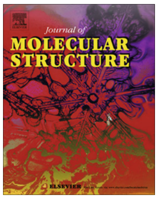
Journal of Molecular Structure 1054–1055 (2013) 367–374

Contents lists available at ScienceDirect

Journal of Molecular Structure

journal homepage: www.elsevier.com/locate/molstruc



Synthesis and structural insights of substituted 2-iodoacetanilides and 2-iodoanilines

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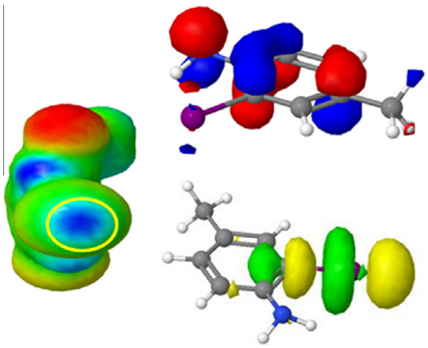
HIGHLIGHTS

- A simple method is applied for the direct iodination of substituted anilines.
- DFT study is conducted understanding the structural features of iodinated products.
- Most of the iodinated products are capable of forming a distinct "Halogen Bonding".
- Noncovalent interaction between the products may reduce the single product yield.

GRAPHICAL ABSTRACT



ARTICLE INFO

Article history:
Received 18 August 2013
Received in revised form 10 September 2013
Accepted 7 October 2013
Available online 15 October 2013

Keywords:
Iodination
Density functional theory
Equilibrium geometry
Vibrational frequencies
Frontier molecular orbitals
Halogen bonding

ABSTRACT

This study reports a simple and efficient method for the direct iodination of substituted anilines with molecular iodine and copper acetate in acetic acid producing 2-iodoacetanilies and 2-iodoanilines. Employing density functional theory (B3LYP) and MidiX basis set, computational study is performed to calculate equilibrium geometries, IR vibrational frequencies, and thermodynamic properties including change of energy, enthalpy and Gibbs free energies. The optimized geometries indicated longer C–I bond distance (2.133 Å) which makes iodine slightly positive. The partial atomic charge profile and electrostatic potential further confirmed that most of the iodinated products are capable of forming a distinct "halogen bonding". The thermodynamic properties disclosed that all iodination reactions are endothermic. Understanding the substituents' effect, molecular frontier orbital (MO) calculations are conducted finding the HOMO, LUMO and HOMO–LUMO gaps for all compounds. The MO calculations revealed that two electron-withdrawing iodine groups have significant influence on lowering the HOMO–LUMO gap compared to one iodine group in the products.

1. Introduction

In numerous transformations, aryl iodides are valuable synthetic intermediate, particularly in metal-catalyzed cross-coupling reactions [1,2]. Electrophilic iodination of anilines, phenols, provides straightforward access to a wide range of essential iodoarene intermediates [3,4], and it was reported that iodine bonded at the *ortho* position to $-NH_2$ or $-NHCOCH_3$ makes the molecule a very convenient synthon for further transformation [5,6]. In synthesis of *N*-substituted-3-alkylisoindoline esters [7], isocoumarin [8] and α-(aminocarbonyl)iminyl radicals [9], aryl iodides provided evidence of their potential applications. Some iodo aromatic compounds are employed in medicine as drugs or diagnostic aids. For instance, a notable imaging agent (iodo-PK11195) and galanthamine

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http://dx.doi.org/10.1016/j.molstruc.2013.10.011

drug synthesized from iodo intermediate are frequently used for treating Alzheimer patients [10,11]. The iodoarenes moiety is also an important structural motif of various bioactive compound, such as berkelic acid methyl ester [12]. The challenge of introducing iodine is particularly important since iodine is preferred over other aromatic halides for some reactions.

Moreover, halogen (especially Br and I) atoms form halogen bonding analogous to hydrogen bonding and these noncovalent interactions play pivotal roles in biological and chemical systems. In halogen bonding [13–15], X atom can act as an electron deficient (electropositive crown or σ-hole) Lewis acid which in turn attracted by electron rich Lewis bases (such as carbonyl oxygen, amine nitrogen). The halogen bonding phenomena are also widely available in the biological molecules such as proteins in which some halogenated ligands form noncovalent halogen bonding with carbonyl oxygen of amino acids [16]. It is also observed that installing halogen atom in some drugs can significantly enhance the performance since halogen atom can enter through the hydrophobic regions of integral membrane proteins [17]. That's why the versatility of the C–I bond makes aryl iodides essential buildings block in medicinal chemistry, supramolecular chemistry, and material science.

Different methods, direct and in direct, are applied for iodoarene synthesis [18–20]. In direct aromatic iodination, the iodonium species directly forms cabon–iodine bond [21]. However, direct halogenations suffer from some difficulties; firstly, the halogens have incredibly dissimilar reactivity, with iodine generally requiring some technique of activation, whereas others are reactive and hazardous chemicals [22]. Secondly, there is a reducing effect of hydrogen iodide produced in the system [23]. Iodination is carried out under oxidative conditions, where iodide ions formed in reactions are oxidized to molecular iodine. The oxidizing agents can degrade sensitive groups, for this reason it is not always feasible. Several iodination methods have been reported using various reagents, such as-py, ICl, MeOH [24]; I_2, $NaNO_2$, H_2O–MeOH [25]; I_2/CAN [26]; KI or I_2/polyvinylpyrrolodone supported H_2O_2/$H_3PW_{12}O_{40}$ in CH_2Cl_2 [27]; I_2–HIO_3 [28]; $NaBO_3{\cdot}4H_2O/I_2$ in ionic liquids [29]; NIS(N-Iodosuccinimide), $[Rh(III)Cp^{*}Cl_2]_2AgSbF_6$, PivOH in 1,2-DCE [30]; $\{[K{\cdot}18\text{-}C\text{-}6]ICl_2\}_n$ [31]. Moreover, Baird and Surridge reported [32] that the iodination of aromatic compounds with iodine and copper(II) halides gave the aryl iodides. It is also indicated that the iodination of less reactive substrates with iodine aluminum(III) and copper(II) chlorides [33] provided the corresponding aryl halides. Although numerous methods related to the iodination of aromatic compound for various transformations are available, there is still a vast need finding of trouble-free, non-hazardous, and cost-effective reagent for the introduction of iodine into an aromatic ring.

In this paper, we report the iodination of 2 or 3-substituted anilines by copper(II) acetate in acetic acid employing one-pot synthesis method. In addition, details quantum chemical investigations have been performed exploring the equilibrium geometries, vibrational frequencies, molecular orbitals of all synthesized compounds.

2. Experimental methods

A typical procedure was followed for one-pot synthesis of substituted 2-iodoaniline and 2-iodoacetanilide from substituted aniline. A mixture of 5 g of substituted aniline **1**–**6** shown in Table 1, granulated iodine (1 mol. equiv.) and copper(II) acetate (1 mol. equiv.) were stirred in 50 mL of glacial acetic for 30 min. The reaction mixture was refluxed for 12 h with constant stirring at 120 °C. Then the reaction mixture was allowed to cool at room temperature. The precipitate of copper(I) iodide was removed by filtration and the filtrate was poured into water and extracted with chloroform (3 × 50 mL). The combined chloroform extracts were washed with sodium hydrogen carbonate solution, sodium thiosulfate solution, distilled water and dried with anhydrous sodium sulfate. A crude semi-solid mass was obtained after removal of solvent. The crude product was purified by column chromatography on silica gel using n-hexane/ethyl acetate as eluant (4:1) and compounds **7**–**24** were isolated.

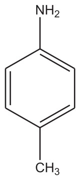
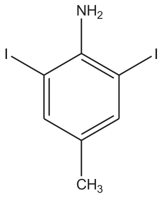
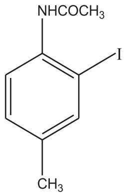
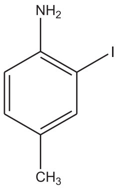
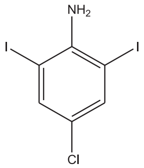
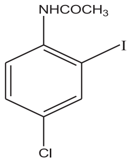
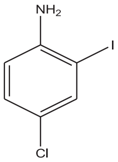
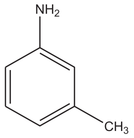
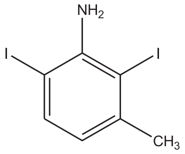
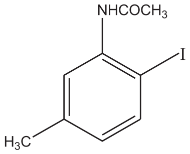
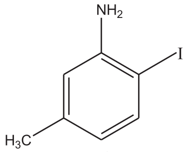
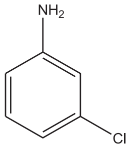
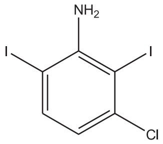
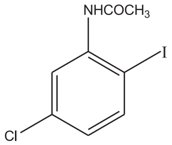
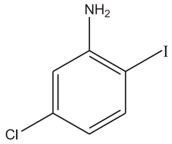
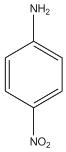
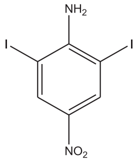
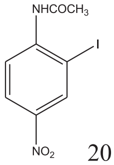
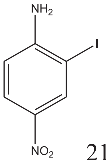
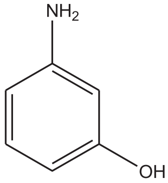
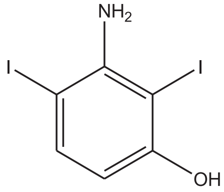
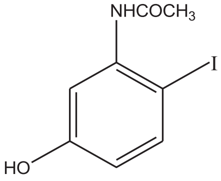
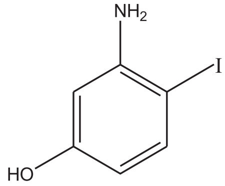
In order to optimize the iodination reaction condition, 4-methyl aniline **1** was considered as starting material and the reaction temperature was varied from 25 °C to 120 °C (supplementary Table S1). It was observed that in low concentration of substrate in acetic acid and stirring the reaction mixture at higher temperature favored 2-iodo-4-methyl-N-ethanoylaniline **8** as a major product. To find out the role of solvent, two solvents, acetic acid or trifluro acetic acid, was used as reaction medium. No desired iodo compound was obtained when the reaction was carried out in trifluro acetic acid at the same condition. Therefore, acetic acid was found to be the best solvent and entry 4 was found to be the optimized condition to synthesize 2-iodo acetanilide.

The substitued-2-iodoacetanilides and 2-iodoanilineswere prepared by a convenient procedure using iodine–copper(II) acetate in acetic acid from their corresponding parent substituted anilines (Scheme 1). Commercially available primary arylamines e.g. *p*-methylaniline **1**, *p*-chloroaniline **2**, *m*-methylaniline **3**, *m*-chloroaniline **4**, *p*-nitroaniline **5** and *m*-aminophenol **6** were used to prepare 2-iodoacetanilide and 2-iodoaniline. The iodination reactions were carried out by stirring the mixture of substituted arylamine **1**–**6** (10.0 mmol), granulated iodine (10.0 mmol) and copper acetate (10.0 mmol) in glacial acetic acid (20 mL) at 120 °C for 12 h. After usual workup, the crude product was purified by column chromatography on silica gel using n-hexane/ethyl acetate (4:1) as eluant, and products **7**–**24** were isolated as shown in the Table 1. Melting points were determined in open capillary tubes in Gallenkamp (England). IR spectra were recorded on a Shimadzu FTIR spectrophotometer with 45 scan and range of 4000–400/cm. ^{1}H NMR and ^{13}C NMR spectra were recorded on a Bruker DPX-400 spectrophotometer (400 MHz) using tetramethylsilane as internal reference. Analytical thin layer chromatography (TLC) was performed on precoated silica gel 60 F_{254} (E. Merck), and the spots were visualized with UV light. Column chromatography was performed on silica gel (60–120 mesh). Elemental analyses (C, H, N) were carried out on Perkin–Elmer 240 C analyzer. All reagents were purchased from E. Merck (Germany) and Fluka (Switzerland). IR and NMR data related to all compounds are presented in the Supplementary materials.

3. Computational details

All calculations were performed with the Gaussian 09 software package [34]. Equilibrium geometries of all compounds (1–24) were first fully optimized and then vibrational frequencies were calculated at density functional theory (B3LYP) using MidiX basis set. Internal energies, enthalpy, free energies, entropy, C_v, and dipole moments of each compound were also investigated. The absence of imaginary frequencies confirmed that the stationary points correspond to minima on the Potential Energy Surface. The MidiX basis set is originally developed from the Huzinaga MIDI basis and applied to H, C, F, S, Cl, Br, and I atoms [35]. The MidiX basis set is comparatively smaller than the popular 6-31G(d); however, it can provide excellent geometries and charge balances with reasonable computational time and accuracy [36]. Since all the compounds of this study contains I atoms, and 6-31G(d) and other related basis sets are not compatible with halogen atoms, MidiX is the appropriate basis set option for these compounds. After computing the optimized structures and vibrational frequencies,

Table 1
Iodination reactions of substituted primary aryl amines **1–6**.

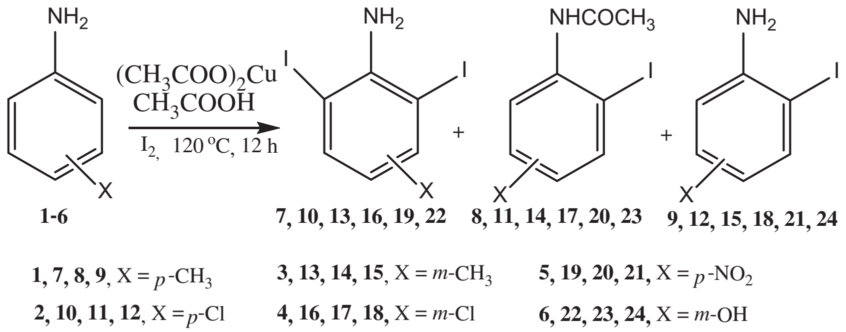
Entry	Aniline	Products			Yield%		
		a	*b*	*c*	*a*	(*b*)	*c*
1	 1	 7	 8	 9	30	(40)	12
2	 2	 10	 11	 12	35	(25)	20
3	 3	 13	 14	 15	35	(20)	16
4	 4	 16	 17	15  18	30	(22)	12
5	 5	 19	 20	 21	38	(20)	15
6	 6	 22	 23	 24	25	(20)	30

molecular orbital calculations were conducted with all compounds using B3LYP/MidiX level of theory for analysing the substitute's effect on the HOMO–LUMO gaps.

4. Results and discussion

All arylamines including 2,6-diiodoaniline (**7, 13, 16, 19, 22**), 2-iodoacetanilide (**8, 11, 14, 17, 20, 23**), and 2-iodoaniline (**9, 12, 15, 18, 21, 24**) are produced in different yield percent. In most cases, substituted-2, 6-diiodoanilines were obtained as a major product. 2, 4-diiodo-5-methylacetanilide and 2, 4, 6-triiodo-5-methylaniline were obtained in trace amount from the iodination reaction of *m*-toluidine **3**. In case of *m*-chloroaniline **4**, 2, 4-diiodoaniline was obtained about 30%.

Shen et al. [37] studied iodination of *m*-chloro aniline **4** with the aid of NIS (*N*-Iodosuccinimide) in acetic acid, unfortunately their process experienced a prolong reaction time in compares to our process. Kraszkiecs and co-workers revealed that iodination of nitrobenzene by diiodine with various oxidants (activated MnO_2, $KMnO_4$, CrO_3, HIO_3, $NaIO_3$, or HIO_4) dissolved in concentrated sulfuric acid (90%), but *p*-nitro aniline **5**, containing both a deactivating nitro group and activating amino group, is susceptible to such iodination system as amino group is readily oxidized [38]. Moreover, we have to compensate the hazardous effects of concentrated sulfuric acid. Our present iodination procedure, on the contrary, does not encounter such difficulties as we employed acetic acid, a mild solvent, easy to recover (to nearly pure form) from reaction system under reduced pressure and is particularly not detrimental in the form of vinegar. In addition, after proper treatment, the byproduct, CuI can be utilized for different catalytic process [39]. A recent study [40] with **5** demonstrated that Ag_2SO_4–I_2 in 1, 2-ethandiol is a useful iodinated agent; however, silver salt is not economical.



Scheme 1.

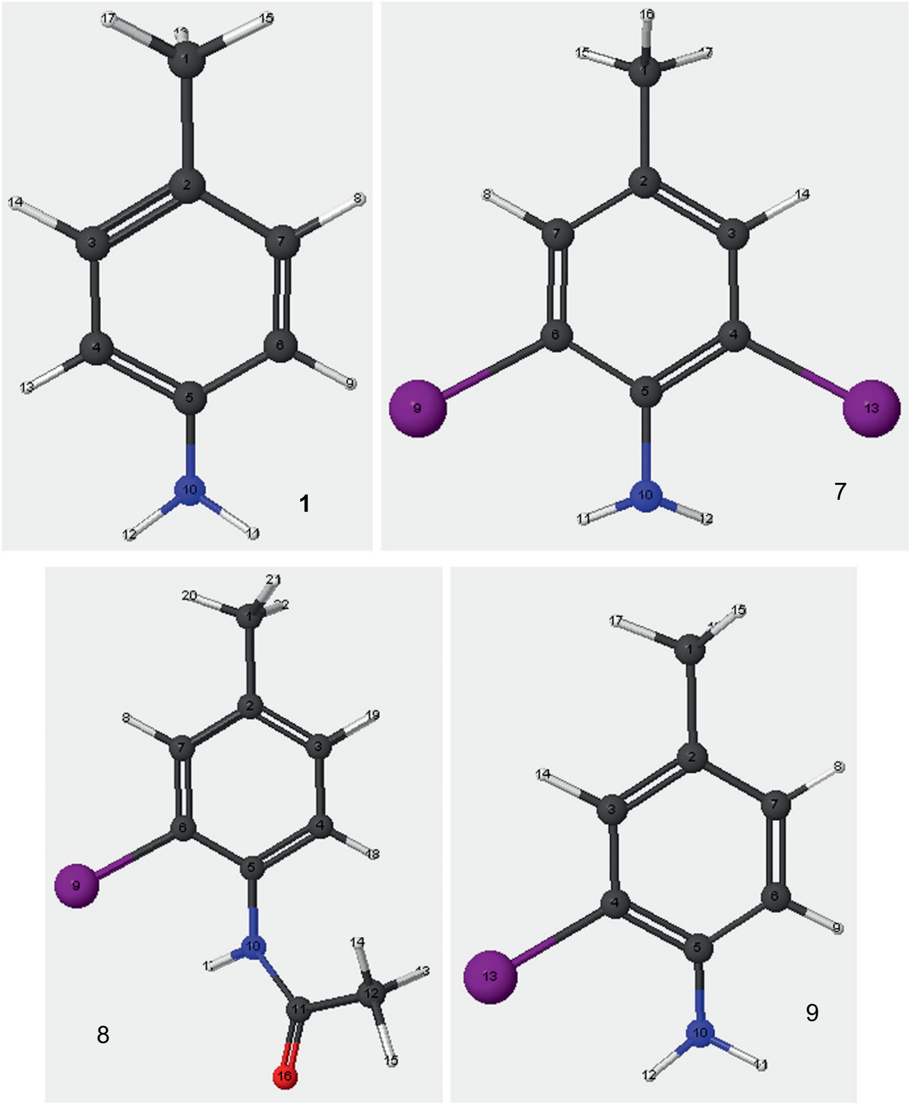


Fig. 1. Optimized structures of the compound **1**, **7**, **8**, and **9** generated at B3LYP/MidiX level of theory.

4.1. Equilibrium geometries

The bond distances (Å), bond angle (°) and dihedral angle (°) of compounds **1**, **7**, **8**, **9**; and **2**, **10**, **11**, **12** are presented in the supplementary Tables S2–S9. Significant changes of bond distance are appeared for iodination sites of the products compared to the reactants. For instance, both C6–I and C4–I bond distances in the compound **7** are 2.132 Å compared to C6–H and C4–H bond distances (1.090 Å) in compound **1** (see Fig. 1 for atom numbering). Similar trend is observed for C6–I (2.130 Å) and C4–I (2.134 Å) bond lengths in compound **8** and **9**, respectively. The bond distance of C4–C5 and C5–C6 are slightly increased in compound **7**, **8** and **9** than compound **1**. The I–C6–C5 bond angle in compound **7** and **8** is 120.1° and 120.6°, respectively whereas I–C4–C3 bond angle in compound **9** is 118.7°. Large elongation of C5–I (2.128 Å) and C3–I (2.128 Å) bonds in compound **10**, I–C9 (2.126 Å) bond in compound **11**, and C3–I (2.127 Å) bond in compound **12** is observed while iodination is performed in compound **2**. The C1–Cl bond distance is nearly unchanged for the iodinated products.

The electrostatic potential of the iodinated products disclosed that I in C–I bond is partially positive and making the carbon slightly negative presented in Fig. 2. The positive hole (σ-hole) in the position of iodine also indicates that these compounds are capable of forming halogen bonding [15]. The characteristic of C–I bond is also confirmed by Mulliken charge calculation. For compound **7**, partial positive charge (0.113) is observed in iodine whereas partial negative charge (−0.239) is appeared in carbon shown in Fig. 3. Similar charge profile is also found in other iodinated products.

4.2. Vibrational frequencies

Experimental and computed vibrational frequencies (without and with scaling) of the compounds **7** and **8** are presented in Table 2. A scaling factor (0.9688) is applied to the for B3LYP vibrational frequencies [41,42]. The experimental asymmetrical and symmetrical N–H stretching of **7** is appeared in the region of 3406 and 3317 cm^{-1}, respectively in very close agreement with the calculated frequencies (3451 and 3367 cm^{-1}) without applying any scaling factor. However, the calculated asymmetrical and symmetrical stretching frequencies with scaling of compound **7** are quite lower compared to the experimental values. The experimental C–H (3037 cm^{-1}) stretching frequencies are consistent with the scaled computed frequencies (3099 cm^{-1}). For compound **8**, the experimental N–H (asymmetrical and symmetrical) stretching frequencies are significantly lower than the unscaled calculated frequencies; however, they are agreed reasonably well with the scaled computed frequencies. The scaled C–N stretching (1291 cm^{-1}) is also well matched with the experimental value (1290 cm^{-1}); nonetheless, the unscaled frequency (1332 cm^{-1}) is somewhat higher than the both frequencies.

A comparison of experimental and computed IR frequencies for compound **10**, **11** and **12** are shown in the supplementary Table S10. The experimental asymmetrical and symmetrical N–H stretching for compound **10** are 3408 and 3317 cm^{-1}, respectively similar to the unscaled computed frequencies (3463 and 3376 cm^{-1}). For N–H stretching, nearly same feature is observed for the compound **12**. However, in case of compound **11**, experimental N–H stretching is close to the scaled computed frequencies. The experimental C–H (sp^2) stretching of **10** and **11** is remarkably lower to both of the computed frequencies; however, it is very close to the scaled frequencies in case of **12**.

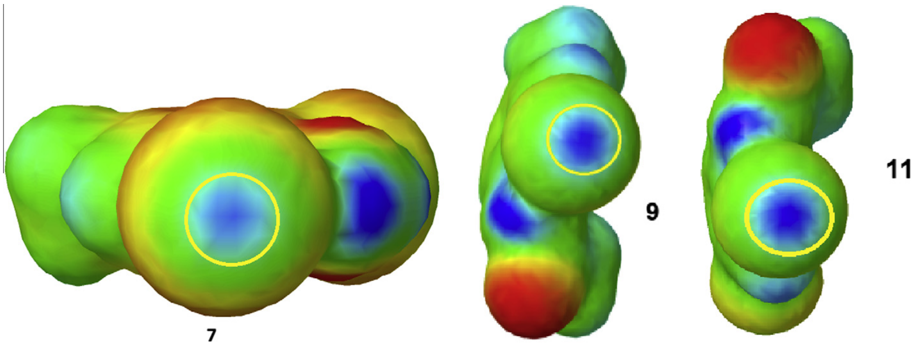


Fig. 2. Electrostatic potential surfaces of iodinated products **7**, **9** and **11**. Yellow circle in the blue region represent the partial positive electrostatic potential for iodine atom. Molecular surfaces were plotted at an electron density of 0.003 e−/bohr 3 with electrostatic potentials from red (−0.06445 hartree) to blue (0.06579 hartree). (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

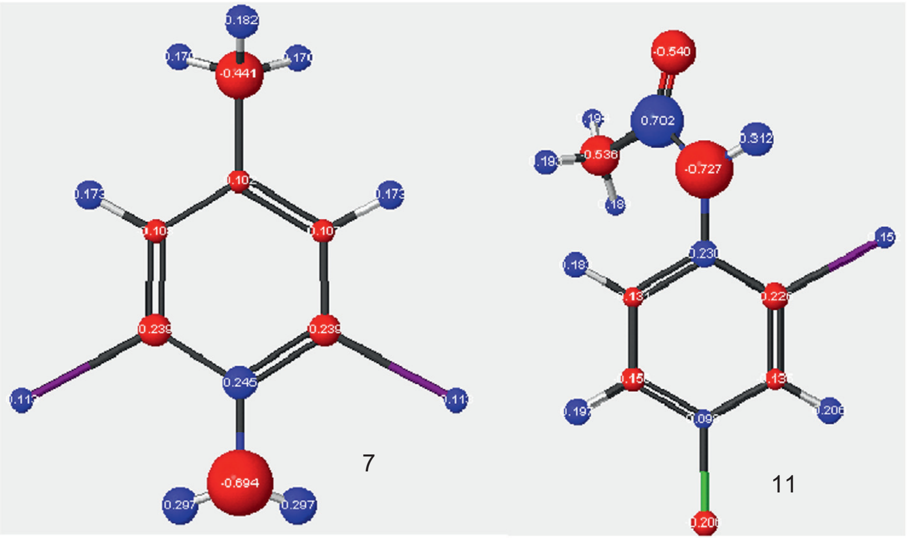


Fig. 3. Partial atomic charge (Mulliken) on compound **7** and **11** where red represent negative and blue represent positive charge. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of this article.)

Table 2
Selected experimental and calculated (without and with scaling) vibrational frequencies (cm^{-1}) of compound **7** and **8**.

Experimental	Calculated without Scaling (intensity)	Calculated with scaling[a]	Assignment[b]
Compound 7			
3406	3451(40.2817)	3343	$\nu_{asym}(NH_2)$
3317	3367(11.4285)	3262	$\nu_{sym}(NH_2)$
3037	3199(4.464)	3099	$\nu(sp^2\ CH)$
2898	3009(36.9285)	2915	$\nu_{sym}(sp^3\ CH)$
1566	1661(85.8755)	1609	$\omega(NH_2)$
1608, 1460	1577(11.3629)	1527	$\nu_{ring} + \theta(sp^3\ CH)$
Compound 8			
3265	3410(35.1665)	3303	$\nu_{asym}(NH_2)$
3021	3175(10.2054)	3076	$\nu_{sym}(NH_2)$
1655	1777(379.892)	1721	$\nu(CO)$
1524	1546(149.982)	1496	$\delta(NH)$
1290	1332(361.296)	1291	$\nu(CN)$
1037	1264(51.8434)	1225	$\delta(CH)$
822	872(28.8633)	844	$\pi(CH)$
681	518(34.3266)	502	$\pi(NH)$

[a] Scaling factor of B3LYP is 0.9688.
[b] ν stretching, δ in-plane bending, π out-plane bending, ω scissoring, θ wagging.

Table 3
Thermodynamic properties (change of energy, enthalpy, and Gibbs free energy in kcal/mol) of all iodination reactions.

Entry→	1	2	3	4	5	6
ΔE	47.45	46.89	48.02	54.07	55.76	50.83
ΔH	35.59	37.02	37.23	41.92	43.84	36.64
ΔG	39.76	38.52	38.21	45.40	45.67	40.14

4.3. Thermodynamic properties of the reactions

Employing B3LYP/MidiX level of theory, the thermodynamic properties of all reactions were calculated and the results are summarized in Table 3. The reaction of entry **1** with iodine and acetic acid produces three products (**7**, **8**, and **9**) along with hydrogen iodide and water. The change of electronic energy, enthalpy and Gibbs free energy of this reaction is 47.45, 35.59 and 39.76 kcal/mol. Nearly similar trends are observed with the reaction of entry **2** and **3** which yield the products (**10**, **11**, and **12**) and (**13**, **14**, and **15**), respectively. However, a moderate change of energy, enthalpy, and free energy is observed for entry **4** and **5** compare to the other reactions. The change of energy, enthalpy, and free energy of the reaction with entry **4** and **5** is 7.18–7.74, 6.33–8.25, and 5.63–7.46 kcal/mol higher than the reactions with entry **1**, **2** and **3.** Nevertheless, the change of thermodynamic energies of the reaction with entry **6** is approximately 3–5 kcal/mol lower than the reaction with entry **4** and **5**. Overall, all iodination reactions found to be endothermic.

4.4. Frontier molecular orbitals

Molecular orbitals calculation is performed with the optimized structure of all compounds using B3LYP/MidiX level of theory. The energy profile of HOMO, LUMO and HOMO–LUMO gap of all compound 1–24 are presented in Table 4. The pictorial view of the HOMO and LUMO orbitals are depicted in Fig. 4. The HOMO and LUMO energy of the entry **1** are 0.31 and −5.30 eV, respectively with a HOMO–LUMO gap of 5.61 eV. In comparison with entry **1**, the two electron-withdrawing halide groups in product **7** significantly decreased the LUMO energy to −1.17 eV whereas the HOMO energy is slightly decreased to −5.41 eV. The overall gap of **7** is 4.24 eV which is 1.37 eV lower than the entry **1**. One halide substituent in the product **9** has less effect on lowering the gap (4.81 eV) compare to the two halide substitutes in **7**. Moreover, incorporating –$NHCOCH_3$ group and one electron withdrawing group in **8** slightly reduced the gap to 5.04 eV.

The frontier molecular orbitals of compound of **2** and **11** are demonstrated in supplementary Fig. S1. Comparison with the product **10**, **11**, and **12**, the lowest HOMO–LUMO gap (4.28 eV) is

Table 4
Energies (eV) of HOMO and LUMO orbitals, HOMO–LUMO gaps are calculated at B3LYP/MidiX level of theory for all compounds 1–24.

	Entry	Product			Entry	Product			Entry	Product		
MO	1	7	8	9	2	10	11	12	3	13	14	15
LUMO+2	2.20	−0.33	−0.39	0.36	1.36	−0.73	−0.90	−0.14	2.19	−0.37	−0.41	0.40
LUMO+1	0.65	−0.62	−0.60	−0.09	0.46	−0.86	−1.01	−0.56	0.72	−0.40	−0.58	−0.10
LUMO	0.31	−1.17	−1.00	−0.70	−0.05	−1.71	−1.39	−1.09	0.29	−1.29	−0.98	−0.68
HOMO	−5.30	−5.41	−6.04	−5.51	−5.35	−5.99	−6.34	−5.87	−5.40	−5.74	−6.09	−5.60
HOMO−1	−6.65	−6.30	−6.66	−6.42	−7.07	−6.74	−6.97	−6.81	−6.45	−6.34	−6.64	−6.33
HOMO−2	−7.98	−7.09	−6.75	−7.03	−7.84	−7.41	−7.11	−7.35	−8.08	−7.11	−6.72	−7.02
GAP	5.61	4.24	5.04	4.81	5.30	4.28	4.95	4.77	5.69	4.45	5.11	4.92
MO	4	16	17	18	5	19	20	21	6	22	23	24
LUMO+2	1.27	−0.75	−0.89	−0.12	1.00	−0.94	−1.24	−0.63	1.95	−0.20	−0.23	0.60
LUMO+1	0.15	−0.81	−1.00	−0.56	−0.27	−1.77	−1.37	−1.17	0.83	−0.28	−0.53	0.10
LUMO	−0.21	−1.58	−1.31	−1.01	−1.37	−1.80	−2.47	−1.61	0.45	−1.18	−0.98	−0.44
HOMO	−5.85	−6.04	−6.41	−5.99	−5.90	−6.21	−6.77	−6.07	−5.38	−5.69	−5.96	−5.43
HOMO−1	−6.83	−6.59	−6.96	−6.71	−7.05	−6.88	−7.06	−6.98	−5.96	−6.01	−6.47	−6.03
HOMO−2	−8.30	−7.21	−7.04	−7.34	−7.30	−7.48	−7.13	−7.28	−7.88	−6.97	−6.72	−7.02
GAP	5.65	4.46	5.10	4.98	4.52	4.41	4.30	4.46	5.83	4.50	4.98	4.99

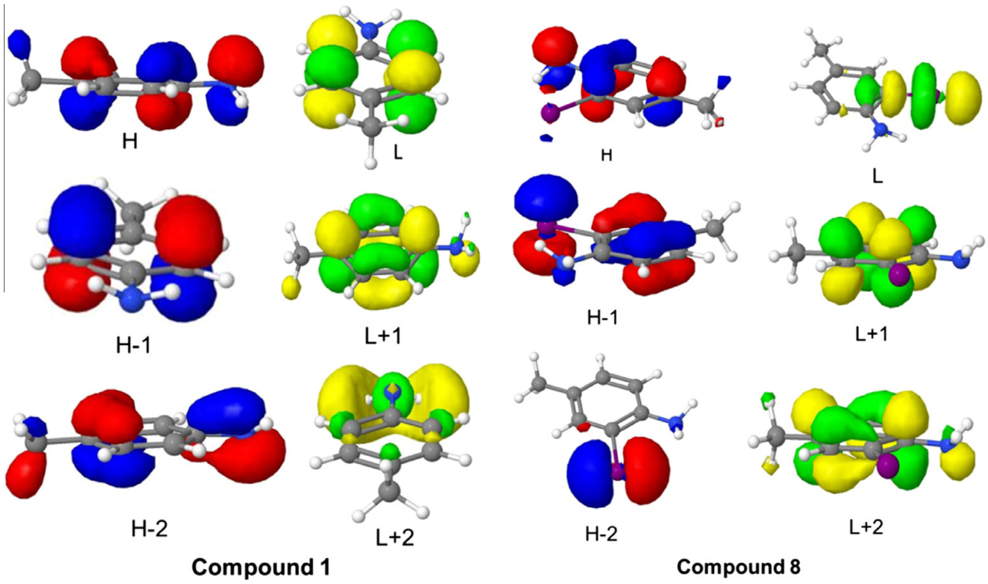


Fig. 4. Frontier molecular orbitals (HOMO, HOMO−1, HOMO−2, LUMO, LUMO+1 and LUMO+2) of compound **1** and **8**.

observed for **10** and the highest gap (4.95 eV) is calculated for **11**. Moreover, similar trends are observed for the products generated from entry **3** and **4**. The presence of NO_2 group in entry **5** and its products **19**, **20**, and **21** does not result any significant change in HOMO and LUMO energies. Nevertheless, remarkable change is noticed for the entry **6** and its related products. For example, the LUMO and HOMO energies of the entry 6 are 0.45 and −5.38 eV, respectively with a gap of 5.83 eV. Installing two iodide groups in product **22** remarkably decreases the gap to 4.50 eV. The HOMO–LUMO gap of one iodide based product **23** and **24** is also lowered to 4.98 and 4.99 eV, respectively. Overall, the small HOMO–LUMO gap indicates high chemical reactivity of products **7**, **10**, **13**, **16** and **22** where two iodine groups are incorporated.

5. Conclusion

This study presents a facile and efficient one-pot iodination of aryl amines synthesizing substituted 2-iodoacetanilides and 2-iodoanilineswith moderate to good yield. Easily recoverable mild acetic acid is being used instead of concentrated sulfuric acid. Another advantage of this procedure is the recycle of byproduct, copper(I) iodide. The computational analysis revealed some interesting features of these of compounds. The elongated C–I bond is observed for all synthesized compounds indicates that these compounds can be used as a starting reagents for medicinal and supramolecular applications. Electrostatic and Mulliken charge calculations confirmed that these iodinated compounds can easily form halogen bond. Our preliminary quantum chemical calculation also confirmed that there is a possibility of forming halogen bonding (I···N) between C–I of compound **8** and $-NH_2$ of compound **7** (Fig. 5). The I···N distance is 3.038 (Å) and the C–I···N angle is 175.8° agreed with the distance and angle usually observed for halogen bonds. The calculated halogen bonding energy between **8** and **7** is −5.31 kcal/mol. This weak noncovalent interaction between the products might have implication on reducing the single product yield. Details computational calculations related to the binding energy between different halogenated products are now underway. The thermodynamic study also unveiled the endothermic nature of these reactions. In future, enhancing the synthetic utility, this method will be applied to other aryl and hetero aryl systems.

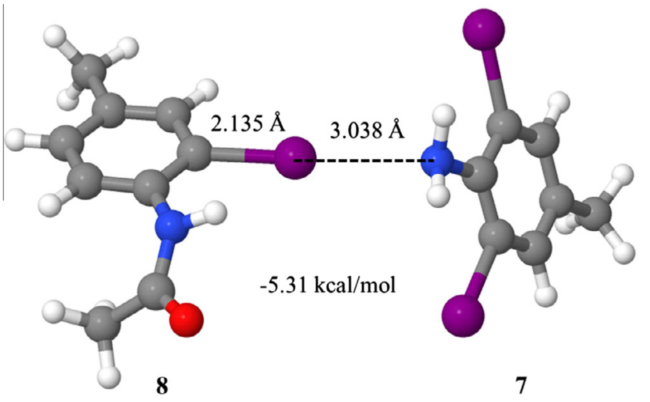


Fig. 5. Halogen bonding between compound **8** and **7** with a binding energy of −5.31 kcal/mol.

Acknowledgements

We gratefully acknowledge the financial assistance of Ministry of National Science Information and Communication Technology (NSICT) Bangladesh. We are thankful to Dr. Kazuaki Shimada, Professor, Department of Chemical Engineering, Iwate University, Japan, and BCSIR, Dhaka for taking NMR spectra. For allocating computational resource and time, we are also thankful to Professor Raymond Poirier, Department of Chemistry, Memorial University, Canada, and the Atlantic Computational Excellence Network (ACE-net) funded by the Canada Foundation for Innovation (CFI), the Atlantic Canada Opportunities Agency (ACOA), and the provinces of Newfoundland & Labrador, Nova Scotia, and New Brunswick.

Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.molstruc.2013.10.011.

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