

A NEW SYNTHESIS OF SOME 1-ALKYL-2,4-DIPHENYLPYRROLES

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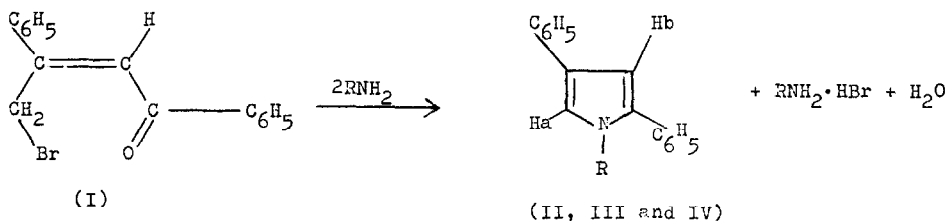
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The chemistry of β -ketoallyl systems has been a subject of investigation in this laboratory for some time (1). As a continuation of these studies, to include γ -ketoallyl systems, we have recently investigated the reaction of trans β -bromo-methylchalcone(I) (from the reaction of N-bromosuccinimide and trans β -methylchalcone in carbon tetrachloride) (2) with certain primary amines in solvent ether. We had originally expected that the resulting products might be γ -ketoallylamines. However, these appear to be, at most, only intermediates in the formation of the products which have been isolated in good yields and assigned the structures of 1-alkyl-2,4-diphenylpyrroles (II, III and IV).

The general reaction is as follows:



<u>Amine</u>	<u>Product</u>	<u>% Yield</u>
methylamine	II, R = CH ₃	69
t-butylamine	III, R = (CH ₃) ₃ C	49
cyclohexylamine	IV, R = C ₆ H ₁₁	77

A typical reaction is carried out by dissolving β -bromomethylchalcone and two molar equivalents of the appropriate amine in ether and stirring for twenty-four hours at room temperature. The reaction mixture is then filtered free of the precipitated amine hydrobromide, washed with water, and dried over sodium sulfate. The solvent is removed by evaporation under reduced pressure and the residue taken up in hot absolute ethanol. Cooling causes the product to crystallize. Purification

is accomplished by recrystallization from absolute ethanol.

A mechanistic scheme suggested (Fig. 1) involves the S_N2 -displacement of bromine from the bromoketone by the amino group, followed by an intramolecular condensation involving amine attack on the carbonyl group and subsequent elimination of a water molecule to form the pyrrole. The more stable trans (relative to cis) configuration of β -bromomethylcinnalzone (2c), in which the bromomethyl group is actually cis to the carbonyl group, would facilitate such a condensation involving a substituted amino group.

II, m.p. 109-110°, gave infrared absorption (CCl_4) at 3000 cm^{-1} (M), 2970 cm^{-1} (M), 2860 cm^{-1} (W), 1604 cm^{-1} (S), 1480 cm^{-1} (S), 1452 cm^{-1} (M), 1387 cm^{-1} (M), 1357 cm^{-1} (M), 1184 cm^{-1} (M), 1056 cm^{-1} (M) and 913 cm^{-1} (M). The n.m.r. spectrum (3) (CCl_4) showed a complex multiplet (10 H) at 2.40-2.93 τ (aromatic protons), a doublet (1 H) at 3.14 τ ($J = 2$ c.p.s.) (pyrrole ring Ha proton), a doublet (1 H) at 3.57 τ ($J = 2$ c.p.s.) (pyrrole ring Hb proton) and a singlet (3 H) at 6.41 τ (methyl protons).

Anal. Calcd. for $C_{17}H_{15}N$: C, 87.52; H, 6.48; N, 6.00. Found: C, 87.72; H, 6.62; N, 5.88.

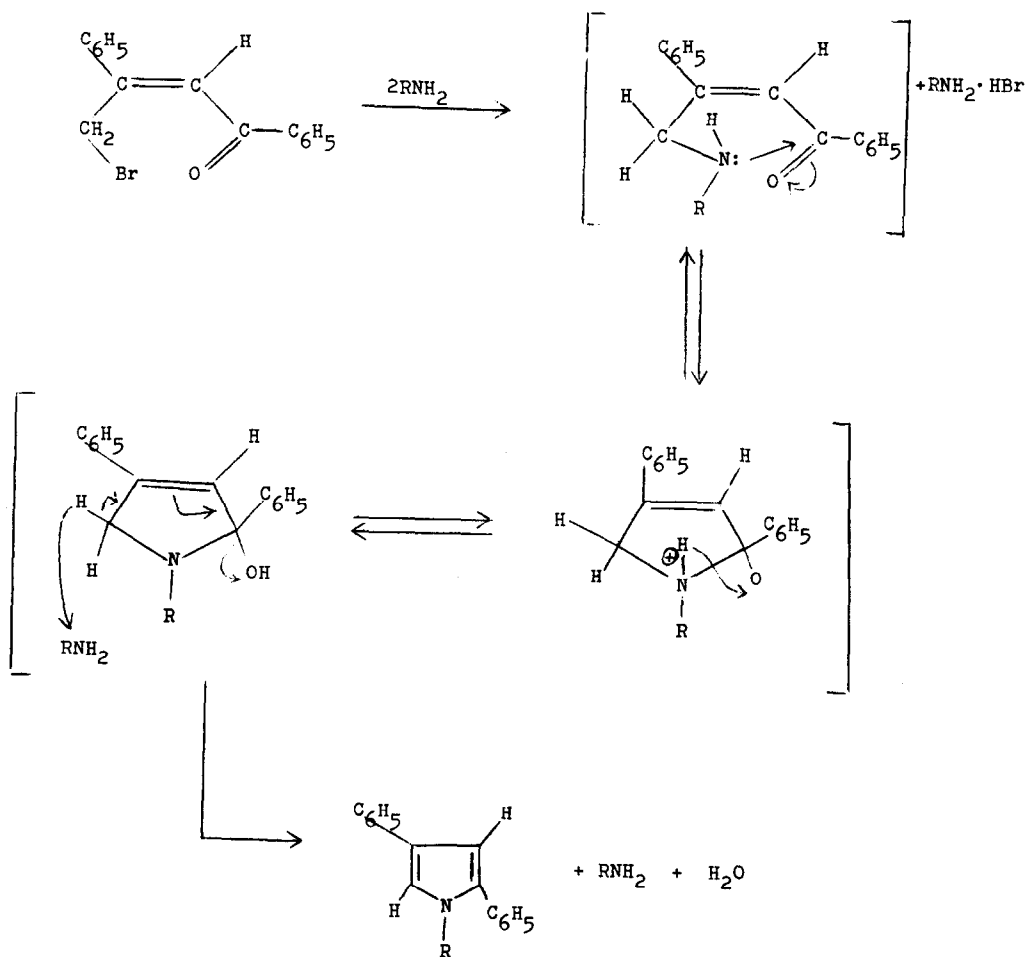
III, m.p. 101-103°, gave infrared absorption (CCl_4) at 3002 cm^{-1} (W), 2965 cm^{-1} (W), 2910 cm^{-1} (S), 1607 cm^{-1} (S), 1485 cm^{-1} (M), 1467 cm^{-1} (M), 1454 cm^{-1} (M), 1441 cm^{-1} (W), 1394 cm^{-1} (W), 1369 cm^{-1} (S), 1351 cm^{-1} (M), 1314 cm^{-1} (W), 1204 cm^{-1} (S), 1178 cm^{-1} (M), 1053 cm^{-1} (W) and 915 cm^{-1} (W). The n.m.r. spectrum (CCl_4) showed a complex multiplet (10 H) at 2.38-2.88 τ (aromatic protons), a doublet (1 H) at 2.91 τ ($J = 2$ c.p.s.) (pyrrole ring Ha proton), a doublet (1 H) at 3.77 τ ($J = 2$ c.p.s.) (pyrrole ring Hb proton) and a singlet (9 H) at 8.56 τ (t-butyl protons).

Anal. Calcd. for $C_{20}H_{21}N$: C, 87.23; H, 7.69; N, 5.09. Found: C, 87.06; H, 7.68; N, 5.02.

IV, m.p. 83.5-85°, gave infrared absorption (CCl_4) at 3005 cm^{-1} (W), 2970 cm^{-1} (W), 2860 cm^{-1} (S), 2775 cm^{-1} (M), 1605 cm^{-1} (S), 1485 cm^{-1} (M), 1452 cm^{-1} (S), 1383 cm^{-1} (M), 1360 cm^{-1} (W), 1341 cm^{-1} (W), 1205 cm^{-1} (W), 1180 cm^{-1} (M),

FIG. 1

Suggested Mechanism of Pyrrole Ring Closure



1056 cm.^{-1} (W), 1041 cm.^{-1} (W), 920 cm.^{-1} (W) and 875 cm.^{-1} (W). The n.m.r. spectrum (CCl_4) showed a complex multiplet (10 H) at 2.40-2.92 τ (aromatic protons), a doublet (1 H) at 2.97 τ ($J = 2$ c.p.s.) (pyrrole ring Ha proton), a doublet (1 H) at 3.67 τ ($J = 2$ c.p.s.) (pyrrole ring Hb proton), a complex multiplet (1 H) at 5.82-6.35 τ (cyclohexyl proton of carbon atom adjacent to nitrogen atom) and a complex multiplet (10 H) at 7.97-9.03 τ (remaining cyclohexyl protons).

Anal. Calcd. for $\text{C}_{22}\text{H}_{23}\text{N}$: C, 87.66; H, 7.69; N, 4.65. Found: C, 87.61; H, 7.81; N, 4.62.

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- The n.m.r. data were determined on a Varian A-60 spectrometer, and are expressed as τ p.p.m. chemical shift using tetramethylsilane (τ 10.0) as an internal standard.