to measure the $^{13}C^{13}C$ spin-spin coupling constants in natural abundance, and it is uncertain, if the above mentioned analysis applies for these conditions. The chemical shifts measured in this work are given in Table 1 and the chemical shift changes upon protonation and deprotonation are shown in Fig. 1 for the three series. The analysis of the $^{13}C^{13}C$ spin-spin coupling constants gives, as a by-product, the connectivity of the carbon skeleton, therefore the chemical shift assignments and the line crossings in Fig. 1 are experimentally valid.

As shown in Fig. 1 the general pattern for the chemical shifts of the carboxyl carbon, the carbon atom bearing the amino group and the carbon atom α to the carboxyl group is rather similar in the ortho-, meta- and para-series. It is remarkable how in the cations the chemical shifts of the carbon atoms within the aromatic ring are closely clustered, whereas in the neutral compounds and the anions the chemical shifts are spread over nearly 50 ppm.

The shielding and deshielding effects for the carbon atoms of a carboxylic acid group or the carbon atoms bearing amino groups upon deprotonation and protonation are subject of a long lasting debate in ^{13}C NMR spectroscopy.[13-16] Despite all efforts a satisfactory theory which predicts quantitatively the observed chemical shift changes is lacking.[16] One point of view is that electric field effects dominate the chemical shift variations, leading to deshielding for the carboxylic carbon atom upon deprotonation and to shielding for the carbon atom bearing the amino group upon protonation. Whether such an electric field effect exists for $^{13}C^{13}C$ spin-spin coupling constants has not yet been investigated. Changes of the chemical shift tensor on protonation or deprotonation could also be discussed as the cause of the "wrong way"[13] shielding and deshielding effects. In comparison with benzoic acid two components of the chemical shift tensor of silver benzoate are deshielded, whereas one is shielded leading to an overall downfield shift of the average.[17] Thus, the situation is certainly more complex than can be seen from high resolution studies.

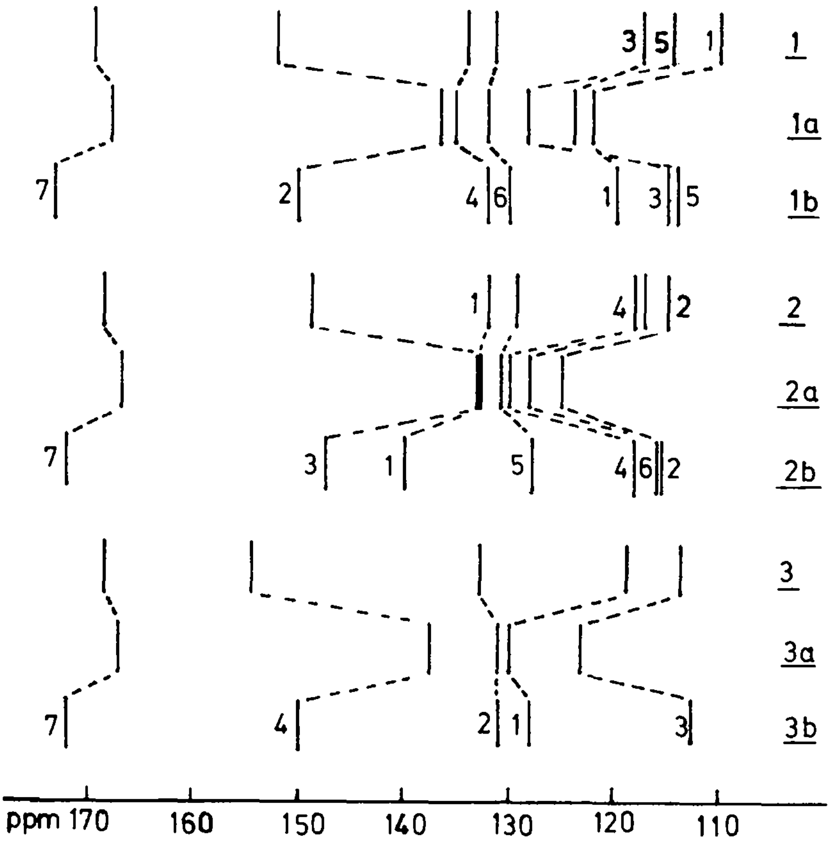


Figure 1. Pattern of ^{13}C chemical shifts changes on protonation and deprotonation of ortho-, meta- and para-aminobenzoic acids.

Table I. ^{13}C chemical shifts of ortho-, meta- and para-aminobenzoic acids 1, 2 and 3, of benzoic acid 4 and aniline 5, their cations 1a, 2a, 3a, 5a and their anions 1b, 2b, 3b and 4b, values given in ppm vs TMS, measured in concentrated solutions of DMSO-d_6.

	C-1	C-2	C-3	C-4	C-5	C-6	C-7
1	110.2	151.7	116.7	134.0	115.0	131.5	169.9
1a	122.1	136.5	124.2	134.7	126.9	132.2	167.8
1b	120.1	150.0	115.3	132.1	114.0	130.1	173.4
2	131.8	115.1	148.9	118.7	129.4	117.6	168.5
2a	132.8	124.7	132.4	129.7	130.8	128.3	166.8
2b	140.0	115.4	147.6	117.9	127.8	115.7	172.2
3	118.7	132.8	114.3	154.6	114..3	132.8	169.1
3a	130.1	131.3	123.5	137.1			166.9
3b	128.1	131.0	112.8	149.9			172.0
4	131.1	129.4	128.5	132.8			167.5
4b	138.6	130.3	129.2	131.8			174.4
5	148.3	114.3	128.9	116.2			
5a	131.4	123.2	129.5	128.0			

Table 2. $^{13}C^{13}C$ spin-spin coupling constants in ortho-, meta- and para-aminobenzoic acids **1**, **2** and **3**, benzoic acid **4** and aniline **5**, their cations **1a**, **2a**, **3a**, **5a** and their anions **1b**, **2b**, **3b** and **4b**, values given in Hz.

	$^1J_{1,2}$	$^1J_{2,3}$	$^1J_{3,4}$	$^1J_{4,5}$	$^1J_{5,6}$	$^1J_{1,6}$	$^1J_{1,7}$
1	62.9	58.9	59.6	53.6	55.7	59.3	72.4
1a	66.3	63.6	57.4	54.2	56.0	59.0	71.7
1b	60.2	60.8	59.1	57.3	55.5	58.7	63.6
2	61.7	61.8	60.4	58.0	56.6	58.7	70.9
2a	59.8	64.8	61.1	53.6	57.0	60.9	71.9
2b	58.7	60.5	57.5	56.7	57.8	60.9	63.3
3	58.4	59.4	59.3				75.2
3a	58.2	57.5	63.6				72.3
3b	58.3	58.4	60.3				67.5
4	58.2	55.0	54.9				71.5
4b	57.7	58.0	55.2				65.9
5	60.6	58.8	56.0				
5a	64.4	56.5	55.7				

2. $^{13}C^{13}C$ spin-spin coupling constants

Qualitative Discussion.

The $^{13}C^{13}C$ spin-spin coupling constants measured in this work are given in Table 2. In all compounds the highest carbon coupling constants are found between C-1 and the carboxylic carbon atoms, $^1J_{1,7}$. The para compound **3** shows the largest value, the values in the ortho compound **1** are about 3 Hz and in the meta compound **2** about 4 Hz smaller and close to benzoic acid (**4**). Thus, the electron donating amino group in **3** increases $^1J_{1,7}$ by about 4 Hz. This relative order holds for the anions as well, where the spin coupling constants for **1b**, **2b** and **3b** are reduced by about 8 Hz in comparison with the neutral compounds. Upon protonation of the amino group only $^1J_{1,7}$ of **3** is reduced significantly by about 3 Hz, whereas the values in **1** and **2** change only slightly by 1 Hz, however for **2** in the opposite direction in comparison with **1** and **3**. This difference in behaviour of **2** can possibly be related to the difference in tautomer partitioning, since protonation of the predominant zwitterionic form **6** of **2** occurs at the carboxyl group and not at the amino group.

Upon protonation of the amino group two carbon coupling constants are mainly affected, $^1J_{1,2}$ and $^1J_{2,3}$ in **1**, $^1J_{2,3}$ and $^1J_{3,4}$ in **2** and $^1J_{3,4}$ which is identical with $^1J_{4,5}$ in **3** and aniline (**5**). For the ortho- and para-compounds and for **5** these values are enhanced by about 4 Hz , whereas the meta compound reacts less significantly. Again this could be explained by the reason given above for **2**. Comparison of the pertinent spin coupling constants of **5** with **3** shows, that the carboxyl group does not have a similar effect as was described for the amino group above.

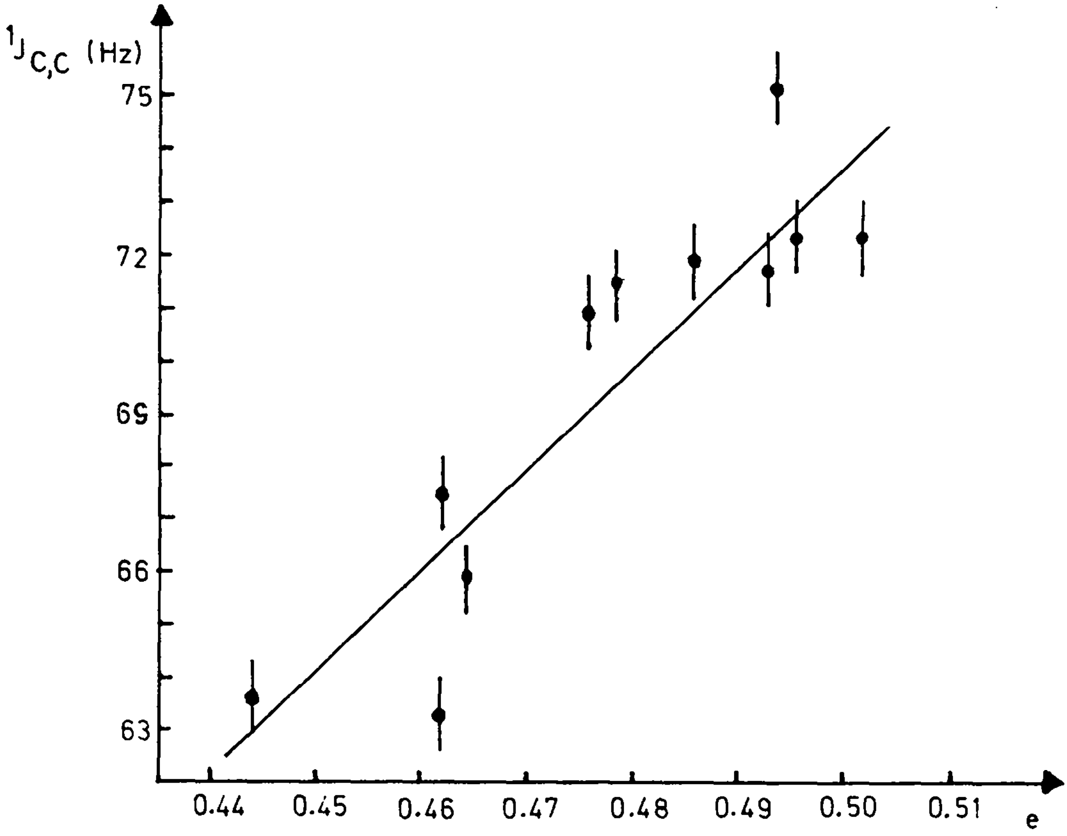


Figure 2. Relationship of the $^{13}C^{13}C$ spin-spin coupling constants between the carboxyl atom and carbon atom 1 and the charge of the carboxyl atom in ortho-, meta- and para-aminobenzoic acids and benzoic acid, their cations and anions.

The remaining spin coupling constants within the benzene ring do not change much upon protonation or deprotonation. This could be taken as evidence that the charge in these molecules is rather localized on the carboxyl or the amino group which is borne out by INDO calculations. This behaviour is quite different from the behaviour of the chemicals shifts as seen from Fig. 1.

Quantitative Correlations.

Attempts to correlate the chemicals shifts or their differences within these compounds with the spin-spin coupling constants of the corresponding carbon atoms failed. This points to the fact, that the physical cause of their variation in is different in this series.[18,19] A calculation of the spin-spin coupling constants using the finite perturbation theory within an INDO-MO program[20] gives rather poor correlations with the experimental values. Whereas in simple hydrocarbons[21] the spin-spin coupling constants correlate well with π-bond order, this attempt fails in the series investigated here.

On protonation or deprotonation the charge at the carbon atoms of the carboxyl group and of the carbon atoms bearing the amino group is varied. For the carboxyl group a linear relationship between the charge generated at the carboxyl carbon atom as calculated with INDO wavefunctions and the $^1J_{1,7}$ spin-spin coupling constant is given in Fig. 2.

The correlation, with r = 0.90 and a standard deviation of 1.8 Hz considering a total spread of the spin coupling constants of about 12 Hz, is not very convincing, however one might admit, that charge effects belong to the physical causes which are responsible for the spin coupling constant variation in this series. Generating higher charge at the carbon atom increases the spin coupling constant. For the carbon atom bearing the amino group a similar correlation does not exist, as the total variation of the spin coupling constants at this carbon atom is only about 4 Hz.

Conclusion

We have shown in this work that the variation of $^{13}C^{13}C$ spin-spin coupling constants in the series of ortho-, meta- and para-aminobenzoic acid, their cations and anions are not related to the variation of chemical shifts. Charge effects are likely one major cause of the changes of the spin coupling constants, however their detailed understanding and quantitative calculation is still far from current knowledge.

Experimental

The commercially available aminobenzoic acids have been recrystallized from water. For the neutral compounds 1 g of material was dissolved in 3 ml DMSO-d_6. A suspension of the aminobenzoic acids in water was treated with excess HCl until all material was dissolved. The filtered solution was evaporated in vacuo and the residue was taken up in DMSO-d_6. The saturated solutions were filtered into 10 mm NMR tubes. A suspension of the aminobenzoic acids in water was treated with one equivalent of NaOH, the filtered solution was evaporated in vacuo, taken up in DMSO-d_6 and the saturated solutions were filtered in 10 mm NMR tubes. The preparations for 4 and 5 were performed accordingly. In two cases (1b,4b) addition of some water was necessary to increase solubility.

The nmr measurements were performed at 305 K on a Bruker WH-400 instrument equipped with a Diablo series 30 disk drive and a 80 k Aspect-2000 computer and a pulse programmer. The decoupler was power gated to prevent excess radiofrequency heating of the samples. Both standard techniques and 1-D INADEQUATE[22] experiments were performed. The 90° pulse for the INADEQUATE measurements was 20μs, a spectral width of 6024 Hz was used leading to a digital resolution of 0.184 Hz after a 64k Fourier Transform. The aquisition time was 5.43 s and a relaxation delay of 10 s was used giving a typical instrument time for one run of about 15 h. Each compound was measured several times. Due to the high viscosity of the ionic solutions, the inherent higher linewidth of the INADEQUATE technique and the similarity of the spin-spin coupling constants within the aromatic ring, the accuracy of these coupling constants should not be considered better than ± 0.7 Hz, whereas for the neutral compounds errors amount to ± 0.3 Hz.

Acknowledgements

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