Syntheses of 3-Methylpyrrole *via* Methyl 4-Methylpyrrole-2-carboxylate. A Thermal Oxazolone–Pyrone Rearrangement†

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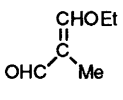
3-Ethoxy-2-methylpropenal with hippuric acid and acetic anhydride gave 4-(3-ethoxy-2-methylallylidene)-2-phenyloxazol-5(4*H*)-one. By successive treatment with methanolic potassium hydroxide, acetic–hydrochloric acid, and methanolic sodium methoxide, methyl 4-methylpyrrole-2-carboxylate was formed in high overall yield, and was converted into 3-methylpyrrole by hydrolysis and decarboxylation. The oxazolone with sodium hydroxide in acetone or dioxane gave 4-(3-hydroxy-2-methylallylidene)-2-phenyloxazol-5(4*H*)-one, isomerized in boiling acetone, or on melting, to 3-benzoylamino-5-methylpyran-2-one. 3-Ethoxy-2-methylpropenal condensed with glycine methyl ester to give an enaminal, cyclized in moderate yield to methyl 4-methylpyrrole-2-carboxylate.

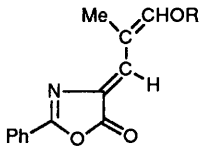
We required a considerable quantity of 3-methylpyrrole (see following paper)[1] and were dissatisfied with existing methods of synthesis.[2] The availability of 3-ethoxy-2-methylpropenal (**1**) in quantity at a reasonable price determined the choice of starting material, and our first experiments explored the possibility of condensing this with nitromethane to form some derivative of 4-nitro-2-methylbutenal, which might have yielded the desired pyrrole by a reductive cyclization. Having failed to find conditions for the initial condensation, we turned to the Erlenmeyer oxazolone synthesis; *i.e.* condensation with hippuric acid and acetic anhydride.

Results and Discussion

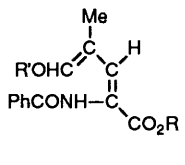
In the classical mode[3] with sodium acetate as catalyst, the product of the synthesis, in low yield, was the acetoxyoxazolone (**2**). Better yields (68%) were obtained by omitting the catalyst, but then the product was the ethoxyoxazolone (**3**). The condensation of preformed 2-phenyloxazol-5(4)-one with the aldehyde (**1**) was also examined. It was found that the usual catalysis by nitrogen bases gave poor results but that toluene-*p*-sulphonic acid at room temperature was effective. Following this indication we tried the sulphonic acid as a catalyst in the Erlenmeyer synthesis and found that the ethoxyoxazolone (**3**) could be produced at room temperature.



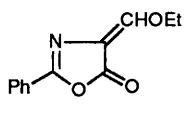
(1)



(2) R = Ac
(3) R = Et
(4) R = H
(5) R = Me



(6) R = Me, R' = Et
(7) R = R' = Et
(8) R = H, R' = Et
(9) R = R' = Me

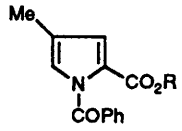


(10)

The oxazolone (**3**) is vinylogous with the 4-alkoxymethyleneoxazolones (*e.g.* (**10**)] extensively explored[4] during the international effort to synthesize penicillin. These compounds have two electrophilic sites, at the exocyclic alkoxylated carbon and at the oxazolone carbonyl. It was not always obvious which of these sites would be attacked by a particular reagent; and so it proved with the present compound. Reaction with methanol or ethanol in the presence of base (potassium hydroxide, sodium alkoxide or, more slowly, triethylamine) smoothly generated the pentadienoic ester derivates (**6**) and (**7**). The oxazolone (**3**) when suspended in boiling dilute aqueous sodium hydroxide was also attacked, slowly, at the carbonyl group, yielding after acidification the pentadienoic acid (**8**). On the other hand, slow addition of a slight excess of strong aqueous sodium hydroxide to a solution of the oxazolone (**3**) in an aprotic solvent such as dioxane or acetone gave the hydroxyallylideneoxazolone (**4**), an acidic substance which resisted ring-opening by further treatment with alkali and which, rather surprisingly, reacted with ethanolic hydrogen chloride to regenerate the ethoxyoxazolone (**3**). Methanolic hydrogen chloride gave the related methoxyoxazolone (**5**) which was also formed directly from the ethoxyoxazolone (**3**) with the same reagent. The methoxyoxazolone with potassium hydroxide or sodium methoxide in methanol afforded, like its ethoxy analogue, a pentadienoic ester (**9**). The hydroxyoxazolone (**4**) could be acetylated to the original product (**2**) of Erlenmeyer synthesis.

The enol ether grouping in the esters (**6**), (**7**), and (**9**) was not sensitive to alkali, but with cold dilute (*ca.* 0.5M) hydrochloric acid in acetic acid cyclization to the *N*-benzoylpyrrole esters (**11**) occurred spontaneously. Cyclization was not necessarily preceded by hydrolysis since protonation of the enol ether may have been followed directly by ring-closure to an alkoxypyrroline which only then lost alcohol. The smoothness and high yield of cyclization, together with the interconversions mentioned in the preceding paragraph, suggest that the *N*-substituted double bonds in the compounds (**2**)–(**9**) have (*Z*)-geometry, as shown. This is the usual geometry for oxazolones produced by the normal Erlenmeyer synthesis.[5] The geometry at the alkoxylated double bond was not examined but it may well be *E* as in the parent aldehyde (**1**).[6] The esters (**11**) were

† No reprints available.



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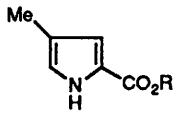
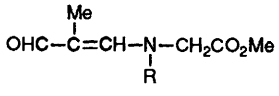


(12) R = H
(13) R = Me

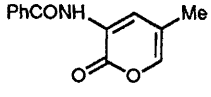
oils and were not purified. Direct alkaline hydrolysis gave 4-methylpyrrole-2-carboxylic acid (**12**), which had to be separated from benzoic acid. Mild methanolysis of the methyl ester (**11**) with a trace of sodium methoxide in methanol gave a mixture of methyl benzoate and methyl 4-methylpyrrole-2-carboxylate (**13**), easily resolved by distillation. The ester (**13**) is a natural product,[7] a trail pheromone for some species of leaf-cutting ants. Three syntheses have been reported,[8–10] but we believe the present synthesis to be preferable, especially for large-scale work since the pyrrole ester can be prepared from the aldehyde (**1**), without isolation of intermediates, in 45% overall yield.

Hydrolysis of the ester (**13**) to the acid (**12**) proceeded easily with aqueous alkali, and decarboxylation to 3-methylpyrrole was conducted in >90% overall yield by heating and then distilling a solution of the acid in an equal weight of sulpholane. Decarboxylation of the pure acid is new, but mixtures with the isomeric 3-carboxylic acid have been decarboxylated in 70% yield [ref. 2(i)(*c*); see later[11] for identity of the acid used]. It was quick and convenient to make the pyrrole, which is sensitive to air and light, as required from the more stable acid.

Another, shorter, but less satisfactory synthesis was also found. The aldehyde (**1**) condensed with glycine methyl ester to afford the enaminal (**14**), also characterized as its crystalline *N*-acetyl derivative (**15**), in fair yield. Cyclization of the enaminal by sodium hydride in dimethyl sulphoxide gave methyl 4-methylpyrrole-2-carboxylate in 26% yield. This synthesis is novel but it does not seem competitive unless the cyclization step can be improved.



(14) R = H
(15) R = Ac



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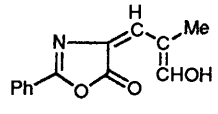

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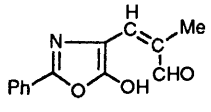
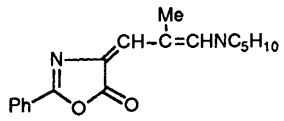


(18)

The yellow hydroxyallylideneoxazolone (**4**) on being melted, or boiled in acetone, formed a colourless isomeric substance identified by its spectra as 3-benzoylamino-5-methylpyran-2-one (**16**). As a thermal rearrangement this is new, and it must be preceded by thermal isomerization to the *E* form (**17**), perhaps by way of a tautomer (**18**). However, an analogous rearrangement in acidic conditions was inferred[12] from the formation of the same pyrone (**16**) in boiling tetrahydrofuran–hydrochloric acid from the piperidinoallylideneoxazolone (**19**), of unknown geometry at the double bonds, which had been prepared from the ethoxymethyleneoxazolone (**10**) and 1-piperidinopropene. In the same paper,[12] condensation of the oxazolone (**10**) and 1,3-dicarbonyl compounds with triethylamine was reported to give, directly, pyrones presumably formed from the initial condensation products. Our oxazolone (**4**), as the anion, did not easily rearrange to the pyrone in boiling aqueous solution; this suggests that the rearranging species may be a zwitterionic tautomer, protonated on nitrogen, of the *E* form (**17**).



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Experimental

Except where otherwise indicated, m.p.s were taken on a Kofler hot stage. 'Hexanes' means the hexane fraction from petroleum, b.p. *ca.* 70 °C. 'Ether' means diethyl ether; 'brine' means saturated aqueous sodium chloride. Methane was used as reactant gas for chemical ionization (CI) mass spectra.

4-(3-Acetoxy-2-methylallylidene)-2-phenyloxazol-5(4H)-one (**2**).—(*a*) A mixture of 3-ethoxy-2-methylpropenal (**1**) (1.14 g; from Fluka), hippuric acid (1.79 g), acetic anhydride (3.06 g), and sodium acetate (0.82 g) was stirred and heated at 50 °C for 6 h and then poured into excess of saturated aqueous sodium hydrogen carbonate. Extraction with ether and treatment of the evaporated extract with methanol gave yellow flakes (0.3 g) of the *acetoxyoxazolone* (**2**), m.p. 181.5–183 °C after recrystallization from methanol (Found: C, 66.2; H, 4.95; N, 5.1. $C_{15}H_{13}NO_4$ requires C, 66.4; H, 4.85; N, 5.2%); δ_H(90 MHz, $CDCl_3$) 8.08 (2 H, m, phenyl 2-, 6-H), 7.88 (1 H, s, allylidene 1-H), 7.54 (3 H, m, phenyl 3-, 4-, 5-H), 6.88 (1 H, d, *J* 2.2 Hz, allylidene 3-H), 2.28 3 H, d, *J* 2.2 Hz, C=CCH$_3$), and 2.24 3 H, s, acetyl CH$_3$); ν_{max}(KBr) 1 785 and 1 765 cm^{-1}.

(*b*) The hydroxyallylideneoxazolone (**4**) (0.17 g) was stirred and heated at 40 °C with acetic anhydride (0.8 ml) and pyridine (2 drops) for 1 h. Evaporation at 1–2 mmHg and recrystallization from chloroform–methanol gave the acetoxyoxazolone (**2**) (0.18 g), m.p. 181–184 °C; the IR spectrum was identical with the product from method (*a*).

4-(3-Ethoxy-2-methylallylidene)-2-phenyloxazol-5(4H)-one.—(*a*) Hippuric acid (1.9 g), 3-ethoxy-2-methylpropenal (1.14 g), and acetic anhydride (3.6 ml) were stirred at 70 °C for 2 h under nitrogen and then poured into aqueous sodium hydrogen carbonate (10%; 80 ml). After 1 h the tan-coloured crystalline solid was collected (1.76 g) and recrystallized from ethanol to give yellow needles of the *ethoxyoxazolone* (**3**), m.p. 134–136 °C (Found: C, 70.0; H, 5.7; N, 5.3. $C_{15}H_{15}NO_3$ requires C, 70.0; H, 5.9; N, 5.4%); δ_H(90 MHz, $CDCl_3$) 8.14 (2 H, m, phenyl 2-, 6-H), 7.59 (3 H, m, phenyl 3-, 4-, 5-H), 7.04 (1 H, s, allylidene 1-H), 6.94 (1 H, s, allylidene 3-H), 4.20 (2 H, q, *J* 7.2 Hz, OCH$_2$), 2.25 (3 H, s, =CCH$_3$), and 1.39 (3 H, t, *J* 7.2 Hz, ethyl CH$_3$); *m/z* (CI) 258 (*M* + H); ν_{max}(paraffin) 1 772 cm^{-1}; λ_{max}($CHCl_3$) 263 and 382 nm (ε 10 200, 36 200).

(*b*) The same reagents with addition of toluene-*p*-sulphonic acid (0.2 g) were stirred at room temperature under nitrogen. The yellow crystalline product began to separate after 45 min and was isolated as before after 33 h (1.57 g).

Methyl 2-Benzoylamino-5-ethoxy-4-methylpenta-2,4-dienoate.—A solution of potassium hydroxide (85%; 1 g) in methanol (30 ml) was added to a stirred suspension of the ethoxyoxazolone (**3**) (20 g) in methanol (70 ml), when the solid soon dissolved and the product crystallized. The mixture was neutralized with acetic acid and enough water was added to complete the crystallization. The product (21 g) was recrystallized for analysis from ethyl acetate and formed

colourless crystals of the *pentadienoic ester* (**6**), m.p. 183–184.5 °C (Found: C, 66.1; H, 6.7; N, 4.6. $C_{16}H_{19}NO_4$ requires C, 66.4; H, 6.6; N, 4.8%); δ_H(90 MHz, $CDCl_3$) 7.95 (2 H, m, Ar 2-, 6-H), 7.55 (3 H, m, Ar 3-, 4-, 5-H), 7.25 (1 H, s, 3-H), 6.70 (1 H, s, 5-H), 3.97 (2 H, q, OCH_2), 3.75 (3 H, s, OCH_3), 1.83 (3 H, s, 4-CH_3), and 1.29 (3 H, t, ethyl CH_3); ν_{max}(paraffin) 3 306, 1 708, 1 646, and 1 611 cm^{-1}; λ_{max}($CHCl_3$) 306 nm (ε 12 050).

Ethyl 2-Benzoylamino-5-ethoxy-4-methylpenta-2,4-dienoate.—Potassium hydroxide (85%; 0.49 g) in ethanol (12 ml) was added to a suspension of the oxazolone (**3**) (2 g) in ethanol (5 ml); a yellow solution was soon formed. Addition of water then caused separation of the product (1.89 g) as white crystals. Recrystallized from ethyl acetate, the *pentadienoic ester* (**7**) had m.p. 156–159 °C (Found: C, 67.4; H, 6.6; N, 4.9. $C_{17}H_{21}NO_4$ requires C, 67.3; H, 6.9; N, 4.6%); δ_H(90 MHz, $CDCl_3$) 7.85 (2 H, m), 7.48 (3 H, m), 7.18 (1 H, s), 6.63 (1 H, s), 4.16 (2 H, q, *J* 7.2 Hz), 3.92 (2 H, q, *J* 7.2 Hz), 1.80 (3 H, s), and 1.25 (6 H, t, *J* 7.2 Hz).

2-Benzoylamino-5-ethoxy-4-methylpenta-2,4-dienoic Acid.—The oxazolone (**3**) (2 g) was heated at reflux in water (4 ml) and sodium hydroxide (2M; 7.2 ml). The filtered solution was acidified to pH 4 and the solid (1.5 g) was collected and washed well with water. Recrystallization from ethyl acetate gave the colourless *pentadienoic acid* (**8**); m.p. 173–174.5 °C (Found: C, 65.6; H, 6.3; N, 4.9. $C_{15}H_{17}NO_4$ requires C, 65.4; H, 6.2; N, 5.1%); δ_H(90 MHz, $CDCl_3$ + $(CD_3)_2SO$) 7.78 (2 H, m), 7.48 (3 H, m), 7.21 (1 H, s), 6.64 (1 H, s), 3.95 (2 H, q, *J* 7.2 Hz), 1.80 (3 H, s), and 1.28 (3 H, t, *J* 7.2 Hz).

4-(3-Hydroxy-2-methylallylidene)-2-phenyloxazol-5(4H)-one.—To the ethoxyoxazolone (**3**) (3 g) in 1,4-dioxane (16 ml), sodium hydroxide (4M; 3.5 ml) was added dropwise. After 30 min, hydrochloric acid (6M; 2.3 ml) was added, followed by water. The precipitated yellow solid was washed well with water and dried (2.03 g). Recrystallization, by dissolution in cold acetone and careful addition of water, or from dichloromethane, gave a crystalline hydrate of the *hydroxyoxazolone* (**4**); m.p. 177.5–179 °C. This could not be fully dehydrated by drying under reduced pressure at moderate temperatures, and stronger heating caused some isomerization, but evolution of water at 130–140 °C was demonstrated (Found: C, 65.1; H, 5.4; N, 5.8. $C_{13}H_{11}NO_3 \cdot 0.6H_2O$ requires C, 65.0; H, 5.1; N, 5.8%); δ_H(90 MHz, $CDCl_3$ + $(CD_3)_2SO$) 8.05 (2 H, m), 7.53 (3 H, m), 7.37 (1 H, s), 6.90 (1 H, s), and 2.20 (3 H, s); *m/z* (CI) 230 (*M* + H); ν_{max}(paraffin) 3 202 and 1 741 cm^{-1}; λ_{max}(acetone) 398 nm (ε 16 000). The same product was obtained with acetone instead of dioxane. It dissolved easily in aqueous sodium hydrogen carbonate and was reprecipitated by acid. It gave no strong colour with ferric chloride.

4-(3-Methoxy-2-methylallylidene)-2-phenyloxazol-5(4H)-one.—(*a*) The hydroxyallylideneoxazolone (**4**) (0.4 g) was stirred with methanol (4 ml) and treated with methanolic hydrogen chloride (from 0.7 ml of acetyl chloride in 10 ml of methanol). After 0.5 h, the yellow solid (0.41 g) was collected and recrystallized from chloroform–methanol. The *methoxyoxazolone* (**5**) had m.p. 198–200.5 °C (Found: C, 69.2; H, 5.4; N, 5.7. $C_{14}H_{13}NO_3$ requires C, 69.1; H, 5.4; N, 5.8%); δ_H(90 MHz, $CDCl_3$ + $(CD_3)_2SO$) 8.10 (2 H, m), 7.53 (3 H, m), 6.95 (1 H, s), 3.87 (3 H, s), and 2.20 (3 H, s); *m/z* (CI) 244 (*M* + H).

(*b*) The ethoxyoxazolone (**3**) (0.6 g) was treated in the same manner (2 h). The yellow crystals (0.52 g) were collected and shown (m.p., mixed m.p., TLC) to be identical with the product from method (*a*).

Methyl 2-Benzoylamino-5-methoxy-4-methylpenta-2,4-dienoate.—The methoxyoxazolone (**5**) (0.4 g) was suspended in methanol (4 ml) and a solution of potassium hydroxide (85%; 0.18 g) in methanol (5 ml) was added. When all solid had dissolved the mixture was neutralized with acetic acid and diluted with water. The white solid (0.36 g) was recrystallized from ethyl acetate to give the *pentadienoic ester* (**9**), m.p. 173–175 °C (Found: C, 65.0; H, 5.9; N, 4.8. $C_{15}H_{17}NO_4$ requires C, 65.4; H, 6.2; N, 5.1%); δ_H(90 MHz, $CDCl_3$) 7.94 (2 H, m), 7.59 (3 H, m), 7.27 (1 H, s), 6.62 (1 H, s), 3.76 (6 H, s), and 1.82 (3 H, s); *m/z* (CI) 276 (*M* + H); λ_{max}($CHCl_3$) 298 nm (ε 13 800). This substance, unlike the analogous esters (**6**) and (**7**), tended to deteriorate to a gum when kept. The same product was obtained when the methoxyoxazolone (**5**) (0.5 g) was stirred for 0.5 h with methanol (8 ml) containing sodium methoxide (3 mg).

4-Methylpyrrole-2-carboxylic Acid.—To the pentadienoic ester (**7**) (3.8 g), suspended in acetic acid (15 ml), hydrochloric acid (6M; 1.5 ml) was added. After 1.5 h the resulting clear solution was diluted with water and extracted with ether (3 × 20 ml). The ether was washed (3 × 20 ml water, 3 × 10 ml aqueous $NaHCO_3$, water), dried ($MgSO_4$), and evaporated. The yellow oil (3.2 g), the benzoylpyrrole ester (**11**; R = Et), had δ_H(90 MHz, $CDCl_3$) 7.76 (2 H, m, phenyl 2-, 6-H), 7.52 (3 H, m, phenyl 3-, 4-, 5-H), 7.02 (1 H, s, pyrrole 5-H), 6.91 (1 H, s, pyrrole 3-H), 3.98 (q, *J* 7.2 Hz, ester CH_2), 2.08 (3 H, s, pyrrole 4-CH_3), and 1.09 (3 H, t, ester CH_3). It was dissolved in ethanol (10 ml), aqueous sodium hydroxide (20 ml of 2M) was added, and the mixture was boiled at reflux for 1 h. Ethanol was removed by evaporation and the residue was acidified with hydrochloric acid (6M). The white precipitate was dried and freed from benzoic acid by recrystallization from chloroform to yield the pyrrole acid (**12**) (1.43 g; 92%); m.p. 194–197 °C (decomp.) [lit.,[11] m.p. 203–204 °C (decomp.)]; δ_H(90 MHz, $CDCl_3$ + $(CD_3)_2SO$) 6.71 (1 H, s, 5-H), 6.69 (1 H, s, 3-H), and 2.07 (3 H, s, 4-CH_3). The same acid was obtained in a similar fashion from the esters (**6**) and (**9**).

Methyl 4-Methylpyrrole-2-carboxylate.—The methyl pentadienoate (**6**) (30 g) was stirred with acetic acid (100 ml) and hydrochloric acid (6M; 12 ml) until dissolution was complete and for *ca.* 10 min thereafter. The mixture was worked up as in the previous experiment to give the benzoylpyrrole ester (**11**; R = Me) as an oil (27 g); δ_H(90 MHz, $CDCl_3$) 7.77 (2 H, m), 7.58 (3 H, m), 7.02 (1 H, s), 6.92 (1 H, s), 3.52 (3 H, s), and 2.07 (3 H, s). This was dissolved in methanol (100 ml) and methanolic sodium methoxide (1%; 5.4 ml) was added. An immediate exothermic reaction subsided after a few minutes and the mixture, after neutralization with acetic acid, was evaporated. Sodium acetate was removed by washing the oily product in ether with water; the recovered oil was dissolved in hexanes and cooled. The crystalline pyrrole ester was filtered off and the residual oil was distilled, b.p. 82–92 °C/15 mmHg, to eliminate methyl benzoate; vacuum sublimation of the residue then gave more pyrrole ester (total, 12 g; 83%). On a larger scale it was better to distil the neutralized and evaporated reaction mixture at *ca.* 20 mmHg through a column (300 × 25 mm) packed with glass helices. When all methyl benzoate had distilled, the column was washed clean by refluxing acetone and distillation was continued without it. The pyrrole ester distilled around 124 °C/19 mmHg; it was dissolved in hexanes (2.5 ml g^{-1}) and chilled to yield large white prisms of the pyrrole ester (**13**), m.p. (capillary) 75–76 °C (lit.,[11] m.p. 73–74 °C); δ_H(90 MHz, $CDCl_3$) 6.78 (1 H, s, 5-H), 6.72 (1 H, s, 3-H), 3.82 (3 H, s, ester CH_3), and 2.09 (3 H, s, 4-CH_3).

3-Methylpyrrole.—Methyl 4-methylpyrrole-2-carboxylate (5 g) was stirred and boiled under reflux with aqueous sodium hydroxide (2M; 50 ml) until all was dissolved (*ca.* 30 min); it was

then cooled and acidified to pH 1. The crystalline precipitate of 4-methylpyrrole-2-carboxylic acid (4.45 g) was collected. The acid (**12**) (2 g) and sulpholane (2 ml) were heated until decarboxylation slackened, then at reflux for another 15 min, and distilled to a head temperature of 200 °C. The distillate (1.35 g) was shaken with one drop of saturated aqueous potassium carbonate, separated, and redistilled. The 3-methylpyrrole (1.19 g), b.p. 142–144 °C, was characterized by preparation of the two crystalline 'phthalides' (see following paper[1]).

N-(2-*Methyl*-3-*oxoprop*-1-*enyl*)*glycine Methyl Ester*.—Sodium methoxide solution (from 1.2 g of sodium and 30 ml of methanol) was added during 40 min to a stirred, ice-cooled mixture of 3-ethoxy-2-methylpropenal (5.7 g) and glycine methyl ester hydrochloride (6.28 g) under nitrogen. One hour later, sodium chloride was removed by filtration and the residue was evaporated. Distillation at 0.1 mmHg in a short-path still (bath 135–140 °C) gave the enaminal (**14**) as a viscous oil (4.67 g); δ_H(60 MHz, $CDCl_3$) 8.88 (1 H, s, CHO), 6.73 (1 H, d, *J* 13.8 Hz, =C*H*–NH), 5.85 (1 H, br, NH), 4.02 (d, *J* 6 Hz, CH_2), 3.74 (3 H, s, ester CH_3), and 1.65 (3 H, s, C–CH_3). A mixture of this compound (3 g) and acetic anhydride (8.5 ml) was heated at reflux under nitrogen for 1 h, cooled, and poured into stirred aqueous sodium hydrogen carbonate. After 2 h, the oil was extracted with dichloromethane and distilled at 130 °C (bath) at 0.1 mmHg in a short-path still. The distillate (3.2 g) crystallized from ether as colourless prisms of the N-*acetyl* derivative (**15**), m.p. 62–64 °C (Found: C, 54.4; H, 6.4; N, 7.1. $C_9H_{13}NO_4$ requires C, 54.3; H, 6.6; N, 7.0%); δ_H(60 MHz, $CDCl_3$) 9.40 (1 H, s, CHO), 7.35 (1 H, s =CH), 4.55 (2 H, s, CH_2), 3.79 (3 H, s, ester CH_3), 2.35 (3 H, s, acetyl CH_3), and 1.85 (3 H, s, CCH_3); ν_{max}(paraffin) 1 758, 1 701, and 1 668 cm^{-1}.

Cyclization of the Enaminal (**14**).—When sodium hydride (60% in mineral oil; 0.5 g) was added to a stirred solution of the enaminal (**14**) (1.57 g) in dry dimethyl sulphoxide (10 ml) under nitrogen, the reaction began immediately. After 3 h the mixture was cooled in ice, with simultaneous addition of hydrochloric acid (2M; 6 ml; final pH = 4). Water was added and the product was extracted into ether (3 × 25 ml); the extract was shaken twice with brine, dried ($MgSO_4$), and evaporated. The residue was recrystallized from hexanes to yield methyl 4-methylpyrrole-2-carboxylate (0.36 g), m.p. 69–72 °C, which was identified (mixed m.p., IR spectrum TLC) with the product reported above. Cyclization with methanolic sodium methoxide gave a lower yield, both in the presence and the absence of methyl formate (added as a water scavenger).

3-*Benzoylamino*-5-*methylpyran*-2-*one*.—(*a*) A solution of the oxazolone (**4**) (0.2 g) in acetone (6 ml) was boiled under reflux for 45 min; the yellow colour faded. Evaporation, and recrystallization of the residue from ethyl acetate, gave the colourless pyrone (**16**) (0.17 g), m.p. 177–179 °C (lit.,[12] m.p. 175–177 °C) (Found: C, 68.0; H, 4.9; N, 6.1. Calc. for $C_{13}H_{11}NO_3$: C, 68.1; H, 4.8; N, 6.1%); δ_H(90 MHz, $CDCl_3$) 8.75 (1 H, s, NH), 8.37 (1 H, d, *J* 2.3 Hz, pyrone 6-H), 7.92 (2 H, m, phenyl 2-, 6-H), 7.58 (3 H, m, phenyl 3-, 4-, 5-H), 7.12 (1 H, br s, 4-H), and 2.05 (3 H, s, CH_3) λ_{max}($CHCl_3$) 320 nm (ε 14 750) [lit.,[12] λ_{max}(dioxane) 320 nm (ε 13 900)].

(*b*) The oxazolone (**4**) (0.1 g) was melted (180 °C; 30 min) and cooled. The solid, recrystallized from ethyl acetate, gave the pyrone (0.09 g).

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