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Synthesis of stilbenes via homocoupling of aryl aldehyde tosylhydrazones

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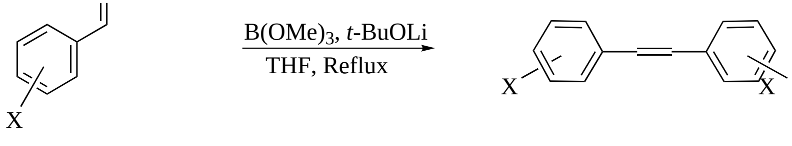
Abstract—Stilbenes are readily prepared in good yields via homocoupling of aryl aldehyde tosylhydrazones in the presence of lithium *tert*-butoxide and trimethyl borate under reflux in THF. © 2001 Elsevier Science Ltd. All rights reserved.

Stilbenes are important synthetic precursors to phenanthrene alkaloids as well as enantiomerically pure 1,2-diphenylethanes, 1,2-diamines, and diols. They also are used as optical brighteners and therapeutic agents for liver disorders. A number of methods have been developed for the preparation of stilbenes based on Wittig-type reactions,[1] reductive coupling of carbonyl compounds,[2] self-coupling of α-lithiated benzylic sulfones,[3] and condensations of aldehyde tosylhydrazones with stabilized carbanions.[4] More recently, Katritsky and co-workers reported a new procedure for the synthesis of stilbenes via reaction of aldehyde tosylhydrazones with benzotriazole-stabilized carbanions.[5]

During our investigation of the alkylation of aryl aldehyde tosylhydrazones with trialkylboranes and alkylboron chlorides,[6] we discovered that reactions involving alkylboron chlorides produced stilbenes rather than alkylation products. To our knowledge, the formation of stilbenes via homocoupling of aryl aldehyde tosylhydrazone has not been reported. Since this method provides a simple and inexpensive method for the preparing stilbenes, we investigated the reaction in the presence of various boron compounds. It was found that trimethyl borate induced excellent yields of stilbene products (Scheme 1).

A series of aryl aldehyde tosylhydrazones were subjected to the reaction sequence. Essentially, all gave excellent yields of stilbenes (Table 1). It should be noted that the successful reaction of the tosylhydrazone of 4-nitrobenzaldehyde (entry 11) required refluxing in DME. Interestingly, aryl aldehyde tosylhydrazones containing electron-withdrawing functionality such as the cyano and nitro groups afforded *trans*-stilbenes as major products. These reactions proceeded relatively slowly.

Although a detailed mechanistic study has not been carried out, the reaction presumably proceeds via the formation of an aryl carbene intermediate as shown in Scheme 2. Trimethyl borate reacts with the lithium tosylate (which precipitates from the reaction mixture) and thus prevents the tosylate from reacting with the aryl carbene intermediate. In fact, benzyl 4-methylphenylsulfone has been observed in the reaction of all aryl aldehyde tosylhydrazones with lithium *tert*-buto2xide in the absence of trimethyl borate, which led to the low yields of stilbenes. In order to confirm the existence of a carbene intermediate, 4-methylstyrene was added to a mixture of 4-methylbenzaldehyde tosylhydrazone, lithium *t*-butoxide and trimethyl borate to trap the carbene intermediate. As expected, 1,2-di-(4-methylphenyl)cyclopropane was isolated. Stoichiometric quantities of lithium *tert*-butoxide and trimethyl borate are required to produce high yields of stilbenes.



Scheme 1.

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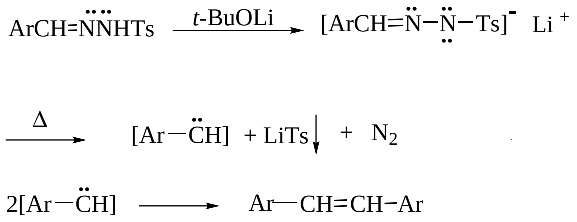
Table 1. Synthesis of stilbenes via aryl aldehyde tosylhydrazones

Entry	X (Scheme 1)	Reaction time (h)	Ratio (*trans*/*cis*)	Yield[a,b]
1	H	6	48/52	82
2	4-F	10	49/51	87
3	4-Cl	8	58/42	87
4	4-Br	7	52/48	83
5	3-Br	7	46/54	80
6	2-Br	7	40/60	85
7	4-Me	5	57/43	81
8	4-MeO	5	48/52	83
9	3-MeO	5	40/60	88
10	2-MeO	5	50/50	79
11	4-NO_2	12	91/9	84
12	4-CN	10	99/1	88

[a] Isolated yield of both *trans* and *cis* isomers.

[b] The physical properties and spectral characteristics of all products were consistent with literature values.



Scheme 2.

The synthesis of stilbene is representative: benzaldehyde tosylhydrazone (3 mmol) is dissolved in 20 mL of dry THF in a dry, argon-flushed, round-bottomed flask equipped with a reflux condenser and stirring bar. Trimethyl borate (3.0 mmol) is then added via syringe followed by lithium *tert*-butoxide (3.0 mmol, 1.0 M solution in hexanes) and the reaction mixture is heated to gentle reflux for 6 h. The mixture is then cooled, hydrolyzed, the organic phase separated and dried (anhydrous $MgSO_4$). Removal of solvent under reduced pressure followed by silica gel column chromatography with hexanes as eluent produces an 82% yield of stilbene.

In conclusion, the homocoupling of aryl aldehyde tosylhydrazones in the presence of trimethyl borate and lithium *tert*-butoxide provides a simple, inexpensive, and efficient route to stilbenes, including stilbenes containing electron-withdrawing functional groups.

Acknowledgements

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