

## SHORT COMMUNICATION

## QUANTUM CHEMICAL STUDIES ON IONIZATION POTENTIALS OF INDOLES

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## ABSTRACT

The experimental ionisation potentials for a number of substituted indoles including 5-fluoroindole, 5-fluoro-3-methylindole and 6-fluoroindole along with accurate ab initio calculations of the IPs for these and 17 related molecules were reported here. It was observed that the fluoro substitution increases the IP of indole. The results predict the IP of 5-fluorotryptophan to be 0.19 eV higher than that of tryptophan.

**Keywords:** Indoles, Ionisation Potentials, Density functional theory, Fluoro indoles.

## INTRODUCTION

Indoles are associated with the different biological properties<sup>1-3</sup>. They exhibit antibacterial, antioxidant, cytotoxic, insecticidal and pronounced hallucinogenic activities. Some of the derivatives of indole are applied as antibiotics in pharmaceuticals. Because of the broad use of indoles in a wide range of fields, such as biochemistry, biology, pharmacology, and agricultural sciences to name a few, indole syntheses that are mild and convenient are of great importance in organic chemistry

The medicinal or drug-action of indoles is related to their electron-donating ability or their acidity. Indoles are expected to be good electron-donors due to the heterocyclic N atom in the molecules. The substitutions can modify the distribution of charges on the various atoms in the indoles. It is, therefore of interest to know the possible ways in which substitutions in the indole systems may influence its activity under the hypothesis that the electron on the heterocyclic N atom in the indole ring is important in performing the task. Fluoro indoles are highly sensitive to environment. The activity of fluoro indoles is also associated with their IPs. No attentions have been paid to the donor activities of fluoro indoles theoretically. We have carried out accurate ab initio calculations and measurements that predict the IP of indole and sixteen substituted indoles including different fluoro substituted derivatives. We wish to report the IPs of indoles in this research articles.

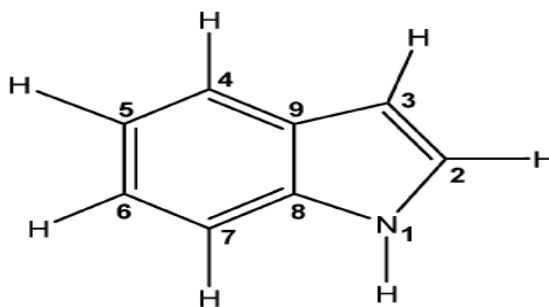


Figure 1. Structure of indole showing numbering convention.

## EXPERIMENTAL

### Computational Calculations

Gaussian98<sup>4</sup> was used for all ground and radical cation calculations in the determination of ionization potentials. Geometry optimizations were carried out with density functional theory (DFT) calculations at the B3LYP/6-31G\* level, where B3LYP denotes the Becke3-Lee-Yang-Parr hybrid functional, B3LYP<sup>5</sup>. Single-point calculations were carried out using the same method and also using B3LYP/6-311+G (2df,2p), which has been found to provide good agreement with experiment<sup>6</sup>.

## RESULTS AND DISCUSSION

Table-1 shows B3LYDFT- calculated adiabatic IPs for a selection of 17 substituted indoles using two basis sets, 6-311+G(2df,2p), and also shows experimental values<sup>7-10</sup>, including seven shown in bold measured in this study after the computations were completed. No adjustments in the computations were made following the new measurements. Figure shows the linear regression plot of the calculated (B3LYP/6-311+G(2df, 2p)) vs. the experimental values. The standard deviation is 0.02 eV. The last column of **Table 1** show values predicted from the regression plot. In this study we focus on the differential effect of 5-fluoro and 6-fluoro substitution. From column 3 of **Table 1** it is seen that the IP for 5F3MI is computed to be 0.190 eV higher than that for 3MI and the measured difference is  $0.190 \pm 0.019$  eV. If the predicted difference is taken from the regression line, the difference is 0.189 eV. For 5FI the computed difference is 0.214, again in excellent agreement with the experimental difference  $0.210 \pm 0.02$  eV. Corresponding results using 6-31G\* were within 0.03 eV of these numbers.

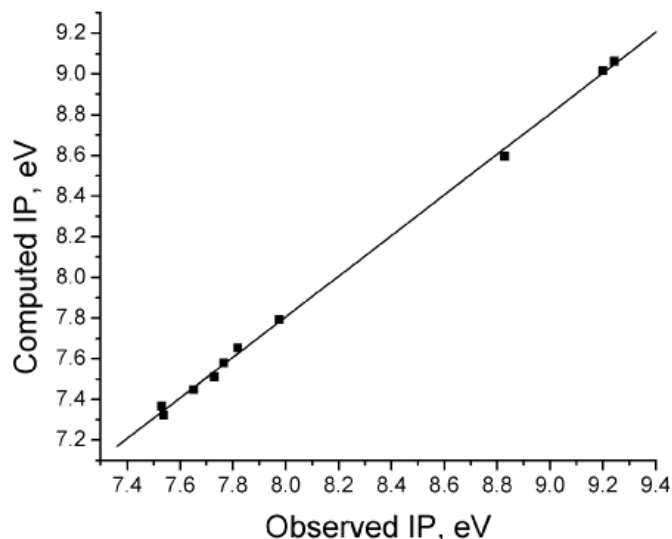
The calculated IP difference between 6FI and indole is 0.074 eV, while the measured value is  $0.054 \pm 0.01$  eV. More pertinent is the calculated IP for 6F3MI, which is 0.092 eV higher than that of 3MI. In the absence of an experimental value for 6F3MI, we use  $0.09 \pm 0.02$  eV for this difference.

Adding fluoro is seen to increase the IP for all indoles, but substitution at the 5 position is the most effective, followed closely by the 7 position. From the 6FI results, one expects the IP of 6FTrp to be at least 0.1 eV lower than that of the 5FTrp. More pertinent is the calculated IP for

**Table 1.** Calculated and Experimental Ionization Potentials (IPs) (eV) of 17 Compounds

name	B3LYP/ 6-31G*	B3LYP/ 6-311 +G(2df, 2p)	experimental IP	predicted IP
5-fluoroindole	7.47	7.793	<b>7.975</b> $\pm$ 0.008	7.986
7-fluoroindole	7.393	7.756		7.949
4-fluoroindole	7.341	7.697		7.891
2-fluoroindole	7.355	7.685		7.878
7-aza-3-methylindole	7.398	7.655		7.848
6-fluoroindole	7.328	7.653	<b>7.819</b> $\pm$ 0.008	7.845
3-fluoroindole	7.295	7.633		7.827
indole	7.276	7.579	7.760 <sup>48</sup> , <b>7.765</b> $\pm$ 0.008	7.771
5-fluoro-3-methylindole	7.212	7.511	<b>7.729</b> $\pm$ 0.009	7.703
7-fluoro-3-methylindole	7.165	7.503		7.697
5-methylindole	7.158	7.449	7.6493 <sup>49</sup> , <b>7.651</b> $\pm$ 0.007	7.643
4-fluoro-3-methylindole	7.097	7.418		7.611
6-fluoro-3-methylindole	7.112	7.413		7.607
2-fluoro-3-methylindole	7.111	7.416		7.609
1-methylindole	7.081	7.366	7.5319 <sup>49</sup> , <b>7.526</b> $\pm$ 0.012	7.558
3-methylindole	7.041	7.321	<b>7.539</b> $\pm$ 0.010	7.514
5-hydroxy-3-methylindole	6.849	7.166		7.357

6F3MI, which is 0.092 eV higher than that of 3MI. In the absence of an experimental value for 6F3MI, we use  $0.09 \pm 0.02$  eV for this difference.



**Figure 2.** Plot of B3LYP/6-311+G(2fd,2p) computed IPs against observed values (points) and linear regression (line).

### CONCLUSIONS

Adding fluoro is seen to increase the IP for all indoles, but substitution at the 5 position is the most effective, followed closely by the 7 position. From the 6FI results, one expects the IP of 6FTrp to be at least 0.1 eV lower than that of 5FTrp. Further, the experiments and calculations reported here show that 5-fluoro substitution increases the IPs of 3-methylindole by 0.19 eV. We have carried out accurate ab initio calculations and measurements that predict the IP of 5FTrp to be 0.19eV higher than that of Trp and the IP of 6FTrp to be 0.09eV higher than that of Trp.

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