

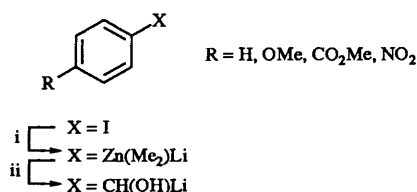
Preparation and reactions of lithium indolyl(dimethyl)zincates

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Lithium indol-3-yl(dimethyl)zincates, prepared by halogen-zinc exchange of 3-iodo-1-phenylsulfonylindoles with lithium trimethylzincate, reacted with benzaldehyde to give the corresponding alcohols.

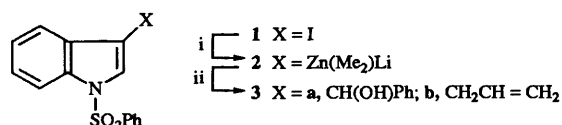
Recently we reported that iodobenzenes possessing various functional groups reacted with lithium trimethylzincate to give lithium dimethyl(aryl)zincates which, in turn, reacted with electrophiles.¹



Scheme 1 Reagents and conditions: i, Me₃ZnLi, THF, -78 °C; ii, R'CHO, -78 °C→room temp.

In order to prepare a new class of indolylzinc derivatives, we have investigated direct halogen-zinc exchange of 2- and 3-iodoindoles with lithium trimethylzincate.

First, the zincate **2**, prepared by treatment of the indole **1** with lithium trimethylzincate at -78 °C in THF, was allowed to react with benzaldehyde to give the desired alcohol **3a** (51%). A similar reaction with the zincate **2** and allyl bromide gave compound **3c** (44%). The metallation when conducted with a combination of lithium trimethylzincate and TMEDA (*N,N,N',N'*-tetramethylethylenediamine) gave the expected products in slightly higher yields. Although 3-lithio-1-phenylsulfonylindole is known to isomerize easily to the thermodynamically stable 2-lithioindole,^{2a,†} no 2-substituted isomers were observed in these reactions. The present method is, therefore, considered to be advantageous for the metallation of the 3-position of indoles.

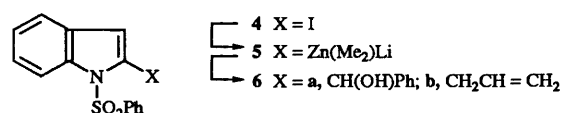


Scheme 2 Reagents and conditions: i, Method A (Me₃ZnLi, THF, -78 °C; 1 h) or Method B (Me₃ZnLi-TMEDA, THF, -78 °C, 1 h); ii, Electrophile -78 °C→room temp.

Electrophile	Method	3	Yield (%)
PhCHO	A	a	51
PhCHO	B	a	61
CH ₂ =CHCH ₂ Br	A	b	44
CH ₂ =CHCH ₂ Br	B	b	56

Similarly, the 2-iodoindole **4** gave compounds **6a** (54%) and **6b** (64%).

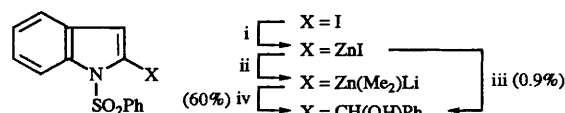
† It has been reported that 1-(*tert*-butyldimethylsilyl)indol-3-yl lithium is a stable species which does not rearrange to the 2-isomer and that 1-(*tert*-butyldimethylsilyl)indol-3-yl zinc chloride had been prepared.^{3b}



Scheme 3 Reagents and conditions: i, Me₃ZnLi-TMEDA, THF, -78 °C, 1 h; ii, Electrophile, -78 °C→room temp.

Electrophile	6	Yield (%)
PhCHO	a	54
CH ₂ =CHCH ₂ Br	b	64

The indol-3-ylzincate **2** was also prepared by allowing indol-3-ylzinc iodide,³ itself obtained from the oxidative addition of active zinc⁴ to the indole **1**, to react with methyl lithium. Indol-3-ylzinc iodides were found not to undergo 1,2-addition to benzaldehyde in the absence of additives. The zincate derived from the reaction of indol-3-ylzinc iodide and methyl lithium showed similar reactivity toward 1,2-addition to give the alcohol (60%). Although this zincate formation demonstrates effective activation of organozinc halides, the halogen-zinc exchange of iodoindoles with lithium trimethylzincate seems to be superior for the preparation of indolylzincates.



Scheme 4 Reagents and conditions: i, active Zn, THF, room temp., 0.5 h; ii, MeLi (2 equiv.), 0 °C, 0.5 h; iii, PhCHO, -78 °C→room temp., 12 h; iv, PhCHO, 0 °C→room temp., 12 h

In summary, the indolylzincates prepared in this work provide a new class of organozinc reagents which complement those already widely used for organic synthesis.⁵

Experimental

Phenyl(1-phenylsulfonylindol-3-yl)methanol

MeLi (1.03 mol dm⁻³ solution in Et₂O; 3.21 cm³, 3.3 mmol) was added at 0 °C to a solution of ZnCl₂-TMEDA⁶ (383 mg, 1 mmol) in THF (5 cm³) and the mixture was stirred at 0 °C for 30 min. It was then cooled to -78 °C and treated with 3-iodo-1-phenylsulfonylindole (383 mg, 1 mmol) in THF (2 cm³). After the resulting mixture had been stirred at -78 °C for 1 h, benzaldehyde (0.20 cm³, 2 mmol) was added to it at the same temperature. The mixture was then gradually warmed to room temperature during 12 h after which it was treated with aq. NH₄Cl (2 cm³), concentrated by removal of THF under reduced pressure, diluted with water (20 cm³) and extracted with CHCl₃ (30 cm³ × 3). The combined extracts were dried (MgSO₄) and evaporated and the crude material was purified by silica gel column chromatography using hexane-AcOEt

(4: 1) as eluent to give a viscous oil (221 mg, 61%); δ_{H} (300 MHz; CDCl_3) 2.24 (1 H, d, J 3.6), 6.02 (1 H, d, J 3.6), 7.15 (1 H, t, J 7.3), 7.24–7.58 (12 H, m), 7.87 (1 H, d, J 7.3) and 7.97 (1 H, d, J 8.4); m/z 363 (M^+ , 52%) (Found: m/z 363.0914. Calc. for $\text{C}_{21}\text{H}_{17}\text{NO}_3\text{S}$: M , 363.0928).

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