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ORIGINAL PAPER

Na_2EDTA: an efficient, green and reusable catalyst for the synthesis of biologically important spirooxindoles, spiroacenaphthylenes and spiro-2-amino-4*H*-pyrans under solvent-free conditions

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Abstract For the first time, the organic salt Na_2EDTA was used as a catalyst for an effective and facile preparation of spiro-4*H*-pyrans via single-pot three-component condensation of isatin/acenaphthoquinone/ninhydrin, malononitrile, and CH-acids through Knoevenagel–Michael–annulation sequence. This new protocol employing Na_2EDTA, which is a green, recyclable, and inexpensive catalyst, offers advantages such as solvent-free and highly efficient reaction conditions, short reaction times (10–15 min), easy work-up and high yields which make it more economic than other environmentally synthetic methods.

Keywords Multi-component reactions (MCRs) · Solvent-free reaction · Green chemistry · Na_2EDTA · Spiro-4*H*-pyrans

Introduction

In recent years, interest in green chemistry [1–3] has developed, and reducing the use of organic solvents and toxic reagents for facile, efficient, and nonpolluting synthetic procedures has become a major challenge for organic chemists. In this area, use of natural materials as a promising catalyst in organic reactions has received a considerable attention due to their green credentials [4, 5]. Furthermore, the combination of multi-component reactions (MCRs) and solvent-free conditions leads to a significant reduction in reaction times, enhancements in conversions, improved selectivity, with several advantages of the eco-friendly approach such as energy savings, waste reduction, easy work-ups, and the avoidance of hazardous organic solvents [6, 7].

So, the design of novel MCRs using solvent-free conditions for the synthesis of simple and complex bioactive heterocycles has remained as a significant topic in the drug discovery process, and analysis of drugs [8, 9]. Among these bioactive heterocycles, pyran ring systems are an important category of oxygen-containing heterocycles. Also, they have broad existence in a variety of important natural compounds, including carbohydrates, alkaloids, polyether antibiotics, pheromones, and iridoids [10]. Pyran-based compounds are widely applied as cosmetics, pigments [11], and potential biodegradable agrochemicals [12]. These compounds display a variety of biological functions including anti-leishmanial [13], anti-HIV [14], antioxidant [15], anti-tumor [16], and central nervous system (CNS) activities and effects [17]; they are also used for the treatment of Alzheimer's disease [18] and schizophrenia [19].

Moreover, spiroheterocycle compounds containing one sp^3 carbon atom common to two rings are found in a number of natural or synthetic molecules [20, 21] and have plenty inimitable virtues [22, 23]. For example, this type of framework has been found as a core structure of many bioactive natural alkaloids such as spirotryprostatins, gelsemine, mitraphylline, horsfiline, chitosenine (Fig. 1) [24]. Molecules with spirocyclic structures are exclusively attractive because the conformational restriction associated with the structural rigidity affects significantly their biological and pharmaceutical activity [25, 26].

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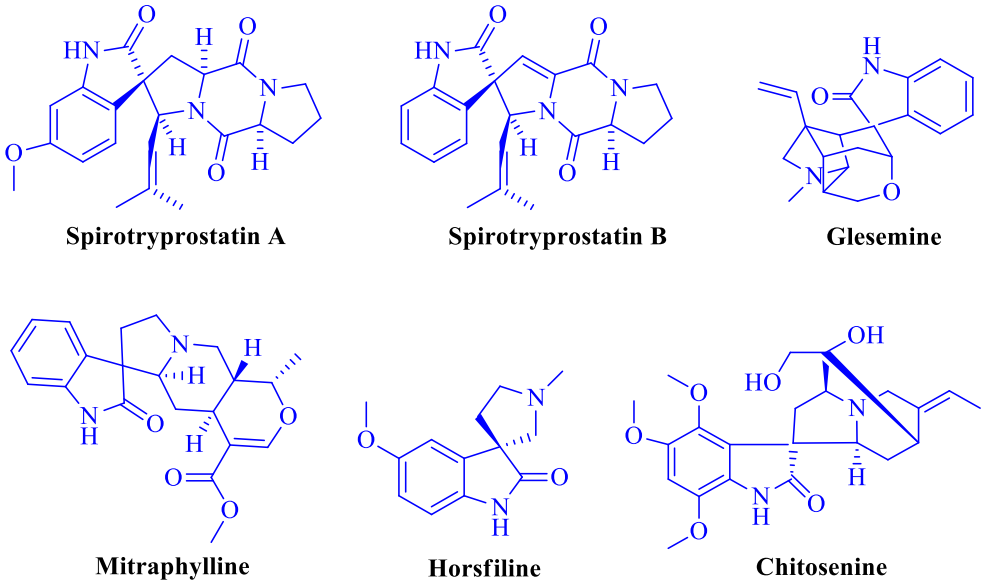


Fig. 1 Some biologically active alkaloids

Furthermore, EDTA (ethylenediaminetetraacetic acid) and its salts are substituted diamines and are used in foods, cosmetic formulations, pharmaceutical products, and manufacturing. Moreover, they are used to treat heavy metal poisoning and to reduce blood cholesterol [27]. Among these salts, we used the ethylenediaminetetraacetic acid disodium salt dehydrate (organic salt Na_2EDTA, Fig. 2) as a solid acid–base bifunctional catalyst for organic synthesis.

Considering the significant potential of spirocyclic compounds, especially when fused to pyran derivatives as a source of valuable drug candidates and with our continued interest in multi-component reactions and our ongoing program for the synthesis of heterocyclic systems based on green chemistry protocols [28–32], herein, we report a green and efficient procedure for the synthesis of spiro-2-amino-4*H*-pyrans, spiroacenaphthylenes, and spirooxindoles **4/5/6** through a single-pot, three-component condensation reaction between isatin/acenaphthoquinone/ninhydrin **1,** malononitrile **2**, and CH-acids **3** in the presence of the catalytic amount of Na_2EDTA as an efficient, eco-friendly, and reusable catalyst under solvent-free conditions at 70 °C (Scheme 1).

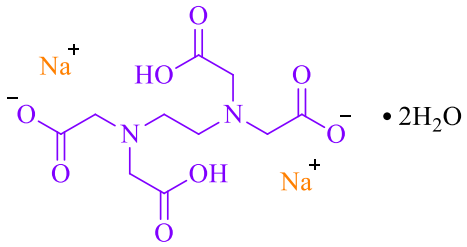


Fig. 2 Structure of Na_2EDTA

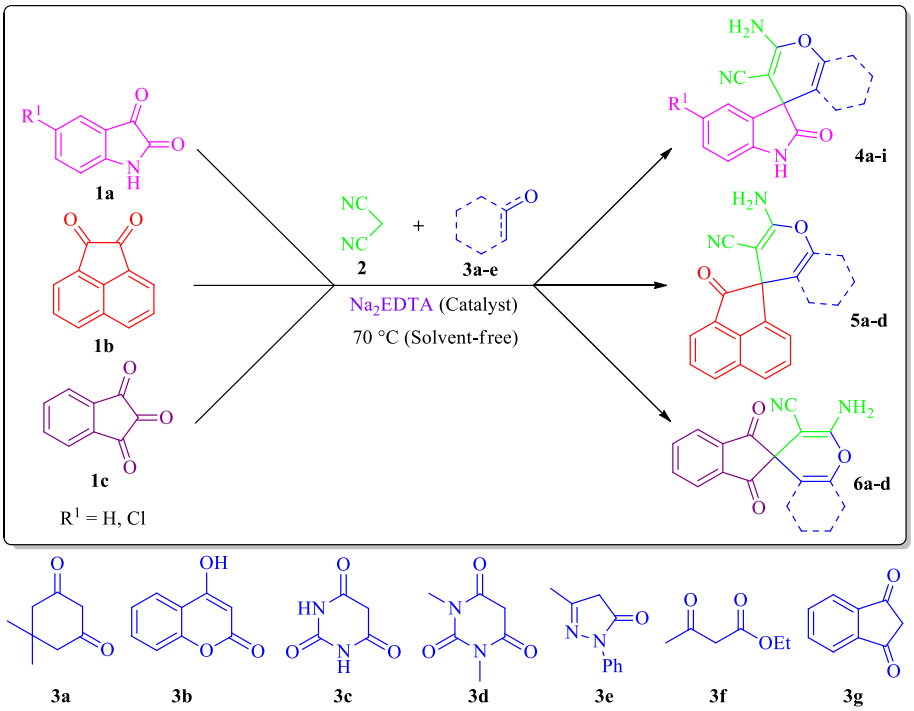
Experimental

General

Melting points and IR spectra of all compounds were determined by using an Electro thermal 9100 apparatus and JASCO FT/IR-460 plus spectrometer. The ^1H NMR and ^{13}C NMR spectra were recorded on a Bruker DRX-300 and 400 Avanve instrument with deuterated dimethyl sulfoxide (DMSO-d_6) as solvent and using TMS as internal reference at 300, 400, 75, and 100 MHz, respectively. Thin-layer chromatography (TLC) was performed on silica-gel Polygram SILG/UV 254 plates. All chemicals were received from chemical producer Merck (Darmstadt, Germany) and Fluka (Buchs, Switzerland) and used without further purification.

General procedure for the synthesis of spirooxindoles, spiroacenaphthylenes, and spiro-2-amino-4*H*-pyrans (4–6)

A mixture of isatin/acenaphthoquinone/ninhydrin)1 mmol) **1a-c**, malononitrile **2** (1 mmol), CH-acid **3a-g** (1 mmol), and 15 mol % of Na_2EDTA was heated under solvent-free conditions at 70 °C for the mentioned time shown in tables. The progress of the reaction was monitored by TLC using EtOAc/*n*-hexane (1:3) as an eluent. Upon completion, the reaction mixture was allowed to cool to room temperature. Then, 5 mL of water was then added to the reaction mixture, the resulting solid was collected by filtration and washed twice with water (2 × 5 mL), and then the pure solid products **4/5/6** were recrystallized from ethanol.



Scheme 1 One-pot, three-component synthesis of spiro-4*H*-pyran derivatives, catalyzed by Na_2EDTA

Selected spectroscopic data of selected and known products are given below:

2-Amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile ***(4a)*** Mp 292–294 °C; IR (KBr): ν_{max} = 3375, 3310, 3143, 2960, 2191, 1725, 1656, 1603, 1465, 1352, 1222, 1178, 1052, 907 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.01 (s, 3H, CH_3), 1.04 (s, 3H, CH_3), 2.08–2.20 (m, 2H, CH_2), 2.53 (s, 2H, CH_2), 6.80 (d, 1H, J = 7.6 Hz, ArH), 6.90 (t, 1H, J = 7.6 Hz, ArH), 6.98 (d, 1H, J = 7.2 Hz, ArH), 7.14 (t, 1H, J = 7.6 Hz, ArH), 7.22 (s, 2H, NH_2), 10.40 (s, 1H, NH).

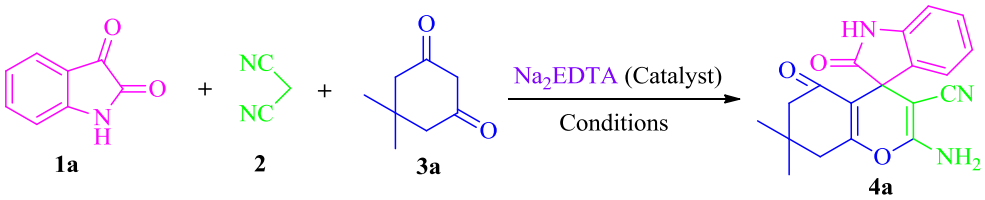
2-Amino-5′-chloro-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile ***(4f)*** Mp 294–295 °C; IR (KBr): ν_{max} = 3360, 3150, 2955, 2192, 1722, 1677, 1648, 1590, 1473, 1347, 1220, 1033, 806, 552 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.03 (s, 6H, $2CH_3$), 2.16 (s, 2H, CH_2), 2.50–2.58 (m, 2H, CH_2), 6.81 (d, 1H, J = 8.1 Hz, ArH), 7.11 (s, 1H, ArH), 7.21 (dd, 1H, J = 8.1 Hz, J = 2.1 Hz, ArH), 7.36 (s, 2H, NH_2), 10.58 (s, 1H, NH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 27.6, 27.9, 32.4, 47.5, 50.3, 57.1, 110.6, 111.1, 117.7, 123.7, 126.1, 128.5, 136.9, 141.3, 141.4, 159.3, 165.1, 178.3, 195.6 ppm.

2′-Amino-7′,7′-dimethyl-2,5′-dioxo-5′,6′,7′,8′-tetrahydro-2H-spiro[acenaphthylene-1,4′-chromene]-3′-carbonitrile ***(5a)*** Mp 271–273 °C; IR (KBr): ν_{max} = 3351, 3274, 3187, 2942, 2194, 1735, 1657, 1461, 1342, 1213, 1154, 1022, 901 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6): δ 1.03 (s, 3H, CH_3), 1.05 (s, 3H, CH_3), 2.04–2.14 (m, 2H, CH_2), 2.64 (s, 2H, H_2), 7.32 (s, 2H, NH_2), 7.40 (d, 1H, J = 6.8 Hz, ArH), 7.66 (t, 1H, J = 6.8 Hz, ArH), 7.83 (t, 1H, J = 8.0 Hz, ArH), 7.92–7.95 (m, 2H, ArH), 8.27 (d, 1H, J = 7.6 Hz, ArH).

2′-Amino-2,5′-dioxo-2H,5′H-spiro[acenaphthylene-1,4′-pyrano[3,2-c]chromene]-3′-carbonitrile ***(5b)*** Mp 295–297 °C; IR (KBr): ν_{max} = 3385, 3280, 3157, 2936, 2192, 1717, 1685, 1652, 1474, 1331, 1226, 1172, 1020, 914 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 7.50 (d, 1H, J = 8.1 Hz, ArH), 7.57 (t, 1H, J = 7.5 Hz, ArH), 7.64–7.81 (m, 5H, ArH, NH_2), 7.89 (t, 1H, J = 7.8 Hz, ArH), 7.99–8.07 (m, 3H, ArH), 8.36 (d, 1H, J = 7.8 Hz, ArH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 52.01, 58.2, 102.6, 112.9, 117.2, 117.6, 121.6, 122.6, 123.2, 125.6, 129.18, 129.5, 130.3, 131.7, 132.7, 134.1, 141,6, 142.1, 152.5, 155.8, 158.8, 158.9, 159.4, 203.6 ppm.

2-Amino-7,7-dimethyl-1′,3′,5-trioxo-1′,3′,5,6,7,8-hexahydrospiro[chromene-4,2′-indene]-3-carbonitrile ***(6a)*** Mp 288–290 °C; IR (KBr): ν_{max} = 3370, 3240, 2955, 2190, 1743, 1712, 1683, 1656, 1592, 1347, 1258, 1161, 1050, 791 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6): δ 1.04 (s, 6H, $2CH_3$), 2.21 (s, 2H, CH_2), 2.63 (s, 2H, CH_2), 7.71 (s,

Table 1 Optimization of the amount of catalyst (Na_2EDTA) and temperature in a one-pot synthesis of the model reaction



Entry	Catalyst (mol %)	Reaction conditions	Time (min)	Isolated yield (%)
1	–	Solvent-free, r.t	100	Trace
2	10	Solvent-free, r.t	75	50
3	15	Solvent-free, r.t	45	72
4	15	Solvent-free, 50 °C	40	80
5	15	Solvent-free, 60 °C	15	90
6	15	Solvent-free, 70 °C	10	94
7	15	Solvent-free, 80 °C	10	95
8	20	Solvent-free, 70 °C	10	92
9	15	Solvent-free, 70 °C	7	90
10	15	H_2O, 70 °C	10	90
11	15	EtOH, 70 °C	10	87
12	–	Solvent-free, 70 °C	10	43

2H, NH_2), 8.00–8.07 (m, 4H, ArH); ^{13}C NMR (300 MHz, DMSO-d_6): δ 27.6, 32.9, 49.3, 52.2, 53.5, 110.4, 117.3, 123.6, 137.1, 141, 160.3, 160.3, 160.35, 166.9, 196.5, 200.2 ppm.

Results and discussion

Considering the importance of spiro-4*H*-pyrans, we were willing to find a practical and general method for their synthesis in high yields and purities and also, because the development of efficient and environmentally friendly synthetic procedures is always desirable, we decided to peruse whether those compounds could be prepared by condensation of isatin/acenaphthoquinone/ninhydrin, malononitrile, and CH-acids through Knoevenagel–Michael–annulation sequence in the absence of any hazardous or toxic catalysts and organic solvents. For this purpose, the condensation reaction between isatin **1a** (1 mmol), malononitrile **2** (1 mmol), and dimedone **3a** (1 mmol) was selected as a model reaction in the presence of different amounts of Na_2EDTA as a catalyst (10, 15 and 20 mol %) at various temperatures (25, 50, 60, 70 and 80 °C). As can be seen in Table 1, the best result was obtained when the reaction was carried out in the presence of 15 mol% of Na_2EDTA at 70 °C in solvent-free conditions, which afforded the corresponding 2-amino-7,7-dimethyl-2′,5-dioxo-5,6,7,8-tetrahydrospiro[chromene-4,3′-indoline]-3-carbonitrile **4a** in 10 min with 94% of yield (Table 1, entry 6).

To explore the scope of the reaction further, the present study is extended to various cyclic ketones and different activated CH-acids using these optimized conditions. All the reactions were complete in 10–15 min and resulted in the formation of the target structures in high yields without the formation of any side products. This one-pot reaction was efficiently promoted using isatin with reduced reaction times and increased yields rather than other cyclic ketones and dimedone reacted rapidly and gave higher yields in comparison with other activated CH-acids (Table 2, entries 1–17).

Recovery of the catalysts is a significant feature in green organic synthesis. Thus, for recyclability of the catalyst, we also investigated the recycling of Na_2EDTA under solvent-free conditions at 70 °C using a selected model reaction of isatin, malononitrile, and dimedone in the presence of Na_2EDTA as a homogeneous catalyst. After the completion of the reaction, 5 mL of water was added to the mixture. The Na_2EDTA was dissolved in water and filtered for the separation of the crude product. The separated product was washed twice with water (2 × 5 mL). The resulting product was subsequently recrystallized from ethanol to give the pure solid. In order to recover the catalyst, since Na_2EDTA is soluble in water, the filtrate was extracted with diethyl ether. The aqueous layer was separated, its solvent was evaporated under reduced pressure, and Na_2EDTA was recovered and reused (Fig. 3).

Table 2 Solvent-free synthesis of spiro-4*H*-pyran derivatives in the presence of Na_2EDTA (15 mol%) as a catalyst at 70 °C

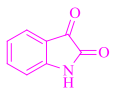
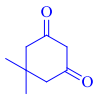
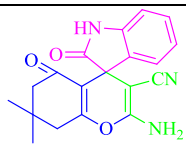
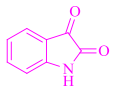
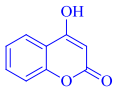
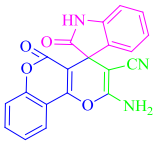
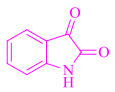
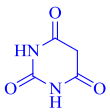
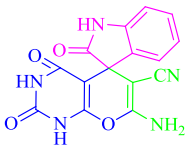
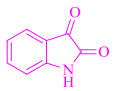
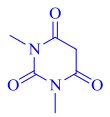
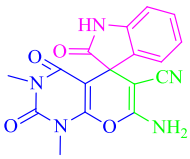
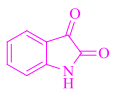
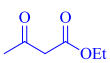
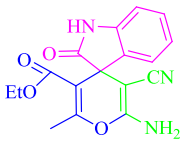
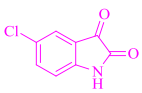
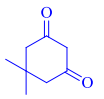
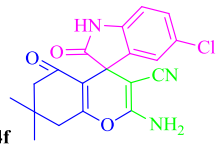
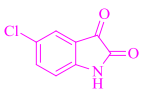
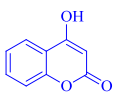
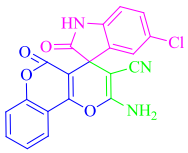
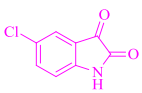
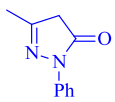
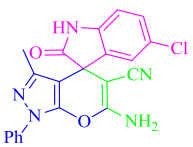
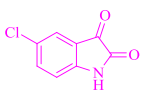
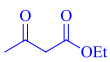
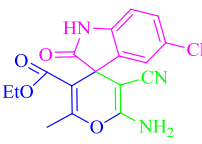
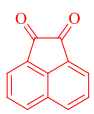
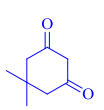
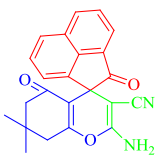
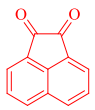
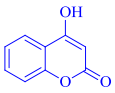
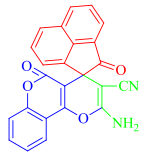
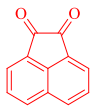
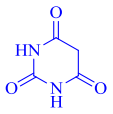
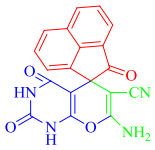
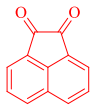
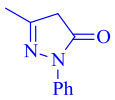
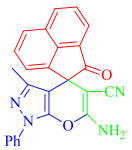
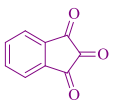
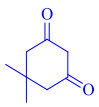
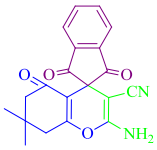
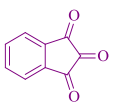
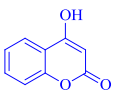
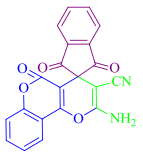
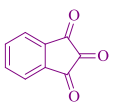
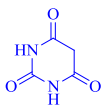
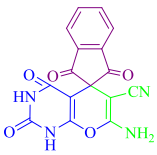
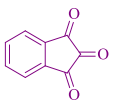
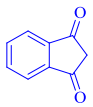
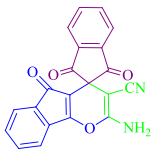
Entry	Cyclic ketone	C−H activated	Product	Time (min)	Yield (%)[a]	M.P. (°C)	
						Observed	Reported
1			**4a** 	10	94	292–294	289–290 [33]
2			**4b** 	10	92	295–296	292–294 [33]
3			**4c** 	15	89	278–280	275–276 [33]
4			**4d** 	15	85	230–231	225–228 [34]
5			**4e** 	15	90	252–254	255–256 [35]
6			**4f** 	10	95	294–295	289–291 [36]
7			**4g** 	10	92	>300	>300 [36]
8			**4h** 	12	87	230–232	226–228 [37]
9			**4i** 	15	89	254–256	256–258 [37]
10			**5a** 	10	94	271–273	270 [38]

Table 2 continued

Entry	Cyclic ketone	C−H activated	Product	Time (min)	Yield (%)[a]	M.P. (°C) Observed	M.P. (°C) Reported
11			**5b** 	12	85	295–297	288–292 [39]
12			**5c** 	15	84	>300	>300 [40]
13			**5d** 	15	90	200–202	197–198 [41]
14			**6a** 	12	92	288–290	290–292 [38]
15			**6b** 	15	84	276–278	280–285 [38]
16			**6c** 	15	88	277–278	275–277 [38]
17			**6d** 	15	85	256–258	255–260 [38]

[a] Isolated yields

As shown in Fig. 3, the catalytic system worked well up to five catalytic runs and slightly reduced the product yield, which may be due to little weight loss of catalyst during each recovery process.

The probable mechanism for the formation of the products using Na_2EDTA, which act as an acid–base bifunctional catalyst in all steps, is outlined in Scheme 2. On the basis of this suggested mechanism, the synthesis of spiro-4*H*-pyrans **4-6** could be achieved through two ways. In two paths, Na_2EDTA is an efficient catalyst to form the olefin **I**, which readily prepares in situ from Knoevenagel condensation of carbonyl group of cyclic ketone **1a–c** with malononitrile **2** (path A) or C–H activated **3a-g** (path B). In continue, Michael addition of C–H activated **3a–g** (path A) or malononitrile **2** (path B) with olefin **I** in the presence of Na_2EDTA finally give intermediate **II**. At the end, intermediate **II** through an intramolecular cyclization by nucleophilic attack of the hydroxyl group on the cyano group producing the desired products **4–6**.

On this mechanism, we suggest that the Na_2EDTA plays a dual role: first, to electrophilically activate the cyclic ketone carbonyl via H-bond formation between one

H-atom of Na_2EDTA and the O-atom of the C=O group, and second, to enhance the nucleophilicity of the C–H activated or malononitrile through deprotonation of the Cα-H by Na_2EDTA.

In order to assess the efficiency and generality of this methodology, the obtained result from the reaction of isatin and malononitrile with dimedone by this method has been compared with those of the previously reported methods (Table 3). It was found that the present method is convincingly superior to the reported methods with respect to reaction time and exhibits broad applicability in terms of yields.

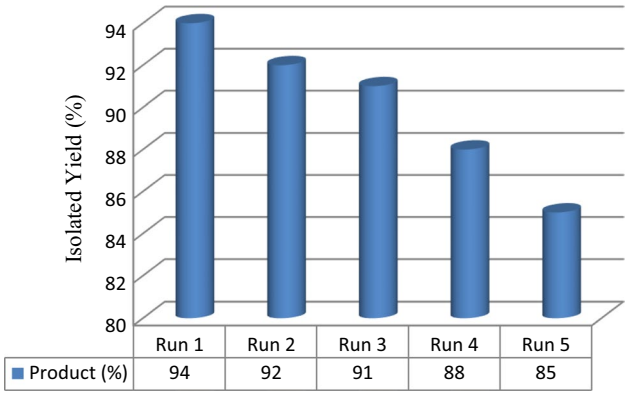
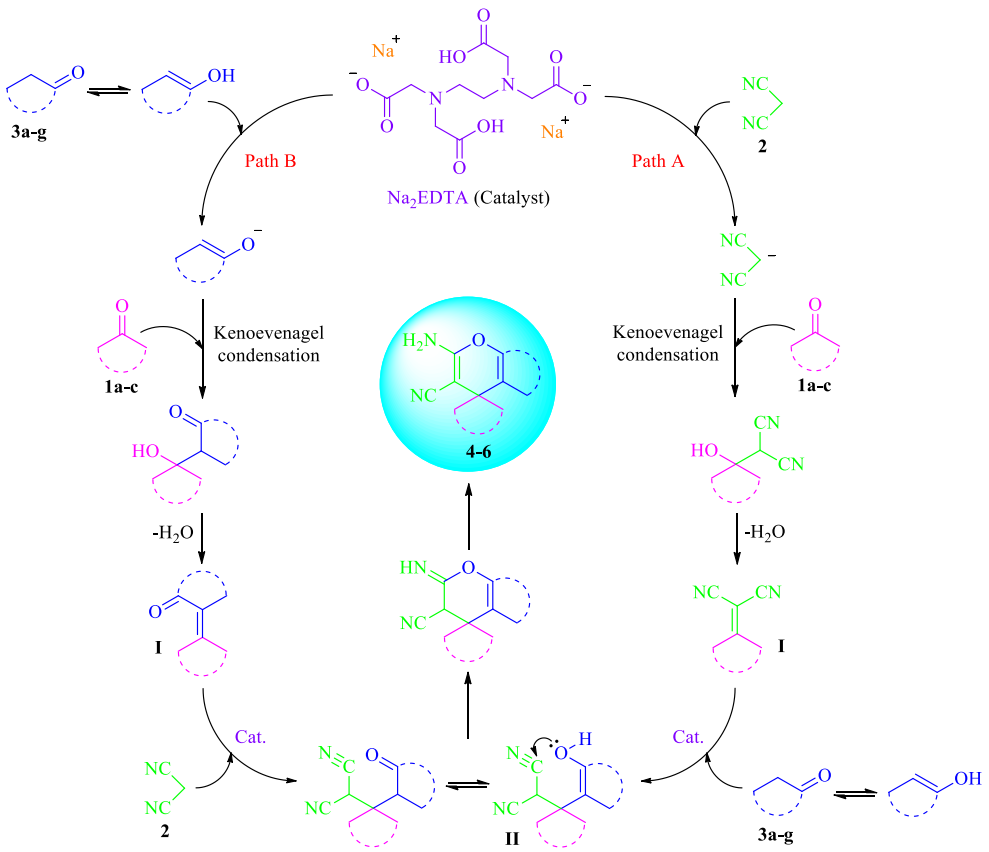


Fig. 3 Results of recycling over five consecutive recycling experiments

Conclusions

In this work, we have demonstrated a simple single-pot, three-component synthesis of spiro-4*H*-pyran derivatives in excellent yields and purities with very short reaction times, from readily available starting materials by using catalytic amount of Na_2EDTA as an environmentally benign solid acid–base bifunctional catalyst, under solvent-free conditions. This green and efficient procedure has a number of advantages such as operational simplicity, easy work-up, use of inexpensive, non-toxic, reusable, easy to handle catalyst without any byproduct, avoidance of hazardous organic solvents, and it may find a wide range of applications in diversity-oriented synthesis, and drug discovery, which make the methodology more attractive than the other conventional



Scheme 2 Proposed mechanism for the formation of spiro-4*H*-pyran derivatives in the presence of Na_2EDTA

Table 3 Comparison of the efficiency of Na_2EDTA with other reported catalysts in the literature for the synthesis of **4a**

Entry	Catalyst/condition	Time (min)	Yield (%)[a]	References
1	TEBA (20 mol %)/H_2O, 60 °C	120	94	Previous work [33]
2	[γ-Fe_2O_3@HAp-Si$(CH_2)_3SO_3H$] (2 mol %)/H_2O, 30 °C	20	75	Previous work [34]
3	EDDA (10 mol %)/H_2O, 60 °C	60	90	Previous work [35]
4	Sodium stearate (10 mol %)/H_2O, 60 °C	180	95	Previous work [36]
5	L-Proline (10 mol %)/H_2O, 80 °C	20	94	Previous work [37]
6	Ni nps/ethylene glycol, rt	5	92	Previous work [38]
7	DBU (10 mol %)/H_2O, reflux	10	90	Previous work [39]
8	$InCl_3$ (20 mol %)/CH_3CN, reflux	90	75	Previous work [42]
9	NH_4Cl (20 mol %)/H_2O, 80 °C	10	92	Previous work [43]
10	β-Cyclodextrin/H_2O, 60 °C	300	90	Previous work [44]
11	Nano MgO (15 mol %)/H_2O, 80 °C	120	93	Previous work [45]
12	$Mg(ClO_4)_2$ (10 mol %)/EtOH, H_2O, 50 °C	30	91	Previous work [46]
13	DMAP (10 mol %)/solvent-free, MWI, 100 °C	5	90	Previous work [47]
14	AHST-MNP (0.07 g)/H_2O, ultrasonic irradiation, 60 °C	105	94	Previous work [48]
15	$Cu(OAc)_2.H_2O$ (15 mol %)/solvent-free, 80 °C	240	86	Previous work [49]
16	Citric acid (20 mol %)/EtOH, H_2O, 80 °C	10	81	Previous work [50]
17	Na_2EDTA (15 mol %)/solvent-free, 70 °C	10	94	Present work

[a] Isolated yields

methods for the synthesis of these biologically important heterocycles.

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References

1. P. Anastas, N. Eghbali, Chem. Soc. Rev. **39**, 301 (2010)
2. P.T. Anastas, J.C. Warner, *Green Chemistry Theory and Practice* (Oxford University, New York, 1998)
3. L. Xu, C. Gu, R. Li, Y. Yu, T. Wang, J. Iran. Chem. Soc. **13**, 597 (2016)
4. N. Hazeri, M.T. Maghsoodlou, F. Mir, M. Kangani, H. Saravani, E. Molashahi, Chin. J. Catal. **35**, 391 (2014)
5. M. Kangani, N. Hazeri, M.T. Maghsoodlou, K. Khandan-Barani, M. Kheyrollahi, F. Nezhadshahrokhabadi, J. Iran. Chem. Soc. **12**, 47 (2015)
6. K. Tanaka, F. Toda, Chem. Rev. **100**, 1025 (2000)
7. B. Pouramiri, E.T. Kermani, J. Iran. Chem. Soc. **13**, 1011 (2016)
8. V.F. Vavsari, G.M. Ziarani, A. Badiei, S. Balalaie, J. Iran. Chem. Soc. **13**, 1037 (2016)
9. K.D. Safa, M. Esmaili, M. Allahvirdinesbat, J. Iran. Chem. Soc. **13**, 267 (2016)
10. L.F. Tietze, G. Kettschau, Hetero Diels-Alder reactions in organic chemistry, in *Stereoselective Heterocyclic Synthesis I*, ed. by P. Metz (Springer, Berlin, Heidelberg, 1997), pp. 1–120
11. G.P. Ellis, Chromenes, chromanones, and chromones, in *The Chemistry of Heterocyclic Compounds Chromenes*, ed. by A. Weissberger, E. C. Taylor, Chap II (Wiley, New York, NY, 1977), pp. 11–139
12. E.A. Hafez, M.H. Elnagdi, A.G.A. Elagemey, F.M.A.A. El-Taweel, Heterocycles **26**, 903 (1987)
13. T. Narender, S. Gupta, Bioorg. Med. Chem. Lett. **14**, 3913 (2004)
14. K. Asres, A. Seyoum, C. Veeresham, F. Bucar, S. Gibbons, Phytother. Res. **19**, 557 (2005)
15. A.J. Johnson, R.A. Kumar, S.A. Rasheed, S.P. Chandrika, A. Chandrasekhar, J. Ethnopharmacol. **130**, 267 (2010)
16. Q.B. Han, N.Y. Yang, H.L. Tian, C.F. Qiao, J.Z. Song, D.C. Chang, S.L. Chen, K.Q. Luo, H.X. Xu, Phytochemistry **69**, 2187 (2008)
17. J. Skommer, D. Wlodkowic, M. Matto, M. Eray, J. Pelkonen, Leukemia Res. **30**, 322 (2006)
18. C. Brühlmann, F. Ooms, P.A. Carrupt, B. Testa, M. Catto, F. Leonetti, C. Altomare, A. Carotti, J. Med. Chem. **44**, 3195 (2001)
19. S.R. Kesten, T.G. Heffner, S.J. Johnson, T.A. Pugsley, J.L. Wright, L.D. Wise, J. Med. Chem. **42**, 3718 (1999)
20. R. Rios, Chem. Soc. Rev. **41**, 1060 (2012)
21. T. Jin, M. Himuro, Y. Yamamoto, Angew. Chem. Int. Ed. **48**, 5893 (2009)
22. H. Diirr, R. Gleiter, Angew. Chem. Int. Ed. **17**, 559 (1978)
23. J. Sun, Y.J. Xie, C.G. Yan, J. Org. Chem. **78**, 8354 (2013)
24. T.L. Pavlovska, R. Redkin, G.V.V. Lipson, D.V. Atamanuk, Mol. Divers. **20**, 299 (2015)
25. R.M. Williams, R.J. Cox, Acc. Chem. Res. **36**, 127 (2003)
26. A. Nandakumar, P. Thirumurugan, P.T. Perumal, P. Vembu, M.N. Ponnuswamy, P. Ramesh, Bioorg. Med. Chem. Lett. **20**, 4252 (2010)
27. R.S. Lanigan, T.A. Yamarik, Int. J. Toxicol. **21**, 95 (2001)
28. M.R. Mousavi, M.T. Maghsoodlou, J. Iran. Chem. Soc. **12**, 743 (2015)
29. M.R. Mousavi, M.T. Maghsoodlou, N. Hazeri, S.M. Habibi-Khorassani, J. Iran. Chem. Soc. **12**, 1419 (2015)
30. M.T. Maghsoodlou, M. Karima, M. Lashkari, B. Adrom, J. Aboonajmi, J. Iran. Chem. Soc. **14**, 329 (2017)
31. P. Dastoorani, M.T. Maghsoodlou, M.A. Khalilzadeh, E. Sarina, Tetrahedron Lett. **57**, 314 (2016)
32. A. Yazdani-Elah-Abadi, M.T. Maghsoodlou, R. Mohebat, R. Heydari, Chin. Chem. Lett. **28**, 446 (2017)
33. S.L. Zhu, S.J. Ji, Y. Zhang, Tetrahedron **63**, 9365 (2007)

34. L. Jalili-Baleh, N. Mohammadi, M. Khoobi, L. Ma'mani, A. Foroumadi, A. Shafiee, Helv. Chim. Acta **96**, 1601 (2013)
35. Y.R. Lee, G.S. Hari, Synthesis **2010**, 453 (2010)
36. L.M. Wang, N. Jiao, J. Qiu, J.J. Yu, J.Q. Liu, F.L. Guo, Y. Liu, Tetrahedron **66**, 339 (2010)
37. Y. Li, H. Chen, C. Shi, D. Shi, S. Ji, Comb. Chem. **12**, 231 (2010)
38. J.M. Khurana, S. Yadav, Aust. J. Chem. **65**, 314 (2012)
39. P. Saluja, K. Aggarwal, J.M. Khurana, Synth. Commun. **43**, 3239 (2013)
40. M. Saeedi, M.M. Heravi, Y.S. Beheshtiha, H.A. Oskooie, Tetrahedron **66**, 5345 (2010)
41. H.R. Safaei, M. Shekouhy, A. Shirinfeshan, S. Rahmanpur, Mol. Divers. **16**, 669 (2012)
42. G. Shanthi, G. Subbulakshmi, P.T. Perumal, Tetrahedron **63**, 2057 (2007)
43. M. Dabiri, M. Bahramnejad, M. Baghbanzadeh, Tetrahedron **65**, 9443 (2009)
44. R. Sridhar, B. Srinivas, B. Madhav, V.P. Reddy, Y.V.D. Nageswar, K.R. Rao, Can. J. Chem. **87**, 1704 (2009)
45. B. Karmakar, A. Nayak, J. Banerji, Tetrahedron Lett. **53**, 5004 (2012)
46. C. Wu, R. Shen, J. Chen, C. Hu, Bull. Korean Chem. Soc. **34**, 2431 (2013)
47. M. Zakeri, M. Mahmoud Nasef, E. Abouzari-Lotf, A. Moharami, M. Heravi, J. Ind. Eng. Chem. **29**, 273 (2015)
48. A.R. Karimi, R. DavoodAbadi, Z. Dalirnasab, Res. Chem. Intermed. **41**, 7427 (2015)
49. F. Mohamadpour, M.T. Maghsoodlou, R. Heydari, M. Lashkari, Res. Chem. Intermed. **42**, 7841 (2016)
50. Z. Karimi-Jaberi, A. Fereydoonnezhad, Iranian. Chem. Commun. **5**, 349 (2017)