Synthetic Applications of Lithiated Tricarbonyl-η^6-arenechromium(0) Complexes: Copper and Palladium Catalysed Substitutions

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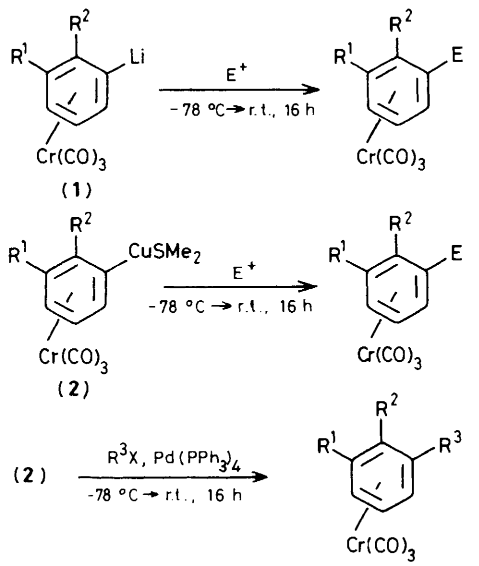
Regioselectively lithiated tricarbonyl-η^6-arenechromium(0) complexes can be acylated and allylated in high yield *via* the analogous arylcopper dimethyl sulphide complexes, and vinylated and arylated *via* palladium catalysed cross coupling of the arylcopper dimethyl sulphide complexes with vinyl and aryl halides.

Recently we reported that, by the use of either chelation control or lateral protection, regioselective lithiation of tricarbonyl-η^6-arenechromium(0) complexes could give access to unusual or normally inaccessible substitution patterns on the arene unit.[1—4] However, it became apparent that the nucleophilicity of the lithiated complexes was abnormally low relative to the basicity and that only a limited range of electrophiles could efficiently substitute for lithium[4] (Table 1). In general, substitution could be achieved with heteroatom electrophiles (entries 1—3), one-carbon electrophiles (entries



4,5),[5] non-enolisable ketones[1,2,5] and to a limited extent, enolisable ketones.[5,6] In contrast, some important classes of electrophile (entries 6—10) were ineffective and the problem was frequently traceable to rapid proton quenching of the lithiated species. We now report methods by which these difficulties can be overcome.

In order to avoid the problem of the basicity of the lithio-complexes, transmetallation to the analogous non-basic copper complexes was carried out.[7] The simple arylcopper reagents, produced from the lithio-complex and one equivalent of copper(I) bromide, proved to be too unreactive. Consequently the recently developed heterocuprates,[8] which use copper(I) dicyclohexylamide or copper(I) diphenylphosphide, were evaluated. Yields were high but it was subsequently found that the use of a copper(I) bromide dimethyl sulphide complex[7,9] (1 equiv.) gave comparable or better yields and these are the ones reported here. The active species is presumed to be the arylcopper dimethyl sulphide complex.

The results are given in Table 2. Acylations were achieved in good yield (entries 1,2,5,6,9) in tetrahydrofuran (THF) at

Table 1. Electrophilic substitution of Li in complexes (**1**) and (**4**).

Entry no.	Substrate	E⁺	Yield (%)
1	(**4**; R = SiPrⁱ₃, X = Li)	I_2[a]	90
2	,,	NBS[b]	54
3	,,	NCS[c]	49
4	(**1**; R¹ = OSiPrⁱ₃, R² = H)	MeI	71
5	(**4**; R = SiPrⁱ₃, X = Li)	Me_2NCHO	33
6	(**1**; R¹ = R² = H)	PrI	0
7	,,	MeCOCl	<20
8	,,	CH_2=$CHCH_2Br$	<10
9	,,	CH_2=CMeBr	0
10	,,	PhBr	0

[a] 1 Equiv. used in benzene solution. [b] NBS = *N*-bromosuccinimide (1 equiv.). [c] NCS = *N*-chlorosuccinimide (1 equiv.).

Table 2. Electrophilic substitution of $CuSMe_2$ in complexes (**2**), (**3**), and (**4**).

Entry no.	Substrate	E⁺	Yield (%)
1	(**2**; R¹ = R² = H)	MeCOCl	75
2	,,	CH_2=CHCOCl	62
3	,,	Me_2C=$CHCH_2Br$	62
4	,,	$\overline{[CH_2]_3CH{=}CHCH}Br$	65
5	(**2**; R¹ = H, R² = OMe)	PhCOCl	57
6	(**2**; R¹ = H, R² = F)	*trans*-PhCH=CHCOCl	47
7	,,	Me_2C=$CHCH_2Br$	67
8	,,	$\overline{[CH_2]_3CH{=}CHCH}Br$	84
9	(**3**; R = CH_2OMe, X = $CuSMe_2$)	MeCOCl	47
10	,,	Me_2C=$CHCH_2Br$	50
11	(**4**; R = SiPrⁱ₃, X = $CuSMe_2$)	$\overline{[CH_2]_3CH{=}CHCH}Br$	58[a]

[a] Reaction time 2 h. Further reaction time produced bromide induced desilylation.

Table 3. Palladium catalysed cross coupling reaction of complexes (**2**) or (**4**) with R³X.

Entry no.	Substrate	R³X	Yield (%)
1	(**2**; R¹ = R² = H)	CH_2=CHBr	95
2	,,	(**5**)	89
3	(**2**; R¹ = H, R² = OMe)	CH_2=CHBr	97
4	(**2**; R¹ = H, R² = F)	,,	87
5	(**4**; R = SiPrⁱ₃, X = $CuSMe_2$)	,,	51
6	(**4**; R = $SiPh_2Bu^t$, X = $CuSMe_2$)	(**5**)	46
7	(**2**; R¹ = R² = H)	PhI	79[a]
8	,,	2-bromopyridine	50[a]
9	,,	3-bromopyridine	20[a]

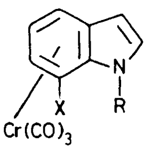
[a] 1 Equiv. of $Pd(PPh_3)_4$ used to preform the arylpalladium halide intermediate.

−78 °C to room temperature (r.t.) during 16 h, even when acidic protons were present (entries 1,9) and were little affected by ring substitution. In no case was over-reaction to alcohols[10] observed. Allylations (entries 3,4,7,8,10,11), which on the lithio-complexes were very poor (Table 1) occurred in 50—84% yield under similar conditions to the acylations. However, other substitutions normally possible with copper reagents,[7] alkylation, 1,4-addition, vinylation, and arylation all failed, even with the heterocuprates.

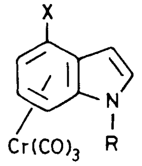
In order to circumvent this, the palladium catalysed cross coupling reaction[11] was considered. Although copper reagents have been little studied in this reaction,[9] the halophilicity of copper suggests that it would be an effective partner for the key halogen–alkyl ligand exchange step. In the event, the cross coupling occurred under mild conditions [lithiated complex, −78 °C, THF–CuBr·SMe$_2$ (1 equiv.) then halide (1 equiv.)–Pd(PPh$_3$)$_4$, −78 °C to r.t.] and in high yield (Table 3), particularly with the more reactive vinyl halides (entries 1—6). The aryl halide couplings (entries 7—9) proved to be less efficient and it was expedient to use one equivalent of tetrakistriphenylphosphinepalladium(0) and to preform the arylpalladium halide intermediate in order to attain good yields.

In contrast to the Heck reaction,[12] the more substituted olefin (**5**) gave yields only slightly less than the simple vinylation (entries 2,6) and this process is a possible alternative for those cases in which the Heck reaction fails.

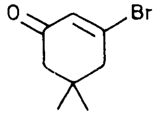
We have, therefore, now developed methods for the application of the (regiocontrolled) lithiated complexes to a wide range of useful substitutions. The origin of the diminished nucleophilicity of these lithiated complexes presumably arises from a combination of the net electron withdrawal from the arene by the chromium unit and its steric hindrance to the in-plane attack of the electrophile on the σ-framework of the anion.



(**3**)



(**4**)



(**5**)

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