A Facile and Convenient Synthesis of the Unknown 1-Aroylmethyl-1*H*-pyrroles

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In the course of our research on pyrrole analogues of econazole, an imidazole chemotherapeutic agent with useful antifungal activities, we needed some 1-aroylmethyl-1*H*-pyrroles as starting material. Surprisingly a survey of the pyrrole literature revealed that no synthesis of these simple products has hitherto been described.

Attempts to prepare 1-aroylmethyl-1*H*-pyrroles by the action of substituted phenacyl bromides on the potassium salt of pyrrole[1,2] failed; the only material recovered being a mixture of products probably derived from the self-condensation of phenacyl bromides as claimed in an earlier report[3]. Furthermore, we tried to prepare the title compounds by the Clauson-Kaas and Tyle method[4] based on the reaction of 2,5-dialkoxytetrahydrofurans with primary amines. These authors and later Josey and Jenner[5] employed a variety of simple aliphatic and aromatic primary amines as starting material to obtain *N*-substituted pyrroles. To our knowledge, phenacylamines have not been used as reagents in the previously reported procedures. Thus, we decided to start from these compounds to prepare the unknown 1-aroylmethyl-1*H*-pyrroles. The reaction was carried out under various experimental conditions[3-7]; but only tars or unreacted materials were generally obtained. In some cases, the title compounds were formed, e.g. by employing acetic acid as solvent, however, the yields were negligible.

Finally, we found that 1-aroylmethyl-1*H*-pyrroles can easily be prepared in good yields by heating the corresponding phenacylamine hydrochlorides (**1**) and 2,5-dimethoxytetrahydrofuran (or 2,5-dioxohexane) in *N*,*N*-dimethylformamide at reflux temperature for a few minutes. Subsequent treatment of the reaction mixture with crushed ice followed by standing overnight at 0–5°C furnished the pyrroles **2** and **3**, respectively as nearly pure solid compounds. Recrystallisation from suitable solvents afforded analytically pure samples. All 1-aroylmethyl-1*H*-pyrroles prepared showed an absorption band in the range of $\nu = 1670$–1710 cm^{-1} for the carbonyl group in the I.R. spectrum (Nujols mulls).

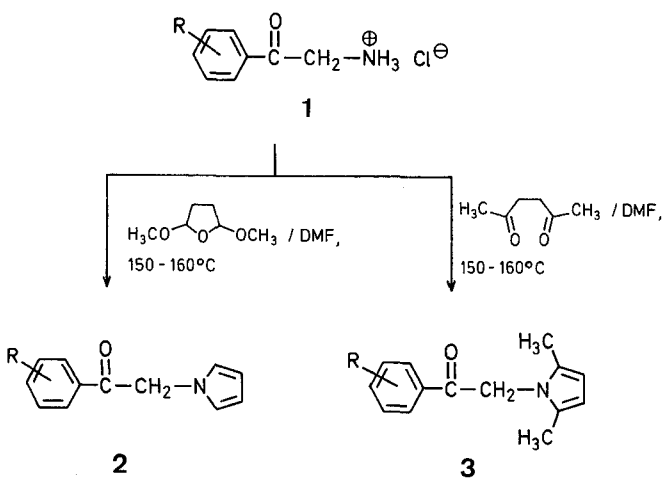

Table. 1-Aroylmethyl-1*H*-pyrroles **2** and **3** prepared

Product No.	R	Yield[a] [%]	m.p. [°C] (solvent)	Molecular formula[b]
2a	H	38	120–125° (cyclohexane)	$C_{12}H_{11}NO$ (185.2)
2b	4-H_3C	50	125–127° (cyclohexane)	$C_{13}H_{13}NO$ (199.2)
2c	4-H_3CO	60	130–132° (ethanol)	$C_{13}H_{13}NO_2$ (215.2)
2d	4-O_2N	78	160–165° (dec.) (benzene)	$C_{12}H_{10}N_2O_3$ (230.2)
3a	H	59	111–115° (cyclohexane)	$C_{14}H_{15}NO$ (213.3)
3b	4-H_3C	43	124–125° (cyclohexane)	$C_{14}H_{15}NO$ (227.3)
3c	4-H_3CO	57	108–109° (cyclohexane)	$C_{15}H_{17}NO_2$ (243.3)
3d	4-O_2N	52	213–215° (dec.) (ethylacetate)	$C_{14}H_{14}N_2O_3$ (258.3)
3e	3-O_2N	24	154–156° (dec.) (cyclohexane)	$C_{14}H_{14}N_2O_3$ (258.3)

[a] Yield of isolated product.

[b] Satisfactory microanalyses obtained: C, ±0.30; H, ±0.22; N, ±0.26.

1-Aroylmethyl-1*H*-pyrroles 2 and 3; General Procedure:

2,5-Dimethoxytetrahydrofuran or 2,5-dioxohexane (11 mmol) is added to a stirred solution of phenacylamine hydrochloride **1** (10 mmol) in dry dimethylformamide (60 ml) heated at 150–160°C. After stirring for 3–5 min at the same temperature, the mixture is poured on crushed ice (200 g) and allowed to stand at 0–5°C over-night. The separated solid is collected by filtration, washed with water, dried, and recrystallised from a suitable solvent (Table).

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