Inorganic Chemistry Communications 14 (2011) 1732–1736

Contents lists available at ScienceDirect

Inorganic Chemistry Communications

journal homepage: www.elsevier.com/locate/inoche

Enhanced catalytic activity of Zr(IV) complex with simple tetradentate Schiff base ligand in the clean synthesis of indole derivatives

Maasoumeh Jafarpour *, Abdolreza Rezaeifard *, Ghorbanali Gorzin

Catalysis Research Laboratory, Department of Chemistry, Faculty of Science, University of Birjand, Birjand, 97179-414, Iran

ARTICLE INFO

Article history:
Received 13 June 2011
Accepted 21 July 2011
Available online 29 July 2011

Keywords:
Indole derivatives
Salphen
Schiff base
Zirconium complexes

ABSTRACT

Zirconium (IV) tetradentate Schiff base (salphen) complex has been successfully used for efficient synthesis of wide variety of indole derivatives in EtOH as a standard green solvent under mild conditions. The investigation of turnover number and reusability of the catalyst indicate well the high efficiency and relative stability of the Zr-complex in this reaction.

The synthesis of relevant organic compounds is a main topic in academic and industrial chemistry and one particular molecular scaffold of interest is the indole. In fact the indole ring system is the most widely distributed heterocycle found in nature. Substituted indoles have been referred to as "privileged structures" owing to their excellent binding ability to many receptors with high affinity and a number of approved drugs has this core in their structures. Indole core is also an important component in many of today's drugs for the treatment of chemotherapy-induced nausea and vomiting, cluster headache, or as antihypertensive, antineoplastic and antimitotic agents. Reviews on this topic continuously appear in literature [1–12].

The chemistry of transition metal complexes with salen-type ligands has been one of the highlights in organometallic chemistry and catalysis. Despite the extensive investigations on the salen-type complexes of middle and late d-block transition metals as catalysts in diverse organic reactions, very few reports have appeared describing the synthesis [13–16], crystal structures [17–19] and catalytic properties of group IV metal complexes with such ligands [20–22].

In continuation of our ongoing research on the development of new eco-friendly organic transformations particularly by mediation of zirconium salts [23–34], herein, we wish to introduce zirconium (IV) salphen complex [Zr(Salphen)Cl_2 (salphen = *N*,*N*′-bis(salicylidene) phenylenediamine dianion ligand)] (Scheme 1) [35] as an easy-made and efficient catalyst for facile synthesis of indole derivatives in ethanol as a sustainable media under mild condition in desired times (Scheme 2).

Preliminary experiments were addressed to condensation of benzaldehyde and indole as model reaction, to determine the best reaction conditions with respect to temperature and reaction time. The use of 1 mmol benzaldehyde and 2.1 mmol indole in 0.5 ml ethanol in the presence of catalytic content of of Zr(salphen)Cl_2 complex (1 mol%) led to desired bisindolylmethane in 95% yield within 10 min at room temperature.

Based on the optimized reaction conditions, the present protocol was applied to a variety of carbonyl compounds and indoles (Table 1) [36]. As shown in Table 1 aromatic aldehydes having both the electron-donating and electron-withdrawing groups afforded bis (indolyl)methane in excellent yields. A rapid condensation of various carbonyl compounds with active 2-methyl indole under the same reaction condition was observed (Table 1, entries 10–15). Moreover, 3-formylindole as a carbonyl compound, gave the corresponding trisindolylmethane in excellent yield (Table 1, entry 14).

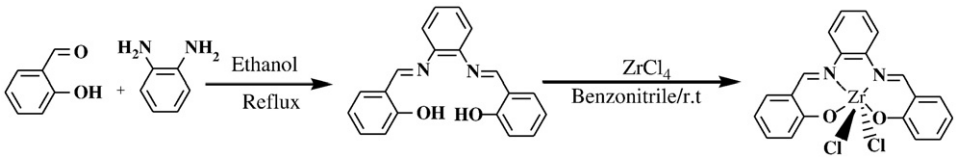
When we applied similar reaction conditions for condensation of isatin and indoles, desired 3,3′-diindolyloxindole derivatives, were secured in 85–90% yields (Table 1, entries 9, 15).

Based on these observations, the following probable mechanisms may be suggested for this reaction (Scheme 3). The role of Zr (Salphen)Cl_2 as a Lewis-acid leading to it's interaction with the carbonyl oxygen atom of aldehydes, thereby increasing the polarization of carbonyl moiety and promoting the condensation reaction.

The high yields of condensation products (85–97%) obtained by this catalytic system in desired times (<1–45 min) indicates the high efficiency of Zr(salphen)Cl_2 catalyst. This was further supported by high turnover numbers obtained for Zr-catalyst in the condensation of benzaldehyde with both indole (3750/24 h) and 2-methyl indole (>5000/24 h) under mild conditions using 5000:10,500:1 molar ratio for benzaldehyde/indol derivatives/catalyst. These promising results

* Corresponding authors. Tel.: +98 561 2502516; fax: +98 561 2502515.
E-mail addresses: mjafarpour@birjand.ac.ir (M. Jafarpour), rrezaeifard@gmail.com, rrezaeifard@birjand.ac.ir (A. Rezaeifard).

1387-7003/$ – see front matter © 2011 Elsevier B.V. All rights reserved.
doi:10.1016/j.inoche.2011.07.017



Scheme 1. Synthesis of Zr(salphen)Cl_2.

for a Schiff base complex once again confirm the high activity and also relative stability of Zr(salphen)Cl_2 during the condensation reaction, inducing us to evaluate the reusability of the catalyst.

The catalyst has been observed to be reusable for the at least three times in multiple sequential condensations by addition of new samples of benzaldehyde and indole to the reaction mixture.

These advantages for this high yielding condensation method offered ready scalability. In the condensation of benzaldehyde and indole as substrates in a semi scale-up procedure (20 times) the related product was secured in 93% yield.

In order to show the merit of the present catalytic protocol in comparison with the other catalytic systems used for the similar reaction particularly by using simple Zr(IV) salts, we have summarized some results obtained in condensation of benzaldehyde and indole (Table 2). These results indicate well the superior catalytic activity of Zr(salphen)Cl_2 than those of other catalytic system in terms of conversion rate and catalyst loading. Moreover, this method uses ethanol as an environmentally benign solvent.

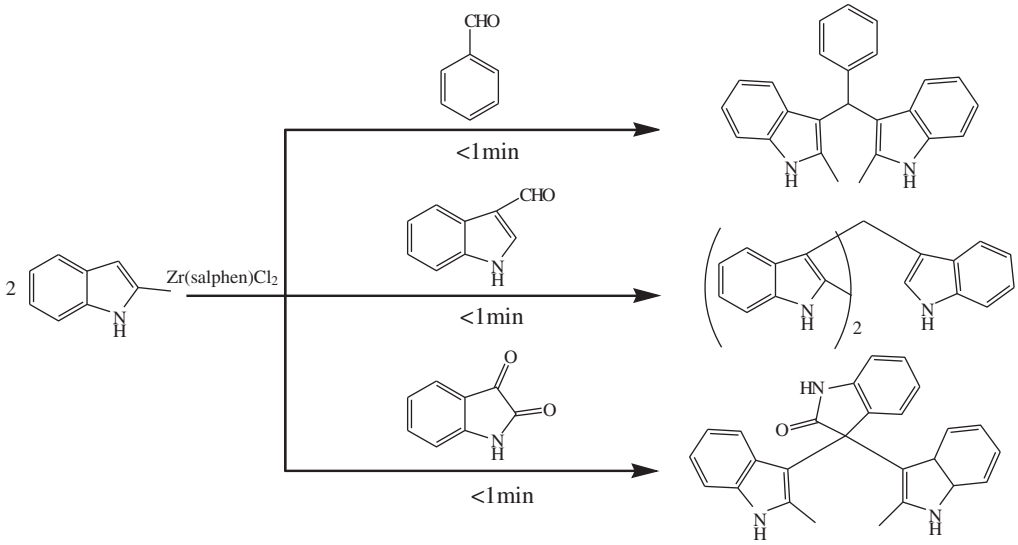
In conclusion, the catalytic activity of Zr(salphen)Cl_2 in synthesis of wide variety of indol derivatives under mild conditions were established. The employment of ethanol as an environmentally benign solvent in this high yielding method along with high turnover numbers and reusability of the catalyst providing ready scalability, makes it more appropriate for practical applications.

Acknowledgement

Support for this work by the Research Council of University of Birjand is highly appreciated.

References

[1] C. Gil, S. Brase, Solid-phase synthesis of biologically active benzoannelated nitrogen heterocycles: an update, J. Comb. Chem. 11 (2009) 175–197.
[2] J. Barluenga, F. Rodriguez, F.J. Fananas, Recent advances in the synthesis of indole and quinoline derivatives through cascade reactions, Chem. Asian J. 4 (2009) 1036–1048.
[3] K. Kruger, A. Tillack, M. Beller, Catalytic synthesis of indoles from alkynes, Adv. Synth. Catal. 350 (2008) 2153–2167.
[4] J.J. Song, J.T. Reeves, F. Gallou, Z.L. Tan, N.K. Yee, C.H. Senanayake, Organometallic methods for the synthesis and functionalization of azaindoles Chem, Soc. Rev. 36 (2007) 1120–1132.
[5] S. Patil, R. Patil, Synthesis and functionalization of indoles through rhodium-catalyzed reactions, Curr. Org. Synth. 4 (2007) 201–222.
[6] J. Hajicek, A review on recent developments in syntheses of the post-secodine indole alkaloids. Part II: Modified alkaloid types Collect, Czech. Chem. Commun. 72 (2007) 821–898.
[7] S. Patil, J.K. Buolamwini, Recent uses of palladium chemistry in indole synthesis Curr, Org. Synth. 3 (2006) 477–498.
[8] G.R. Humphrey, J.T. Kuethe, Practical methodologies for the synthesis of indoles, Chem Review 106 (2006) 2875–2911.
[9] S. Cacchi, G. Fabrizi, Synthesis and functionalization of indoles through palladium-catalyzed reactions, Chem Review 105 (2005) 2873–2920.
[10] S. Agarwal, S. Cammerer, S. Filali, W. Frohner, J. Knoll, M.P. Krahl, K.R. Reddy, H.J. Knolker, Novel routes to pyrroles, indoles and carbazoles – applications in natural product synthesis, Curr. Org. Chem. 9 (2005) 1601–1614.
[11] M.A. Metwally, S. Shaaban, B.F. Abdel-Wahab, G.A. El-Hiti, 3-acetylindoles: synthesis, reactions and biological activities, Curr Org. Chem. 13 (2009) 1475–1496.
[12] M. Bandini, A. Eichholzer, Catalytic functionalization of indoles in a new dimension, Angew Chem. Int. Ed. 48 (2009) 9608–9644.
[13] W.H. Leung, E.Y.Y. Chan, E.K.F. Chow, I.D. Williams, S.M. Peng, Metal complexes of a chiral quadridentate Schiff base, J. Chem. Soc., Dalton Trans. (1996) 1229–1236.
[14] M. Pasquali, F. Marchetti, A. Landi, C. Floriani, Preparations and structures of NN′-ethylenebis(salicylideneiminato)-titanium(III) derivatives, J. Chem. Soc., Dalton Trans. (1978) 545–549.
[15] G. Dell_Amico, F. Marchetti, C. Floriani, Peripheral electrophilic properties of dichloro[NN′-ethylenebis(salicylideneiminato)]titanium(IV): a route leading to a stable Ti-H-B unit, J. Chem. Soc., Dalton Trans. (1982) 2197–2202.



Scheme 2. Synthesis of indole derivatives in the presence Zr(salphen)Cl_2 (1 mol%) in ethanol at room temperature.