

Mechanism of Anionic Dearomatizing Reactions of Diphenylphosphinamide Derivatives: A Theoretical and Experimental Study

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Abstract: The mechanism of the anionic dearomatisation of phosphinamide derivatives has been investigated both theoretically and experimentally. The potential-energy surface of model reactions was studied at the Becke3LYP/6-31+G* level of theory, and according to this study, a pre-reactive complex is formed between the alkyllithium and the phosphinamide. This complex evolves preferentially through NC_α-metalation of the phosphinamide. The

intramolecular nucleophilic addition of the carbanion to the *ortho* position of the aromatic ring leads to the dearomatised products, in a reaction that has been shown to be under thermodynamic control. Coordinating co-solvents,

such as hexamethyl phosphoramide (HMPA) or *N,N'*-dimethyl-*N,N'*-propylene urea (DMPU), appear to influence the reaction by favouring the formation of solvent-separated ion pairs. The cyclisation reaction of allylphosphinamide derivatives was also studied. It was found that both the α - and γ -attack of the allyl anion can take place, however the formation of the seven-membered ring products derived from the γ -attack are clearly favoured.

Keywords: anions • dearomatization • density functional calculations • lithiation • phosphinamides • solvent effects

Introduction

The addition of main-group organometallic reagents to aromatic compounds is an efficient method for breaking down the conjugate π system of an aromatic ring and has been extensively used for the preparation of functionalised alicyclic and acyclic compounds.^[1] In arenes these dearomatising reactions are generally limited to polycyclic systems.^[2] On the

other hand, conjugate addition to aromatic hydrocarbons bearing electron-withdrawing groups (e.g., aldehyde and ketone,^[3] imines,^[4] carboxylic acid,^[5] carboxylic ester,^[6] carboxamides,^[7] acyl halide,^[8] nitriles,^[9] oxazolidines,^[10] oxazolines,^[11] triazenes^[12]) has much wider scope as revealed by the application of this methodology to the synthesis of several natural products^[13] and non-natural analogues.^[14] In *N*-benzylcarboxamides,^[15] phenyl sulfones,^[16] *N*-benzylsulfonamides^[17] and *N*-benzylidiphenylphosphinamides,^[18] the dearomatisation may take place intramolecularly through an anionic cyclisation reaction.

We have recently shown in a synthetic^[19] and NMR^[20] study that upon treatment of *N*-benzyl-*N*-methylidiphenylphosphinamide **1a** (Scheme 1) with *sec*-butyllithium in tetrahydrofuran (THF) at -90°C the mechanism of the cyclo-dearomatising reaction involves the formation of a dimeric precomplex **I** between the starting phosphinamide and the base, which evolves by *ortho*-directed and benzylic lithiation to give the lithium intermediates **II** and **III**, respectively. The benzylic anion **III** undergoes a cyclisation through intramolecular attack at the *ortho* position of a P-substituted phenyl ring leading to the four possible dearomatised diastereoisomers **IV–VII**. The reaction progresses to yield an equilibrium mixture of derivatives **IV** and **V**, plus the *ortho*-lithiated intermediate **II**. Compounds **III** to **VII** have been identified as monomeric, whereas **II** has been assigned as di-

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Supporting information for this article is available on the WWW under <http://www.chemeurj.org/> or from the author. It contains Cartesian coordinates and energies of the stationary points located, ³¹P{¹H} NMR spectra showing the product distribution in the dearomatization–protonation reaction of **1b** and 1D gTOCSY NMR spectra of compounds **3a** and **3b**.