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UNEXPECTED AFFECTS OF Me_3Si-X ON REACTIONS OF HIGHER ORDER CYANOCUPRATES

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Abstract: The assumed compatibility of Me_3SiCl with higher order cyanocuprates has been studied by both chemical and spectroscopic (^1H, ^7Li, ^{29}Si NMR) means. Both types of experiments confirm that Me_3Si-X significantly alters the composition of both homo ($R_2Cu(CN)Li_2$) and mixed ($RR'Cu(CN)Li_2$) reagents.

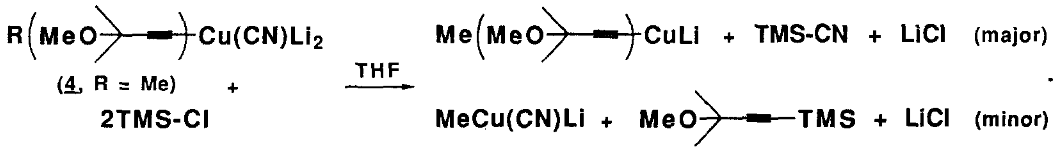
The remarkable impact of TMS-Cl in conjugate addition reactions of organocopper and organocuprate complexes has lead to widespread acceptance of this additive.[2] Since there is no measurable interaction of TMS-Cl with α,β-unsaturated ketones, it's role has been considered to be one of trapping the intermediate enolate reversibly formed from the addition of a copper anion to the β-position of the enone.[2f] Implied in this scenario is the complete compatibility of the cuprate with TMS-Cl. There is growing evidence, however, that such an assumption is incorrect,[2a,b] and indeed the significant modification of both lower order (L.O.)[3] and higher order (H.O.)[4] cuprates by $BF_3 \cdot Et_2O$ has recently been demonstrated. We now report that TMS-halides undergo an immediate and irreversible reaction with H.O. cuprates, affording different species which appear to be responsible for the chemistry observed.

The unanticipated affect of TMS-Cl was initially noted in 1,2-additions of $Bu_2Cu(CN)Li_2$ (1) to an α-substituted aldehyde 2. While 1 itself adds to 2 at -78° over 4 h to afford (after hydrolysis) a 1:1 mix of syn and anti diastereomers 3a,b, the same reaction conducted in the presence of 2 equiv TMS-Cl leads to a 7:1 ratio. This is curious, since the additive is presumed to exert an influence only with respect to reaction rate,[2f] coming into play after the 1,2-addition has occurred. Mixed cuprates 4 and 5 (see Table I), which by themselves are relatively unreactive under these conditions, not only now lead to 3a,b in high yields, but to ratios on the order of 12-13:1. Other trimethylsilyl halides were also examined, as summarized in Table I. Interestingly, Me_2SiCl_2 gave results similar to TMS-Cl, while TMS-Br was the reagent of choice here, affording an impressive 17-19:1 ratio in excellent yield.[5] It also assisted in consuming 2 more rapidly than did the other silyl additives.

From these surprisingly diastereoselective additions it was anticipated that TMS-Cl might be altering the cuprates themselves, perhaps by infiltration of the cluster or by removal of RLi (or R'Li) from the dianion as observed with BF_3.[4] We therefore turned to low temperature, high field ^1H, ^7Li, and ^{29}Si NMR to examine the nature of the interaction between H.O. cuprates and TMS-Cl. Homocuprate $Me_2Cu(CN)Li_2$ (6), as well as mixed cuprates 4 and 5 (R = Me), were all studied in THF. Treatment of 6 (which by itself gives a single peak in the ^1H NMR spectrum at δ -1.59 ppm) with 2TMS-Cl (δ 0.38 ppm) at -92° leads to new peaks at δ -1.44, 0.02, and in particular, at 0.31 ppm corresponding to TMS-CN. Upon warming to -80°, the new peaks all grow at the expense of the original two species present. Additional peaks at δ -0.04 and -1.31 ppm also appear (Fig. 1).[6,7] The remarkable occurrence of TMS-CN reveals that TMS-Cl is sequestering the cyano ligand from the H.O. cuprate.[8] The necessary outcome of this action is the generation of a lower order cuprate, R_2CuLi, plus LiCl (Eq. 1). Thus, the peak in the ^1H NMR furthest upfield in Figure 1 is predominantly Me_2CuLi, and not $Me_2Cu(CN)Li_2$! The ^{29}Si NMR (Fig. 2) confirms the presence of TMS-CN as the major species.

$$\mathrm{Me_2Cu(CN)Li_2} + \mathrm{2TMS\text{-}Cl} \xrightarrow[\leq -78^\circ]{\mathrm{THF}} \mathrm{Me_2CuLi} + \mathrm{TMS\text{-}CN} + \mathrm{TMS\text{-}Cl} + \mathrm{LiCl} \qquad ...(1)$$

Cuprates 4 and 5 (R = Me) were examined in a like manner. Reagent 4, with an acetylenic moiety isoelectronic with the cyanide ligand, follows two pathways of interaction with TMS-Cl (Eq. 2). That is, both TMS-CN and silylated acetylene ($MeOC(Me)_2C{\equiv}C$-TMS) are observed in the PMR spectrum, the former in excess. The ^{29}Si NMR spectrum at -85° corroborates the existence of these two species (Fig. 3), as does the ^7Li NMR, where the singlet for 4 (alone) moves from δ-0.70 ppm to a LiCl-like δ-0.10 (LiCl/MeOH as internal standard labelled as δ 0.00 ppm).

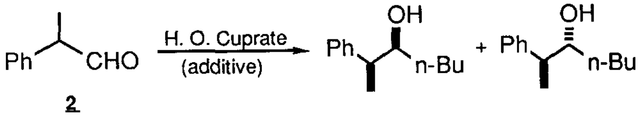


...(2)

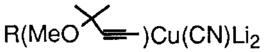
The mixed cuprate 5 (R = Me), in addition to surrendering its nitrile ligand to TMS-Cl, also gives up a small but observable percentage of the 2-thienyl group, to form 2-trimethylsilylthiophene as established by ^{29}Si NMR (Fig. 4). The proton NMR in the δ 0.5 to -2.0 ppm region shows the usual signals for TMS-Cl, TMS-CN, and both cuprates MeCu(CN)Li and Me(2-Th)CuLi (Fig. 5). The ^7Li NMR spectrum for 5 + 2TMS-Cl displays a dramatic shift from δ-0.92 (for 5 alone) to δ -0.06 ppm, again very close to that for LiCl.

The importance of TMS-CN, together with TMS-Cl, for enhancing diastereoselective 1,2-additions was checked chemically by comparison experiments using cuprates 4 (R = n-Bu) and 7 ($Bu(MeOC(Me)_2C{\equiv}C)CuLi$) on educt 2 (Scheme 1). From Eq. 2, it was expected that competitive removal of the acetylene group from 4 by TMS-Cl would decrease consumption of 2, since the remaining MeCu(CN)Li is unreactive under these conditions (case 1).[9] The 1,2-addition of preformed 7 in the absence of TMS-CN (case 3) was expected to suffer at least in terms of the

Table I. Effects of R_3Si-X on Reactions of H.O. Cuprates with Aldehyde 2 in THF at -78°.



2

	Additive	3a	:	3b	Yield (%)[a]
n-$Bu_2Cu(CN)Li_2$ 1	none	1		1	52-72[b]
	TMS-Cl	7		1	45 [b,c]
 4 (R = n-Bu)	none	no reaction			-- [b]
	TMS-Cl	10		1	88 [b]
	TMS-Br	17-19		1	97 [d]
	TMS-I	7		1	37 [b,]
	TMS-OTf	10		1	8 [b,c]
	Me_2Cl_2	12		1	20 [b,c]
R (2-Th)$Cu(CN)Li_2$ 5 (R = n-Bu)	none	1.5		1	23[b,c,]
	TMS-Cl	14		1	98 [b]

[a] By quantitative GC analyses. [b] After 4h. [c] Mostly starting material remains. [d] After 1.5h.

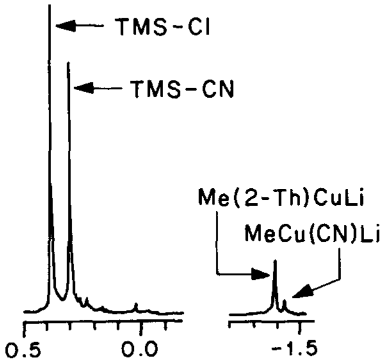


Figure 5. ^1H NMR for: $Me(2-Th)Cu(CN)Li_2 + 2TMS-Cl$

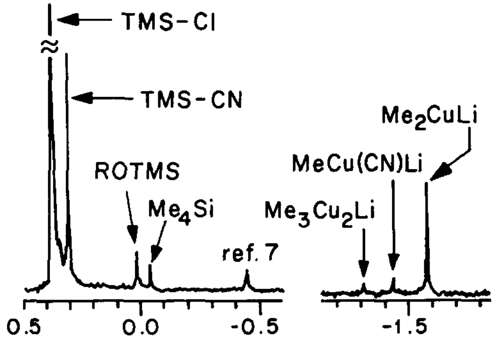


Figure 1. ^1H NMR of 6 + 2TMS-Cl at -80°

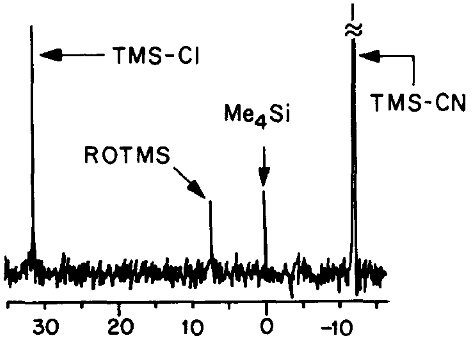


Figure 2. ^{29}Si NMR of 6 + 2TMS-Cl at -80°

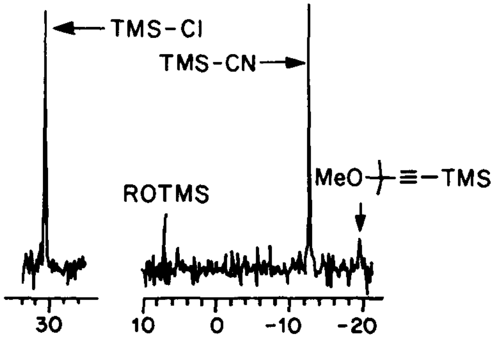


Figure 3. ^{29}Si NMR of 4 (R = Me) + 2TMS-Cl at -85°

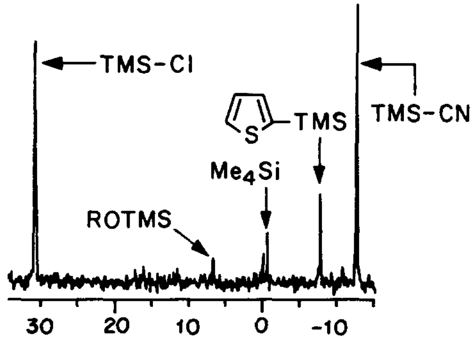
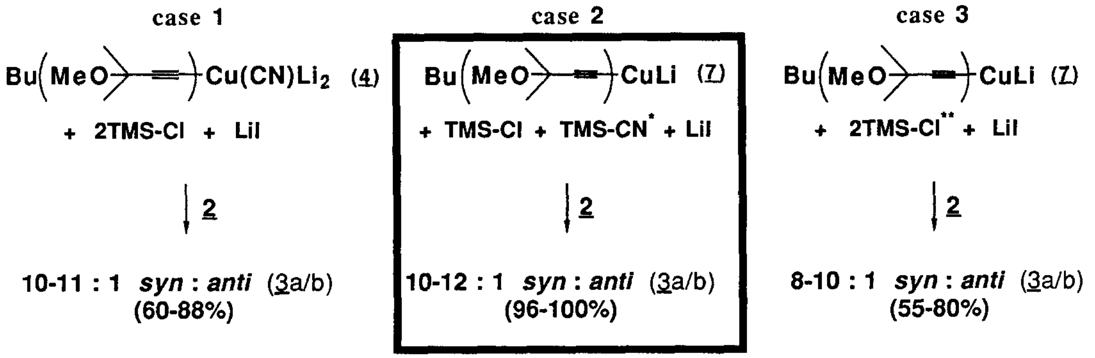


Figure 4. ^{29}Si NMR of 5 (R = Me) + 2TMS-Cl at -80°

syn:anti ratio of 3a:3b formed. The best case scenario was predicted to be that where 7 is reacted in the presence of both TMS-CN and TMS-Cl (case 2). In the event, indeed the highest yields and ratios of products are realized when both of these additives are in the medium.

Scheme 1.



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* Using 1eq TMS-CN alone gave 35% products (7 : 1) + mainly cyanohydrin. **The reaction with 2TMS-CN gave only a 50% yield as a mix (8.5 : 1) of diastereomers; the major competing process was cyanohydrin formation.

In summary, H.O. cuprates are not compatible with TMS-Cl, but react at low temperatures to form L.O. cuprates and TMS-CN. The presence of this in-situ formed additive (i.e. TMS-CN) leads to increased Cram selectivities for L.O. cuprate 1,2-additions in an as yet undetermined way. These spectroscopic and chemical data also suggest that L.O. cuprates are themselves unaffected by these additives,[10] although TMS-X derivatives clearly play a still elusive role in various types of cuprate coupling processes.

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References and Notes

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4. B.H. Lipshutz. E.L. Ellsworth, T.J. Siahaan, J. Am. Chem. Soc., 110, 4834 (1988).
5. The generality of these observations is presently being investigated.
6. The minor peak at δ -0.45 is due to an impurity in the MeLi.
7. NMR spectra were recorded for all pure species prepared individually.
8. The TMS-Br reacts with H.O. mixed cuprates to a far greater extent (by ^{1}H NMR) at -78° than does TMS-Cl to give much higher percentages of TMS-CN.
9. LiI (1 equiv) was added to the H.O. cuprate to provide this by-product of L.O. cuprate formation.
10. E.g., the ^{29}Si NMR spectrum of $\mathrm{Me(MeOC(Me)_2C{\equiv}C)CuLi}$ + 2TMS-Cl shows no $\mathrm{MeOC(Me)_2C{\equiv}C\text{-}TMS}$.

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