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# UNEXPECTED REACTIVITY OF ALLYL MAGNESIUM CHLORIDE WITH NITROARENES. A GENERAL METHOD OF SYNTHESIS OF N-ALLYL-N-ARYLHYDROXYLAMINES AND N-ALLYLANILINES

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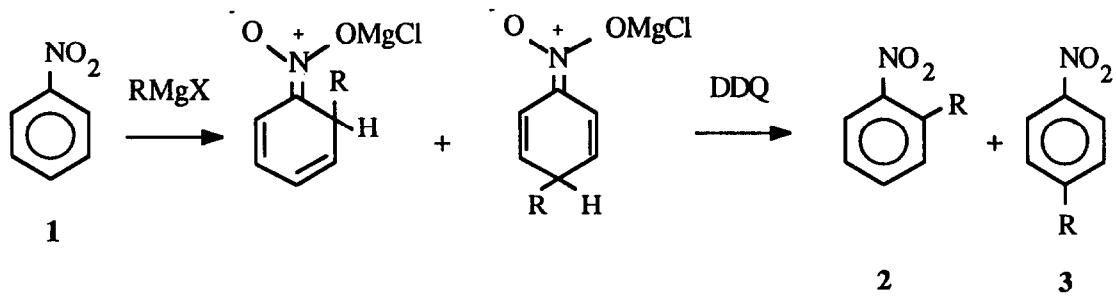
*Abstract: In contrast to alkyl Grignard reagents, the allyl reagent reacts with nitroarenes via 1,2 addition to the nitro group. The "in situ" treatment of the unstable intermediate adduct with $LiAlH_4$ in the presence of catalytic Pd/C provides a general synthesis of N-allyl-N-arylhydroxylamines or N-allylanilines.*

Only recently, have some fundamental aspects been clarified of the reactivity of nitroarenes with strong basic carbanions, such as RMgX and RLi, which attack to the nitroarenic system irreversibly. It is now established[1,2] that alkyl reagents (e.g. MeMgX) predominantly undergo conjugate addition to the nitroarenic substrate (Scheme 1).

SCHEME 1




This reaction is of wide applicability and generally results in good yields of ring alkylated products[1,3], although, in some instances a side redox process with formation of stable nitroarene radical anions may occur[4]. The redox process becomes substantial when steric hindrance factors become important both in the substrate and in the nucleophilic carbanion[5].

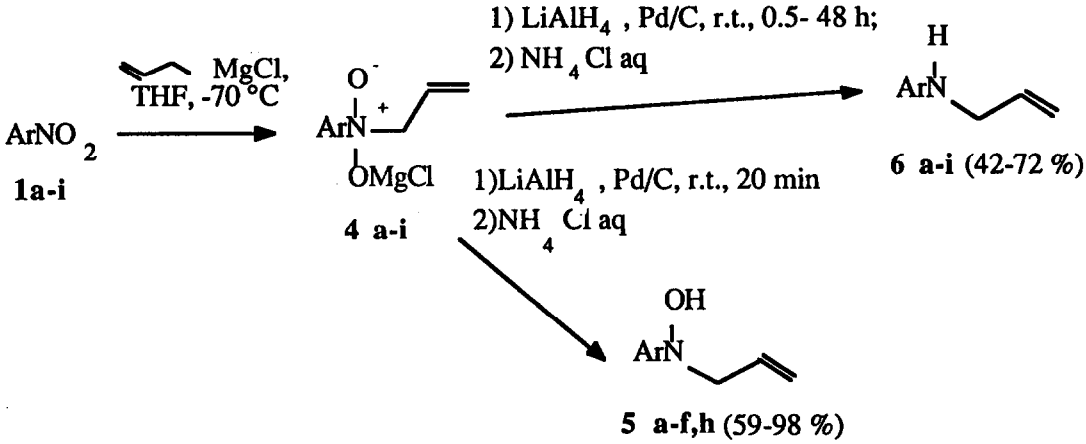
We report now, that the course of the reaction of nitroarenes with allyl magnesium chloride completely differs from the pattern with the alkyl Grignard reagents.

When allylmagnesium chloride is allowed to react with an equimolecular amount of nitrobenzene (**1a**, Scheme 2) at -70 °C, an irreversible 1:1 adduct is very likely formed. We

were not able to identify the structure of this adduct, since it decomposed during our attempts to trap or isolate it.

The 'in situ' treatment of the reaction mixture with lithium aluminum hydride (1.4 : 1) in the presence of 0.1/1 moles of palladium on charcoal for about 20 min at room temperature led to N-allyl-N-phenylhydroxylamine (**5a**, 98%). This strongly suggests that a structure like **4** must be assigned to the 1:1 adduct. Therefore the allyl Grignard reagent gives almost exclusively 1,2 addition to the nitroarenic system. No ring alkylated products as **2** or **3** (Scheme 1) were obtained after treatment of the reaction mixture with DDQ.

SCHEME 2




a) Ar = phenyl; b) Ar = 4-chlorophenyl; c) Ar = 3-chlorophenyl; d) Ar = 4-diphenylyl;
e) Ar = 2-fluorophenyl; f) Ar = 3-methoxyphenyl; g) Ar = 4-methoxyphenyl;
h) Ar = 2-naphthyl; i) Ar = 5-(1-methylindolyl)

These findings are very surprising, since, in the reaction of alkyl Grignard reagents, N-alkylated products are generally negligible (2-3 %) with the exception of benzyl derivatives for which N-alkylation can account in some cases for about 15% of the reaction versus 60-70 % of ring alkylation.[6]

Predominant N-attack has been observed in the reaction of aryl Grignard or lithium reagents[7,8,9]. However the two reactions are only apparently connected. In fact, in contrast with the present results, in the reaction of arylmagnesium halides, two moles of reagent are always consumed per mole of substrate to give diarylhydroxylamine magnesium salt, diarylnitroxide, and magnesium phenoxide, even in the presence of a deficiency of Grignard compound[10]. Although the mechanism is not yet completely understood, very likely an initial O-arylation[7,8], followed by a phenoxide elimination to nitroso compound, and finally by an 1,2 addition of ArMgX to the nitroso derivative, occurs[11].

The reaction of allylmagnesium chloride seems to be general since it can be successfully applied to a variety of nitroarenes[12]. However, when strongly electron-donating substituents, such as methoxy or pyrrolic NMe (compounds **1g** and **1i** respectively), were linked at positions conjugated with the nitro function, it was not found possible to stop the reduction at the hydroxylamine stage, but complete reduction to amines **6** was always observed. In all other cases, in order to obtain a complete reduction to N-allylanilines **6**, a larger excess of $LiAlH_4$ (2.5 : 1) and longer reaction times (36-48 h) were required[13].

The use of $LiAlH_4$ and Pd/C is essential to obtain the hydroxylamine **5** or amine derivative **6** while the acyclic double bond is not affected. Lithium aluminum hydride alone or other hydrides were demonstrated to be unable to accomplish the reduction. In contrast with the aliphatic nitroderivatives, no reduction occurs with an excess of Grignard reagent.[14]

In conclusion, this reaction represents an important route to obtain N-allyl-N-arylhydroxylamines, since to our knowledge, a general synthetic method for these compounds is not yet reported. Moreover, it provides a further, quite simple method of synthesis of N-allylanilines.

Finally, our present results tend to the notion that the present-day lack of knowledge of the precise reactivity of RMgX and RLi towards nitroarenes can be ascribed to the failure in discovering how the unstable intermediates can be converted into stable derivatives. As the conjugate addition was realized when it was found to be possible to convert nitronate adducts into nitroso or nitro derivatives using a Lewis acid[15] or an oxidizing agent[2,16] respectively, so in the present system the 1,2-addition has been realized when we succeeded in decomposing the hypothetical tetrahedral adduct **4** to N-allylhydroxylamine derivatives with a specific reagent.

**References and notes**

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12. Yields and physical data for compounds **5** follow:

**5 a** : 98%; oil; $^1$H-NMR ($CDCl_3$) $\delta$ 3.70-4.03 (m, 2H, $-CH_2-$); 4.88-5.45 (m, 2H, $=CH_2$); 5.67-6.38 (m, 1H, -CH=); 6.70 (bs, 1H, OH); 6.87-7.52 (m, 5H, arom); IR (film): $\nu_{OH}$ 3392 cm$^{-1}$ (broad); m/z: 149 ($M^+$), 133, 132, 130, 108, 106, 77, 76, 51, 41. Anal Calcd for $C_9H_{11}NO$: C, 72.48; H, 7.38; N, 9.39%; Found C, 72.40; H, 7.35; N, 9.40%.

**5 b** : 96%; oil; $^1$H-NMR ($CDCl_3$) $\delta$ 3.70-3.97 (m, 2H, $-CH_2-$); 4.97-5.42 (m, 2H, $=CH_2$); 5.60-6.30 (m, 1H, -CH=); 6.87-7.50 (m, 5H, arom + OH); IR (film): $\nu_{OH}$ 3360 cm$^{-1}$ (broad); m/z: 183.0449 ($M^+$, calcd for $C_9H_{10}ClNO$ 183.0451), 167, 142, 140, 130, 111, 75, 41.

**5 c** : 75%; oil; $^1$H-NMR ($CDCl_3$) $\delta$ 3.67-4.10 (m, 2H, $-CH_2-$); 5.03-5.50 (m, 2H, $=CH_2$); 5.62-6.33 (m, 1H, -CH=); 6.80-7.43 (m, 5H, arom + OH); IR (film): $\nu_{OH}$ 3387 cm$^{-1}$ (broad); m/z: 183.0450 ($M^+$, calcd for $C_9H_{10}ClNO$ 183.0451), 167, 164, 142, 140, 130, 111, 75, 41.

**5 d** : 98%; mp 68-9 °C; $^1$H-NMR ($CDCl_3$) $\delta$ 3.77-4.17 (m, 2H, $-CH_2-$); 5.08-5.50 (m, 2H, $=CH_2$); 5.67-6.57 (m, 1H, -CH=); 7.07-7.83 (m, 10H, arom + OH); IR (KBr): $\nu_{OH}$ 3397 cm$^{-1}$ (broad); m/z: 209 ($M^+$-16), 206, 182, 168, 152, 140, 115, 76, 41. Anal Calcd for $C_{15}H_{15}NO$: C, 80.00; H, 6.67; N, 6.22%; Found C, 79.80; H, 6.70; N, 6.20%.