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AN ANOMALOUS METALATION OF A TRIMETHYLSILYL GROUP

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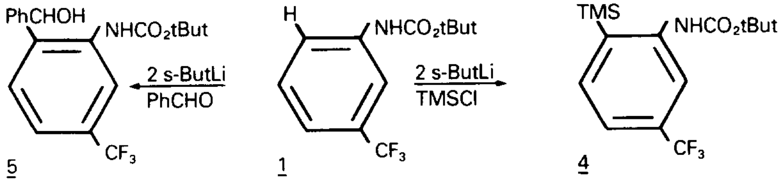
Abstract: Metalation of 4 followed by traping with electrophiles unexpectedly provided products from metalation on the trimethylsilyl group.

The ortho directed metalation of anilines is an attractive route to fused ring heterocycles. This method is of special interest with electron deficient anilines that fail to react under classical electrophilic aromatic substitution procedures.

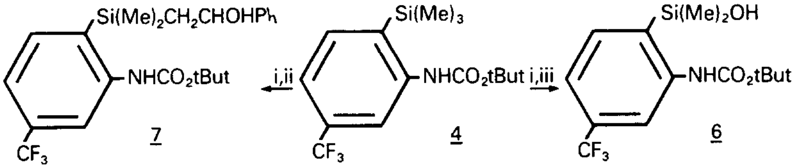
Our interest was in the directed metalation of trifluoromethyl substituted anilines. It is known that the metalation of trifluoromethylbenzenes yield mostly ortho products.[1] The directed metalation of t-butyl phenylcarbamates also provide ortho products.[2] Also there are several examples of metalation into the 2-position of a benzene substituted 1,3- with two ortho directing groups.[3]

We proposed to carry out the lithiation of t-butyl[3-(trifluoromethyl)phenyl]-carbamate (1) with the expectation that lithiation would occur at the 2-position. It was found however that treatment of 1 with s-butyl lithium in THF at -40°C for 1 hour, followed by the addition of the electrophiles TMSCl or PhCHO gave conversion to the substituted products 4 and 5 as analytically pure solids after chromatography and crystallization (Scheme I). The ^{1}H and ^{13}C NMR of 4 and 5 showed that the metalation and substitution had occurred on the 6-position instead of the expected 2-position of 1.



SCHEME I

The use of trimethylsilyl as a blocking group by Mills and Snieckus suggests that lithiation of 4 would be directed to the 2-position.[4] However, treatment of 4 with 2-equivalents of t-butyl lithium in THF at -40°C and addition of DMF produced the silanol 6. Alternatively, treatment of 4 with 2-equivalents of t-butyl lithium in THF at -40°C followed by addition of benzaldehyde provided 7.



i = 2 s-butLi, ii = PhCHO, iii = DMF

SCHEME II

The silanol 6 can be seen to result from lithiation of 4 on the trimethylsilyl group, followed by a Peterson type of reaction on quenching with DMF. The product 7 was obtained from the -40°C reaction of the anion with benzaldehyde followed by a -40°C quench with HOAc, and again shows that the metalation is directed to the trimethylsilyl group.

The directed metalation of the trimethylsilyl group in 4 although contrary to our expectations appears to be consistent with a number of directed lithiations in the literature in which metalation occurs on a kinetically acidic site in preference to thermodynamically available alternatives.[6] This metalation provides a novel route to a silicon stabilized anion which may prove useful in Peterson olefination-type reactions[5] or other chemistry mediated by anions α to silicon.

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