Tetrahedron. Vol. 25, pp 527 to 540. Pergamon Press 1969. Printed in Great Britain

# REACTIONS OF DIMETHYL ACETYLENEDICARBOXYLATE—II

## REACTION WITH PHENACYLAMINES[1]

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(*Received in the UK* 30 *July* 1968; *Accepted for publication* 23 *August* 1968)

**Abstract**—Dimethyl acetylenedicarboxylate reacts with phenacylanilines to give simple 1:1 adducts, arising out of a Michael type of addition. NMR studies of these adducts reveal that they have the maleate geometry. Chemical shift non-equivalence of the diastereotopic phenacyl methylene protons in some of these adducts has been observed and this is attributed to the restricted rotation about the aryl nitrogen bond. Under the influence of an acid catalyst and in some cases without any catalyst, the Michael adducts are cyclyzed to dimethyl 1-aryl-4-phenylpyrrole-2,3-dicarboxylates. The Michael adducts, under basic conditions, undergo a Dieckmann-type of cyclization to give methyl 1-aryl-5-benzoyl-4-hydroxypyrrole-2-carboxylates.

SEVERAL reactions of acetylenic esters employing various nucleophiles are reported in the literature. Nucleophiles in general, add to acetylenic esters giving rise to simple 1:1 adducts, arising out of a Michael type of addition.[2] The nucleophilic addition of amines to acetylenic esters, for example, can give rise to a mixture of enamines of maleate and fumarate geometry, arising out of a *cis* or *trans* type of addition.[3] If the attacking nucleophiles contain suitably positioned functional groups (carbonyl or double bonds), then the intermediates formed in these reactions could undergo cyclization giving rise to heterocyclic compounds. This principle has been recently used in the facile synthesis of several heterocyclic compounds.[4]

In an earlier communication,[1] we reported the facile addition of few phenacylanilines, such as phenacylaniline, phenacyl-*o*-toluidine, phenacyl-*o*-ethylaniline and phenacyl-*p*-chloroaniline with dimethyl acetylenedicarboxylate. The object of the present investigation was to examine the stereochemistry of the addition of different phenacylamines with dimethyl acetylenedicarboxylate and also to use the enamines formed in these reactions, for the synthesis of different pyrrole derivatives.

*Enamine adducts and their stereochemistry*. The phenacylamines used include, phenacylaniline (I), phenacyl-*o*-toluidine (VII), phenacyl-*o*-ethylaniline (X), phenacyl-*p*-chloroaniline (XIII), phenacyl-*p*-bromoaniline (XVI), phenacyl-*p*-iodoaniline (XIX), phenacyl-*p*-toluidine (XXII), phenacyl-*p*-anisidine (XXV) and phenacyl-α-naphthylamine (XXVIII). In each case, we could isolate only one isomer of the enamine adduct.

The reaction of a secondary amine such as I with dimethyl acetylenedicarboxylate would be expected to proceed through a resonance stabilized zwitterionic intermediate II. This intermediate can pick up a proton, either internally from the attacking nucleophile to give the *cis*-addition product III, which has a maleate geometry or externally from the solvent, yielding the *trans*-addition product IV, which has the

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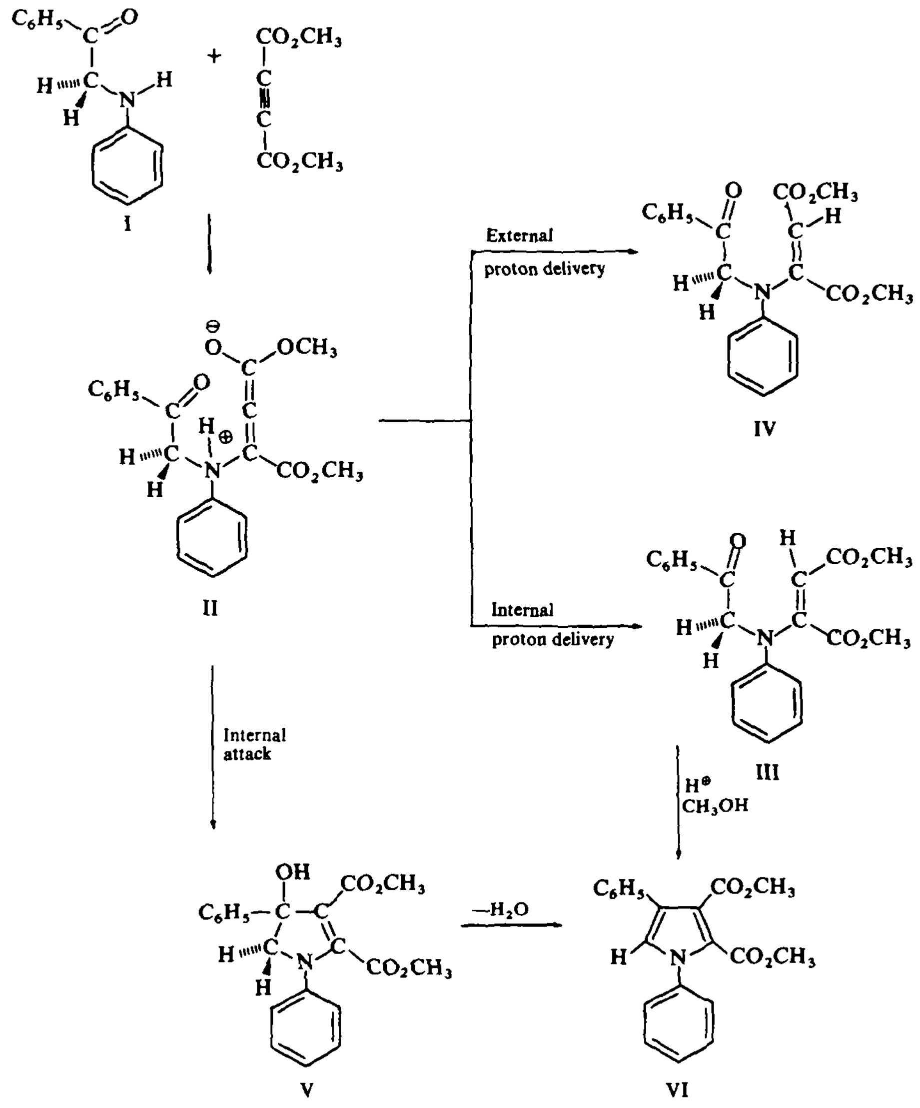
fumarate geometry. Another possible mode for the reaction of the zwitterionic intermediate is to have an internal attack of the carbanion center on the suitably positioned carbonyl group, giving rise to the pyrrole derivative VI, through the intermediate V (Scheme I). From the reaction of phenacylaniline with dimethyl

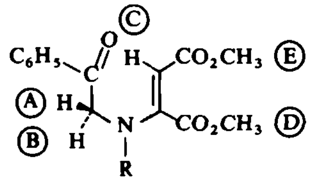
SCHEME I



acetylenedicarboxylate, the only product that could be isolated, besides polymeric material, was a 53% yield of dimethyl phenacylanilinomaleate (III).[1,*] The structure of this adduct has been based on its NMR spectrum. The NMR spectrum of III

[*] The stereochemistry of this product and other enamines were not assigned earlier, but they were assumed to be of the fumarate type.

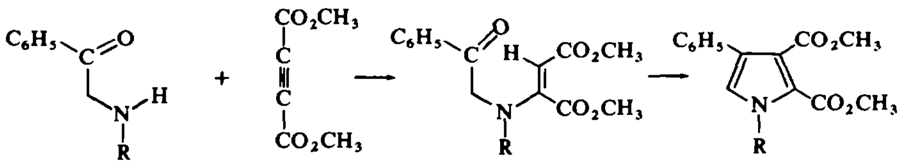
TABLE 1. CHEMICAL SHIFTS (τ) OF PROTONS IN DIMETHYL PHENACYLAMINOMALEATES ($CDCl_3$)



| Compound | R | A | B | C | D | E | Aromatic (multiplet) | Other substituents |
|---|---|---|---|---|---|---|---|---|
| III | $C_6H_5$ | 4·99 | | 5·29 | 6·40 | 6·46 | 2·30 | |
| VIII | $o$-$CH_3C_6H_4$ | 4·91 | 5·18 | 5·39 | 6·35 | 6·41 | 2·34 | 7·63 (methyl) |
| XI | $o$-$C_2H_5C_6H_4$ | 4·93 | 5·29 | 5·46 | 6·40 | 6·46 | 2·30 | 7·24 (methylene)<br>8·71 (methyl) |
| XIV | $p$-$ClC_6H_4$ | 5·01 | | 5·26 | 6·33 | 6·40 | 2·41 | |
| XVII | $p$-$BrC_6H_4$ | 5·01 | | 5·26 | 6·33 | 6·38 | 2·42 | |
| XX | $p$-$IC_6H_4$ | 5·02 | | 5·25 | 6·32 | 6·36 | 2·48 | |
| XXIII | $p$-$CH_3C_6H_4$ | 4·97 | | 5·29 | 6·31 | 6·37 | 2·33 | 7·69 (methyl) |
| XXVI | $p$-$OCH_3C_6H_4$ | 4·99 | | 5·31 | 6·33 | 6·39 | 2·58 | 6·19 (methoxyl) |
| XXIX | α-Naphthyl | 4·82 | 5·07 | 5·36 | 6·40 | 6·44 | 2·2 | |

(Table 1) showed two sharp singlets at 6·40 τ (3H) and 6·46 τ (3H) respectively, due to the methylene protons and a broad multiplet centered around 2·30 τ (10H) due to the phenyl protons. The vinylic proton appeared as a sharp singlet at 5·29 τ. The observed position of the vinylic proton in this enamine compares favourably with the values reported for similar enamines, having maleate geometry.[3a,c,e] Similarly, the enamines obtained from the reaction of other phenacylamines studied, also have the maleate geometry (Scheme II) and the vinylic protons in these adducts appear around 5·30 τ (Table 1).

SCHEME II



VII: R = $o$-$CH_3C_6H_4$
X: R = $o$-$C_2H_5C_6H_4$
XIII: R = $p$-$ClC_6H_4$
XVI: R = $p$-$BrC_6H_4$
XIX: R = $p$-$IC_6H_4$
XXII: R = $p$-$CH_3C_6H_4$
XXV: R = $p$-$CH_3OC_6H_4$
XXVIII: R = α-Naphthyl
XXX: R = Cyclohexyi

VIII: R = $o$-$CH_3C_6H_4$
XI: R = $o$-$C_2H_5C_6H_4$
XIV: R = $p$-$ClC_6H_4$
XVII: R = $p$-$BrC_6H_4$
XX: R = $p$-$IC_6H_4$
XXIII: R = $p$-$CH_3C_6H_4$
XXVI; R = $p$-$CH_3OC_6H_4$
XXIX: R = α-Naphthyl

IX: R = $o$-$CH_3C_6H_4$
XII: R = $o$-$C_2H_5C_6H_4$
XV: R = $p$-$ClC_6H_4$
XVIII: R = $p$-$BrC_6H_4$
XXI: R = $p$-$IC_6H_4$
XXIV: R = $p$-$CH_3C_6H_4$
XXVII: R = $p$-$CH_3OC_6H_4$
XXXI: R = Cyclohexyl

The exclusive formation of the maleates in the reaction of phenacylamines with dimethyl acetylenedicarboxylate, even in the presence of a proton donating solvent such as methanol reveals that the stereospecific collapse of the zwitterionic intermediates via intramolecular protonation is the major pathway in these reactions. In addition, steric factors will also favour the formation of the maleates. Based on steric considerations, one would expect the maleates to be more stable than the fumarates, as there is less crowding of the substituent groups in these isomers.

It is pertinent to observe that some of the zwitterionic intermediates, formed in the reaction of phenacylamines with dimethyl acetylenedicarboxylate, undergo cyclization to give pyrrole derivatives. Thus, in the reaction of phenacyl-$p$-chloroaniline with dimethyl acetylenedicarboxylate in methanol, besides a 78% yield of the maleate XIV, a 17% yield of dimethyl 1-($p$-chlorophenyl)-4-phenylpyrrole-2,3-dicarboxylate (XV) was also isolated. The yield of XV increased, as was reported earlier, when aprotic solvents were employed. Similarly, pyrrole derivatives were isolated from the reactions of XVI, XIX, XXII and XXV with dimethyl acetylenedicarboxylate. An extreme case was the reaction of phenacylcyclohexylamine (XXX), where only the cyclized pyrrole derivative XXXI was formed, when the reaction was carried out in methanol. No maleate could be isolated from this reaction.

It is interesting to note that in dimethyl phenacyl($o$-toluidino)maleate (VIII), dimethyl phenacyl($o$-ethylanilino)maleate (XI), and dimethyl phenacyl-α-naphthylaminomaleate (XXIX), obtained from the reactions of VII, X and XXVIII respectively,

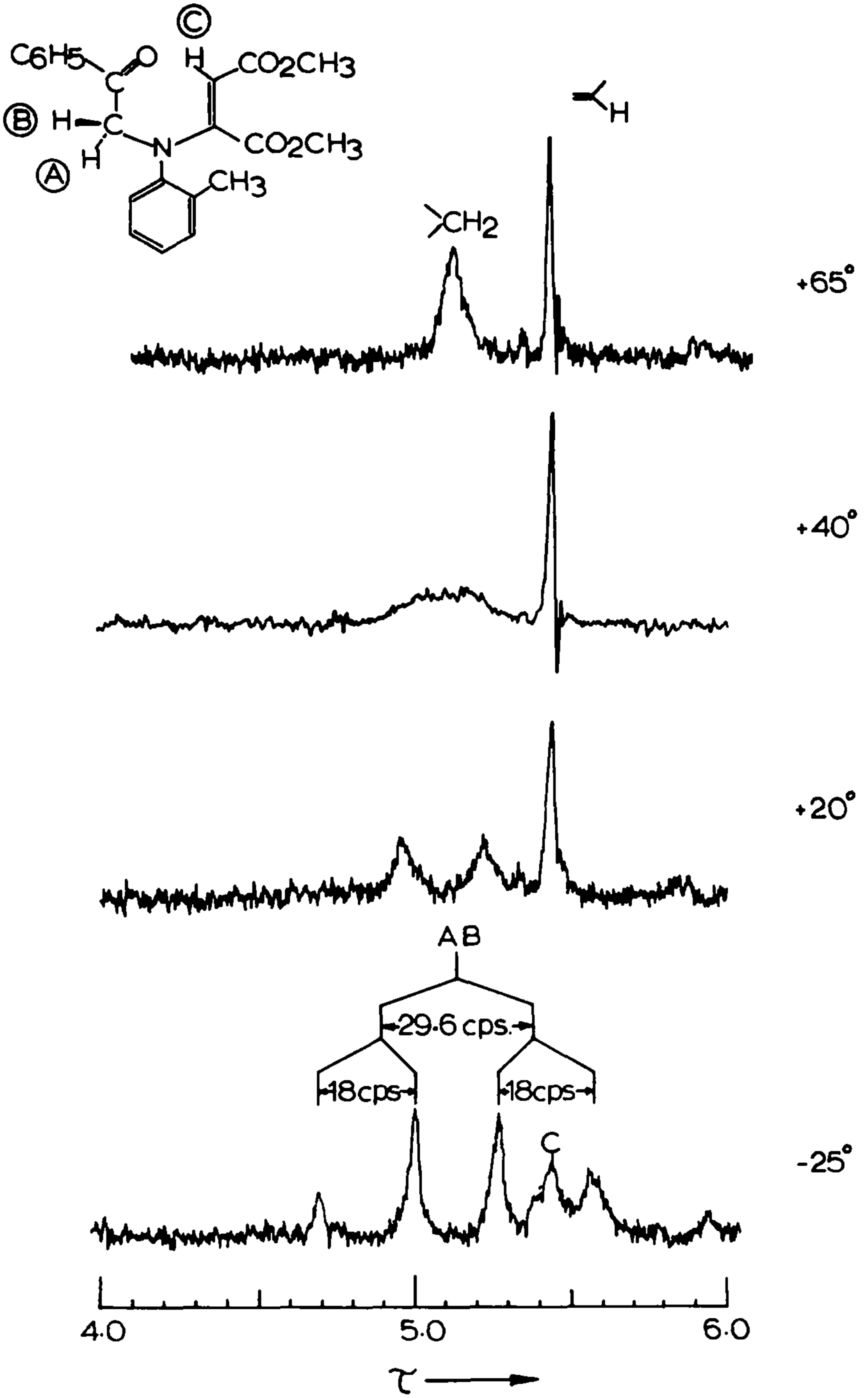


FIG. 1. Temperature dependent NMR spectrum of dimethyl phenacyl(*o*-toluidino)maleate at 60 mcs.

the geminal methylene protons of N-phenacyl group exhibit chemical shift nonequivalence in NMR. A temperature dependent study reveals that in the NMR spectrum of VIII, for example, the methylene protons appear as broad singlets centered around 5·13 τ both at 65° and 40°. At 20°, the methylene protons show two separate signals at 4·93 τ and 5·20 τ, respectively and at −20° the signals appear as an AB type quartet centered at 5·07 τ, with a coupling constant (J) of 18 c/s and a chemical shift difference (δ) of 29·6 c/s between the two protons (Fig. 1). In comparison, the methylene protons of the N-phenacyl group in dimethyl phenacyl(*p*-toluidino)maleate (XXIII), appear as a sharp signal, which remains unchanged even at low temperatures (−25°). The occurrence of chemical shift nonequivalence observed for the geminal methylene protons in *o*-substituted dimethyl phenacylanilinomaleates (VIII, XI and XXIX) may be traced to the restricted rotation around the benzene to nitrogen bond. Similar chemical shift nonequivalence of diastereotopic protons in cyclic and acyclic amides have been recently reported in the literature.[5]

The IR spectra of the enamine maleates show one ester band at 1740 $cm^{-1}$ and the α,β-unsaturated ester and keto carbonyl bands, as a strong peak at 1700 $cm^{-1}$. In a high resolution IR spectrometer (Perkin–Elmer Model 521), the 1700 $cm^{-1}$ peak appears as two separate absorptions at 1700 and 1689 $cm^{-1}$, respectively. The band at 1689 $cm^{-1}$ is assigned to the keto carbonyl, on the basis of the position of the C=O peak in the original phenacylamine. The UV spectra of the enamine maleates, shown two absorption maxima around 244 mμ and 290 mμ, respectively.

*Dimethyl* 1,4-*diarylpyrrole*-2,3-*dicarboxylates*. The enamine adducts obtained from the reaction of phenacylanilines undergo cyclization to 1,4-dairylpyrroles. Thus, dimethyl phenacylanilinomaleate (III) gave a 21% yield of dimethyl 1,4-diphenylpyrrole-2,3-dicarboxylate (VI). Similarly, dimethyl phenacyl(*o*-toluidino)maleate (VIII), dimethyl phenacyl(*o*-ethylanilino)maleate (XI) and dimethyl phenacyl(*p*-chloroanilino)maleate (XIV) gave the corresponding pyrroles IX, XII and XV respectively, in yields ranging between 54 to 72%. During the present investigation, we were able to isolate several 1,4-diarylpyrroles (XVIII, XXI, XXIV, XXVII and XXXI) in good yields, directly from the reactions of the corresponding phenacylamines with dimethyl acetylenedicarboxylate. Our attempts to carry out the cyclization of the maleate XXIX, employing hydrogen chloride as catalyst have been unsuccessful.

The NMR spectra of few dimethyl 1-aryl-4-phenylpyrrole-2,3-dicarboxylates have been reported.[1] Table 2 lists the spectra of several pyrroles. A typical pyrrole exhibits signals at 3·17 τ, assigned to the α-pyrrolyl proton, and at 6·15 τ and 6·30 τ, assigned to 3- and 2-carbomethoxy protons, respectively.* Aromatic protons appear around 2·6 τ as a complex multiplet. In the IR spectra of these pyrroles, the ester bands due to the 3- and 2-carbomethoxy group consistently appear around 1725 $cm^{-1}$ and 1695 $cm^{-1}$, respectively. The UV spectra of these pyrroles are characterized by absorption bands around 242 mμ and a shoulder around 280 mμ.

With a view to confirming the structure of the 1,4-diarylpyrroles formed from the enamine adducts, we attempted some degradative studies with dimethyl 1-(*p*-chlorophenyl)-4-phenylpyrrole-2,3-dicarboxylate (XV). Treatment of XV with methanolic

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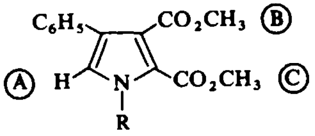
* The NMR assignment of 2- and 3-carbomethoxy protons is tentative and is based on the assumption that the 2-position in the pyrrole ring is more electron rich than the 3-position.

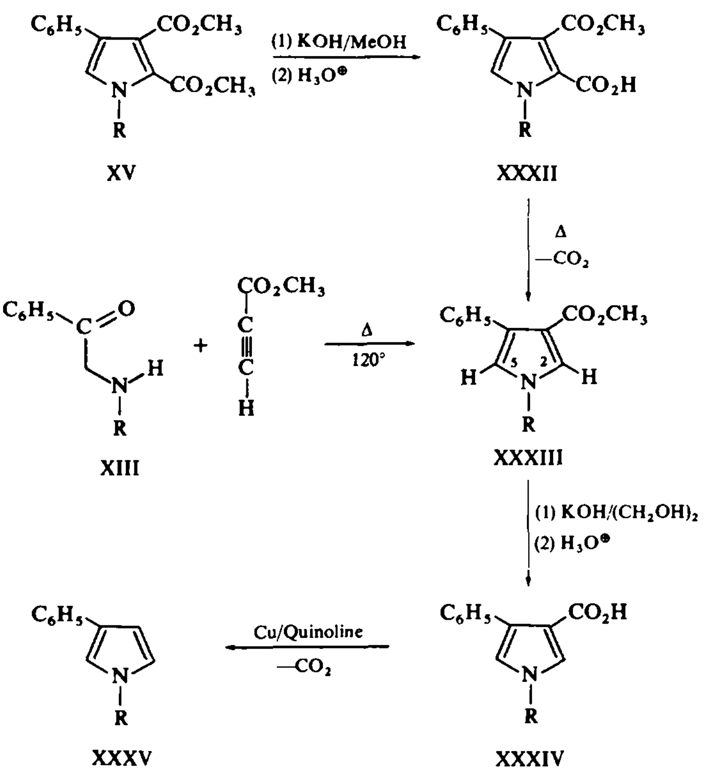
TABLE 2. CHEMICAL SHIFTS (τ) OF PROTONS IN DIMETHYL N-SUBSTITUTED-4-PHENYLPYRROLE-2,3-DICARBOXYLATES ($CDCl_3$)



| Compound | R | A | B | C | Aromatic (Multiplet) | Other substituents |
|---|---|---|---|---|---|---|
| VI | $C_6H_5$ | 3·05 | 6·15 | 6·30 | 2·59 | |
| IX | $o$-$CH_3C_6H_4$ | 3·10 | 6·15 | 6·33 | 2·67 | 7·91 (methyl) |
| XII | $o$-$C_2H_5C_6H_4$ | 3·02 | 6·16 | 6·27 | 2·58 | 7·55 (methylene), 8·89 (methyl) |
| XIV | $p$-$ClC_6H_4$ | 3·02 | 6·17 | 6·27 | 2·58 | |
| XVIII | $p$-$BrC_6H_4$ | 3·04 | 6·17 | 6·27 | 2·57 | |
| XXI | $p$-$IC_6H_4$ | 3·03 | 6·15 | 6·26 | 2·48 | |
| XXIV | $p$-$CH_3C_6H_4$ | 3·07 | 6·14 | 6·35 | 2·63 | 7·58 (methyl) |
| XXVII | $p$-$OCH_3C_6H_4$ | 3·04 | 6·15 | 6·28 | 2·70 | 6·17 (methoxyl) |
| XXXI | Cyclohexyl | 2·95 | 6·21 | 6·24 | 2·66 | 5·13 (tertiary), 8·53 (cyclohexyl) |

potassium hydroxide, gave a 72% yield of methyl 1-(*p*-chlorophenyl)-2-carboxy-4-phenylpyrrole-3-carboxylate (XXXII). The acid XXXII underwent decarboxylation at its m.p., to give a 91% yield of methyl 1-(*p*-chlorophenyl)-4-phenylpyrrole-3-carboxylate (XXXIII). It is generally observed that in the hydrolysis of pyrrole 2,3-dicarboxylates, the ester group in the 2-position is more easily attacked,[4b, e] although this need not always be the case.[6] With a view to establishing the structure of XXXIII and thereby, the mode of hydrolysis of the pyrrole derivative XV, we attempted an independent synthesis of XXXIII. Treatment of phenacyl-*p*-chloroaniline (XIII) with methyl propiolate at 120° for 7 hr in a sealed tube, resulted in the formation of a 65% yield of methyl 1-(*p*-chlorophenyl)-4-phenylpyrrole-3-carboxylate, identical in all respects with XXXIII, obtained from the hydrolysis of XV, followed by decarboxylation (Scheme III). A further confirmation of structure XXXIII for the decarboxylated product was provided by its NMR spectrum which shows a sharp singlet at 6·27 $\tau$ (3H), due to one carbomethoxy group and a multiplet centered around 2·62 $\tau$ (9H), due to the phenyl protons. In addition, the spectrum shows two distinct doublets at 2·32 $\tau$ (1H) and 3·0 $\tau$ (1H), with a coupling constant of 2·5 c/s.

SCHEME III



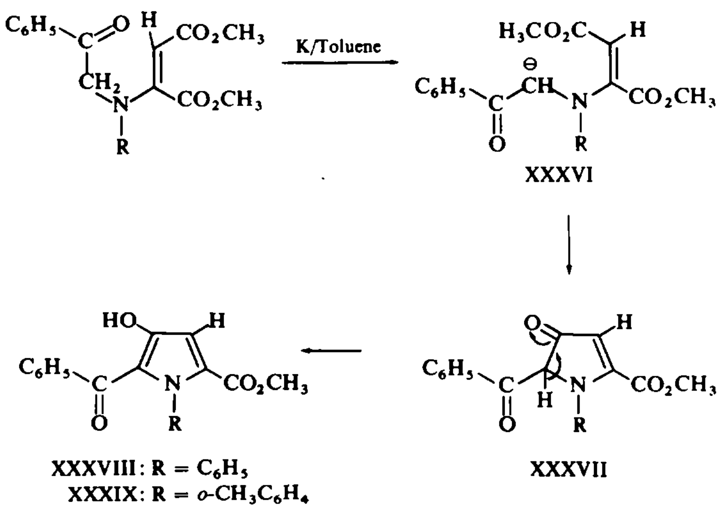
R = $p$-Cl—$C_6H_4$

Of these, the doublet at 2·32 $\tau$ is assigned to the 2-pyrrolyl proton, as it would be more deshielded due to the presence of the 3-carbomethoxy group; the doublet at 3·0 $\tau$ is assigned to the 5-pyrrolyl proton. It has been reported[7] that in pyrrole derivatives, the coupling constant between the 2- and 5-protons is around 2·2 c/s, whereas, the coupling constant between the 3- and 5-protons is of the order of 1·5 c/s. The observed value of 2·5 c/s for the coupling constant between the two pyrrolyl protons in XXXIII, is in agreement with the assigned structure.

Drastic hydrolysis of XXXIII gave a 97% of 1-(*p*-chlorophenyl)-4-phenylpyrrole-3-carboxylic acid (XXXIV). Treatment of XXXIV with copper powder in quinoline gave 1-(*p*-chlorophenyl)-3-phenylpyrrole (XXXV) in a 65% yield (Scheme III). The structures of all these intermediates were confirmed on the basis of their analytical results and spectral data.

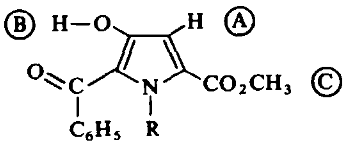
*Dieckmann cyclization of the enamine adducts.* The Michael adduct obtained from the reaction of methyl N-ethylglycinate with dimethyl acetylenedicarboxylate, under basic condition gives dimethyl 1-ethyl-4-hydroxypyrrole-2,3-dicarboxylate.[4d] Similarly, dimethyl phenacylanilinomaleate (III) gave a 30% yield of methyl 1-phenyl-5-benzoyl-4-hydroxypyrrole-2-carboxylate (XXXVIII). The reaction is assumed to proceed through a carbanion intermediate (XXXVI), which undergoes cyclization as shown in Scheme IV. Similarly, the reactions of dimethyl phenacyl-*o*-toluidinomaleate (VIII), dimethyl phenacyl-(*o*-ethylanilino)-maleate (XI), dimethyl phenacyl-(*p*-chloroanilino)-maleate (XIV), dimethyl phenacyl-(*p*-bromoanilino)-maleate (XVII), and dimethyl phenacyl-α-naphthylaminomaleate (XXIX) gave rise to the corresponding pyrrole derivatives in yields ranging between 30–60%.

SCHEME IV



XXXVIII: R = $C_6H_5$
XXXIX: R = $o\text{-}CH_3C_6H_4$
XXXX: R = $o\text{-}C_2H_5C_6H_4$
XXXXI: R = $p\text{-}ClC_6H_4$
XXXXII: R = $p\text{-}BrC_6H_4$
XXXXIII: R = α-Naphthyl

TABLE 3. CHEMICAL SHIFTS (τ) OF PROTONS IN METHYL 5-BENZOYL-4-HYDROXY-1-ARYLPYRROLE-2-CARBOXYLATES (CCDl$_3$)



| Compound | R | A | B | C | Aromatic (Multiplet) | Other substituents |
|---|---|---|---|---|---|---|
| XXXVIII | $C_6H_5$ | 3·30 | — | 6·31 | 2·82 | |
| XXXIX | $o$-$CH_3C_6H_4$ | 3·30 | −0·09 | 6·33 | 2·96 | 8·09 (methyl) |
| XXXX | $o$-$C_2H_5C_6H_4$ | 3·30 | −0·15 | 6·33 | 2·90 | 7·82 (methylene), 8·18 (methyl) |
| XXXXI | $p$-$ClC_6H_4$ | 3·28 | 0·05 | 6·27 | 2·89 | |
| XXXXII | $p$-$BrC_6H_4$ | 3·30 | 0·04 | 6·30 | 2·95 | |
| XXXXIII | α-Naphthyl | 3·28 | −0·03 | 6·46 | 2·63 | |

The IR spectra of these pyrroles are characterized by the presence of strong absorption bands at 3497 $cm^{-1}$ (OH group), 1730 $cm^{-1}$ (ester carbonyl group) and 1615 ± 10 $cm^{-1}$ (chelated carbonyl group). The UV spectra of these pyrroles are characterized by strong absorption bands at 216 mμ, 200 mμ and 332 mμ. The NMR spectra of these pyrroles (Table 3) displayed a signal at 3·30 τ assigned for the β-pyrrolyl proton and at 6·32 τ due to the 2-carbomethoxy protons. The protons due to the OH group appear around −0·5 τ.

## EXPERIMENTAL

All m.ps are uncorrected and were determined in a Thomas–Hoover m.p. apparatus. IR spectra were determined in either a Perkin–Elmer model 137 or 521 IR spectrometer and UV spectra on a Cary 14-R spectrometer. NMR traces were taken on a Varian A-60 spectrometer, using TMS as an internal standard.

*Starting materials.* Phenacylamines were prepared as per reported procedures.[8,9] In this way, phenacylaniline, m.p. 98°, phenacyl-*o*-toluidine, m.p. 88°, phenacyl-*o*-ethylaniline, m.p. 55°, phenacyl-*p*-chloroaniline, m.p.. 165°, phenacyl-*p*-bromoaniline, m.p. 162°, phenacyl-*p*-iodoaniline, m.p. 157°, phenacyl-*p*-toluidine, m.p. 134°, phenacyl-*p*-anisidine, m.p. 93°, phenacyl-α-naphthylamine, m.p. 124° and phenacylcyclohexylamine, m.p. 124° were obtained in good yields.

### *Reactions of dimethyl acetylenedicarboxylate*

(a) *With phenaeyl-*p*-bromoaniline.* Dimethyl acetylenedicarboxylate (2·2 g, 0·015 mole) was added to a soln of XVI (4·35 g, 0·015 mole) in a mixture (1 : 1) of MeOH and $CHCl_3$ (50 ml) over a period of 30 min and then heated under reflux for 2 hr. Removal of the solvent under vacuum gave a mixture of products (4·5 g) which was fractionally crystallized from MeOH to give 1·3 g (20%) of XVII, m.p. 137°. (Found: C, 55·54; H, 4·18; N, 3·52. $C_{20}H_{18}NO_5Br$ requires: C, 55·55; H, 4·16; N, 3·24%); IR spectrum (KBr): 3030, 2882 (CH), 1741 (ester C═O), 1700 (α,β-unsaturated ester C═O), 1594, 1565 and 1484 $cm^{-1}$ (C═C); UV spectrum (MeOH): 243 mμ (ε 19,900) and 288 (18,000).

From the mother liquor, 3·2 g (52%) of XVIII was isolated, m.p. 151°, on recrystallization from MeOH. (Found: C, 57·65; H, 3·99; N, 3·39. $C_{20}H_{16}NO_4Br$ requires: C, 57·99; H, 3·86; N, 3·38%); IR spectrum (KBr): 3058, 2915 (C—H), 1725, 1710 (ester C═O), 1601, 1548, 1508 and 1491 $cm^{-1}$ (C═C); UV spectrum (MeOH): 243 mμ (ε 32,400) and 286 (9400) shoulder.

(b) *With phenacyl-*p*-iodoaniline.* To a soln of XIX (2·3 g, 7 mmole) in a mixture (1 : 1) of MeOH and $CHCl_3$ (50 ml) was added 1 g (7 mmole) of dimethyl acetylenedicarboxylate, and the mixture heated under reflux for 2 hr. Removal of the solvent under vacuum gave a product (1·6 g) which was fractionally crystallized from MeOH to give 0·5 g (16%) of XX, m.p. 147°. (Found: C, 50·07; H, 3·70; N, 3·25. $C_{20}H_{18}NO_5I$ requires: C, 50·10; H, 3·75; N, 2·92%); IR spectrum (KBr): 3030, 2880 (C—H), 1743 (ester C═O), 1697 (α,β-unsaturated ester, C═O), 1595, 1570 and 1484 $cm^{-1}$ (C═C); UV spectrum (MeOH): 242 mμ (ε 25,000) and 289 (14,000).

The mother liquor, after removal of XX gave 1·1 g (36%) of XXI, m.p. 132°, after recrystallization from MeOH. (Found: C, 51·71; H, 3·36; N, 3·09. $C_{20}H_{16}NO_4I$ requires: C, 52·06; H, 3·47; N, 3·03%); IR spectrum (KBr): 3058, 2940 (C—H), 1725, 1705 (ester C═O), 1600, 1546 and 1491 $cm^{-1}$ (C═C); UV spectrum (MeOH): 246 mμ (ε 32,700) and 284 (9400) (shoulder).

(c) *With phenacyl-*p*-toluidine.* (i) Dimethyl acetylenedicarboxylate (0·9 g, 0·006 mole) was added to a soln of XXII (1·2 g, 0·005 mole), dissolved in a mixture (1 : 1) of MeOH and $CHCl_3$ (20 ml) and the mixture heated under reflux for 4 hr. Removal of the solvent under vacuum gave a solid (1·5 g), which on fractional crystallization from MeOH gave 0·85 g (48%) of XXIII, m.p. 120–121°. (Found: C, 68·71; H, 5·96; N, 3·67. $C_{21}H_{21}NO_5$ requires: C, 68·66; H, 5·72; N, 3·81%); IR spectrum (KBr): 3030, 2967 (C—H), 1748 (ester C═O), 1701 (α,β-unsaturated ester, C═O), 1580 (C═C), 1220 and 1149 $cm^{-1}$ (ester O—C—O); UV spectrum (MeOH): 246 mμ (ε 21,900) and 290 (22,700).

The mother liquor yielded 0·1 g (8%) of the phenacyl-*p*-toluidine, m.p. 134° (mixture m.p.). In addition, 0·55 g (32%) of XXIV, m.p. 107 was obtained. (Found: C, 72·28; H, 5·50; N, 3·98. $C_{21}H_{19}NO_4$ requires: C, 72·19; H, 5·48; N, 4·01%); IR spectrum (KBr): 3030, 2967 (C—H), 1721, 1697 (ester C═O), 1618, 1543, 1508 and 1473 $cm^{-1}$ (C═C); UV spectrum (MeOH): 233 mμ (ε 25,300) and 273 (8050).

In a separate run, 0·8 g of XXIII was treated with 0·5 ml conc HCl in MeOH, and heated under reflux for 2 hr. Removal of the solvent yielded 0·55 g (73%) XXIV, m.p. 107°. In addition, 0·05 g (6%) of phenacyl-*p*-toluidine, m.p. 134° (mixture m.p.), was isolated.

(ii) In another run, dimethyl acetylenedicarboxylate (1·6 g, 0·01 mole) and phenacyl-*p*-toluidine (2·7 g, 0·01 mole), dissolved in THF (25 ml) were refluxed for 2 hr. The reaction gave 2·1 g (50%) of XXIV, m.p. 107°, and 0·05 g (1%) of XXIII, m.p. 120–121°.

(d) *With phenacyl-p-anisidine.* Treatment of dimethyl acetylenedicarboxylate (2·84 g, 0·02 mole) with XXV (4·8 g, 0·02 mole) in a refluxing mixture (1:1) of MeOH and $CHCl_3$ (40 ml) for 4 hr, gave 4 g of a product which was chromatographed on alumina. Elution with pet. ether (b.p. 60–80°) gave 1·2 g (20%) of XXVII, m.p. 131·5°. (Found: C, 69·11; H, 5·27; N, 3·78. $C_{21}H_{19}NO_5$ requires: C, 69·03; H, 5·24; N, 3·83%); IR spectrum (KBr): 3050, 2941 (C—H), 1724, 1693 (ester C═O), 1608, 1546 and 1511 $cm^{-1}$ (C═C); UV spectrum (MeOH): 236 mμ (ε 24,000) and 287 (8500) (shoulder).

Further elution of the alumina column with MeOH gave 2·6 g (41%) of XXVI, m.p. 150°. (Found: C, 65·64; H, 5·69; N, 3·50. $C_{21}H_{21}NO_6$ requires: C, 65·77; H, 5·48; N, 3·65%); IR spectrum (KBr): 3040, 2911 (CH), 1735 (ester C═O), 1692 (α,β-unsaturated ester C═O), 1587, 1575 and 1492 $cm^{-1}$ (C═C); UV spectrum (MeOH): 244 mμ (ε 21,500) and 288 (22,200).

In addition, 0·8 g (16%) of XXV, m.p. (mixture m.p.), was recovered.

(c) *With phenacyl-α-naphthylamine.* Treatment of dimethyl acetylenedicarboxylate (2·84 g, 0·02 mole) with phenacyl-α-naphthylamine (5 g, 0·02 mole) in MeOH (25 ml) and $CHCl_3$ (20 ml) for 2 hr gave 5·6 g (73%) of XXIX, m.p. 148°, after recrystallization from $CHCl_3$ and MeOH (1:1). (Found: C, 71·37; H, 5·29; N, 3·41. $C_{24}H_{21}NO_5$ requires: C, 71·45; H, 5·25; N, 3·27%); IR spectrum (KBr): 3040, 2915 (C—H), 1733 (ester C═O), 1692 (α,β-unsaturated ester C═O), 1587, 1570 and 1490 $cm^{-1}$ (C═C); UV spectrum (MeOH): 239 mμ (ε 18,300), 274 (17,600) and 287 (15,900).

(f) *With phenacylcyclohexylamine.* Dimethyl acetylenedicarboxylate (1·7 g, 0·012 mole) was added to a soln of phenacylcyclohexylamine (2·5 g, 0·012 mole) dissolved in 25 ml MeOH and the mixture refluxed for 2 hr. Removal of the solvent gave 2·9 g (74%) of XXXI, m.p. 105°, after recrystallization from MeOH. (Found: C, 70·04; H, 6·49; N, 3·79. $C_{20}H_{23}NO_4$ requires: C, 70·36; H, 6·79; N, 4·10%); IR spectrum (KBr): 2941, 2857 (C—H), 1724, 1706 (ester C═O), 1548, 1508 and 1481 $cm^{-1}$ (C═C); UV spectrum (MeOH): 246 mμ (ε 14,100), and 298 (3000).

*Hydrolysis of dimethyl 1-(p-chlorophenyl)-4-phenylpyrrole-2,3-dicarboxylate.* A suspension of XV (7·75 g, 0·02 mole) in 100 ml MeOH was refluxed with 2·24 g (0·04 mole) KOH for 2 hr. Most of the solvent was removed under vacuum, and the residue was treated with water. Acidification with HCl and extraction with ether gave 5·2 g (72%) of XXXII, m.p. 169–171° (d). (Found: C, 64·18; H, 4·20; N, 4·02. $C_{19}H_{14}NO_4Cl$ requires: C, 64·13; H, 3·96; N, 3·93%); IR spectrum (KBr): 2965, 2857 (C—H), 1735 (ester C═O), 1684 (acid C═O), 1605, 1550, 1512 and 1490 $cm^{-1}$ (C═C); NMR spectrum ($CDCl_3$): 2·62 τ (phenyl, 9H), 3·08 τ (5-pyrrolyl, 1H) and 6·27 τ (3-carbomethoxy, 3H).

*Decarboxylation of methyl 1-(p-chlorophenyl)-2-carboxy-4-phenylpyrrole-3-carboxylate.* Compound XXXII (3·5 g, 0·01 mole) was heated in an oil bath (180–200°) for 30 min. It melted with evolution of $CO_2$. The mixture, on cooling, was extracted with ether and the extract was washed with $NaHCO_3$ aq to remove unchanged acid. Removal of the solvent under vacuum gave a product, which was recrystallized from MeOH to give 2·8 g (91%) of XXXIII, m.p. 130°. (Found: C, 69·47; H, 4·60; N, 4·25. $C_{18}H_{14}NO_2Cl$ requires: C, 69·34; H, 4·53; N, 4·49%). IR spectrum (KBr): 3030 (C—H), 1709 (ester, C═O), 1647, 1587, 1511 and 1488 $cm^{-1}$ (C═C); NMR spectrum ($CDCl_3$): 2·32 τ (2-pyrrolyl, 1H, doublet, $J$ = 2·5 c/s), 3·0 τ (5-pyrrolyl, 1H, doublet, $J$ = 2·5 c/s), 2·62 τ (phenyl, 9H) and 6·27 τ (3-carbomethoxy, 3H).

*Reaction of methyl propiolate with phenacyl-p-chloroaniline.* A mixture of methyl propiolate (1·6 g, 19 mmole) and phenacyl-*p*-chloraniline (1·8 g, 7 mmole) was heated in a sealed tube at 120° for 7 hr. On cooling, the mixture was triturated with MeOH and the product recrystallized from MeOH gave 1·3 g (65%) of XXXIII, m.p. 130° (mixture m.p.). In addition, 0·2 g (11%) of the unchanged phenacyl-*p*-chloroaniline was recovered.

*Hydrolysis of methyl 1-(p-chlorophenyl)-4-phenylpyrrole-3-carboxylate.* A solution of XXXIII (1·5 g, 0·005 mole) in ethyleneglycol (10 ml) was mixed with an ethyleneglycol soln of KOH (0·6 g in 10 ml). The mixture was heated under reflux for 4 hr (200°). Most of the solvent was removed under vacuum and the resulting mixture was acidified, treated with water and extracted with ether. Removal of the solvent from the ether extract gave 1·35 g (97%) of XXXIV, m.p. 185°, after recrystallization from MeOH. (Found: C, 68·12; H, 3·94; N, 4·38. $C_{17}H_{12}NO_2Cl$ requires: C, 68·57; H, 4·03; N, 4·70%); IR spectrum (KBr): 3030, 2897 (C—H), 1689 (acid C═O), 1592, 1517 and 1497 $cm^{-1}$ (C═C); NMR spectrum ($CDCl_3$): 2·20 τ (2-pyrrolyl, 1H, doublet, $J$ = 2·5 c/ps), 2·98 τ (5-pyrrolyl, 1H, doublet, $J$ = 2·5 c/ps) and 2·58 τ (phenyl, 9H).

*Decarboxylation of 1-(p-chlorophenyl)-4-phenylpyrrole-3-carboxylic acid.* A mixture of XXXIV (1 g, 0·034 mole) and 0·5 g Cu powder was heated with freshly distilled quinoline (15 ml) to 250° in an oil bath for 2 hr. The mixture on cooling, was poured over ice and extracted with ether. The extract was washed with dil HCl and then with $NaHCO_3$aq. After drying over $MgSO_4$, the solvent was removed to give 0·55 g (65%) of XXXV m.p. 140° (d); after recrystallization from a mixture (1:1) of MeOH and $CHCl_3$. (Found: C, 75·54; H, 4·80; N, 5·40. $C_{16}H_{12}NCl$ requires: C, 75·73; H, 4·73; N, 5·52%); IR spectrum (KBr): 3058 (C—H), 1603, 1533 and 1511 $cm^{-1}$ (C═C).

*Methyl 5-benzoyl-4-hydroxy-1-phenylpyrrole-2-carboxylate* (XXXVIII). A mixture of dimethyl phenacylanilinomaleate (3·2 g; 0·01 mole) and K (0·4 g; 0·01 g atom) was refluxed in dry toluene (30 ml) for 2 hr, then cooled, poured over crushed ice and extracted with ether to remove all toluene. The aqueous layer was then acidified with dil HCl and extracted with $CH_2Cl_2$. The extract was dried over $Na_2SO_4$ and the solvent removed to give 0·9 g (30%) of XXXVIII, m.p. 117°, after recrystallization from MeOH. (Found: C, 70·94; H, 4·84; N, 4·22. $C_{19}H_{15}NO_4$ requires: C, 71·02; H, 4·71; N, 4·36%); IR spectrum (KBr): 3497 (O—H), 1730 (ester C═O), 1618 (chelated, C═O); UV spectrum (MeOH): 260 mμ (ε 13,000), 305 (9800) and 331 (9000)

*Methyl 5-benzoyl-4-hydroxy-1-(o-tolyl)-pyrrole-2-carboxylate* (XXXIX). A soln of dimethyl phenacyl(*o*-toluidino)maleate (2·2 g, 6 mmole) in 30 ml dry toluene was refluxed with K (0·3 g; 0·0075 g atom) for 2 hr. The mixture, on cooling, was poured over crushed ice and extracted with ether to remove all toluene. Acidification of the aqueous extract with dil HCl, followed by extraction with $CH_2Cl_2$ gave 0·95 g (47%) of XXXIX, m.p. 89°, after recrystallization from MeOH. (Found: C, 71·17; H, 5·14; N, 4·49. $C_{20}H_{17}NO_4$ requires: C, 71·63; H, 5·11; N, 4·18%); IR spectrum (KBr): 3472 (O—H), 3067, 2941 (C—H), 1730 (ester C═O), 1618 (chelated, C═O), 1575, 1525 and 1490 $cm^{-1}$ (C═C); UV spectrum (MeOH): 259 mμ (ε 14,600), 299 (10,400) and 332 (9600).

*Methyl 5-benzoyl-1-(o-ethylphenyl)-4-hydroxypyrrole-2-carboxylate* (XXXX). A soln of dimethyl phenacyl(*o*-ethylanilino)maleate (1·7 g, 0·0045 mole) in dry toluene (20 ml) was added to a suspension of finely divided K (0·2 g, 0·005 g atom) in 10 ml toluene. The mixture was refluxed for 2 hr, cooled and poured over crushed ice. Extraction with ether removed all toluene and the aqueous layer was subsequently treated with dil HCl and then extracted with $CH_2Cl_2$. Removal of the solvent gave 0·9 g (60%) of XXXX, m.p. 146·5°, after recrystallization from MeOH. (Found: C, 72·14; H, 5·70; N, 4·02. $C_{21}H_{19}NO_4$ requires: C, 72·19; H, 5·48; N, 4·01%); IR spectrum (KBr): 3425 (O—H), 3185, 2959 (C—H), 1729 (ester C═O), 1608 (chelated, C═O), 1565, 1527, 1486 and 1458 $cm^{-1}$ (C═C); UV spectrum (MeOH): 259 mμ (ε 14,100), 302 (10,000) and 334 (9500).

*Methyl 5-benzoyl-1(p-chlorophenyl)4-hydroxypyrrole-2-carboxylate* (XXXXI). A mixture of dimethyl phenacyl(*p*-chloroanilino)maleate (2·16 g, 0·005 mole) and finely divided K (0·3 g, 0·0075 g atom) was refluxed in dry toluene (40 ml) for 2 hr. After cooling, the reaction mixture was poured over crushed ice and extracted with ether. The aqueous layer was acidified with dil HCl and extracted with $CH_2Cl_2$. Removal of the solvent gave a product, which on recrystallization from MeOH gave 500 mg (27%) of XXXXI, m.p. 180°. (Found: C, 63·72; H, 4·08; N, 4·01. $C_{19}H_{14}NO_4Cl$ requires: C, 64·13; H, 3·97; N, 3·94%); IR spectrum (KBr): 3497 (O—H), 1729 (ester C═O), 1595 (chelated, C═O), 1575 and 1527 $cm^{-1}$ (C═C); UV spectrum (MeOH): 258 mμ (ε 13,000), 300 (9100) and 336 (7800).

*Methyl 4-benzoyl-1(p-bromophenyl)4-hydroxypyrrole-2-carboxylate* (XXXXII). A soln of dimethyl phenacyl-α-naphthylaminominomaleate (2·2 g, 0·005 mole) and finely divided K (0·2 g, 0·005 g atom) was refluxed in dryl toluene (40 ml) for 2 hr. The solvent was removed under vacuum and the residue poured over The product on recrystallization from MeOH gave 0·95 g (35%) of XXXXII, m.p. 175–176°. (Found: C, 57·47; H, 3·78; N, 3·41. $C_{19}H_{14}NO_4Br$ requires: C, 57·00; H, 3·53; N, 3·50%); IR spectrum (KBr): 3484 (O—H), 1730 (ester C═O), 1595 (chelated, C═O), 1572 and 1531 $cm^{-1}$ (C═C); UV spectrum (MeOH): 258 mμ (ε 12,300), 304 (9400) and 338 (7500).

*Methyl 5-benzoyl-4-hydroxy-1-(α-naphthyl)pyrrole-2-carboxylate* (XXXXIII). A mixture of dimethyl phenacyl-α-naphthylaminomaleate (2·2 g, 0·005 mole) and finely divided K (0·2 g; 0·005 g atom) was refluxed in dryl toluene (40 ml) for 2 hr. The solvent was removed under vacuum and the residue poured over crushed ice. Extraction with ether removed all toluene and the aqueous layer was treated with dil HCl and then extracted with $CH_2Cl_2$. Removal of the solvent gave 1·0 g (45%) of XXXXIII, m.p. 138°, after recrystallization from MeOH. (Found: C, 74·66; H, 4·70; N, 3·70. $C_{23}H_{17}NO_4$ requires: C, 74·38; H, 4·61; N, 3·77%); IR spectrum (KBr): 3947 (C—H), 1730 (ester, C═O) 1600 (chelated, C═O), 1515 and 1458 $cm^{-1}$ (C═C); UV spectrum (MeOH): 224 mμ (ε 71,200), 262 (15,800) 287 (14,550), 296 (14,580) and 332 (9800).

*Acknowledgement*—The authors thank Professor C. N. R. Rao for his help in getting the NMR spectra of several compounds reported in this paper. We thank Dr. M. K. Saxena and Mr. Anil Kumar for partial experimental assistance and Mr. A. H. Siddiqui for his help in microanalysis. One of us (SKK) is thankful to the authorities of the Indian Institute of Technology, Kanpur for the award of a Research Assistantship.

## REFERENCES

[1] For part I in this series, see, S. K. Khetan, J. G. Hiriyakkanavar and M. V. George, *Tetrahedron* **24**, 1567 (1968).

[2] For a recent review, see, E. Winterfeldt, *Angew. Chem.* (Internat. Ed.) **5**, 423 (1967).

[3] For some of the amine additions, see, [a] R. Huisgen, K. Herbig, A. Siegl and H. Huber, *Chem. Ber.* **99**, 2526 (1966);
[b] K. Herbig, R. Huisgen and H. Huber, *Ibid.*, **99**, 2546 (1966);
[c] J. E. Dolfini, *J. Org. Chem.* **30**, 1298 (1965);
[d] W. E. Truce and D. G. Brady, *Ibid.*, **31**, 3543 (1966);
[e] E. Winterfeldt and H. Preuss, *Chem. Ber.* **99**, 450 (1966);
[f] T. Y. Chen, H. Kato and M. Ohta, *Bull. Chem. Soc. Japan* **39**, 1618 (1966); *Chem. Abstr.* **65**, 13635 (1966);
[g] R. Huisgen, B. Giese and H. Huber, *Tetrahedron Letters* 1883 (1967).

[4] For some of these additions, see, [a] J. B. Hendrickson, R. Rees and J. F. Templeton, *J. Am. Chem. Soc.* **86**, 107 (1964);
[b] D. S. James and P. E. Fanta, *J. Org. Chem.* **27**, 3346 (1962);
[c] E. Winterfeldt, *Chem. Ber.* **97**, 1952 (1964);
[d] E. Winterfeldt and H. J. Dillinger, *Ibid.* **99**, 1558 (1966);
[e] U. K. Pandit and H. O. Huisman, *Rec. Trav. Chim.* **85**, 311 (1966); *Chem. Abstr.* **65**, 10555 (1966).

[5] Y. Shvo, E. C. Taylor, K. Mislow and M. Raban, *J. Am. Chem. Soc.* **89**, 4910 (1967).

[6] A. H. Corwin, *Heterocyclic Compounds* (Edited by R. C. Elderfield) Vol. I; p. 304. Wiley, New York, N.Y. (1950).

[7] J. W. Emsley, J. Feeney and L. H. Sutcliff, *High Resolution Nuclear Magnetic Resonance Spectroscopy* Vol. II; p. 789. Pergamon Press, Oxford (1966).

[8] A. Bichler, *Ber. Dtsch Chem. Ges.* **25**, 2860 (1892).

[9] F. Kunckell, *Ibid.* **30**, 574 (1897).