

Synthesis of 1-Acyl-1*H*-pyrroles from Cyclic 2-(Acylmethyl)-1,3-diketones via Rearrangement involving Transannular Interaction

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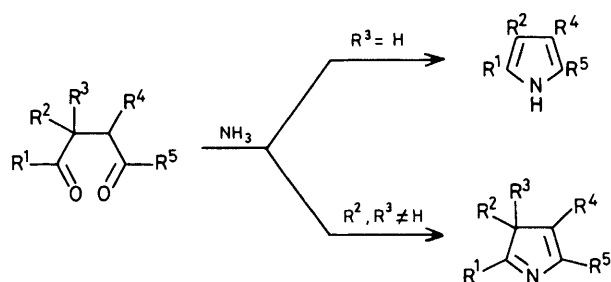
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Cyclic 2-(acylmethyl)-1,3-diketones are converted into 1-acyl-1*H*-pyrroles in high yields by ammonium acetate in acetic acid, via rearrangement of a hydroxypyrroline intermediate.

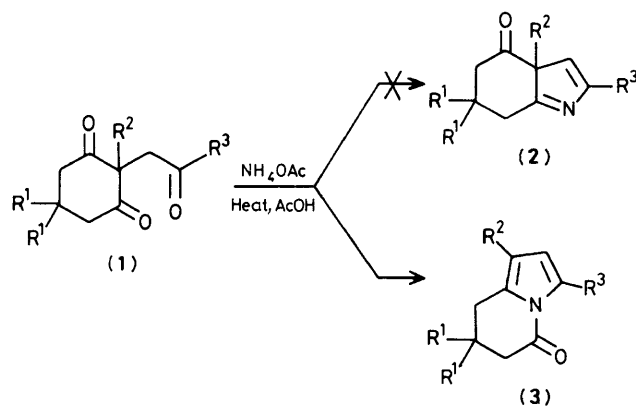
An attractive, although apparently unexplored, approach to the little-known¹ 3*H*-pyrrole ring system is the modified Paal-Knorr reaction between ammonia and a 2,2-disubstituted 1,4-diketone (Scheme 1). As part of a continuing search for new syntheses of this ring system,² we treated the triketone (**1a**) with ammonium acetate in refluxing acetic acid, isolating, however, not the 3*H*-pyrrole (**2a**), but the rearranged bicyclic 1-acyl-1*H*-pyrrole (**3a**) in 96% yield.[†] Com-

pounds (**1b–g**)[‡] likewise gave the products (**3b–g**) (72–93%), and the indanedione derivatives (**4**; R = Me, Ph) gave the analogous tricyclic products (**5**) (55, 65%). We thus report a simple, novel, and high yielding synthesis of 1-acyl-1*H*-pyrroles in which the amide function forms part of a fused lactam ring.

Treatment of compounds (**1**) overnight in liquid ammonia gave essentially quantitative yields of the hydroxypyrrolines (**6**), which on heating in acetic acid, or to their melting points without solvent, were converted in very high yields into the pyrroles (**3**). Compounds (**6**) thus appear to be intermediates in the reaction shown in Scheme 2. Their conversion into the 1*H*-pyrroles (**3**) may be either by dehydration to the 3*H*-pyrroles (**2**) followed by two successive acyl [1,5]-shifts [disfavoured by the observed transformation (**4**) → (**5**) which would require a highly strained intermediate by this route], or as shown in Scheme 3. The key feature in the second mechanism is a transannular interaction between an amide nitrogen atom and a carbonyl group in a medium ring; there is



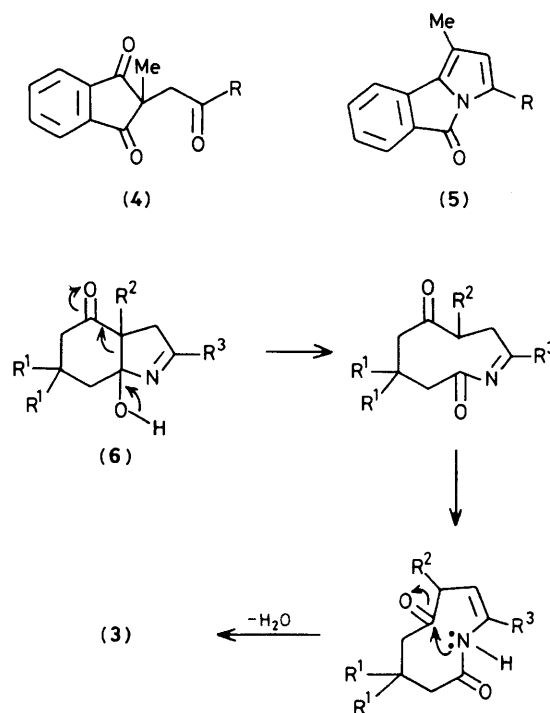
Scheme 1



	a	b	c	d	e	f	g
R ¹	Me	Me	Me	Me	H	H	H
R ²	Me	PhCH ₂	Me	PhCH ₂	Me	PhCH ₂	Me
R ³	Ph	Ph	Me	Me	Ph	Ph	Me

Scheme 2

[†] Satisfactory elemental analyses were obtained for compounds (**1**), and (**3**)–(**6**). Representative spectral data are as follows: compound (**3a**), i.r., ν_{max} (Nujol): 1710 (C=O), 1360, and 1320 cm^{-1} ; ^1H n.m.r., δ (CDCl_3): 1.04 (6H, s), 1.96 (3H, s), 2.44 (2H, s), 2.58 (2H, s), 6.04 (1H, s), and 7.2–7.4 (5H, m). Compound (**6a**), i.r., ν_{max} (Nujol): 3125 (OH), 1705 (C=O), 1600 (C=N), and 1048 cm^{-1} (C–O); ^1H n.m.r., δ (CDCl_3): 0.78 (3H, s), 1.03 (3H, s), 1.35 (3H, s), 2.09 (2H, s), 2.12, 2.50 (2H, ABq), 2.76, 3.62 (2H, ABq), 5.60 (1H, br. s), and 7.2–7.8 (5H, m).



Scheme 3

[‡] Prepared, like (**1a**), by sequential dialkylation of cyclic 1,3-diketones.

precedent for cyclisations of this type in the literature,^{3,4} although not apparently with pyrrole formation. The reaction fails to take place with acyclic 1,3-diketone derivatives, further supporting this mechanism.

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