Tetrahedron Letters 58 (2017) 1834–1838

Contents lists available at ScienceDirect

Tetrahedron Letters

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

Tandem and chemoselective synthesis of benzil derivatives from styrene and arene diazonium salts

Vilas G. Jadhav, Sachin A. Sarode, Jayashree M. Nagarkar *

Department of Chemistry, Institute of Chemical Technology, Matunga, Mumbai 400019, India

ARTICLE INFO

Article history:
Received 24 January 2017
Revised 22 March 2017
Accepted 25 March 2017
Available online 28 March 2017

Keywords:
Benzil
Styrene
Tandem synthesis
Selenium dioxide
Arene diazonium salts

ABSTRACT

A facile and practically applied protocol for synthesis of benzil derivatives using styrene and arene diazonium salts is reported. $Pd(OAc)_2/SeO_2$ catalytic system was found to be efficient for chemoselective synthesis of benzil. Selenium dioxide works well as an oxidant under milder reaction conditions. Moderate to very good yields of the desired products were obtained.

Benzil, an aromatic 1,2 diketone is an important intermediate in chemical industry having wider applications in pharmaceuticals.[1–3] Various biologically active heterocyclic compounds, such as triazine[4], quinoxaline[5] and imidazole[3] can be synthesized from 1,2 diketones. Recently benzil derivatives have been found to show antitumor activity.[6] They are also reported as photosensitive agents and photoinitiators.[7]

Benzils can be prepared from oxidation of benzyl phenyl ketone.[8,9] Arene alkene[10,11] and arene alkyne[12,13] (Scheme 1) which can be easily obtained from Heck and Sonogashira reactions are also employed to obtain benzils. Oxidation of olefins for the formation of fine chemicals using transition metal catalysts in combination with peroxides, peracids, and other oxidizing reagents has been widely employed.[14–17] An alkene can be oxidized to aldehyde and epoxides. Therefore, selective oxidation of alkene towards the desired product is the promising challenge.[18,19] Hurran et al. synthesized benzil from benzyl phenyl ketone using SeO_2.[20] Riley et al. first reported stilbene to benzil oxidation using selenium dioxide as an oxidant at higher temperatures in the range of 190 to 235 °C[21,22]. Selenium dioxide is known to be active at higher temperatures.

Recently, dimethyl sulfoxide-iodine as a novel system for the oxidation of alkynes and alkenes to benzils have been reported. However, the reaction was carried out at high temperature.[23] Wan et al. reported Ru catalyzed oxidation of stilbene in presence of TBAI/TBHP oxidants giving benzil derivatives[11]. Graphene oxide was used for the preparation of benzil from cis stilbene with moderate yield.[24,25] Sun et al. reported an efficient I_2-H_2O catalytic system for the synthesis of benzil derivatives.[10]

All above reported methods require starting material stilbene. It is synthesized by reacting styrene with arene halide in presence of palladium catalyst which is a very well known Heck-Mizoroki reaction. Arene diazonium salts were used instead of arene halide with styrene as a coupling partner in the Heck-Matsuda(HM) reaction.[26–28] The rate of reaction is very high even at room temperature. Keeping all these merits in mind, we planned the direct synthesis of benzil from styrene and arene diazonium salts.

Arene diazonium salts are found to be alternative reagent for arene halide.[29] They have attracted much attention in the area of organic synthesis due to their higher reactivity.[30,31] Diazonium salts can be easily prepared from inexpensive anilines and are stable for long periods. In continuation with our work with arene diazonium salts for C—C[32,33] and C—N[34] coupling reactions here in we report one pot synthesis of benzil derivatives using arene diazonium salts and styrene in presence of catalytic amount of $Pd(OAc)_2$ and SeO_2. Therefore, to develop collective methodology which will reduce one step of the formation and separation process for stilbene and also achieve chemoselective oxidation of stilbene would be highly desirable.

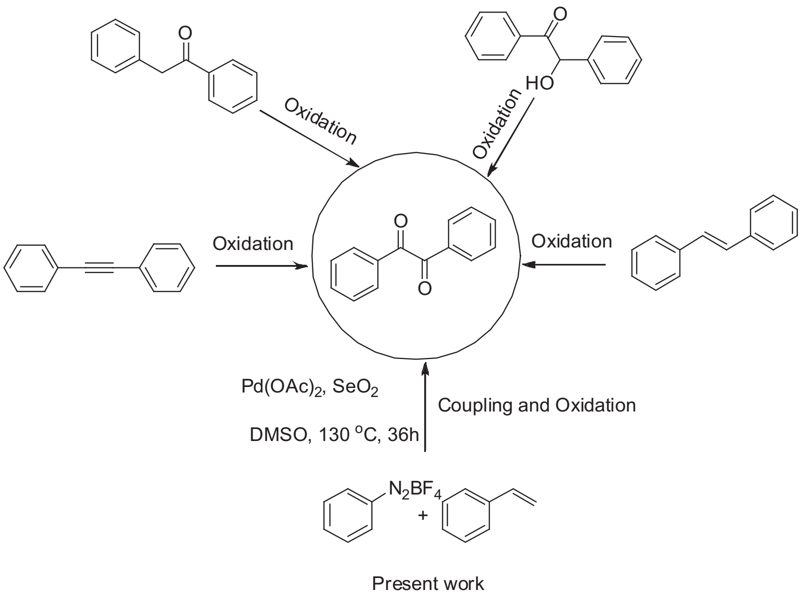
Results and discussion

Initially the reactions of styrene (1 mmol) with p-toluenediazonium salt (1.2 mmol) in DMSO solvent with various catalytic systems and oxidants were carried out and the results are presented

---

* Corresponding author.
E-mail address: jm.nagarkar@ictmumbai.edu.in (J.M. Nagarkar).

http://dx.doi.org/10.1016/j.tetlet.2017.03.076
0040-4039/© 2017 Elsevier Ltd. All rights reserved.

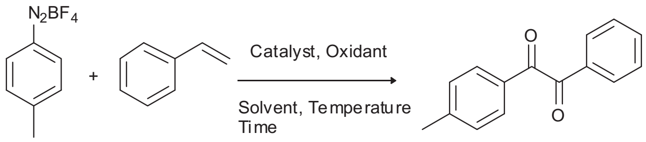


Scheme 1. Different route towards synthesis of benzil.

in Table 1. The reaction of styrene and p-toluenediazonium salt with $Pd(OAc)_2$ (0.5 mol%) and TBHP (2 eq.) furnished only trace amount of diketone along with aldehyde and phenol as side products (Table 1 entry 1). The reaction did not proceed without catalyst (Table 1 entry 2). The reaction was carried out in presence of copper bromide as a co-catalyst with atmospheric molecular oxygen at 120 °C. 15% of the desired product was obtained along with bromo benzene in presence of copper bromide as per Sandmayer reaction[35] (Table 1 entry 3). where as copper acetate gave 19% of the desired product (Table 1 entry 3 and 4).

Even though we increased the reaction time up to 72 h, only 28% of the desired product was obtained (Table 1 entry 5). Then we applied different oxidants such as KIO_4, I_2, and $K_2S_2O_8$. benzoyl peroxide and SeO_2. KIO_4 furnished 10% of diketone whereas molecular iodine produced only trace amount of diketone giving 4-Methyl stilbene, and methyl iodobenzene as byproducts at 120 °C (Table 1 entry 6, 7). $K_2S_2O_8$ was unable to give benzil where as benzoyl peroxide offered 20% yield (Table 1 entry 8, 9). When the reaction was carried out with SeO_2 for 24 h at 120 °C, we got 76% yield of the desired product chemoselectively. (Table 1 entry 11) With these interesting results, various parameters such as catalyst loading, temperature and reaction time have been optimized. We studied the reaction for $Pd(OAc)_2$ loading from 0.1 mol% to 1 mol%. It was found that 0.5 mol% of catalyst yielded 76% of the benzil derivative (Table 2 entry 4). Moreover, no significant increase in the yield of desired product above 0.5 mol% of $Pd(OAc)_2$ was observed. Hence 0.5 mol% was the optimum amount of catalyst required for the reaction.

Table 1
Optimization of the reaction parameters.[a]



Entry	Catalyst	Oxidant	Temperature (°C)	Time (h)	Yield[b] (%)
1	$Pd(OAc)_2$	TBHP	100	12	Trace
2	–	TBHP	100	12	–
3	$Pd(OAc)_2/CuBr_2$	O_2	120	24	15
4	$Pd(OAc)_2/Cu(OAc)_2$	O_2	120	24	19
5	$Pd(OAc)_2/Cu(OAc)_2$	O_2	120	72	28
6	$Pd(OAc)_2$ $Cu(OAc)_2$	KIO_4	120	24	10
7	$Pd(OAc)_2$ $Cu(OAc)_2$	I_2	120	24	Trace
8	$Pd(OAc)_2$ $Cu(OAc)_2$	$K_2S_2O_8$	120	12	–
9	$Pd(OAc)_2$ $Cu(OAc)_2$	Benzoyl peroxide	120	24	20
10	$Pd(OAc)_2/Cu(OAc)_2$	SeO_2	120	24	74
11	$Pd(OAc)_2$	SeO_2	120	24	76

[a] Reaction conditions: styrene (1 mmol), diazonium salt (1.2 mmol), DMSO (2 mL), Catalyst (0.5:0.5 mol%), Oxidants (2 eq), O_2 (1 atm).
[b] Isolated yield.