REACTION OF 2-AMINOPYRROLE and 1-ALKYL-2-AMINOPYRROLE WITH DMAD: MICHAEL ADDITION *VS* DIELS-ALDER REACTION

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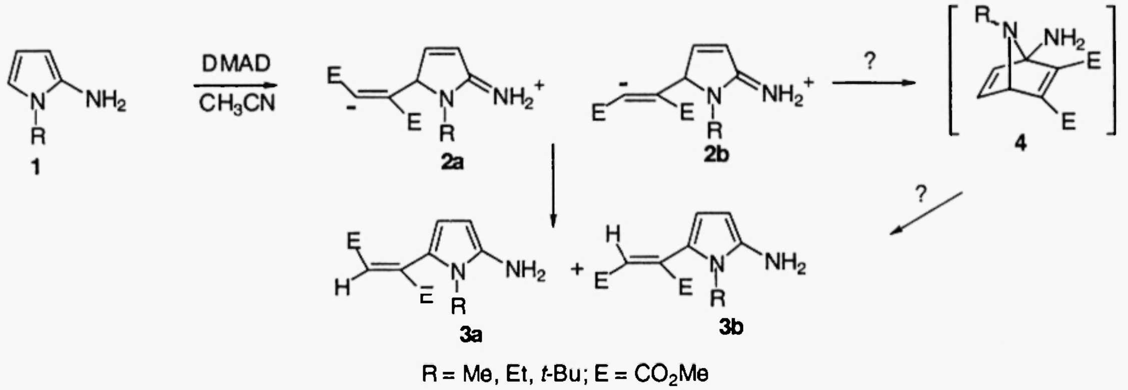
Abstract: 2-Aminopyrrole and 1-substituted-2-aminopyrroles react with DMAD in less than two minutes to give a mixture of *E* and *Z vinyl* pyrroles (Michael adducts). No evidence of Diels-Alder cycloaddition was found even at –35°C.

Recently we reported the first preparation of 2-aminopyrrole and 1-substituted 2-aminopyrroles without further substitution on the ring.[1] All previously reported examples of 2-aminopyrroles contain an electron-withdrawing group or a phenyl ring on the pyrrole nucleus.[2] These groups stabilise the electron-rich pyrrole ring. In their absence the newly synthesised 2-aminopyrroles are stable only in solution and are not isolable. It has been found, however, that 2-aminopyrrole and 1-alkyl-2-aminopyrroles can be protonated and isolated as stable tetraphenylborate salts.[3] Treatment of the salt with triethylamine regenerates the 2-aminopyrrole. In this communication we report that 2-aminopyrroles generated by this method react rapidly with dimethyl acetylenedicarboxylate (DMAD) to give Michael adducts. This is the first reported Michael addition reaction of 2-aminopyrrole derivatives.

Reactions were carried out in NMR tubes by dissolving the tetraphenylborate salt in deuteroacetonitrile and adding triethylamine (1 equivalent) to generate the 2-aminopyrrole **1**. Excess (3 equivalents) DMAD was added, and the reaction was over in less than two minutes -- the time it took to mix the reagents and take an NMR spectrum. No starting material (salt or 2-aminopyrrole) was evident after two minutes. NMR spectra for reactions of 1-alkyl-2-aminopyrroles were consistent with the presence of the *E* and *Z* vinyl pyrroles **3a and 3b**. When 1-*t*-butyl-2-aminopyrrole was used, for example, the NMR spectrum of the reaction mixture indicated the presence of two *t*-butyl groups in a ratio of *ca* 6:4 and two sets of methoxy groups in the same ratio. The vinyl protons in **3a** and **3b** appeared as singlets at δ 6.65 and 5.75 respectively. Assignment of *E* and *Z* stereochemistry of the vinyl pyrroles was based on a NMR correlation by Noland.[4] In this study, of a number *E*/*Z* pairs obtained from the reaction of substituted pyrroles with DMAD, the vinyl singlet at lower field is from the *E* isomer. Similarly *E* and *Z* adducts were formed in a ratio of *ca* 1:1 when the methyl and ethyl derivatives were studied. When the reaction was carried out with 2-aminopyrrole, decomposition took place and no adduct or any other identifiable product was detected by



R = Me, Et, *t*-Bu; E = CO_2Me

NMR. Reactions were run on a preparative scale but adducts decomposed during column chromatography and could not be isolated.

NMR spectra of the reaction mixtures indicated the presence of another product that contained two methoxy groups. This product was precipitated as a white solid by adding water to the acetonitrile reaction mixture. The solid was found by NMR and FABMS to be the tetraphenylborate salt of 2-triethylammonio-2-butenedioic acid dimethyl ester. An identical solid could be isolated simply be reacting DMAD with triethylammonium tetraphenylborate in acetonitrile. This by-product was the result of the addition of triethylamine to DMAD to give a zwitterion that was then trapped by a proton.[5]

Experimental[6] and theoretical studies[7] indicate that pyrroles react with DMAD to give initially a zwitterion **2** (Michael adduct). Proton transfer results in vinyl pyrroles analogous to **3a** and **3b**. The zwitterion can cyclize to give the 7-azabicyclo[2.2.1]hepta-2,5-diene **4** (Diels-Alder adduct).[6] It has been shown that the Diels-Alder process is favoured in the absence of weak acids.[8] In light of this the 2-aminopyrrole **1** was generated by adding $NaBH_4$ or $NaCNBH_3$ to the solution of the *t*-butyl salt in deuteroacetonitrile. The acidic proton was removed as hydrogen gas. DMAD was then added but only vinyl pyrroles were detected by NMR. Diels-Alder adducts obtained from pyrroles are often unstable. Reaction of 1-*t*-butyl-2-aminopyrrole with DMAD was carried out at –35°C. The reaction was followed to completion (30 min) by NMR but no Diels-Alder adduct **4** was detected. No change occurred as the reaction mixture was warmed to probe temperature. From these results it is not possible to determine if the Diels-Alder adduct **4** ever formed during the reaction.

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