www.pharmaerudition.org

ISSN: 2249-3875

International Journal of Pharmaceutical Erudition

Research for Present and Next Generation

FEB. 2022

Vol: 11 Issue:04

(47- 50)

ISSN 2249-3875

International Journal of Pharmaceutical Erudition

Research Paper

SYNTHESIS OF NOVEL SUBSTITUTED ISATIN DERIVATIVES

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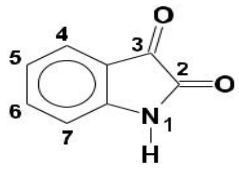
Isatin (1H-indole-2,3-dione) and its derivatives represent an important class of heterocyclic compounds that can be used as precursors for drug synthesis. Since its discovery, a lot of research work has been done regarding the synthesis, chemical properties, and biological and industrial applications of isatin. In this review, we have reported several novel methods for the synthesis of N-, C2-, and C3-substituted and spiro derivatives of isatin. The isatin moiety also shows important chemical reactions such as oxidation, ring expansion, Friedel–Crafts reaction and aldol condensation. These reactions, in turn, produce several biologically viable compounds like 2-oxindoles, tryptanthrin, indirubins, and many more. We have also summarized some recently reported biological activities exhibited by isatin derivatives, like anti-cancer, anti-bacterial, anti-diabetic and others. Special attention has been paid to their anti-cancer activity, and various anti-cancer targets such as histone deacetylase, carbonic anhydrase, tyrosine kinase, and tubulin have been discussed in detail. Other applications of isatin derivatives, such as in the dye industry and in corrosion prevention, have also been discussed.

Key Words: 1H-indole-2,3-dione, derivatives of isatin, novel methods

INTRODUCTION

Isatin (1H-indole-2,3-dione, Figure 1) was first obtained by Erdman and Laurent in 1841 as a product from the oxidation of indigo by nitric and chromic acids.



Heterocyclic compounds are an important class of organic compounds having vivid biological and pharmacological properties.1,2 Isatin (1H-indole-2,3-dione), also known as indenedione and indole quinone, is one such biologically active heterocyclic moiety. It has a nitrogen atom at position 1 and two carbonyl groups at positions 2 and 3 (Fig. 1). It comprises two cyclic rings, one of which is six-membered and the other is five-membered. Both of the rings are planar. The six-membered ring has an aromatic character, whereas the five-membered ring possesses an anti-aromatic character. The biological and pharmacological data obtained from the scientific literature are summarized in Electronic Supplementary Information (ESI) 1. A graphical survey of the application of isatin in the synthesis of other heterocyclic systems is presented in ESI 2, and ESI 3 contains a summary of metal complexes and some organometallic derivatives of isatin.

Isatin Synthesis

Sandmeyer Synthesis

One of the most famous techniques for the synthesis of isatin is Sandmeyer method. Aniline reacts with chloral hydrate and hydroxylamine hydrochloride conducting

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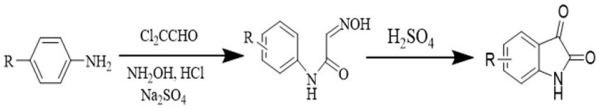
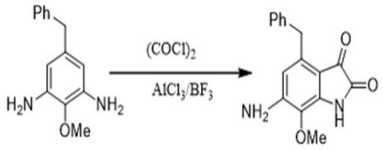
aqueous solution of sodium sulfate to produce an isonitrosoacetenilide. In this way, isonitrosoacetenilide in the presence of sulphuric acid easily converted into isatin analogs.



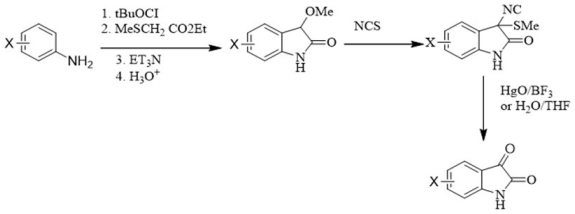
Stolle Synthesis

This method is very effective for the synthesis of isatin and its derivatives. The substituted isatin is synthesized by converting substituted aniline in the presence of oxalyl chloride and Lewis acids like BF3 or AlCl3. This method is also very useful to synthesize 1-Maryland polycyclic istan from phenothiazine, phenoxazine, dibenzoazepine and indol.



Gassman Synthesis

Gassman introduced a new approach, to synthesize isatin. This method involves the characteristics relationship between electrons donating, an electron withdrawing group, to convert aniline to intermediate 3-methylthyiooxidinol. In this intermediate, the methyl group is oxidized by N-chlorosucinamide, which is proceeded by the hydrolysis of the chlorinated intermediate.



Isatin derivatives are well known malleable substances, which are acted as forerunners for the synthesis of heterocyclic compounds [27]. Isatin derivatives play a vital role in the medicines because it used as bactericide [28], used for viral infections [29], anti-HIV [30], fungicide [31], anti-epileptic [32], anti-neoplastic [33], for the treatment of Mycobacterium [34] and anti- instigative [35]. Isatin derivative like 5-hydroxy isatin and spirobenzodiazepine, also used to reduce depression [36] (Figure 5). Few derivatives of isatin like 3-p-(p-(alkoxycarbonyl)phenyl)carbonyl)phenyl) imino-1-aminomethyl-2-indolinone is found to be effective against tuberculosis [37]. 5-[2(3)-dialkyl aminoalkoxy] Indole 2,3-dione is one of the important isatin derivative used against aminoalkane (histamine) [38]. Isatin derivatives are used for the treatment of malaria. 4-aminoquinoline derivatives were found to be efficacious versus Plasmodium falciparum [39]. Such derivatives can be obtained both from natural and synthetic source. tryptanthrin wellknown isatin derivative obtained from Chinese herb [40].

The synthesis of isatins **iia-h** starting from

ISSN 2249-3875

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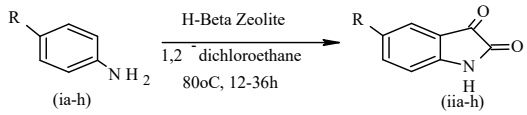
anilines **ia-h** by using oxalyl chloride as the acylating agent a reusable catalyst in the presence 1,2-dichloroethane as solvent at 80 °C under heterogeneous conditions . The methodology superior catalyst homogeneous Lewis acid catalysts like SnCl4 and BF3.Et2O.The procedure requires simple filtration of the catalyst and evaporation of the solvent to obtain good yields of isatins 48–79%.



RESULT AND DISSCUTION

Compound	% yield	Rf value	Mol. Formula
Iia	79.07	0.65	$C_8H_5NO_2$
Iib	61.27	0.71	$C_9H_7NO_2$
Iic	68.33	0.69	$C_{11}H_{11}NO_2$
Iid	71.01	0.81	$C_8H_4ClNO_2$
Iie	49.82	0.76	$C_8H_4FNO_2$
Iif	48.11	0.52	$C_9H_7NO_2$
Iig	54.42	0.49	$C_8H_4N_2O_4$
Iih	66.13	0.62	$C_{10}H_7NO_4$

SUMMARY AND CONCLUSION

The present work, which has undertaken is bonafied, and novel for the synthesis of isatin derivatives. All synthesize compounds were tested for the preliminary tests, physical constants and TLC.

REFERENCE

1. Parrick, J.; Yahya, A.; Ijaz, A.S.; Yizun, J. *J. Chem.Soc., Perkin Trans. 1* **1989**, 2009.

2. Valentine, J.J.; Nakanishi, S.; Hageman, D.L.; Snider, R.M.; Spencer, R.W.; Vinick, F.J. *Bioorg. Med. Chem.Lett.* **1992**, *2*, 333.

3. Robinson, R.P.; Donahue, K.M. *J. Org. Chem.***1991**, *56*, 4805.

4. Kraynack, E.A.; Dalgard, J.E.; Gaeta, F.C.A. *Tetrahedron Lett.* **1998**, *39*, 7679.

5. Baker, A.D.; Wong, D.; Lo, S.; Bloch, M.; Horozoglu, G.; Goldman, N.L.; Engel, R.; Riotta, D.C. *Tetrahedron Lett.* **1978**, 215.

6. Lokmane, E.; Larina, L.; Mazeika, I.; Freimanis, J. *Latv. P.S.R. Zinat. Akad. Vestis, Kim. Ser.* **1980**, 699.

7. Benincori, T.; Fusco, R.; Sannicolo, F. *Gazz. Chim.Ital.* **1990**, *120*, 635.

8. Cheng, Y.; Goon, S.; Meth-Cohn, O *J.Chem. Soc.,Perkin Trans. 1.* **1998**, 1619.

9. Kurihara, T.; Nasu, K.; Mizuhara, Y.; Hayashi, K. *Chem. Pharm. Bull.* **1982**, *30*, 2742.

10. Chupakhin, O.N.; Rusinov, V.L.; Beresnev, D.G.; Neunhoeffer, H. *J. Heterocycl. Chem.***1997**, *34*, 573.

11. Parrick, J.; Yahya, A.; Ijaz, A.S.; Yizun, J. *J. Chem. Soc., Perkin Trans. 1* **1989**, 2009.

12. Valentine, J.J.; Nakanishi, S.; Hageman, D.L.; Snider, R.M.; Spencer, R.W.; Vinick, F.J. *Bioorg. Med. Chem. Lett.* **1992**, *2*, 333.

13. Robinson, R.P.; Donahue, K.M. *J. Org. Chem.* **1991**, *56*, 4805.

14. Kraynack, E.A.; Dalgard, J.E.; Gaeta, F.C.A. *Tetrahedron Lett.* **1998**, *39*, 7679.

15. Baker, A.D.; Wong, D.; Lo, S.; Bloch, M.; Horozoglu, G.; Goldman, N.L.; Engel, R. Riotta, D.C. *Tetrahedron Lett.* **1978**, 215.

16. Lokmane, E.; Larina, L.; Mazeika, I.; Freimanis, J. *Latv. P.S.R. Zinat. Akad. Vestis, Kim. Ser.* **1980**, 699.

17. Benincori, T.; Fusco, R.; Sannicolo, F. *Gazz. Chim. Ital.* **1990**, *120*, 635.

Conflict of Interest

The authors declare that they have no conflict of interest