

Sergio Baroni, Riccardo Stradi*

Istituto di Chimica Organica della Facoltà di Farmacia, Università di Milano,
Viale Abruzzi 42, 20131 Milano, Italy

Maria Luisa Saccarello

Medea Researches, Via Pisacane 34/A, 20129 Milano, Italy

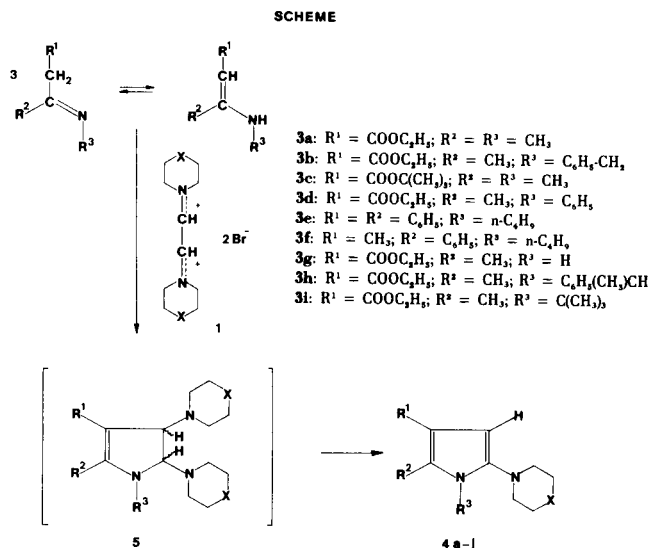
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Diimmonium salt **1** reacts with enamines **3** affording α -amino-pyrroles **4**. The synthetic potential of this reaction is discussed.

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The potential of diimmonium dibromides **1**, which are easily available from 1,1,2,2-tetraaminoethanes **2** by reaction with acetyl bromide (**2**), has attracted our attention in recent years for the synthesis of nitrogen containing heterocycles such as imidazoles (**3**) (**4**) (**5**) or indoles (**6**).

In this paper we wish to report our findings on a new entry to pyrrole derivatives **4** directly from diimmonium salts **1** and enamines of general formula **3**.



The aminopyrrole structure assigned to **4a-j** was inferred on the basis of analytical, $^1\text{H-Nmr}$ and mass spectrometry data. The α -position of the amino group was

Fig. 1

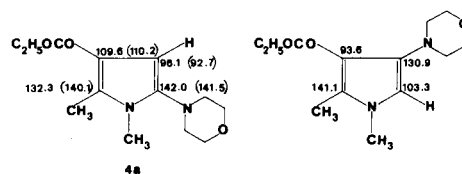
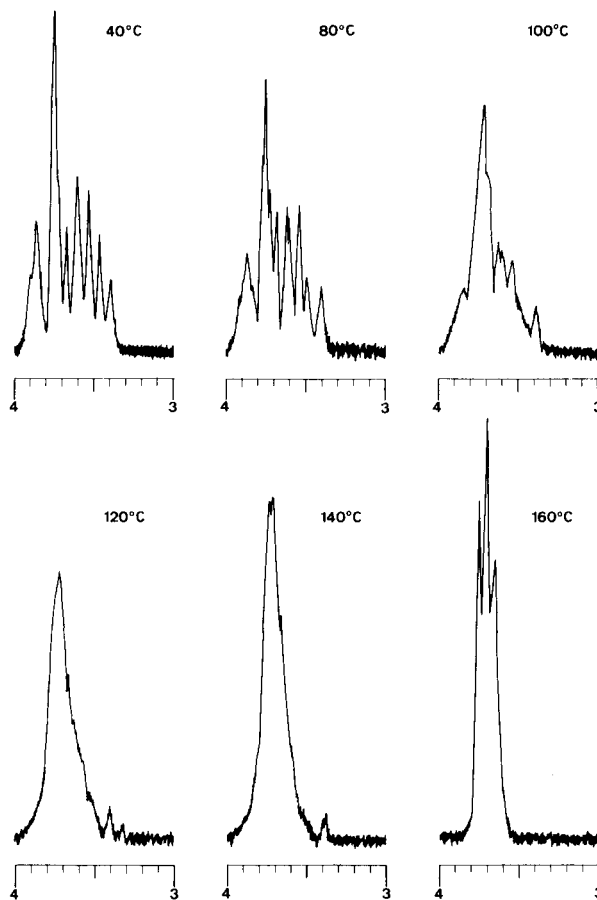


Fig. 2



Enamines **3a-i** react under mild conditions with diimmonium salts **1** affording the amino pyrroles **4a-j** with yields of preparative interest as the main reaction product.

It is noteworthy to observe that the yields of 2-amino-4-carbomethoxy-5-methylpyrrole (**4g**) obtained directly from 3-aminocrotonate **3g** are low. Better results are given by debenzoylation of 1-benzyl-2-morpholino-4-carbomethoxy-5-methylpyrrole (**4b**) which afforded **4g** with good over all yields.

The formation mechanism of pyrrole derivatives **4a-j** is explained in terms of a double electrophilic attack of the diimmonium salt **1** on the nitrogen and the β -carbon atom of the enaminic form of **3**. The 2,3-dihydropyrroles **5** thus formed lose the amino group under the reaction conditions, affording α -aminopyrroles **4** (Table 1).

Table 1

Compound	R ¹	R ²	R ³	X	Chromatographic eluant	Yield (a) %	M.p. (°C) (from)	H _β p.m.r. [CDCl ₃]	Found % (Required %)		
									C	H	N
4a	COOC ₂ H ₅	CH ₃	CH ₃	O	C ₆ H ₆ /C ₂ H ₅ OAc 80:20	45	67 (P.E.)	6.15	62.01 (61.88)	8.15 (7.99)	10.94 (11.10)
4b	COOC ₂ H ₅	CH ₃	CH ₂ C ₆ H ₅	O	C ₆ H ₆ /C ₂ H ₅ OAc 90:10	70	51 (P.E.)	6.23	69.10 (69.39)	7.40 (7.37)	8.41 (8.53)
4c	COOC(CH ₃) ₂	CH ₃	CH ₃	O	C ₆ H ₆ /C ₂ H ₅ OAc 90:10	60	104 (i-C ₃ H ₇) ₂ O	5.93	64.49 (64.26)	9.00 (8.83)	10.00 (9.99)
4d	COOC ₂ H ₅	CH ₃	C ₆ H ₅	O	C ₆ H ₆ /C ₂ H ₅ OAc 80:20	30	123 (dec) (i-C ₃ H ₇) ₂ /i-C ₃ H ₇ OH 50:50	6.13	68.83 (68.77)	7.15 (7.05)	8.83 (8.91)
4e	C ₆ H ₅	C ₆ H ₅	n-C ₄ H ₉	O	C ₆ H ₆	50	52 (P.E.)	6.03	79.69 (79.86)	7.62 (7.73)	7.60 (7.77)
4f	CH ₃	C ₆ H ₅	n-C ₄ H ₉	O	C ₆ H ₆ /C ₂ H ₅ OH 80:20	—(b)	—	6.26	—	—	—
4g	COOC ₂ H ₅	CH ₃	H	O	(C ₂ H ₅) ₂ O	20	118 Pentane/(i-C ₃ H ₇) ₂ O 50:50	5.73	60.60 (60.48)	7.50 (7.61)	11.48 (11.76)
4h	COOC ₂ H ₅	CH ₃	CH ₃	N-CH ₃	—	80	132 (i-C ₃ H ₇) ₂ O	6.03	62.01 (61.88)	8.15 (7.99)	10.94 (11.10)
4i	COOC ₂ H ₅	CH ₃	C ₆ H ₅ (CH ₂) ₂ CH-	O	(C ₂ H ₅) ₂ O	83	76 (P.E.)	6.20	70.33 (70.15)	7.71 (7.65)	8.29 (8.18)
4j	COOC ₂ H ₅	CH ₃	C(CH ₃) ₃	O	C ₆ H ₆ /(C ₂ H ₅) ₂ O 90:10	46	114 (i-C ₃ H ₇) ₂ O	6.20	65.41 (65.28)	9.00 (8.90)	9.46 (9.52)

(a) Of isolated product. (b) Only impure samples could be isolated from the mixture because of the great instability of this compound.

determined for compound **4a** by analysis of its ¹³C spectrum and extended by analogy to all pyrrole derivatives synthesized during this study.

Figure 1 shows the experimental values of the ring carbon chemical shifts together with those calculated, which were obtained by additional substituent effects (7,8).

The two values are in good agreement, whereas those calculated for the β-morpholino isomer are quite different from the experimental ones.

The structural assignment discussed above is confirmed by the ¹H-Nmr analysis of 1-*t*-butyl derivative **4j**. The spectra of **4j** recorded in DMSO at increasing temperatures show a clear modification of the signals associated with the morpholine CH₂-O-CH₂ system (Figure 2). This behaviour is consistent only with a close position between the *t*-butyl and the morpholino groups hindering the free rotation of the latter.

The preparative interest of this reaction fails when enamines, in which R' = H or methyl, are reacted with diimmonium salts. ¹H-Nmr monitoring of the reaction revealed the formation of the expected pyrrole derivative but all attempts to isolate it in a pure state failed. This fact justifies the conclusion that α-aminopyrroles bearing a hydrogen atom or an alkyl group at C₄ are very unstable compounds.

Further work is in progress to investigate the relationship between structure and stability in this class of derivatives more fully.

EXPERIMENTAL

Enamines 3a-i.

The enamines **3a**, **3d**, **3e**, **3f** and **3g** are known compounds and were

prepared according to the literature methods (9)(10)(11)(12). Compound **3b** (b.p. 1.0, 170-180°), **3c** (b.p. 0.2, 75-80°), **3h** (b.p. 1.0, 130°), and **3i** (b.p. 2.5, 132°) were prepared mixing an equimolecular amount of two reactants in the presence of molecular sieves. The enamines were purified by distillation at reduced pressure.

2-Aminopyrroles 4a-j. General Procedure.

To a suspension of freshly prepared diimmonium dibromide **1** (0.01 mole) in dry dichloromethane (80 ml.), a solution of freshly distilled enamine **3** (0.01 mole) and triethylamine (2.02 g., 0.02 mole) dissolved in dry dichloromethane (40 ml.) was added. The mixture was stirred at room temperature for 2 hours, washed with water, the organic layer was dried over magnesium sulphate and the solvent removed under reduced pressure to give the crude aminopyrrole **4**. The product was purified by column chromatography on silica gel (ratio silica gel/crude product 50:1) using the eluents shown in Table 1).

Debenzylation of 1-Benzylpyrrole (4b).

To a stirred solution of sodium (313 mg., 13.6 mmoles) in liquid ammonia (80 ml.) cooled at -60°, a solution of pyrrole **4b** (2.23 g., 6.8 mmoles) in tetrahydrofuran (10 ml.) was added dropwise. The reaction mixture was stirred for 1 hour, methanol (2 ml.) was added, the ammonia was evaporated on a warm water bath (~35-40°). The reaction residue was washed with water and extracted with dichloromethane. The organic layer was dried with anhydrous magnesium sulphate and the solvent removed under reduced pressure. The crude residue was purified by column chromatography on silica gel (ratio silica gel/crude product (40:1) and eluted with ethyl ether; yield 1.12 g. (80%).

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