Gazi University Journal of Science
GU J Sci
28(2):195-199 (2015)

An Economical and Green Synthesis of Spiro[diindeno [1,2-b:2,1-e]pyridine-11,3-indoline]-trione Derivatives through Multi-Component Reaction by Br¢nsted Acidic Ionic Liquid Catalyst

Majid M. HERAVI[1,♠], Zeinab TEYMURI[1], Narges KARIMI[1], Yahya S. BEHESHTIHA[1],
Niloofar TAVAKOLI[2]

[1]*Department of chemistry, School of sciences, Alzahra University, 1993891176, Vanak, Tehran, Iran*
[2]*Department of Chemistry, Faculty of Sciences, Islamic Azad University, Mashhad Branch, 91735413, Mashhad, Iran*

Received: 10/09/2013 Revised: 14/12/2014 Accepted:25/12/2014

ABSTRACT

Synthesis of spiro[diindenopyridine-indoline]-triones by one-pot condensation of 1,3-indandione, isatin and aniline by Brønsted acid ionic liquid (BAIL),1-(4-sulfonicacid)butyl-3-methylimidazolium hydrogen sulfate ([$(CH_2)_4SO_3$HMIM][HSO_4]), as reusable and an economical catalyst in water under reflux condition.

Keywords: Water; Ionic liquid; Isatin; Aniline; 1,3-indandione

1. INTRODUCTION

Recently, an excellent attention has been centered on the employment of water as a green solvent in organic transformations. Water may be a favorable solvent for chemical reactions as a result of it's safe, non-toxic, environmentally friendly, without delay obtainable, and cheap compared to organic solvent.[1-3] Since the pioneering studies by Breslow [4,5] on Diels-Alder reactions, there has been an increasing recognition that organic reactions will proceed well in aqueous media providing key blessings over organic solvents like rate insolubility of the ultimate products that facilitates their isolation.

The fast assembly of molecular various compounds is a very important goal of artificial chemical science and one of the key paradigms of recent drug discovery. One strategy that probably meets the goals of synthesis and library production is multicomponent reactions (MCRs), during which three or a lot of beginning materials area unit brought along in varied, convergent, and atom-efficient approach to quickly build up molecular structure and complication.[6-8] They offer vital benefits over typical linear step synthesis by reducing time and by saving cash, energy, and raw materials, that so leads to each economic and environmental advantages. At a similar time, diversity will be achieved from buildup libraries by simply varying each component.

[♠] Corresponding author, e-mail: mmh1331@yahoo.com

Aniline emerged as associate analgesic drug, its cardiac-suppressive facet effects countered with caffein.[9] 1,3-indandione a crucial member of the category of 1,3-dicarbonyl compounds yields a good vary of compounds of chemical and pharmaceutical interest with completely different substrates.[10]

Isatin and its derivatives have fascinating biological actives and broad used as precursors for several natural product.[11] particularly, oxindol derivatives at C3 as spirocarbo- and heterocyclics extremely enhance biological activity.[12] As an example, spirotryprostatin A, a natural organic compound isolated from the fermentation broth of fungus, has been known as a new inhibitor of microtubule assembly (Figure 1).

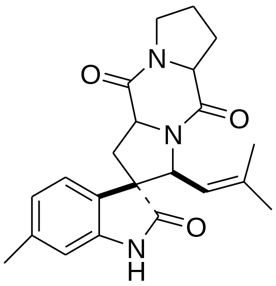


Figure 1. Spirotryprostain A

Ionic liquid (ILs) are receiving an upsurge of interest as green solvents in varied catalyst and no catalytic chemical and organic chemistry transformation.[13] In recent years, sulfonyl-functioned acidic ILs have emerged as promising acid catalysts in replacement of conventional homogeneous and heterogeneous acidic catalysts as a result of their versatile, nonvolatilisable, noncorrosive, immune to hydrolytic decomposition, and incompatible with several organic solvent.[14] These ILc have exhibited important catalytic potential in several organic reactions like esterfication,[15] polyhydroquinoline,[16] and Pechmann reaction.[17]

2. EXPERIMENTAL

All the chemicals were purchased from Merck Company. Melting points were measured using Barnstead Electro thermal. GC Mass analysis was performed using the Agilent 6890 GC system Hp-5 capillary 30m×530μm×1.5μm nominal. IR spectra were recorded as KBr disc on the FT-IR Brucker Tensor 27 spectrometers. ^{1}HNMR spectra were recorded on a Bruker AQS-AVANCE Spectrometer at 500 MHz, Using TMS as an internal standard.

2.1 *Preparation of Brønsted acidic ionic liquid*

For the current study, Brønsted acidic ionic liquid was ready in keeping with the literature procedure.[18] The obtained ionic liquid was used as catalysts for synthesis of spiro[diindenopyridine-indoline]-triones.

2.2 *General Procedure for the Synthesis of Spiro[diindenopyridine-indoline]-triones*

(0.1 g, 31.6 mol%) [(CH2)$_4$SO$_3$HMIM][HSO4] was added to a mix of the 1,3-indandione 1 (2 mmol), aniline 2 (1 mmol) isatin 3 (1 mmol) in water (5 mL) was stirred below reflux for an suitable amount of time. When completion of the reaction, as indicated by TLC, the reaction mixture was extracted with dichloromethane. The acidic IL is insoluble within the organic product. The crude product was pure by recrystallization from ethanol (5 mL) and water (10 mL).

2.3 *Spectral Data for Selected Compounds*

2.3a 5-phenyl-5H-spiro[diindeno[1,2-b:2',1'-e]pyridine-11,3'-indoline]-2',10,12-trione (4a)

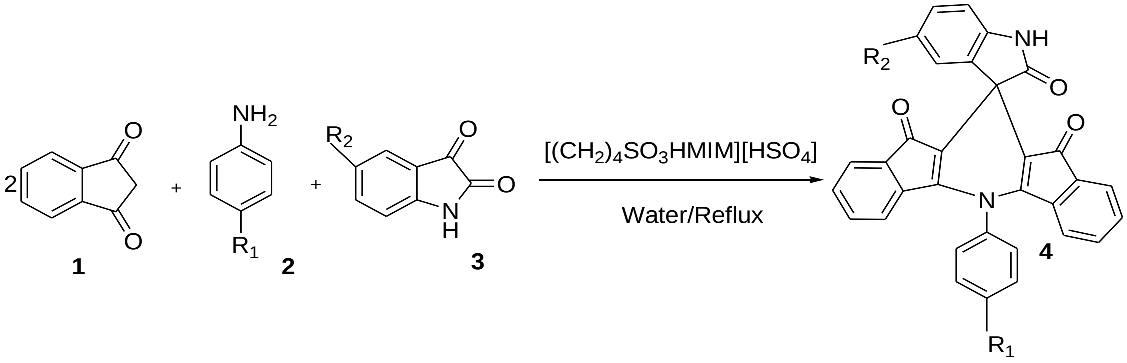
Mp >300^{o}C; IR (KBr), νmax 3435 (NH), 1700 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d6) δH: 10.60 (s, 1H, NH), 8.05-6.41 (m, 15H, ArH), 5.26 (d, J=6 Hz, 2H, ArH) ppm.

2.3b*5-(4-Nitrophenyl)-5H-spiro[diindeno[1,2-b:2',1'-e]pyridine-11,3'-indoline]-2',10,12-trione (4d).*
Mp >300 °C; IR (KBr) νmax 3335 (NH), 1710 (C=O) cm^{-1}; ^{1}H NMR (DMSO-d6) δH: 10.63 (s, 1H, NH), 8.58-6.85 (m, 14H, ArH), 5.55 (d, J = 6.0 Hz, 2H, ArH) ppm.

2.3c *5-(4-Bromophenyl)-5H-spiro[diindeno[1,2-b:2',1'-e]pyridine-11,3'-indoline]-2',10,12-trione -trione (4f).*
Mp >300°C; IR (KBr) νmax 3493 (NH), 1702(C=O) cm^{-1}; ^{1}H NMR (DMSO-d6) δH: 10.62 (s, 1H, NH), 8.14-6.81 (m, 14H, ArH), 5.56 (d, J = 6 Hz, 2H, ArH) ppm.

3. RESULTS AND DISCUSSION

In continuation of our interest within the synthesis of heterocycles by ILc as a catalyst,[19] herein we have a tendency to report a green and sensible technique for synthesis of spiro[diindenopyridine-indoline]-triones by one-pot condensation of 1,3-indandione, isatin and aniline by Brønsted acid ionic liquid (BAIL),1-(4-sulfonicacid)butyl-3-methylimidazolium hydrogen sulfate ([(CH$_2$)$_4$SO$_3$HMIM][HSO$_4$]), as recyclable and an economical catalyst (Scheme 1and Figure 2).



Scheme 1. Synthesis of spiro[diindenopyridine-indoline]-triones4

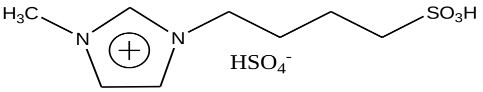


Figure 2. 1-(4-Sulfonic acid)butyl-3-methylimidazolium hydrogen sulfate ([$(CH_2)_4SO_3HMIM][HSO_4]$)

In order to check the generality of this procedure, a series of assorted isatin and aniline were applied. The results are shown in Table 1. To reaction of 1,3-indandione, isatin and aniline was at first investigated using numerous catalysts like $NiCl_2$, $Cu(bpdo)_2.2H_2O$ and ILc in water beneath reflux condition (Table2). Although 4a is generated within the presence of those catalysts, solely $[(CH_2)_4SO_3HMIM][HSO_4]$ resulted during a high chemical yield. To optimize the catalyst loading, 0.06 g and 0.08 g was tested however the yields weren't sensible. A 0.1g loading of 1-(4-Sulfonic acid) butyl-3-methylimidazolium hydrogen sulfate was sufficient to push the reaction forward and better amounts of catalyst didn't increase the yields considerably (Table 3).

Table 1. Synthesis spiro[diindenopyridine-indoline]-triones

Compound **4**	R_1	R_2	Time (h)	Yield (%)
a	H	H	1.45	82
b	Me	H	1.20	87
c	OMe	H	1.3	90
d	NO_2	H	2	75
f	Br	H	2.40	88
g	H	Br	2.10	78
h	Me	Br	2	88
i	OMe	Br	2.15	87
j	NO_2	Br	2.30	79
k	Br	Br	3.30	77

Table 2. Catalytic activity of various catalysts for the reaction of 1,3-indandione, aniline and isatin in water under reflux condition

Entry	Catalyst	Time (h)	Yield[a] (%)
1	$NiCl_2$ (0.06 g)	2.20	72
2	$Cu(bpdO)_2.2H_2O$ (0.06 g)	2.20	68
3	$[(CH_2)_4SO_3HMIM][HSO_4]$ (0.06 g)	2.20	74

[a]Isolated yield

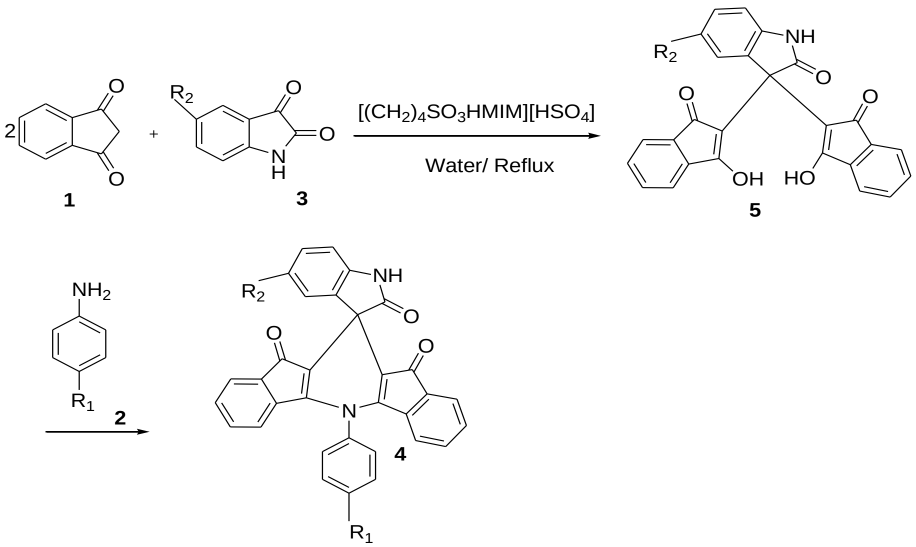
In another investigation, the model reactions were meted out in numerous solvents (acetonitrile, water, dichloromethane and ethanol). Among them, water was proven to be the most effective solvent and was the selected for further investigation under reflux conditions. It ought to be noted that everyone compounds were known and their physical information were compared with those of authentic compounds and found to be identical.

Table 3. Optimization amount of [$(CH_2)_4SO_3$HMIM][HSO_4] for synthesis spiro[diindenopyridine-indoline]-triones

Entry	Catalyst (g)	Time (h)	Yield^a (%)
1	0.06	1.45	61
2	0.08	1.45	75
3	0.1	1.45	82

^{a}Yields refer to the pure isolated products

The catalyst within the aqueous phase may be recovered by removing the water underneath vacuum and washing with ethoxyethane (10 mL) and drying at 50°C, underneath vacuum for 1h, and reutilized two occasions, and yields were comparable the primary run (with the yields of the merchandise 4a being 82%, 75%, and 66%, respectively). The planned mechanism for the synthesis of spiro[diindenopyridine-indoline]-triones within the presence of [$(CH_2)_4SO_3$HMIM][HSO_4] could tentatively be visualized to occur via a tandem bicycle sequence of reactions as represented in Scheme 2, first involve: 1,3-indandione (**1**) and isatin (**3**) were reacted then intermediate (**5**) and aniline were reacted within the presence of catalyst underneath identical reaction condition, the product 4a was obtained in 82% yield.[20]



Scheme 2. Synthesis of Spirooxindole 4a

4. CONCLUSION

In conclusion, we've described a straightforward one-pot four component reaction involving 1,3-indandione, isatin and aniline for the synthesis of a series of Spiro[diindenopyridine-indoline]-triones derivatives in water below reflux condition. Significantly, valuable options of this methodology embrace the upper yields of the product, short times and green procedure that create it a helpful method for the synthesis of those necessary compounds.

ACKNOWLEDGEMENTS

We are grateful to Alzahra University Research Council for partial support of this work

CONFLICT OF INTEREST

No conflict of interest was declared by the authors.

.

REFERENCES

1. Li, C.J. and Chan, T.H. Organic reactions in aqueous media. Wiley, New York.

2. Grieco, P.A. Thomson Science, Glasgow, Scotland.

3. Li, C.J., “Organic Reactions in Aqueous Media with a Focus on Carbon−Carbon Bond Formations”, A Decade Update; Chem. Rev. 105: 3095-3166.

4. Breslow, R., “Hydrophobic effects on simple organic reactionsin water”, Acc Chem. Res. 24: 159-164.

5. Breslow, R., “Determining he geometries of transition states by use of antihydrophobic additives in water”, Acc Chem. Res. 37: 471-478.

6. Yoshida, H., Fukushima, H., Ohshita, J. and Kunai, A., “CO$_2$ Incorporation reaction using arynes: straightforward access to benzoxazinone”, J. Am. Chem. Soc. 128: 11040-11041, (2006).

7. Duan, X.H., Liu, X.Y., Guo, L.N., Liao, M.C., Liu, W.M. and Liang, Y.M., “Palladium- Catalyzed one-pot synthesis of highly substituted furans by a three-component annulation reaction”, J. Org. Chem. 70: 6980-6983 (2005).

8. Zhu, J. Bienayme(Eds.), H., “Multicomponent Reactions”, Wiley-VCH, Weinheim, 2005.

9. Wilcox, R.W, "The treatment of influenza in adults", *Medical News*, 15: 931-932 (1900).

10. Junck, H., and Sterk, H. “Synthesen mit nitrilen, 19.mitt.: die partielle retro-michael-addition von tetracyanäthylen an indandion-1,3”, Tetrahedron Lett. 40: 4309-4310 91968).

11. Xue, J., Zhang, Y., Wang, X.I., Fun, H.K. and Xu, J.-H., “Photoinduced reactions of 1-Acetylisatin with Phenylacetylenes”, Org. Lett. 2: 2583-2586 (2000).

12. Marti, C.; Carreira, E.M., “Inspiration from Natural Products”, Eur. J. Org. Chem. 2209-2219 (2003).

13. Jain, N., Kumar, A.,Chauhan, S. and Chauhan, S.M.S., “Chemical and biochemical transformations in ionic liquids”, Tetrahedron 61: 1015-1060 (2005).

14. Gu, Y., Shi, F. and Deng, Y., ”Esterification of aliphatic acids with olefin promoted by Brønsted acidic ionic liquids”, J. Mol. Catal. A: Chem. 212: 71-75 (2004).

15. Gu, Y., Zhang, J., Duan Z. and Deng, Y., “Pechmann Reaction in Non-Chloroaluminate Acidic Ionic Liquids under Solvent-Free Conditions”, Adv. Synth. Catal. 347: 512-516 (2005).

16. Cole, A.C., Jensen, J.L., Ntai, L., Tran, K.L.T., Weaver, K.J., Forbes, D.C. and Davis, J.H. “Novel Brønsted Acidic Ionic Liquids and Their Use as Dual Solvent−Catalysts”, J. Am. Chem. Soc. 124: 5962-5963 (2002).

17. Heravi, M.M., Saeedi, M., Karimi, N., Zakeri, M., Beheshtiha, Y.S. and Davoodnia, A., “Brønsted Acid Ionic Liquid [(CH$_2$)$_4$SO$_3$HMIM][HSO$_4$] as Novel Catalyst for One-Pot Synthesis of Hantzsch Polyhydroquinoline Derivatives”, Synth. Commun. 40: 523-529 (2010).

18. Wang, W., Shao, L., Cheng, W., Yang, J. and He, M., “Brønsted acidic ionic liquids as novel catalysts for Prins reaction”, Catal. Commun. 9: 337-341 (2008).

19. Heravi, M.M., Zakeri, M., Karimi, N., Saeedi, M., Oskooie, H.A. and Tavakoli, N.H., “Acidic Ionic Liquid [(CH$_2$)$_4$SO$_3$HMIM][HSO$_4$] a green media for the simple and straightforward synthesis of 2,4,5-trisubstituted imidazoles”, Synth. Commun. 40: 1998-2006 (2010).

20. Ghahremanzadeh, R., Shakibaei, G.I., Ahadi S. and Bazgir, A., “One-Pot, Pseudo Four-Component Synthesis of a Spiro[diindeno[1,2-*b*:2′,1′-*e*]pyridine-11,3′-indoline]-trione Library”, J. Comb. Chem. 12: 191-194 (2010).