

SYNTHESIS OF N-(*o*-AMINO ARYL) PYRROLES BY PAAL-KNORR REACTION

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ABSTRACT

N-(*o*-nitro aryl)- and N-(*o*-acetamino aryl)-2, 5-dimethyl pyrroles are synthesized by Paal-Knorr reaction by condensing acetyl acetone with *o*-nitro anilines and *o*-acetamino anilines respectively. Reduction of the nitro aryl pyrroles and hydrolysis of acetamino aryl pyrroles yielded the corresponding N-(*o*-amino aryl)-2, 5-dimethyl pyrroles.

PREPARATION of N-(amino aryl) pyrroles from 1, 4-dicarbonyl compounds and phenylenediamines has limited application due to the simultaneous or exclusive formation of bis pyrrole derivatives and to the possible formation of isomers when benzene-substituted phenylenediamines are made use of.¹⁻⁷ Synthesis of N-(nitro aryl) and N-(acetamino aryl) pyrroles and their conversion to the amino aryl pyrroles by reduction and hydrolysis respectively appears to be a more convenient route.

Bulow and Dick⁸ condensed diacetyl succinate with *p*-nitro aniline and *p*-amino acetanilide in refluxing acetic acid and obtained the corresponding N-substituted pyrroles. Hazelwood *et al.*² prepared the N-substituted pyrroles from acetyl acetone and a variety of aromatic primary amines including *m*- and *p*-nitro anilines and *m*- and *p*-amino acetanilides. They carried out the reaction in refluxing ethanolic acetic acid or in the presence of traces of hydrochloric acid and reported that *o*-nitro aniline did not react under these conditions. During their studies on N-aryl pyrrole carboxylic acids Piatteli and Minale⁹ showed that the monoacetals of 1, 4-dicarbonyl compounds can be made use of in Paal-Knorr reaction. The successful preparation of N-(*o*-nitro phenyl)-2, 5-dimethyl pyrrole from *o*-nitro aniline and its reduction to the corresponding amino compound was reported by the present authors.⁷

During our studies on the synthesis of phthalamic acid derivatives as plant growth substances, we were in need of some substituted anilines with bulky groups in *ortho* position as potential intermediates and chose, among

other types, some *o*-(*N*-pyrrolyl) anilines, *i.e.*, *N*-(*o*-amino aryl) pyrroles, for this purpose. These compounds are now synthesized adopting two methods and the relative merits of the methods are studied. In the first place, benzene substituted *o*-nitro anilines have been condensed with acetyl acetone to give *N*-(*o*-nitro aryl)-2,5-dimethyl pyrroles, followed by reduction to the corresponding *N*-(*o*-amino aryl)-2, 5-dimethyl pyrroles. Secondly, *o*-amino acetanilides, on reaction with the same diketone, yielded *N*-(*o*-acetamino aryl) pyrroles which on hydrolysis gave the respective *N*-(*o*-amino aryl) pyrroles (Chart I). The condensation of 4-methyl-, 5-methyl-, 4-chloro and

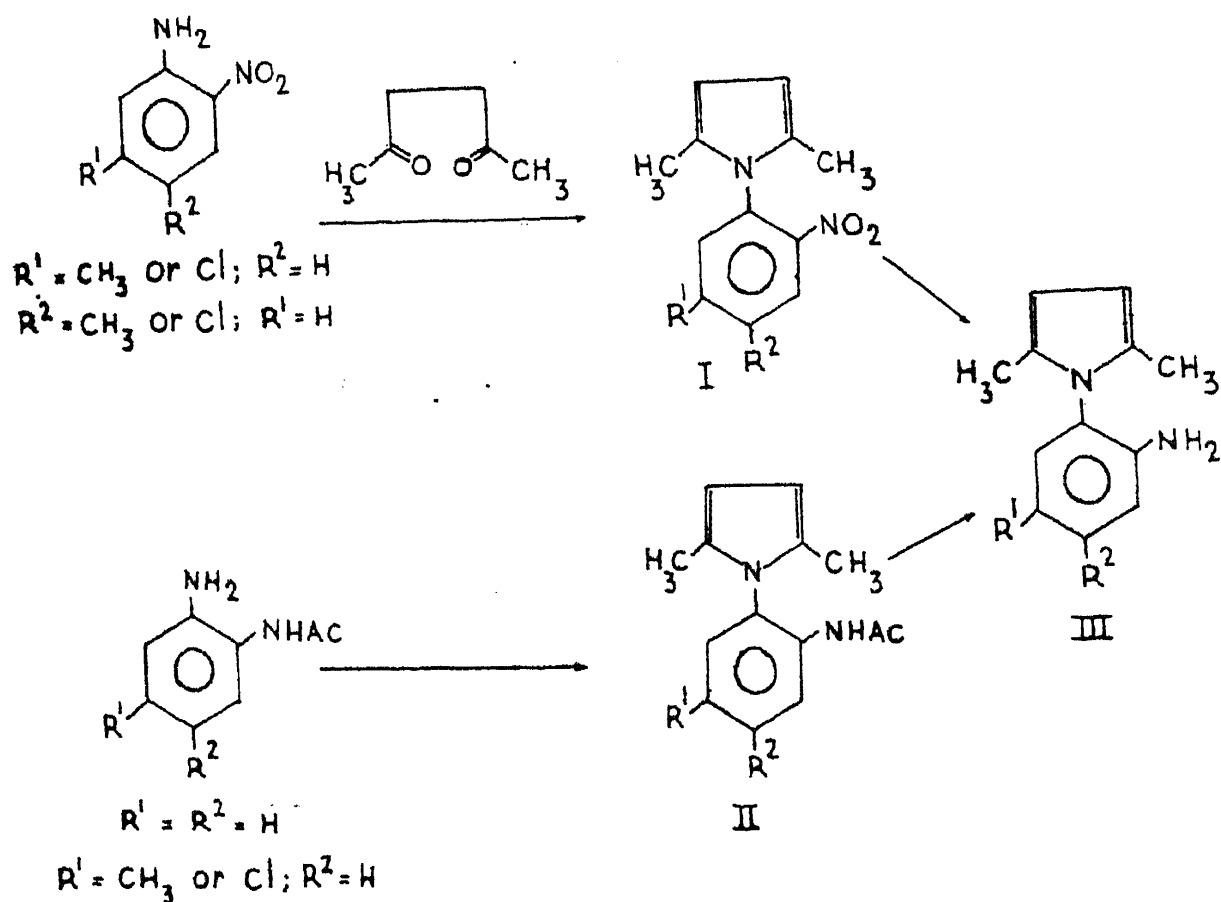


CHART - I

5-chloro-2-nitroanilines with acetyl acetone in refluxing glacial acetic acid resulted in the formation of the corresponding *N*-(*o*-nitro aryl)-2, 5-dimethyl pyrroles (I). *o*-Amino acetanilide, 2-acetamino-5-methyl aniline and 2-acetamino-5-chloro aniline readily reacted with acetyl acetone in acetic acid at room temperature to give the respective *N*-(*o*-acetamino aryl)-2, 5-dimethyl pyrroles (II). These compounds are included in Table I. Reduction of (I) under neutral and mild conditions using aqueous ferrous sulphate and iron powder and hydrolysis of (II) by prolonged refluxing in alkali yielded the corresponding *N*-(*o*-amino aryl)-2, 5-dimethyl pyrroles (III) (Table II).

The synthesis of nitro aryl pyrroles followed by reduction appears to be better method for the preparation of amino aryl pyrroles compared to the

TABLE I

N-(o-nitro aryl) and N-(o-acetamino aryl)-2, 5-dimethyl pyrroles I and II

S. No.	Name	% Yield	M.P.	Mol. formula	% Nitrogen	
					Found	Calculated
<i>N-(o-nitro aryl)-2, 5-dimethyl pyrroles (I)</i>						
1.	N-(2-nitro phenyl)-2, 5-dimethyl pyrrole ⁷	23	85	C ₁₂ H ₁₂ N ₂ O ₂	12·82	12·96
2.	N-(2-nitro-4-methyl phenyl)-2, 5-dimethyl pyrrole*	87	115	C ₁₃ H ₁₄ N ₂ O ₂	12·36	12·17
3.	N-(2-nitro-5-methyl phenyl)-2, 5-dimethyl pyrrole	33	50	C ₁₃ H ₁₄ N ₂ O ₂	12·26	12·17
4.	N-(2-nitro-4-chloro phenyl)-2, 5-dimethyl pyrrole†	56	112	C ₁₂ H ₁₁ ClN ₂ O ₂	11·40	11·18
5.	N-(2-nitro-5-chloro phenyl)-2, 5-dimethyl pyrrole	25	73	C ₁₂ H ₁₁ ClN ₂ O ₂	11·60	11·18
<i>N-(o-acetamino aryl)-2, 5-dimethyl pyrroles (II)</i>						
1.	N-(2-acetamino phenyl)-2, 5-dimethyl pyrrole*	78	79	C ₁₄ H ₁₆ N ₂ O	12·43	12·28
2.	N-(2-acetamino-5-methyl phenyl)-2, 5-dimethyl pyrrole*	76	80	C ₁₅ H ₁₈ N ₂ O	11·80	11·57
3.	N-(2-acetamino-5-chloro phenyl)-2, 5-dimethyl pyrrole*	75	90	C ₁₄ H ₁₅ ClN ₂ O	10·81	10·67

* Recrystallized from petroleum ether.

† Recrystallized from ethanol.

second method, mainly due to the difficulty in hydrolysis of the acetamino compounds. The observation of Bulow and Dick⁸ that N-(*p*-acetamino phenyl)-2, 5-dimethyl-3, 4-dicarbethoxy pyrrole underwent only partial

conversion to *N*-(*p*-amino phenyl)-2, 5-dimethyl-3, 4-dicarboxy pyrrole after refluxing in 30%–alkali for two days lends support to this view.

EXPERIMENTAL: GENERAL PROCEDURES

Method I

(a) *N*-(2-nitro aryl)-2, 5-dimethyl pyrroles (I).—A mixture of the substituted *o*-nitro aniline (0.04M), acetyl acetone (10 ml; excess) and acetic acid (20 ml) was refluxed for seven hours. The contents were poured on crushed ice and the separated product was subjected to steam-distillation. The steam volatile product was collected, and dried under vacuum. Further purification was effected by crystallization from suitable solvent if found necessary.

TABLE II

N-(*o*-amino aryl)-2, 5-dimethyl pyrroles (III)

S. No.	Name	% yield		M.P.	Mol. formula	% Nitrogen	
		(H) of (I)	(HOH) of (II)			Found	Calculated
1.	<i>N</i> -(2-amino phenyl)-2, 5-dimethyl pyrrole	81	25	74	C ₁₂ H ₁₄ N ₂	15.20	15.10
2.	<i>N</i> -(2-amino-4-methyl phenyl)-2, 5-dimethyl pyrrole	37	..	58	C ₁₃ H ₁₆ N ₂	14.32	14.00
3.	<i>N</i> -(2-amino-5-methyl phenyl)-2, 5-dimethyl pyrrole	23	20	40	C ₁₃ H ₁₆ N ₂	14.25	14.00
4.	<i>N</i> -(2-amino-4-chloro-phenyl)-2, 5-dimethyl pyrrole*	59	..	93	C ₁₂ H ₁₃ ClN ₂	12.92	12.69
5.	<i>N</i> -(2-amino-5-chloro-phenyl)-2, 5-dimethyl pyrrole*	25	20	57	C ₁₂ H ₁₃ ClN ₂	13.02	12.69

* Purified by passing petroleum ether solution through alumina column.

(b) *N*-(2-Amino aryl)-2, 5-dimethyl pyrroles (III) by reduction of (I).—The foregoing nitro compound (0.01M), iron powder (5 g), ferrous sulphate (6 g) and distilled water (30 ml) were refluxed for three hours. The reaction mixture was filtered and the residue subjected to steam-distillation. The steam volatile product was collected, dried under vacuum and further purified wherever found necessary.

Method II

(a) *N*-(2-Acetamino aryl)-2, 5-dimethyl pyrroles (II).—Acetonyl acetone (0.01M) was added to the *o*-amino acetanilide (0.01M), dissolved in glacial acetic acid (10 ml), the mixture left aside for two hours and then diluted with ice-cold water. *N*-(2-acetamino aryl)-2, 5-dimethyl pyrrole that separated was filtered and recrystallized from a suitable solvent.

(b) *N*-(2-Amino aryl)-2, 5-dimethyl pyrroles (III) by hydrolysis of (II).—Potassium hydroxide solution (20 ml; 30%) was added to the above acetamino compound (1 g) and the mixture refluxed for twenty-four hours. Steam-distillation of the mixture yielded the pure *N*-(2-amino aryl)-2, 5-dimethyl pyrroles.

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