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# Electrophilic Amination of Diarylzincs and Triarylzincates with Acetone -(2,4,6-Trimethylphenylsulfonyl) Oxime and with O-Methylhydroxylamine

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## ELECTROPHILIC AMINATION OF DIARYLZINCS AND TRIARYLZINCATES WITH ACETONE -(2,4,6-TRIMETHYLPHENYL SULFONYL)OXIME AND WITH O-METHYLHYDROXYLAMINE

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**Abstract:** Diarylzincs and triarylzincates react efficiently with acetone O-(2,4,6-trimethylphenylsulfonyl)oxime and O-methylhydroxylamine in the presence of CuCN to give amines in good yields.

There has been a great deal of interest in the electrophilic amination of carbanions and detailed reviews on this subject have appeared which outline the use of aminating reagents for the combination of the amino group, "NH<sub>2</sub><sup>+</sup>" with various organometallics. <sup>1</sup> A number of new reagents have also been identified, for example, N,O-bis(trimethylsilyl)hydroxylamine<sup>2</sup>, lithium t-butyl N-tosyl-oxycarbamate<sup>3</sup>, N-protected oxaziridines<sup>4</sup>, 1-chloro-

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1-nitrosocyclohexane<sup>5</sup>, acetone O-(2,4,6-trimethylphenylsulfonyl) oxime<sup>6</sup>, 4,4-bis (trifluoromethyl)benzophenone O-(methylsulfonyl)oxime<sup>7</sup> and bis(2,2,2-trichloroethyl) azodicarboxylate.<sup>8</sup> However, great emphasis has been placed on organolithiums.<sup>1,3a-c,4,5,9</sup> Grignard reagents <sup>1,6,7,9</sup>, organocoppers <sup>1,2,3,9</sup> and organoboranes<sup>10</sup> as the organometallics to be aminated with the exception of some reports on the amination of organozinc enolates<sup>3a,5,11</sup> and a few unsuccesful attempts.<sup>1,3d,8,12</sup> An electrophilic amination protocol by oxidative decomposition of lithium and zinc amidocyanocuprates has also been reported.<sup>13</sup>

The importance of organozinc reagents <sup>14-17</sup> due to their easy preparation, high reactivity as zinc-copper reagents and excellent functional group tolerance as well as Li, Mg and Cu to Zn transmetallation ability has stimulated us to the development of amination methods for organozinc reagents. We report herein our results in studies on the amination of organozinc

reagents, 1 with acetone O-(2,4,6-trimethylphenylsulfonyl) oxime, 2 and O-methyl-hydroxylamine, 3 (Scheme 1).

$$RM + Mc_{2}C = NOSO_{2} \longrightarrow Mc \xrightarrow{THF, rt, 3h} [Mc_{2}C = NR] \xrightarrow{Hydrolysis} RNH_{2}$$

$$\frac{1}{2}$$

$$RM + McONH_{2} \xrightarrow{1. THF, rt, 3h} RNH_{2}$$

$$\frac{1}{3} \xrightarrow{Hydrolysis} 4$$

$$M: ZnCl, 1/2 Zn, 1/3 ZnLi (or MgBr), ZnCl/CuCN, 1/2 Zn/CuCN, 1/3 ZnM' (M': Li or MgBr)/CuCN, Cu(CN)ZnCl, 1/2 CuZnCl$$

Scheme 1

Initial electrophilic amination studies of the organozines were conducted on phenylzine chloride and diphenylzine prepared from phenyllithium, lithium triphenylzineate and zine homo-and heterocuprates, i.e. diphenylzine cuprate and phenylzine cyanocuprate. As can be seen in Table 1, the direct amination of phenylzine chloride, diphenylzine and lithium triphenylzineate with 2 were dissapointing, however in the presence CuCN, reaction results in the formation of aniline in good yields (Table 1, entries 4,9,13). Amination of triphenyllithium zineate catalyzed with 20 mol % CuCN gave the highest yield (entry 13). Optimization experiments indicated that the yield is strongly dependent on the amount of CuCN (Table 1, entries 11, 12). However, stoichiometric zine cyanocuprate (Table 1, entries 16-20) and zine cuprate (Table 1, entry 21) did not give higher amination yields. The use of a mixed zineate, Me<sub>2</sub>PhZnLi<sup>18</sup> (RM/2=2) rather than Ph<sub>3</sub>ZnLi was not found more succesful for amination (Table 1, entry 14).

As we already observed<sup>6</sup> Lewis acid character of  $MgCl_2$  leading to an increasing yield and/or shorter reaction time in the Cu (I) catalyzed reaction of phenylmagnesium bromide with 2, we also tried the CuCN catalyzed amination of phenylzine bromide derivated phenylzine chloride and diphenylzine and bromomagnesium triphenylzineate with 2 (Table 1, entries 22-25). By comparison of Table 1, entries 4 and 22; 9 and 23; 13 and 25, it can be easily seen that CuCN catalyzed amination of phenylzine reagents result in higher yields if they are prepared by Mg to Zn metallation rather than Li to Zn metallation. To support the role of MgCl<sub>2</sub> in

 

 Table 1 Electrophilic amination of arylzinc reagents, 1 with acctone O-(2,4,6-trimethlylphenylsulfonyl) oxime, 2 and O-methlyhydroxylamine, 3<sup>[a]</sup>.

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Entry	RM <sup>[b,c]</sup>	CuCN mol %	Aminating reagent	Reaction of Temp.	conditions <sup>[d]</sup> Time, h	Yield of RNH <sub>2</sub> % <sup>[e]</sup>
1	PhZnCl	_	2	rt	3	0
2	PhZnCl	10	2	rt	3	25 <sup>[[]</sup>
3	PhZnCl <sup>[g]</sup>	20	2	rt	3	10
4	PhZnCl	20	2	гt	3	58
5	PhZnCi <sup>th</sup>	20	2	rt	3	32
6	PhZnCl	100	2	rt	3	12
7	Ph <sub>2</sub> Zn		2	rt	3	0
8	Ph_Zn <sup>[g]</sup>	20	2	rt	3	31
9	PhoZn	20	2	rt	3	44
10	Ph <sub>a</sub> ZnLi	_	2	rt	3	.0
11	PhyZnLi	5	2	rt	3	57
12	Ph <sub>3</sub> ZnLi	10	2	rt	3	52
13	Ph,ZnLi	20	2	rt	3	70
14	Me_PhZnLi <sup>[i]</sup>	20	2	ч	3	59
15	Ph <sub>a</sub> ZnLi <sup>[j]</sup>	20	2	rt	3	79,70 <sup>[k]</sup>
16	PhCu(CN)ZnCl	—	2	rt	3	<b>5</b> 6
17	PhCu(CN)ZnCl	-	2	rt	1	38 <sup>[1]</sup>
18	PhCu(CN)ZnCl <sup>[n</sup>	ป	2	0°C	l	57
19	PhCu(CN)ZnCl		2	0°C, r	t 0.75	52
20	PhCn(CN)ZnCl		2	-15°C	C,rt 1,2	53
21	Ph <sub>2</sub> Cu ZnCl	_	2	-15°C	L,n 1,2	49
22	PhZnCl	20	2	rt	3	65,65 <sup>[k]</sup>
23	Ph <sub>2</sub> Zn	20	2	rt	3	68
24	Ph <sub>3</sub> ZnMgBr		2	h	3	23
25	Ph <sub>3</sub> ZnMgBr	20	2	rt	3	85
26	p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ZnCl	20	2	rt	3	49 <sup>[k]</sup>
27	(p-C11 <sub>3</sub> C <sub>6</sub> 11 <sub>4</sub> ) <sub>2</sub> Zn	i 20	2	rt	3	45 <sup>(k)</sup>
28	(p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ) <sub>3</sub> ZnMg	Br 20	2	n	3	55 <sup>[k]</sup>

 $RM + 2 \text{ or } 3 \longrightarrow RNH_2$   $1 \qquad 4$ 

Ent	ry RM <sup>[b,c]</sup>	CuCN mol %	Aminating reagent	Reaction Temp.	conditions <sup>[d]</sup> Time, h	Yield of RNH <sub>2</sub> % <sup>[e]</sup>
29	p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> ZnCl	20	2	rt	3	54 <sup>[k]</sup>
30	$(p-CH_3OC_6H_4)_2Zn$	20	2	rt	3	51 <sup>[k]</sup>
31	(p-CH_OC_H_),ZnMgBt	20	2	rt	3	61 <sup>[k]</sup>
32	PhZnCl	_	3	rt	3	0
33	PhZnCl	20	3	rt	3	70
34	Ph <sub>2</sub> Zn	20	3	rt	3	70
35	PhzZnLi	_	3	rt	3	33
36	PhzZnLi	20	3	rt	3	92, 89 <sup>[:1]</sup>
37	PhCu(CN)ZnCl	_	3	rt	3	40
38	Ph <sub>2</sub> CuZnCl	_	3	rt	3	42
39	$(p-CH_3C_6H_4)_2Zn$	20	3	rt	3	65 <sup>[k]</sup>
40	(p-CH <sub>3</sub> C <sub>6</sub> H <sub>4</sub> ) <sub>3</sub> ZnMgBr	20	3	rt	3	62 <sup>[k]</sup>
41	(p-CH <sub>3</sub> OC <sub>6</sub> H <sub>4</sub> ) <sub>2</sub> Zn	20	3	rt	3	65 <sup>[k]</sup>
42	$(p-CH_3OC_6H_4)_2ZnMgB$	r 20	3	rt	3	63 <sup>[k]</sup>

- [a] Phenylzinc reagents in entries 1-21 and 32-38 were prepared by transmetallaton of phenyllith.um. Phenylzinc reagents and other organozinc reagents in entries 22-31 and 39-42 were prepared by transmetallation of the corresponding organomagnesium bromides.
- [b] RZnCl, R<sub>2</sub>Zn and R<sub>3</sub>ZnLi (or R<sub>3</sub>ZnMgBr) were prepared by treating an ethereal solution of RLi (or RMgBr) (1,2 and 3 equiv, respectively) with anhydrous ZnCl<sub>2</sub> (1 equiv) in THF at 0°C and stirring for 15 minutes.
- [c] PhCu(CN)ZnCl and Ph<sub>2</sub>CuZnCl were prepared by transmetallation of PhCu(CN)Li and Ph<sub>2</sub>CuLi, respectively. PhCu(CN)Li was prepared by treating an ethereeal solution of PhLi (1 equiv) with CuCN (1 equiv) at 15 °C, stirring for 15 minutes and then by adding anhydrous ZnCl<sub>2</sub> (1 equiv) to PhCu(CN)Cl solution at -15°C and stirring again for 15 minutes. Ph<sub>2</sub>CuLi was prepared by treating and ethereal solution of PhLi (2 equiv) with CuI (1 equiv) at -15 °C and adding ZnCl<sub>2</sub> (1 equiv) to Ph<sub>2</sub>CuLi solution as above.
- [d] Reactions were carried out with 1.5 or 3.0 mmol aminating reagent, 2 or 3. RM/2= 1.5 and RM/3 = 2 for RZnCl, R<sub>2</sub>Zn and R<sub>3</sub>ZnLi (or R<sub>3</sub>ZnMgBr); RM/2 (or 3) = 2 for RCu(CN)ZnCl and R<sub>2</sub>CuZnCl.
- [e] Yield determined as average of two or more runs by GC using internal standard technique and based on 2 or 3 unless otherwise noted.
- [f] Yield of aniline purified by column chromatography.
- $[g] Ph_2Zn/2 = 1$
- <sup>[h</sup> <sup>h</sup>HMPA was used as cosolvent (THF/HMPA= 3.7/1).
- [i] Me<sub>2</sub>PhZnLi was prepared by treating Me<sub>2</sub>Zn (1 equiv) with PhLi (1 equiv) at 0°C and stirring for 15 minutes. Me<sub>2</sub>PhZnLi/2 = 2.
- [j] MgCl<sub>2</sub>, 20 mol % was addet to the reaction mixture.
- [k] Yield of amine isolated as N-benzoyl derivative.
- [1] Yield of aniline was found to be 36% and 32% after a reaction time of 0.25 and 0.5 h, respectively.
- [m]PhCu(CN)ZnCl/2 = 2.25
- [n] Yield of aniline purified by distillation.

electrophilic amination of carbanions with 2, the CuCN catalyzed amination of lithium triphenylzineate was also carried out in the presence of  $MgCl_2$  (20 mol %) (Table 1, entry 15). The reaction led to a yield of 79 %, which is higher than that of lithium zineate (70%), but not much lower than that of bromomagnesium zineate (85%).

We also examined the efficiency of O-methylhydroxylamine, **3** as an aminating reagent for phenylzine reagents (Table 1, entries 32-38). CuCN catalyzed amination of triphenyllithium zincate gave the highest yield (Table 1, entry 36) again compared to the other phenylzine reagents. In addition, **3** seems to be a more efficient reagent than **2** for the amination of diarylzines and triarylzineates.

We also used p-tolyl and p-anisylzinc reagents prepared from corresponding Grignard reagents to be aminated with both 2 and 3. Amination of dip-tolylzinc with 3 (Table 1, entry 39) and amination of trip-tolylbromomagnesium zincate with 2 and 3 (Table 1, entries 28 and 40) resulted in higher yields (55-65 %). Amination of dip-anisylzinc with 3 (Table 1, entry 41) and trip-anisylbromomagnesium zincate with 2 and 3 (Table 1, entries 31 and 42) also led to similar yields (61-65 %).

In conclusion, we revealed that diarlyzines and triarylyzineates prepared by Mg to Zn transmetallation and less efficiently by Li to Zn transmetallation undergo facile amination with 2 and 3 to give amines in good yields. Further investigations into the amination of alkylzines and functional group containing organozines are currently in progress.

#### **Experimental Section**

Typical procedure for the CuCN catalyzed reaction of bromomagnesium triaryl- zincates with acetone O-(2,4,6-trimethylphenylsulfonyl)oxime, **2** or O-methyl-hydroxylamine, **3**.

Under nitrogen atmosphere, to a flask containing ZnCl<sub>2</sub> (0.613 g, 4.50 mmol) at 0°C dry THF (10 ml) was injected and PhMgBr (13.5 mmol) in ether was added dropwise. The mixture was stirred at 0°C for 20 minutes and then the temperature was allowed to rise to room temperature. CuCN (0.614 g, 0.90 mmol) was added. After stirring the mixture for 15 minutes, a solution of 2 (0.765 g, 3.00 mmol) in THF (6 ml) or 3 (0.047 g, 2.25 mmol) in THF (4 ml) was added and stirring was continued for 3 hours. For hydrolytic workup after amination with 2, the mixture was stirred at room temperature with 12 N HCl (10 ml) for 2 hours. The aqueous phase was washed with ether, made basic with conc. NaOH and the free amine was extracted with ether (4x30 ml). The organic layer was dried over Na, SO<sub>4</sub>. The crude material obtained after evaporation of solvent in vacuo was purified by distillation or flash chromatography on silicagel with etherpetroleum ether (5:4) to give pure amine whose GC and spectral data matched those of authentic material. After amination with 3, hydrolysis of the mixture was also carried out with saturated solution of NH<sub>4</sub>Cl/NH<sub>3</sub> (5:1) (10 ml). The aqueous phase was extracted with ether and the crude material was purified with column chromatography to give amine as above. After hydrolytic workup, amine was also isolated as N-benzoyl derivative.<sup>19</sup>

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