The Synthesis and Chemistry of Azolenines.† Part 4.[1] Preparation and Rearrangement of some 3,5-Diaryl-2*H*-pyrrole-2,2-dicarboxylic Esters

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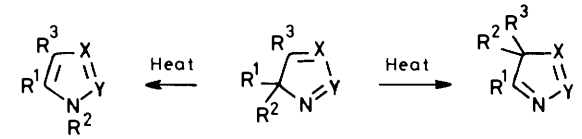
Oxidation of diethyl 3,5-diaryl-3,4-dihydro-2*H*-pyrrole-2,2-dicarboxylates (**3**) with chloranil in refluxing xylene gives not the 3,5-diaryl-2*H*-pyrrole-2,2-dicarboxylates (**4**) as reported by an earlier group, but instead the rearranged, isomeric, 1*H*-pyrrole-1,2-dicarboxylates (**5**). 2*H*-Pyrroles (**4**) may be obtained from the dihydropyrroles (**3**) using DDQ in benzene at room temperature; they rearrange to the isomers (**5**) in boiling xylene *via* an acyl [1,5]-sigmatropic shift from carbon to nitrogen, a novel process in the 2*H*-pyrrole series. Thermal analyses indicate that the rearrangement is concerted, with negligible charge separation in the transition state. Other novel 3,5-diaryl-1*H*-pyrrole-2-carboxylic acid derivatives are described.

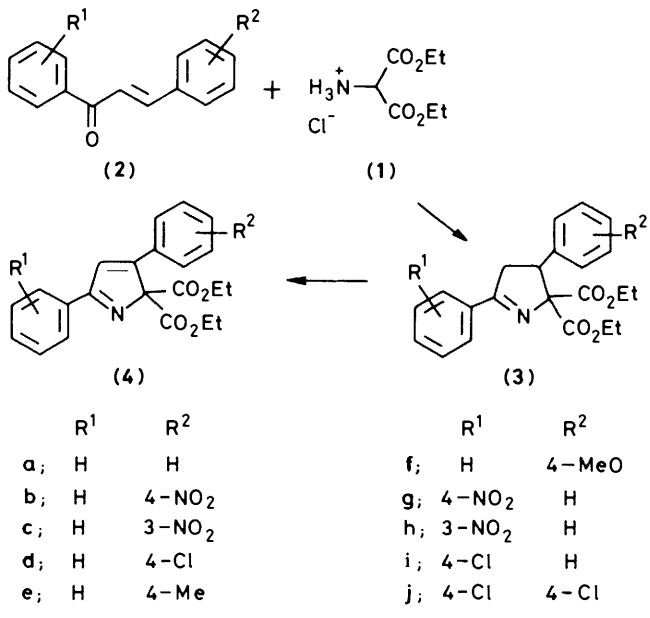
Thermal [1,5]-sigmatropic rearrangements involving migration of a substituent from the tetrahedral carbon atom to a second ring atom (carbon or nitrogen) (Scheme 1) is a characteristic reaction of azolenines.†[2] While reactions of this type have been investigated in depth for a wide range of substituents in the 3*H*-pyrazole series (van Alphen-Hüttel rearrangements[2b]), detailed studies with 2*H*-pyrroles have been restricted to migrations of alkyl or aryl groups.‡[3] Further, with only one exception,[4] migrations in the latter series have been exclusively to carbon, whereas for 3*H*-pyrazoles competitive shifts to carbon and nitrogen have been observed, especially for migrating acyl groups. In the only three papers we have found which report rearrangements of 2-acyl-2*H*-pyrroles,[5–7] the C-3 position, to which the acyl (ester) group migrated, was unsubstituted. It was thus of interest to study rearrangements of structures in which C-3 already bears a substituent.

We selected for the study the diesters (**4**) (Scheme 2), since two synthetic routes to compounds of this type have already been described;[8,9] in such structures there was the possibility that an ester group may migrate to C-3, unsubstituted C-4, or N.

Robert and co-workers reported that pyrolysis of a mixture of diethyl aminomalonate hydrochloride (**1**) and 1,3-diphenylpropenone (chalcone) (**2a**) without solvent gave the dihydropyrrole (**3a**), which could be oxidised to the 2*H*-pyrrole (**4a**) with 2,3,5,6-tetrachloro-1,4-benzoquinone (chloranil) in boiling xylene.[9] Since the method was later extended to give a series of dihydropyrroles (**3**),[10] it appeared to offer a promising general route to 2*H*-pyrroles of type (**4**). We thus adopted this approach.



Scheme 1. X, Y = CR^4 or N



	R^1	R^2		R^1	R^2
a;	H	H	f;	H	4-MeO
b;	H	4-NO_2	g;	4-NO_2	H
c;	H	3-NO_2	h;	3-NO_2	H
d;	H	4-Cl	i;	4-Cl	H
e;	H	4-Me	j;	4-Cl	4-Cl

Scheme 2.

Results and Discussion

The dihydropyrrole (**3a**) was prepared as described by Robert and co-workers (54%); its melting point and spectroscopic properties were identical with reported data.[9,11] Oxidation with chloranil in boiling xylene for 10 h gave a product (60%) the analysis for which was consistent with the molecular formula $C_{22}H_{21}NO_4$ and whose melting point (102—103 °C) was identical with that reported[9] for the 2*H*-pyrrole (**4a**). The ^1H n.m.r. spectrum (60 MHz) showed signals for the ethoxy groups at δ 1.15 (6 H, t), and 4.22 (4 H, q, somewhat br) also in excellent agreement with published data, although there was in addition a sharp singlet at δ 6.31 not reported previously. However, at 90 MHz the ethyl signals resolved into two triplets (δ 1.14 and 1.16) and two quartets (δ 4.21 and 4.25) as indeed was reported in a subsequent paper by the French group.[11] These data are inconsistent with the proposed structure (**4a**), for while the protons in each methylene group are diastereotopic and might be expected to give rise to the observed two quartets, the protons on the two methyl groups are all magnetically equivalent and should produce only one triplet. The ^{13}C n.m.r. spectrum revealed pairs of signals each for methyl, methylene, and carbonyl carbon atoms (δ 13.49 and 13.87, 60.94 and 64.57,

† The term azolenines refers to non-aromatic isomers of azoles.
‡ [3,3] Sigmatropic rearrangements involving substituted allyl groups have also been studied.[3c]

Table 1. Physical and analytical data for 2*H*-pyrroles (**4**).

Compound	R^1	R^2	Method	Reaction time (h)	Yield (%)	M.p. (°C)[a]	$M^{+\cdot}$	Formula	Found (%) (Required) C	H	N
(**4a**)	H	H	A	5	63	97	363	$C_{22}H_{21}NO_4$	72.55 (72.7)	5.7 (5.8)	3.7 (3.85)
(**4b**)	H	4-NO_2	A	5	63	122[b]	408	$C_{22}H_{20}N_2O_6$	64.65 (64.7)	5.0 (4.95)	6.8 (6.85)
(**4c**)	H	3-NO_2	A	5	80	130	408	$C_{22}H_{20}N_2O_6$	64.6 (64.7)	4.9 (4.95)	6.9 (6.85)
(**4d**)	H	4-Cl	A	5	78	133	397	$C_{22}H_{20}ClNO_4$	66.55 (66.4)	5.05 (5.1)	3.4 (3.5)
(**4e**)	H	4-Me	A	24	72	112—113	377	$C_{23}H_{23}NO_4$	73.2 (73.2)	6.1 (6.1)	3.6 (3.7)
(**4f**)	H	4-MeO	A	8	58	104	393	$C_{23}H_{23}NO_5$	70.2 (70.15)	5.9 (5.6)	3.55 (3.6)
(**4g**)	4-NO_2	H	B	4	60	119—121[b]	408	$C_{22}H_{20}N_2O_6$	64.95 (64.7)	5.0 (4.95)	6.7 (6.85)
(**4h**)	3-NO_2	H	A	5	82	144	408	$C_{22}H_{20}N_2O_6$	64.9 (64.7)	4.9 (4.95)	6.75 (6.85)
(**4i**)	4-Cl	H	B	4	65	90	397	$C_{22}H_{20}ClNO_4$	66.55 (66.4)	5.2 (5.1)	3.6 (3.5)
(**4j**)	4-Cl	4-Cl	A	48	75	123	432	$C_{22}H_{19}Cl_2NO_4$	60.85 (61.1)	4.45 (4.4)	3.05 (3.25)

[a] From aqueous methanol unless otherwise indicated. [b] From methanol.

and 151.31 and 161.38, respectively), which together with i.r. signals at 1 770, 1 735, and 1 695 cm^{-1} showed the compound to be a carbamate with the rearranged structure (**5a**)*. Interestingly, only scattered reports of pyrrole-1,2-dicarboxylic esters have appeared,[12] and none seem to be known having aryl substituents.

Since 2*H*-pyrroles are known to rearrange thermally, it appeared that compound (**4a**) was being formed, and subsequently converted into (**5a**) under the vigorous conditions employed. We thus attempted the oxidation under milder conditions. Chloranil in refluxing toluene (4—24 h) also gave the rearranged compound (**5a**), while unchanged starting material was recovered when benzene was used as solvent, even after 24 h under reflux. Subsequently, we found that when stirred in benzene at room temperature with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ), the dihydropyrrole (**3a**) was converted into the desired 2*H*-pyrrole (**4a**) in good yield. Compound (**4a**) had a melting point of 97 °C, which could not be raised on further recrystallisation; in the ^1H n.m.r. spectrum there was only one triplet and one quartet, respectively at δ 1.19 and 4.23 (showing that the magnetic non-equivalence of the methylene protons is not resolved at 90 MHz), and the ring methine gave a singlet at δ 7.38. In the ^{13}C n.m.r. spectrum ($CDCl_3$) the ester methyl, methylene, and carbonyl signals were at respectively δ 13.81, 62.41, and 176.71, while the pyrrole ring carbon atom signals for C-2 to C-5 respectively were at δ 92.26, 163.01, 125.68, and 165.72, confirming the structure to be a 2*H*-pyrrole-2,2-dicarboxylic ester. When refluxed in xylene, compound (**4a**) was converted in high yield into the isomer (**5a**), showing that the suspected rearrangement was taking place under these conditions. We thus report the first authenticated example of an acyl migration from C to N in the 2*H*-pyrrole series.

To establish both the generality of this synthetic approach to compounds (**4**), and the effect of benzene ring substituents on their rearrangement, we converted a series of chalcones (**2**) into the corresponding dihydropyrroles (**3**), and attempted to oxidise them to 2*H*-pyrroles.

Two different modifications of the method of Robert and co-workers[10] gave the dihydropyrroles (**3**) in improved yields. In the first the aminomalonate salt (**1**) and the chalcone (**2**) were heated together with anhydrous potassium carbonate under nitrogen; in the second, the reactants (**1**) and (**2**) were heated under reflux in toluene in the presence of toluene-*p*-sulphonic acid. Both methods gave 60—85% yields of the dihydropyrroles (**3**).

In most cases the oxidation was accomplished in good yield using DDQ in benzene as above, stirring being continued for 5—48 h (method A). For some examples, however, this led to complex mixtures; in these cases chloranil in refluxing toluene (method B) was found to be suitable. Conditions employed, yields, physical, and analytical data for 2*H*-pyrroles (**4**) are shown in Table 1, while i.r. and ^1H n.m.r. spectroscopic data are in Table 2. Two peaks are observed in the carbonyl region of the i.r. (respectively near 1 750 and 1 725 cm^{-1}), while in the ^1H n.m.r. spectra the methylene quartets show no evidence of splitting. The 2*H*-pyrrole methine proton signal (δ 7.28—7.54) is seen to be particularly sensitive to the 3-aryl ring substituent; in other reported examples of 3,5-diaryl-2*H*-pyrroles it is in the range δ 7.0—7.3.[13]

In order to compare physical and spectroscopic properties of the 2*H*-pyrroles with their rearranged isomers, a series of diesters (**5**) was prepared either from the dihydropyrroles (**3**) with chloranil in xylene (method C), or by thermal rearrangement of compounds (**4**) by refluxing in benzene (method D). The reactions were found to be general, and proceeded in high yields (60—85%); no evidence was found of products having an ester group in the 3- or 4-position. Physical and analytical data for the products (**5**) are in Table 3, and spectroscopic data in Table 4. I.r. carbonyl absorptions are found near 1 770 (carbamate) and 1 695 cm^{-1} (pyrrole ester), a third peak being observed in some cases near 1 730 cm^{-1}; in most ^1H n.m.r. spectra, two sets of methyl and methylene signals are observed.

The rearrangements of a number of 2*H*-pyrroles [(**4a**), (**4b**),

* Robert and co-workers have now reported the compound to be (**5a**) and not (**4a**), from an *X*-ray structure determination (A. Laarif, F. Théobald, M. Birouk, and J.-F. Robert, *Acta Crystallogr., Sect. C* 1984, **40**, 1278).

Table 2. I.r. and ^{1}H n.m.r. spectroscopic data for 2*H*-pyrroles (**4**)

Compound	R^1	R^2	$\nu_{max.}$ (Nujol)/cm^{-1}	δ_H ($CDCl_3$)[a] Me[b]	CH_2[c]	4-H[d]	5-ArH	3-ArH
(**4a**)	H	H	1 755, 1 730, 1 610, 1 230, 1 055, 780, 760	1.186	4.228	7.377	7.4—7.55(3 H, m) 8.01—8.12(2 H, m)	7.25—7.41(3 H, m) 7.61—7.74(2 H, m)
(**4b**)	H	4-NO_2	1 765, 1 725, 1 595, 1 515, 1 350, 1 225, 1 050, 855, 780, 755	1.230	4.267	7.533	7.45—7.55(3 H, m) 8.02—8.15(2 H, m)	7.849(2 H, m) 8.248(2 H, m)
(**4c**)	H	3-NO_2	1 755, 1 725, 1 605, 1 530, 1 350, 1 230, 1 060, 900, 740	1.245	4.282	7.543	7.4—7.65(4 H, m)[e] 8.04—8.15(2 H, m)	7.95—8.27(2 H, m) 8.568(1 H, t)
(**4d**)	H	4-Cl	1 750, 1 735, 1 610, 1 240, 1 050, 1 015, 840	1.210	4.243	7.367	7.4—7.55(3 H, m) 8.01—8.12(2 H, m)	7.372(2 H, m) 7.622(2 H, m)
(**4e**)	H	4-Me	1 750, 1 720, 1 610, 1 240, 1 060, 900, 835, 780	1.201	4.231	7.343	7.4—7.6(3 H, m) 8.02—8.13(2 H, m)	2.368(3 H, s) 7.200(2 H, m), 7.574(2 H, m)
(**4f**)	H	4-MeO	1 755, 1 725, 1 600, 1 260, 1 225, 1 060, 835, 785, 705	1.205	4.236	7.279	7.4—7.6(3 H, m) 8.01—8.12(2 H, m)	3.832(3 H, s) 6.919(2 H, m), 7.649(2 H, m)
(**4g**)	4-NO_2	H	1 745, 1 715, 1 610, 1 530, 1 345, 1 240, 1 080, 1 055, 860, 850	1.210	4.262	7.387	8.256(2 H, m) 8.331(2 H, m)	7.35—7.48(3 H, m) 7.55—7.77(2 H, m)
(**4h**)	3-NO_2	H	1 755, 1 730, 1 605, 1 530, 1 350, 1 225, 1 100, 1 055, 855, 780, 750	1.210	4.262	7.445	8.25—8.50(2 H, m) 8.866(1 H, t)	7.35—7.75(6 H, m)[e]
(**4i**)	4-Cl	H	1 745, 1 730, 1 605, 1 260, 1 230, 1 100, 1 055, 1 015, 845, 770	1.186	4.233	7.377	7.430(2 H, m) 8.003(2 H, m)	7.25—7.50(3 H, m) 7.60—7.75(2 H, m)
(**4j**)	4-Cl	4-Cl	1 750, 1 720, 1 600, 1 245, 1 100, 1 060, 840	1.210	4.243	7.392	7.442(2 H, m) 7.991(2 H, m)	7.352(2 H, m) 7.608(2 H, m)

[a] Digital resolution ±0.005 p.p.m. [b] Triplet, *J* 7.0 Hz. [c] Quartet, *J* 7.0 Hz. [d] Signal overlaps aryl region, but is clearly identifiable. [e] Includes 1 H from other aryl ring.

Table 3. Physical and analytical data for 1*H*-pyrrole diesters (**5**)

Compound	R^1	R^2	Method	Reaction time (h)	Yield (%)	Solvent	M.p. (°C)	$M^{+\cdot}$	Formula	Found (%) (Required) C	H	N
(**5a**)	H	H	C	10	74	95% EtOH	102—103	363	$C_{22}H_{21}NO_4$	72.9 (72.7)	5.8 (5.8)	3.8 (3.85)[a]
(**5b**)	H	4-NO_2	C	2	58	$CHCl_3$–MeOH	122	408	$C_{22}H_{20}N_2O_6$	65.0 (64.7)	4.9 (4.95)	7.0 (6.85)
(**5c**)	H	3-NO_2	C	2	68	$CHCl_3$–MeOH	83—84	408	$C_{22}H_{20}N_2O_6$	64.55 (64.7)	4.8 (4.95)	6.7 (6.85)
(**5d**)	H	4-Cl	C	2	70	95% EtOH	87—88	397	$C_{22}H_{20}ClNO_4$	66.4 (66.4)	4.9 (5.1)	3.5 (3.5)
(**5e**)	H	4-Me	C	2	65	MeOH	94	377	$C_{23}H_{23}NO_4$	73.2 (73.2)	6.1 (6.15)	3.65 (3.7)
(**5f**)	H	4-MeO	C	2	62	MeOH	75	393	$C_{23}H_{23}NO_5$	70.5 (70.2)	5.6 (5.85)	3.4 (3.55)
(**5g**)	4-NO_2	H	C	2	82	$CHCl_3$–MeOH	105	408	$C_{22}H_{20}N_2O_6$	65.0 (64.7)	4.95 (4.95)	6.45 (6.85)
(**5h**)	3-NO_2	H	D	36	73	$CHCl_3$–MeOH	71	408	$C_{22}H_{20}N_2O_6$	65.0 (64.7)	4.8 (4.95)	6.8 (6.85)
(**5i**)	4-Cl	H	C	4	85	95% EtOH	103	397	$C_{22}H_{20}ClNO_4$	66.25 (66.4)	4.9 (5.1)	3.75 (3.5)
(**5j**)	4-Cl	4-Cl	C	10	80	95% EtOH	139—140	432	$C_{22}H_{19}Cl_2NO_4$	60.75 (61.1)	4.5 (4.4)	3.05 (3.25)

[a] Calc. for $C_{22}H_{21}NO_4$.

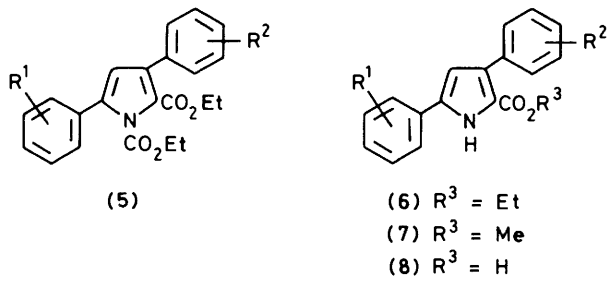
(**4e**), (**4f**), (**4g**), (**4i**), and (**4j**)] were studied by differential scanning calorimetry. At a heating rate of 10 °C min^{-1}, traces for each compound showed an endotherm corresponding to the melting temperature, followed by a strong exotherm at 140 ± 2 °C. This latter corresponds to the rearrangement giving rise to an (aromatic) 1*H*-pyrrole; that it occurs at essentially the same temperature regardless of the aryl ring substituents suggests that the rearrangement is a concerted [1,5] sigmatropic shift with negligible charge separation in the transition state (Scheme 3). Insensitivity of rearrangement rates to substituents on (non-migrating) aryl groups has been observed in the 3*H*-pyrazole series.[14]

During the course of this work we observed that oxidation of the dihydropyrroles (**3**) using either DDQ (method E) or active manganese dioxide (method F) in boiling benzene, resulted in their conversion into the monoesters (**6**). These latter could also be prepared from the diesters (**5**) by refluxing in DMSO (method G) or by stirring with aqueous ethanolic NaOH at room temperature (method H). Further, we found that the diesters (**5**) could be selectively converted either into the

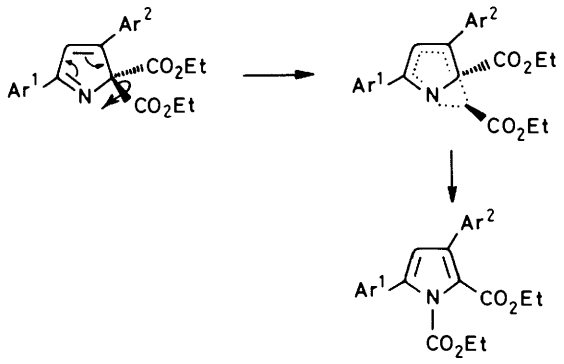
Table 4. I.r. and ^{1}H n.m.r. spectroscopic data for 1*H*-pyrroles diesters (**5**)

Compound	R^1	R^2	$\nu_{max.}$ (Nujol)/cm^{-1}	δ_H ($CDCl_3$)[a] Me	CH_2	4-H	5-ArH	3-ArH
(**5a**)	H	H	1 770, 1 735, 1 695, 1 290, 1 240, 1 230, 1 060, 1 025, 780, 770	1.142 1.162	4.206 4.252	6.313	7.2–7.6(10 H, m)	
(**5b**)	H	4-NO_2	1 770, 1 705, 1 520, 1 350, 1 245, 1 115, 760	1.176 1.201	4.242 4.291	6.352	7.43(5 H, s)	7.694(2 H, m) 8.237(2 H, m)
(**5c**)	H	3-NO_2	1 770, 1 695, 1 530, 1 355, 1 280, 1 240, 1 020, 765, 695	1.186[b]	4.233 4.309	6.357	7.42(5 H, s)	7.524(1 H, t) 7.860(1 H, d), 8.170(1 H, d), 8.432(1 H, s)
(**5d**)	H	4-Cl	1 770, 1 690, 1 330, 1 245, 1 150, 1 020, 775	1.162 1.196	4.223 4.267	6.288	7.25–7.6(9 H, m)	
(**5e**)	H	4-Me	1 770, 1 690, 1 330, 1 280, 1 245, 1 150, 1 110, 1 020, 830, 765	1.147 1.201	4.223 4.247	6.303	7.39(5 H, s)	2.363(3 H, s) 7.174(2 H, m), 7.429(2 H, m)
(**5f**)	H	4-MeO	1 765, 1 690, 1 330, 1 295, 1 250, 1 145, 1 020, 855, 830, 770	1.147 1.205	4.223 4.247	6.288	7.35(5 H, s)	3.808(3 H,s) 6.908(2 H, m), 7.475(2 H, m)
(**5g**)	4-NO_2	H	1 770, 1 720, 1 670, 1 510, 1 345, 1 240, 1 145, 1 100, 1 025, 860, 755	1.201 1.230	4.247 4.316	6.449	7.618(2 H, m) 8.240(2 H, m)	7.25—7.55(5H,m)
(**5h**)	3-NO_2	H	1 760, 1 730, 1 705, 1 515, 1 355, 1 310, 1 250, 1 205, 1 100, 1 020, 745	1.220[b,c]	4.236 4.296	6.493	7.3—7.9(7 H, m), 8.15—8.35(2 H, m)	
(**5i**)	4-Cl	H	1 780, 1 695, 1 340, 1 285, 1 255, 1 100, 1 030, 840, 715	1.181 1.205	4.221 4.282	6.313	7.25—7.6(9 H, m)	
(**5j**)	4-Cl	4-Cl	1 770, 1 730, 1 690, 1 330, 1 280, 1 245, 1 150, 1 020, 840, 765	1.196[b]	4.221 4.280	6.269	7.25—7.5(8 H, m)	

[a] Digital resolution, ±0.005 p.p.m. [b] Two triplets not resolved. [c] Solvent $CDCl_3$–$(CD_3)_2SO$.

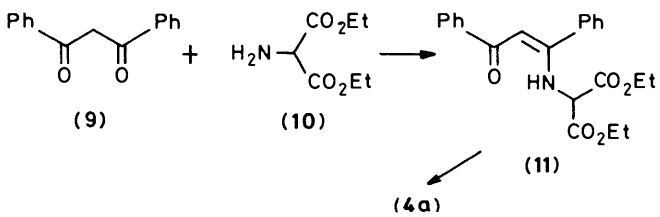


Scheme 3.



monomethyl esters (**7**) (methanolic KOH at room temperature; method I), or into the carboxylic acids (**8**) (aqueous ethanolic NaOH, reflux; method J). Since few 3,5-diarylpyrrole-2-carboxylic acid derivatives have been reported previously,[15] we have prepared some examples of compounds (**6**)—(**8a**) to record their physical (Table 5), and spectroscopic (Table 6) properties. Compound (**8a**) appears to be the first reported example of a 3,5-diaryl-1*H*-pyrrole-2-carboxylic acid. This, and other examples prepared in these laboratories, developed intense violet colours in solution.

Finally, attempts were made to prepare 2*H*-pyrroles (**4**) by methods which did not require an oxidation step. Using a procedure analogous to that reported by Umio and co-workers,[8] 1,3-diphenylpropane-1,3-dione (**9**) (Scheme 4) and



Scheme 4.

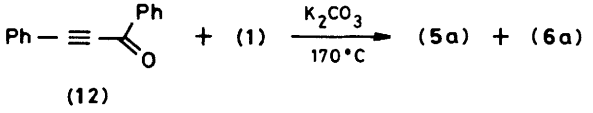
diethyl aminomalonate (**10**) were converted into the enamine (**11**) (68%) which was cyclised to the pyrrole (**4a**) (46%) using ethyl polyphosphate in chloroform. Compounds (**9**) and (**10**) when heated together, dry at 170 °C, or in refluxing dimethylformamide, gave the ester (**6a**) as the sole isolated product. In contrast, a mixture of the salt (**1**), the diketone (**9**) and potassium carbonate when heated at 170 °C gave a 1:1 mixture of the esters (**5a**) and (**6a**). The alkynone (**12**), likewise when heated dry with the salt (**1**) and potassium carbonate (Scheme 5), gave a mixture of the same two esters (**5a**) and (**6a**), this time in a ratio of 1:7.5.

In view of the ready availability of substituted chalcones (**2**), the route of Scheme 2 appears to be the most general and convenient for preparing the 2*H*-pyrrole diesters (**4**).

Table 5. Physical and analytical data for 1*H*-pyrrole-2-carboxylic acid derivatives (**6**), (**7**), and (**8a**)

Compound	R^1	R^2	Method	Reaction time (h)	Yield (%)	Solvent	M.p. (°C)	$M^{+\cdot}$	Formula	Found (%) (Required) C	H	N
(**6a**)	H	H	F	15	72	95% EtOH	142[a]	291	$C_{19}H_{17}NO_2$			
(**6b**)	H	4-NO_2	F	15	56	$CHCl_3$–MeOH	208	336	$C_{19}H_{16}N_2O_4$	68.1 (67.85)	4.9 (4.8)	8.2 (8.3)
(**6d**)	H	4-Cl	E	6	62	95% EtOH	185[b]	325	$C_{19}H_{16}ClNO_2$	69.9 (70.05)	4.8 (4.95)	4.15 (4.3)
(**6e**)	H	4-Me	F	15	75	MeOH	170	305	$C_{20}H_{19}NO_2$	79.1 (78.7)	5.9 (6.25)	4.4 (4.6)
(**6f**)	H	4-MeO	G	2	76	MeOH	135	321	$C_{20}H_{19}NO_3$	74.8 (74.75)	5.8 (5.95)	4.1 (4.35)
(**6g**)	4-NO_2	H	E	24	68	$CHCl_3$–MeOH	213	336	$C_{19}H_{16}N_2O_4$	67.75 (67.85)	4.65 (4.8)	7.95 (8.3)
(**6h**)	3-NO_2	H	F	15	75	MeOH	183	336	$C_{19}H_{16}N_2O_4$	68·0 (67.85)	5.0 (4.8)	8.15 (8.3)
(**6i**)	4-Cl	H	H	24	78	95% EtOH	180	325	$C_{19}H_{16}ClNO_2$	69.95 (70.05)	5.0 (4.95)	4.45 (4.3)
(**6j**)	4-Cl	4-Cl	G	2	70	95% EtOH	192	359	$C_{19}H_{15}Cl_2NO_2$	63.1 (63.35)	4.2 (4.2)	3.7 (3.9)
(**7a**)	H	H	I	4	63	95% EtOH	179[c]	277	$C_{18}H_{15}NO_2$			
(**7e**)	H	4-Me	I	4	68	95% EtOH	173	291	$C_{19}H_{17}NO_2$	78.35 (78.3)	6.05 (5.9)	4.6 (4.8)
(**7i**)	4-Cl	H	I	4	75	95% EtOH	170	311	$C_{18}H_{14}ClNO_2$	69.7 (69.35)	4.9 (4.5)	4.5 (4.5)
(**7j**)	4-Cl	4-Cl	I	4	72	95% EtOH	186	345	$C_{18}H_{13}Cl_2NO_2$	62.25 (62.4)	3.9 (3.8)	3.85 (4.05)
(**8a**)	H	H	J	16	64	95% EtOH	180	263	$C_{17}H_{13}NO_2$	77.2 (77.5)	4.7 (5.0)	5.0 (5.3)

[a] Lit.,[15a] 140—144 °C. [b] With sublimation. [c] Lit.,[15d] 182 °C.



Scheme 5.

Experimental

I.r. spectra were recorded on a Perkin Elmer 577 spectrophotometer and calibrated against polystyrene; n.m.r. spectra (^1H, 89.56 MHz; ^{13}C, 22.53 MHz) were recorded on a JEOL FX-90Q instrument with $SiMe_4$ as internal reference, and mass spectra on a Hitachi RMS-4 spectrometer. Thermal analyses were carried out on a Rigaku 'Thermoflex' instrument, operating in the TG/DSC mode; 5 mg samples were used, the temperature being increased from 20 °C at a rate of 10 °C min^{-1}. Substituted chalcones were prepared by standard procedures.[16]

Preparation of the Dihydropyrroles (**3**).—*With potassium carbonate.* A mixture of the ester salt (**1**) (10 mmol), the appropriate chalcone (**2**) (10 mmol), and anhydrous K_2CO_3 (50 mmol) was heated, with vigorous stirring under N_2, in a flask fitted with a reflux condenser, at 170—190 °C for 30 min. The cooled product was shaken with a mixture of water and chloroform, and the separated chloroform layer was dried ($MgSO_4$) and evaporated, and the residue recrystallised (95% EtOH).

With toluene-p-*sulphonic acid in toluene.* The ester salt (**1**) (5 mmol) and the appropriate chalcone (**2**) (5 mmol) were heated under reflux in toluene (100 ml) for 16 h in the presence of a catalytic quantity of toluene-*p*-sulphonic acid. The solvent was removed under reduced pressure and the residue recrystallised as above.

Data for novel dihydropyrroles: (**3i**) (56%), m.p. 126 °C (Found: C, 66.4; H, 5.7; N, 3.3. $C_{22}H_{22}ClNO_4$ requires C, 66.1; H, 5.55; N, 3.5%); $\nu_{max.}$ (Nujol) 1 745, 1 730, 1 625, 1 270, 1 215, 835, and 790 cm^{-1}; δ_H ($CDCl_3$) 0.830 (3 H, t), 1.293 (3 H, t), 3.1—4.0 (4 H, m), 4.1—4.6 (3 H, m), 7.226 (5 H, s), 7.403 (2 H, m), and 7.925 (2 H, m); and (**3j**) (80%), m.p. 158—9 °C (Found: C, 61.2; H, 4.9; N, 3.2. $C_{22}H_{21}Cl_2NO_4$ requires C, 60.85; H, 5.1; N, 3.2%); $\nu_{max.}$ (Nujol) 1 745, 1 725, 1 620, 1 280, 1 215, 1 095, 1 015, and 825 cm^{-1}; δ_H ($CDCl_3$) 0.898 (3 H, t), 1.303 (3 H, t), 3.1—4.0 (4 H, m), 4.1—4.6 (3 H, m), 7.201 (4 H, s), 7.405 (2 H, m), and 7.922 (2 H, m). For known dihydropyrroles:[10] (**3a**) (65%), m.p. 93 °C (lit., 94 °C); (**3b**) (68%), m.p. 153 °C (lit., 153—4 °C); (**3c**) (56%), m.p. 116 °C (lit., 116—7 °C); (**3d**) (78%), m.p. 120 °C (lit., 119—20 °C); (**3e**) (75%), m.p. 81 °C (lit., 82 °C); (**3f**) (72%), m.p. 106—7 °C (lit., 108 °C); (**3g**) (70%), m.p. 155 °C (lit., 157 °C); and (**3h**) (68%), m.p. 130 °C (lit., 130 °C).

Oxidation to 2H-*Pyrroles* (**4**).—*Method A.* The appropriate dihydropyrrole (**3**) (10 mmol), and DDQ (10 mmol) were stirred together in benzene (50 ml) at 25 °C for periods in the range 5—48 h (Table 1). The mixture was filtered, the residue washed with benzene (2 × 10 ml), and the combined filtrates evaporated under reduced pressure. The residue was recrystallised.

Method B. The dihydropyrroles (**3g**) or (**3i**) (10 mmol) and chloranil (15 mmol) were refluxed together in toluene (100 ml) for 4 h. The products were isolated as for method A.

Preparation of 1H-*Pyrrole*-1,2-*dicarboxylic Esters* (**5**).—*Method C.* This was as described for the diesters (**4**) (method B) except that the reaction was conducted in refluxing xylene until the conversion from (**3**) to (**5**) was complete (2—10 h; Table 3). Products were isolated as for method A.

Method D. The 2*H*-pyrrole (**4h**) (0.01 mol) was refluxed in

Table 6. I.r. and ^{1}H n.m.r. spectroscopic data for 1*H*-pyrrole-2-carboxylic acid derivatives, (**6**), (**7**), and (**8**)

				δ_H ($CDCl_3$)[a]					
Compound	R^1	R^2	$\nu_{max.}$ (Nujol)/cm^{-1}	Me	CH_2	4-H	NH	5-ArH	3-ArH
(**6a**)	H	H	3 300, 1 655, 1 605, 1 275, 1 210, 1 140, 1 030, 770, 705	1.205	4.238	6.603[b]	9.696	7.2—7.7(10 H, m)	
(**6b**)	H	4-NO_2	3 310, 1 660, 1 600, 1 515, 1 345, 1 295, 1 270, 1 140, 1 025, 870	1.274	4.304	6.657[b]	9.545	7.2—7.7(5 H, m)	7.764(2 H, m) 8.238(2 H, m)
(**6d**)	H	4-Cl	3 310, 1 655, 1 290, 1 270, 1 135, 1 090, 1 020, 815, 775	1.254	4.270	6.579[b]	9.516	7.2—7.7(5 H, m)	7.346(2 H, m) 7.521(2 H, m)
(**6e**)	H	4-Me	3 320, 1 655, 1 295, 1 275, 1 140, 1 035, 820, 780, 770	1.225	4.242	6.588[b]	9.680	7.1—7.7(9 H, m), 2.372(3 H, s)	
(**6f**)	H	4-MeO	3 315, 1 670, 1 295, 1 275, 1 185, 1 145, 1 030, 850, 820	1.230	4.242	6.569[b]	9.620	7.2—7.7(5 H, m)	3.813(3 H, s) 6.909 (2 H, m) 7.523(2 H, m)
(**6g**)	4-NO_2	H	3 310, 1 665, 1 515, 1 335, 1 270, 1 215, 1 145, 1 110, 1 040, 860	1.196[d]	4.221[d]	7.020[c,d]	12.304[d]	8.212[d](4 H, s)	7.3—7.6[d](5H,m)
(**6h**)	3-NO_2	H	3 400, 1 680, 1 535, 1 515, 1 350, 1 265, 1 210, 1 135, 1 040	1.220	4.252	6.720[b]	9.940	7.519(1 H, t), 7.931(1 H, m) 8.134(1 H, m), 8.466(1 H, t)	7.2—7.7(5 H, m)
(**6i**)	4-Cl	H	3 310, 1 655, 1 385, 1 295, 1 275, 1 210, 1 140, 1 095, 1 025, 820, 780	1.259	4.280	6.603[b]	9.300	7.2—7.7(9 H, m)	
(**6j**)	4-Cl	4-Cl	3 340, 1 665, 1 290, 1 275, 1 210, 1 145, 1 100, 1 025, 820	1.249	4.272	6.623[b]	9.410	7.2—7.7(8 H, m)	
(**7a**)	H	H	3 305, 1 665, 1 605, 1 275, 1 215 1 140, 1 010, 770, 700	3.784		6.623[b]	9.410	7.2—7.7(10 H, m)	
(**7e**)	H	4-Me	3 310, 1 665, 1 605, 1 295, 1 275, 1 210, 1 135, 1 010, 815, 775	3.744		6.579[b]	9.633	7.1—7.7(9 H, m)	2.368(3 H, s)
(**7i**)	4-Cl	H	3 320, 1 675, 1 605, 1 290, 1 265, 1 215, 1 135, 1 010, 820, 765	3.779		6.591[b]	9.545	7.2–7.6(9 H, m)	
(**7j**)	4-Cl	4-Cl	3 310, 1 680, 1 285, 1 270, 1 210, 1 135, 1 095, 1 020, 1 010, 805	3.398[d]		6.728[d]	12.055[d]	7.31—7.60[d](4 H, m)	7.414[d](2 H, m) 7.899[d](2 H, m)
(**8a**)	H	H	3 440, 3 020—2 500, 1 670, 1 645, 1 605, 1 300, 1 275, 920, 765, 700			6.615[c,d]	10.160[d]	7.1—7.9[d](10 H, m)	

[a] Digital resolution ±0.005 p.p.m. [b] $^4J_{HH}$ 3.1 Hz. [c] $^4J_{HH}$ 2.6 Hz. [d] Solutions in $(CD_3)_2SO$.

benzene for 36 h. The solvent was evaporated and the residue was recrystallised.

Preparation of Ethyl 1H-*Pyrrole-2-carboxylates* (**6**).—*Method E.* Experimental details as for method A, only the benzene solution was refluxed for periods from 2—24 h (Table 5).

Method F. The dihydropyrrole (**3**) (10 mmol) and active MnO_2[17] (8.7 g, 100 mmol) were stirred together in refluxing benzene (azeotropic removal of water formed) until the starting material was no longer detectable by t.l.c. (SiO_2; eluant $CHCl_3$). The cooled mixture was filtered, the residue washed with hot benzene (2 × 10 ml), and the filtrate was evaporated and the residue recrystallised.

Method G. The appropriate diester (**5**) (10 mmol) was refluxed in DMSO (50 ml) for 2 h. The cooled mixture was poured into ice–water, the residue was extracted into ether (3 × 25 ml), the ether solution was dried and evaporated, and the residue recrystallised.

Method H. A solution of the appropriate diester (**5**) (10 mmol) in 5% aqueous ethanolic (1:1) NaOH solution (50 ml) was stirred at 25 °C for 16 h. The solution was cooled to 0 °C, acidified to pH 2.5 with 2 M HCl, and the resulting crystalline precipitate was filtered off, washed with water, and recrystallised.

Preparation of Methyl Esters (**7**): *Method I.*—A solution of the appropriate diester (**5**) (10 mmol) in 10% methanolic KOH (20 ml) was stirred at 25 °C for 4 h. The solution was cooled to 0 °C and the product isolated as for the ethyl ester, method H.

Preparation of Carboxylic Acids (**8**): *Method J.*—Conditions as for method H, only the solution was heated under reflux for 16 h prior to acidification and isolation of the product.

Preparation of the Enamine (**11**).—A mixture of 1,3-diphenylpropane-1,3-dione (**9**) (2.24 g, 10 mmol), diethyl aminomalonate (**10**) (1.75 g, 10 mmol), and a catalytic amount of toluene-*p*-sulphonic acid was heated under reflux in benzene (25 ml) for 10 h. The benzene was evaporated under reduced pressure, and the residue recrystallised from ethanol to yield the *enamine* (**11**) (2.6 g, 68%), needles, m.p. 107 °C (Found: C, 69.05; H, 6.2; N, 3.6. $C_{22}H_{23}NO_5$ requires C, 69.3; H, 6.1; N, 3.7%); $\nu_{max.}$(Nujol) 3 410, 1 755, 1 735, 1 605, 1 570, 1 550, 1 245, 1 160, 1 030, 760, and 700 cm^{-1}; δ_H ($CDCl_3$), 1.26 (6 H, t, *J* 7 Hz), 4.23 (4 H, q, *J* 7 Hz), 4.75 (1 H, d, *J* 9 Hz), 5.94 (1 H, s), 7.2—7.4 (8 H, m), 7.8—8.0 (2 H, m), and 11.6 (1 H, br s).

Cyclisation of the Enamine (**11**) *to the* 2H-*Pyrrole* (**4a**).—The enamine (**11**) (1.0 g, 2.6 mmol) and ethyl polyphosphate (20 g) were heated together under reflux in chloroform (20 ml) for 17 h. The chloroform was removed under reduced pressure, the

residue was treated with ice and water, and the resulting mixture was extracted exhaustively with ether. The ether extracts were washed with 5% NaOH solution (2 × 50 ml) and with water (3 × 50 ml), dried $MgSO_4$), and evaporated. The brown residue was purified by preparative t.l.c. (SiO_2; eluant $CHCl_3$) to yield after recrystallisation ($CHCl_3$–EtOH), a product (0.44 g, 46%), identical in all respects with the 2*H*-pyrrole (**4a**).

Reaction between 1,3-*Diphenylpropynone* (**12**) *and the Aminomalonate Salt* (**1**).—The propynone (**12**) (2.06 g, 10 mmol), the aminomalonate salt (**1**) (2.12 g, 10 mmol), and anhydrous K_2CO_3 (1.38 g, 10 mmol) were heated together on an oil-bath at 170 °C for 30 min. The crude product was extracted with $CHCl_3$ (2 × 20 ml), the mixture was washed with water (2 × 20 ml), the $CHCl_3$ phase was dried ($MgSO_4$), and the solvent evaporated. The residue was purified by preparative t.l.c. (SiO_2; eluant benzene–ethyl acetate) to give three products, respectively (**5a**) (10%), (**6a**) (75%), and (**10**) (15%) by weight.

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