Simulation of ^{13}C NMR chemical shifts for polychlorinated and polybrominated oxybenzenes with two-particle increment scheme

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A two-particle system of OY—Cl and OY—Br mixed increments for predicting ^{13}C NMR chemical shifts of polyhalogenated polyoxybenzenes has been developed. It has been found that only the *ortho-* and *para*-interactions of the OY and Hal substituents contribute significantly to the ^{13}C chemical shifts and that the *ortho*-effects of the OY located between Hal and H and those of the OY located between two Hal atoms are different. Additional effects are due to solvating solvents. The increment scheme is predictive over the whole class of compounds under consideration and may be realized on personal computers.

Key words: ^{13}C NMR, electronic and steric effects, increment scheme, polychlorinated and polybrominated oxybenzenes.

The determination of the structure of molecules by ^{13}C NMR is principally based on the known topological dependence of their chemical shifts. The spectra can be predicted with the aid of empirical additive schemes which assume the statistical averaging of random factors. These schemes should have an accuracy comparable with the resolving power of the method and should be simple in use. Moreover, the increment schemes for various types of compounds should be constructed on the same principle, reflecting the continuous character of the variation of physicochemical properties of molecules upon slight variation in their structure.

A simple procedure for the estimation of ^{13}C NMR chemical shifts for polysubstituted benzenes[1,2] assumes that the effects of the substituents, which can be determined from the spectra of monosubstituted derivatives, are independent, and works well only for simpler compounds[3—5] in which the collective effect of the substituents on the chemical shifts of the ring carbon atoms is small. However, ignoring the interaction of the substituents results in noticeable discrepancies between the calculated and experimental values for *para*-disubstituted benzenes,[1,3,6] and for *ortho*-disubstituted compounds and more complex molecules the calculation error may be as high as 5—7 ppm.[7—9]

The difference between the calculated and experimental chemical shifts may be reduced almost to zero by introducing many-particle increments;[10] however, as a rule, they are unsuitable for other compounds (beyond the array studied). In addition, the observed variations of the chemical shifts are caused not only by topological factors (the arrangement of the substituents), but depend as well on the conditions of the experiment. For example, phenols may form hydrogen bonds with the solvent, whose effect on the ^{13}C chemical shifts can be as high as 2 ppm.

The optimal way to create universal empirical schemes for calculating ^{13}C NMR chemical shifts is to look for two-particle increments similar to atom-atom potentials in molecular mechanics. This approach has proved itself for polysubstituted benzenes with substituents of a similar kind, $C_6H_{(6-n)}X_n$ (X = Cl, Br, *etc.*),[11—13] and polyoxybenzenes (OY = OH, OMe, and OPh),[14] whose ^{13}C NMR chemical shifts are represented as individual and collective (two-particle) increments. Standard deviations proved to be comparable with the experimental error, which made it possible to predict the spectra of new compounds with good accuracy.

In the present work we extend this method[11—14] to ^{13}C NMR chemical shifts of polychlorinated and polybrominated oxybenzenes containing either identical or different OY substituents (Y = H, Me, Ph). The preliminary results were reported previously.[15]

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Table 1. Experimental (calculated) ^{13}C NMR chemical shifts for some polychlorinated monooxybenzenes

Pos. of the subst.	Solvent	δ, TMS						Ref.
		C-1	C-2	C-3	C-4	C-5	C-6	
1- OH-Benzenes								
2-Cl	$CDCl_3$	151.8	120.3	129.2	121.5	128.5	116.5	16
	C_6H_{12}	152.3	120.7	129.3	121.4	128.6	116.9	17
		(151.8)	(120.5)	(129.2)	(121.2)	(127.0)	(117.2)	
	Acetone	153.2	120.4	130.1	120.8	128.3	117.1	10
		(153.3)	(121.2)	(129.2)	(120.8)	(127.0)	(117.2)	
3-Cl	$CDCl_3$	156.3	116.1	135.1	121.3	130.6	113.9	16
		(157.7)	(116.2)	(134.9)	(120.1)	(130.3)	(113.9)	
	Acetone	158.8	115.8	134.5	119.7	130.9	114.3	10
		(158.8)	(116.2)	(134.9)	(120.1)	(130.3)	(113.9)	
4-Cl	$CDCl_3$	154.1	116.8	129.7	125.9			16
		(154.8)	(117.3)	(129.2)	(124.5)			
	Acetone	156.6	117.1	129.5	123.9			10
		(156.3)	(117.3)	(129.2)	(124.0)			
$2,3-Cl_2$	$CDCl_3$	152.9	119.2	132.8	122.3	128.2	114.6	16
		(153.6)	(118.7)	(133.1)	(122.0)	(128.3)	(114.7)	
	Acetone	154.9	119.5	133.1	121.4	128.2	115.3	10
		(155.2)	(119.4)	(133.1)	(121.6)	(128.3)	(114.7)	
$2,4-Cl_2$	$CDCl_3$	150.3	120.6	128.7	125.9	128.7	117.3	16
		(150.5)	(121.7)	(129.3)	(125.7)	(127.5)	(117.4)	
	Acetone	152.4	121.4	129.5	124.3	128.2	118.1	10
		(152.0)	(121.9)	(129.3)	(124.7)	(127.5)	(118.1)	
$2,5-Cl_2$	$CDCl_3$	152.0	118.5	129.7	121.8	133.9	116.8	16
		(153.3)	(119.5)	(130.4)	(120.9)	(133.1)	(116.8)	
	Acetone	154.1	119.5	131.1	120.8	132.9	116.9	
$2,6-Cl_2$	$CDCl_3$	148.1	121.3	128.5	121.3			16
		(148.5)	(121.8)	(127.5)	(121.3)			
	Acetone	149.3	122.1	128.8	121.2			10
		(149.2)	(125.6)	(127.5)	(121.3)			
$3,4-Cl_2$	$CDCl_3$	154.6	117.7	133.1	124.4	131.0	115.4	16
		(155.7)	(118.0)	(133.1)	(124.0)	(131.1)	(115.2)	
$2,3,4-Cl_3$	Acetone	153.6	121.1	131.4	123.6	128.8	115.8	10
		(153.7)	(121.2)	(132.1)	(124.0)	(129.2)	(115.2)	
$2,3,5-Cl_3$	Acetone	155.3	118.8	133.8	121.0	132.7	115.5	10
		(155.6)	(118.2)	(134.3)	(121.2)	(133.5)	(115.5)	
$2,3,6-Cl_3$	Acetone	150.8	121.2	131.8	121.7	128.6	120.6	10
		(150.6)	(120.8)	(131.9)	(121.7)	(128.4)	(121.2)	
$2,4,5-Cl_3$	Acetone	153.0	120.4	131.0	122.7	131.0	118.2	10
		(152.1)	(119.9)	(130.7)	(124.8)	(131.9)	(117.9)	
$2,4,6-Cl_3$	$CDCl_3$	147.1	121.8	128.2	125.5			16
		(147.5)	(121.9)	(127.9)	(125.1)			
	Acetone	148.8	122.9	128.4	124.5			10
		(148.1)	(124.1)	(127.9)	(125.1)			
$3,4,5-Cl_3$	Acetone	156.9	116.8	134.0	121.1			10
		(157.0)	(116.1)	(134.9)	(121.7)			
$2,3,4,5-Cl_4$	Acetone	153.4	120.5	133.0	122.5	131.8	116.4	10
		(153.4)	(119.4)	(133.9)	(123.0)	(133.1)	(115.8)	
$2,3,4,6-Cl_4$	Acetone	149.7	122.5	130.3	123.9	128.8	121.0	10
		(149.9)	(123.3)	(131.9)	(124.3)	(130.7)	(119.6)	
$2,3,5,6-Cl_4$	Acetone	151.8	120.0	131.6	121.8	131.6	120.0	10
		(153.1)	(120.2)	(131.9)	(123.1)	(130.7)	(119.6)	
$2,3,4,5,6-Cl_5$	$CDCl_3$	148.3	119.9	131.6	125.2			16
		(149.1)	(118.6)	(132.2)	(123.9)			
	Acetone	150.3	121.1	131.2	123.8			10
		(150.1)	(120.9)	(132.2)	(123.9)			
1-OMe-Benzenes								
2-Cl	CCl_4	155.0	122.8	130.0	120.8	127.1	111.7	18
		(155.2)	(123.0)	(129.2)	(121.9)	(127.0)	(112.1)	
4-Cl	$CDCl_3$	158.2	115.2	129.3	125.5			6
		(158.3)	(115.7)	(129.2)	(125.2)			
$2,3-Cl_2$	$CDCl_3$	156.5	121.4	133.7	122.1	127.6	110.1	18
		(157.1)	(121.2)	(133.1)	(122.7)	(128.3)	(110.1)	
$2,6-Cl_2$	$CDCl_3$	152.6	129.6	129.0	125.0			18
		(152.0)	(129.9)	(127.5)	(124.9)			
	Acetone	153.2	130.0	130.1	126.1			19
		(152.0)	(129.9)	(130.1)	(124.9)			
$2,3,4-Cl_3$	$CDCl_3$	154.9	122.9	132.2	125.0	127.9	110.3	18
		(155.8)	(123.0)	(132.1)	(125.2)	(129.2)		
$2,3,6-Cl_3$	$CDCl_3$	153.7	128.9	132.3	125.8	128.4	127.8	18
		(153.5)	(128.1)	(131.9)	(125.4)	(128.4)	(127.3)	
$2,4,6-Cl_3$	DMSO	150.7	128.8	128.0	128.2			20
		(151.0)	(130.0)	(127.9)	(128.7)			
$2,3,5,6-Cl_4$	Acetone	155.5	128.1	132.6	127.2			19
		(155.5)	(126.0)	(132.2)	(126.7)			
1-OPh-Benzenes								
$2,4,5-Cl_3$	$CDCl_3$	152.0	124.4	131.2	127.2	131.3	120.9	21
		(152.1)	(124.4)	(130.7)	(126.9)	(131.9)	(120.9)	
$2,4,6-Cl_3$	$CDCl_3$	146.1	130.6	128.9	130.9			21
		(145.9)	(131.6)	(127.9)	(130.6)			
$3,4,5-Cl_3$	$CDCl_3$	156.2	118.3	134.5	125.2			21
		(156.6)	(119.2)	(134.9)	(124.6			
$2,3,5,6-Cl_4$	$CDCl_3$	149.3	127.9	132.3	127.4			21
		(150.4)	(127.6)	(132.2)	(129.0)			
$2,3,4,5,6-Cl_5$	$CDCl_3$	147.3	128.8	132.2	130.6			21
		(147.5)	(128.2)	(132.0)	(129.3)			

Table 2. Experimental (calculated) ^{13}C NMR chemical shifts for some polychlorinated monooxybenzenes which have not been used in constructing the increment scheme (3)

Position of the substituent	Solvent	δ, TMS						
		C-1	C-2	C-3	C-4	C-5	C-6	Reference
				1,2-(OH)$_2$-Benzenes				
3-Cl	Acetone	146.8	142.2	120.7	120.5	120.3	114.4	10
		(147.5)	(142.2)	(121.2)	(119.3)	(120.8)	(113.3)	
4-Cl	Acetone	144.5	146.4	115.6	123.8	119.7	116.5	10
		(144.6)	(147.5)	(115.9)	(124.1)	(119.7)	(117.0)	
3,4-Cl$_2$	Acetone	145.5	143.9	119.3	122.7	120.1	114.3	10
		(145.9)	(144.0)	(119.4)	(122.3)	(121.2)	(115.0)	
3,5-Cl$_2$	Acetone	147.4	141.6	121.0	119.9	123.7	114.4	10
		(148.2)	(140.8)	(121.9)	(119.8)	(124.4)	(114.2)	
3,6-Cl$_2$	Acetone	143.4		120.5	119.4			10
		(143.3)		(119.4)	(120.5)			
4,5-Cl$_2$	Acetone	145.5		116.8	121.7			10
		(145.9)		(117.8)	(122.3)			
3,4,5-Cl$_3$	Acetone	145.5	143.0	121.2	120.6	123.0	115.0	10
		(145.7)	(142.5)	(121.2)	(120.3)	(123.7)	(115.9)	
3,4,6-Cl$_3$	Acetone	142.1	144.5	118.6	122.9	120.5	119.6	10
		(141.7)	(144.4)	(117.9)	(123.1)	(120.8)	(119.8)	
3,4,5,6-Cl$_4$	Acetone	143.0		119.5	122.5			10
		(142.7)		(119.4)	(122.5)			
				1-OH,2-OMe-Benzenes				
3-Cl	Acetone	152.4	144.9	128.3	121.4	125.7	116.2	22*
		(151.2)	(143.6)	(127.3)	(120.8)	(124.4)	(113.8)	
4-Cl	Acetone	146.6	149.1	112.9	124.4	121.5	116.8	22*
		(145.0)	(148.8)	(113.2)	(125.2)	(121.4)	(117.1)	
5-Cl	Acetone	148.1	147.2	113.1	119.9	126.1	116.0	22*
		(148.1)	(145.9)	(114.3)	(120.8)	(125.8)	(116.0)	
6-Cl	Acetone	143.9	149.3	110.7	120.3	120.3	122.5	22*
		(142.2)	(149.8)	(111.0)	(120.4)	(121.4)	(122.1)	
3,4-Cl$_2$	Acetone	151.0	146.2	127.3	123.3	126.0	116.5	22*
		(149.6)	(145.5)	(127.5)	(123.4)	(125.2)	(115.1)	
3,5-Cl$_2$	Acetone	152.9	144.2	129.5	120.8	129.0	116.4	22*
		(151.9)	(142.3)	(130.5)	(120.9)	(128.9)	(114.3)	
3,6-Cl$_2$	Acetone	148.9	145.9	126.9	121.5	126.1	120.6	22*
		(146.9)	(145.4)	(127.4)	(120.5)	(124.4)	(119.5)	
4,5-Cl$_2$	Acetone	147.4	148.3	114.0	122.1	123.7	117.1	22*
		(146.3)	(147.2)	(115.1)	(123.4)	(124.2)	(117.9)	
4,6-Cl$_2$	Acetone	143.0	149.7	111.5	124.2	120.8	121.7	22*
		(140.9)	(150.1)	(111.5)	(125.1)	(121.5)	(123.3)	
5,6-Cl$_2$	Acetone	145.5	148.0	111.2	120.4	124.9	119.4	22*
		(144.1)	(147.8)	(112.3)	(121.2)	(124.0)	(120.3)	
3,4,5-Cl$_3$	Acetone	151.2	145.4	128.8	121.8	128.6	117.1	22*
		(149.4)	(144.0)	(129.3)	(122.4)	(127.7)	(116.0)	
3,4,6-Cl$_3$	Acetone	146.8	147.8	126.1	123.2	126.1	120.8	22*
		(145.1)	(146.5)	(126.1)	(123.1)	(124.8)	(120.7)	
3,5,6-Cl$_3$	Acetone	149.9	144.5	128.7	121.1	126.9	119.7	22*
		(147.8)	(143.8)	(127.9)	(120.8)	(125.2)	(119.1)	
4,5,6-Cl$_3$	Acetone	144.5	148.0	112.1	123.2	123.0	120.4	22*
		(142.6)	(146.7)	(113.2)	(123.7)	(123.0)	(122.1)	
3,4,5,6-Cl$_4$	Acetone	148.6	145.3	128.3	122.7	127.2	120.8	22*
		(145.6)	(144.3)	(127.5)	(122.7)	(126.7)	(120.3)	

* An experiment without the assignment of signals.

** The calculation does not support the initial assignment of signals.

*** This paper.

Table 2. (Continued)

Position of the substituent	Solvent	δ, TMS						
		C-1	C-2	C-3	C-4	C-5	C-6	Reference
				1-OH,4-OMe-Benzenes				
2-Cl	Acetone	147.8	121.1	114.8	154.3	115.7	118.1	23*
		(147.0)	(121.6)	(115.1)	(154.5)	(115.8)	(117.0)	
3-Cl	Acetone	154.2	117.7	123.1	149.5	114.8	115.1	23*
		(152.1)	(116.7)	(123.3)	(149.0)	(112.2)	(114.9)	
2,3-Cl_2	Acetone	148.9	121.3	122.4	150.6	112.4	115.2	23*
		(147.7)	(119.8)	(112.2)	(150.4)	(121.4)	(116.5)	
2,6-Cl_2	Acetone	154.9	116.7	129.9	146.1	129.9	116.7	23*
		(154.0)	(114.8)	(129.7)	(145.6)	(129.7)	(114.8)	
2,3,5-Cl_3	Acetone	151.5	119.9	127.8	147.1	129.5	116.3	23*
		(150.4)	(119.9)	(128.5)	(146.0)	(129.4)	(115.0)	
2,3,6-Cl_3	Acetone	144.8	121.2	120.9	150.5	113.0	123.1	23*
		(144.4)	(121.2)	(120.2)	(150.8)	(110.3)	(122.3)	
2,3,5,6-Cl_4	Acetone	147.8	120.8	127.9	148.6	127.9	120.8	23*
		(147.9)	(119.9)	(126.6)	(148.2)	(126.6)	(119.9)	
				1,2-(OMe)$_2$-Benzenes				
3-Cl	$CDCl_3$	154.7	146.3	129.1	122.7	125.0	111.7	***
		(153.7)	(145.2)	(129.3)	(121.4)	(124.4)	(111.0)	
4-Cl	$CDCl_3$	148.0	149.7	112.2	125.8	120.4	112.2	***
		(147.9)	(150.4)	(113.2)	(125.8)	(121.4)	(114.3)	
3,4-Cl_2	$CDCl_3$	153.2	147.6	128.3	125.4	125.4	111.8	***
		(152.1)	(147.1)	(127.5)	(124.0)	(125.2)	(112.3)	
3,5-Cl_2	$CDCl_3$	154.8	145.2	129.8	122.5	129.6	112.5	***
		(154.4)	(143.9)	(130.5)	(121.5)	(128.9)	(111.5)	
3,6-Cl_2	$CDCl_3$	151.4	151.4	127.1	125.8	125.8	127.1	***
		(149.7)	(149.7)	(127.5)	(124.5)	(124.5)	(127.5)	
4,5-Cl_2	$CDCl_3$	149.1	149.1	113.7	124.2	124.2	113.7	***
		(148.8)	(148.8)	(115.1)	(124.0)	(124.0)	(115.1)	
3,4,5-Cl_3	$CDCl_3$	152.8	146.2	129.6	124.1	129.0	112.4	***
		(151.9)	(146.8)	(129.3)	(123.0)	(127.7)	(113.2)	
3,4,5,6-Cl_3	$CDCl_3$	150.6	150.6	129.2	128.3	128.3	129.2	***
		(148.6)	(148.6)	(127.5)	(126.7)	(126.7)	(127.5)	
				1,3-(OH)$_2$-Benzenes				
4-Cl	DMSO	(153.7)	104.0	(157.4)	109.8	130.1	107.7	18**
		(156.5)	(104.3)	(154.0)	(111.7)	(129.8)	(108.4)	
				1,3-(OMe)$_2$-Benzenes				
2,4,5,6-Cl_4	$CDCl_3$	152.6	123.6		125.4	131.2		18
		(152.9)	(121.1)		(122.4)	(131.5)		
				1,4-(OMe)$_2$-Benzenes				
2-Cl	$CDCl_3$	150.1	123.7	116.9	154.6	114.0	113.6	***
	$CDCl_3$	149.4	123.0	112.7	153.9	113.3	116.2	18
		(149.1)	(123.6)	(115.2)	(153.4)	(113.0)	(112.7)	
2,3-Cl_2	$CDCl_3$	151.1	123.8	123.8	151.1	110.7	110.7	***
		(150.9)	(121.8)	(121.8)	(150.9)	(110.7)	(110.7)	
2,5-Cl_2	$CDCl_3$	150.0	121.7	115.6	150.0	121.7	115.6	***
		(150.2)	(121.8)	(112.8)	(150.2)	(121.8)	(112.8)	
2,6-Cl_2	$CDCl_3$	147.0	130.2	115.2	156.4	115.2	130.2	***
		(145.8)	(130.5)	(113.5)	(158.1)	(113.5)	(130.5)	
2,3,5-Cl_3	$CDCl_3$	153.1	121.8	130.4	147.6	127.7	112.0	***
		(153.7)	(120.6)	(128.7)	(147.2)	(127.9)	(110.8)	
2,3,5,6-Cl_4	$CDCl_3$	151.2	128.3	128.3	151.2	128.3	128.3	***
		(151.7)	(126.6)	(126.6)	(151.7)	(126.6)	(126.6)	
				1,2,3-(OMe)$_3$-Benzenes				
4,5,6-Cl_3	$CDCl_3$	150.7	147.6	150.7	124.5	127.6	124.5	***
		(149.5)	(144.2)	(149.5)	(122.1)	(126.3)	(122.1)	

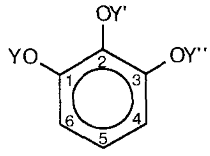
Experimental

The ^{13}C NMR data for polyhalogenated oxybenzenes (Table 1) were taken from papers of various authors. The ^{13}C NMR spectra of polychlorinated oxybenzenes in various solvents and the information on the methods for their synthesis are given in Refs. 6, 10, 16—23. The NMR data for polychlorinated veratrole and 3,4,5-trimethoxybenzenes (Table 2) were partly published in Ref. 24 (initially without assignment of the signals[25]). The spectra of polybrominated oxybenzenes (Table 3) are given in Refs. 17—19, 26—27.

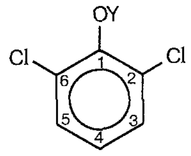
For multiple-parameter regression analysis, only NMR data on polychlorinated and polybrominated monooxybenzenes were used (see Tables 1 and 3). The standard least-squares method was supplemented by the known technique of the adjustment of multiple-parameter linear regression.[28] Only 22 and 19 parameters for ^{13}C NMR chemical shifts in chloro- and bromooxybenzenes remained ultimately nonzero (Table 4), and the standard error was 0.67 and 0.87 ppm, respectively.

Results and Discussion

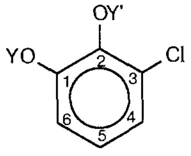
Prediction of ^{13}C NMR chemical shifts in polyhalogenated oxybenzenes may be based on the analysis of a modest number of monooxy substituted compounds and the use of increments for polychloro-, polybromo-, and polyoxybenzenes.[11—14] The transition to polyhalobenzenes with several oxygen-containing groups can be carried out according to the following scheme: the OY—OY′ increment in **c** is identical to that in **a** and the OY—Cl increment in **c** is identical to that in **b** (the relationships for OY—Br are similar).



a



b



c

The chemical shifts for a number of chlorinated monooxybenzenes (see Table 1) were determined in both inert and solvating solvents. These data comprise a statistical ensemble that embraces all of the structural situations and the main types of effects of the medium for polychlorooxybenzenes. The available set of experimental data is quite representative for revealing the basic factors determining the variations in the chemical shifts in this class of compounds.

In the two-particle approximation, the chemical shift of a k-th carbon atom C_k in a polysubstituted benzene is represented by the sum of contributions:

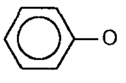
$$\delta C_k = \delta C_0 + \sum_i P_k^{\,i} + \sum_{i,j} \Gamma_k^{\,ij} , \qquad (1)$$

where δC_0 is the chemical shift in the unsubstituted benzene (128.5 ppm); $P_k^{\,i}$ is the individual increment of a substituent in monosubstituted benzene C_6H_5X where X occupies the i-th position with respect to C_k; $\Gamma_k^{\,ij}$ is the contribution to the shielding of C_k caused by the nonadditivity of the effects of the i-th and j-th substituents. $\Gamma_k^{\,ij}$ for polychlorinated and polybrominated benzenes[11—13] is determined by the sum of the two-particle increments:

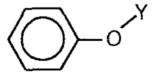
$$\Gamma_k^{\,ij} = \sum_{i,j} \{R_k^{\,ij}\ l_k^{\,ij} + S_k^{\,ij}\ (l_k^{\,ij})^2\} , \qquad (2)$$

where $l_k^{\,ij}$ is the number of two-particle heterosubgraphs with the C_k atom and $R_k^{\,ij}$ and $S_k^{\,ij}$ are linear and square coefficients.

In the case of polyoxybenzenes all of the $S_k^{\,ij}$ are equal to zero, and $P_k^{\,i}$ and $R_k^{\,ij}$ depend on the type of substituent OY and are divided into two constituents: the increment of O (**1**) and the increment of Y in the OY group (**2**):



1



2

Therefore,

$P_k = PO_k + PY_k$, and $R_k = R(O—O)_k + R(OY—O)_k$.

New mixed Cl—O increments were determined in a similar way to the O—O increments.[13,14]

Chemical shifts in phenols and other hydroxybenzenes are affected by the formation of hydrogen bonds in specific solvents. This is taken into account as a modification to the basic topological factors.[14] Assuming that some of the mixed Hal—O increments also depend on the solvent, we introduced modifiers to the corresponding increments for neutral solvents. With due regard for this, Eq. (1) takes the form:

$$\delta C_k = \delta C_0 + \sum_i (PCl, PO + PY)_k^{\,i} + \qquad (3)$$
$$+ \sum_{i,j} [R(Cl—Cl), R(O—O), R(OY—O), R(O—Cl), R(OY—Cl)_k^{\,ij}\ l_k^{\,ij}\ ].$$

The equation for the chemical shifts in polybrominated polyoxybenzenes is similar.

The $R(Cl—Cl)_k$ and $R(O—O)_k$ values are related to the Cl and O atoms, and $R(OY—O)_x$ reflects the effect of substituent Y in the corresponding two-particle heterosubgraph on the chemical shifts in a benzene ring (irrespective of the type of substituent Y′ in the neighboring Y′—O group). The same is true for $R(Br—Br)$. Mixed $R(O—Cl)$ and $R(O—Br)$ increments do not depend on Y, while $R(OY—Cl)$ and $R(OY—Br)$, on the contrary, describe the effects of various Y.

Table 3. Experimental (calculated) ^{13}C NMR chemical shifts for some polybrominated oxybenzenes

Position of the substituent	Solvent	δ, TMS C-1	C-2	C-3	C-4	C-5	C-6	Reference
1-OH,2-Br	C_6H_{12}	153.3 *(152.7)	110.7 (110.5)	132.3 (131.8)	121.7 [121.4]	129.7 (128.9)	116.6 (116.4)	17
1-OMe,2-Br	CCl_4	155.8 *(156.2)	111.9 (111.9)	133.1 (133.1)	121.3 [122.1]	127.9 (127.9)	111.5 (111.5)	18
1-OH,4-Br	$CDCl_3$	153.9 *(154.9)	117.2 [117.4]	132.5 [132.0]	113.2 (111.8)			18
	**DMSO	156.8	117.6	132.1	110.1			26
1-OPh,4-Br	$CDCl_3$	156.5 *(155.4)	120.3 [120.5]	132.5 [132.0]	115.6 (114.8)			18
1-OH,2,6-Br_2	$CDCl_3$	149.3 (150.5)	110.0 (110.9)	131.9 (131.7)	122.3 (122.7)			18
1-OMe,2,6-Br_2	Acetone	154.8 (154.8)	118.6 (119.0)	133.6 (132.6)	127.5 (126.3)			19
1-OH,2,4-Br_2	$CDCl_3$	151.5 (151.7)	110.8 (111.1)	134.0 (134.6)	112.7 (112.8)	132.0 (132.4)	117.4 (117.6)	18
1-OH,2,4,6-Br_3	$CDCl_3$	150.5 (149.3)	112.4 (111.4)	133.9 (134.2)	111.3 (111.1)			18
1-OMe,2,4,6-Br_3	$CDCl_3$	153.7 (153.7)	118.9 (119.5)	134.9 (135.1)	117.3 (117.5)			18
1-OH,2-OMe,4,5-Br_2	$CDCl_3$	145.3 *(145.5)	146.3 (147.4)	115.2 [115.9]	115.0 (114.6)	113.6 (115.3)	119.0 [119.2]	27
1,2-OMe,3,4,5,6-Br_4	$CDCl_3$	151.9 (151.9)		122.3 (121.3)	124.3 (125.2)			***

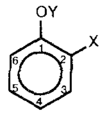
* The values given in brackets do not require mixed Br,O increments.

** The calculation refers to $CDCl_3$.

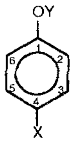
*** This paper.

The information on polychlorooxybenzenes is quite diverse (Tables 1 and 2), while that on polybromooxybenzenes is rather limited.[17–19,26,27] NMR data for only 11 compounds are known (43 different ^{13}C chemical shifts, see Table 3). Nevertheless, we managed to find a set of OY—Br increments similar to those for OY—Cl (Table 4), which are sufficiently predictive to reveal the false assignment of some signals. This proves that the increments found are fully suitable for describing the spectra of all of the polybrominated polyoxybenzenes. Though the limiting amount of experimental data did not allow us to obtain meaningful statistics for some of the increments or to discuss the effect of the solvent, the magnitude of the random error can nevertheless be estimated.

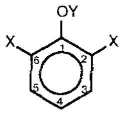
Table 4. OY—Cl and OY—Br mixed increments added to Cl—Cl, Br—Br,[12] and OY—OY′[14] increments



E



F



G

Structural unit	C_k	X = Cl Y = H	(+solv.)	Y = Me	Y = Ph	X = Br Y = H	Y = Me
E	C-1	−4.85	0.41	−4.85	−4.85	−6.70	−6.70
	C-2	−1.31	0.75	2.67	3.90	0.55	3.50
	C-3	—	—	—	—	−0.25	1.10
	C-4	—	−0.45	—	—	—	—
	C-5	—	—	—	—	1.55	0.60
	C-6	−0.51	—	−3.60	−0.60	−1.00	−4.40
F	C-1	0.41	—	0.41	0.41	0.18	0.18
	C-4	−1.33	—	−1.33	−1.33	−2.10	−2.10
G	C-1	−4.10	−0.22	−4.10	−5.23	−5.64	−5.64
	C-2	−1.17	0.75	8.38	5.37	0.40	10.01
	C-3	—	—	—	—	0.85	1.77
	C-4	−0.35	—	1.20	0.93	0.14	2.98

The regression analysis of the full experimental matrix (see Tables 1 and 2) corresponding to Eq. (3) showed that it contains more zero terms than was expected and that some of the contributions are within the limits of experimental error. In addition to experimental values for 28 polychlorinated monooxybenzenes, Table 1 presents chemical shifts calculated from Eq. (3) for inert and specific solvents. For calculations of the OY—Cl increments, 109 experimental points and 22 parameters were finally used (the standard error was 0.67 ppm). The OY—Br system was described by 19 parameters with a standard error of 0.87 ppm. As Tables 1—3 indicate, the calculated values are in good agreement with the experimental data.

Table 4 presents the OY—Cl and OY—Br mixed increments. Among them, all of the *ipso-* and *para-*increments corresponding to the 1—OY, 4—Hal subgraph and almost all of the type 1—OY, 2—Hal and

1—OY, 2,6—Hal_2 *ipso*-increments (except for Y = Ph for the latter) do not depend on Y. Their values are mostly determined by mesomeric and steric interactions between the halogen and O atoms. An additional effect of the substituent is observed when Y = Ph is located between two halogen atoms. The increases in the effects of monosubstituted benzenes C_6H_5OY due to the *ortho*-effects of OY in the OY—Hal fragments are substantially different depending on whether or not there is second halogen atom in the *ortho*-position with respect to O.

The O—Hal *ortho*-combination exerts no *para*-effect on an unsubstituted carbon atom (this increment is not given in Table 4); therefore, the slight 1—4 effects for OY substituents located between two halogen atoms are associated with the deflection of OY out of the plane of the ring. In structures with a 1,2-disubstituted fragment **1**, the OPh group makes no additional contribution to the chemical shifts, which confirms the absence of steric contacts of OPh with its nearest neighbors. It is likely that the two rings in halogenated diphenyl ethers of this type are predominantly mutually perpendicular.

Table 2 demonstrates the potential of the new increment scheme for predicting the chemical shifts of polychlorinated polyoxybenzenes, which were not used for its construction. One of the reasons for the limitedness of the basic experimental material is the relatively large number of incorrect assignments, which could only be disclosed in the course of statistical analysis. These mistakes not only increased the calculation error, but also lead to insurmountable problems in formulating the basic postulates of the increment scheme. It should be emphasized that most of the signals given in Table 2 have not yet been assigned at all.

As can be seen from Table 2, the calculations as a whole are in good agreement with the experimental data, which confirms the predictive ability of the set of increments obtained. It should also be emphasized that for developing the increment scheme, only reliably assigned signals, rather than full spectra of compounds, may be used, since the structural information that is lacking will be filled by the representative ensemble of spectra.

In some cases calculation errors are as high as 2—3 ppm (see Table 2) and cannot be decreased in terms of the system of increments under consideration (in these cases dissimilar experimental values correspond to the same topological code).

This may be due to the fact that the orientation of the orbital of the electron pair of the oxygen atom with respect to the benzene ring differs from a certain average orientation for this topological symbol over the ensemble of compounds. The increment scheme may be further refined for the needs of a particular problem, however, at the cost of its simplicity and versatility.

Below we present an example of the calculation of chemical shifts for 1,4-OMe, 2-Cl-C_6H_3.[18] The shifts of chlorobenzene were taken as the initial values, in order to use previously obtained results,[11—13] and the O and OMe increments[14] were summed up.

$$
\begin{aligned}
\delta(\text{C-1}) = {} & \delta[(\text{C-2})(C_6H_5Cl) + ipso(\text{OMe}) + \\
& + para(\text{OMe}) + (\text{O—O})(1\text{—}4) + \\
& + (\text{C-1})(\text{OMe—Cl})] = \\
& = 128.6+31.54-7.84+1.64-4.85 = 149.09\ , \\
\delta(\text{C-2}) = {} & \delta[(\text{C-1})(C_6H_5Cl) + ortho(\text{OMe}) + \\
& + meta(\text{O})] + \delta[(\text{C-2})(\text{OMe-Cl})] = \\
& = 134.3 - 14.02 + 0.62 + 2.67 = 123.57\ , \\
\delta(\text{C-3}) = {} & \delta[(\text{C-2})(C_6H_5Cl) + meta(\text{O}) + \\
& + ortho(\text{OMe})] = \\
& = 128.6 + 0.62 - 14.02 = 115.2\ , \\
\delta(\text{C-4}) = {} & \delta[(\text{C-3})(C_6H_5Cl) + ipso(\text{OMe}) + \\
& + para(\text{OMe}) + (\text{O—O})(1\text{—}4)] = \\
& = 129.7 + 31.54 - 7.84 + 1.64 = 153.4\ , \\
\delta(\text{C-5}) = {} & \delta[(\text{C-4})(C_6H_5Cl) + ortho(\text{OMe}) + \\
& + meta(\text{O})] = \\
& = 126.4 - 14.02 + 0.62 = 113.0\ , \\
\delta(\text{C-6}) = {} & \delta[(\text{C-3})(C_6H_5Cl) + ortho(\text{OMe}) + \\
& + meta(\text{OMe})] + \delta[(\text{C-6})(\text{OMe—Cl})] = \\
& = 129.7 - 14.02 + 0.62 - 3.6 = 112.7\ .
\end{aligned}
$$

The calculation not only agrees with the experiment, but also points out that the C-3 and C-6 signals should be reassigned.

The approach proposed makes it possible to systematize the array of existing compounds of this class which have not yet been examined by NMR, as well as the peculiarities of the electron and conformational effects of OY substituents on carbon atoms of polyhalogenated polyoxybenzenes. The chemical shifts are calculated with higher reliability than with the aid of expert systems based on the compilation of spectral fragments from banks, however large they may be.

It is important in practice that the increment scheme provide sufficiently correct information on the ^{13}C NMR spectra of any of haloaromatic compounds. Therefore, the results of the study of the topological properties of the ^{13}C NMR spectra of polyhalogenated oxybenzenes can be used, for example, for investigating dangerous environmental pollutants such as polyhalogenated dibenzo-*p*-dioxins[29] and dibenzofurans. Despite its complex appearance, Eq. (3) can easily be algorithmized, since all of its terms are similar. This makes it possible to develop computer programs to simulate the ^{13}C NMR spectra, which would be more reliable than those based on the fragmentary compilation of a database.

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