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Ru(III)-exchanged FAU-Y zeolite as an efficient heterogeneous catalyst for preparation of oxindoles

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ABSTRACT

Ru(III)-exchanged FAU-Y zeolite was used as an efficient reusable heterogeneous catalyst for preparation of oxindoles from condensation reaction of indoles with isatins under very mild reaction conditions.

Keywords: Oxindoles, catalysis, Indoles, FAU-Y Zeolite.

INTRODUCTION

Indole framework occur in many pharmacologically and biologically active compounds[1], and the chemistry of indoles has been and continues to be one of the most active areas of heterocyclic chemistry[2,3]. Oxindole derivatives are also, based on indole framework and are well known as laxatives, anti bacterial and anti inflammatory agents[4,5]. Although, there exist some natural sources for these heterocyclic compounds, –for example, the marine alkaloid Convolutamydine A, from the marine bryozoan *Amathia convoluta*[6] – oxindole derivatives have been prepared by different methods such as acid catalyzed reaction of indoles and isatin[7], silica sulfuric acid catalysis[8], $KAl(SO_4)_2$ catalysis under microwave conditions[9], bismuth triflate catalysis[10] and few others. All of these methods have their own drawbacks such as long reaction times, non-environment friendly solvents, low yields of products, *etc.* In continuation of our program aimed at developing new efficient methodologies for the preparation of indole derivatives using ruthenium based catalysts[11-14], we describe here an efficient method for the synthesis of oxindoles. We have recently reported that, Ruthenium chloride hydrate smoothly acts as homogeneous catalyst in one-pot trimerization of indoles under oxidative conditions[15]. Application of solid catalysts in organic transformation, on the other hand, have very important role because, solid acids have many advantages such as simplicity in handling, thermal stability, ease of recycling and more environmentally safe disposal. Also, wastes and by-products can be minimized or avoided by developing cleaner synthetic routes. In this contribution, we have devised an efficient synthesis of oxindoles from electrophilic substitution reaction of indoles with isatins using Ru(III)-exchanged Zeolite Y.

RESULTS AND DISCUSSION

Typical results of the Ru(III)-exchanged zeolite Y catalyzed condensation of indoles with isatins are shown in Table 1. Treatment of indole (2 mmol) with isatin (1 mmol) in the presence of Ru(III)-exchanged zeolite Y (Ru-Y, 10 mol %) in 1,2-dichloroethane (10 mL) under reflux conditions, furnished an excellent yield of the product **1a** in a rather short time (93 %, 30 min.). After filtration of the solid catalyst, which was saved for recycling, the reaction mixture was purified by using preparative TLC (Hexanes:Ethylacetate 10:4). The NMR data was consistent with those previously reported for 3,3-di(1*H*-indole-3-yl)indolin-2-one[16].

As it is shown, this method worked with a variety of substrates. One interesting example is the reaction of 3-methylindole with isatin (entry 4), which provided the alcohol product **4a**, while the other reported methods were failed in this reaction.

With regard to the isatin moiety, the present protocol is noteworthy, because condensation with 1-methylisatin and 5-cyanoisatin gave corresponding products in acceptable yields (Table 1, entries 7,8).

In order to evaluate reusability of the solid catalyst, the reaction of indole and isatin was carried out in presence of the recycled catalyst in successive runs. These results are shown in Table 2.
As it is shown, only 8% loss of efficiency in terms of the product yield was observed after five runs, which promises minimization of the waste.

In conclusion, we have developed a convenient route to oxindole derivatives. The advantages of the present protocol are ease of work-up, little waste and high yields of products.

General procedure for condensation of indoles with isatins

Preparation of the catalyst: Zeolite FAU-Y (1 g) was added to a solution of ruthenium chloride hydrate (0.05 M, 15 mL) and stirred at room temperature for 24 h. The mixture was then filtered and washed with two 20 mL portions of distilled water, dried at 300 °C overnight and characterized by XRD patterns.

To a solution of indole (2 mmol) and isatin (1 mmol) in 1,2-dichloroethane, catalyst (10 mol%) was added and the reaction mixture was heated in an oil bath under reflux conditions for the time specified in Table 1. After completion of the reaction, the mixture was filtered, and the filtrate was purified by using preparative TLC. The same procedure was also used for the other products listed in Table 1.

Characterization data for the products

3,3-di(1*H*-indol-3-yl)indolin-2-one, 1a.

White solid, mp 310-312 °C, IR (KBr): ν (cm^{-1}); 758, 1012, 1103, 1336, 1473, 1614, 1706, 3056, 3280, 3323, 3427. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.51 (2H, t, *J*=7.5 Hz), 6.59 (1H, t, *J*=7.5 Hz), 6.62 (2H, s), 6.69 (1H, d, *J*=7.7 Hz), 6.72 (2H, t, *J*=7.5 Hz), 6.88 (1H, t, *J*=7.6 Hz), 6.97 (1H, d, *J*=7.4 Hz), 7.02 (4H, t, *J*=7.65 Hz), 9.78 (1H, s), 9.89 (2H, s) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 53.41, 110.48, 112.47, 115.14, 119.01, 119.13, 121.62, 122.26, 125.05, 125.21, 126.55, 128.70, 135.45, 137.77, 142.17, 179.60 ppm. Anal. Calcd for $C_{24}H_{17}N_3O$: C, 79.32; H, 4.72; N, 11.56; found: C, 79.35; H, 4.75; N, 11.55.

3,3-di(2-methyl-1*H*-indole-3-yl)indolin-2-one, 3a

White solid, mp 297-299 °C, IR (KBr): ν (cm^{-1}); 611, 686, 740, 760, 1018, 1176, 1298, 1421, 1458, 1616, 1712, 2927, 3055, 3330, 3417. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 2.11 (3H, s), 2.30 (3H, s), 6.41 (1H, d, *J*= 7.6 Hz), 6.80-6.85 (3H, m), 6.98-7.09 (4H, m), 7.37 (2H, d, *J*= 7.5 Hz), 7.82 (1H, d, *J*= 7.6 Hz), 7.92 (1H, d, *J*= 8.2 Hz), 10.39 (1H, s), 10.51 (1H, s), 10.92 (1H, s) ppm. Anal. Calcd for $C_{26}H_{21}N_3O$: C, 79.77; H, 5.41; N, 10.73; found: C, 79.78; H, 5.40; N, 10.72.

3-hydroxy-3-(3-methyl-1*H*-indol-2-yl)indolin-2-one, 4a

White solid, IR (KBr): ν (cm^{-1}); 748, 1001, 1064, 1093, 1124, 1209, 1242, 1328, 1467, 1622, 1685, 1716, 2833, 2941, 3222, 3357. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 2.01 (1H, br), 2.08 (3H, s), 6.90 (1H, d, *J*= 7.8 Hz), 7.16 (1H, t, *J*= 7.1 Hz), 7.21 (1H, t, *J*= 7.0 Hz), 7.29-7.34 (3H, m), 7.44 (1H, d, *J*= 7.4 Hz), 7.58 (1H, d, *J*= 7.8 Hz), 8.30 (1H, s), 8.75 (1H, s) ppm. Anal. Calcd for $C_{17}H_{14}N_2O_2$: C, 73.37; H, 5.07; N, 10.07; found: C, 73.43; H, 5.10; N, 10.09.

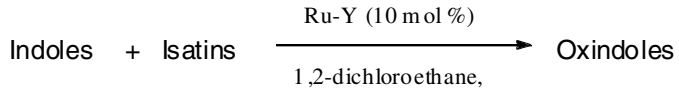
3,3-di(5-cyano-1*H*-indole-3-yl)indolin-2-one, 5a

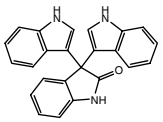
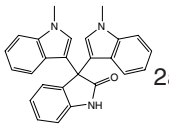
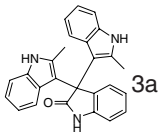
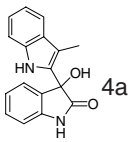
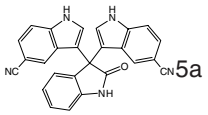
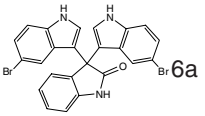
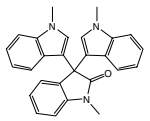
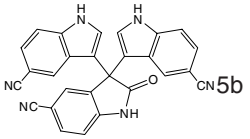
White solid, mp 273-275 °C, IR (KBr): ν (cm^{-1}); 752, 810, 1101, 1228, 1346, 1469, 1618, 1670, 1706, 2223, 3259, 3338. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.87 (1H, t, *J*= 7.0 Hz), 6.91-6.95 (3H, m), 7.10-7.18 (4H, m), 7.31 (2H, d, *J*= 8.3 Hz), 7.62 (2H, s), 9.98 (1H, s), 10.64 (2H, s) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 52.93, 102.03, 110.85, 113.14, 115.98, 121.45, 122.59, 124.62, 125.32, 125.99, 126.98, 128.81, 133.79, 139.47, 141.39, 179.39 ppm. Anal. Calcd for $C_{26}H_{15}N_5O$: C, 75.53; H, 3.66; N, 16.94; found: C, 75.55; H, 3.65; N, 16.94.

3,3-di(5-bromo-1*H*-indole-3-yl)indolin-2-one, 6a

White solid, mp 264-266 °C, IR (KBr): ν

Table 1: Ru(III)-exchanged zeolite Y catalyzed condensation of indoles with isatins



Entry[a]	Indole	Product	Time (min.)	Yield[b] (%)
1	Indole	 1a	30	93[c]
2	1-methylindole	 2a	20	98[c]
3	2-methylindole	 3a	25	95
4	3-methylindole	 4a	60	75
5	5-cyanoindole	 5a	45	80
6	5-Bromoindole	 6a	45	82
7	1-methylindole	 2b	15	85
8	5-cyanoindole	 5b	75	60

[a]All products were characterized by ^{1}H NMR, ^{13}C NMR and IR data

[b]Isolated yields

[c]Identified by comparison with authentic samples[16]

Table 2: Reaction of indole and isatin in presence of the recycled catalyst in successive runs

Run	Catalyst loading (%)	Product	Time (min.)	Yield[(a)] (%)
1	10	1a	30	93[b]
2	10	1a	30	93
3	10	1a	30	90
4	10	1a	30	88
5	10	1a	30	85

[a]Isolated yields.
[b]Identified by comparison with authentic samples[16]

(cm^{-1}); 651, 675, 750, 798, 885, 1101, 1463, 1562, 1616, 1712, 3280, 3323, 3427. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.75 (2H, d, *J*= 2.4 Hz), 6.79 (1H, t, *J*= 7.4 Hz), 6.86 (1H, d, *J*= 7.7 Hz), 6.97 (2H, dd, *J*= 8.6, 1.7 Hz), 7.02-7.08 (4H, m), 7.32 (2H, d, *J*= 1.3 Hz), 9.87 (1H, s), 10.12 (2H, s) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 53.65, 110.43, 112.32, 113.51, 114.64, 122.27, 123.65, 124.47, 125.42, 126.29, 127.89, 128.40, 134.26, 136.29, 141.50, 179.64 ppm. Anal. Calcd for $C_{24}H_{15}Br_2N_3O$: C, 55.31; H, 2.90; N, 8.06; found: C, 55.35; H, 2.92; N, 8.05.

1-methyl-3,3-bis(1-methyl-1*H*-indol-3-yl)indolin-2-one, 2b

White solid, mp 232-234 °C, IR (KBr): ν (cm^{-1}); 742, 1014, 1083, 1128, 1157, 1251, 1334, 1371, 1467, 1608, 1714, 2925, 3051. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 3.40 (3H, s), 3.74 (6H, s), 6.92 (2H, s), 6.99 (2H, t, *J*=7.4 Hz), 7. 04 (1H, d, *J*=7.8 Hz), 7.08 (1H, t, *J*=7.5 Hz), 7.21 (2H, t, *J*=7.5 Hz), 7.32 (2H, d, *J*=8.3 Hz), 7.35 (2H, d, *J*=8.1 Hz), 7.38 (1H, t, *J*=7.4 Hz), 7.51 (1H, d, *J*=7.3 Hz) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 27.08, 33.20, 53.19, 108.62, 109.72, 114.17, 119.43, 121.84, 121.96, 123.13, 125.72, 126.89, 128.46, 129.19, 134.74, 138.20, 143.38, 178.30 ppm. Anal. Calcd for $C_{27}H_{23}N_3O$: C, 79.97; H, 5.72; N, 10.36; found: C, 79.95; H, 5.74; N, 10.35.

3,3-di(5-cyano-1*H*-indole-3-yl)-5-cyanoindolin-2-one, 5b

White solid, mp 289-291 °C, IR (KBr): ν (cm^{-1}); 754, 812, 1470, 1618, 1704, 2224, 3259, 3340. ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 6.94 (2H, d, *J*=2.5 Hz), 7.01 (1H, d, *J*=8.3 Hz), 7.18 (2H, dd, *J*=8.3, 1.3 Hz), 7.29 (1H, d, *J*=8.5 Hz), 7.33 (2H, d, *J*=8.3 Hz), 7.53 (1H, s), 7.69 (2H, s), 10.45 (1H, s), 10.78 (2H, s) ppm. ^{13}C NMR (125 MHz, $CDCl_3$, 25 °C): δ = 53.10, 102.13, 110.87, 113.19, 115.98, 121.44, 122.60, 124.68, 125.39, 125.99, 126.98, 128.84, 133.86, 139.47, 141.49, 179.70 ppm. Anal. Calcd for $C_{27}H_{14}N_6O$: C, 73.96; H, 3.22; N, 19.17; found: C, 74.01; H, 3.24; N, 19.17.

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REFERENCES

1. Zhang, H.-C.; Ye, H.; Moretto, A. F.; Brumfield, K. K.; Maryanoff, B. E. *Org. Lett.* **2**: 89 (2000).
2. Gilchrist, T.L. *Heterocyclic Chemistry*; Academic Press: London, 231 (1997).
3. Humphrey, G.R.; Kuethe, J.T. *Chem. Rev.* **106**: 2875 (2006).
4. Popp, F.D. *J. Heterocyc. Chem.* **21**: 1367 (1984).
5. Garrido, F.; Ibanez, J.; Gonalons, E.; Giraldez, A. *Eur. J. Med. Chem.* **10**: 143 (1975).
6. Kamano, Y.; Zhang, H.P.; Ichihara, Y.; Kizu, H.; Komiyama, K.; Itokawa, H.; Pettit, G.R. *Tetrahedron Lett.* **36**: 2783 (1995).
7. Bergman, J.; Eklund, N. *Tetrahedron* **36**: 1445 (1980).
8. Azizian, J.; Mohammadi, A.A.; Karimi, N.;

Mohammadizadeh, M.R.; Karimi, A.R. *Catalysis Communications* **7**: 752 (2006).
9. Azizian, J.; Mohammadi, A.A.; Karimi, A.R.; .; Mohammadizadeh, M.R. *J. Chem. Res. Synop.* **6**: 424 (2004).
10. Yadav, S.S.; Subbareddy, B.V.; Kamakolanu, U. G. *Synthesis* **24**: 4121 (2006).
11. Tabatabaeian, K.; Mamaghani, M.; Mahmoodi, N. O.; Khorshidi, *A. Can. J. Chem.* **84**: 1541 (2006).
12. Tabatabaeian, K.; Mamaghani, M.; Mahmoodi, N. O.; Khorshidi, A. *J. Mol. Catal. A* **270**: 112 (2007).
13. Tabatabaeian, K.; Mamaghani, M.; Mahmoodi, N. O.; Khorshidi, A. *Tetrahedron Lett.* **49**: 1450 (2008).
14. Tabatabaeian, K.; Mamaghani, M.; Mahmoodi, N. O.; Khorshidi, A. *Can. J. Chem.* **87**: 1213 (2009).
15. Tabatabaeian, K.; Mahmoodi, N.O.; Ghoraninia, M.; Khorshidi, A.; *Orient. J. Chem.* **24**(1): 101 (2008).
16. Bowen, K.; Qin, Y.; He, Q.; Huang, Z.; Wang, F. *Tetrahedron Lett* **46**: 1751 (2005).