



A base-mediated three-component coupling reaction for the synthesis of phosphorohydrazones

Jun Wen, Liang Dong, Liang Yang, Tao Jiang, Sheng Hu, Tong-Zai Yang, Xiao-Lin Wang*

Institute of Nuclear Physics and Chemistry, China Academy of Engineering Physics, Mianyang 621900, Sichuan Province, China

ARTICLE INFO

Article history:

Received 11 June 2013

Received in revised form 14 September 2013

Accepted 18 September 2013

Available online 2 October 2013

Keywords:

Phosphorohydrazones

Three-component

P–N ligand

Fluorescent sensor

ABSTRACT

A simple and efficient three-component coupling reaction for the synthesis of phosphorohydrazones was developed. Both aldehydes and ketones participated in the reaction to afford the corresponding phosphorohydrazones in moderate-to-good yields. Moreover, a novel P–N ligand was synthesized by this method, which can act as a fluorescent sensor for iron ion.

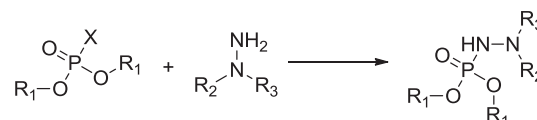
© 2013 Elsevier Ltd. All rights reserved.

1. Introduction

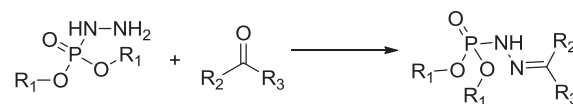
Heteroatom compounds containing P–N bonds are well known to be chemically stable and hence are widely used in catalysis,¹ metal extraction, bio-organic chemistry,² and so on. Further, highly efficient methods for synthesizing these compounds have been reported.³ In particular, phosphorohydrazones possess a diverse range of bioactivities, such as antitumor, antibacterial, and antiangiogenic activity⁴ and are valuable intermediates for building blocks in natural products.⁵ However, there are very few reported methods for the synthesis of phosphorohydrazones. The Atherton–Todd reaction (Scheme 1) is used as a major strategy for the synthesis of phosphorohydrazones,⁶ but a mixed product is often obtained because of the presence of two N–H bonds in the hydrazine group. Condensation of phosphorohydrazidates with carbonyl compounds⁷ and conjugate addition of dialkyl phosphites with diazenes can also afford phosphorohydrazones,⁸ but the practical applicability of these methods is severely restricted because of the need for special substrate sources.

Sulfonylhydrazones are valuable intermediates for organic synthesis; they are used as an in situ source of diazo compounds in many types of transition-metal-catalyzed reactions.⁹ Nevertheless, such heavy metals are toxic and contamination of the final product by the metal catalysts is undesirable, which calls for the development of transition-metal-free reactions. We have recently

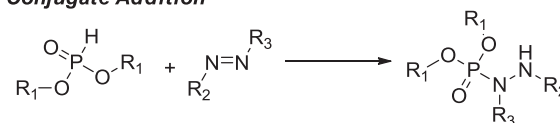
Atherton–Todd Methods



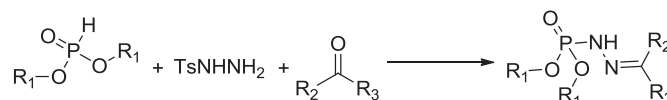
Condensation Reaction



Conjugate Addition



Our Work



Scheme 1. Methods for the preparation of phosphorohydrazones.

* Corresponding author. Tel./fax: +86 816 2484289; e-mail address: xlwang@caep.ac.cn (X.-L. Wang).

reported an effective method for the synthesis of pyrazoles by the one-pot condensation of α,β -unsaturated carbonyl compounds with tosylhydrazide in the absence of any transition-metal

catalyst.¹⁰ Herein, we report a base-mediated three-component coupling reaction of dialkyl phosphites, tosylhydrazide, and carbonyl compounds (Scheme 1) that affords a wide variety of substituted phosphorohydrazones in moderate-to-good yields.

2. Results and discussion

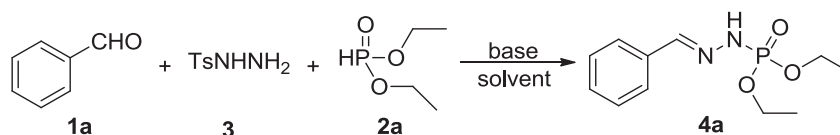
For the initial optimization of the reaction conditions, the condensation of benzaldehyde **1a**, tosylhydrazide **3**, and diethyl phosphite **2a** was selected as a model reaction system. The results are listed in Table 1. When the reaction was carried out in *N,N*-dimethylformamide (DMF) with K_2CO_3 as the base, the desired product **4a** was isolated in 46% yield (entry 1). A similar yield was obtained in the reaction carried out with K_3PO_4 as the base (entry 2). Other bases, such as NaOH, Cs_2CO_3 , and MeONa (entries 3–5), however, gave only trace amounts of the desired product, and no product was detected in the absence of the base (entry 6). These results implied that the presence of a base is crucial for the success of the reaction. Screening of solvents (entries 7–10) revealed that 1,4-dioxane was the most suitable for the reaction, affording the desired product in 76% yield. Screening of base amounts on a small scale (entries 8, 11–13) indicated that 3 equiv of K_2CO_3 was the optimal amount for the reaction, in which case 76% product yield was obtained (entry 8). Increasing the reaction temperature dramatically increased the product yield, with 60 °C being the optimal temperature. Higher temperatures were unfavorable because of the

71% yield. A heteroarene carbonyl compound, such as thiophene-3-carbaldehyde also gave the desired product **4h** in 70% yield. When acetophenone was used as the substrate under the optimized conditions, the product **4i** was obtained but in poor yield (35%). Therefore, we optimized the reaction conditions, including the type of base and temperature, and obtained **4i** in fairly good (68%) yield when the reaction was performed at 80 °C using K_3PO_4 as the base. Under these conditions, substituted acetophenone and benzophenone could afford the corresponding phosphorohydrazones **4j–l** in moderate yields.

Reactions employing various dialkyl phosphites with substituted benzaldehydes and tosylhydrazide were also investigated; the results are summarized in Table 3. H-Phosphite diesters bearing different alkyl groups could react smoothly under the optimized reaction conditions to afford the products **5**. Di-*tert*-butyl phosphite gave the corresponding product **5d** in relatively lower yield (55%) than that with the other dialkyl phosphites, probably because of the steric effect. Dibenzyl or diallyl phosphite, too, gave the desired products **5e** and **f** in 72% and 43% yields, respectively.

We speculated that the reaction started with the condensation of tosylhydrazide with the carbonyl compound to form the tosylhydrazone, base will deprotonate the proton of –NHTs and then kick out Tosyl group to form the diazo compound.¹¹ Thereafter, the intermediate diazo compound was trapped by a dialkyl phosphite to give the final product. The main byproduct is *N,N'*-dialkenylhydrazine, which is formed via self-coupling of the diazo compound

Table 1
Optimization of reaction conditions^a



Entry	Base	Base amount (equiv)	Solvent	Temp (°C)	Yield (%) ^b
1	K_2CO_3	3	DMF	60	46
2	K_3PO_4	3	DMF	60	41
3	NaOH	3	DMF	60	Trace
4	Cs_2CO_3	3	DMF	60	Trace
5	MeONa	3	DMF	60	Trace
6	—	—	DMF	60	NR
7	K_2CO_3	3	DMSO	60	Trace
8	K_2CO_3	3	1,4-Dioxane	60	76
9	K_2CO_3	3	Toluene	60	23
10	K_2CO_3	3	EtOH	60	11
11	K_2CO_3	1	1,4-Dioxane	60	14
12	K_2CO_3	1.5	1,4-Dioxane	60	22
13	K_2CO_3	2	1,4-Dioxane	60	51
14	K_2CO_3	3	1,4-Dioxane	rt	NR
15	K_2CO_3	3	1,4-Dioxane	40	25
16	K_2CO_3	3	1,4-Dioxane	80	66

^a Reaction conditions: **1a** (0.5 mmol), **2a** (0.75 mmol), **3** (0.625 mmol), base (3.0 equiv), solvent (2 mL), 24 h, in air.

^b Isolated yield.

greater amount of by-products formed (entries 14–16).

Under the optimized conditions, we next evaluated the substrate scope by extending the reaction to various carbonyl compounds. The results of the coupling reactions of diethyl phosphite, tosylhydrazide, and carbonyl compounds mediated by a base are summarized in Table 2. Benzaldehydes with electron-rich and electron-deficient substituents afforded the corresponding phosphorohydrazones **4a–g** in moderate-to-good yields. The results indicated that benzaldehydes with electron-withdrawing substituents can give the corresponding products in better yields. The sterically hindered 2-bromobenzaldehyde did not affect the result and gave the desired product **4g** in

(Scheme 2).¹²

Phosphorohydrazones may find application in coordination chemistry and metal extraction as well. Thus, to expand the practical utility of this synthetic method, we applied the coupling reaction to the preparation of a novel 1,1'-bi-2-naphthol (BINOL) ligand **7**. As depicted in Scheme 3, **7** was prepared in 53% yield by the reaction of binaphthalene dialdehyde **6** with tosylhydrazide and diisopropyl phosphite under the optimized conditions. The fluorescence spectra of **7** in DMF exhibited a broad emission peak, with λ_{max} at 408 nm (Fig. 1). We then tested the fluorescence response of **7** toward a series of metal ions. As shown in this figure, the fluorescence of **7** was clearly quenched upon the

Download English Version:

<https://daneshyari.com/en/article/5217592>

Download Persian Version:

<https://daneshyari.com/article/5217592>

[Daneshyari.com](https://daneshyari.com)