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Substituent effects on the reaction of trityl chlorides with Grignard reagents

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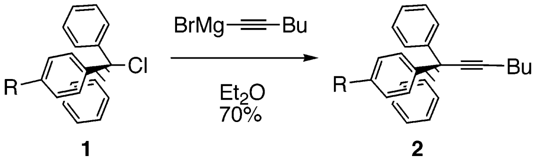
Abstract

The result of the substitution of trityl chlorides with Grignard reagents was found to be highly dependent on the solvent and the nature of the substituents on the trityl group. In THF, electron donating substituents were found to give high yields of Grignard addition while electron withdrawing substituents were found to give mostly reduction to the corresponding triphenyl methane via hydride abstraction from the solvent. © 2000 Elsevier Science Ltd. All rights reserved.

As part of an ongoing program geared toward the synthesis of cooperative chemical sensors,[1] we required a facile preparation of bis-tritylacetylene compounds bearing a variety of substitution on the trityl groups. Literature precedent indicated that trityl chlorides could be substituted with acetylene Grignard reagents in ethereal solvents to give good yields of the tritylacetylene (Eq. (1)).[2,3] Therefore, this class of compounds appeared to be easily accessible.



(1)

Our initial synthetic target required a *meta*-amino substitution pattern. Thus, the tosyl protected trityl chloride **3** was treated with acetylene Grignard in THF. However, the only product obtained was that of reduction (**4**) with no addition of the Grignard reagent observed (Eq. (2)). Using benzene as the solvent,[4] the trityl acetylene **5** was produced in good yields with no reduction observed.[5] Clearly, THF promoted the reduction and was ultimately the reductant in the reaction. Further work demonstrated that the reduction process could not always be avoided. For example, the benzyl protected trityl chloride **6** gave mostly the product of

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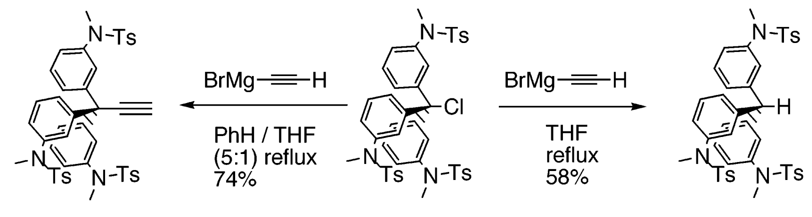
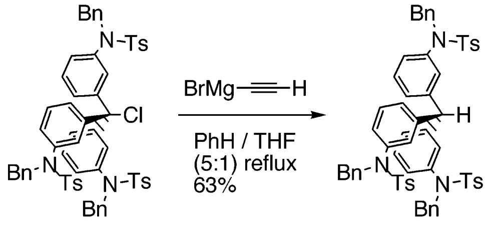
reduction (**7**) with little substitution (<10%) under a variety of conditions (Eq. (3)). Our interest in this class of compounds prompted an investigation into the substituent effects on the reduction process involved in Eqs. (2) and (3).



5 **3** **4**

(2)

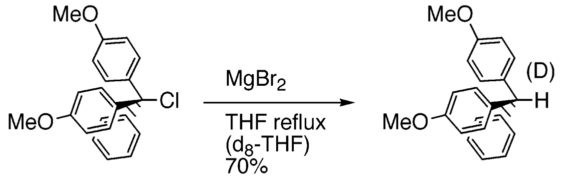


6 **7**

(3)

Toward this end, four substituted trityl chlorides were treated with excess ethyl Grignard at two different concentrations in THF (Table 1). In general, electron donating groups tended to promote Grignard addition while electron withdrawing groups favored the reduction product. Higher concentration generally gave higher ratios of the Grignard addition product (compare entries 5 and 6). The sterically imposing tosyl amine groups inhibited Grignard addition to the extent that only reduction was observed at either concentration (entries 7 and 8). The yields of compound **8a** were better overall than the other substituted trityl chlorides owing to side reactions which are apparent in the latter cases.

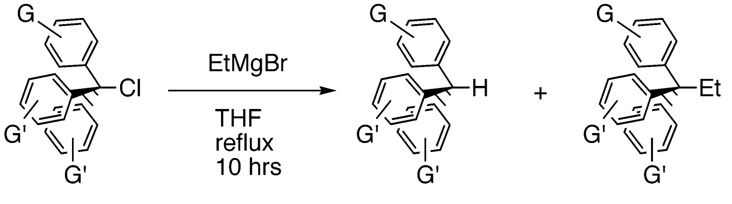
In principle, the mechanism of this reduction could entail a carbocation or a radical intermediate. The reduction of trityl chlorides with lithium amides has been studied by Newcomb and proceeds via electron transfer which produces a trityl radical.[6] The radical abstracts a hydrogen atom from the resulting aminyl radical and gives the product of reduction. However, the results in Table 1 appeared to be more consistent with a pathway in which a trityl carbocation abstracts a hydride from the solvent.[7,8] Indeed, reaction of compound **8a** with a Lewis acid, $MgBr_2$, in THF gives exclusively the reduction product in 70% yield (Eq. (4)). The reaction was repeated in d_8-THF and the product contained >95% deuterium incorporation by mass spectrometry. Therefore the reduction products presented in Table 1 likely result from Lewis acid promoted hydride abstraction from THF.



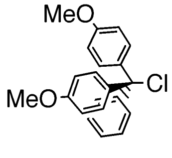
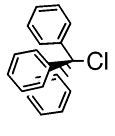
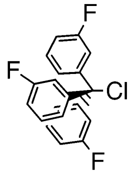
8a **9a**

(4)

Table 1[a]

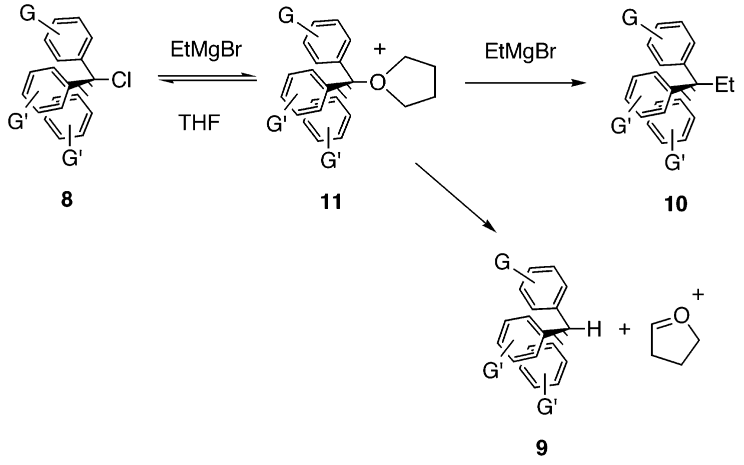


8 **9** **10**

Entry	Trityl chloride	Concentration (M)	Ratio **9**:**10**	Yield (%)
1	 **8a**	0.012	1:5.0	87
2	**8a**	0.1	1:4.4	80
3	 **8b**	0.012	1:1.6	51
4	**8b**	0.1	1:2.9	58
5	 **8c**	0.012	9.1:1	50
6	**8c**	0.1	1.1:1	55
7	**3**	0.012	>20:1	58
8	**3**	0.1	>20:1	45

[a] All new compounds gave satisfactory spectroscopic analysis.

A simple mechanism consistent with these results is presented in Scheme 1. The magnesium salts aid in the dissociation of the trityl chloride to the solvent associated trityl cation (**11**).[6,9] This cation then partitions between addition of the Grignard reagent (**10**) and abstraction of a hydride from the coordinated solvent (**9**). Thus, electron withdrawing groups destabilize the trityl cation making it more reactive and prone to hydride abstraction, while electron donating groups stabilize the cation which can then be trapped by the Grignard reagent. Increased overall



Scheme 1.

concentration leads to a higher ratio of Grignard addition as this is a bimolecular reaction. Steric constraints imposed by large substituents disfavor the addition of the Grignard reagent leading to predominance of the reduction product.

In summary, we have found that the addition of Grignard reagents to trityl chlorides is dependent on both the solvent and the substituents on the trityl group. Electron donating groups give higher yields of products which favor Grignard addition while electron withdrawing groups and sterically demanding groups favor reduction to the triphenyl methane derivative via hydride abstraction.

Acknowledgements

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