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

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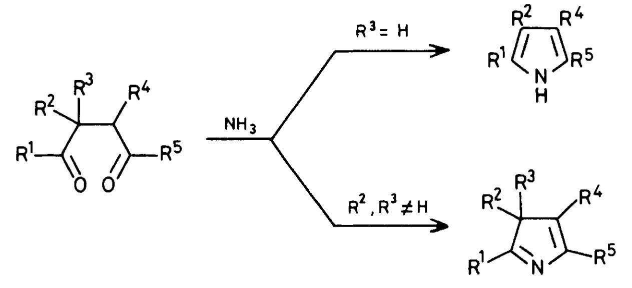
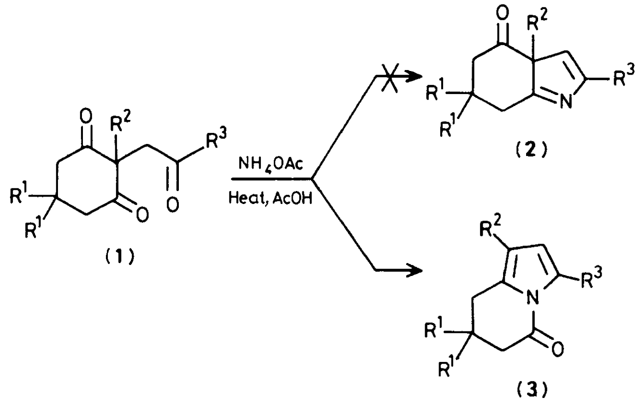
Cyclic 2-(acylmethyl)-1,3-diketones are converted into 1-acyl-1*H*-pyrroles in high yields by ammonium acetate in acetic acid, *via* rearrangement of a hydroxypyrroline intermediate.

An attractive, although apparently unexplored, approach to the little-known[1] 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.† Compounds (**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.



Scheme 1

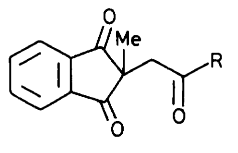


(**1**) (**2**) (**3**)

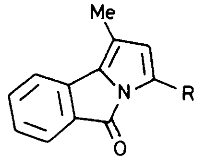
	a	b	c	d	e	f	g
R^1	Me	Me	Me	Me	H	H	H
R^2	Me	$PhCH_2$	Me	$PhCH_2$	Me	$PhCH_2$	Me
R^3	Ph	Ph	Me	Me	Ph	Ph	Me

Scheme 2

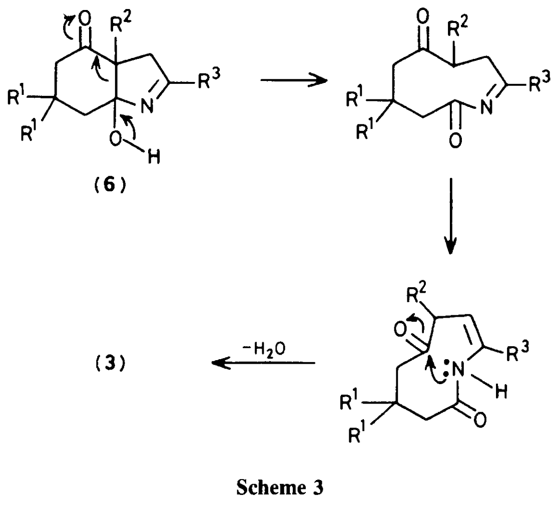
Treatment of compounds (**1**) overnight in liquid ammonia gave essentially quantitative yields of the hydroxypyrrolines (**6**), which on heating in acetic acid, or to their melting points without solvent, were converted in very high yields into the pyrroles (**3**). Compounds (**6**) thus appear to 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



(**4**)



(**5**)



Scheme 3

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† 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}; ^{1}H 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); ^{1}H 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).

‡ 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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