

Silylcupration of N-phenyl-N-ethynyl-aniline: a Versatile Route to Functionalized N,N-bis(phenyl)enamines

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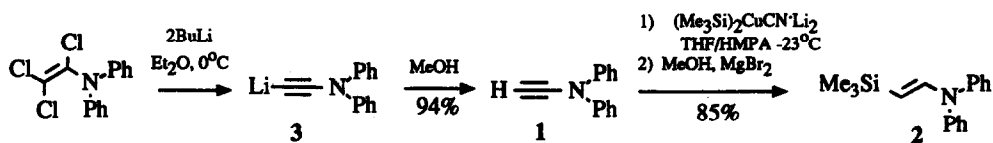
Abstract: *The silylcupration of N-phenyl-N-ethynyl-aniline, occurs regioselectively leading to silylation at the β -carbon atom. Subsequent reaction of the resulting vinyl copper adduct with electrophiles, opens a new flexible route to functionalized enamines.*

In an earlier paper⁽¹⁾ the silylcupration of suitably N-protected propargylic amines showed a high degree of regio and stereocontrol, affording an easy way for obtaining, after quenching with electrophiles, 2-substituted allylamines.

Our interest in the field of unsaturated nitrogen containing compounds as potentially biologically active building blocks⁽²⁾, coupled with our current studies of metallo-metallation reactions on terminal acetylenes bearing heteroatoms on the lateral chain^(1,3,4), prompted us to report here our further work in which the silylcupration of N-phenyl-N-ethynyl-aniline (1) has been studied.

Addition of $(\text{Me}_3\text{Si})_2\text{CuCN}\cdot\text{Li}_2$ to (1) at -23°C occurs very rapidly and only the (E)-enamine (2) bearing the trimethylsilyl group at the β -carbon, was recovered⁽⁵⁾ in the crude mixture, after quenching with

methanol, and isolated in 85% yield after workup and distillation⁽⁶⁾ (Scheme 1).



Scheme 1

The geometry of the double bond in compound (2) has been determined by means of the value of 16.6 Hz of the *J* in the ¹H NMR which is typical from a *trans* ethylenic proton coupling.

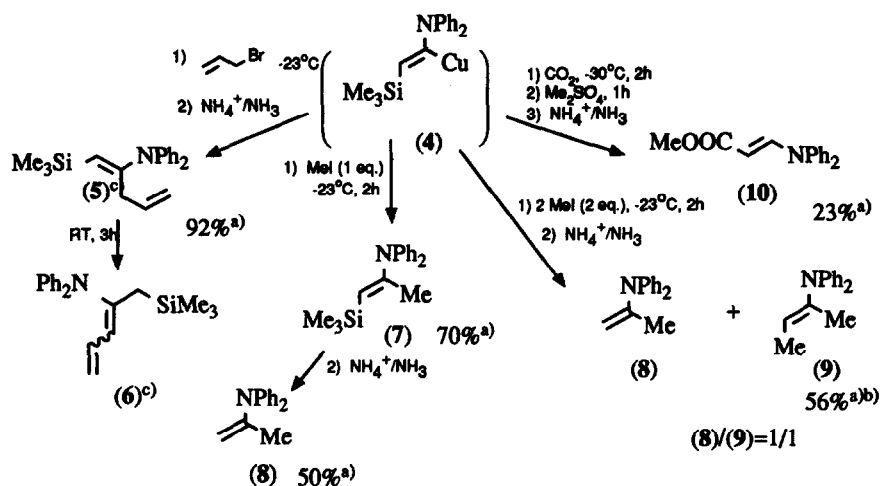
To our knowledge, the preparation of Group -14 organometallic enamines such as (2) is unprecedented, with the exception of one report⁽⁷⁾ dealing with the formation of 2,2-bis(dimethylamino)vinyl trichlorosilane by reaction of silicon tetrachloride and vinylidenebisdimethylamine.

It is worth noting that in the metallo-cuprate addition, the regioselectivity is reversed as compared with that previously observed in the carbocupration of (1)⁽⁸⁾: this result supports our previous observations^(1,3) on the regiochemical outcome in the metallo-metallation of alkynyl systems⁽⁹⁾.

To achieve functionalization at the α-position of the enamine (2), quenching of the vinylcopper intermediate (4) with electrophiles other than a proton was performed, and the results are summarized in Scheme 2.

Adduct (4) reacts smoothly with a highly reactive electrophile, such as allylbromide, affording in high yields the expected compound (5), which isomerizes at room temperature to the corresponding dienamino derivative (6). Moreover reaction with methyl iodide affords compound (7), detectable in the reaction mixture by GC/MS analysis, and which undergoes a very fast displacement of the trimethylsilyl group, only compound (8) being in fact isolated after aqueous workup with ammonium buffer solution. In the presence of excess of electrophile, compound (9) resulting from a double functionalization, was also detected in sizeable amount in the crude reaction mixture. Accordingly, quenching of (4) with a large excess of CO₂, followed by methylation, led to (10) as the sole product⁽¹⁰⁾ although in rather low yield.

The enhanced reactivity of the 2-trimethylsilyl-ethenylamine-type compound at the silicon-substituted carbon atom, can be easily understood considering that enamines are ambident conjugated systems with high, but variable, nucleophilicity at both the nitrogen and the β-carbon atoms. The normal tendency of enamines to interact with electrophiles⁽¹¹⁾, is strengthened in the case under study, in the presence of a good leaving group such as the trimethylsilyl moiety⁽¹²⁾, and fits with an interesting feature of these compounds for which in



Scheme 2

a) Gaschromatographic yield

b) Total yield of (8) and (9)

c) $^1\text{H-NMR}$: 6.37-6.98 (m, 10H), 5.93 (m, 1H, $J_{\text{trans}}=17.2$ Hz, $J_{\text{cis}}=10.2$ Hz, $^3J=6.7$ Hz), 5.14 (s, 1H), 5.1-4.92 (m, 2H), 3.12 (m, 2H), 0.20 (s, 9H)

MS: 307 (55), 306 (34), 292 (10), 234 (14), 226 (12), 191 (20), 190 (96), 167 (16), 140 (24), 77 (15), 73 (10)

(6) $^1\text{H-NMR}$: 7.37-6.98 (m, 10H), 6.60 (m, 1H), 5.82 (d, 1H, $J=11.1$ Hz), 4.98-4.84 (m, 2H), 1.98 (s, 2H), 0.21 (s, 9H)
MS: 307 (17), 306 (10), 292 (3), 234 (6), 191 (5), 190(28), 167 (4), 140 (6), 77 (15), 73 (100), 51 (3)

solution an apparent dynamic equilibrium is established⁽⁷⁾ with carbon-metal bonds, rapidly making and breaking.

In summary, the silylcupration of N-phenyl-N-ethynyl-aniline, provides a new flexible entry to the not easily accessible class of functionalized enamines. Among the others, the advantage offered by the high reactivity of the C-Si bond in (2) and (7) overcomes the difficulties encountered in the alkylation of ketone enamines in which complex mixtures are formed^(10,13). Finally, derivative (6) bearing a dienammino as well as an allylsilane moiety, is of high synthetic interest and studies directed to the exploitation of the reactivity of this new building block are currently underway in our laboratory.

References and notes

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5. The silylcupration performed *in situ* on compound 3, a key intermediate in the synthesis of 1 (scheme 1), afforded compound 2 in 70% yield and without loss of stereo- and regiochemistry (see also Ficini, J.; Barbara, C.; *Bull. Soc. Chim. Fr.*, 1964, 4. 871).
6. In a typical procedure 193 mg (1 mmol) of (1) were added at -23°C to a THF/HMPA solution of $(\text{Me}_3\text{Si})_2\text{CuLi}\cdot\text{LiCN}$. After 2 hours the solution was treated with MeOH at -23°C , stirred for ten minutes, and the solvent evacuated. The crude mixture was added with anhydrous diethylether and solid MgBr_2 and stirred for 20 min.; the solid was filtered and eliminated. 230 mg of (2) solid crystalline (m.p. $84-85^{\circ}\text{C}$) were recovered after removal of solvent and purification by Kugel-Rhor distillation (b.p. $=90^{\circ}\text{C}$ at 0.01 mm Hg). The only E isomer was spectroscopically detected. (2): $^1\text{H-NMR}$: 7.4-7.0 (m, 10H), 6.91 (d, 1H, $J=16.6$ Hz), 4.42 (d, 1H, $J=16.6$ Hz), 0.07 (s, 9H); $^{13}\text{C-NMR}$: 145.8, 143.4, 129.7, 124.3, 124.1, 99.7, 0.2; IR: 3039 (w), 2960 (w), 1586 (s), 1256 (s), 974 (m); MS: 267 (23), 266 (24), 252 (33), 194 (18), 77 (100), 59 (42), 51 (22).
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