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Pyridine-Catalysed Desulfonylative Addition of β-Diketones to Arylazosulfones via Diaziridine Rearrangement

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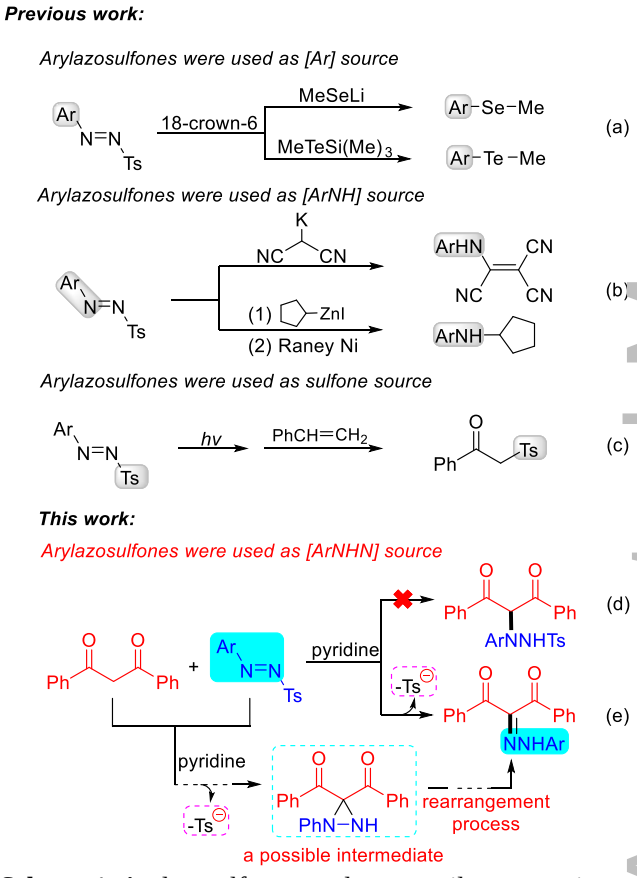
Abstract: A pyridine-catalysed desulfonylative addition of β-diketones to arylazosulfones was developed to obtain diazenyl β-dicarbonyl compounds. The aryldiazenyl group was observed in the desired product from arylazosulfones, and this diazenylation reaction was achieved via a possible rearrangement process based on diaziridine ring cleavage. The scope of the protocol was investigated and a plausible mechanism was given.

Keywords: Diketones; arylazosulfones; desulfonylative addition; pyridine

Finding a direct and simple approach to construct nitrogen-containing organic compounds has attracted increasing attention and research interest in synthetic organic chemistry because nitrogen-containing organic compounds have wide applications in organic synthesis, chemical industry, and biological systems.[1,2] Among the developed C–N synthetic methods, the diazenylation reaction is an efficient protocol for the synthesis of azo compounds and their analogues. Reflecting on the development of the diazenylation transformation, general methods that incorporate an organic compound with a R-N_2 moiety are processes that couple diazonium salts with a suitable carbon-nucleophile to give carbodiazenylation compounds.[3] Nevertheless, aryldiazonium salts are unstable to store due to their potentially dangerous and explosive chemical property. Although hydrazine salts[4] and triazenes[5] could be used as diazenyl group precursors for the synthesis of different nitrogen-containing compounds, these incorporated diazenyl transformations should be assisted by a transition-metal catalyst or complicated conditions. Accordingly, finding a stable, alternative and easily available substrate for use as a diazenyl source under simple conditions still has significant challenges.

Arylazosulfones, which are important building blocks,[6] were widely applied as aryl,[7] arylamine,[8]



Scheme 1. Arylazosulfones used as versatile partners in different reactions.

or sulfone sources[9a] *via* chemical bond (C–N, N–N, and N–S) cleavage under different conditions (Scheme 1a–1c). On the other hand, arylazosulfones also have been demonstrated as versatile radical partners in photochemical coupling reactions due to their good photochemical behaviors for constructing various organic molecules.[9] Recently, we employed electron-deficient diazene as the electrophile in phosphine- promoted cyclization to produce nitrogen-

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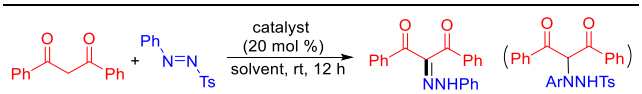
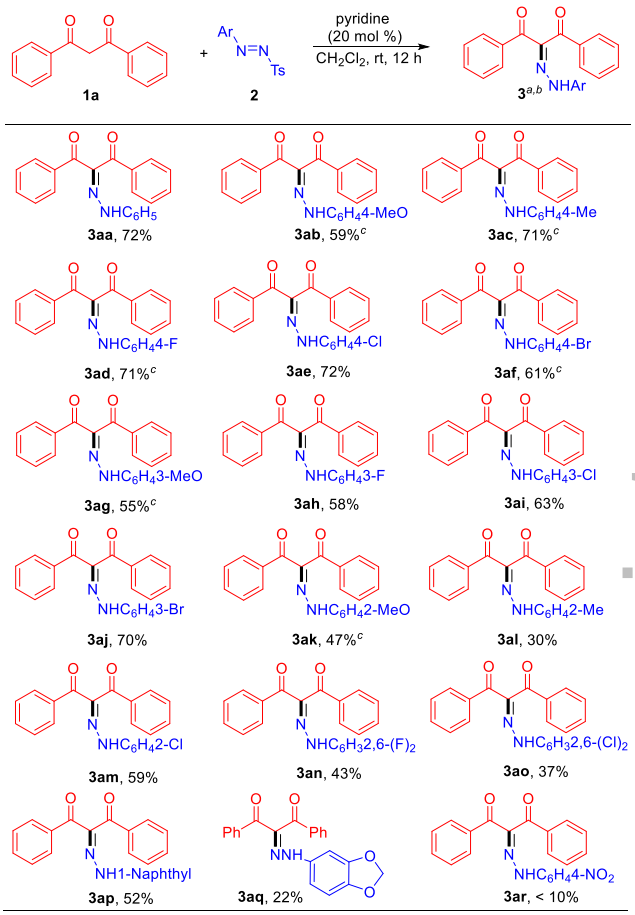
Table 1. Optimization of the reaction conditions.[a)]



1a 2a 3aa *Not found*

Entry	Catalyst	Solvent	Yield (%)[b]
1	Pyridine	CH_2Cl_2	31[c]
2	Pyridine	CH_2Cl_2	72
3	Pyridine	CH_2Cl_2	42[d]
4	Pyridine	CH_2Cl_2	41[e]
5	Pyridine	CH_2Cl_2	27[f]
6	Pyridine	$CHCl_3$	39
7	Pyridine	DCE	62
8	Pyridine	Et_2O	51
9	Pyridine	Benzene	40
10	Pyridine	DMF	20
11	Pyridine	DMSO	63
12	Pyridine	Methanol	55
13	(2-Me)Pyridine	CH_2Cl_2	37
14	(4-MeO)Pyridine	CH_2Cl_2	32
15	DBU	CH_2Cl_2	43
16	DMAP	CH_2Cl_2	30
17	DABCO	CH_2Cl_2	32
18	Et_3N	CH_2Cl_2	< 5
19	Ph_3P	CH_2Cl_2	ND[g]

[a)] Reaction conditions: **1a** (0.20 mmol), **2a** (0.20 mmol), catalyst (0.04 mmol, 20 mol %), solvent (2.0 mL), rt, for 12 h. [b)] Isolated yield. [c)] 10 mol% pyridine was used. [d)] 50 mol% pyridine was used. [e)] At 0 °C. [f)] At 40 °C. [g)] No desired product was detected.



Scheme 2. The Scope of arylazosulfones. [[a)] Reaction conditions: **1a** (0.20 mmol), **2** (0.20 mmol), pyridine (0.02 mmol, 20 mol %), CH_2Cl_2 (2.0 mL), rt, for 12 h. [b)] Isolated yield. [c)] 20 mol % DBU was used.]

containing heterocycles.[10] Due to our ongoing research interest in the reaction of arylazosulfones, we explored the possibility of other cyclization reactions *via* multicomponent reaction processes. Unexpectedly, an unusual desulfonylative transformation was observed when arylazosulfones were mixed with β-diketones in the presence of a pyridine catalyst, producing an unimaginable carbodiazenylation product, but the conventional Michael addition product was not observed (Scheme 1d and 1e).[11] Combined with the above-mentioned results, we speculated that this rearrangement process should be carried out during coupling transformation for the generation of carbodiazenylation products, and as far as we know, in reported pioneering studies, rearrangement reactions have never occurred in the reaction of arylazosulfones. Herein, we report a pyridine-catalysed desulfonylative condensation reaction of β-diketones with arylazosulfones for the preparation of carbodiazenylation products *via* diaziridine rearrangement.

Initially, we selected 1,3-diphenylpropane-1,3-dione (**1a**) and phenyl-2-tosyldiazene (**2a**) as the model substrates to begin our investigation of the optimized reaction conditions, and the results are listed in Table 1. The addition of 10 mol % pyridine to a solution of **1a** and **2a** at room temperature gave the desired carbodiazenylation product **3aa** with a 31% yield; this compound was characterized by NMR spectroscopy and HRMS analysis (Table 1, entry 1). The amount of pyridine had an obvious effect on the product yield; an 72% yield of **3aa** was obtained by increasing the amount of pyridine to 20 mol%, but a better yield was not achieved with a further improvement in the catalyst loading amount (Table 1, entries 2 and 3). The efficiency of the reaction is sensitive to temperature; 41% and 27% yields were obtained when the reaction was carried out at 0 °C and 40 °C, respectively (Table 1, entries 4 and 5). Furthermore, we attempted to examine the reaction efficiency by screening various solvents, and CH_2Cl_2 was confirmed to be the best solvent while using pyridine as the catalyst; low yields of condensation product **3aa** were obtained when another chlorinated (DCE and $CHCl_3$), or nonpolar/weak polar solvent was used as the medium (Table 1, entries 6-9). With the utilization of a polar solvent, such as DMF or DMSO, 20% and 63% yields of **3aa** were obtained, respectively (Table 1, entries 10 and 11). Furthermore, a 55% yield of **3aa** was obtained when the reaction was performed in the protonic solvent (Table 1, entry 12). When we switched the substituents in pyridine, better yields were not afforded (Table 1, entries 13 and 14). Upon further investigation of the effect of other tertiary amides on the reaction, pyridine was

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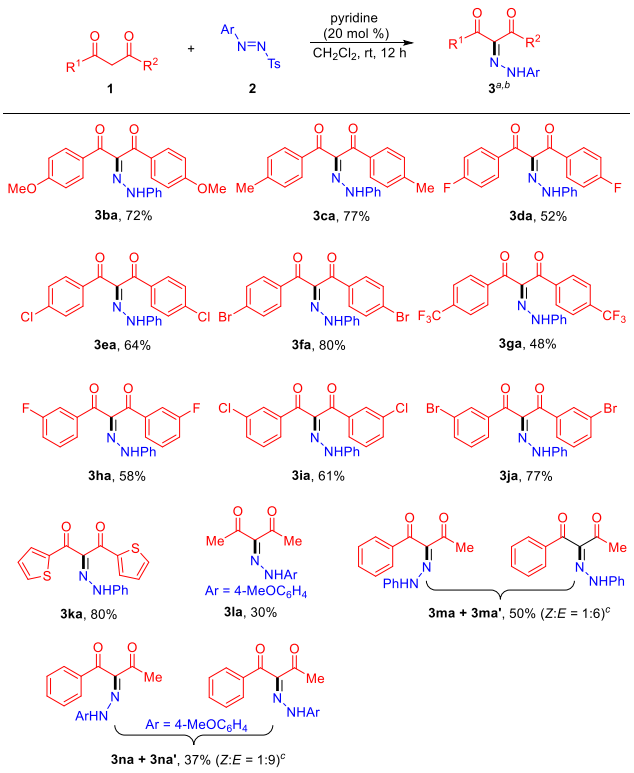


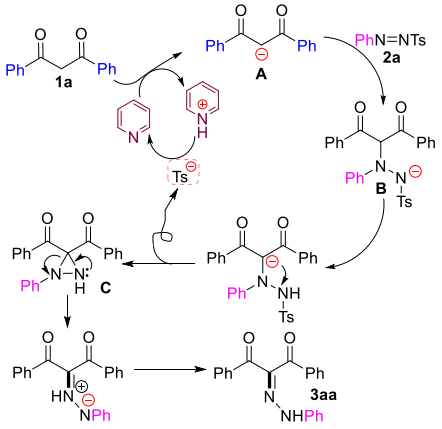
Scheme 3. The scope of β-diketones. [a] Reaction conditions: **1** (0.20 mmol), **2** (0.20 mmol), pyridine (0.02 mmol, 20 mol %), CH_2Cl_2 (2.0 mL), rt, for 12 h. [b] Isolated yield. [c]The ratio was determined by ^1H NMR.]

found to be the best one (Table 1, entries 15–18). On the other hand, Ph_3P is ineffective in the reaction (Table 1, entry 19).

By using the optimized conditions, a variety of arylazosulfones were employed to react with 1,3-diphenylpropane-1,3-dione (**1a**) to explore the substrate scope of the pyridine-catalysed desulfonylative reaction, and the results are listed in Scheme 2. Arylazosulfone **2** with different substituents on the phenyl rings could couple well with **1a** and provide the corresponding diazenylative products in moderate to good yields. Arylazosulfone **2** with an electron-rich group, such as MeO and Me, on the *para*-position of the phenyl rings reacted with **1a** to afford the desired products **3ab** and **3ac** in moderate to good yields. Meanwhile, substrate **2** with a halogen group (F, Cl or Br) on the *para*-position of the benzene rings afforded the corresponding products (**3ad**−**3af**) in 61−72% yields. When the substituent (MeO, F, Cl or Br) was located at the *meta*-position of the benzene rings in substrate **2**, the corresponding product (**3ag**−**3aj**) was obtained in 55−70% yields. When the substituent (MeO, Me, or Cl) was further moved to the *ortho*-position of the benzene ring, however, lower yields (30−59%) were afforded owing to the steric hindrance (**3ak** *vs*. **3ab** and **3ag**; **3al** *vs*. **3ac**; **3am** *vs*. **3ae** and **3ai**). Furthermore, the reactions of substrate **2** with two halogen groups afforded the desired products **3an** and **3ao** in 43% and 37% yield, respectively. On the other hand, when 1-(naphthalen-1-yl)- and (benzo[d][1,3]dioxol-5-yl)-2-tosyldiazene were employed, the reaction also occurred and generated the desired products **3ap** and **3aq** in modest yields. However, only a trace amount of desired product (**3ar**) was observed when the substituent was deformed to a stronger electron-poor group (NO_2).

To further evaluate the scope of this diazenylation reaction, the scope of the reaction was expanded to include other β-diketones (**1**), and the reactions proceeded smoothly to give the desired products with satisfactory yields in most of the cases, as illustrated in Scheme 3. In general, the efficiency of the reaction was insensitive to the substituents on the aromatic rings in diverse aromatic β-diketones. For example, aromatic β-diketones with an electron-rich group, such as MeO or Me, on the phenyl ring reacted with **2a** to afford the corresponding products **3ba** and **3ca** with 72% and 77% yields, respectively. As expected, β-diketones with different halogen groups, could react smoothly with **2a** to generate the desired products (**3da**−**3fa**) in 52−80% yields. For the CF_3-substituted aromatic β-diketones involved in the reaction, the desired product **3ga** was afforded in a 48% yield. Furthermore, by using a substrate with a halogen group on the *meta*-position (**1h**−**1j**) of the phenyl ring, the efficiency of the reaction was still maintained (**3ha** *vs* **3da**, **3ia** *vs* **3ea** and **3ja** *vs* **3fa**). For β-diketone **1** having a heteroaromatic group, the anticipated product (**3ka**) was isolated in 80% yield. A 30% yield of the desired product **3la** was obtained when aliphatic β-diketone (acetylacetone) was used in the reaction. On the other hand, when benzoylacetone (**1m**) was employed to react with phenyl-2- and 4-methoxyphenyl-2-tosyldiazene, corresponding products existing with two stereoisomers were obtained in 50% and 37% yields with ratios of 1:6 and 1:9, respectively.

According to the above-mentioned observations and corresponding reported work, a plausible reaction mechanism was proposed in Scheme 4. β-Diketone **1a** was transferred to its anionic form, intermediate **A**, in the presence of the pyridine catalyst and concomitantly formed pyridine salt. Subsequent addition of the anionic intermediate **A** to phenyl-2-tosyldiazene **2a** generated intermediate **B**, which transformed to the unstable diaziridine derivative **C**



Scheme 4 Proposed mechanism.

via intramolecular tandem H^+ transfer and a nucleophilic substituted desulfonylation procedure. Note that the pyridine catalyst regenerated by the reaction of Ts^- with the pyridine salt. Finally, the desired product **3aa** was obtained via C–N bond cleavage rearrangement in diaziridine derivative **C** and another intramolecular H^+ transfer pathway. In order to perform in-depth research on the reaction mechanism, necessary control experiments were conduced (see the ESI for details), which implied that we could not determine whether there is another reaction path (e.g. underwent the diazonium salt procedure) to generate carbodiazenylation product.[3,6-9]

In conclusion, we have developed a pyridine-catalysed desulfonylative addition of β-diketones to arylazosulfones for obtaining diazenyl β-dicarbonyl compounds, and arylazosulfone was first successfully employed as an aryldiazenyl source through a rearrangement process to achieve an unprecedented interesting addition reaction. Further investigations on the potential value of arylazosulfones in organic synthesis are underway in our laboratory.

Experimental Section

General Procedure for this diazenylation reaction: To a stirred solution of β-diketone (0.20 mmol) with arylazosulfone (0.20 mmol) in 2.0 mL of CH_2Cl_2 at room temperature was added pyridine (0.04 mmol). The reaction mixture was stirred at room temperature for 12 h. Then the solvent was removed in vacuo and the residue was purified by column chromatography on silica gel (10:1 petroleum ether/EtOAc) to give the pure product. It should be noted that the products **3ad**−**3af** and **3ah**−**3aj** were purified by column chromatography on silica gel (6:1 petroleum ether/CH_2Cl_2).

Acknowledgements

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Adv. Synth. Catal. **Year**, *Volume*, Page – Page

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