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Electrocatalytic Synthesis of Spirooxindole-Chromene Derivatives in Ethanol/DMSO Media using a Fe-Mn-O Composite as an Efficient Working Electrode

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Abstract

An efficient and sustainable method was developed for electrocatalytic multicomponent synthesis of spirooxindole-chromene derivatives *via* a green one-pot, three component condensations of cyclic-1,3-diones, malononitrile and isatins inside an undivided cell where potassium bromide was applied as electrolyte in ethanol/DMSO (95/5 v/v) media, and a practical Fe-Mn-O composite was used as cathode electrode. The presented electrosynthesis approach proved to be reliable and cost-effective for the synthesis of target compounds in 83-91% yields. In this method, we highlight the utility of electrosynthesis method for the preparation of diverse spirooxindole-chromen derivatives that can be a breakthrough for production of vital drugs.

***Keywords*:** Cyclic-1,3-diones, Electrocatalytic multicomponent synthesis,Isatins, Malononitrile, Spirooxindole-chromene derivatives.

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Introduction

In recent years, the invention of rapid, environmentally friendly and cost-effective synthetic protocols to facilitate the preparation of biologically active compoundshas become an essential part of research in organic and medicinal chemistry[1]. The spirooxindole system is considered as the core framework of a numerous natural alkaloids, involving spirotryprostatins A-B, [2] horsfiline[3], NITD609[4], gelsemine[5], cyclopamine B[6], gelseverine[7], strychnofoline[8], rhynchophylline[9], elacomine[10], and marcfortine A[11]. Beside the notable task of the spirooxindole arrangement in the anti-HIV[12], anticancer[13], antimalarial[14], and antitubercular drugs[15], this system can be applied as progesterone receptor modulator[16] and MDM2 inhibitor[17] (Figure 1).

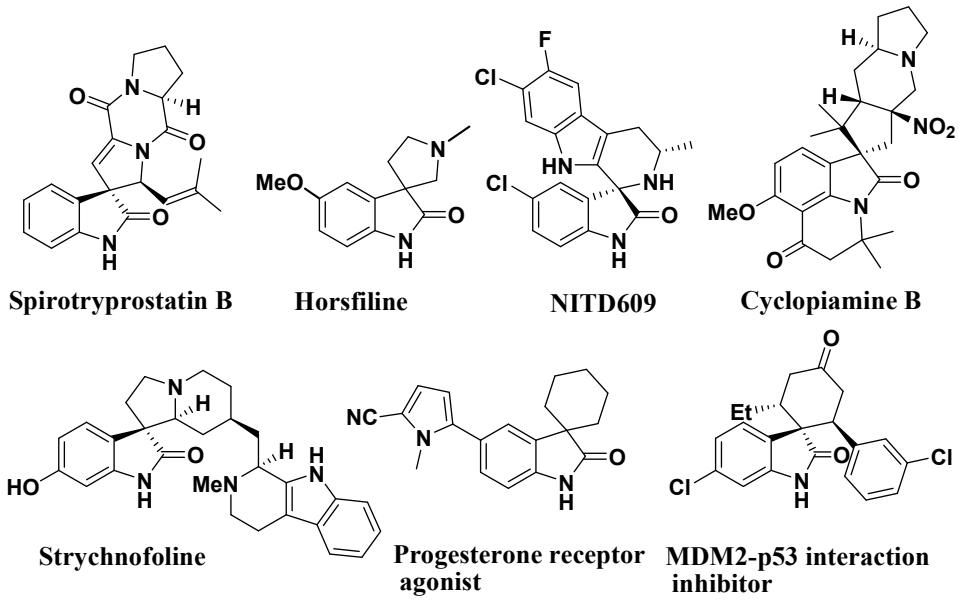


Figure 1. Selected alkaloids and biological spiro-cyclic compounds possessing oxindole motif.

Furthermore, 4*H*-pyran skeleton and their derivatives are the "privileged" structures of numerous oxygen-containing heterocyclic natural compounds. In recent years, organic chemists have been fascinated by the noteworthy pharmacological and biological characteristics of 4*H*-pyran. These materials are applicable as anti-tumor[18], anticonvulsant [19] , anti-inflammatory[20] , anti-cancer [21], anti-HIV[22], cytotoxic[23], antimalarial[24], and antidyslipidemic[25] compounds. Also, they have been considered as the inhibitors of insulin-regulated aminopeptidase (IRfAP) for improving memory and having potential calcium channel antagonists [26](Figure 2).

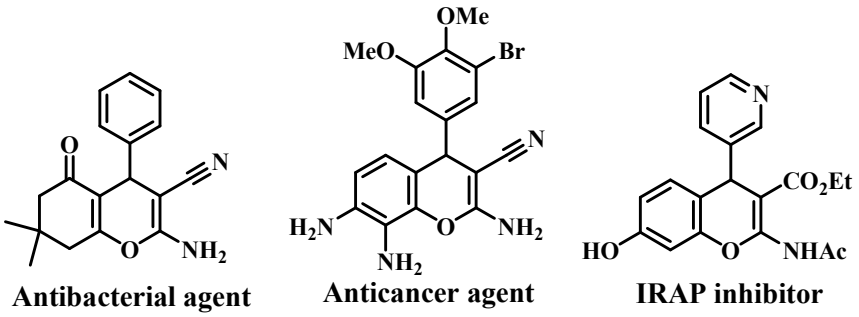
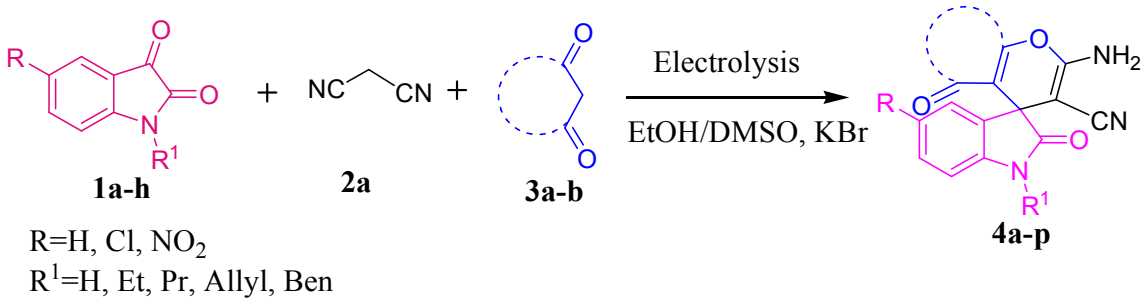


Figure 2. Selected examples of potential pharmaceuticals based on 4*H*-pyran.

Due to the above-mentioned notable reports, a combination of a spirooxindole and 4*H*-pyran rings may offer a significant improvement in biological activities or create new medicinal properties[27].Definitely, synthesis of novel building blocks of 3,3-disubstituted oxindole containing 4*H*-pyrans have been interesting and challenging for organic chemists owning to their biological activities that make this materials considerable candidates for clinical pharmaceuticals[28]. Due to the environmental pollution in recent years,many attempts have focused on the development of new environment-friendly strategies for the removal of the environmental pollutants. In this regard, the green chemistry approach, initiated in the 1990s, offers unique characteristics to develop and make products in benign conditions [29]. Moreover, multicomponent reactions (MCRs) reveal a key role in the recognition of the goals of green chemistry[30]. As a result, the combination of multi-component reactions technology with the green chemistry concepts exhibits an imperative potential in the development of innovative green and cost-effective synthesis strategies[31].

One approach to address this issue involves electrocatalytic multicomponent reaction, in which three or more starting materials are combined together in electrochemical cells in the presence of appropriate electrolyte and working electrodes to generate target products.Noteworthy, the growth of research in organic electrochemistry during recent years has made electrosynthesis as one of the most competitive protocols of modern organic chemistry and provided the organic chemists with a novel and versatile synthetic device of great promise. Inspired by the concept of green chemistry and in the continuation of our efforts for the electrosyntheius of oxindole-based chromene structures, we have investigated the electrosynthesis of spirooxindole-chromene derivatives by one-pot three component reactions between isatin derivatives, malononitrile, and cyclic-1,3-dions, in the presence of potassium bromide with the electrolyte and ethanol/DMSO media as a solvent (Scheme 1).



Scheme 1. electrosynthesis of chromene-derivatives (**4a-p**) using isatines (**1a–h**), malononitrile (**2a**), and cyclic-1,3-diones (**3a–b**).

Experimental

General

All solvents and starting materials were purchased from Merck and Sigma-Aldrich used without any additional purification. Analytical TLC was carried out using Merck 0.2mm silica gel 60 F-254 Al-plates. ^{1}H NMR spectra was recorded on a Bruker Avance DRX-500 machine using DMSO-d_6 as solvent and TMS as an internal standard at room temperature. FT-IR spectra of samples were obtained on ABB Bomem MB100 spectrometer with potassium bromide (KBr) pellets. Melting points were determined using an Electrothermal 9100 apparatus and are uncorrected. Controlled-current coulometry and preparative electrolysis were performed via a SAMA potentiostat/galvanostat (Isfahan-Iran). The Fe-Mn-O cathode (5 cm^2), graphite anode (5 cm^2) were used as working electrodes.

Fabrication of Fe-Mn-O composite as the working electrode

In this procedure, 0.1 g of $Fe(NO_3)_3.9H_2O$ and 0.24 g of $Mn(Ac)_2.4H_2O$ (with Fe/Mn molar ratio of 1:4) were dissolved in doubled-distilled water in order to create a clear condition under magnetic stirring. This solution was added to 20 mL of 0.5 M tartaric acid in ethanol media and stirred for 1 h. After that the obtained solution was centrifuged and the remaining materials was washed with ethanol and dried. Finally, the obtained material was annealed at 500 ^{0}C for 1 h.[46]

General procedure for the synthesis of spirooxindole-chromene derivatives

Isatin (**1a**), malononitrile (**2a**) and cyclohexan-1,3-dion (**3a**) (molar ratio: 1:1.1) and potassium bromide (0.5 mmol) in ethanol/DMSO media (20 ml) was placed in an undivided cell equipped with a magnetic stirrer, Fe-Mn-O composite cathode (5 cm^2), graphite anode (5 cm^2) for electrosynthesis of spirooxindole-chromene derivatives. The temperature was adjusted at 45 °C and the current was fixed at 100 mA in order to obtain a current density of 20 mA cm^{-2}. 0.1 F mol^{-1} of electricity was

passed through the electrochemical system within 60 min. The progress of synthesis route was checked by TLC analysis (ethyl acetate/*n*-hexane 1/3). The resultant mixture was kept at room temperature to become cold, then residue was condensed under the desired pressure and the resulting solid phase was separated via a simple filter and washed with ether and dried. The target compounds were characterized using some analytical techniques such as m.p., FT-IR, and NMR.

Data of representative examples

2-amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4a)**

White solid; Yield 89%; m.p. 299-301 °C;IR (KBr) ν (cm^{-1}) 3382, 3110, 3145, 2960, 2927, 2883, 2191, 1720, 1683, 1659, 1607, 1470, 1345, 1325, 1225, 741.^{1}H NMR (500 MHz, DMSO-d_6) δ= 1.01 (3H, s, CH_3), 1.04 (3H, s, CH_3), 2.14 (2H, AB_q, CH_2), 2.50 (1H, s, CH_2), 3.1 (1H, s, CH_2), 6.80 (1H, d, *J* = 7.50, Ar-H), 6.89 (1H, t, *J* = 7.50, Ar-H), 6.98 (1H, d, *J* = 7.00, Ar-H), 7.14 (3H, s br, Ar-H, NH2), 10.33 (1H, s br, NH).

2-amino-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4b)**

white solid; Yield 90%; m.p. 302-304 °C;IR (KBr) ν (cm^{-1}) 3358, 3278, 3116, 2951, 3032, 2811, 2199, 1720, 1679, 1651, 1607, 1466, 1357, 1216, 1080, 1019, 758.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.92 (2H, s, CH_2), 2.34 (2H, m, CH_2), 2.66 (2H, s, CH_2), 6.78 (1H, d, *J* = 7.50, Ar-H), 6.88 (1H, *J* = 7.50, Ar-H), 7.01 (1H, d, *J* = 6.50, Ar-H), 7.13 (1H, *J* = 7.50, Ar-H), 7.22 (2H, s br, NH_2), 10.40 (1H, s br, NH).

2-amino-5'-chloro-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4c)**

white solid; Yield 84%; m.p. 290-292 °C;IR (KBr) ν (cm^{-1}) 3370, 3298, 3165, 2960,2931,2887,2199, 1733, 1679, 1647, 1611, 1478, 1353, 1220, 1168, 1055, 806, 564.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.02 (6H, s, CH_3), 1.05 (2H, m, CH_2), 2.15 (2H, s, CH_2), 2.57 (2H, m, CH_2), 6.80 (1H, d, *J* = 8.00, Ar-H), 7.11 (1H, s, Ar-H), 7.19 (1H, d, *J* = 8.50, Ar-H), 7.34 (2H, s br, NH^2), 10.55 (1H, s br, NH).

2-amino-5'-chloro-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4d)**

white solid; Yield 83%; m.p. 290-291 °C;IR (KBr) ν (cm^{-1}) 3370, 3226, 3253, 3185, 2968, 2899, 2831, 2199,1728,1675, 1651, 1615, 1482, 1353, 1225, 1011, 729.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.94 (2H, s, CH_2), 2.25 (2H, m, CH_2), 2.65 (2H, s, CH_2), 6.79 (1H, d, *J* = 8.00, Ar-H),

6.88 (1H, *J* = 7.50, Ar-H), 7.15 (1H, s, Ar-H), 7.19 (1H, d, *J* = 9.00, Ar-H), 7.32 (2H, s br, NH_2), 10.55 (1H, s br, NH).

2-amino-7,7-dimethyl-5'-nitro-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4e)**

white solid; Yield 87%; m.p. 300-302 °C;IR (KBr) ν (cm^{-1}) 3390, 3361, 3193, 2968, 2935, 2875, 2191, 1748, 1683, 1647, 1607, 1518, 1478, 1462, 1353, 1337, 1229, 1063, 560.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.02 (6H, s, CH_3), 2.17 (2H, AB_q, CH_2), 2.52 (1H, d, *J* = 19.50, CH_2), 2.66 (1H, d, *J* = 17.50, CH_2), 7.02 (1H, d, *J* = 7.50, Ar-H), 7.46 (2H, s br, NH_2), 7.97 (1H, s, Ar-H), 8.15 (1H d, *J* = 7.00, Ar-H), 11.18 (1H, s br, NH).

2-amino-5'-nitro-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4f)**

white solid; Yield 89%; mp 299-301 °C;IR (KBr) ν (cm^{-1}) 3298, 3173, 2960, 2879,2191, 2191, 1736, 1679, 1627, 1603, 1514, 1482, 1458, 1337,1305, 1212, 1136,1076, 1015, 951, 838, 697,556,540.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.95 (2H, s, CH_2), 2.25 (2H, s, CH_2), 2.68 (2H, s, CH_2), 7.01 (1H, s, Ar-H), 7.38 (2H, s br, NH_2), 8.01 (1H, s, Ar-H), 8.14 (1H, s, Ar-H), 11.32 (1H, s br, NH).

2-amino-1'-ethyl-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4g)**

White solid; Yield 84%; m.p. 267-271 °C;IR (KBr) ν (cm^{-1}) 3418, 3278, 3149, 2984, 2960, 2931, 2871, 2195, 1708, 1679, 1651, 1607, 1466, 1373, 1345, 1321, 1225, 1225, 1050, 758.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.00 (3H, s, CH_3), 1.04 (3H, s, CH_3), 1.17 (3H, t, *J* = 7.00, CH_3), 2.12 (2H, AB_q, CH_2), 2.57 (2H, AB_q, CH_2), 3.71 (2H, m, CH_2), 6.96 (1H, t, *J* = 7.00, Ar-H), 7.03 (2H, m, Ar-H), 7.24 (1H, m, Ar-H, NH_2).

*2-amino-1'-ethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile***(4h)**

White solid; Yield 86%; m.p. 254-256 °C;IR (KBr) ν (cm^{-1}) 3378, 3302, 3245, 3181, 2992, 2974, 2191, 1679,1603, 1490,1470, 1349, 1216, 758.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.17 (3H, t, *J* = 6.50, CH_3), 1.92 (2H, s, CH_2), 2.19 (2H, m, CH_2), 2.66 (2H, s, CH_2), 3.70 (2H, t, *J* = 6.00, CH_2), 6.95 (1H, t, *J* = 7.00, Ar-H), 7.01 (1H, d, *J* = 7.00, Ar-H), 7.06 (1H, d, *J* = 7.00, Ar-H), 7.23 (3H, m, ArH, NH_2).

2-amino-7,7-dimethyl-2',5-dioxo-1'-propyl-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4i)**

White solid; Yield 83%; m.p. 251-254 °C;IR (KBr) ν (cm^{-1}) 3431, 3278, 3169, 2964, 2931, 2887, 2195, 1695, 1659, 1635, 1607,1490, 1466,1353, 1321, 1225, 1047, 753.^{1}H NMR (500 MHz, DMSO-d_6) δ 0.09 (3H, t, *J* = 7.00, CH_3), 0.95 (3H, s, CH_3), 1.02 (3H, s, CH_3), 1.62 (2H, d, *J* = 6.50, CH_2), 2.12 (2H, AB_q, CH_2), 2.56 (2H, m, CH_2), 3.62 (2H, m, CH_2), 6.95 (1H, t, *J* = 7.50, Ar-H), 7.02 (2H, m, Ar-H), 7.22 (1H, t, *J* = 7.50, Ar-H), 7.27 (2H, s br, NH_2).

1'-allyl-2-amino-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4k)**

White solid; Yield 89%; m.p. 234-236 °C;IR (KBr) ν (cm^{-1}) 3431, 3278, 3165, 2960, 2203, 1700, 1679, 1663, 1349, 758.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.09 (3H, s, CH_3), 1.14 (3H, s, CH_3), 2.20 (2H, AB_q, CH_2), 2.53 (2H, AB_q, CH_2), 4.43 (2H, s, CH_2), 4.84 (2H, s, CH_2), 5.28 (1H, d, *J* = 7.50, CH_2), 6.95 (1H, t, *J* = 7.50, Ar-H), 7.02 (2H, m, Ar-H), 7.22 (1H, t, *J* = 7.50, Ar-H), 7.27 (2H, s br, NH_2).

*1'-allyl-2-amino-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile***(4l)**

White solid; Yield 90%; m.p. 250-254 °C;IR (KBr) ν (cm^{-1}) 3406, 3314, 3249, 3197, 2963, 2974, 2887, 2179, 1712, 1667, 1611, 1478, 1462, 1349, 1200, 1068, 745, 496.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.93 (2H, s, CH_2), 2.22 (2H, s, CH_2), 2.68 (2H, s, CH_2), 4.30 (2H, AB_q, CH_2), 5.16 (1H, d, *J* = 10.00, CH), 5.45 (1H, d, *J* = 12.00, CH), 5.85 (1H, m, CH), 6.87 (1H, d, *J* = 6.50, Ar-H), 6.97 (1H, m, Ar-H), 7.08 (1H, d, *J* = 5.50, Ar-H), 7.21 (1H, s br, Ar-H), 7.24 (1H, s br, NH_2).

2-amino-1'-benzyl-7,7-dimethyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **(4m)**

White solid; Yield 86%; m.p. 289-291 °C;IR (KBr) ν (cm^{-1}) 3330, 3253, 3205, 2968, 2887, 2191,1712, 1675, 1655, 1603, 1353, 1216, 1047, 753.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.03 (3H, s, CH_3), 1.06 (3H, s, CH_3), 2.18 (2H, AB_q, CH_2), 2.60 (2H, AB_q, CH_2), 4.91 (2H, AB_q, CH_2), 6.69 (1H, d, *J* = 7.00, Ar-H), 6.97 (1H, m, Ar-H), 7.08 (1H, m, Ar-H), 7.13 (1H, m, Ar-H), 7.30 (4H, m, Ar-H), 7.49 (2H, s br, NH_2).

*2-amino-1'-benzyl-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile***(4n)**

White solid; Yield 87%; m.p. 265-267°C; IR (KBr) ν (cm^{-1}) 3378, 3290, 3241, 3169,3064, 2960,2935, 2899,2875, 2195,1691, 1671,1607, 1486,1349, 1087, 749. ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.95 (2H, s, CH_2), 2.25 (2H, AB_q, CH_2), 2.70 (2H, s, CH_2), 4.90 (2H, AB_q, CH_2), 6.68

(1H, d, *J* = 7.00, Ar-H), 6.96 (1H, t, *J* = 6.50, Ar-H), 7.11 (2H, t, *J* = 6.50, Ar-H), 7.27 (2H, s, Ar-H, NH_2), 7.30 (2H, m, Ar-H), 7.50 (2H, d, *J* = 6.50, Ar-H).

2'-amino-7',7'-dimethyl-2,5'-dioxo-5',6',7',8'-tetrahydro-2H-spiro[acenaphthylene-1,4'-chromene]-3'-carbonitrile **(4o)**

White solid; Yield 83%; m.p. 265-267 °C; ^{1}H NMR (500 MHz, DMSO-d_6) δ 1.02 (3H, s, CH_3), 1.04 (3H, s, CH_3), 2.08 (2H, AB_q, CH_2), 2.63 (2H, m, CH_2), 7.33 (2H, s, Ar-H), 7.39 (1H, s, Ar-H), 7.66 (1H, s, Ar-H), 7.83 (1H, s, Ar-H), 7.93 (2H, s br, NH_2), 8.27 (1H, d, *J* = 6.00, Ar-H); IR (KBr) ν (cm^{-1}) 3370, 3298, 3249,3181, 2984, 2931, 2883, 2191, 1720, 1683, 1663, 1603, 1345, 1216, 778.

2'-amino-2,5'-dioxo-5',6',7',8'-tetrahydro-2H-spiro[acenaphthylene-1,4'-chromene]-3'-carbonitrile **(4p)**

White solid; Yield 84%; m.p. 250-252 °C;IR (KBr) ν (cm^{-1}) 3360, 3314, 3241, 3189, 3052, 2984, 2943, 2883, 2187, 1720, 1663, 1595,1349,1204, 782.^{1}H NMR (500 MHz, DMSO-d_6) δ 1.93 (2H, s, CH_2), 2.16 (2H, s, CH_2), 2.71 (2H, s, CH_2), 7.73 (2H, s, Ar-H), 7.39 (1H, s, Ar-H), 7.41 (1H, s, Ar-H), 7.65 (1H, s, Ar-H), 7.81 (1H, s, Ar-H), 7.93 (2H, s br, NH_2), 8.27 (1H, s,Ar-H).

Results and Discussion

In continuation of our previous reports for electrosynthesis of heterocyclic compounds [32], the three reaction of isatin (**1a**), malononitrile (**2a**) and cyclohexan-1,3-dion (**3a**) (molar ratio: 1:1.1) were chosen as a model reaction and the static study was carried out to determine the reaction parameters for obtaining the optimized conditions. This reaction proceeded in alcoholic media inside of an undivided cell as a pattern reaction. Some important variables including temperature, reaction media (ethanol, methanol, n-propanol and ethanol/DMSO) and the applied current were tested in detail. On the first step, the results of solvent and current density screening showed that ethanol/DMSO (95/5) at a current density of 20 mA cm^{-2} (I = 100 mA , electrode surface = 5 cm^2) with Fe-Mn-O cathode and graphite anode provides considerable high yields and short synthesis times. Ethanol as alcoholic synthesis media revealed superior properties in comparison with propanol and methanol at temperature of 45 °C.

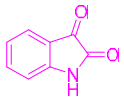
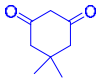
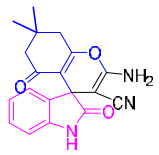
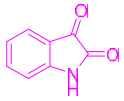
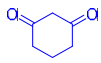
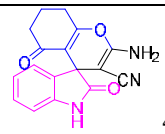
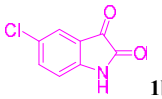
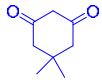
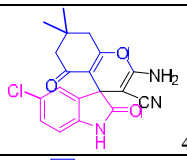
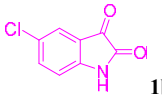
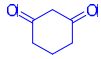
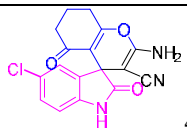
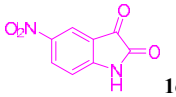
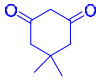
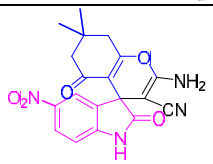
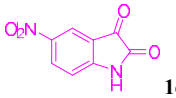
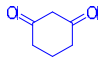
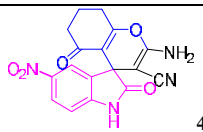
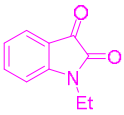
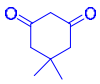
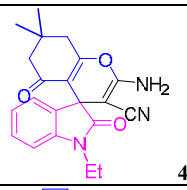
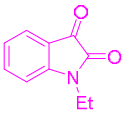
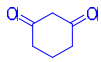
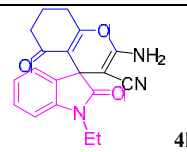
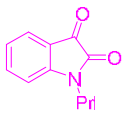
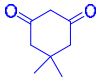
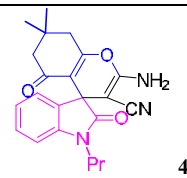
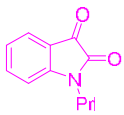
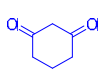
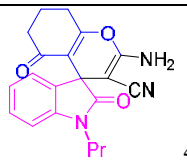
Table 1. Optimization of the reaction conditions for the electrosynthesis of 2-amino-2',5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3'-indoline]-3-carbonitrile **4a.**

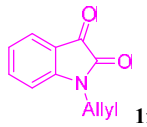
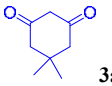
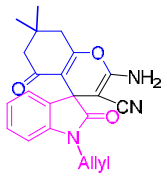
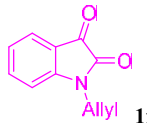
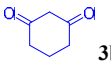
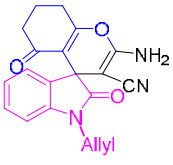
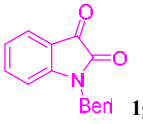
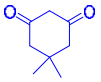
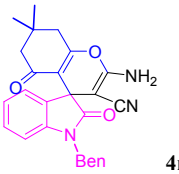
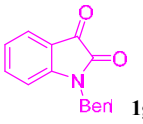
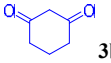
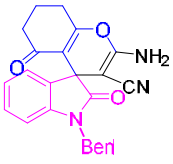
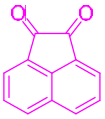
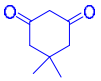
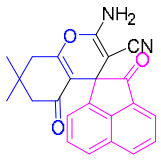
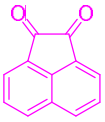
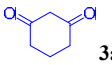
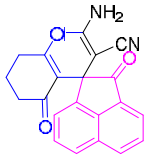
Entry	Solvent(20 ml)	Temp. (°C)	I (mA)	Current density (mA cm^{-2})	Electricity passed($Fmol^{-1}$)	Time (min)	Yield(%)[b] 4a
1	MeOH	r.t	25	5	0.1	60	44
2	MeOH	40	25	5	0.1	30	68
3	n-PrOH	r.t	25	5	0.1	60	57
4	n-PrOH	40	25	5	0.1	30	65
5	EtOH	r.t	25	5	0.1	60	70
6	EtOH	40	25	5	0.1	30	78
7	EtOH/DMSO	r.t	25	5	0.1	60	75
8	EtOH/DMSO	40	25	5	0.1	30	80
9	EtOH/DMSO	40	50	10	0.1	60	88
10	EtOH/DMSO	45	100	20	0.1	60	91
11	EtOH/DMSO	45	100	40	0.1	65	86
12	EtOH/DMSO	45	200	40	0.1	60	81
13	EtOH/DMSO	50	200	50	0.1	60	72
14	EtOH/DMSO	50	250	50	0.1	70	67
15	EtOH/DMSO	50	250	50	0.1	90	55

[a]Reaction conditions: Isatin (1a), malononitrile (2) and 3-amino-1*H*-pyrazol-5(4*H*)-one (3a) (molar ratio: 1.1:1), KBr (0.5 mmol), Fe-Mn-O cathode (5 cm^2), graphite anode (5 cm^2) were used.

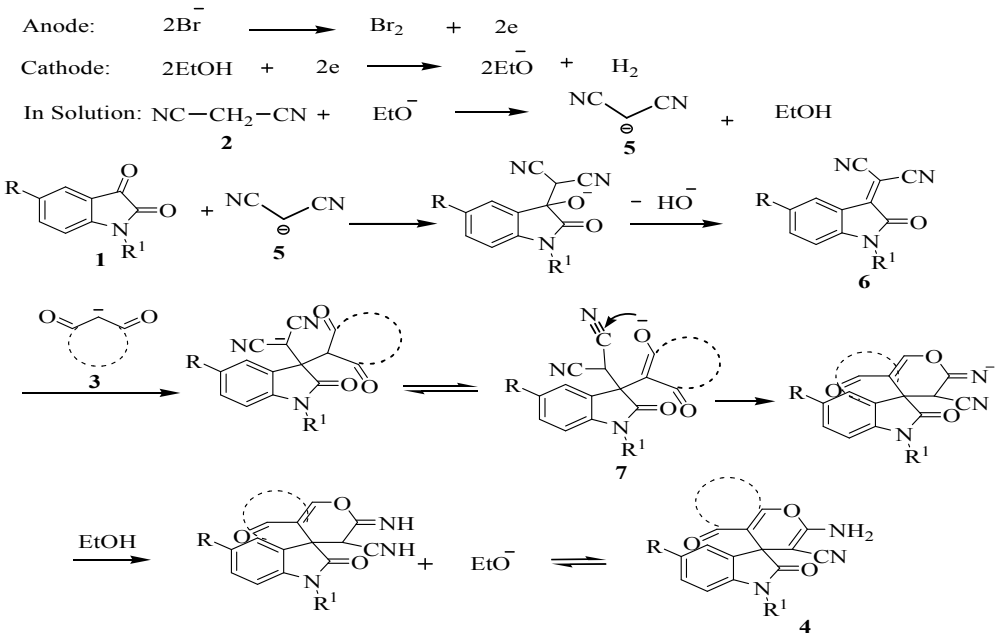
According to the previous studies[33-45], the plausible mechanism suggested in Scheme 2 seems to be reasonable for the one-pot three-component electrochemically reaction of isatin (**1**), malononitrile (**2**), and cyclohexan-1,3-dion (**3**). The first step includes the formation of an ethoxide anion from deprotonating of ethanol occurred in cathode surface (Scheme 2). On the next step, malononitrile anion (**5**) was producing by reaction of ethoxide anion and malononitrile. In continuation, the 2-(2-oxoindolin-3-ylidene)malononitrile (**6**) obtainedfrom the Knoevenagel condensation between isatin (**1**) and malononitrile anion (**6**) upon losing a hydroxide anion. Michael addition of the cyclic-1,3-dions anion (**3**), generated from the hydroxide anion, on the intermediate (**6**) affords the 3,3-disubstituted isatin intermediate (**7**). The final products (**4a-p**) are obtained by the intramolecular cyclization and tautomerization of the intermediate (**7**). The regeneration of the ethoxide anion in the final step starting of the new reaction cycle with malononitrile.

Table 2. The electrosynthesis of chromene-derivatives (**4a-p**) using isatines (**1a–h**),malononitrile (**2a**), and cyclic-1,3-diones (**3a–b**).

Entry	Isatin Derivatives	Cyclic-1,3-dion	Product	Yields(%)	m.p. (lit.)/ (obsd.) (°C)
1	 **1a**	 **3a**	 **4a**	91	300-304[33]/299-301
2	 **1a**	 **3b**	 **4b**	90	304-305[34]/302-305
3	 **1b**	 **3a**	 **4c**	84	290-292[35]/290-292
4	 **1b**	 **3b**	 **4d**	83	293-295[36]/290-291
5	 **1c**	 **3a**	 **4e**	87	296-298[37]/300-302
6	 **1c**	 **3b**	 **4f**	89	306-307[38]/299-301
7	 **1d**	 **3a**	 **4g**	84	274-276[39]/269-271
8	 **1d**	 **3b**	 **4h**	86	254-255[39]/254-256
9	 **1e**	 **3a**	 **4i**	83	255-257[40]/251-254
10	 **1e**	 **3b**	 **4j**	85	245-247[40]/244-246

11	 **1f**	 **3a**	 **4k**	89	232-236[41]/234-236
12	 **1f**	 **3b**	 **4l**	90	252-254[42]/250-254
13	 **1g**	 **3a**	 **4m**	86	281-282[35]/289-291
14	 **1g**	 **3b**	 **4n**	87	290-292[43]/291-291
15	 **1h**	 **3a**	 **4o**	83	266-268[44]/265-267
16	 **1h**	 **3a**	 **4p**	84	246-248[45]/250-252

[a]Reaction conditions: Isatin (**1a-m**), malononitrile (**2a**) and cyclic-1,3-diones (**3a-b**) (molar ratio: 1:1:1), KBr (0.5 mmol), Fe-Mn-O cathode (5 cm^2), graphite anode (5 cm^2) were used.



Scheme 2. The plausible mechanism of the electrocatalytic Synthesis of Spirooxindole-Chromene Derivatives.

Conclusion

In conclusion, a sustainable and promising electrochemical method was applied for multicomponent combination of isatins, malononitrile, and cyclic-1,3-dions into in order to synthesize spiro[chromene-4,3'-indoline]-3-carbonitrile derivatives in appreciable yield. The designed electrocatalytic method protocol provides a convenient and efficient route to create spirocyclic oxindole systems with fused functionalized chromene fragment which can be considered as the promising 'privileged drug scaffold' especially in pharmacy and medicine purposes. In addition, the developed electrocatalytic multicomponent protocol utilizes facile equipment and reagents involving an undivided cell, available electrodes, and simple starting materials. Furthermore, it is easily carried out, and the reaction products are crystallized from the reaction mixture.

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