

REACTIONS OF METHYLCOPPER AND CHIRAL ORGANOCUPRATES WITH 1-NITRO-2-PHENYLETHENE AND OF LITHIUM DIMETHYLCUPRATE WITH METHYL 3(NITROPHENYL)PROPENOATES

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Abstract—Organocopper compounds like methylcopper, lithium dimethylcuprate, chiral lithium methyl-(*S*)-2(1-dimethylaminoethyl)-phenylcuprate and lithium menthoxy(methyl)cuprate react with 1-nitro-2-phenylethene to give the conjugate addition product 1-nitro-2-phenylpropane in moderate yields. In the reaction with lithium methyl-(*S*)-2(1-dimethylaminoethyl)phenylcuprate 2% asymmetric induction was obtained. The reaction between lithium dimethylcuprate and methyl 3(4-nitrophenyl)propenoate gave the corresponding azoxy compound and no conjugate addition product, while methyl 3(3-nitrophenyl)propenoate gave some conjugate addition.

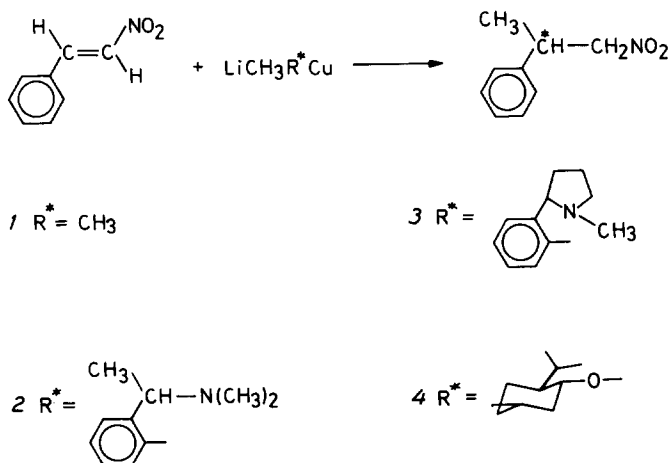
Organocuprates are valuable reagents in several addition reactions.¹ We have earlier investigated reactions between mixed chiral cuprates and several enones² and enoates^{3,4} and also organocopper reactions of 1,3,5-trinitrobenzene.^{5,6} We are therefore interested in reactions between cuprates and unsaturated compounds also containing a nitro group. We describe here the reactions between 1-nitro-2-phenylethene and methyl copper, lithium dimethylcuprate (1), lithium methyl-(*S*)-2-(2-*N*-methylpyrrolidiny)phenylcuprate(2), lithium methyl-(*S*)-2-(1-*N,N*-dimethylaminoethyl)phenylcuprate (3) and lithium menthoxy(methyl)-cuprate (4), respectively (Scheme 1). The last two chiral reagents gave some asymmetric induction.

Bowlus⁷ has described the reaction between 1-nitro-2-phenylethene and lithium dimethylcuprate. Langer and Seebach⁸ reacted some nitro-olefins with lithium diorganocuprates in chiral solvents and obtained some asymmetric induction. Bartoli *et al.* reported that Grig-

nard reagents added to nitroarenes, giving addition products;⁹ in the presence of copper(I) halide the nitro group was reduced.¹⁰ Furthermore, Severin and Schmitz have reported that addition of a large excess of Grignard reagent to 1,3,5-trinitrobenzene gave trialkyl-trinitrocyclohexanes.¹¹ Some organocopper compounds add to 1,3,5-trinitrobenzene in pyridine to give Meisenheimer compounds in reactions which are analogous to conjugate addition.^{6,12,13} Nitrobenzene has been used to oxidise mixed lithium diorganocuprates (LiRR'Cu) to *R-R'* although the fate of the nitrobenzene is not known.¹⁴ In the present work we also explored the reactions between lithium dimethylcuprate and methyl 3(nitrophenyl)propenoates.

RESULTS AND DISCUSSION

As observed by Bowlus,¹⁷ 1-nitro-2-phenylethene is very reactive towards lithium dimethylcuprate giving the conjugate addition product in moderate yield. A polymeric



Scheme 1.

material is also formed, which is similar to that obtained on anionic polymerisation of the starting material.¹⁵ When the temperature is lowered the amount of solid polymeric material increases at the expense of the conjugate addition product.

When lithium iodide is present methylcopper adds to 1-nitro-2-phenylethene in reasonable yield with less formation of polymeric material. Methylcopper, from which the lithium iodide had been removed, reacted less and it therefore seems probable that the lithium iodide aids in solubilising the methyl copper or by forming an heterocuprate such as LiMeICu (see Ref. 16). Thus methylcopper plus lithium iodide here offer a preparative advantage over lithium dimethylcuprate.

We also investigated the addition to 1-nitro-2-phenylethene of the mixed chiral organocuprates (LiMeR*Cu) lithium methyl-(*S*)-2-(2-*N*-methylpyrrolidinyl)phenylcuprate (2),¹⁷ lithium methyl(*S*)-2(1-*N*,*N*-dimethylaminoethyl)phenylcuprate (3),⁴ and lithium menthoxy-methyl)phenylcuprate (4).^{18,19} The yields of conjugate addition product were moderate and some polymer was formed (Table 1). Cuprate 3 gave a 2% excess (e.e.) of the *R* enantiomer; this was established after reduction to 2-phenylpropylamine with known absolute configuration.²⁰⁻²²

Table 1. Reactions between organocopper reagents and 1-nitro-2-phenylethene. Yields are given in per cent after distillation (product 1-nitro-2-phenylpropane and substrate) or recrystallisation (polymer)

Reagent	Temp. °C	Yields	
		Product	Polym. Subst.
MeCu (no LiI)	0	13	13
MeCu, 2 eq. (no LiI)	0	20	6
MeCu + LiI	0	50	2
<u>1</u>	0	33	10
<u>1</u>	-40	31	17
<u>1</u>	-78	4	8
<u>2</u> (no LiI)	0	6 (no e.e.)	10
<u>3</u> (no LiI)	-40	22 (2% e.e.)	6
<u>4</u>	-40	12 (1% e.e.)	1

The result of the reaction between cuprate 4 and 1-nitro-2-phenylethene, 12% isolated yield and 1% e.e. of (*R*)-1-nitro-2-phenylpropane, might be compared with reactions between lithium alkylmenthoxy cuprates with 2-cyclohexenone.^{18,19}

Lithium dimethylcuprate in tetrahydrofuran reacted readily with methyl 3(4-nitrophenyl)propenoate to give the corresponding azoxy compound in 45% yield, whereas no conjugate addition was observed. The reaction is reminiscent of the formation of azoxybenzenes in some copper(I) oxide-promoted reactions²³ as well as in Grignard reactions.⁹ Methyl 3(3-nitrophenyl)propenoate gave some conjugate addition (23%) in THF; in toluene the azoxy compound was the predominant product. The *ortho* isomer gave a vigorous and complex reaction.

The results show that an aromatic nitro group *ortho* or *para* to an attached enoate system prevents conjugate addition and that the nitro groups can take part in side reactions, especially in non-polar solvents.

EXPERIMENTAL

The organometallic reactions were performed under purified N₂. Methoxylithium, 2(1-*N*,*N*-dimethylaminoethyl)phenyllithium and 2-(2-*N*-methylpyrrolidinyl)phenyllithium were prepared from (-)-menthol, *S*(-)-*N*,*N*-dimethyl-1-phenylethylamine and *S*(-)-*N*-methylphenylpyrrolidine, respectively, and BuLi in ether at room temp. The reactions were checked with Gilman tests I and II.²⁴

Methylcopper was prepared from MeLi and copper(I) iodide in ether at 0°. In some reactions the ethereal mixture was centrifuged, the ether was drawn off and the methylcopper washed with fresh ether (Table 1). The proper organolithium compound was then added to the methylcopper at 0° to form the mixed, chiral cuprates 2, 3 and 4, respectively. Lithium dimethylcuprate (1) was prepared analogously.

1-Nitro-2-phenylpropane. 1-Nitro-2-phenylethene (20 mmol in 10 ml dry ether) was added drop by drop to a cold (Table 1) and stirred soln or suspension of the cuprate or organocopper compound (22 mmol monomer) in ether. The total volume after addition was 40 ml. The mixture was added after 30 min to a saturated NH₄Cl/NH₃ (pH 8) sol. A white, sparingly soluble material separated and was filtered off and recrystallised from EtOH, m.p. 225–230°, yields see Table 1. Found: C, 63.1, H, 5.4, N, 9.2 and O, 22.3. Calc. for (C₉H₉NO₂)_n: C, 64.4, H, 4.7, N, 9.4, O, 21.5% and M 149.1*n*. MS 284.1168. IR(KBr): 1555 s, 1380 s cm⁻¹. ¹H NMR(270 MHz, CDCl₃, 333 K): δ 7.4(phenyl, m), 4.50, 4.25, 3.77 (CH-CH, chain, m, *J* 3 Hz, 11 Hz and 7 Hz).

The ethereal layer was dried and the residue distilled in a Kugelrohr, b.p. 84°/10 Pa, to give 1-nitro-2-phenylpropane, yields see Table 1. IR(neat): 1555s, 1380 s cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 7.3 (5H, m), 4.45 (2H, d, 7 Hz), 3.5 (1H, m, 7Hz) and 1.27 (3H, d, 7 Hz). The distillation residue was not investigated.

2-Phenylpropylamine. 1-Nitro-2-phenylpropane (1.6 g) was reacted with metallic Fe in boiling HCl.²² The product was distilled in a Kugelrohr, b.p. 50°/130 Pa, to give 0.56 g (41%) 2-phenylpropylamine. IR(neat): 3370, 3300 and 1600 cm⁻¹. ¹H NMR (60 MHz, CDCl₃): δ 7.4 (5H, m), 2.88 (3H, m CH₂-CH), 1.35 (2H, b, NH₂) and 1.25 (3H, d, 7 Hz, CH₃). 1-Nitro-2-phenylpropane, [α]_D²⁵ = -0.040 (benzene, 0.50) gave *R*(+)-2-phenylpropylamine²⁰ (e.e. 2%),²¹ [α]_D²⁵ = +0.60 (EtOH, 0.049).

Reactions with methyl (nitrophenyl)propenoates. The lithium dimethylcuprate (60 mmol) was prepared in toluene or tetrahydrofuran (50 ml). The ester (25 mmol, dissolved in 50 ml toluene or THF) was added to the reagent at 0°. The mixture was worked up when all the substrate was consumed according to glc.

Methyl 3(2-nitrophenyl)propenoate. The substrate was consumed immediately and the mixture turned dark. After the usual work-up, tlc of the crude product showed several blue, red and yellow products. The mixture was not further investigated.

Methyl 3(3-nitrophenyl)propenoate. Immediately after the ester had been added to the cuprate the soln turned bright yellow-red, the colour disappeared and a yellow ppt (methylcopper) appeared. The substrate was consumed within 2.5 hr. After the usual work-up the methyl 3(3-nitrophenyl)butanoate was recrystallised from EtOH to give 0.77 g (23%) of colourless material, m.p. 113–115°. IR(KBr): 1715 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 8.4–7.4 (4H, m), 4.30 (3H, dd + m), 3.75 (3H, s) and 0.83 (3H, d, 7 Hz). When the reaction was performed in toluene 0.30 g dimethyl 3',3'-azoxybis-3-phenylpropenoate was formed, m.p. 125–130°. MS: *m/e* = 366.130 (M⁺, 73%); 350.127 (M⁺-16, 100%). IR(KBr) 1710 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 8.5 (1H), 8.3 (1H, m), 8.1 (1H, m), 7.5–7.8 (7H, m), 6.55 (2H, dd, 6 Hz), 3.84 (3H, s), 3.83 (3H, s). UV (EtOH, log ε): 275 nm, 4.5 and 3.20 nm, sh 4.2.

Methyl 3(4-nitrophenyl)propenoate. The reactions were performed in toluene or THF; in both solvents dimethyl 4',4'-azoxybis-3-phenylpropenoate was formed. In THF 7 mmol substrate gave 0.40 g(54%) and in toluene 0.26 g(34%) azoxy compound after recrystallisation from EtOH, m.p. 150–152°. IR(KBr): 1710, 1520, 1350 and 1175 cm⁻¹. ¹H NMR (270 MHz, CDCl₃): δ 8.27 (1H, d, 16 Hz), 8.15 (1H, d, 16 Hz), 7.67 (1H, d, 16 Hz), 7.64 (1H, d, 16 Hz), 7.59 (2H, d, 8.5 Hz), 7.57 (2H, d, 8.5 Hz), 6.46 (1H, d, 16 Hz), 6.44(1H, d, 16 Hz), 3.77 (3H, s) and 3.78 (3H, s). MS: *m/e* = 366(M⁺); 350 (M⁺-16).

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