Letter

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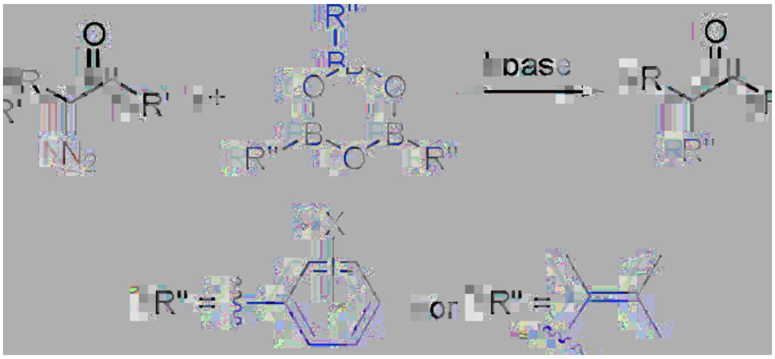

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Arylation and Vinylation of α-Diazocarbonyl Compounds with Boroxines

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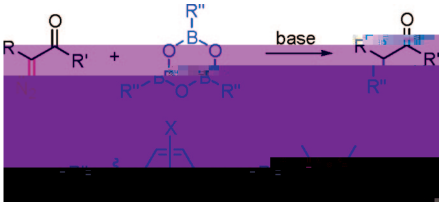
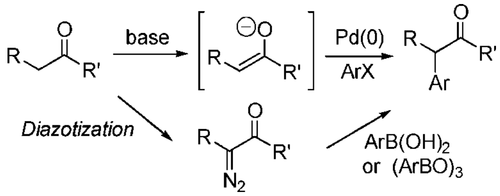
ABSTRACT



An alternative approach for α-arylation and α-vinylation of carbonyl compounds is described: reaction between aryl- or vinylboroxines with α-diazocarbonyl compounds leads to the formation of α-arylated or α-vinylated carbonyl compounds under mild conditions.

α-Arylation and α-vinylation of carbonyl compounds are very important in organic synthesis. Although various approaches have been developed for these purposes, they usually suffer drawbacks in one way or another. Recently, palladium-catalyzed α-arylation and α-vinylation of carbonyl compounds, which are mostly developed by Buchwald and Hartwig, have been shown to provide simple and efficient methods to introduce aryl and vinyl groups to the α carbon of carbonyl compounds.[1,2] However, these catalytic processes have to be carried out under strong basic conditions. An indirect approach toward α-arylated carbonyl compounds would be the arylation of the corresponding α-diazocarbonyl compounds, which could be easily available through diazotization of the corresponding carbonyl compounds under mild conditions (Scheme 1). In this paper, we report an alternative α-arylation method by the reaction of α-diazocarbonyl compounds with easily accessible arylboroxines. This approach also applies to α-vinylation by using the corresponding vinylboroxines.

Scheme 1. α-Arylation of Carbonyl Compounds



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(2) For selected recent publications, see: (a) Hama, T.; Culkin, D. A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 4976. (b) Takemiya, A.; Hartwig, J. F. *J. Am. Chem. Soc.* **2006**, *128*, 14800. (c) Martín, R.; Buchwald, S. L. *Angew. Chem., Int. Ed.* **2007**, *46*, 7236. (d) Huang, J.; Bunel, E.; Faul, M. M. *Org. Lett.* **2007**, *9*, 4343. (e) Liao, X.; Weng, Z.; Hartwig, J. F. *J. Am. Chem. Soc.* **2008**, *130*, 195. (f) Durbin, M. J.; Willis, M. C. *Org. Lett.* **2008**, *10*, 1413. (g) Vo, G. D.; Hartwig, J. F. *Angew. Chem., Int. Ed.* **2008**, *47*, 2127.

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could be further improved by using 1,2-dichloroethane (DCE) as solvent (entry 13). Since three phenyl groups in one phenylboroxine can be theoretically transferred to the product, we proceeded to reduce the amount of phenylboroxine. One equivalent of boroxine afforded satifactory results (entry 13). When the phenylboroxine was further reduced, the reaction became sluggish and the yield was diminished due to the side reactions of diazo substrate (entry 15).

In Hooz and Brown's reports, only the diazo compounds without α-substitution (N_2CHA, A = CN, CO_2Et, COMe, COPh, etc.), in most cases the ethyl diazoacetate, were investigated. As a general α-arylation method, more diazo substrates with structural diversity have to be employed. Thus, the optimized reaction conditions were applied to the reaction of **5a** with various α-diazocarbonyl compounds (Table 2). The α-phenylation products were obtained in moderate to high yields in all cases. Reaction with α-alkyl substituted diazo esters gave the α-phenyl-substituted aliphatic esters in good yields (entries 2−4). When the alkyl group was replaced by hydrogen, the reaction became sluggish but the yield remained high (entries 5). Reaction with α-diazoamide also worked well (entry 6), thus providing an efficient way for α-arylation of amides.

The results for the reaction with α-diazoketones are also summarized in Table 2 (entries 7−9). The slightly diminished yields in these cases as compared with α-diazoesters might be attributed to the decreased reactivity of the substrates under the reaction conditions, which resulted in 1, 2-H shift side reactions. Finally, the α-aryl-α-diazoacetates were also studied (entries 10−13). Reactions with these substrates needed a higher temperature to reach completion. The electron-donating group was found to facilitate the reaction (entry 12). Since the α-aryl-α-diazoacetates are easily available from the corresponding α-arylacetates,[11] this process constitutes a practical access to α,α-diaryl-substituted acetates.

Furthermore, a series of arylboroxines were examined through the reaction with *p*-tolyldiazoacetate **6** under the same conditions at 100 °C. As shown in Table 3, the reactions all proceeded well to afford diaryl-substituted acetate products **7a−h**. It was noted that the reaction was significantly accelerated by electron-withdrawing substituents of arylboroxines (entries 4−6).

[redacted]

It is worthwhile to note that both the arylboroxine substrate reacti9s79.3(the)79.3ldiazesubstrateint(is)-9.3(reaction)-9.3caon substituents (Table entriesTable entries

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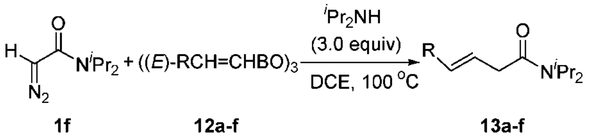
nylation by using vinylboroxine. With α-diazo amide **1f**, vinylboroxines **12a−f** were applied to the similar reaction conditions, and the results are summarized in Table 4. In all cases, the reaction occurred smoothly, giving α-vinylation products in moderate to good yields. The byproduct attributed from the shift of the double bond to the α,*β* position were not detected in these cases. The same α-vinylation reaction has also been tested with diazo ester **1a**. In that case, the major product of *β*,*γ*-unsaturated ester was accompanied by small amount of α,*β* unsaturated ester as minor product.

Table 4. Reaction of Vinylboroxines **12a−f** with **1f**[a]

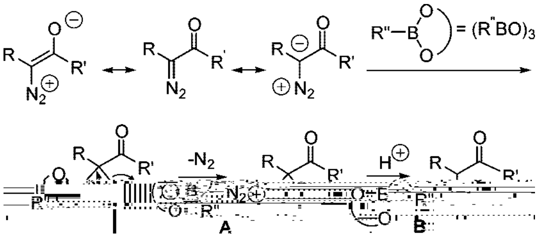


entry	**12**, R	time (h)	yield (**13**, %)[b]
1	**12a**, C_6H_5	12	**13a**, 65
2	**12b**, *p*-$CH_3C_6H_4$	11	**13b**, 88
3	**12c**, *p*-ClC_6H_4	10	**13c**, 77
4	**12d**, 1-naphthyl	13	**13d**, 74
5	**12e**, *n*-pentyl	24	**13e**, 45
6	**12f**, $BnOCH_2CH_2-$	22	**13f**, 61

[a] Reaction conditions: **1f** (1 equiv), **12a−f** (1 equiv). [b] Isolated yield.

The mechanism of this α-arylation and α-vinylation is thought to be similar to the reaction of α-diazo compounds with alkylborane (Scheme 2).[3,4] The reaction is initiated by nucleophilic attack of the diazo carbon to boroxine, generating intermediate **A**, followed by 1,2-migration of R″ from boron to carbon to give **B**. Hydrolysis of **B** leads to the product. The additive of diisopropylamine has been found to significantly improve the yield of the reaction. It was observed that adding diisopropylamine could markedly slow down the reaction. Since diazo compounds are generally sensitive to acids, we speculate that the role of diisopropylamine is to neutralize the reaction system by interact with boroxine or acidic species generated during the reactions, thus preventing the diazo substrate from decomposition.

Scheme 2. Mechanistic Rationale



In summary, we have developed a general approach for α-arylation and α-vinylation by the reaction of α-diazocarbonyl compounds with boroxines. Since the reaction conditions are mild and both diazo compounds and boroxines are easily available, this reaction should find an application in organic synthesis.

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Supporting Information Available: Experiment procedure, characterization data, ^1H and ^{13}C NMR spectra for all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

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