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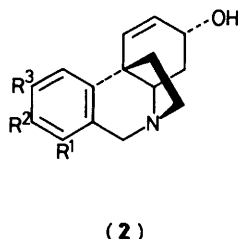
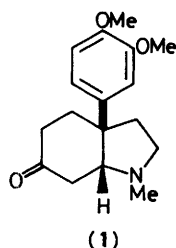
The Reaction of α,β -Unsaturated Ketones with 1-Substituted 3-Arylsuccinimides: A Facile Entry into the Cyclopenta[*c*]pyrrole Heterocyclic Ring System

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The condensation of succinimides of the type (3) with α,β -unsaturated ketones in the presence of a catalytic quantity of sodium hydride yields, in one step, derivatives of cyclopenta[*c*]pyrrole represented by (8), (9), and (10).

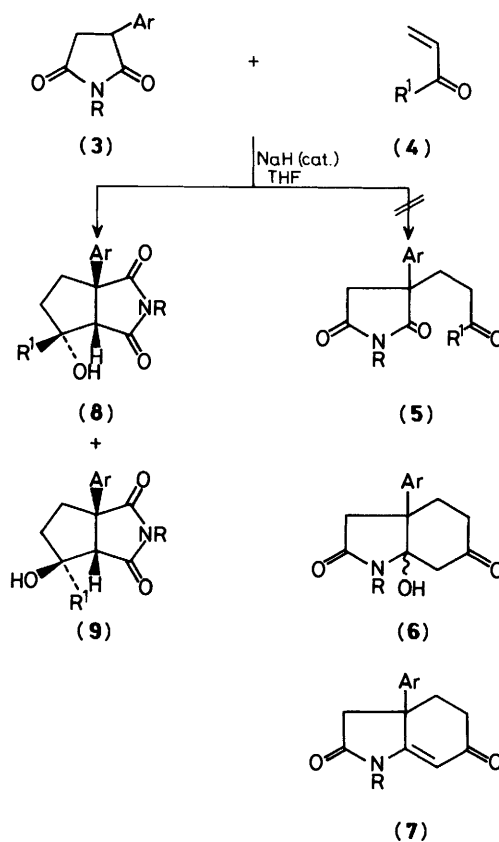
In exploring a new route to the synthesis of mesembrine (1) and related *Sceletium* alkaloids¹ and extending it to the synthesis of some *Amaryllidaceae* alkaloids² such as matridine (2a), crinine (2b), and powelline (2c), we encountered a novel reaction when



- a; R¹ = H, R² = R³ = OMe
 b; R¹ = H, R²R³ = OCH₂O
 c; R¹ = OMe, R²R³ = OCH₂O

3-(3,4-dimethoxyphenyl)succinimide³ was treated with methyl vinyl ketone (MVK) (4; R¹ = Me) in the presence of a catalytic quantity of sodium hydride in anhydrous tetrahydrofuran. The reaction was exothermic and the mixture furnished, after a brief period under reflux and chromatography over basic alumina, a colourless crystalline product (81%) which consisted of a 1:1 mixture of two closely related compounds an elemental analysis of which corresponded to that of a 1:1 adduct of (3; R = Me, Ar = 3,4-dimethoxyphenyl) and MVK. The i.r.* and n.m.r.* spectra, which clearly precluded the expected structures (5), (6) or (7), established it as a mixture of (8a) and (9a), the assumption here being that the *cis* fusion of the two five-membered rings is more stable than the *trans* orientation.

It was immediately apparent that the Michael adduct (5), the primary product of the reaction, underwent an unexpected intramolecular aldol type of reaction at its 4-position activated by the carbonyl function at the 5-position to yield (8) and (9) instead of the normal Robinson-type of reaction leading to (6) or (7). It was established that this reaction was indeed quite



R = R¹ = Me,
 Ar = 3,4-dimethoxyphenyl

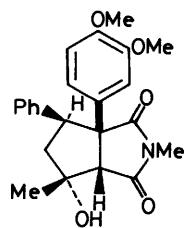
	Yield (%) of (8) and (9)
(8) and (9)	
a; R = R ¹ = Me, Ar = 3,4-dimethoxyphenyl	80
b; R = Pr, R ¹ = Et, Ar = 3,4-dimethoxyphenyl	60
c; R = Me, R ¹ = benzyl, Ar = 3-methoxyphenyl	65
d; R = Me, R ¹ = phenethyl, Ar = 3-methoxyphenyl	70
e; R = Me, R ¹ = n-C ₃ H ₇ , Ar = 3-methoxyphenyl	70
f; R = allyl, R ¹ = Me, Ar = 3-methoxyphenyl	68
g; R = R ¹ = Me, Ar = 4-tolyl	80
h; R = R ¹ = Me, Ar = 4-chlorophenyl	56
i; R = R ¹ = Me, Ar = 3-chlorophenyl	79
j; R = R ¹ = Me, Ar = 3-thienyl	63

* (8a): ν_{max} . 3 540 (OH), 1 780 and 1 710 cm⁻¹ (imide carbonyl); δ_{H} (200 MHz, CDCl₃) 1.51 (3 H, s), 1.55 (1 H, dd, *J* 14 and 7 Hz), 1.91 (2 H, m), 2.05 (1 H, s, exchangeable with D₂O), 2.45 (1 H, dd, *J* 14 H and 7 Hz), 3.03 (3 H, s), 3.25 (1 H, s), 3.85 (3 H, s), 3.87 (3 H, s), 6.81 (1 H, d, *J* 8 Hz), 6.91 (1 H, dd, *J* 8 and 3 Hz), and 7.01 (1 H, d, *J* 3 Hz).

general with respect to 1-substituted 3-arylsuccinimides (**3**) and α,β -unsaturated ketones (**4**) providing, in one step and in 50 to 80% yield, a 1:1 mixture of compounds of the type (**8**) and (**9**) representing the cyclopenta[*c*]pyrrole heterocyclic ring system. Although the basic ring system is known and easy to construct,⁵ the 1-aryl substituted derivatives of the system have not, to date, been described in the literature.

The diastereoisomers (**8**) and (**9**) can be separated by careful chromatography on basic alumina or by flash chromatography on silica gel and their structures secured by highfield ¹H n.m.r. coupled with n.O.e. difference experiments.

In the case of β -mono substituted α,β -unsaturated ketones, two pairs of diastereoisomeric products are possible. In the one case examined, with *trans*-4-phenylbut-3-en-2-one and (**3**; R = Me, Ar = 3,4-dimethoxyphenyl) only two diastereoisomers resulted and the major isomer which was isolated was assigned the structure (**10**) after extensive n.O.e. difference determinations.



(10)

Wijnberg and Speckamp⁴ report that the condensation of 1-methyl-3-phenylsuccinimide (**3**; R = Me, Ar = Ph) with MVK (**4**; R¹ = Me) under a variety of conditions to yield (**5**; R = Me, Ar = Ph) gave 'inferior' results. No mention was made of the conditions used or whether the expected product (**5**; R = Me, Ar = Ph) was isolated at all.

Further transformation of compounds of the type (**8**) and (**9**) will be reported elsewhere.

Acknowledgements

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- 3 This and other 3-arylsuccinimides were prepared essentially according to the procedure of C. A. Miller and L. M. Long, *J. Am. Chem. Soc.*, 1951, **73**, 4895.
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