

## First Example of Electrophilic Substitution by Addition–Elimination ( $\sigma$ -Substitution) in Pyrrole†

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Reaction of 1-methylpyrrole with *N*-chloroacetanilide leads to the incorporation of an acetanilide moiety in the pyrrole ring by addition–elimination.

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Pyrrole and its derivatives undergo electrophilic substitution in typical  $S_E2$  fashion<sup>1,2</sup> but, unlike furan,<sup>3</sup> no examples of electrophilic substitution by addition–elimination or a  $\sigma$ -substitution mechanism<sup>4</sup> have been reported. We now report the

first example of addition–elimination ( $\sigma$ -substitution) in pyrrole chemistry.

1-Methylpyrrole (**1**) (1 mol) was chlorinated with *N*-chloroacetanilide (NCA; 1 mol) and acetic acid (0.2 mol) as previously reported for pyrrole.<sup>5</sup> A highly exothermic reaction occurred and HCl was produced; NCA could not be detected iodometrically after mixing the reagents. Gas chromatographic analysis indicated the presence of chloropyrroles, acetanilide, and two compounds with long retention times. These products were isolated and identified (<sup>1</sup>H n.m.r.,

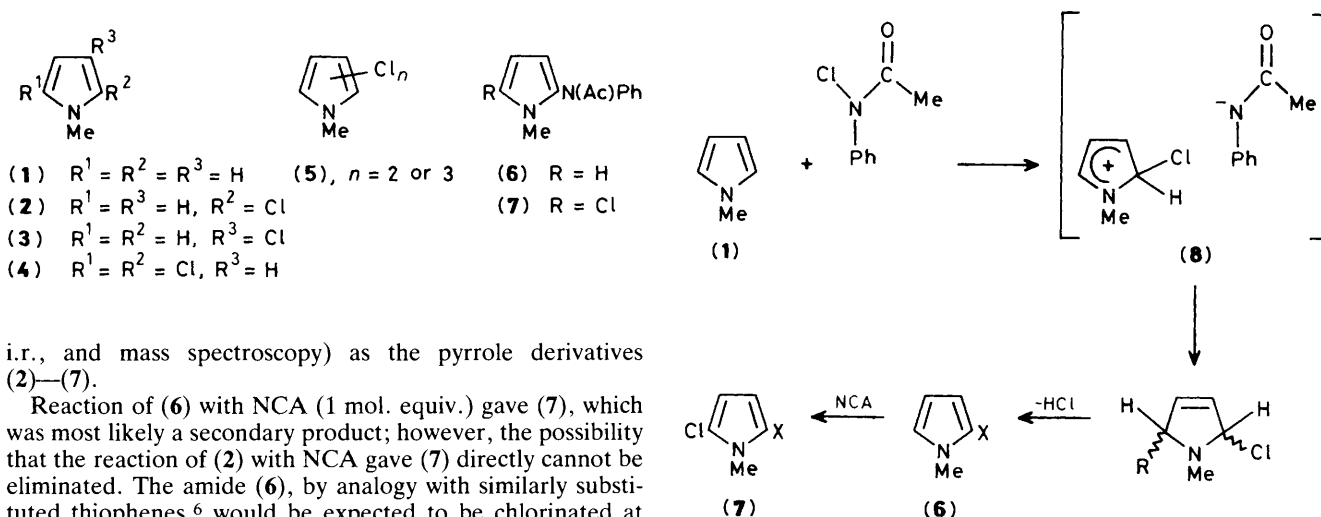
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† Presented at the 191st National Meeting of the American Chemical Society, New York City, April 1986, abstract no. 286; taken in part from the Masters thesis of I. B.

**Table 1.** Influence of reaction conditions on product yields.

Reaction conditions <sup>a</sup>			% Yield <sup>b</sup>						
(1)	NCA	Acid	(1)	(2)	(3)	(4)	(5)	(6)	(7)
0.2	0.2 <sup>c</sup>	—	16	23	12	18	1	13	7
0.2	0.2	0.04(AcOH)	21	21	5	20	1	13	5
0.2	0.2	0.04(HCl)	32	11	2	18	6	10	8

<sup>a</sup> Concentrations in mol dm<sup>-3</sup> in CH<sub>2</sub>Cl<sub>2</sub>. <sup>b</sup> G.l.c., naphthalene as the internal standard. <sup>c</sup> HCl (determined as AgCl) produced in 21% yield.



i.r., and mass spectroscopy) as the pyrrole derivatives (2)—(7).

Reaction of (6) with NCA (1 mol. equiv.) gave (7), which was most likely a secondary product; however, the possibility that the reaction of (2) with NCA gave (7) directly cannot be eliminated. The amide (6), by analogy with similarly substituted thiophenes,<sup>6</sup> would be expected to be chlorinated at either C-5 or C-3. The possibility of chlorination at C-3 was eliminated on steric grounds.

There appear to be two reasonable routes for the incorporation of an acetanilide moiety into (1). (i) Reaction of 1-methylpyrrole (1) with NCA could give an ion pair consisting of a  $\sigma$ -complex and the anion of acetanilide which could collapse<sup>7</sup> to give a 2,5-adduct.<sup>3</sup> Elimination of HCl would give (6). Similar adducts have been reported to be formed during the amination of arenes<sup>4</sup> with  $NCl_3$ - $AlCl_3$ . (ii) Radical chain addition of the acetanilido radical to (1) could lead to (6). Such a process would be analogous to the reaction of *N*-bromosuccinimide (but not *N*-chlorosuccinimide) with arenes to give *N*-arylsuccinimide derivatives.<sup>8</sup> These reactions needed an initiator and in its absence no reaction occurred.

The reaction of (1), NCA, and acetic acid in CH<sub>2</sub>Cl<sub>2</sub> was carried out in the dark, under an argon atmosphere and with solutions that had been degassed by freeze-thaw cycles. Under these conditions (6) and (7) were observed in a total yield of 13% (% of total area) by g.l.c., compared with a total yield of 10% when the reaction was carried out under ambient light and with undegassed samples. These results eliminated the possibility of a radical chain mechanism. The following is proposed to explain the formation of (6) and (7) (Scheme 1).

Products (2)—(7) are the result of competing attacks on the pyrrole ring by NCA and its conjugate acid.<sup>5</sup> Reactions were run in the presence of HCl and without added acid. The results are summarized in Table 1. Increasing acidity results in more secondary chlorination products and recovered (1), but the total yield of (6) and (7) does not vary appreciably. This would seem to suggest that protonation of NCA is slower than attack of (1) by NCA. This is being studied further.

Two factors have been proposed to explain the formation of a 2,5-addition product in the nitration of furan with acetyl nitrate:<sup>9</sup> the nucleophilicity of the acetate ion and the dienic character of furan which makes ion pair collapse faster than

deprotonation. It is proposed that the same two factors are responsible for the formation of (6).

Kao and co-workers<sup>10</sup> performed calculations which indicated that when a substituent is a  $\pi$ -electron donor the inhibition of electron delocalization from nitrogen is greater when the substituent is at C-2 than at C-3. These results<sup>10</sup> indicate that 2-halogenopyrroles are more dienic in character than the 3-halogenopyrroles or the parent pyrroles.

This enhanced dienic character should also be reflected in the energies of the transition states leading from ion pair (8) to (2) (deprotonation) and (6) (collapse). The formation of the amide (6) is a result of the presence of the nucleophilic anion of acetanilide in (8) and the effect of a 2-chloro substituent on the aromaticity of the pyrrole ring.

Received, 3rd March 1986; Com. 281

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