

# **An extraction of the Isatin from the Couroupita Guianensis (cannon ball tree) and A novel synthesis of the N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4]thiadiazole]-3',5'-diyl)diacetamide from the Isatin**

**Rahul R. Tripathi\*, Ratnamala P. Sonawane**

The Institute of Science, 15 Madam Cama Road, Fort, Mumbai - 400032, Maharashtra, India

\*E-mail address: [rahulmax01991@gmail.com](mailto:rahulmax01991@gmail.com)

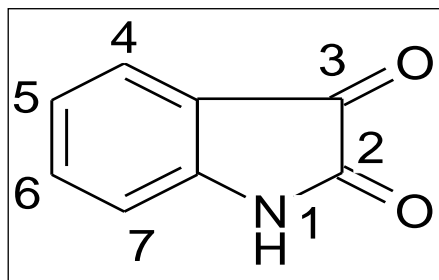
## **ABSTRACT**

Isatins are synthetically versatile substrates, where they can be used for the synthesis of a large variety of Isatins and heterocyclic compounds. In this, the isatin were extracted from the floral material of Couroupita guianensis commonly known as an Cannon ball tree. After that, a novel heterocyclic spiro derivative having an IUPAC name N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4]thiadiazole]-3'5'-diyl)diacetamide were synthesized, which may be used as raw material for drug synthesis. A spiro compound N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4]thiadiazole]-3'5'-diyl)diacetamide were synthesise by refluxing Isatin And thiosemicarbazone in ethanol and then on heating with acetic anhydride underwent to cyclization into intermediate that on acetylation of the NH and NH<sub>2</sub> groups afforded the spiro compound.

**Keywords:** Couroupita guianensis, Isatin, thiosemicarbazone.

## **1. INTRODUCTION**

Isatins (1H-indole-2,3-dione) are synthetically versatile substrates, where they can be used for the synthesis of a large variety of heterocyclic compounds, such as indoles and quinolines, and as raw material for drug synthesis [1-4,8-9]. Isatins have also been found in mammalian tissue and their function as a modulator of biochemical processes has been the subject of several discussions [11]. The advances in the use of isatins for organic synthesis during the last twenty-five years, as well as a survey of its biological and pharmacological properties are reported in this review and in the accompanying supplementary information [6]. Isatin (1H-indole-2,3-dione, Scheme 1) was first obtained by Erdman and Laurent in 1841 as a product from the oxidation of indigo by nitric and chromic acids [12].



**Scheme 1.** 1H-indole-2,3-dione.

The synthetic versatility of isatin has led to the extensive use of this compound in organic synthesis. Three reviews have been published regarding the chemistry of this compound: the first by Sumpter, in 1954, a second by Popp in 1975, and the third on the utility of isatin as a precursor for the synthesis of other heterocyclic compounds. The synthetic versatility of isatin has stemmed from the interest in the biological and pharmacological properties of its derivatives. These properties are more fully detailed in the supplementary material. In nature, isatin is found in plants of the genus *Isatis*, in *Calanthe discolor* LINDL. and in *Couroupita guianensis* Aubl., and has also been found as a component of the secretion from the parotid gland of *Bufo* frogs, and in humans as it is a metabolic derivative of adrenaline [12,13]. Substituted isatins are also found in plants, for example the melosatin alkaloids (methoxy phenylpentyl isatins) obtained from the Caribbean tumorigenic plant *Melochia tomentosa* as well as from fungi: 6-(3'-methylbuten-2'-yl)isatin was isolated from *Streptomyces albus* and 5-(3'-methylbuten-2'-yl)isatin from *Chaetomium globosum*. Isatin has also been found to be a component of coal tar [12-13]. Isatin (2,3-dioxindole) is an endogenous compound identified in humans, and its effect has been studied in a variety of systems. Biological properties of isatin include a range of actions in the brain and offer protection against certain types of infections. Isatin has anxiogenic, sedative, anticonvulsant activities and acts as a potent antagonist on atrial natriuretic peptide receptors in vitro. A series of p-substituted isatin semicarbazones have shown anticonvulsant activity in MES, scPTZ and scSTY tests. Various isatin-N-Mannich bases of isatin-3-thiosemicarbazones have shown antiviral and tuberculostatic activity [12-13]. Methisazone (N-methyl isatin-3-thiosemicarbazone) was found to be an effective compound against variola and vaccinia viruses and have also shown promising antimicrobial activity. The cannon ball tree possesses (*Couroupita guianensis* Aubl), antibiotic, antifungal, antiseptic, and analgesic qualities [14-31].

## 2. EXPERIMENTAL

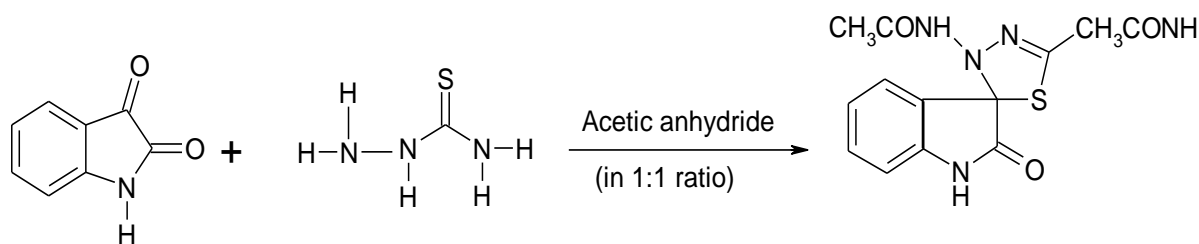
### 2. 1. Extraction and the purification of Isatin from the couroupita Guianesis

The floral material of *couroupita guianensis* were taken from the Borivali National park, Mumbai, Maharashtra, India. the floral parts Dried, powdered (500 g) floral parts were extracted with  $\text{CHCl}_3$  using soxhlet extractor and concentrated in a rotary vacuum evaporator. The residue thus obtained was dissolved in  $\text{CH}_2\text{Cl}_2$  and passed through a column of silica gel to remove the colouring material. The resulting solution was concentrated and chromatographed on silica gel column (5 × 50 cm, 60-120 mesh) using  $\text{CH}_2\text{Cl}_2$  containing

slowly increasing amounts of methanol as eluent (flow rate: 2.5 ml/min). Fractions of 250 ml were collected monitored by HPLC (Shimadzu, Japan). (Yield of Isatin-0.600 gm) Melting point – 202 °C.

## 2. 2. Novel synthesis of N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4]thiadiazole]-3',5' diyl)diacetamide

With the aim to prepare compounds as promising biologically active substances we carried out in this study acetylation with acetic anhydride of thiosemicarbazide prepared from substituted isatin and in continuation of our work on Spiro compounds. Compound was prepared by refluxing isatin and thiosemicarbazide in ethanol. Which on heating to 115-120 °C for 4 h with acetic anhydride yields isatin-3-thiosemicarbazone which underwent cyclization into intermediate that on acetylation of the NH and NH<sub>2</sub> groups afforded tetrahydro-1,3,4-thiadiazole-2-spiro-3-indol-2-one 3a-c in 71 % yield. M.P. (274-275 °C).



**Scheme 2.** Synthesis of N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4]thiadiazole]-3',5' diyl)diacetamide from isatin.

Melting points were determined in open capillary tubes on a Thomas Hoover melting point apparatus and are uncorrected. The purity of the compounds was confirmed by thin layer chromatography using silica gel glass plates as stationary phase, chloroform and methanol (9:1) as mobile phase.

The IR spectra were recorded on a Perkin FT-IR instrument using KBr disc method and <sup>1</sup>H NMR spectra and <sup>13</sup>C NMR were recorded at 90 MHz on a Jeol FX 90Q FT-NMR spectrophotometer using DMSO-d<sub>6</sub> as solvent and TMS as an internal standard.

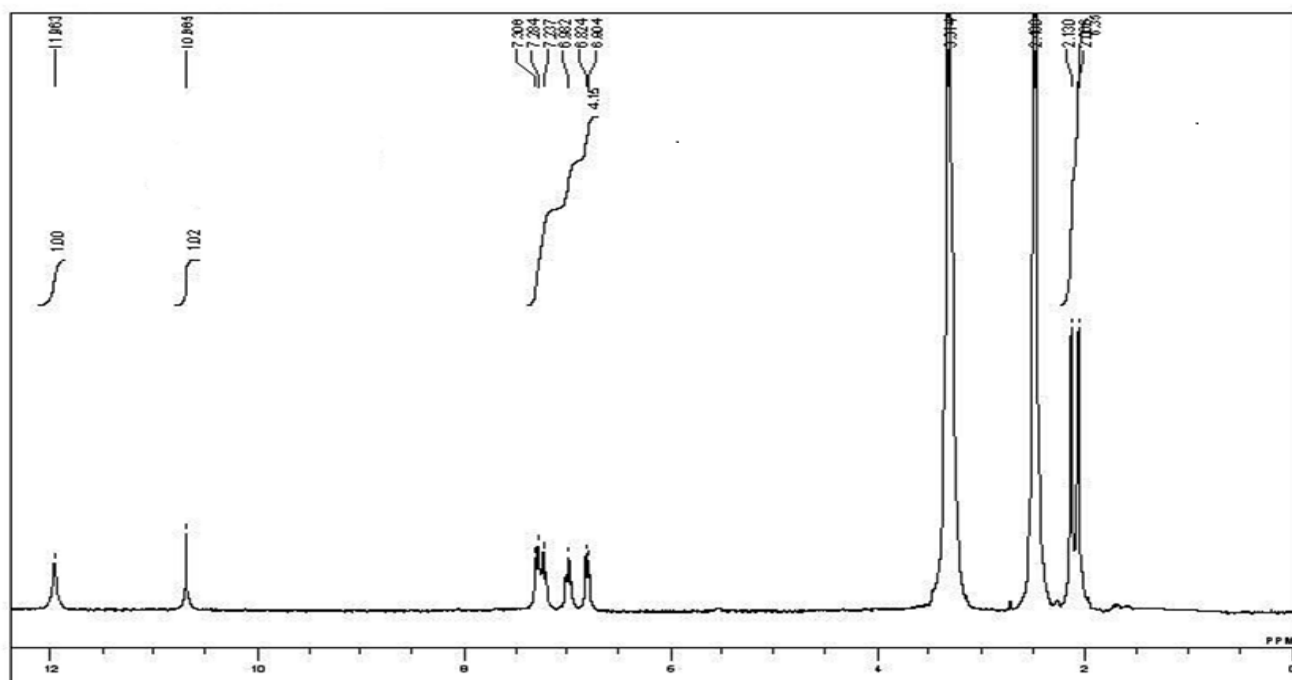
## 3. RESULTS AND DISCUSSION

### 3. 1. <sup>1</sup>H indole-2,3-dione (Isatin)

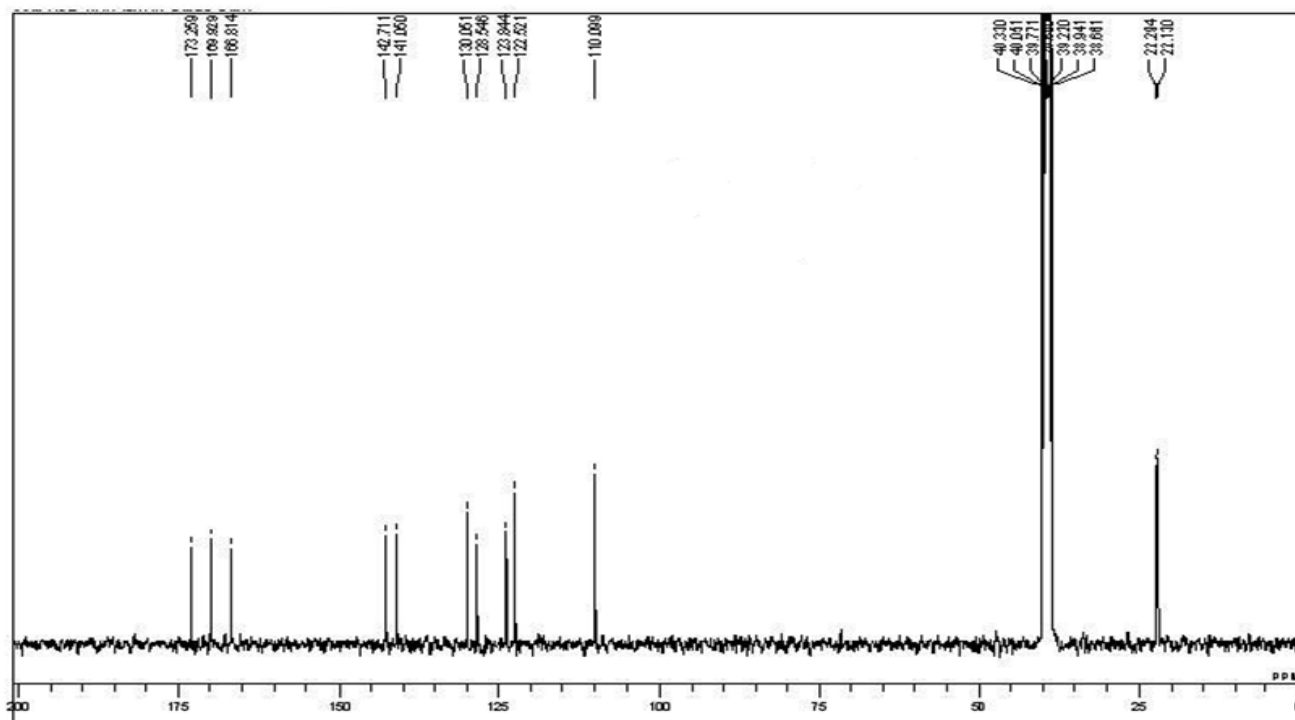
IR (KBr): 3207 cm<sup>-1</sup> (-NH), 1743.4 cm<sup>-1</sup> and 1691.12 cm<sup>-1</sup> (C=O), 1294.83 cm<sup>-1</sup> (C-N stretching), 1457.97 cm<sup>-1</sup> (C=C), 1097.25 & 1073.06 cm<sup>-1</sup> (C-O stretching), below 900 cm<sup>-1</sup> benzenoid ring. MS m/z (%) = 147.2 (M<sup>+</sup> 40), 119.0(100), 105.0(2), 90.0(70), 77.0(8), 65.0(40), 52.0(12), 43.0(12).

### 3. 2. N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4] thiadiazole]-3'5'-diyl)diacetamide

<sup>1</sup>H NMR δppm: 11.93(s), 10.70 (s), peak at aromatic region (6-8), 2.13 (s, 3H, CH<sub>3</sub>), 2.06 (s), 3H, CH<sub>3</sub>, the signals for the the -NH proton were D<sub>2</sub>O exchangeable. <sup>13</sup>C NMR δppm: peak at, 166.814, 169.924, 173.25 – amide carbonyl group, 110.09 (s), 141.06(s), 142.711(s), 22.10(s, 3H, CH<sub>3</sub>), 22.20(s, 3H, CH<sub>3</sub>), remaining signal fall in the aromatic region (122.521, 128.54, 123.844, 130.06).



**Fig. 1.** Proton NMR - N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4]thiadiazole]-3'5'-diyl)diacetamide.



**Fig. 2.** CARBON 13-NMR - N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4]thiadiazole]-3'5'-diyl)diacetamide.

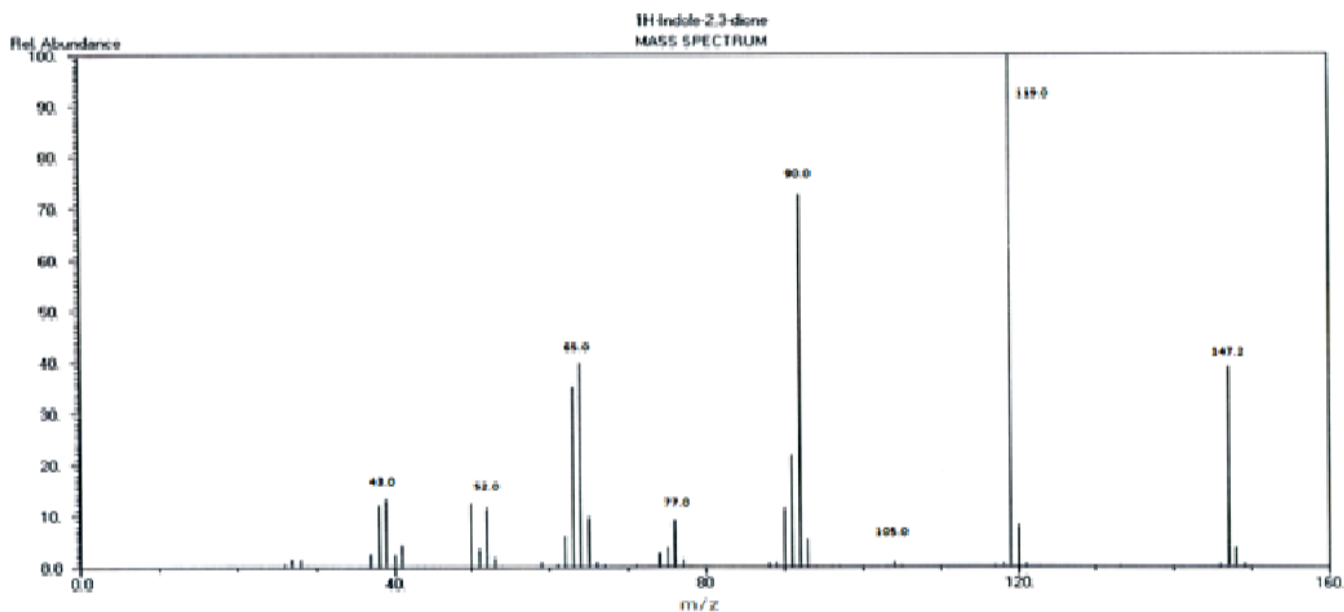


Fig. 3. Mass spectra of indole-2,3-dione (Isatin).

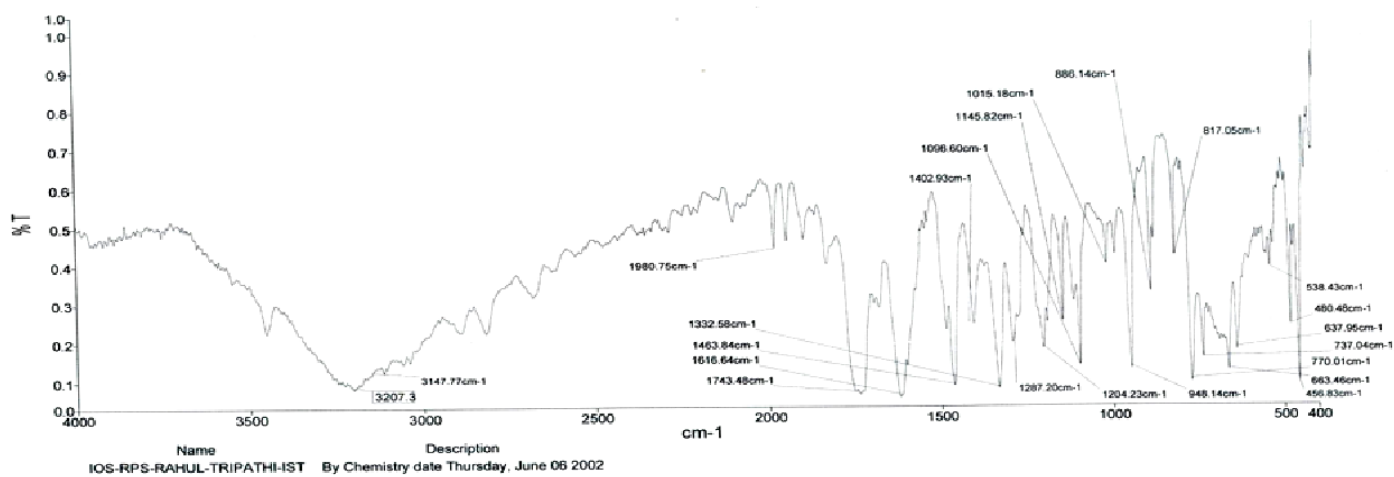


Fig. 4. Infra-red spectra of indole-2,3-dione (Isatin).

#### 4. CONCLUSION

We had extracted an Isatin from the floral parts of an cannon ball ntree ( couroupita guianesis) and synthesize the novel N,N'-(2-oxo-3'H-spiro[indoline-3,2'-[1,3,4] thiadiazole]-3'5'-diyl)diacetamide which may show some biological activity . We believe that, since the compound is an derivative of the semicarbazone it may posses an biological activity like anticonvulsant, anti tuberculosis, etc. the spiro compound prepared may be use for further research purpose.

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