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Electronic structures and reactivities of iodinating agents in the gas phase and in solutions: a density functional study

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The electronic and spatial structures of a broad spectrum of neutral compounds with X—Hal (X = N, O, Cl; Hal = Cl, Br, I) bonds and their protonated forms and of different electronic states of triiodide cation, I_3^+, were determined from density functional B3LYP/6-311G* quantum chemical calculations. The effects of the structure of these compounds on the parameters of electrophilic reactivity were revealed and the thermochemical characteristics of homolytic and heterolytic X—Hal bond dissociation and of iodine transfer in hydroxyl-containing solvents were calculated. Due to low homolytic bond dissociation energies of X—I, the formation of molecular iodine and triiodide cation I_3^+ becomes thermodynamically favorable and the cation should act as iodinating agent alternative to acylhypoiodites and *N*-iodoimides. The solvation effects of MeOH and CH_2Cl_2 on the X—Hal bond homolysis and heterolysis were determined using the PCM model.

Key words: halogenation, reactivity, iodinating agents, quantum chemistry, DFT B3LYP/6-311G* quantum chemical method.

Compounds with iodine—heteroatom bonds, such as iodine chloride, hypoiodites (HOI, MeCOOI, CF_3COOI, *etc.*),[1,2] *N*-iodoimides (*N*-iodosuccinimide (NIS);[1,3—5] *N*-iodosaccharine (NISAC);[6] 1,3-diiodo-5,5-dimethylhydantoin (DIH);[7] tetraiodoglycoluril (TIG);[8] *etc.*) are widely used as electrophilic iodinating agents. Common to all these compounds is that the iodine atom is bonded to a more electronegative atom and therefore polarization of the iodine—heteroatom bond reduces the electron density on the iodine atom, thus making it more electrophilic in character.

In contrast to *N*-iodoimides and ICl that are stable compounds, alkyl- and acylhypoiodites are often only postulated as kinetically independent intermediates (in some cases this is only based on indirect data).

Experimental studies of the state of the solutions containing or generating electrophilic iodine present difficulties. Because of this, reliable data on the reactivities of compounds RXI (X = O, N, Cl) and on the mechanisms of transfer of electrophilic iodine to substrates are unavailable so far. In this work, in order to theoretically estimate the effect of the structure of the RXI compounds on their reactivities in the ground and protonated states, density functional B3LYP/6-311G* quantum chemical calculations using the natural bonding orbital (NBO) scheme were carried out for the first time. The calculations were performed using the GAUSSIAN 98W program package[9] (B3LYP hybrid density functional method; B3 Becke exchange functional[10] and the Lee—Yang—Parr (LYP) correlation functional;[11] 6-311G(d) full-electron basis set for the H, N, C, O, F, and S atoms). At present, the method employed is commonly used for the description of thermodynamic characteristics. Geometric parameters of all molecules calculated were fully optimized and the absence of imaginary vibrational frequencies confirmed the stationary character of corresponding points on the potential energy surface. For the iodine atom we used a relativistic potential including a total of forty-six core electrons and the 6-311G* basis set (10s9p5d) for the valence electrons.[12] This basis set provides a more flexible description of the region of valence electrons compared to the 6-31G basis set because it uses three functions for the representation of any valence atomic orbital (AO).

The molecules under study were ICl, HOI, MeOI, MeCOOI, CF_3COOI, CF_3SO_2OI, $HOSO_2OI$, NIS, TIG, DIH, and NISAC. For comparison, we also studied the corresponding bromo and chloro derivatives, namely, HOBr, HOCl, *N*-bromosuccinimide (NBS), and *N*-chlorosuccinimide (NCS).

The Mulliken atomic charges of iodine $q(\mathrm{I})$ and heteroatom $q(\mathrm{X})$, the X—I bond lengths, the Wiberg indices ($W_{\mathrm{I-X}}$), the energies of the lowest unoccupied MOs

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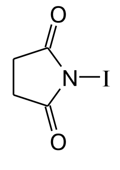
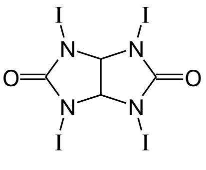
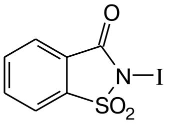


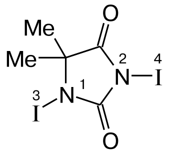
NIS



TIG



NISAC



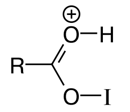
DIH

(E_{LUMO}), and degrees of the LUMO localization on atoms (C^2) expressed as the sums of the squared coefficients of the AO contributions to the corresponding MOs are listed in Table 1.

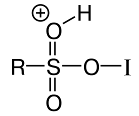
According to calculations, the electron density deficiency on iodine atom increases as follows: I—Cl (0.178) < < MeOI (0.235) < HOI (0.259) < TIG (0.255) < NIS (0.273) < MeCOOI (0.283) < DIH (0.268, 0.289) < < CF_3COOI (0.341) < NISAC (0.343) < $HOSO_2OI$ (0.376) < CF_3SO_2OI (0.400). The degree of polarization of the X—I bond increases while the Wiberg index (quantity characterizing the order of a chemical bond) decreases in the same order. By and large, there is a linear correlation between the q(I) values and the Wiberg indices and therefore both parameters can be taken as electrophilicity criteria for the iodine compounds studied. The iodine atoms in the DIH molecule are nonequivalent, the atom in position 4 between two C=O groups being the most electrophilic in character.

According to calculations, NISAC is the strongest electrophilic iodinating agent among those existing as free stable compounds, but it can also iodinate only activated arenes in neutral media.[6] It is well known that the reactivities of iodinating agents enhance in acid media. For instance, NIS in CF_3SO_3H,[3] as well as $BF_3—H_2O$ [5] or NIS [4] and TIG [8] in sulfuric acid can iodinate nitrobenzene and some other deactivated arenes and the iodinating activity of iodine chloride increases as the sulfuric acid concentration increases.[13] One can suggest that the reason for the enhanced reactivities of the RXI compounds in acid media consists in that protonation increases their electrophilic character and favors transfer of electrophilic iodine to solution. As far as we know no experimental data that allow one to compare the contributions of these factors are available, although it was reported[3,14] that NIS and TIG rapidly lose iodine in trifluoromethanesulfuric acid and sulfuric acid solutions, respectively (^{13}C NMR data).

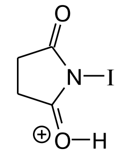
Hypoiodites of sulfuric and carboxylic acids, as well as NIS, TIG, DIH, and NISAC can be protomated both at heteroatoms bonded to the iodine atom and at doubly bonded oxygen atoms of C=O and S=O groups. According to calculations, the heats of formation of monoprotonated structures of the second type are ~20 kcal mol^{-1} lower than those of the alternative structures (similar conclusion was drawn recently[5] in a B3LYP/6-311G** quantum chemical study of various protonated forms of NCS). Besides, protonation at the nitrogen atom of *N*-halogenimides results in ring opening and formation of acylium ions.[5] Based on this, we analyzed the following most stable forms of the protonated structures of the reagents mentioned above.



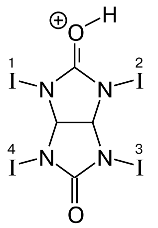
R = CH_3, CF_3



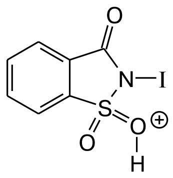
R = CF_3, OH



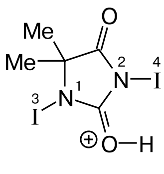
NIS—H^+



TIG—H^+



NISAC—H^+



DIH—H^+

For the protonated form TIG—H^+, Table 1 lists the parameters of the N—I(1) group in which the iodine atom is characterized by the highest electrophilicity. The DIH molecule can alternatively be protonated at two nonequivalent carbonyl groups. According to calculations, the DIH—H^+ form protonated at the C=O group of the carbamide fragment —NCON— is about 6 kcal mol^{-1} more stable.

It is clear that protonation causes a noticeable increase in the electrophilicity of iodine atom. Of course, this effect is most pronounced in those RXI compounds where protonation occurs at the O atom bonded to the I atom (H_2O^+I, $MeO^+(H)I$, and ICl^+H). Nevertheless, protonation of distant (from the iodine atom) O atoms of the C=O and S=O groups also causes a marked decrease in the atomic charge of iodine. The electron density deficiency on the iodine atom in the protonated forms of the RXI compounds increases as follows: TIG—H^+ (0.420) ≈ DIH—H^+ (0.419, 0.433) < NIS—H^+ (0.444) < < NISAC—H^+ (0.484) < ICl^+H (0.499) < $MeCO^+HOI$ (0.537) < CF_3CO^+HOI (0.584) < $IOSO_2OH_2{}^+$ (0.590) < < $MeOH^+I$ (0.600) ≈ $CF_3SO_2{}^+HOI$ (0.603) < H_2O^+I (0.668).

Trends to elongation, polarization, and a decrease in the Wiberg indices of the X—I bonds are also observed in

Table 1. Mulliken atomic charges of iodine q(I) and heteroatom q(X), X—I bond lengths (d), Wiberg indices ($W_{\text{I—X}}$), and LUMO energies (E_{LUMO}) and their localization (C^2) on atoms of the RXI molecules and their protonated forms obtained from B3LYP/6-311G* NBO calculations

Compound	q(I)	q(X)	d/nm	$W_{\text{X—I}}$	$-E_{\text{LUMO}}$/eV	C^2 (%)
	e					
HO—I	0.259	–0.675	2.043	0.894	3.14	I, 0.64; O, 0.41
H_2O^+I	0.668	–0.750	2.135	0.552	10.76	I, 0.66; O, 0.29
CH_3OI	0.235	–0.473	2.053	0.863	3.07	I, 0.65; O, 0.39
CH_3O^+HI	0.600	–0.601	2.123	0.599	10.12	I, 0.63; O, 0.30
CH_3COOI	0.283	–0.451	2.068	0.759	3.51	I, 0.67; O, 0.29
CH_3COH^+OI	0.537	–0.366	2.110	0.631	9.08	I, 0.66; O, 0.25
CF_3COOI	0.341	–0.451	2.072	0.728	4.27	I, 0.68; O, 0.28
CF_3CO^+HOI	0.584	0.358	2.122	0.592	9.80	I, 0.67; O, 0.23
$IOSO_2OH$	0.376	–0.575	2.065	0.742	4.42	I, 0.68; O, 0.30
$IOSO_2OH_2{}^+$	0.590	–0.553	2.119	0.588	9.68	I, 0.67; O, 0.26
CF_3SO_2OI	0.400	–0.581	2.064	0.727	4.66	I, 0.67; O, 0.30
$CF_3SO(OH^+)OI$	0.603	–0.545	2.116	0.574	9.64	I, 0.65; O, 0.24
Cl—I	0.178	–0.178	2.385	0.972	4.25	I, 0.68; Cl, 0.54
$IClH^+$	0.499	0.136	2.483	0.771	11.19	I, 0.66; Cl, 0.37
NIS	0.273	–0.598	2.065	0.797	2.72	I, 0.81; N, 0.44
$NIS—H^+$	0.444	–0.585	2.080	0.765	7.81	I, 0.77; N, 0.44
TIG	0.255	–0.562	2.090	0.820	3.43	I, 0.21; N, 0.12
$TIG—H^+$ [a]	0.420	–0.566	2.089	0.758	7.64	I, 0.15; N, 0.09
NISAC	0.343	–0.787	2.059	0.796	3.10	I, 0.82; N, 0.43
$NISAC—H^+$	0.484	–0.779	2.081	0.739	7.35	I, 0.77; N, 0.41
DIH	0.268	–0.619	2.063	0.811	3.13	I(3), 0.40;
	(I(3))	(N(1))	(N(1)—I(3))	(N(1)—I(3))		N(1), 0.26
	0.289	–0.625	2.063	0.795		I(4), 0.41;
	(I(4))	(N(2))	(N(2)—I(4))	(N(2)—I(4))		N(2), 0.23
$DIH—H^+$	0.433	–0.629	2.078	0.761	7.61	I(4), 0.50;
	(I(4))	(N(2))	(N(1)—I(3))	(N(2)—I(4))		N(2), 0.28;
	0.419	–0.586	2.078	0.762		I(3), 0.27;
	(I(3))	(N(1))	(N(2)—I(4))	(N(1)—I(3))		N(1), 0.15
MIH2	0.282	–0.627	2.056	0.801	2.63	I, 0.83; N, 0.43
$I_3{}^+$	0.470	0.265	2.720	0.972	9.95	I(1), 0.29; I(2), 0.48;
	(I(2))	(I(1), I(3))	(I(1)—I(2))	(I(1)—I(2))		I(3), 0.29
NBS	0.181	–0.509	1.864	0.891	2.19	Br, 0.97; N, 0.63
$NBS—H^+$	0.318	–0.509	1.868	0.881	7.44	Br, 0.92; N, 0.61
NCS	0.149	–0.513	1.864	0.950	1.50	Cl, 0.01; N, 0.82
$NCS—H^+$ [b]	0.262	–0.515	1.703	0.954	7.07	Cl, 0.01; N, 0.12
HOCl	0.128	–0.555	—	0.979	2.59	Cl, 0.72; O, 0.61
H_2O^+Cl	0.476	–0.606	1.767	0.794	11.18	Cl, 0.74; O, 0.45
HOBr	0.168	–0.588	1.872	0.952	2.90	Br, 0.68; O, 0.51
H_2O^+Br	0.553	–0.658	1.930	0.696	11.16	Br, 0.73; O, 0.37

[a] Listed are the data for the N—I(1) group; the atomic charges q(I) of other iodine atoms are q(I(2)) = 0.576, q(I(3)) = 0.499, and q(I(4)) = 0.505.

[b] The LUMO is mainly localized on the $4p_z$ and $5p_z$ orbitals of the carbon atom of protonated C=O group ($C^2{}_{\text{C}}$ = 0.73).

the same order, although the changes in these parameters do not obey regular patterns.

The LUMO populations (C^2) listed in Table 1 show that for all the R—X—I compounds studied this orbital is mainly localized on the iodine atoms. This substantiates that the iodine atom is the electrophilic center in the molecules under study. Protonation leads to noticeable decrease in the LUMO energy and to even greater increase in the contribution of this orbital to the iodine AO. The compounds with N—I bonds represent exceptions because their protonation causes almost no change in the contribution of this orbital to the iodine AO. The decrease in the LUMO energies corresponds to an increase in the atomic charge deficiency of iodine in both neutral and protonated forms of RXI molecules. There is an approximate linear correlation between the calculated q(I) values and the LUMO energies with two exceptions, ICl and ICl^+H (here, the LUMO energies are too low

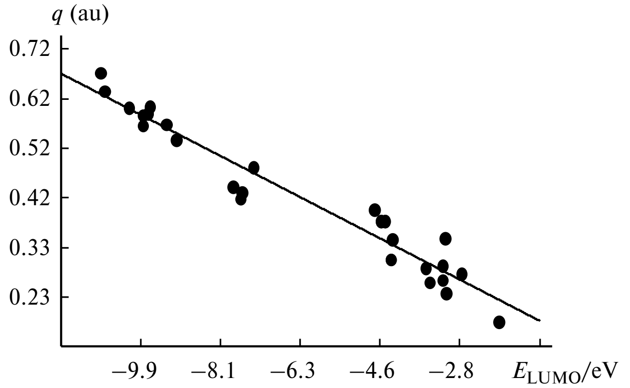


Fig. 1. Correlation between the atomic charges of iodine in compounds RX—I and RXH$^+$I and the LUMO energies (S = 0.03, r = 0.971).

compared to the corresponding q(I) values). A possible reason is that the calculated energies are underestimated, because the experimental electron affinity (EA) values of ICl are −1.48,[15] −1.78,[16] and −2.41 eV (see Ref. 17). When using an average experimental electron affinity value of −1.89 eV for the LUMO energy of ICl, the corresponding point falls on the common plot (Fig. 1)

$$q(\text{I}) = 0.13 - 0.05E_{\text{LUMO}} \quad (r = 0.971, S = 0.03).$$

Since protonation of substrates with N—I bonds causes a relatively small increase in the parameters related to the electrophilicity of iodine atoms, calculations show that compounds TIG—H$^+$, DIH—H$^+$, NIS—H$^+$, and NISAC—H$^+$ are less electrophilic in character in the acid media compared to the protonated compounds with the Cl—I and O—I bonds.

It has been known for long that hypohalogen-containing acids HOHal (Hal = Cl, Br, I), their ethers and esters ROHal, as well as *N*-halogenimides and *N*-halogenamides can act as both free radicals and electrophiles depending on the reaction conditions and substrate type (see, *e.g.*, a review[18] and Refs 19 and 20). This is first of all due to the possibility for both homolytic and heterolytic dissociation of X—I bonds to occur; however, no quantitative experimental data that allow one to estimate the effects of the structure of these compounds on the proportions of the two types of bond dissociation have been reported so far. We calculated the enthalpies and free energies of homolytic and heterolytic dissociation of X—I bonds in the neutral and protonated forms of the compounds under study (Scheme 1) and in some related compounds with X—Cl and X—Br bonds (Table 2). Halogen cations Hal$^+$ were calculated using the data for the most stable triplet states.

Scheme 1

$$\text{RX—Hal} \rightleftharpoons \text{RX}^{\bullet} + \text{Hal}^{\bullet}$$

$$\text{RX—Hal} \rightleftharpoons \text{RX}^{-} + \text{Hal}^{+}$$

$$\text{RX(H}^{+}\text{)—Hal} \rightleftharpoons \text{RXH} + \text{Hal}^{+}$$

Hal = Cl, Br, I

Table 2. B3LYP/6-311G* calculated enthalpies (ΔH) and free energies of reactions of the compounds containing X—Hal bonds in the free and protonated forms in the gas phase (ΔG_g) and in solutions (ΔG_s) in methanol and dichloromethane

Reaction	ΔH	ΔG_g	ΔG_s/kcal mol^{-1}	
	kcal mol^{-1}		MeOH	CH_2Cl_2
$HOI \rightleftharpoons HO^{\bullet} + I^{\bullet}$ (1)	44.86	37.90	45.97	64.39
$HOI \rightleftharpoons HO^{-} + I^{+}$ (2)	283.57	276.77	120.73	158.01
$H_2O^{+}I \rightleftharpoons H_2O + I^{+}$ (3)	40.53	33.16	54.08	48.28
$CH_3OI \rightleftharpoons CH_3O^{\bullet} + I^{\bullet}$ (4)	32.39	23.77	33.68	52.58
$CH_3OI \rightleftharpoons CH_3O^{-} + I^{+}$ (5)	255.14	246.79	120.17	150.42
$CH_3OHI^{+} \rightleftharpoons CH_3OH + I^{+}$ (6)	49.71	41.41	46.44	47.72
$CH_3COOI \rightleftharpoons CH_3COO^{\bullet} + I^{\bullet}$ (7)	34.46	27.13	34.75	54.16
$CH_3COOI \rightleftharpoons CH_3COO^{-} + I^{+}$ (8)	218.03	209.50	92.02	118.95
$CH_3COH^{+}OI \rightleftharpoons CH_3COOH + I^{+}$ (9)	55.07	46.20	46.91	50.47
$CF_3COOI \rightleftharpoons CF_3COO^{\bullet} + I^{\bullet}$ (10)	38.60	29.01	39.91	58.78
$CF_3COOI \rightleftharpoons CF_3COO^{-} + I^{+}$ (11)	192.41	183.35	75.45	98.94
$CF_3COH^{+}OI \rightleftharpoons CF_3COOH + I^{+}$ (12)	38.48	29.81	33.88	33.10
$CF_3SO_2OI \rightleftharpoons CF_3SO_2O^{\bullet} + I^{\bullet}$ (13)	32.92	23.25	36.20	54.12
$CF_3SO_2OI \rightleftharpoons CH_3SO_2O^{-} + I^{+}$ (14)	164.33	156.30	56.42	76.84
$CF_3SOO(H^{+})OI \rightleftharpoons CF_3SO_3H + I^{+}$ (15)	37.02	29.54	23.66	28.40
$IOSO_2OH \rightleftharpoons HOSO_2O^{\bullet} + I^{\bullet}$ (16)	33.35	23.55	35.83	53.79

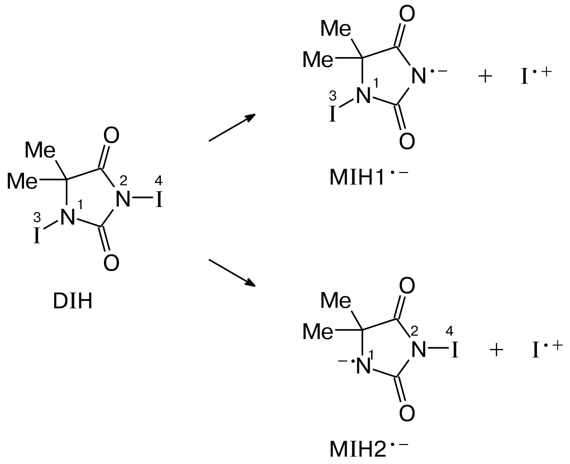
(*to be continued*)

Table 2 (*continued*)

Reaction	ΔH	ΔG_g	ΔG_s/kcal mol^{-1}	
	kcal mol^{-1}		MeOH	CH_2Cl_2
$IOSO_2OH \rightleftharpoons HOSO_2O^- + I^+$ (17)	174.91	166.07	62.09	84.35
$IOSOO(H^+)OH \rightleftharpoons H_2SO_4 + I^+$ (18)	37.48	29.39	28.54	31.92
$ClI \rightleftharpoons Cl^\bullet + I^\bullet$ (19)	45.60	39.49	45.17	64.18
$ClI \rightleftharpoons Cl^- + I^+$ (20)	205.61	199.66	72.63	99.21
$ClH^+I \rightleftharpoons HCl + I^+$ (21)	18.25	11.69	13.90	15.02
NIS $\rightleftharpoons$ Succinimide$^\bullet$ + I$^\bullet$ (22)	56.77	49.88	58.55	77.73
NIS $\rightleftharpoons$ Succinimide$^-$ + I$^+$ (23)	218.01	209.34	110.17	130.65
NIS—H$^+$ $\rightleftharpoons$ Succinimide + I$^+$ (24)	64.28	55.30	53.64	56.72
NISAC $\rightleftharpoons$ Saccharine$^\bullet$ + I$^\bullet$ (25)	42.39	33.57	42.67	61.75
NISAC $\rightleftharpoons$ Saccharine$^-$ + I$^+$ (26)	193.18	185.12	81.89	106.73
NISAC—H$^+$ $\rightleftharpoons$ Saccharine + I$^+$ (27)	57.97	49.44	38.08	44.48
TIG $\rightleftharpoons$ Triiodoglycoluril$^\bullet$ + I$^\bullet$ (28)	36.72	27.08	—	—
TIG $\rightleftharpoons$ Triiodoglycoluril$^-$ + I$^+$ (29)	198.58	189.09	—	—
TIG—H$^+$ $\rightleftharpoons$ Triiodoglycoluril+ I$^+$ (30)	65.73	57.06	—	—
DIH $\rightleftharpoons$ MIH2$^\bullet$ + I$^\bullet$ (31)	38.31	29.24	40.43	58.08
DIH $\rightleftharpoons$ MIH2$^-$ + I$^+$ (32)	211.25	202.63	108.99	128.76
DIH $\rightleftharpoons$ MIH1$^\bullet$ + I$^\bullet$ (33)	48.67	40.72	47.82	67.63
DIH $\rightleftharpoons$ MIH1$^-$ + I$^+$ (34)	206.57	199.45	101.85	123.72
DIH—H$^+$ $\rightleftharpoons$ MIH1 + I$^+$ (35)	64.18	56.10	50.21	55.43
DIH—H$^+$ $\rightleftharpoons$ MIH2 + I$^+$ (36)	65.23	55.96	49.11	54.70
$HOBr \rightleftharpoons HO^\bullet + Br^\bullet$ (37)	46.96	39.89	48.53	48.33
$HOBr \rightleftharpoons HO^- + Br^+$ (38)	317.00	310.09	147.18	186.18
$H_2O^+Br \rightleftharpoons H_2O + Br^+$ (39)	61.27	53.67	73.32	68.33
NBS $\rightleftharpoons$ Succinimide$^\bullet$ + Br$^\bullet$ (40)	61.50	54.43	65.98	64.28
NBS $\rightleftharpoons$ Succinimide$^-$ + Br$^+$ (41)	254.06	245.21	141.49	161.43
NBS—H$^+$ $\rightleftharpoons$ Succinimide + Br$^+$ (42)	97.37	88.24	84.55	86.76
$HOCl \rightleftharpoons HO^\bullet + Cl^\bullet$ (43)	47.81	40.67	49.81	49.46
$HOCl \rightleftharpoons HO^- + Cl^+$ (44)	344.64	337.66	171.98	211.54
$H_2O^+Cl \rightleftharpoons H_2O + Cl^+$ (45)	79.11	71.38	91.23	86.72
NCS $\rightleftharpoons$ Succinimide$^\bullet$ + Cl$^\bullet$ (46)	66.52	59.29	70.06	69.40
NCS $\rightleftharpoons$ Succinimide$^-$ + Cl$^+$ (47)	285.88	276.87	169.09	190.78
NCS—H$^+$ $\rightleftharpoons$ Succinimide + Cl$^+$ (48)	126.45	117.25	114.78	115.18
$I_2 + I^+ \rightleftharpoons I_3^+$ (49)	−54.29	−48.00	−40.06	−43.84
$HOI + I_2 \rightleftharpoons HO^- + I_3^+$ (50)	216.98	228.77	129.05	114.17
$H_2O^+I + I_2 \rightleftharpoons H_2O + I_3^+$ (51)	−13.76	−14.85	14.02	4.43
$CH_3OI + I_2 \rightleftharpoons CH_3O^- + I_3^+$ (52)	200.85	198.78	80.10	106.57
$CH_3O^+HI + I_2 \rightleftharpoons CH_3OH + I_3^+$ (53)	−4.59	−6.60	6.38	3.87
$CH_3COOI + I_2 \rightleftharpoons CH_3COO^- + I_3^+$ (54)	163.73	118.21	51.96	75.10
$CH_3COH^+OI + I_2 \rightleftharpoons CH_3COOH + I_3^+$ (55)	0.77	−1.80	6.85	6.62
NIS + $I_2 \rightleftharpoons$ Succinimide$^-$ + I_3^+ (56)	163.71	161.34	70.10	86.80
NIS—H$^+$ + $I_2 \rightleftharpoons$ Succinimide + I_3^+ (57)	9.98	7.29	13.57	12.87
$ClI + I_2 \rightleftharpoons Cl^- + I_3^+$ (58)	151.31	151.66	32.57	55.36
$ClH^+I + I_2 \rightleftharpoons HCl + I_3^+$ (59)	−36.05	−36.31	−26.16	−28.83
$CF_3COOI + I_2 \rightleftharpoons CF_3COO^- + I_3^+$ (60)	138.11	135.35	35.38	55.09
$CF_3COH^+OI + I_2 \rightleftharpoons CF_3COOH + I_3^+$ (61)	−15.81	−18.19	−6.18	−10.75
$CF_3SO_2OI + I_2 \rightleftharpoons CF_3SO_2O^- + I_3^+$ (62)	110.03	108.30	16.36	32.99
$CF_3SOO(H^+)OI + I_2 \rightleftharpoons CF_3SO_3H + I_3^+$ (63)	−17.27	−18.46	−16.40	−15.45
$IOSO_2OH + I_2 \rightleftharpoons HOSO_2O^- + I_3^+$ (64)	120.61	118.06	22.02	40.50
$IOSOO(H^+)OH + I_2 \rightleftharpoons H_2SO_4 + I_3^+$ (65)	16.82	18.62	−11.52	−11.93
DIH + $I_2 \rightleftharpoons$ MIH1$^-$ + I_3^+ (66)	152.27	151.45	61.79	79.87
DIH—H$^+$ + $I_2 \rightleftharpoons$ MIH1 + I_3^+ (67)	13.60	11.94	10.15	11.58
DIH + $I_2 \rightleftharpoons$ MIH2$^-$ + I_3^+ (68)	156.96	154.62	68.92	84.91
DIH—H$^+$ + $I_2 \rightleftharpoons$ MIH2 + I_3^+ (69)	14.64	11.80	9.05	10.85

Two compounds, TIG and DIH, represent a particular case. Their molecules contain more than one iodine atom, thus being different from other compounds studied. In this study we were not interested in determining the thermochemical characteristics of consecutive, stepwise elimination of all iodine atoms from the TIG molecule and calculated the dissociation parameters only for one N—I bond, which results in triiodoglycoluril (TRIG). For DIH, we calculated the thermodynamic parameters of elimination of iodine atoms from positions 1 and 2 to give radical and anionic species 2-iodo-5,5-dimethylhydantoin (MIH2$^{\bullet}$, MIH2^{-}) and 1-iodo-5,5-dimethylhydantoin (MIH1$^{\bullet}$, MIH1^{-}), respectively, (Scheme 2).

Scheme 2



The dissociation energies of two types of N—I bonds in the protonated form DIH—H^{+} were calculated analogously; the N(1)—I(3) and N(2)—I(4) bond dissociation results in MIH2 and MIH1, respectively. According to calculations, radical MIH2$^{\bullet}$ is 10.36 kcal mol^{-1} more stable than radical MIH1$^{\bullet}$; for this reason, the N(1)—I(3) bond is weaker in the homolytic dissociation reaction compared to the N(2)—I(4) bond (see Table 2). On the contrary, heterolysis of the N(2)—I(4) bond is expected to occur easier. In the protonated form DIH—H^{+} both N—I bonds show almost the same strength. Thus, calculations predict that, thermodynamically, the loss of an iodine atom by the DIH molecule in neutral media will most probably be followed by the formation of MIH2. By and large it should be noted that the N—I bond strengths in the *N*-iodoimides studied increase in the order TIG < DIH < NISAC < NIS. It is of considerable practical and theoretical value to answer a question concerning the relative reactivity of DIH and MIH2, *i.e.*, does the reactivity of DIH increase or decrease upon the loss of the first iodine atom? Calculations of the MIH2 molecule revealed a decrease in the electrophilic reactivity parameters of the iodine atom in position 2 compared to the reactivity of DIH (see Table 1).

Comparison of the results of calculations of structurally similar halo derivatives RXHal (X = O, N; Hal = Cl, Br, I) suggests the following. Based on all criteria (atomic charge of Hal, Wiberg index, and LUMO energies), the iodine-containing compounds have the highest degree of electrophilicity. Calculations predicted the increase in electrophility of RXHal compounds in the order RXCl < RXBr < RXI (see Table 1). At first glance, this is quite unexpected and is antiparallel to the order of increasing the electrophilicity of halogens ($I_2 < Br_2 < Cl_2$). At the same time this relationship becomes understandable with allowance for the fact that polarization of the $X^{\delta-}$—$Hal^{\delta+}$ bond in these molecules should increase in the order Cl < Br < I due to the higher electronegativity of the O and N atoms compared to those of the Hal atoms.

As far as we know, no measurements of the electrophilic or free-radical relative reactivity of hypohalites ROHal and *N*-halogenimides were reported as yet. However, the conclusion about the highest electrophilic activity of RXI compounds (see above) can to some extent be substantiated by the experimental data,[5] according to which the NIS—BF_3—H_2O system can iodinate deactivated arenes at 0—5 °C, whereas chlorination and bromination under the action of NCS and NBS, respectively, in the same medium occurs only at 75—105 °C. Nevertheless, it is often reported that hypochlorites and hypobromites are more reactive than hypoiodites in electrophilic reactions (see, *e.g.*, a review[2]). The results of our calculations show that this order of reactivities is determined by molecular chlorine and bromine liberated upon X—Cl and X—Br (X = O, N) bond homolysis rather than intrinsic electrophilicity of hypochlorites and hypobromites (that is rather low according to calculations).

For clear reasons, protonation of the compounds studied leads to an abrupt decrease in the heterolytic bond dissociation energies of X—Hal, but the homolytic bond dissociation energies also usually remain lower. Here, the exceptions are the protonated forms IOH_2^{+}, $CF_3C(OH^{+})OI$, and especially $ClHI^{+}$, for which heterolytic dissociation becomes more probable (see Table 2, Eqs (3), (12), and (21)).

Among the most widely used methods of iodination are those involving NIS, ICl, or the reaction systems in which acyl- and alkylhypoiodites are generated as a result of redox transformations in aprotic nonpolar solvents (CH_2Cl_2, MeCN), and in alcohols or acetic acid (*i.e.*, in neutral or weak acid media). A number of examples is provided by the systems I_2—HgO—AlkOH, I_2 (or ICl)—$AgOCOCF_3$, I_2—$PhI(OAc)_2$—AcOH, I_2—$PhI(OCOCF_3)_2$, I_2—$MeCO_3H$, ICl—Bu^{t}OK, and I_2—$Hg(OAc)_2$).[1] Calculations of the thermodynamic functions (see Table 2) showed with certainty that neutral forms of these reagents cannot act as sources of I^{+} cations under these conditions. From this it follows that the RX—I compounds act as iodinating agents and that their relative electrophilic reactivities can be estimated using the characteristics listed in Table 1. Therefore, *N*-iodosaccharine is expected to possess the highest electrophilic reactivity in neutral media among the available RX—I reagents.

But the results obtained suggest the possibility of yet another route of electrophilic iodination. Relatively low homolytic dissociation energies of X—I bonds should lead to formation of molecular iodine upon recombination of free iodine radicals. Indeed, the formation of molecular iodine is explicitly or implicitly reported in most studies on the iodination involving hypoiodites. In turn, iodine formed can interact with electrophilic I^+ cation and with neutral and especially protonated forms of the RXI reagents, thus producing an equilibrium amount of triiodide cation I_3^+ in the reaction solutions (Scheme 3).

Scheme 3

$$I^+ + I_2 \rightleftharpoons I_3^+$$

$$RXI + I_2 \rightleftharpoons RX^- + I_3^+$$

$$RX(H^+)I + I_2 \rightleftharpoons RXH + I_3^+$$

This intermediate is of great interest, because it is known with certainty that the species is a true iodinating agent in strong acid media (see, *e.g.*, Refs 21 and 22). The stoichiometry of the ion was proved and the characteristics of its absorption spectra were determined. The electronic and spatial structures of the I_3^+ ion in the complexes $I_3^+AlCl_4^-$ and $I_3^+AsF_6^-$ are also known.**[23]**

Optimization of the structure of the I_3^+ ion (I(1)—I(2)—I(3)) predicts a trigonal geometry (bond angle of 107.8°) and the singlet state that is 9.66 kcal mol^{-1} more stable than the triplet state. The calculated equilibrium geometric parameters and electronic characteristics of the singlet state of the I_3^+ ion are listed in Table 1. It should be noted that the structure of the I_3^+ ion is similar to the T-shaped configurations of polyvalent iodine(III) derivatives RIX_2 (bond angle X—I—X is about 90—100°)**[24]** and the complexes $I_3^+AlCl_4^-$ and $I_3^+AsF_6^-$ (bond angles I—I—I are 101—104°).**[23]**

The calculated thermodynamic characteristics of the reactions of formation of I_3^+ cation (see Eqs (49)—(69)) are listed in Table 2. The results obtained clearly show that generation of this cation from molecular iodine and I^+ ion (see Eq. (49)) is thermodynamically favorable and that the proportion of the decomposition channel of the protonated forms $RXIH^+$ to I_3^+ is much higher than the decomposition to monocation I^+ in acid media or the decomposition to iodine radical upon homolysis of X—I bonds (*cf.*, for instance, Eqs (1), (3) and (51); Eqs (7), (9) and (55); Eqs (22), (24) and (57); Eqs (10), (12) and (61); Eqs (13), (15) and (63); and Eqs (16), (18) and (65)). Moreover, calculations predict almost complete decomposition of protonated iodine chloride ClH^+I (see Eq. (59)) and protonated hypoiodite intermediates of strong acids (see Eqs (61) and (63)) to I_3^+ in the presence of iodine. The results calculations provide a correct explanation for the presence of noticeable concentrations of I_3^+ cation in the reaction solutions of acylhypoiodites, NIS or TIG detected earlier**[25]** in the absorption spectra.

Thus, calculations predict that the protonated forms $RXIH^+$ and I_3^+ are true electrophilic intermediates of iodination by the reagents under study in acid media. The ratio of these species should depend on the reagent concentration and on the nature of the solvent used. Often, it is the I_3^+ cation that would limit the electrophilic reactivity of the protonated reagents of the types R—X—I and ICl.

The results presented above were obtained for the reagents in the gas phase. To obtain a better approximation to actual iodination conditions (the process usually proceeds in solvents), we for the first time estimated the effect of medium on the solvation characteristics of certain reagents under study and products of their decomposition by the B3LYP/6-311G* method using the polarized continuum model (PCM).**[26]** (Unfortunately, we failed to determine the solvation characteristics of TIG in the framework of the PCM model, because the calculations led to unrealistically overestimated ΔG_{solv} value of about ~60000 kcal mol^{-1}.) The solvents considered were MeOH and CH_2Cl_2 as typical examples of real protic and aprotic media. The calculated solvation energies of the compounds RXHal and products of their decomposition are listed in Table 3 and the calculated changes in the total energies of homolytic and heterolytic dissociation of the X—Hal bonds in MeOH and CH_2Cl_2 are given in Table 2. Comparison of these values with the results of gas-phase calculations (see Table 2) shows that the heterolytic dissociation energies of the X—Hal bonds become nearly halved due to high solvation energies ΔG_{solv} of the ionic species; nevertheless, they remain much higher than the homolytic dissociation energies of these bonds. We also found that solvents have a relatively weak effect on the changes in the X—Hal bond dissociation energies of the protonated substrates $RX(H^+)I$.

We also calculated the solvation effects for iodine and I_3^+ cation (see Table 3) and the changes in the total energy of formation of I_3^+ in solutions (see Table 2). In this case the thermodynamic probability of I_3^+ formation from iodine and MeOI in solvents also considerably increases compared to the gas phase (see Table 2, Eq. (52)). At the same time the decomposition of the protonated form MeO^+HI to I_3^+ in solvents becomes 6—12 kcal mol^{-1} less probable than in the gas phase (see Table 2, Eq. (53)). This follows from the somewhat higher solvation energy of methyloxonium ion MeO^+HI compared to that of the I_3^+ cation (see Table 3).

Table 3. Effect of solvents on the solvation characteristics of RXHal compounds and decomposition products obtained from B3LYP/6-311G* calculations using the PCM model

Compound	$-\Delta G_{solv}$/kcal mol^{-1}		Compound	$-\Delta G_{solv}$/kcal mol^{-1}		Compound	$-\Delta G_{solv}$/kcal mol^{-1}	
	MeOH	CH_2Cl_2		MeOH	CH_2Cl_2		MeOH	CH_2Cl_2
HOI	7.40	4.00	I_2	1.84	2.62	$IOSO_2O^-$	59.00	48.32
H_2O^+I	78.90	57.54	HOBr	7.25	3.72	$HOSO_2O^{\bullet}$	11.34	6.16
MeOI	3.59	2.99	H_2O^+Br	84.08	61.69	$HOSO_2O^-$	69.08	53.19
MeO^+HI	59.53	46.52	HOCl	7.03	3.29	H_2SO_4	19.60	9.84
CH_3COOI	4.11	3.45	H_2O^+Cl	86.73	64.08	$Br^{\bullet}$	0.37	0.47
$CH_3C(OH^+)OI$-*anti*	57.53	45.32	$I^{\bullet}$	0.85	1.22	Br^+ tripl	64.87	51.07
CF_3COOI	2.07	1.93	I^+ tripl	57.92	46.00	$Cl^{\bullet}$	0.16	0.12
CF_3COH^+OI	60.14	43.97	I_3^+ (T) singl	45.40	37.75	Cl^+ tripl	67.60	53.04
CF_3SO_2OI	3.90	3.27	$MeO^{\bullet}$	3.14	2.12	Cl^-	76.53	62.56
$CF_3SOO(H^+)OI$	55.22	42.35	MeO^-	84.77	66.23	HCl	1.93	0.83
$IOSO_3H$	13.36	7.55	MeOH	5.57	3.36	HBr	1.52	0.83
$IOSOO(H^+)OH$	68.53	49.99	$HO^{\bullet}$	6.02	2.61	HI	0.84	0.95
ICl	1.21	1.86	HO^-	113.04	84.78	Monoiodohydantoin-1	8.40	5.66
ICl^+H	55.92	43.90	H_2O	7.34	3.66	Monoiodohydantoin-2	9.22	6.16
NIS	8.47	6.63	$CH_3COO^{\bullet}$	4.76	3.17	Succinimide	11.18	7.03
$NIS-H^+$	58.32	45.03	CH_3COO^-	73.71	58.26	Succinimide$^{\bullet}$	8.41	5.99
NISAC	12.70	7.72	CH_3COOH	7.73	4.08	Succinimide$^-$	59.98	49.90
NISAC—H+	53.49	41.19	$CF_3COO^{\bullet}$	1.25	0.82	Saccharine	15.92	9.38
DIH	7.73	4.95	CF_3COO^-	62.45	51.00	Saccharine$^{\bullet}$	13.42	7.98
$DIH-H^+$	47.03	37.24	CF_3COOH	7.01	3.81	Saccharine$^-$	68.04	50.46
NBS	10.76	6.54	$CF_3SO_2O^{\bullet}$	1.29	1.35	MIH1$^{\bullet}$	10.42	6.50
NBS—H+	63.16	47.19	$CF_3SO_2O^-$	54.76	45.88	MIH2$^{\bullet}$	6.44	4.69
NCS	9.25	6.06	CF_3SO_3H	11.14	5.79	MIH1$^-$	57.25	44.86
NCS—H+	67.04	48.57	$IOSO_2O^{\bullet}$	4.33	3.77	MIH2$^-$	54.17	43.87

When carrying iodination reactions involving stable reagents similar to *N*-iodoimides or iodine chloride in hydroxyl-containing solvents, a question always arises as to does transfer of iodine to substrate occur immediately from the reagents or the reagents only act as sources of active iodine that is transferred to solution? The vast majority of the published studies ignores this question, but transfer of iodine from NIS and TIG to solutions of trifluoromethanesulfuric and sulfuric acids was detected experimentally.[3,14] In this study, based on the calculated thermodynamic characteristics, we first calculated the changes in the free energy of iodine transfer from ICl, NIS, and NISAC to H_2O, MeOH, and H_2SO_4 in the gas phase and in solution in MeOH (Table 4). To estimate the effect of the nature of halogen on these exchange processes, identical calculations were carried out for NBS and NCS.

The data listed in Table 4 show almost no transfer of iodine to solutions with formation of reactive hypohalogenite species for ICl unlike *N*-halogenimides; therefore, ICl should act as a "true" iodinating agent. At the same time calculations for NIS and especially NISAC predict a significant degree of iodine transfer. Thus, both *N*-iodoimides and hypoiodite species RO—I that are in equilibrium with one another should act as iodinating species in hydroxyl-containing solvents. It should be noted

Table 4. B3LYP/6-311G* calculated free energies (ΔG) of the reactions of compounds containing X—Hal bonds with hydroxyl-containing compounds in the gas phase (I, $\varepsilon = 0$) and in methanol (II, $\varepsilon = 32.6$)

Reactions	ΔG/kcal mol^{-1}	
	I	II
$ClI + H_2O \rightleftharpoons HCl + HOI$	13.27	14.62
$ClI + MeOH \rightleftharpoons HCl + MeOI$	11.95	14.47
$ClI + H_2SO_4 \rightleftharpoons HCl + IOSO_3H$	16.15	22.37
$ClI + AcOH \rightleftharpoons HCl + AcOI$	14.49	19.06
$NIS + H_2O \rightleftharpoons$ $\rightleftharpoons$ Succinimide + HOI	1.81	0.13
$NIS + MeOH \rightleftharpoons$ $\rightleftharpoons$ Succinimide + MeOI	0.49	−0.02
$NIS + H_2SO_4 \rightleftharpoons$ $\rightleftharpoons$ Succinimide + $IOSO_3H$	4.69	7.89
$NIS + AcOH \rightleftharpoons$ $\rightleftharpoons$ Succinimide + AcOI	3.03	4.57
$NISAC + H_2O \rightleftharpoons$ Saccharine + HOI	0.45	−0.47
$NISAC + MeOH \rightleftharpoons$ $\rightleftharpoons$ Saccharine + MeOI	−0.86	−0.62
$NISAC + H_2SO_4 \rightleftharpoons$ $\rightleftharpoons$ Saccharine + $IOSO_3H$	3.33	7.29
$NBS + H_2O \rightleftharpoons$ Succinimide + HOBr	4.37	5.00
$NCS + H_2O \rightleftharpoons$ $\rightleftharpoons$ Succinimide + HOCl	8.45	7.80

that the degree of iodine transfer to solution decreases with an increase in the acid properties of the hydroxyl-containing component ROH, while comparison of the data for NIS, NBS, and NCS suggests a dramatic increase in stability in this order.

Summing up, the reactivities of most iodinating agents should be determined by various electrophilic iodinating species existing in solutions rather than a single structure, which is due to thermodynamically probable formation of I_3^+ cation and iodine exchange between the reagents and hydroxyl-containing solvents.

Experimental

All calculations were carried out on a workstation at the Tomsk Polytechnical University. The dissociation energies of the compounds calculated were corrected for zero-point vibrational energy (ZPVE) and reduced to normal conditions (298.15 K, 1 atm) using thermal corrections to the enthalpy and free energy.

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