Article

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Efficient Synthesis of 3,3′-diaryloxindoles Catalyzed by L-prolinate Anion Immobilized onto Amberlite as a Novel Heterogeneous Organocatalyst

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L-prolinate anion immobilized onto amberlite IRA900OH ([Amb]L-Prolinate) is reported as a new, reusable and cheap organocatalyst for the condensation of indoles with isatins to afford the corresponding 3,3′-diaryloxindol derivatives in ethanol under reflux condition. [Amb]L-Prolinate was achieved by the treatment of a MeOH/H_2O solution of L-proline with amberlite IRA900OH at 60 °C. The procedure for heterogenization of L-proline organocatalyst is based on non-covalent ion-pair immobilization of L-proline on the surface of anion-exchange resin amberlite IRA900OH (AmbIRA900OH) as a commercially accessible cationic polymer support. The prepared heterogeneous organocatalyst was well characterized by using of FTIR, TGA, DTG, XRD and elemental analysis techniques. The catalytic activity of the catalyst was also examined in the reaction of indole and isatin. The catalyst has been recovered and its reusability confirmed in 8 runs.

Keywords: L-proline; Anion-exchange resin; Organocatalyst; 3,3′-Diaryloxindole; Heterogeneous Catalyst.

INTRODUCTION

The past decade has witnessed a renaissance of organocatalysis in the field of asymmetric catalysis[1] and has developed into a practical synthetic paradigm since its genesis nearly 30 years ago.[2] Several advantages such as cost-effectiveness and wide range of synthetic application justify the use of organocatalysis. The absence of metal in organocatalyst brings an undeniable advantage considering both the principles of "green chemistry" and the economic point of view.[3] At the same time immobilization and recycling of organocatalysts has experienced a very good growth.[4,5] Actually, organocatalytic methods often require catalyst loadings as high as 30 mol% for the achievement of high conversions in reasonable reaction times. This is the main reason for the need of an efficient immobilization and recycling procedure. Moreover, immobilization of anorganocatalyst may enhance its activity and stereoselectivity.[6]

One of the efficient methods for the heterogenizing an organic molecule is its immobilization onto solid supports. The immobilization of organocatalysts can be achieved through both covalent and noncovalent bonding which lead to (i) the formation of covalent bond between catalyst and substrate, and (ii) the procedures that designed on the base of noncovalent interactions such as hydrogen bonding or ions pair intractions. One of the most important challenges with catalyst immobilization is to retain the activity and stereoselectivity of the immobilized catalysts. Moreover, another important aspect of immobilized catalysts is the separation, which should be achieved by a simple operation such as filtration.[8] The proline catalyzed Robinson annulation was one of the earliest examples of an enantioselective reaction using an organic catalyst.[9]

In recent years, trials are being made by using amino acids, especially L-proline and proline-derivatives to catalyze essential transformations in the fine chemical and pharmaceutical industries. The interest in this field has thus increased spectacularly in the last few years.[10] It is noticeable that the immobilization methods for the heterogenization of L-proline require the use of synthetic materials that are more expensive than proline or need tedious experimental methods. L-proline is commercially available at low cost but often employed at high catalyst loading. Nevertheless, efforts of improving or modifying its catalytic activities, taking advantage of particular properties of

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the support, would rationalize the immobilization in many cases.[11]

Oxindoles are known to show biological and pharmacological activities.[12-14] Particularly, 3,3′-diaryloxindole moiety is an integral common structural motif of many natural products, clinical drugs and biologically active compounds and is known to possess anticonvulsant, antibacterial, anti-inflammatory, antiprotozoal and mechanism-specific anti proliferative properties.[15,16] The various biological activities of oxindole derivatives have attracted the attention of many synthetic chemists.[17,18] Therefore, considerable efforts have been made to synthesize analogues of 3,3′-di(indolyl)oxindole derivatives, which were prepared by the reaction of isatin and indoles using various catalysts. The reported procedures consist of using catalysts such as nano-SiO_2/TiO_2,[19] SAMSNs,[20] $LiClO_4$,[21] Sulfamic acid,[22] p-TSA,[23] boron trifluoride supported on nano-SiO_2,[24] CSA,[25] proliniumtriflate (ProTf),[26] I_2,[27,28] Amberlyst-15,[29] $ZrCl_4$,[30] $Cu(OTf)_2$,[31] $FeCl_3$,[32] KSF,[33] ionic liquids,[34-36] β-cyclo-dextrin,[37] $H_6P_2W_{18}O_{62}$,[38] $Bi(OTf)_3$,[39] silica sulfuric acid (SSA),[40] ceric ammonium nitrate (CAN),[41] montmorillonite-K10 clay[42] and $KAl(SO_4)_2.12H_2O$.[43]

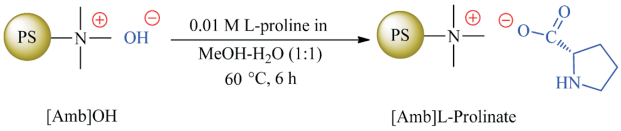
However, most of the methods are flawed by aspects such as unsatisfactory yield, prolonged reaction time, inconvenient availability of reagent, toxic solvents and expensive catalysts. Hence, there is a need to develop eco-safe methodology for the synthesis of oxindoles. Considering the significance of all above discussed aspects and in continuation of our interest in the applications of ion-exchange resins for click synthesis of 1,4-disubstituted-1*H*-1,2,3-triazoles,[44,45] we decided to explore the catalytic activity of the ion-exchange resin amberlite IRA900OH (AmbIRA900OH) as a cationic polymer support for the ion-pair immobilization of L-proline anion via ionic interaction between carboxylate group of L-prolinate and quaternary ammonium cation of the cationic Amb support. This heterogeneous catalyst was used as an efficient, reusability, cheap and commercially accessible catalyst for the one-pot three-component synthesis of 3,3′-diaryloxindol derivatives in ethanol.

RESULTS AND DISCUSSION

Catalyst preparation

The procedure followed to obtain the ion–pair immobilization of L-prolinate anion on the cationic polymer resin is outlined in Scheme 1. The strategy consists of building up suitable heterogeneous macroporous polymer-supported L-prolinate catalyst on the surface of commercially available amberlite IRA-900OH (mesh 16–50). Preparation of the heterogeneous polymer-supported L-prolinate catalyst by this procedure is facile and straightforward. In a typically procedure AmbIRA900OH was treated with a solution of 0.01 M L-proline at 60 °C to achieve [Amb]L-prolinate hybrid.

Scheme 1 Preparation of [Amb]L-prolinate hybrid



[Amb]OH [Amb]L-Prolinate

Characterization of [Amb]L-prolinate catalyst

IR spectra

The ion–pair immobilization of L-prolinate anion on the polymer resin can be confirmed by characterizing the pure AmbIRA900OH, pristine L-proline and [Amb]L-prolinate hybrid using FT-IR spectroscopy, as shown in Figure 1. The FT-IR spectrum of pristine L-proline shows characteristic stretching frequencies include: N-H asymmetric stretching at 3056 cm^{-1} and carboxylate (COO^-) asymmetric and symmetric stretching at 1622 and 1380 cm^{-1}, respectively (Figure 1a). These bands are observed as new peaks in the FT-IR spectrum of [Amb]L-prolinate hybrid when compared with the FT-IR spectrum of pure AmbIRA900OH (Figure 1b vs. a). The carboxylate (COO^-) asymmetric and symmetric stretching are presented in [Amb]L-prolinate and found to shift to lower positions at 1615 and 1375 cm^{-1}respectively (Figure 1b). In addition, the band at 3056 cm^{-1} corresponding to the asymmetric

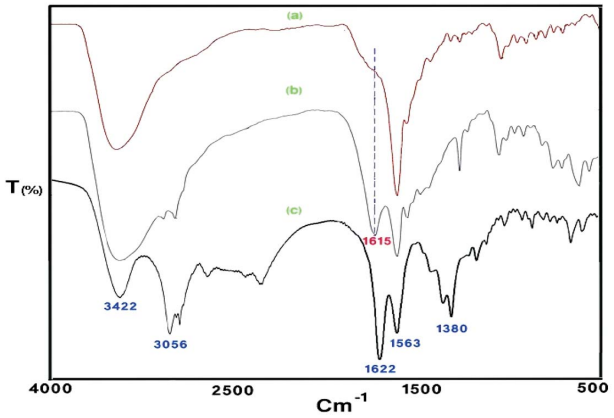


Fig. 1. FT-IR spectrum of [Amb]OH (a), [Amb]L-prolinate (b) and pristine L-proline (c).

stretching vibration of the N-H group in L-proline is also found at 3056 cm^{-1} in FT-IR spectrum of [Amb]L-prolinate. All the results from the comparison of FT-IR spectra encourage us to anticipate that the L-prolinate anion successfully loaded onto the polymer surface through ionic interaction using ion-pair binding between carboxylate group of L-prolinate and quaternary ammonium cation of the cationic Amb support.

TGA and DTG analysis

Thermogravimetric analysis (TGA) and differential thermal analysis (DTG) associated with the decomposition profiles of the AmbIRA900OH, pristine L-proline and [Amb]L-prolinate hybrid under a nitrogen atmosphere provide further evidence for the immobilization of L-prolinate anion onto the polymer surface (Figure 2 and Figure 3). The 100% weight loss of pristine L-proline appears at 215-250 °C on the base of its TGA and DTG curves and assigned to the successive cleavage of the L-proline at this interval (Figure 2c and 3c).The TGA curve of pure AmbIRA900OH shows three weight loss step intervals at 65-100 °C, 150-250 °C and 370-470 °C. The first weight loss interval at 65-100 °C is most probably due to a loss of adsorbed water (weight loss = ca. 11 wt.%). The second weight loss interval at 150-250 °C presumably assigned to the loss of some functional groups (weight loss = ca. 19wt.%) and finally the third weight loss interval at 370-470 °C (weight loss = ca. 34 wt.%) could presumably assigned to partial polymer decomposition (Figure 2b). Figure 3b displays the DTG curve of AmbIRA900OH and is in accordance with the weight loss steps from its TGA curve. The TGA curve of [Amb]L-prolinate hybrid displays four weight loss steps include: 60-100 °C,150-250 °C, 250-370 °C and 370-470 °C intervals (Figure 2a). These four weight loss peaks are well distinguished in the corresponding DTG curve (Figure 3a).

Obviously, in comparison with AmbIRA900OH, a new decomposition interval is observed in TGA and DTG curves of [Amb]L-prolinate hybrid (weight loss = ca. 15 wt.%). This weight loss is assigned to the successive cleavage of L-prolinate anion loaded on the surface of the polymer and also referred to the content of L-prolinate moiety on the Amb-cationic support. The calculation from TG curve was indicated that 1.3 mmol of L-prolinate organocatalyst is loaded per 1 g of the [Amb]L-prolinate hybrid. It is noticeable that the decomposition temperature of L-prolinate anion in [Amb]L-prolinate hybrid has been increased to 250-370 °C in comparison with the decomposition temperature of pristine L-proline (215-250 °C). These observations mean that the thermal stability of the L-prolinate has been increased in comparison with the pristine L-proline and also explain the carboxylate asymmetric and symmetric stretching shifts to lower positions in FT-IR spectrum of [Amb]L-prolinate hybrid (Figure 1b).

The increased decomposition temperature of the L-prolinate suggests that the guest/host interaction was done through the ion-pair exchanges between hydroxyl and L-prolinate anions on the surface of ion-exchange resin and is an indirect proof for the presence of ion-pair interaction between L-prolinate anions and quaternary ammonium cations on the surface of cationic support (Fig. 3a vs. c). The high loading of L-prolinate on the surface of Amb (15 wt.%), together with the unique ion-pair binding behaviors between L-prolinate and Amb-cation, makes the [Amb]L-prolinate hybrid efficient and stable in the reaction system.

XRD

The crystalline nature of [Amb]L-prolinate hybrid

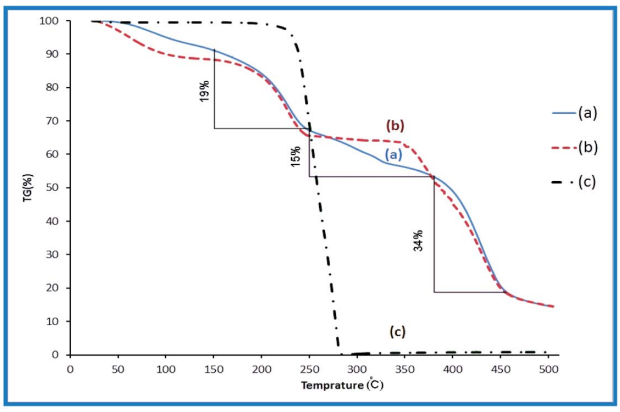


Fig. 2. TGA curve of [Amb]L-prolinate (a), [Amb]OH (b) and pristine L-proline (c).

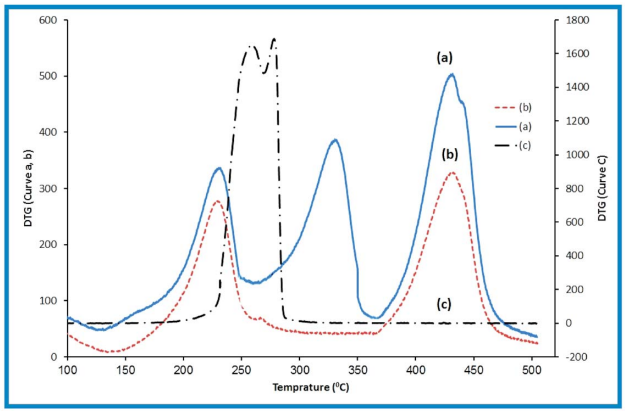


Fig. 3. DTA curve of [Amb]L-prolinate (a), [Amb]OH (b) and pristine L-proline (c).

confirms that L-prolinate is non-conveniently supported on cationic polymer support *via* ion-pair immobilization. The main intense diffraction peaks of pristine L-proline based on the standard spectrum (Figure 4a) are observed in the XRD pattern of [Amb]L-prolinate hybrid due to the presence of the L-prolinate on the Amb support thanks to a favorable ion-pair binding with quaternary ammonium cations of the ion-exchange resin (Figure 4b vs. a). This technique gives robustness to the catalytic system and on the other hand lets the L-prolinate organocatalyst to be flexible, mobile and free on the surface of the polymer at the same time. Moreover, the thermal stability of organocatalyst has been improved by this way. These mentioned advantages are characteristic properties of homogeneous and heterogeneous catalysts which have been included in [Amb]L-prolinate hybrid.

Optimization of the reaction conditions

After preparation and characterization of [Amb]L-prolinate catalyst, its catalytic activity was investigated in a reaction for the synthesis of 3,3′-diaryloxindol derivatives. To optimize the reaction conditions, the reaction of indole and isatin was selected as the model reaction to examine the effect of [Amb]L-prolinate catalyst (2-15 mol%) under a variety of conditions (Table 1).

The present optimization studies revealed that the best result was achieved by caring out the reaction in the presence of 10 mol % of [Amb]L-prolinate under reflux condition in ethanol (Table 1, entry 9). The yield smoothly increased with the catalyst load up to 10 mol% and use of larger amounts of the catalyst (15 mol%) did not improve the yield while decreasing the amount of the catalyst led to decreased yield. Using the optimized conditions, the reaction of indole derivatives and isatin derivatives was explored with using 10 mol% of [Amb]L-prolinate under reflux condition in ethanol (Scheme 2, Table 2). All the products were cleanly isolated with simple filtration and recrystallization from hot ethanol. As Table 2 shows, in all the cases, indoles and isatins substituted with either electron-donating or electron-withdrawing groups smoothly underwent the reaction and gave the target products in good to excellent yields (3a-v).

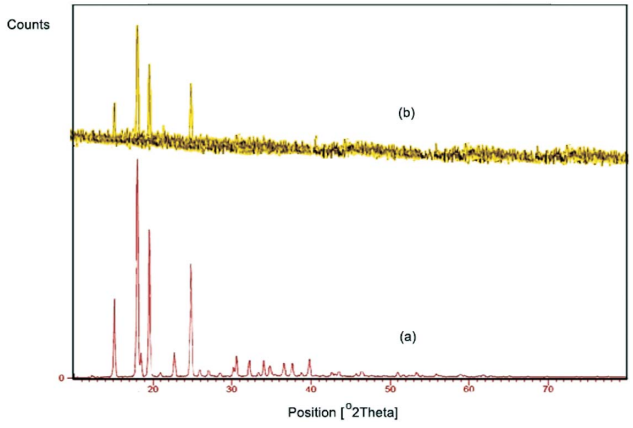
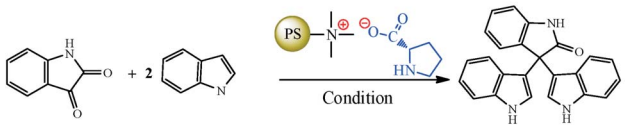


Fig. 4. XRD pattern of pristine L-proline (a) and [Amb]L-prolinate (b).

On the basis of forgoing results, we proposed a plausible mechanism to explain the formation of 3 from isatin (1) and indole (2) using [Amb]L-prolinate as catalyst. Initially, 1 reacts with L-prolinate anion of catalyst to form an iminium carboxylate (I). Then, L-prolinate anion abstracts a proton from the indole to form the intermediate indolyl anion (II). In the next step, Michael addition of indolyl anion (II) to the iminium carboxylate (I) furnishes intermediate III. Reaction of another mole of indole with III, results in the formation of final product **3** (Scheme 3).

The recovery and reuse of a catalyst is highly prefera-

Table 1. Investigation of catalytic activity of [Amb]L-prolinatefor the synthesis of 3,3′-diaryloxindol3a under various conditions



Entry	Conditions	Temperature (°C)	[Amb]L-prolinate	Time (min)	Yield (%)[a]
1	neat	100	2	55	55
2	CH_2Cl_2	reflux	2	50	60
3	CH_3CN	reflux	2	45	65
4	THF	65	2	50	60
5	DMF	100	2	40	68
6	H_2O/DMF	100	5	30	75
7	H_2O	reflux	5	35	80
8	CH_3CH_2OH	reflux	5	25	90
9	CH_3CH_2OH	reflux	10	10	98
10	CH_3CH_2OH	reflux	15	15	98

[a] Yield refer to isolated and pure product.

Scheme 2 Synthesis of 3,3′-diaryloxindol derivatives catalyzed by [Amb]L-prolinate

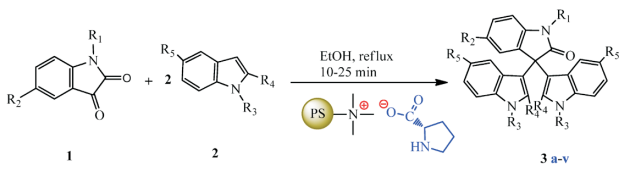
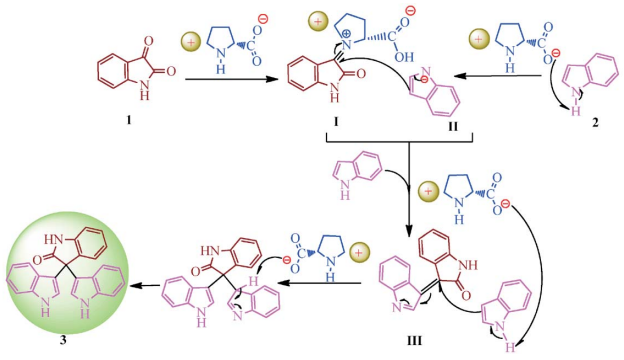


Table 2. Synthesis of 3, 3′-diaryloxindol derivatives (3a-v) catalyzed by [Amb]L-prolinate

Entry	1	2	Produt	Time (min)	Yield (%)[a]	m.p. (°C)	
						Found	Reported
1	R_1=R_2=H	R_3=R_4=R_5=H	**3a**	10	98	312-314	> 300 [21]
2	R_1=Me, R_2=H	R_3=R_4=R_5=H	**3b**	15	89	291-293	291–293 [37]
3	R_1=H, R_2=F	R_3=H, R_4=H, R_5=Br	**3c**	10	81	298-304	-
4	R_1=H, R_2=OMe	R_3=R_4=R_5=H	**3d**	15	98	-	-
5	R_1=H, R_2= NO_2	R_3=H, R_4=Me, R_5=H	**3e**	10	96	288-300	-
6	R_1=H, R_2=OMe	R_3=H, R_4=Me, R_5=H	**3f**	8	86	286-290	-
7	R_1=H, R_2=H	R_3=H, R_4=H, R_5=Br	**3g**	10	82	301-303	298–300 [33]
8	R_1=H, R_2=F	R_3=R_4=R_5=H	**3h**	15	84	298-304	> 250 [36]
9	R_1=H, R_2=F	R_3=H, R_4=Me, R_5=H	**3i**	8	83	234-236	-
10	R_1=Me, R_2=H	R_3=H, R_4=Me, R_5=H	**3j**	15	89	287-289	271–273 [34]
11	R_1=H, R_2=H	R_3=Me, R_4=H, R_5=H	**3k**	15	83	300-303	298-300 [21]
12	R_1=H, R_2=Cl	R_3=Me, R_4=H, R_5=H	**3l**	10	84	302-305	298-300 [21]
13	R_1=H, R_2=H	R_3=H, R_4=Me, R_5=H	**3m**	15	99	289-291	297-299 [21]
14	R_1=H, R_2=Cl	R_3=R_4=R_5=H	**3n**	15	79	296-298	> 300 [21]
15	R_1=H, R_2=NO_2	R_3=R_4=R_5=H	**3o**	5	97	293-295	298–299 [39]
16	R_1=H, R_2=Cl	R_3=H, R_4=H, R_5=Br	**3p**	8	89	300-303	> 300 [33]
17	R_1=H, R_2=NO_2	R_3=H, R_4=H, R_5=Br	**3q**	5	85	299-301	-
18	R_1=H, R_2=OMe	R_3=H, R_4=H, R_5=Br	**3r**	10	82	300-305	-
19	R_1=Me, R_2=H	R_3=H, R_4=H, R_5=Br	**3s**	10	81	304-306	-
20	R_1=H, R_2=OMe	R_3=Me, R_4=H, R_5=H	**3t**	9	82	291-293	-
21	R_1=H, R_2=F	R_3=Me, R_4=H, R_5=H	**3u**	15	80	298-300	-
22	R_1=H, R_2=Br	R_3=R_4=R_5=H	**3v**	10	94	309-311	309–310 [29]

[a] Yield refer to pure and separated products.

Scheme 3 Plausible mechanism for the formation of 3 from 1 and 2



ble for a greener process. For this purpose, the reusability of [Amb]L-prolinate was examined up to eight consecutive cycles (fresh + seven cycles) for the synthesis of 3,3′-diaryloxindol 3a. From Figure 5, It can be seen that [Amb]L-prolinate can be reused up to 8 runs without need to reload and the yield difference between the first and 8th runs is only 5% which indicated that the catalyst efficiency is almost completely maintained during 8 consecutive runs. The nitrogen content of the fresh and reused catalyst was measured by using of elemental analysis and the comparison of the nitrogen contents indicated that the catalyst lost only 4% of its nitrogen content after 8 runs. This is a good proof for very low leaching account of L-proline organocatalyst from [Amb]L-prolinate catalyst into the reaction mixture during 8 runs and also confirms that the catalytic

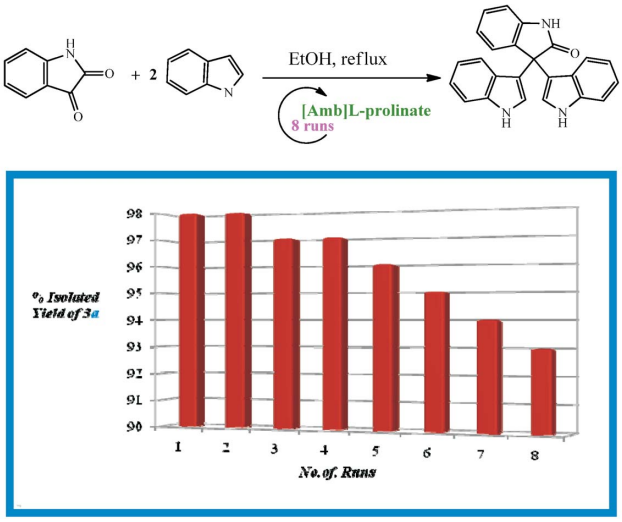


Fig. 5. Recycling of [Amb]L-prolinate for the synthesis of 3a.

ability of [Amb]L-prolinate almost completely has been remained stable after 8 runs in agreement with the recyclability study.

In addition, to show the efficiency of this method in comparison with other reported procedures, we selected the reaction of indole and isatin for the synthesis of 3,3′-di(1H-indol-3-yl)indolin-2-one 3a as a representative model. The reaction catalyzed by [Amb]L-prolinate is superior, compared to literature data, with respect to the catalyst, yield and reaction times. As shown in Table 3, our procedure gave the best yield and requires less time than other protocols.

CONCLUSIONS

We have developed a simple and highly efficient method for the preparation of of 3,3′-diaryloxindoles from indoles and isatins using 10 mol% of L-prolinate-amberlite ([Amb]L-Prolinate) as a new heterogeneous organocatalyst in ethanol under reflux condition. The non-covalent immobilization strategy was used for the heterogenization of L-proline *via* ion-pair immobilization on the surface of amberlite hydroxide. This methodology made the organocatalyst to be mobile and flexible which not only helped the supported catalyst to be as powerful as its non-supported form, but also made it to be easily recoverable with simple filtration. The method offers several advantages including high yield of products, short reaction time, recyclability of the catalyst, and easy experimental work-up procedure.

EXPERIMENTAL

^{1}H NMR spectra of samples were recorded at a Bruker Advanced DPX 400-MHz spectrometer. X-ray diffraction (XRD) patterns were recorded on a Philips X'PERT-Pro-MPD diffractometer using Cu Ka radiation (k = 1.542 Å). A continuous scan mode was used to collect 2 h from 5 to 40. Fourier transform infrared (FT-IR) spectra were obtained as potassium bromide pellets in the range400–4000 cm^{-1} using an AVATAR 370 Thermo Nicolet spectrophotometer. Elemental analyses (C, H, and N) were performed with a Heraeus CHN-O-Rapid analyzer. The thermogravimetric and differential thermogravimetric (TG–DTG) analysis was performed on Netsch STA449c. The sample weight was *ca*. 10 mgand was heated from room temperature up to 600 °C with 10 °C/min using alumina sample holders.

Preparation of the[Amb]L-Prolinate catalyst: Amberlite IRA-900OH (mesh 16–50, 1 g) was suspended in 10mL of a 1M solutionof L-proline in MeOH:H_2O (1:1). The system was heated at 60 °C for 6 h. The filtration of the reaction mixture followed by washing with MeOH:H_2O (1:1) (2 × 10 mL) and H_2O (2 × 10 mL) afforded [Amb]L-Prolinate catalyst. The prepared catalyst was collected and dried under vacuum

General procedure for the [Amb]L-Prolinate catalyzed synthesis of 3,3'-Diaryloxindol derivatives: Indole (2 mmol) and isatin (1 mmol), were placed together in a round-bottom flask containing 5 mL of EtOH. [Amb]L-Prolinate catalyst (0.08 g, 10 mol%), was added to the mixture. The suspension was magnetically stirred at reflux condition for appropriate time according to (Table 2). After completion of the reaction as followed by TLC (n-hexane: ethyl acetate; 3:1), the catalyst was filtered and washed with hot ethanol (2 × 5 mL). The recovered catalyst was washed with acetone, dried and stored for other similar consecutive runs. The filtrate mixture was recrystallized to provide the

Table 3. Comparison of the catalytic efficiency of [Amb]L-prolinate with various catalysts reported for the synthesis of 3a

Ref	Yield (%)	Time (min)	Conditions	Catalysts	Entry
This work	98	10	EtOH/reflux	[Amb]L-prolinate (10 mol%)	**1**
[32]	98	15	MeCN/r.t (sonication)	$FeCl_3$	**2**
[29]	94	30	H_2O/70 °C	Amberlyst-15	**3**
[35]	93	60	r.t	Ionic liquid	**4**
[40]	94	120	DCM/RT	Silica sulfuric acid	**5**
[41]	95	180	EtOH/RT (sonication)	CAN	**6**
[38]	95	30	H_2O/60 °C	Heteropolyacid	**7**
[20]	98	10	H_2O/60 °C	SAMSNs	**8**
[21]	93	240	EtOH/60 °C	$LiClO_4$ (20 mol%)	**9**
[23]	92	20	CH_2Cl_2/ r.t	p-TSA (10 mol%)	**10**
[22]	89	120	EtOH: H_2O (1:1 v/v)/r.t	Sulfamic acid (20 mol%)	**11**
[19]	85	30	solvent-free/50 °C	Nano TiO2/SiO_2 (0.04 g)	**12**
[33]	90	25	EtOH/reflux	KSF	**13**
[24]	95	20	CH_3OH/r.t	Nano-SiO_2–BF_3-CH_3OH	**14**

pure crystals of 3,3′-diaryloxindol derivatives. The products are known compounds and are characterized by IR and NMR spectroscopy data for new compounds. Their melting points are compared with reported values.[19-43]

Selected spectroscopic data: 5-Methoxy-3,3′-di(1*H*-indol-3-yl)indolin-2-one (3d) (R_1=H, R_2=OMe, R_3=R_4=R_5=H): IR (KBr): 3350 (-NH), 1680 cm-1 (-C=O), 1200 cm-1 (C-O); ^{1}H NMR (DMSO, 400 MHz): δ = 3.618 (s, 3H, OCH_3), 6.80-6.81 (m, 3H,Ar-H), 6.83 (d, *J* = 2.8 Hz, 1H, Ar-H), 6.89 (d, *J* = 2.4 Hz, 2H, Ar-H), 6.91-6.93 (m, 1H, Ar-H), 7.02 (t, *J* = 7.6 Hz, 2H, Ar-H), 7.25 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.36 (d, *J* = 7.6 Hz, 2H, Ar-H), 10.45 (s, 1H, amidic NH), 10.96 (s, 2H, NH). ^{13}CNMR (DMSO, 400 MHz): δ = 179.1 (C=O), 155.1, 137.4, 136.4, 135.2, 126.1, 124.8, 121.4, 121.2, 118.7, 114.7, 112.6, 112.5,112.1, 110.3, 56.5 (O–CH_3), 53.5 (C-3) ppm. **5-Methoxy-3,3′-di(2-methyl-1*H*-indol-3-yl)indolin-2-one(3f)** (R_1=H, R_2=OMe, R_3=H, R_4=Me, R_5=H): mp 286-290 °C; ^{1}H NMR (DMSO, 400 MHz): δ = 1.96 (s, 3H, CH_3), 2.11 (s, 3H, CH_3), 3.58 (s, 3H, OCH_3), 6.51(d, *J* =8 Hz, 1H, Ar-H), 6.65 (q, *J* = 8 Hz, 2H, Ar-H), 6.76(d, *J* = 7.2 Hz, 2H, Ar-H), 6.80-6.83 (m, 1H, Ar-H), 6.88-6.99 (m, 3H, Ar-H), 7.23-728 (m, 2H, Ar-H), 10.40 (s, 1H, amidic NH), 10.87 (s, 2H, NH) ppm. ^{13}CNMR (DMSO, 400 MHz): δ = 179.6 (C=O), 155.0, 137.4, 135.4, 135.2, 134.4, 132.4, 127.8, 119.5, 118.6, 114.1, 113.3, 112.4,110.4, 99.5, 55.84 (O–CH_3), 53.34 (C-3), 13.7 (CH_3) ppm. **5-Methoxy-3,3′-di(5-bromo-1*H*-indol-3-yl)indolin-2-one (3r)** (R_1=H, R_2=OMe, R_3=H, R_4=H, R_5=Br): mp 300-305 °C; ^{1}H NMR (DMSO, 400 MHz): δ = 3.38 (s, 3H, OCH_3), 7.07 (s, 1H, Ar-H), 7.22 (dd, J_1 = 8.4 Hz, J_2 = 8.8 Hz 3H), 7.37-7.41 (m, 4H, Ar-H), 7.96 (s, 1H, Ar-H), 8.27 (d, *J* = 7.6 Hz, 2H, Ar-H), 11.38 (s, 2H, NH), 11.48 (s, 1H, amidic NH) ppm. ^{13}CNMR (DMSO, 400 MHz): δ = 179.1 (C=O), 1148.0, 143.0, 136.3, 134.7, 127.4, 126.9, 126.2, 124.4, 122.7, 120.7, 114.6, 112.8, 111.8, 110.6, 101.2 (O–CH_3), 53.6 (C-3) ppm. **1-methyl-3,3-di(5-bromo-1H-indol-3-yl)indolin-2-one (3s)** (R_1=Me, R_2=H, R_3=H, R_4=H, R_5=Br): mp 304-306 °C; ^{1}H NMR (DMSO, 400 MHz): δ = 3.7 (3H, s, -NCH_3), 6.75 (s, 1H, Ar-H), 6.87 (d, *J* = 6.8 Hz 1H, Ar-H), 6.96 (s, 3H, Ar-H), 7.18 (d, *J* = 8.0 Hz, 2H, Ar-H), 7.38 (d, *J* = 12.8 Hz, 4H, Ar-H), 10.60 (s, 1H, amidic NH), 11.30 (s, 2H, NH) ppm. ^{13}CNMR (DMSO, 400 MHz): δ = 178.8 (C=O), 155.3, 136.2, 135.2, 127.5, 126.6,124.0, 123.1,122.6, 114.3, 113.8, 113.1, 112.4, 111.1, 101.2, 55.8 (C-3), 53.1 (-NCH_3) ppm. **5-Methoxy-3,3′-di(1-methyl-1H-indol-3-yl)indolin-2-one(3t)** (R_1=H, R_2=OMe, R_3=Me, R_4=H, R_5=H): mp 291-293 °C; ^{1}H NMR (DMSO, 400 MHz): δ = 3.37 (s, 3H, OCH_3), 3.7(s, 6H, 2 × -CH_3), 6.84-6.88 (m, 4H, Ar-H), 6.93 (s, 3H, Ar-H), 7.11 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.27 (d, *J* = 7.6 Hz, 2H, Ar-H), 7.39 (d, *J* = 8.0 Hz, 2H, Ar-H), 10.48 (s, 1H, amidic NH) ppm. ^{13}CNMR (DMSO, 400 MHz): δ = 179.0 (C=O), 155.2, 137.9, 136.3, 135.1, 129.0, 126.5, 121.6,121.5, 119.0, 114.0, 112.7,110.4, 110.2, 55.7 (O–CH_3), 53.4 (C-3), 32.8 (CH_3) ppm. **5-Fluoro-3,3′-di(1-methyl-1H-indol-3-yl)indolin-2-one(3u)** (R_1=H, R_2=F, R_3=Me, R_4=H, R_5=H): mp 298-300 °C (Lit[22] mp: > 300 °C); ^{1}H NMR (DMSO, 400 MHz): δ = 3.77 (s, 6H, 2 × -CH_3), 6.89 (d, *J* = 6.8 Hz, 2H, Ar-H), 6.96-7.01 (m, 3H, Ar-H), 7.10 (d, *J* = 8.0 Hz, 4H, Ar-H), 7.26 (d, *J* = 7.2 Hz, 2H, Ar-H), 7.40(d, *J* = 7.6 Hz, 2H, Ar-H), 10.7 (s, 1H, amidic) ppm. ^{13}CNMR (DMSO, 400 MHz): δ = 179.0 (C=O), 159.6, 157.21, 137.9, 136.7, 129.1, 126.4, 121.7, 121.3, 119.0, 114.8, 113.3, 113.0, 110.9, 110.3, 53.4 (C-3), 32.8 (CH_3) ppm.

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REFERENCES

1. Berkessel, A.; Gröger, H. *Asymmetric Organocatalysis: From Biomimetic Concepts to Applications in Asymmetric Synthesis*; Wiley-VCH: Weinheim, Germany, 2005.
2. Hajos, Z. G.; Parrish, D. R. *J. Org. Chem*. **1974**, *39*, 1615.
3. Rajjak, I. J. *Catal*. **2014**, *2014*, 1-35.
4. Gruttadauria, M.; Giacalone, F.; Noto, R. *Chem. Soc. Rev.* **2008**, *37*, 1666.
5. Cozzi, F. *Adv. Synth. Catal*. **2006**, *348*, 1367.
6. Gruttadauria, M.; Giacalone, F.; Mossuto Marculescu, A.; Salvo, A. M. P.; Noto, R. *ARKIVOC* **2009**, *viii*, 5-15.
7. Zhang, L.; Luo, S.; Cheng, J.-P. *Catal. Sci. Technol*. **2011**, *1*, 507-516.
8. Trindade, A. F.; Gois, P. M. P.; Afonso, C. A. M. *Chem. Rev.* **2009**, *109*, 418-514.
9. Yamada, S.-I.; Otani, G. *Tetrahedron Lett*. **1969**, *10*, 4237-4240.
10. Martín-Rapún, R.; Fan, X.; Sayalero, S.; Bahramnejad, M.; Cuevas, F.; Pericàs, M. A. *Chem. Eur. J.* **2011**, *17*, 8780-8783.
11. Jimeno, C.; Sayalero, S.; Pericàs, M. A. In *Heterogenized Homogeneous Catalysts for Fine Chemicals*; Barbaro, P.; Liguori, F.; Eds.; Springer: New York, 2010; Chapter 4, pp 123-170.
12. Bolotov, V. V.; Drugovina, V. V.; Yakovleva, L. V.; Bereznyakova, A. I. *Khim.-Farm. Zh.* **1982**, *16*, 58-61.
13. Pajouhesh, H.; Parsons, R.; Popp, F. D. *J. Pharm. Sci*. **1983**, *72*, 318-321.
14. Marti, C.; Carreira, E. M. *Eur. J. Org. Chem*. **2003**, *63*, 2209-2219.
15. Joshi, K. C.; Pathak, V. N.; Jain, S. K. *Pharmazie* **1980**, *35*, 677.
16. Pope, F. D. *J. Heterocycl. Chem*. **1984**, *21*, 1641-1645.
17. Klumpp, D. A.; Yeung, K. Y.; Prakash, G. K. S.; Olah, G. A.

J. Org. Chem. **1998**, *63*, 4481-4484.
18. Jursic, B.; Stevens, E. D. *Tetrahedron Lett*. **2002**, *43*, 5681-5683.
19. Haghighi, M.; Nikoofar, K. *J. Saudi Chem. Soc*. **2014**, In Press.
20. Mehrasbi, E.; Sarrafi, Y.; Tajbakhsh, M. *Res. Chem. Intermed*. **2015**, *41*, 6777-6787.
21. Rad-Moghadam, K.; Gholizadeh, S. *Iran. J. Catal.* **2014**, *4*, 41-47.
22. Brahmachari, G.; Banerjee. *ACS Sustain. Chem. Eng*. **2014**, *2*, 411-422.
23. Yu, J.; Shen, T.; Lin, Y.; Zhou, Y.; Song, Q. *Synth. Commun.* **2014**, *44*, 2029-2036.
24. Saffar-Teluri, A. *Res. Chem. Intermed*. **2014**, *40*, 1061-1067.
25. Alinezhad, H.; Haghighi, A.; Salehian, F. *Chin. Chem. Lett.* **2010**, *21*, 83-186. Shiri, M. *J. Iran. Chem. Soc.* **2013**, *10*, 1019-1023.
26. Shiri, M. *J. Iran. Chem. Soc*. **2013**, *10*, 1019-1023.
27. Paira, P.; Hazra, A.; Kumar, S.; Paira, R.; Sahu, K. B.; Naskar, S.; Saha, P.; Mondal, S.; Maity, A.; Banerjee, S.; Mondal, N. B. *Med. Chem. Lett*. **2009**, *19*, 4786-4789.
28. Reddy, B. V. S.; Rajeswari, N.; Sarangapani, M.; Prashanthi, Y.; Ganji, R. J.; Addlagatta, A. *Bioorg. Med. Chem. Lett.* **2012**, *22*, 2460-2463.
29. Sarrafi, Y.; Alimohammadi, K.; Sadatshahabi, M.; Norozipoor, N. *Monatsh. Chem*. **2012**, *143*, 1519-1522.
30. Jafarpour, M.; Rezaeifard, A.; Gazkar, S.; Danehchin, M. *Transit. Met. Chem*. **2011**, *36*, 685-690.
31. Praveen, C.; Ayyanar, A.; Perumal, P. T. *Bioorg. Med. Chem. Lett.* **2011**, *21*, 4072-4077.
32. Kamal, A.; Srikanth, Y. V. V.; Khan, N. A.; Shaik, T. B.; Ashraf, M. *Bioorg. Med. Chem. Lett*. **2010**, *20*, 5229-5231.
33. Nikpasand, M.; Mamaghani, M.; Tabatabaeian, Kh.; Samimi, H. A. *Synth. Commun*. **2010**, *40*, 3552-3560.
34. Karimi, N.; Oskooi, H.; Heravi, M. M.; Saeedi, M.; Zakeri, M.; Tavakoli, *N. Chin. J. Chem*. **2011**, *29*, 321-323.
35. Rad-Moghadam, K.; Sharifi-Kiasaraie, M.; Taheri-Amlashi, H. *Tetrahedron* **2010**, *66*, 2316-2321.
36. Indrasena, A.; Riyaz, Sd.; Naidu, A.; Dubey, P. K. *Heterocycl. Lett.* **2014**, *4*, 349-354.
37. Subhendu, N.; Pritam, S.; Rupankar, P.; Priyankar, P.; Abhijit, H.; Krishnendu, S. B.; Sukdeb, B.; Nirup, M. B. *J. Chem. Res*. **2009**, 3, 174-177.
38. Alimohammadi, K.; Sarrafi, Y.; Tajbakhsh, M. *Monatsh. Chem*. **2008**, *139*, 1037-1039.
39. Yadav, J. S.; Reddy, B. V. S.; Gayathri, K. U.; Meraj, S.; Prasad, A. R. *Synthesis* **2006**, *24*, 4121-4123.
40. Azizian, J.; Mohammadi, A. A.; Karimi, N.; Mohammadizadeh, M. R.; Karimi, A. R. *Catal. Commun*. **2006**, *7*, 752-755.
41. Wang, Sh. Y.; Ji, Sh. J. *Tetrahedron* **2006**, *62*, 1527-1535.
42. Chakrabarty, M.; Sarkar, S.; Harigaya, Y. *J. Chem. Res*. **2005**, 540-542.
43. Azizian, J.; Mohammadi, A. A.; Karimi, A. R.; Mohammadizadeh, M. R. *J. Chem. Res*. **2004**, *6*, 424-426.
44. Keshavarz, M.; Iravani, N.; Ghaedi, A.; ZareiAhmady, A.; Vafaei-Nezhad, M.; Karimi, S. *SpringerPlus* **2013**, *2*, 64.
45. Albadi, J.; Keshavarz, M. *Synth. Commun*. **2013**, *43*, 2019-2030.

