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REVERSIBILITY IN THE REACTION OF PENTACHLOROPHENYLLITHIUM WITH AROMATIC NITRILES

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SUMMARY

The formation of a mixture of 2,4-diarylquinazolines from the reaction of pentachlorophenyllithium with benzonitrile followed by *p*-tolunitrile is a consequence of the reversibility of the reaction of pentachlorophenyllithium with aromatic nitriles. The reversibility was confirmed by the elimination of pentachlorophenyllithium from pentachlorophenyl *p*-tolyl ketone *N*-lithio imine. When the ketone *N*-lithio imine was heated in the presence of mesitylene, the adduct of tetrachlorobenzyne with mesitylene was obtained in good yield, accompanied by *p*-tolunitrile.

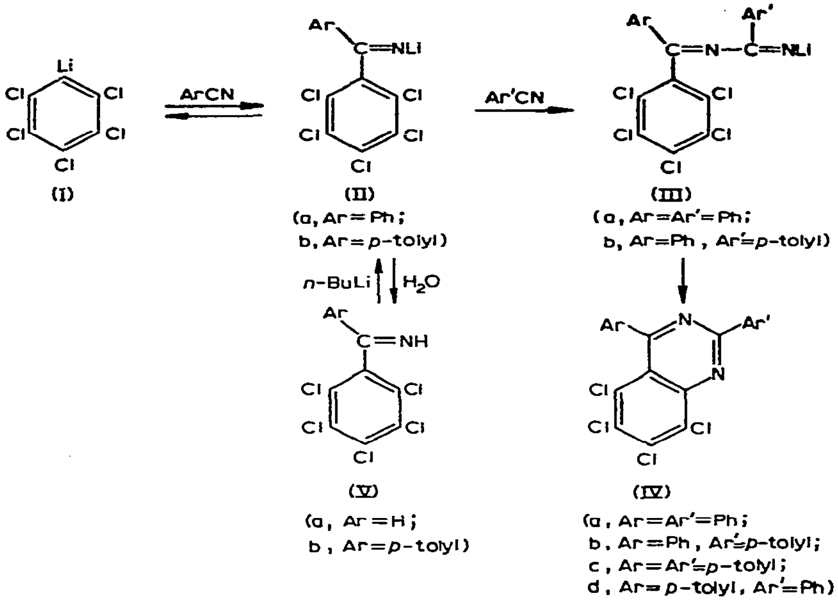
INTRODUCTION

The addition of organomagnesium and organolithium compounds to nitriles to give ketone imines (and thence ketones) is a well known general reaction. The reaction is not normally regarded as reversible, and we are aware of no previous evidence for such reversibility, although it has been reported that a related reaction, *viz.* the addition of a ketimate salt to dichlorofluoroacetonitrile, is reversible[1].

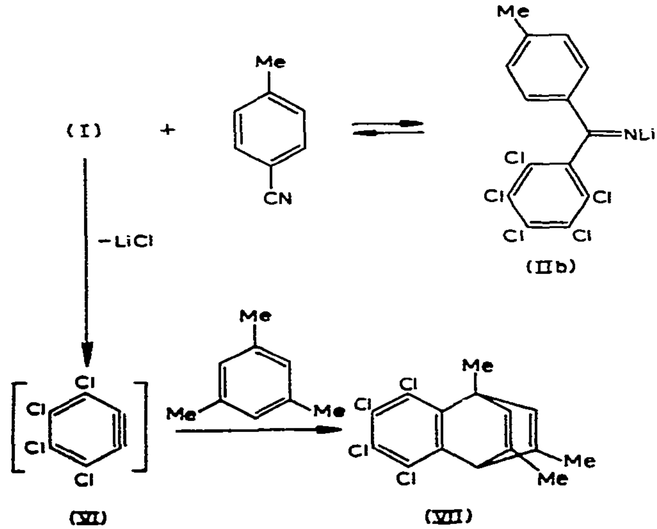
RESULTS AND DISCUSSION

We have recently reported the reaction of pentachlorophenyllithium (I) with two moles of benzonitrile, leading to 5,6,7,8-tetrachloro-2,4-diphenylquinazoline (IVa) by the route shown in Scheme 1[2]. Attempts to extend this reaction to the synthesis of 5,6,7,8-tetrachloro-4-phenyl-2-*p*-tolylquinazoline (IVb) by the use of one mole of benzonitrile followed by a second mole of *p*-tolunitrile led in every case to a mixture of products. The components of the mixture could not be separated, but the mass spectrum showed molecular ions at *m/e* 432 and 446, indicating that besides the expected product [(IVb); M^+ 432], some 5,6,7,8-tetrachloro-2,4-di-*p*-tolylquinazoline (IVc) had been formed. [A rough indication of the relative proportions of (IVb) and (IVc) was given by the ratio 1/1 for the intensities of the signals at *m/e* 432 and 446.] A possible explanation for these results was that the reaction between pentachlorophenyllithium (I) and benzonitrile, leading to pentachlorophenyl phenyl ketone

SCHEME 1



SCHEME 2



N-lithio imine (IIa) is reversible*. We have substantiated this hypothesis by studying both the addition of pentachlorophenyllithium to benzonitrile or *p*-tolunitrile and the reverse reaction.

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* As a consequence the mixture of products probably also contained some of the other possible quinazolines, (IVa) and (IVd).

The forward reaction, using one mole of nitrile, was straightforward; thus, hydrolysis of the reaction product from pentachlorophenyllithium (I) and benzonitrile and *p*-tolunitrile gave pentachlorophenyl phenyl ketone imine (Va) (61%) and pentachlorophenyl *p*-tolyl ketone imine (Vb) (59%) respectively.

For studying the reverse reaction, the ketone *N*-lithio imine (IIb) was prepared in diethyl ether solution from the ketone imine (Vb) and n-butyllithium. When the resulting solution was heated under reflux for 2 h, and then hydrolysed, pentachlorobenzene (I) was isolated from the products in 7% yield, and *p*-tolunitrile was detected by means of its IR absorption at 2235 cm^{-1}. The reverse reaction was carried essentially to completion when the ketone *N*-lithio imine (IIb) was heated in the presence of mesitylene. In this medium, pentachlorophenyllithium (I) decomposed to tetrachlorobenzyne (VI) which was trapped as its adduct with mesitylene, 5,6,7,8-tetrachloro-1,4-dihydro-1,3,9-trimethyl-1,4-ethenonaphthalene (VII)[3]. The adduct (VII) was isolated in 70% yield, and *p*-tolunitrile was isolated in 39% yield.

Benkeser and Broxterman have recently reported[4] that the addition of crotylmagnesium bromide to isopropyl tert-butyl ketone is reversible. It may be predicted that other examples of reversible organolithium and organomagnesium addition reactions will be found; the possibility should certainly be taken into account in mechanistic studies using sterically hindered reagents (*cf.* ref. 5).

EXPERIMENTAL

All operations involving organolithium compounds were carried out under an atmosphere of dry, oxygen-free nitrogen. ^{1}H NMR spectra were recorded at 60 MHz for solutions in deuterochloroform, with tetramethylsilane as internal standard.

Pentachlorophenyllithium

Solutions of pentachlorophenyllithium were prepared from hexachlorobenzene by the literature method[6].

Attempted syntheses of 5,6,7,8-*tetrachloro-4-phenyl-2-p-tolylquinazoline*

(*a*). A solution of pentachlorophenyllithium, from hexachlorobenzene (5.7 g, 20 mmoles), in diethyl ether (200 ml) was stirred at −20° as benzonitrile (2.0 g, 20 mmoles) in diethyl ether (50 ml) was added dropwise during 10 min. The mixture was stirred at room temperature for 1 h. *p*-Tolunitrile (7.0 g; 60 mmoles) in diethyl ether (50 ml) was added, and the mixture was stirred and heated under reflux for 3 h. Water (100 ml) was added, and the organic layer was worked up. Chromatography of the product (silica) gave a mixture of 2,4-diaryl-5,6,7,8-tetrachloroquinazolines (3.0 g).

(*b*). A solution of pentachlorophenyl phenyl ketone imine (3.54 g; 10 mmoles) was stirred at −75° as n-butyllithium (5.0 ml of 2.23 *M* solution in hexane) was added. The mixture was allowed to warm to 10° during 1 h, and *p*-tolunitrile (4.6 g; 39 mmoles) in diethyl ether (50 ml) was added dropwise. The mixture was heated under reflux for 3 h, hydrolysed, and worked up as in (*a*), to give a mixture of quinazolines (2.3 g), M^+ 432, 446.

Pentachlorophenyl phenyl ketone imine

A solution of pentachlorophenyllithium, from hexachlorobenzene (5.7 g), in diethyl ether (200 ml) was stirred at −20° as benzonitrile (2.0 g) was added during 10 min. The mixture was stirred at room temperature for 1 h. Water (100 ml) was added, and the ether layer was separated, dried, and evaporated. Chromatography of the residue (silica gel) gave pentachlorophenyl phenyl ketone imine (eluted with 4/1 benzene/light petroleum) (4.3 g; 61%), m.p. 118–119°, τ −1.00 and 0.12 (broad singlets, total 1 H; exchangeable H; NH), 2.45 (m, 5 H; Ph). (Found: C, 44.5; H, 1.9, N, 3.9; M^+, 351. $C_{13}H_6Cl_5N$ calcd.: C, 44.1; H, 1.7; N, 4.0%; M^+, 351.)

Pentachlorophenyl p-tolyl ketone imine

A similar procedure, using *p*-tolunitrile (2.34 g), gave pentachlorophenyl *p*-tolyl ketone imine (4.3 g; 59%), m.p. 145–146°, τ −1.00 and 0.15 (broad s, total 1 H; exchangeable H; NH), 2.60 (m, 4 H; aromatic H), 7.60 (s, 3 H; CH_3) (Found: C, 46.0; H, 2.3; N, 3.9; M^+, 365. $C_{14}H_8Cl_5N$ calcd.: C, 45.7; H, 2.1; N, 3.8%; M^+, 365.)

Elimination of pentachlorophenyllithium from pentachlorophenyl p-tolyl ketone N-lithio imine

(*a*). n-Butyllithium (5.0 ml of a 2.25 *M* solution in hexane) was added to a stirred solution of pentachlorophenyl *p*-tolyl ketone imine (3.68 g) in diethyl ether (200 ml) at −75°. The solution was heated under reflux for 1 h. Water (100 ml) was added, and the ether layer was separated, dried, and evaporated. The residue showed a strong absorption maximum at 2235 cm^{-1}, and chromatography on silica yielded pentachlorobenzene (175 mg; 7%).

(*b*). The experiment was repeated on twice the scale using a mixture of diethyl ether (200 ml) and mesitylene (150 ml) as solvent, and a heating period of 2 h. Following removal of the solvents by distillation under reduced pressure, chromatography of the residue gave 5,6,7,8-tetrachloro-1,4-dihydro-1,3,9-trimethyl-1,4-ethenonaphthalene (eluted with light petroleum) (4.65 g, 70%) m.p. 120–121° (lit.[3] m.p. 110°) τ 3.95 (quintet, 2 H), 5.15 (t, 1 H), 7.88 (s, 3 H), 8.08 (d, 6 H), and *p*-tolunitrile (eluted with 30% benzene/light petroleum) (0.92 g, 39%), identical (IR) with an authentic specimen.

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