Synthetic Approaches to Fused Heteroaromatic Compounds by the Condensation Reactions of Functional Pyrroles (1)

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Condensation reactions of the "functionalized" pyrroles which were obtained by one pot synthesis of aziridines and acetylenic dipolarophiles were discussed. On treatments of 3,4-di- and 2,3,4-tribenzoylpyrroles with hydrazine hydrate and phosphorus pentasulfide, the several pyrrolopyridazine derivatives and fused thiophenes, respectively, were prepared. The structure proofs for the products of the reaction of the 2,3,4-tribenzoylpyrrole (**9a**) with hydrazine hydrate were based on the ^{13}C FT-nmr spectrum of the corresponding ^{13}C-enriched compounds.

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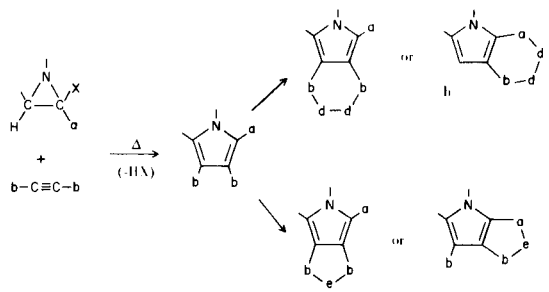
It is well established that 1,3-dipolar cycloaddition, the generality of which was recognized by Huisgen (2) in a series of researches, is one of the most useful methods for the synthesis of heterocycles, in particular five membered ring compounds (3).

An interest in the general problem of synthesizing fused heterocyclic systems such as 2,3-dihydro-2*H*-pyrrolo[3,4-*d*]oxazole (4), 4,5-dihydrofuro[3,4-*b*]pyrrole (5), 1*H*-imidazo[4,5-*d*]pyridazin-4(5*H*)one (6), *N*-aminopyrazolo-[4,5-*d*]pyridazine (7), and "non-classical" thiophene (8,9) by "functionalized" cycloadditions with 1,3-dipoles led us to explore analogous synthetic approaches.

In this paper the author describes further applications of functionalized pyrroles obtained by one pot synthesis with 1,3-dipolar cycloadditions to the synthesis of fused heteroaromatic compounds, as illustrated in Scheme I.

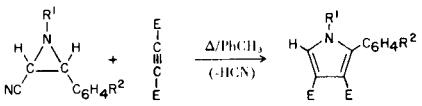
Scheme I



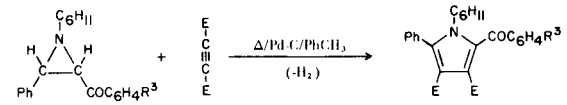
The functionalized pyrroles, *i.e.*, 3,4-dicarbomethoxypyrroles **5** (10), 3,4-dibenzoylpyrroles **6** and **7**, and 2,3,4-tribenzoylpyrroles **9** were prepared by the cycloadditions of cyanoaziridines **1** and **2** (10,11) with dimethyl acetylenedicarboxylate **3** or dibenzoylacetylene **4a**, and by the cycloadditions of benzoylaziridines **8** (12) with dibenzoylacetylenes **4** under dehydrogenating condition in refluxing toluene, respectively (Scheme II).

Their spectral and analytical data are shown in Table I, II, and III. The ir absorptions at about 1710 or 1660 cm^{-1} indicate the presence of carbonyl groups, the pmr spectra show aromatic protons and the other substituents, and the mass spectra and the elemental analysis clearly establish the structure. In this synthesis the primary cycloadduct, *eg.*, a Δ^3-pyrroline could not be isolated,

Scheme II



	R^1	R^2	E	E	R^1	R^2
1a	C_6H_{11}	H	3 $COOCH_3$	5a $COOCH_3$	C_6H_{11}	H
1b	C_6H_{11}	*o*-Cl	4a COPh	5b $COOCH_3$	C_6H_{11}	*o*-Cl
1c	C_6H_{11}	*p*-Cl		5c $COOCH_3$	C_6H_{11}	*p*-Cl
1d	C_6H_{11}	*p*-CH_3		5d $COOCH_3$	C_6H_{11}	*p*-CH_3
1e	C_6H_{11}	*p*-CH_3O		5e $COOCH_3$	C_6H_{11}	*p*-CH_3O
2a	$PhCH_2$	H		6a COPh	C_6H_{11}	H
2b	$PhCH_2$	*o*-Cl		6b COPh	C_6H_{11}	*o*-Cl
2c	$PhCH_2$	*p*-Cl		6c COPh	C_6H_{11}	*p*-Cl
2d	$PhCH_2$	*p*-CH_3		6d COPh	C_6H_{11}	*p*-CH_3
2e	$PhCH_2$	*p*-CH_3O		6e COPh	C_6H_{11}	*p*-CH_3O
				7a COPh	$PhCH_2$	H
				7b COPh	$PhCH_2$	*o*-Cl
				7c COPh	$PhCH_2$	*p*-Cl
				7d COPh	$PhCH_2$	*p*-CH_3
				7e COPh	$PhCH_2$	*p*-CH_3O



	R^3		R^3	E
8a	H	4a COPh	9a H	COPh
8b	*p*-Cl	4b COC_6H_4Cl-*p*	9b H	COC_6H_4Cl-*p*
8c	*p*-CH_3	4c $COC_6H_4CH_3$-*p*	9c H	$COC_6H_4CH_3$-*p*
			9d *p*-Cl	COPh
			9e *p*-Cl	COC_6H_4Cl-*p*
			9f *p*-Cl	$COC_6H_4CH_3$-*p*
			9g *p*-CH_3	COPh
			9h *p*-CH_3	COC_6H_4Cl-*p*
			9i *p*-CH_3	$COC_6H_4CH_3$-*p*

and when the dehydrogenative reagent was omitted in the reaction of **8a**, a complex mixture containing the pyrrole **9a** as the major product was obtained. Thus, one pot synthesis of the pyrroles from aziridines and acetylenic compounds are apparently general (13).

The successful application of this reaction to the condensed heteroaromatics was the reaction of 3,4-dibenzoylpyrroles with excess hydrazine hydrate in ethanol to give the pyrrolo[3,4-*d*]pyridazines. This ring system, which is of interest because of its relationship to isoindoles, has been scarcely investigated since its first synthesis by Buu-Hoï, *et al.*, in 1959 (14,15).

On treatment of all the dibenzoylpyrroles **6** and **7** with hydrazine hydrate, the three pyrrolo[3,4-*d*]pyridazines

Table I

Dimethyl 2-Aryl-1-cyclohexylpyrrole-3,4-dicarboxylates **5a-e**

Compound	Yield, %	M.p. °C	Ir (a) cm^{-1} ν COO	Nmr (in chloroform-d) cyclohexyl	ester CH_3	CH_3	aromatic	CH_3	M^+, m/e	Found, % (Calcd.) C	H	N
5a	27	106-109	1716	0.7-2.1	3.57	3.74	7.25-7.40		341	70.23	6.99	4.27
									$C_{20}H_{23}O_4N$	(70.36	6.79	4.10)
5b	46	117-119	1712	1.1-2.2	3.62	3.83	7.27-7.52		375	64.10	6.03	3.82
									$C_{20}H_{22}ClO_4N$	(63.91	5.90	3.73)
5c	61	124-127	1718	1.3-1.9	3.69	3.85	7.24-7.42		375	63.69	5.90	3.85
									$C_{20}H_{22}ClO_4N$	(63.91	5.90	3.73)
5d	45	98-101	1711	1.0-2.0	3.66	3.83	7.22-7.38	2.41	355	70.97	7.16	3.72
									$C_{21}H_{25}O_4N$	(70.96	7.09	3.94)
5e	40	104-106	1712	1.1-2.1	3.75	3.94	7.00-7.46	3.90	371	67.88	6.94	3.67
									$C_{21}H_{25}O_5N$	(67.90	6.78	3.77)

(a) In chloroform. The center of a broad absorption.

Table II

1-Cyclohexyl- and 1-Benzyl-2-aryl-3,4-dibenzoylpyrroles **6a-e** and **7a-e**

Compound	Yield %	M.p. °C	Ir (a) cm^{-1} ν C=O	Nmr (in chloroform-d) aromatic	N-CH- (b)	$-CH_2-$ (c)	$-CH_3$	M^+, m/e	Found, % (Calcd.) C	H	N
6a	72	196-197	1655	7.05-7.75	3.86	1.40-2.21		433	82.82	6.54	3.52
								$C_{30}H_{27}O_2N$	(83.11	6.28	3.23)
6b	43	193-194	1650	7.05-7.84	3.65	1.32-2.41		467	76.74	5.34	2.81
								$C_{30}H_{26}ClO_2N$	(76.99	5.60	2.99)
6c	72	233-233.5	1655	7.09-7.74	3.83	1.35-2.17		467	76.79	5.52	2.82
								$C_{30}H_{26}ClO_2N$	(76.99	5.60	2.99)
6d	68	214-215	1640 1660	7.07-7.75	3.91	1.37-2.18	2.33	447	82.94	6.51	3.01
								$C_{31}H_{29}O_2N$	(83.19	6.53	3.13)
6e	81	217-219	1640 1660	6.78-7.73	3.81	1.35-2.20	3.77	463	80.14	6.25	3.09
								$C_{31}H_{29}O_3N$	(80.32	6.31	3.02)
7a	76	149-149.5	1655	6.90-7.73		5.06		441	85.55	5.08	3.00
								$C_{31}H_{23}O_2N$	(85.33	5.25	3.17)
7b	55	150-151	1650	6.90-7.70		4.90-5.03 (d)		475	78.30	4.63	2.79
								$C_{31}H_{22}ClO_2N$	(78.23	4.66	2.94)
7c	80	160-161	1640 1665	6.90-7.72		5.05		475	78.36	4.78	3.07
								$C_{31}H_{22}ClO_2N$	(78.23	4.66	2.94)
7d	82	147-147.5	1640 1665	6.80-7.74		5.07	2.28	455	84.12	5.49	3.18
								$C_{32}H_{25}O_2N$	(84.37	5.53	3.07)
7e	85	195-195.5	1635 1665	6.75-7.73		5.08	3.76	471	81.28	5.17	2.69
								$C_{32}H_{25}O_3N$	(81.51	5.34	2.97)

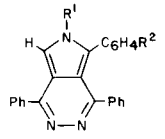
(a) Potassium bromide disk. (b) Broad singlet. (c) Cyclohexyl-H on **6a-e** and benzyl-H on **7a-e**. (d) AB-quartet; J = 15 Hz.

Table III

1-Cyclohexyl-5-phenyl-2,3,4-triaroylpyrroles **9a-i**

Compound	Yield, %	M.p. °C	Ir (a) cm^{-1} ν C=O	Nmr (in chloroform-d) aromatic	N-C*H*- (d)	-CH_2-	-CH_3	M^+, m/e	Found, % (Calcd.)		
9a	29	189-190 (b)	1660	6.9-7.75	4.05	0.9-2.05		537	82.41	5.85	2.73
								$C_{37}H_{31}O_3N$	(82.65	5.81	2.61)
9b	46	226.5-228 (b)	1655	6.9-7.75	4.05	0.9-2.05		605	73.47	4.84	2.40
								$C_{37}H_{29}Cl_2O_3N$	(73.26	4.82	2.31)
9c	15	175-175.5 (c)	1660	6.8-7.75	4.05	0.9-2.05	2.20	565	82.77	6.21	2.62
							2.26	$C_{39}H_{35}O_3N$	(82.80	6.24	2.48)
9d	45	210-211 (c)	1665	6.9-7.65	4.05	0.9-2.1		571	77.74	5.12	2.59
								$C_{37}H_{30}ClO_3N$	(77.68	5.29	2.45)
9e	46	212-213 (c)	1660	6.9-7.65	4.05	0.9-2.05		639	69.48	4.22	2.27
								$C_{37}H_{28}Cl_3O_3N$	(69.33	4.40	2.19)
9f	29	226-227 (c)	1665	6.8-7.65	4.05	0.9-2.05	2.20	599	78.14	5.63	2.50
							2.28	$C_{39}H_{34}ClO_3N$	(78.05	5.71	2.33)
9g	32	185-186 (c)	1662	6.9-7.65	4.05	0.9-2.05	2.28	551	82.92	6.11	2.79
								$C_{38}H_{33}O_3N$	(82.73	6.03	2.54)
9h	35	217-217.5 (b)	1655	6.9-7.75	4.05	0.9-2.15	2.32	619	73.56	5.28	2.36
								$C_{38}H_{31}Cl_2O_3N$	(73.55	5.04	2.26)
9i	17	200.5-201 (b)	1662	6.8-7.65	4.05	0.9-2.05	2.21	579	82.75	6.47	2.54
							2.29 (e)	$C_{40}H_{37}O_3N$	(82.87	6.43	2.42)

(a) Potassium bromide disk. (b) From *n*-hexane-benzene. (c) From ethanol-benzene. (d) Broad singlet. (e) MeX 2(6H).



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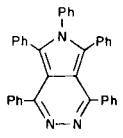

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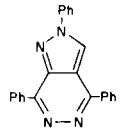

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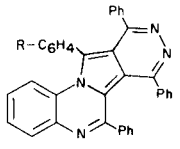


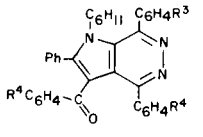
13a R NO_2
13b R H

(**10a**) $R^1 = PhCH_2$, $R^2 = H$; (**10b**) $R^1 = PhCH_2$, $R^2 = p$-Cl; (**10c**) $R^1 = PhCH_2$, $R^2 = p$-CH_3) were produced in good yields (73-89%). In other cases the products could not be purified by recrystallizations because of decomposition. By a similar method, pentaphenylpyrrolo[3,4-*d*]pyridazine (**11**), triphenylpyrazolo[3,4-*d*]pyridazine (**12**) and 7-aza-indolidino[1,2-*d*]pyridazines **13a** and **13b** were easily obtained in fairly good yields from the corresponding dibenzoyl compounds.

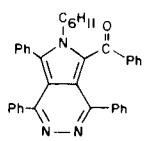
The structures of these products were supported by the disappearance of the peak at 1650 cm^{-1} in the ir spectra indicative of carbonyl groups, and by the corresponding parent peaks of the mass spectra and the satisfactory elemental analysis.

In contrast, the reaction of 1-cyclohexyl-5-phenyl-2,3,4-tribenzoylpyrroles **9a** with excess hydrazine hydrate in ethanol readily gave a pyrrolopyridazine derivative, the constitution of which was determined by the appearance of the peak at 1548 cm^{-1} on the ir spectra being attributed to the C=N linkage, the mass spectra (M^+ 537), and the correct elemental analysis. Although the literature references (16) have strongly suggested that the condensation product is the pyrrolo[2,3-*d*]pyridazine **14a** instead of the pyrrolo[3,4-*d*]pyridazine **15**, the direction of cyclization was confirmed by the ^{13}C FT-nmr spectra of the ^{13}C-enriched product **14a'** obtained from 2,3,4-tribenzoylpyrrole **9a'** which were labeled on the carbonyl-carbon of the 2-benzoyl group. The ^{13}C FT-nmr spectrum of **9a'** showed an enhanced peak at 190.6 ppm. Since an enhanced peak at 147.5 ppm was observed in **14a'**, the labeled benzoyl group in **9a'** was apparently incorporated into an aromatic ring in **14a'**.

The tribenzoylpyrroles **9b** and **9c** were also converted into the corresponding pyrrolo[2,3-*d*]pyridazines **14b** and **14c**, respectively. In the uv and visible spectra of these



14a R^3 R^4 H
14b R^3 H, R^4 *p*-Cl
14c R^3 *p*-Cl, R^4 H



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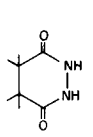
products **14a**, **14b**, and **14c** were observed the same absorption maxima at 244 and 300 nm.

On the other hand, an attempt to prepare a cyclic hydrazide **16**, which is known to form from the reaction of esters of succinic acid and phthalic acid with hydrazine (17), from the dicarbomethoxypyrrole **17** (10b) were unsuccessful, giving only a dihydrazide **18** in 50% yield.



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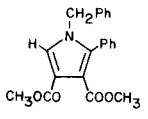

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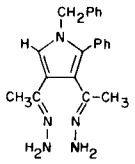

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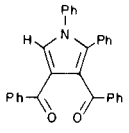
Potts, *et al.*, (8b) have found that the substitution pattern of the pyrrole moiety is critical for a formation of the nonclassical thiophene ring system by the action of phosphorus pentasulfide on the 3,4-dibenzoylpyrroles, and that the products from 5-unsubstituted pyrroles such as **19** and **20** were the corresponding dithiobenzoylpyrroles (8b,d). These findings were also confirmed in the present experiments. The pyrrole **6a** reacted with excess phosphorus pentasulfide in refluxing pyridine to afford red amorphous crystals, which were immediately converted in the air into yellow products. The red crystals are probably the nonclassical thiophene **21**. The final yellow product was determined to be the 3,4-dithiobenzoylpyrrole **22** by the ir absorption band at 1075 cm^{-1} in the C=S stretching region, the mass spectrum (M^+ 465) and the correct elemental analysis.



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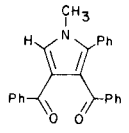

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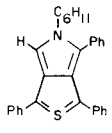

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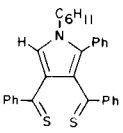

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On the other hand, the reaction of **9a** with phosphorus pentasulfide in refluxing pyridine gave stable dark red needles which had a parent peak at 554 in the mass spectrum and showed satisfactory elemental analysis as the pyrrolothiophene **23**. The structure of the nonclassical thiophene **24** may be excluded on the basis of its failure to react with *N*-phenylmaleimide, dimethyl acetylenedicarboxylate, and dibenzoylacetylene.

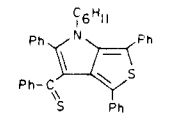
The considerably stable nonclassical thiophene **26** was obtained by action of phosphorus pentasulfide on the pyrrole derivative **25** (18) as red crystals. Although **26** could not be isolated in the pure state, treatment of the crude product with *N*-phenylmaleimide in refluxing xylene for 52 hours gave the 1:1 cycloadduct **27**. The nmr spectrum of **27** showed the bridgehead protons at 5.05 and 5.23 (AB-quartet, J = 9.0 Hz), and the mass spectrum and the elemental analysis was also satisfactory.

Table IV

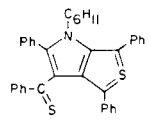
1-Cyclohexyl- and 1-Benzyl-2-aryl-3-cyanoaziridines **1a-e** and **2a-e**

Compound	Yield %	M.p. (b) °C	Ir (a) cm^{-1} ν C≡N *trans*	Ir (a) cm^{-1} ν C≡N *cis*	Nmr (in chloroform-d), aromatic	aziridine ring *trans*	aziridine ring *cis* (AB-q;	aziridine ring J, Hz)	-CH_2- (c)	Found, % (Calcd.) C	H	N
1a	80	101 (d)	2190	2250	7.25-7.6	4.07	2.34	2.91 (6.0)	1.0-2.1			
1b	57	62-65	2200	2270	7.2-7.6	4.16	2.47	3.19 (6.0)	1.1-2.2	69.32 (69.09	6.45 6.57	10.82 10.74)
1c	61	137-138		2250	7.25-7.45		2.36	2.89 (5.0)	1.1-2.2	69.17 (69.09	6.57 6.57	10.97 10.74)
1d	72	102-105	2220	2250	7.1-7.5	4.03	2.30	2.87 (6.0)	1.1-2.2 (e)	79.76 (79.95	8.41 8.39	11.60 11.66)
1e	13	103-105		2220	6.88-7.40		2.31	2.89 (6.0)	1.1-2.0 (f)	75.13 (74.96	7.85 7.86	10.92 10.93)
2a	28	85-86		2240	7.20-7.48		2.42	3.01 (5.8)	3.72	81.90 (82.02	5.90 6.03	11.72 11.96)
2b	30	96-97		2240	7.18-7.55		2.56	3.33 (6.3)	3.68 3.79 (13.7)	71.59 (71.51	4.79 4.88	10.23 10.42)
2c	36	137-137.5		2240	7.20-7.46		2.45	3.00 (5.8)	3.69 3.78 (13.7)	71.42 (71.51	4.78 4.88	10.44 10.42)
2d	10	115-115.5		2250	7.12-7.40		2.39	2.98 (5.9)	3.66 3.73 (13.8) (g)	82.51 (82.22	6.21 6.50	11.24 11.28)
2e	28	102-103		2240	6.83-7.38		2.38	2.98 (6.1)	3.72 (h)	77.20 (77.25	6.01 6.10	10.48 10.60)

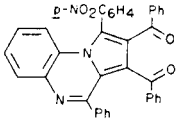
(a) Potassium bromide disk. (b) Compounds **1a-e** were recrystallized from ether-petroleum ether and **2a-e** from ethanol. (c) Cyclohexyl-H on **1a-e** and benzyl-H on **2a-e**. (d) See: Reference 11 (m.p. 108.5-110.5°). (e) CH_3: 2.34 (*cis*), 2.38 (*trans*). (f) CH_3O; 3.82. (g) CH_3; 2.32. (h) CH_3O; 3.75.



23



24



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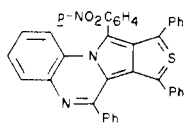

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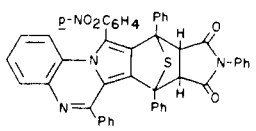

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EXPERIMENTAL

General.

Melting points were determined on a Yanagimoto micromelting point apparatus and are uncorrected. Infrared spectra were obtained on a Jasco IR-G or a Hitachi EPI-G3 spectrophotometer. Visible and ultra-violet spectra were taken on a Hitachi 139 spectrophotometer. ^1H nmr spectra were measured on a JEOL 4H-100 instrument. ^{13}C nmr spectra were recorded on a JEOL FX-60 pulsed Fourier transformation nuclear magnetic resonance spectrometer operating at 15.040 MHz. Samples were observed in 10-mm.o.d. tubes, at 0.1-0.2 M solutions in deuteriochloroform at 30°. Chemical shifts are given in parts per million downfield from tetramethylsilane as zero. Partial proton decoupling was used to distinguish between individual carbon atoms. Mass spectra were obtained on a JEOL 01SG-2 mass spectrometer.

2-Aryl-3-cyano-1-cyclohexylaziridines (**1a-e**) and 2-Aryl-1-benzyl-3-cyanoaziridines (**2a-e**) (11). General Procedure.

The cyanoaziridines **1** and **2** were prepared by the Gabriel method (12b) from 1-aryl-1,2,dibromo-2-cyanoethanes which were obtained by bromination of the substituted cinnamonitriles (19) and used without further purification. The products **1** and **2** were recrystallized from ether-petroleum ether and ethanol, respectively. Their spectral and analytical data are tabulated in Table IV.

Dimethyl 2-Aryl-1-cyclohexylpyrrole-3,4-dicarboxylates (**5a-e**) (10). General Procedure.

A solution of 2.2 mmoles of **1** and 7 mmoles of dimethyl acetylenedicarboxylate **3** was heated under reflux in 20 ml. of toluene for 22 hours. Evaporation of the solvent *in vacuo* gave a syrup, from which the product was isolated by chromatography on alumina with benzene-chloroform as eluent, and was recrystallized from ethanol containing small portions of *n*-hexane (Table I).

1-Cyclohexyl- and 1-Benzyl-2-aryl-3,4-dibenzoylpyrroles (**6a-e**) and (**7a-e**). General Procedure.

A solution of 2.2 mmoles of **1** and **2**, and the equimolar dibenzoylacetylene (**4a**) was refluxed in 50 ml. of toluene for 5-10 hours. After evaporation of the solvent, the residue was recrystallized from ethanol to afford **6a-e** and **7a-e**, respectively (Table II).

1-Cyclohexyl-5-phenyl-2,3,4-triaroylpyrroles (**9a-i**). General Procedure.

A mixture of 1.5 mmoles of **8** (12) and 1.8 mmoles of diaroylacetylene **4** (20) with 1 g. of 10% palladium-carbon was heated in 40 ml. of refluxing toluene for 5-8 hours. The product isolated after a usual workup was purified by recrystallization from ethanol-benzene or *n*-hexane-benzene to give **9a-i** (Table III).

5-Aryl-6-benzyl-1,4-diphenylpyrrolo[3,4-*d*]pyridazine (**10a-c**). General Procedure.

To a solution of 0.55 mmole of **7** in 20-50 ml. of ethanol was added dropwise 6 ml. of 100% hydrazine hydrate. After stirring and heating at 60° for 30 minutes the mixture was cooled to room temperature from which pure yellow needles of **10** crystallized.

Compound **10a**.

This compound was obtained in 84% yield, m.p. 214-217°; ir (potassium bromide): 1530 cm^{-1}; ms: M^+ m/e 437.

Anal. Calcd. for $C_{31}H_{23}N_3$: C, 85.10; H, 5.29; N, 9.61. Found: C, 84.85; H, 5.18; N, 9.43.

Compound **10b**.

This compound was obtained in 73% yield, m.p. 221-222°; ir (potassium bromide): 1530 cm^{-1}; ms: M^+ m/e 471.

Anal. Calcd. for $C_{31}H_{22}ClN_3$: C, 78.89; H, 4.70; N, 8.90. Found: C, 78.86; H, 4.55; N, 8.81.

Compound **10c**.

This compound was obtained in 89% yield, m.p. 187-189°; ir (potassium bromide): 1537 cm^{-1}; ms: M^+ m/e 451.

Anal. Calcd. for $C_{32}H_{25}N_3$: C, 85.11; H, 5.58; N, 9.31. Found: C, 85.24; H, 5.47; N, 9.28.

1,4,5,6,7-Pentaphenylpyrrolo[3,4-*d*]pyridazine (**11**).

In a similar manner as above for **10a-c**, the treatment of 100 mg. (0.2 mmole) of 3,4-dibenzoyl-1,2,5-triphenylpyrrole (21) with excess hydrazine hydrate in ethanol containing a small portion of benzene at 70° gave 50 mg. (50%) of **11**, m.p. 255-258°; ir (potassium bromide): 1547 cm^{-1}; ms: M^+ m/e 499.

Anal. Calcd. for $C_{36}H_{25}N_3$: C, 86.54; H, 5.04; N, 8.41. Found: C, 86.39; H, 5.21; N, 8.32.

1,4,6-Triphenylpyrazolo[3,4-*d*]pyridazine (**12**).

In a similar manner as above for **10a-c**, the treatment of 100 mg. (0.28 mmole) of 3,4-dibenzoyl-1-phenylpyrazole (22) with excess hydrazine hydrate in 1-propanol at 90° gave 80 mg. (81%) of **12**, m.p. 254-256°; ir (potassium bromide): 1563 cm^{-1}; ms: M^+ m/e 348.

Anal. Calcd. for $C_{23}H_{16}N_4$: C, 79.29; H, 4.63; N, 16.08. Found: C, 79.57; H, 4.34; N, 16.03.

5-(*p*-Nitrophenyl)-1,4,12-triphenylpyridazine[4,5-*a*]pyrrolo[1,2-*a*]-quinoxaline (**13a**) and 1,4,5,12-Tetraphenylpyridazino[4,5-*a*]pyrrolo[1,2-*a*]quinoxaline (**13b**).

In a similar manner as above for **10a-c**, the treatment of 100 mg. of 2,3-dibenzoyl-1-(*p*-nitrophenyl)-4-phenylpyrrolo[1,2-*a*]-quinoxaline **25** (18) and 2,3-dibenzoyl-1,4-diphenylpyrrolo[1,2-*a*]-quinoxaline (18) with excess hydrazine hydrate gave **13a** and **13b** respectively.

Compound **13a**.

This compound was obtained in a yield of 71%, m.p. 316-317° dec.; ir (potassium bromide): 1520, 1350 cm^{-1}; ms: M^+ m/e 570.

Anal. Calcd. for $C_{37}H_{23}N_5O_2$: C, 78.02; H, 4.02; N, 12.30. Found: C, 77.89; H, 3.89; N, 12.09.

Compound **13b**.

This compound was obtained in a yield of 50%, m.p. 314° dec.; ir (potassium bromide): 1548 cm^{-1}; ms: M^+ m/e 525.

Anal. Calcd. for $C_{37}H_{29}N_4$: C, 84.71; H, 4.61; N, 10.68. Found: C, 84.67; H, 4.88; N, 10.44.

7-Aroyl-5-cyclohexyl-1,4-diaryl-6-phenylpyrrolo[1,2-*d*]pyridazine (**14a-c**). General Procedure.

In a similar manner as above for **10a-c**, the treatment of 0.6 mmole of **9a-c** with excess hydrazine hydrate in ethanol-benzene (4:1) gave compounds **14**.

Compound **14a**.

This compound was obtained in a yield of 67%, m.p. 286-288°; ir (potassium bromide): 1548, 1660 cm^{-1}; ms: M^+ m/e 533; λ max (chloroform): 244.0 nm (log ε = 4.57), 300.0 nm (log ε = 4.11).

Anal. Calcd. for $C_{37}H_{31}ON_3$: C, 83.27; H, 5.87; N, 7.87. Found: C, 83.06; H, 5.92; N, 8.11.

Compound **14b**.

This compound was obtained in a yield of 41%, m.p. 254-256°; ir (potassium bromide): 1544, 1656 cm^{-1}; ms: M^+ m/e 601; λ max (chloroform): 244.0 nm (log ε = 4.57), 300.0 nm (log ε = 4.15).

Anal. Calcd. for $C_{37}H_{29}Cl_2ON_3$: C, 73.75; H, 4.85; N, 6.97. Found: C, 73.73; H, 4.62; N, 6.83.

Compound **14c**.

This compound was obtained in a yield of 81%, m.p. 255.5°; ir (potassium bromide): 1540, 1662 cm^{-1}; ms: M^+ m/e 567; λ max (chloroform): 244.0 (log ε = 4.65), 299.5 nm (log ε = 4.23).

Anal. Calcd. for $C_{37}H_{30}ClON_3$: C, 78.22; H, 5.32; N, 7.40. Found: C, 78.04; H, 5.29; N, 7.48.

^{13}C-Labeled 1-Cyclohexyl-5-phenyl-2,3,4-tribenzoylpyrrole (**9a'**).

A mixture of 1.5 g. of ^{13}C-labeled 2-benzoyl-1-cyclohexyl-3-phenylaziridine (23) and 1.5 g. of dibenzoylacetylene with 1.5 g. of 5% palladium-carbon was heated in 120 ml. of refluxing toluene. The product isolated after a usual workup was purified by recrystallization from ethanol-benzene to give 780 mg. (29%) of **9a'**, m.p. 187-188°; ^{13}C nmr (deuteriochloroform): 24.77, 26.23, 33.22, 59.86 (cyclohexyl-carbon), 190.61 (enhanced; carbon of 2-benzoyl carbonyl), 191.02 (included into the enhanced peak; carbon of 3-benzoyl carbonyl), 192.16 (carbon of 4-benzoyl carbonyl).

^{13}C-Labeled 7-Benzoyl-5-cyclohexyl-1,4,6-triphenylpyrrolo[1,2-*d*]-pyridazine (**14a'**).

The preparation was followed as described above for **14a**. From 400 mg. of **9a'**, 345 mg. (87%) of **14a'** was obtained, m.p. 285-287°; ^{13}C nmr (deuteriochloroform): 24.69, 26.15, 33.14, 59.21 (cyclohexyl-carbon), 146.03 (carbon of the position 1), 147.49 (enhanced; carbon of the position 4), 192.49 (carbon of 7-benzoyl carbonyl).

Reaction of **17** with Hydrazine Hydrate.

A solution of 100 mg. (0.29 mmole) of **17** (m.p. 83.0-83.5°; lit. (10b) 98°) and 3 ml. of 100% hydrazine hydrate in 20 ml. of ethanol was heated at 70°. The mixture was concentrated to *ca.* 5 ml. precipitating crude white crystals. The product was recrystallized from 20% aqueous ethanol to give white needles of 1-benzyl-2-phenylpyrrole-3,4-dicarbohydrazide (**18**), 50 mg. (51%), m.p. 88-90°; ir (potassium bromide): 1550, 1600, 1650 cm^{-1}; pmr (deuteriochloroform): 3.87 (broad s, 4H, NH-NH_2), 4.88 (s, 2H, benzyl), 6.85-7.57 (m, 13H, aromatic); ms: M^+ m/e 349.

The Reaction of **6a** with Phosphorus Pentasulfide.

The procedures for the reactions of **19** and **20** by Potts, *et al.*, (8d) were followed. A mixture of 100 mg. of **6a**, 300 mg. of phosphorus pentasulfide, and 15 ml. of dry pyridine was refluxed for 5 hours. After cooling, the reaction mixture was poured into 10% aqueous sodium hydroxide solution. A dark red solid separated and was immediately converted into a yellow substance on filtration. This product was recrystallized from acetic anhydride to afford yellow crystals of **22**, m.p. 187-190°; ir (potassium bromide): 1075 cm^{-1}; pmr (deuteriochloroform): 5.82 (s, 1H, H-5), 7.15-7.5 and 7.92-8.04 (m, 15H, aromatic), 1.4-2.4 (m, cyclohexyl); ms: M^+ m/e 465.

Anal. Calcd. for $C_{30}H_{27}NS_2$: S, 13.76. Found: S, 13.79.

The Reaction of **9a** with Phosphorus Pentasulfide.

In a similar manner as above, a mixture of 500 mg. of **9a**, 2.0 g. of phosphorus pentasulfide, and 90 ml. of dry pyridine was refluxed under a nitrogen atmosphere for 5 hours. After cooling, the reaction mixture was poured into 10% aqueous sodium hydroxide solution. A dark red solid precipitated and was separated by chromatography on silica-gel with *n*-hexane-benzene as eluent into four fractions and then the solvent of each fraction was evaporated. The residues were recrystallized from ethanol to afford the following. From the first fraction 6 mg. of dark red needles, m.p. 226-229° was obtained; ir (potassium bromide): 1650 (broad), 1065 cm^{-1}; ms: M^+ m/e 457. From the second fraction 46 mg. of dark red crystals of 6-benzoyl-4-cyclohexyl-1,3,5-triphenylthieno[3,4-*b*]pyrrole **23**, m.p. 229-231° was obtained; ir (potassium bromide): 1058, 1085 cm^{-1}; pmr (deuteriochloroform): 0.37-2.08 (m, cyclohexyl), 7.10-8.08 (m, aromatic); λ max (chloroform): 275 (log ε = 4.37), 341 (log ε = 4.21), 478.5 (log ε = 3.91); ms: M^+ m/e 553.

Anal. Calcd. for $C_{37}H_{31}NS_2$: C, 80.25; H, 5.64; N, 2.53; S, 11.58. Found: C, 80.45; H, 5.66; N, 2.44; S, 11.33.

From the third fraction, 6 mg. of yellow crystals, m.p. 188-189°, was obtained; ir (potassium bromide): 1400, 1597 cm^{-1}; pmr (deuteriochloroform): 1.1-2.1 (m, cyclohexyl), 4.8 (broad s, 1H), 5.78 (s, 1H), 7.20-7.44, 7.9-8.1 (m, aromatic); ms: M^+ m/e 465. From the last fraction, 12 mg. of **9a** was recovered.

The Reaction of **25** with Phosphorus Pentasulfide and The Cycloaddition Reaction of The Product with *N*-Phenylmaleimide.

In a manner similar to that described above, a mixture of 900 mg. of **25**, 3 g. of phosphorus pentasulfide, and 100 ml. of dry pyridine were refluxed for 5 hours. After cooling, the reaction mixture was poured into 10% aqueous sodium hydroxide solution. A red solid precipitated and was dried under reduced pressure, and then 650 mg. of the product was treated with 200 mg. of *N*-phenylmaleimide in 30 ml. of refluxing toluene for 52 hours. After removal of the solvent, the residue was chromatographed on alumina using benzene as eluent affording yellow crystals which was recrystallized twice from ethanol-benzene: 50 mg. of **27**, m.p. 254-257°; ir (potassium bromide): 1522, 1350, 1778, 1717 cm^{-1}; pmr (deuteriochloroform): 5.05, 5.23 (AB-q, J = 9 Hz), 6.6-7.9 (m, aromatic); ms: M^+ m/e 746, 714 (M^+-32).

Anal. Calcd. for $C_{41}H_{30}N_4O_4S$: C, 75.59; H, 4.05; N, 7.50; S, 4.29. Found: C, 75.61; H, 4.21; N, 7.36; S, 4.47.

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