Chinese Chemical Letters 27 (2016) 619–622

Contents lists available at ScienceDirect

Chinese Chemical Letters

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

Original article

Enantioselective synthesis of 10-allylanthrones *via* iridium-catalyzed allylic substitution reaction

Zheng-Le Zhao [a,b], Qing Gu [b], Xin-Yan Wu [a,*], Shu-Li You [a,b,*]

[a] Key Laboratory for Advanced Materials and Institute of Fine Chemicals, East China University of Science and Technology, Shanghai 200237, China
[b] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai 200032, China

ARTICLE INFO

Article history:
Received 26 January 2016
Received in revised form 18 February 2016
Accepted 19 February 2016
Available online 2 March 2016

Keywords:
Allylic substitution
Anthrone
Asymmetric catalysis
Enantioselectivity
Iridium

ABSTRACT

A highly enantioselective allylic substitution reaction of anthrones with aromatic or aliphatic allyl carbonates was realized by using iridium catalyst prepared from $[Ir(COD)Cl]_2$ and BHPphos. Substituted 10-allylanthrones were obtained in excellent yields and with excellent enantioselectivity and regioselectivity (up to 98% yield, 99% *ee*) under mild conditions.
© 2016 Chinese Chemical Society and Institute of Materia Medica, Chinese Academy of Medical Sciences. Published by Elsevier B.V. All rights reserved.

1. Introduction

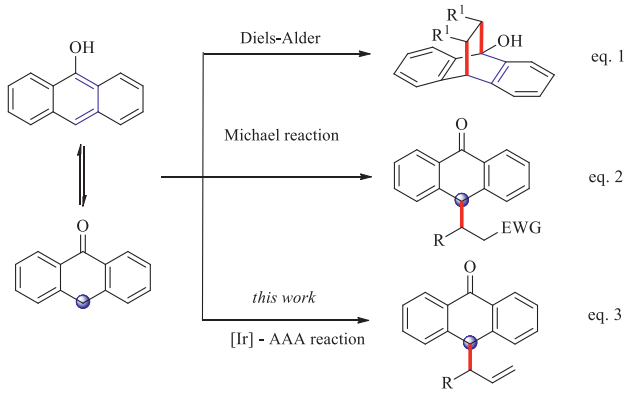
Anthrones and their derivatives play an important role in medicinal chemistry and organic synthesis [1]. Many anthrone derivatives exhibit interesting biological activity, such as antimicrobial, antipsoriatic, telomerase inhibiting, and antitumor activity [2]. Over the past several years, considerable efforts have been devoted to the construction of anthrone derivatives in an enantioselective manner. In this regard, 9-anthrol, the enol tautomer of anthrone, has been generally used as a diene component in asymmetric Diels–Alder cycloaddition reactions with a variety of dienophiles (Scheme 1, eq. 1) [3]. For instance, in 2006, Tan and coworkers demonstrated a highly enantioselective Diels–Alder reaction of anthrones and phenylmaleimides with chiral bicyclic guanidine as catalyst, giving bridged Diels–Alder cycloadducts in excellent yields and enantioselectivity [3f]. In addition, anthrone could also serve as a nucleophile at the C10 position exemplified by the Michael addition to α,β-unsaturated carbonyls [4], and nitroalkenes [5] (Scheme 1, eq. 2). Despite of the fact that remarkable progresses have been made toward various transformations of anthrones by organocatalysis, little attention has been paid on transition-metal catalyzed asymmetric reactions of anthrones. The chemoselectivity between O- and C-atom is considered as a main challenge in this reaction due to the equilibrium between anthrol and anthrone [6]. Thus the development of an efficient chemo- and enantioselective reaction is highly desirable for construction of valuable functionalized anthrones in both academic and industrial laboratories. With our continuing interest in allylic substitution reactions [7,8], we recently found that anthrones are suitable carbon-nucleophiles in Ir-catalyzed asymmetric allylic substitution reaction (Scheme 1, eq. 3). Herein we report our preliminary results from this study.

2. Experimental

General procedure for iridium-catalyzed enantioselective allylic alkylation: A flame-dried Schlenk tube was cooled to room temperature and filled with argon. To this flask were added $[Ir(COD)Cl]_2$ (5.7 mg, 0.01 mmol, 2 mol%), phosphoramidite ligand BHPphos **L4** (13.5 mg, 0.02 mmol, 4 mol%), THF (0.5 mL) and *n*-propylamine (0.5 mL). The reaction mixture was heated at 50 °C for 30 min and then the volatile solvents were removed *in vacuo* to give a pale yellow solid. After that, a solution of allylic carbonate **1** (0.55 mmol, 110 mol%) and anthrone (0.50 mmol) in 3.0 mL CH_2Cl_2, and *t*-BuOLi (40 mg, 0.50 mmol, 100 mol%) were added. After the reaction was complete (monitored by TLC), the crude reaction mixture was filtrated with celite and washed with EtOAc.

E-mail address: xinyanwu@ecust.edu.cn.
* Corresponding authors at: Key Laboratory for Advanced Materials and Institute of Fine Chemicals, East China University of Science and Technology, Shanghai 200237, China.
E-mail addresses: xinyanwu@ecust.edu.cn (X.-Y. Wu), slyou@sioc.ac.cn (S.-L. You).

http://dx.doi.org/10.1016/j.cclet.2016.02.017
1001-8417/© 2016 Chinese Chemical Society and Institute of Materia Medica, Chinese Academy of Medical Sciences. Published by Elsevier B.V. All rights reserved.



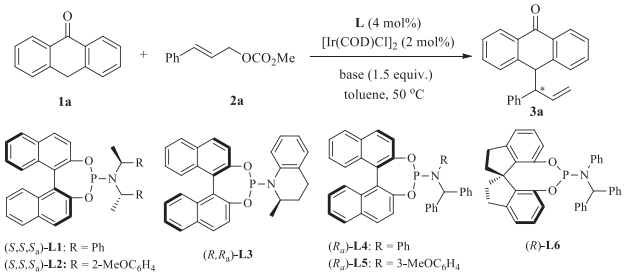
Scheme 1. Catalytic asymmetric reactions of anthrone.

The solvents were removed under reduced pressure. The ratio of branched and linear product was determined by ^{1}H NMR of the crude reaction mixture. Then the residue was purified by silica gel column chromatography (PE/acetone = 20/1 to 10/1) to afford the desired product **3**. The characterization data of the products are summarized in the Supporting information.

3. Results and discussion

At the outset of our study, we chose cinnamyl methyl carbonate (**2a**) as the electrophile to test the allylic substitution reaction of anthrone **1a**. In the presence of an iridium catalyst prepared from $[Ir(COD)Cl]_2$ (2 mol%) and (S,S,S_a)-**L1** (4 mol%) [9], the allylic alkylation reaction of anthrone with 1.5 equiv. of *t*-BuOLi as base in toluene proceeded smoothly to give the C10 allyl substituted product exclusively in 73% yield and 89% *ee* (Table 1, entry 1). The reaction with the Alexakis ligand (**L2**) gave the product in a better yield (93%) but with slightly lower *ee* (80%) (Table 1, entry 2). The reactions with THQphos (**L3**) and *N*-arylhydrylaniline derived phosphoramidites (**L4**, **L5**) developed in our group [10] afforded excellent results. BHPphos (**L4**) was found to be the most efficient ligand, affording **3a** in 95% yield and 95% *ee* (Table 1, entry 4). When the scaffold of the ligand was switched from BINOL to SPINOL, good yield was obtained with decreased enantioselectivity (Table 1, entry 6, 90% yield, −79% *ee*). It is remarkable that almost no *O*-allylation product and only trace amount of linear allylation product were observed in all cases. Encouraged by these preliminary results, we subsequently examined the effect of bases in this reaction. These results in Table 1 indicated that *t*-BuOLi (Table 1, entry 4) was the most suitable one among the bases tested for the present reaction (Table 1, entries 7–11). When no external base was added, the reaction was much slower, providing **3a** in 50% yield and 92% *ee* (Table 1, entry 12).

Table 1
Screening of ligands and bases.[a]



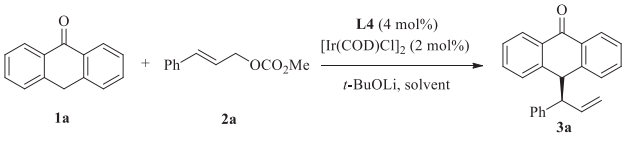
Entry	Ligand	Base	Time (h)	Yield (%)[b]	*ee* (%)[c]
1	**L1**	*t*-BuOLi	24	73	89
2	**L2**	*t*-BuOLi	24	93	80
3	**L3**	*t*-BuOLi	10	90	89
4	**L4**	*t*-BuOLi	10	95	95
5	**L5**	*t*-BuOLi	10	90	95
6	**L6**	*t*-BuOLi	24	90	−79
7	**L4**	DBU	24	–	–
8	**L4**	DMAP	24	74	89
9	**L4**	Cs_2CO_3	24	64	92
10	**L4**	*t*-BuONa	10	60	95
11	**L4**	*t*-BuOK	10	68	94
12	**L4**	–	48	50	92

[a] Reaction conditions: $[Ir(COD)Cl]_2$ (2 mol%), **L** (4 mol%), **1a** (0.50 mmol), **2a** (0.55 mmol, 1.1 equiv.), base (0.75 mmol, 1.5 equiv.), toluene (3 mL) at 50 °C.
[b] Isolated yield.
[c] Determined by HPLC analysis.

Under the above conditions (Table 1, entry 4), several solvents were further evaluated. The results are summarized in Table 2. The reaction proceeded to complete in CH_2Cl_2 at room temperature, giving the desired product in almost quantitative yield with the best enantioselectivity (97% *ee*) (Table 2, entry 5 *vs.* entries 1–4). A survey of the loading of the base and catalyst revealed that 1 equiv. of *t*-BuOLi and 2 mol% of $[Ir(COD)Cl]_2$ provided the best results (Table 2, entry 7, 98% yield, 99% *ee*). There was a decrease in yield when the catalyst loading was further reduced to 0.5 mol% (Table 2, entry 9, 70% yield, 96% *ee*).

With the optimized conditions in hand, we investigated the substrate scope of this allylic substitution reaction. We are pleased to find that cinnamyl carbonates bearing an either electron-deficient or electron-donating group (4-F, 4-Br, 4-OMe, 4-Me, 4-*i*-Bu, 3-Cl, 3-OMe, 3-Me, 2-OMe, Table 3, entries 2–10) could exclusively give the branched allyl substituted products in excellent yields and enantioselectivity (96%–98% yields, 91%–98% *ee*). The *ortho* methoxy substituted cinnamyl carbonate could also provide the desired product (**3aj**) in 97% yield and 91% *ee* (Table 3, entry 10). 1-Naphthyl and 2-thienyl cinnamyl carbonates (**2k**-**2l**) were also tolerated, affording products in 92% yield, 98% *ee* (entry 11) and 94% yield, 97% *ee* (entry 12), respectively. Alkylallyl carbonates (Me, Et) could occur smoothly, but with slightly decreased ee values (entries 13–14, 88% yield, 81% *ee*; 82% yield, 78% *ee*). It is notable that anthrones bearing varied substituents could also be tolerated. The reactions with 4,5-dichloroanthrone and 1,8-dihydroxy-9-[10H]-anthracenone gave their corresponding products in 95% yield, 90% *ee* (entry 15) and 92% yield, 95% *ee* (entry 16), respectively. The absolute configuration of the products was determined by VCD calculation of product **3ae** (98% *ee*) as *R* (see the Supporting Information for details).

Table 2
Screening of solvents and catalyst loading.[a]



Entry	Solvent	*t*-BuOLi (equiv.)	Temp (°C)	Time (h)	Yield (%)[b]	*ee* (%)[c]
1	Toluene	1.5	50	10	95	95
2	CH_3CN	1.5	50	10	85	95
3	Hexane	1.5	50	24	73	94
4	THF	1.5	50	10	93	94
5	CH_2Cl_2	1.5	r.t.	10	96	97
6	CH_2Cl_2	1.2	r.t.	10	96	98
7	CH_2Cl_2	1.0	r.t.	10	98	99
8[d]	CH_2Cl_2	1.0	r.t.	10	95	97
9[e]	CH_2Cl_2	1.0	r.t.	10	70	96

[a] Reaction conditions: $[Ir(COD)Cl]_2$ (2 mol%), **L4** (4 mol%), **1a** (0.50 mmol), **2a** (0.55 mmol, 1.1 equiv.), *t*-BuOLi, solvent (3 mL).
[b] Isolated yield.
[c] Determined by HPLC analysis.
[d] 1 mol% of $[Ir(COD)Cl]_2$ was used.
[e] 0.5 mol% of $[Ir(COD)Cl]_2$ was used.

Download English Version:

https://daneshyari.com/en/article/1253951

Download Persian Version:

https://daneshyari.com/article/1253951

Daneshyari.com