Synthesis and Tautomeric Structure of some 2*H*-Pyrazolo[3,4-*d*]pyridazines

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A number of substituted 2*H*-pyrazolo[3,4-*d*]pyridazines, pyridazin-7(6*H*)ones, and -pyridazine-4,7(5*H*,6*H*)diones have been prepared from the 3,4-diacyl-, 3-carbethoxy-4-acyl-, 3-carbethoxy-4-cyano-, and 3,4-dicarbethoxy-pyrazole derivatives and hydrazine hydrate. The structures of the compounds prepared were inferred from their elemental analyses and spectral data. On the basis of spectroscopic data it was concluded that pyrazolopyridazinones have the oxo form, whereas the monohydroxymono oxo structure is preferred for pyrazolopyridazinediones.

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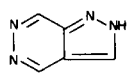
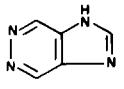
In spite of the marked similarity between 2*H*-pyrazolo[3,4-*d*]pyridazine, I, and the purine analog namely 1*H*-imidazo[4,5-*d*]pyridazine, II, only the chemistry of the latter has been throughly investigated (1). A literature survey revealed that only four derivatives of I have been reported (1-4). In an attempt to help remedy this situation we have extended our previous studies (5-8) on the reactions of hydrazonoyl halides, III, bearing additional functionality, ZCO-, with β-diketones and β-keto esters to synthesis of I. These reactions proved useful for synthesis of pyrazoles, IV, with ortho functional groups capable of forming the pyridazine ring. In the present report the results of the application of this approach for synthesis of five series of pyrazole derivatives namely VIII to XII (Scheme 1) and the use of the latter in synthesis of several derivatives of pyrazolopyridazines XIII to XVI, pyrazolopyridazinones XVII to XX, and pyrazolopyridazinediones, XXI (Scheme 2) are outlined. In addition the tautomeric structures of XVII to XXI are also discussed.



I



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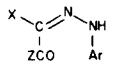
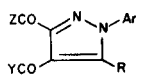


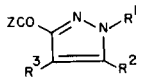
III



IV

Addition of *N*-arylcarbethoxymethanehydrazonoyl chloride (II, X = Cl, Z = OC_2H_5) (8) to a solution of the sodium salts of acetylacetone and dibenzoylmethane at room temperature in ethanol afforded the corresponding pyrazoles VIII and IX, respectively. Similar treatment of

Scheme 1



Series	R^2	R^3	Z
V	CH_3	$COCH_3$	C_6H_5
VI	C_6H_5	COC_6H_5	C_6H_5
VII	CH_3	COC_6H_4	C_6H_5
VIII	CH_3	$COCH_3$	OC_2H_5
IX	C_6H_5	COC_6H_5	OC_2H_5
X	C_6H_5	$COOC_2H_5$	OC_2H_5
XI	C_6H_5	CN	OC_2H_5
XII	C_6H_5	CN	C_6H_5

a $R^1 = C_6H_5$ d $R^1 = p\text{-}ClC_6H_5$
b $R^1 = p\text{-}CH_3C_6H_4$ e $R^2 = C_6H_5$, $R^2 = p\text{-}CH_3C_6H_4$
c $R^1 = p\text{-}CH_3OC_6H_4$ f $R^1 = C_6H_5$, R = $p\text{-}BrC_6H_4$

III (X = Cl, Z = OC_2H_5) with sodium salt of ethyl benzoylacetate gave the pyrazole derivatives X. The structures of VIII to X were derived from their analytical data (Table 1) and their chemical behaviour. For example, all compounds VIII to X gave no color with ethanolic ferric chloride solution and did not couple with benzenediazonium ion in presence of sodium acetate or sodium hydroxide. In addition the products X were recovered unchanged when refluxed in ethanolic hydrochloric acid, thus excluding the isomeric structure XA. The spectral data (ir and uv) in Table 2 for these products were consistent with their assigned structures. Finally the structures of these compounds were established by their pmr spectra. Thus, the spectra of VIII in deuterated chloroform exhibited two singlets near δ 2.70 and 2.40 ppm assignable to the 4-$COCH_3$ and 5-CH_3 protons, respectively. The spectra of X in the same solvent showed a quintet at δ 1.20 (6H, J = 7 Hz) due to two overlapped triplets corresponding to 3- and 4-$COOCH_2CH_3$ protons. Also,

Scheme 2

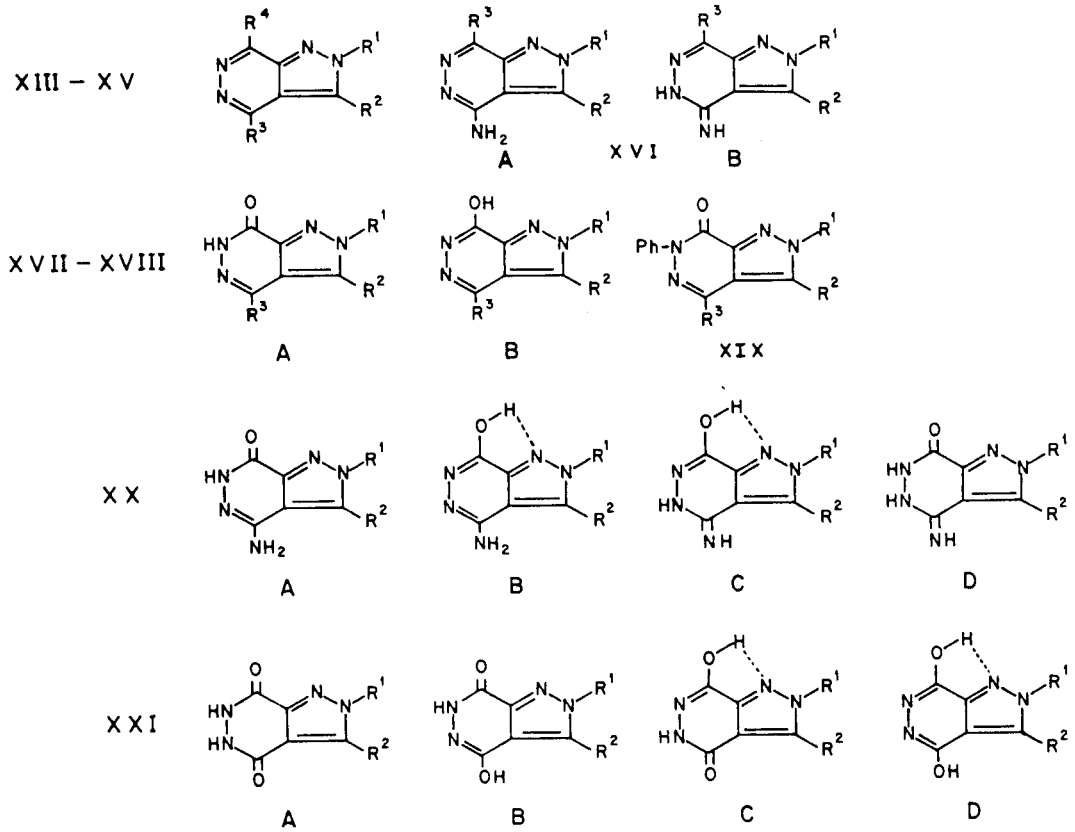


Table 1

Substituted Pyrazoles

Compound No.	1-Aryl	M.p., °C	Molecular Formula	C % Calcd.	C % Found	H % Calcd.	H % Found	N % Calcd.	N % Found
			1-Aryl-3-carbethoxy-4-acetyl-5-methylpyrazoles, VIII						
VIIIa	C_6H_5	56-57	$C_{15}H_{16}N_2O_3$	66.16	66.07	5.92	5.89	10.29	10.26
VIIIb	p-$CH_3C_6H_4$	119	$C_{16}H_{18}N_2O_3$	67.11	66.90	6.34	6.35	9.79	9.70
VIIIc	p-$CH_3OC_6H_4$	54	$C_{16}H_{18}N_2O_4$	63.65	63.61	6.00	6.02	9.27	9.20
VIIId	p-ClC_6H_4	92	$C_{15}H_{15}ClN_2O_3$	58.73	57.73	4.93	4.87	9.13	9.05
			1-Aryl-3-carbethoxy-4-benzoyl-5-phenylpyrazoles, IX						
IXa	C_6H_5	159-160	$C_{25}H_{20}N_2O_3$	75.74	75.39	5.08	5.08	7.07	7.22
IXb	p-$CH_3C_6H_4$	128	$C_{26}H_{22}N_2O_3$	76.08	75.53	5.40	5.47	6.83	6.76
IXc	p-$CH_3OC_6H_4$	140-142	$C_{26}H_{22}N_2O_3$	73.22	72.97	5.20	5.29	6.57	6.30
IXd	p-ClC_6H_4	158-159	$C_{25}H_{19}ClN_2O_3$	69.68	69.74	4.44	4.58	6.50	6.43
			1-Aryl-3,4-dicarbethoxy-5-phenylpyrazoles, X						
Xa	C_6H_5	93-94	$C_{21}H_{20}N_2O_4$	69.21	69.12	5.53	5.49	7.68	7.53
Xd	p-ClC_6H_4	86-87	$C_{21}H_{19}ClN_2O_4$	63.24	63.35	4.80	4.61	7.02	7.00
			1-Aryl-3-carbethoxy-4-cyano-5-phenylpyrazoles, XI						
XIa	C_6H_5	193	$C_{19}H_{15}N_3O_2$	72.99	72.75	4.32	4.12	12.88	12.61
XIc	p-$CH_3OC_6H_4$	130	$C_{20}H_{17}N_3O_3$	69.15	69.00	4.93	5.03	12.10	12.13
XId	p-ClC_6H_4	135	$C_{19}H_{14}ClN_3O_2$	65.64	64.62	4.17	4.05	11.58	11.68
			1-Aryl-3-benzoyl-4-cyano-5-phenylpyrazoles, XII						
XIIa	C_6H_5	190	$C_{23}H_{15}N_3O$	79.06	79.00	4.33	4.18	12.02	11.89
XIIc	p-$CH_3OC_6H_4$	210	$C_{24}H_{17}N_3O_2$	76.02	75.73	4.52	4.11	11.08	11.06
XIId	p-ClC_6H_4	227	$C_{23}H_{14}ClN_3O$	71.97	72.00	3.68	3.49	10.94	10.81

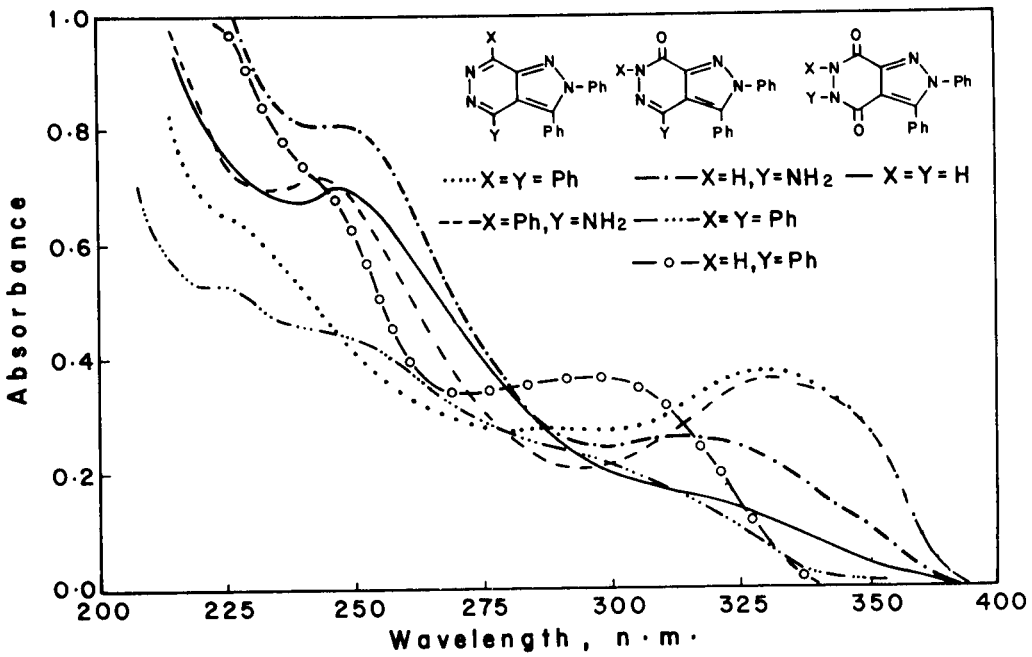
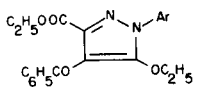


Fig. 1. Electronic absorption spectra of some substituted 2*H*-pyrazolo[3,4-*d*]pyridazine, 2*H*-pyrazolo[3,4-*d*]pyridazin-7(6*H*)-ones, and 2*H*-pyrazolo[3,4-*d*]pyridazine-4,7(5*H*,6*H*)dione in ethanol.

they exhibited a septet at δ 4.30 ppm (4H, J = 7 Hz) due to two overlapped quartets assignable to the 3- and 4-$COOCH_2CH_3$ groups. The spectra of IX in deuteriochloroform were relatively simple in their patterns as compared with that of VIII and X, they showed the characteristic signals due to the 3-$COOCH_2CH_3$ and aromatic protons. The data are summarized in Table 2.

Reaction of benzoylacetonitrile with III (X = Cl, Z = OC_2H_5) in ethanol in presence of sodium ethxodie yielded 1,5-diaryl-3-carbethoxy-4-cyanopyrazoles, XI.



XA

Similar treatment of III (X = Br, Z = C_6H_5) with sodium salt of benzoylacetonitrile in ethanol produced 1,5-diaryl-3-benzoyl-4-cyanopyrazoles, XIII. The structures of the products XI and XII have been identified by elemental analysis and their spectra (ir, uv, pmr). In particular XI and XII showed a band near 2240 cm^{-1} (C≡N). The uv absorption pattern was of typical pyrazole derivatives, Table 2.

When 3,4-diacylpyrazoles V to VII (8) were treated with hydrazine hydrate in refluxing ethanol, the corresponding 2*H*-pyrazolo[3,4-*d*]pyridazines XIII to XV were produced, respectively. The structures of these products, indicated by their preparative route and elemental analysis data, were supported by their spectral properties, Table 3. For example the ir spectra showed no carbonyl bands. Also, the location of the methyl group on a pyridazine carbon atom in XIII and XV was evidenced by the downfield shift (δ 2.50 and 2.97 ppm, respectively) of the signal for the acetyl group at C-4 in the corresponding pyrazoles V (δ 2.23 ppm) and VII (δ 2.53 ppm). The electronic absorption pattern of XIII to XV in ethanol was characterized by the presence of two intense bands (log ε > 4) in the 310-330 and 230-270 nm regions; whereas the starting pyrazoles V to VII showed a single absorption maximum in the 245-265 nm region. The data are given in Table 3.

Hydrazinolysis of VIII and IX gave XVII and XVIII respectively. The ir and uv spectra indicate that the latter products appear to have the keto structures XVII-A and XVIII-A (Scheme 2) rather than the hydroxy forms XVII-B and XVIII-B, respectively. For example, in their infrared they exhibited a sharp and strong band near 1690 cm^{-1} and a broad band in the region 3200-3170 cm^{-1}, assignable to CO and NH of a cyclic hydrazide group. The electronic absorption patterns of XVII and XVIII were also compatible with assigned structures. Thus, the uv absorption curve of XVIIIa, taken as an example of the series prepared, is reproduced in Fig. 1 together with that of compound XIX. The latter represents the fixed keto

Table 2

Compound No.	λ max (Ethanol) nm	δ (Deuteriochloroform) (multiplicity, assignment) (a)	CH_3CO	PhCO	ν (Potassium bromide) cm^{-1}	C = N	C ≡ N
		1-Aryl-3-carbethoxy-4-acetyl-5-pyrazoles, VIII					
VIIIa	278 (4.165)	2.70 (s, 4-$COCH_3$), 2.50 (s, 5-CH_3)	1675		1740	1617	
VIIIb	273 (4.372)	2.73 (s, 4-$COCH_3$), 2.35 (s, 5-CH_3)	1670		1735	1620	
VIIIc	283 (4.521)	2.60 (s, 4-$COCH_3$), 2.40 (s, 5-CH_3)	1670		1738	1615	
VIIId	280 (4.102)		1675		1740	1620	
		1-Aryl-3-carbethoxy-4-benzoyl-5-phenyl pyrazoles, IX					
IXa	250 (4.361)			1649	1740	1610	
IXb	240 (4.472)	2.40 (s, 1-p-CH_3Ar)		1645	1738	1616	
IXc	240 (4.531)	3.85 (s, 1-p-CH_3OAr)		1640	1740	1620	
IXd	245 (4.126)			1650	1742	1617	
		1-Aryl-3,4-dicarbethoxy-5-phenyl pyrazoles, X					
Xa	253 (4.160)	1.20 (quintet) (b), 6H, 3,4-(-$COOCH_2CH_3$)$_2$; 4.30 (septet) (c), 4H, 3,4-(-$COOCH_2CH_3$)$_2$			1725, 1700	1610	
Xd	256 (4.250)	1.23 (quintet) (b), 6H, 3,4-(-$COOCH_2CH_3$)$_2$; 4.30 (septet) (c), 4H, 3,4-(-$COOCH_2CH_3$)$_2$			1740, 1720	1615	
		1-Aryl-3-carbethoxy-4-cyano-5-phenyl pyrazoles, XI					
XIa	260 (4.589) sh, 233 (4.878)				1725	1617	2240
XIc	275 (4.451) sh, 245 (4.741)	3.85 (s, 1-*p*-CH_3OAr)			1725	1615	2235
XId	265 (3.759) sh, 237 (4.050)				1730	1610	2235
		1-Aryl-3-benzoyl-4-cyano-5-phenyl pyrazoles, XII					
XIIa	250 (4.040)			1660		1610	2240
XIIc	258 (4.550)	3.80 (s, 1-*p*-CH_3OAr)		1655		1610	2240
XIId	255 (4.480)			1655		1615	2240

(a) All compounds exhibit a multiplet signal in the 7.00-8.50 ppm region due to ArH protons. Compounds in series V, VI and VIII each showed a triplet at 1.10-1.45 (3H, J = 7 Hz, -OCH_2-CH_3) and a quartet at 4.0-4.2 (2H, J = 7 Hz, -OCH_2CH_3). (b) Two overlapped triplets. (c) Two overlapped quartets.

Table 3

Substituted 2*H*-pyrazolo[3,4-*d*]pyridazines

Compound No.	Substituents 2-Ar	7-Ar	M.p., °C	Molecular Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found	λ max (EThanol) (log ε) nm	δ (Deuteriochloroform) ppm (a)
3,4-Dimethyl-2,7-diaryl-2*H*-pyrazolo[3,4-*d*]pyridazines, XIII												
XIIIe	C_6H_5	p-$CH_3C_6H_4$	252	$C_{20}H_{18}N_4$	76.40	76.60	5.77	5.77	17.82	17.73	315 (4.14), 245 (4.30	2.33, 2.80, 2.73
XIIIb	p-$CH_3C_6H_4$	C_6H_5	214	$C_{20}H_{18}N_4$	76.40	76.13	5.77	5.91	17.82	17.72	320 (4.22), 270 (4.08)	2.26, 2.60, 2.73
XIIId	p-ClC_6H_4	C_6H_5	282	$C_{19}H_{15}ClN_4$	68.16	68.11	4.51	4.40	16.73	17.42	315 (4.12), 245 (4.37)	2.80 2.97
3,4-Diphenyl-2,7-diaryl-2*H*-pyrazolo[3,4-*d*]pyridazines, XIV												
XIVa	C_6H_5	C_6H_5	195	$C_{29}H_{20}N_4$	82.05	79.55	4.75	5.15	13.20	12.46	330 (4.29), 230 (4.50)	
XIVb	p-$CH_3C_6H_4$	C_6H_5	198	$C_{30}H_{22}N_4$	82.16	82.35	5.28	5.25	12.77	12.41	325 (4.30), 225 (4.55)	2.37
XIVd	p-ClC_6H_4	C_6H_5	208	$C_{29}H_{19}ClN_4$	75.89	75.90	4.17	4.21	12.20	12.05	327 (4.28), 225 (4.56)	
XIVe	C_6H_5	p-$CH_3C_6H_4$	200	$C_{30}H_{22}N_4$	82.16	82.05	5.28	5.22	12.77	12.74	335 (4.26), 240 (4.38)	2.43
XIVf	C_6H_5	p-BrC_6H_4	220	$C_{29}H_{19}BrN_4$	69.19	69.30	3.73	3.73	11.18	10.75	325 (4.46), 240 (4.57) sh	
3-Phenyl-4-methyl-2*H*-pyrazolo[3,4-*d*]pyridazines, XV												
XVa	C_6H_5	C_6H_5	226	$C_{24}H_{18}N_4$	79.53	79.41	5.00	5.12	15.46	15.51	317 (4.19), 230 (4.44)	2.50
XVb	p-$CH_3C_6H_4$	C_6H_5	240	$C_{25}H_{20}N_4$	80.41	80.33	5.39	5.44	15.00	15.06	315 (4.16), 250 (4.16) sh	2.26, 2.46
XVd	p-ClC_6H_4	C_6H_5	232	$C_{24}H_{17}ClN_4$	72.63	72.51	4.32	4.35	14.11	14.55	315 (4.22), 240 (4.43) sh	
XVe	C_6H_5	p-$CH_3C_6H_4$	232	$C_{25}H_{20}N_4$	80.41	79.51	5.39	5.40	15.00	14.89	323 (4.18), 232 (4.40)	2.44
XVf	C_6H_5	p-BrC_6H_4	242	$C_{24}H_{17}BrN_4$	65.31	65.05	4.16	4.34	13.62	13.56	323 (4.23), 232 (4.43)	
3-Phenyl-4-amino-2,7-diaryl-2*H*-pyrazolo[3,4-*d*]pyridazines, XVI (a)												
XVIa	C_6H_5	C_6H_5	304	$C_{23}H_{17}N_5$	76.01	75.98	4.71	4.70	19.27	19.30	330 (4.10), 297 (4.39	6.00 (b)

(a) ν (Potassium bromide) 3480, 3260, 3070 cm^{-1} (NH_2). (b) Broad.

tautomer of XVIIIa. It is obvious that both XIX and XVIIIa have identical spectra. This identity suggests that XVIII exists in the oxo form in solution of low dielectric constant.

Reaction of 4-cyanopyrazole derivatives XI and XII with hydrazine hydrate afforded products identified as XVI and XX, respectively. There are two possible tautomeric forms for XVI, whereas four tautomeric structures can be written for XX (Scheme 2). The ir spectrum of XVI in potassium bromide seems to be compatible with the amino form XVI-A rather than the imino structure XVI-B, as it revealed three bands at 3430, 3260 and 3070 cm^{-1} assignable to an NH_2 group. Furthermore, the uv spectrum of XVIa is similar to that of XIVa (Fig. 1) indicating that both XIVa and XVIa have similar chromophoric systems. The structure XVI-A was also supported by the appearance of a two protons broad signal at δ 6.00 in the pmr spectrum of XVIa in deuterated dimethylsulfoxide. The latter signal disappeared upon shaking the solution with deuterium oxide and a new peak due to the DOH proton resonance appeared at δ 4.50 ppm. The spectra of XX also indicate that they exist predominantly in the oxoamino form XX-A. The other tautomeric structures XX-B to XX-D seemed to be incompatible with the data obtained. As shown in Fig. 1 the absorption patterns of XIVa and XXa are quite similar. The slight bathochromic shift exhibited by the π-π* band of XXa might be due to the greater auxochromic effect of the 6-amino substituent as compared with the 6-phenyl group in XIVa. The same conclusion that XX is best represented by the aminooxo structure XX-A was reached from the infrared absorption. The appearance of bands at 3480, 3300 and 3200 (NH_2(and 1670 (CO) cm^{-1} in the spectra of XX lend support to the assigned strucuture.

When refluxed in hydrazine hydrate the pyrazoles X readily gave XXI. Theoretically each of the latter products can have four tautomeric structures namely: the dioxo form XXI-A, the dihydroxy form XXI-D and the two monohydroxymonooxo forms XXI-B and XXI-C. The spectral properties of the compounds prepared seem to be not in favour of both structures XXI-A and XXI-D. The ir spectra in potassium bromide showed, in each case, bands assignable to cyclic hydrazide CO (~1650 cm^{-1}) and broad band with some structure in the region 2500-3300 cm^{-1} corresponding to overlapped hydrogen bonded NH and OH groups. These data appear to be compatible with monohydroxy-monooxo structures XXI-B and XXI-C. The latter structure XXI-C is expected to be more stable than XXI-B because of the possible intramolecular hydrogen bonding. However, comparison of the uv spectra of XXIa with that of XXa in ethanol (Fig. 1) revealed that both compounds exhibited identical absorption pattern. This identity suggests that structure XXI-B is the predominant

Table 4

Substituted 2*H*-Pyrazolo[3,4-*d*]pyridazinones

Compound No.	2-Ar	M.p., °C	Molecular Formula	C, % Calcd.	C, % Found	H, % Calcd.	H, % Found	N, % Calcd.	N, % Found	λ max (Ethanol) (log ε) nm	ν (Potassium bromide) NH (OH)	ν (Potassium bromide) CO
XVIIa	C_6H_5	280-282	$C_{13}H_{12}N_4O$	64.98	65.04	5.03	5.29	23.32	23.58	283 (3.88), 233 (4.35)	3190	1665
XVIIb	*p*-$CH_3C_6H_4$	269.	$C_{14}H_{14}N_4O$	66.12	66.30	5.55	5.73	22.03	22.50	280 (4.08); 235 (4.50)	3200	1670
XVIIc	*p*-$CH_3OC_6H_4$	270-273	$C_{14}H_{14}N_4O_2$	62.21	62.16	5.22	5.42	20.73	20.88	277 (4.12); 245 (4.29)	3200	1670
XVIId	*p*-ClC_6H_4	278-280	$C_{13}H_{11}ClN_4O$	56.84	56.96	4.03	4.17	20.39	20.79	290 (4.00); 243 (4.51)	3190	1680
			3,4-Diphenyl-2-aryl-2*H*-pyrazolo[3,4-*d*]pyrodazin-7-(6*H*)ones, XVIII									
XVIIIa	C_6H_5	287-290	$C_{23}H_{16}N_4O$	75.80	75.77	4.42	4.57	15.37	15.47	300 (4.12), 245 (4.40) sh	3180	1680
XVIIIc	*p*-$CH_3OC_6H_4$	274-276	$C_{24}H_{18}N_4O_2$	73.08	72.88	4.60	4.72	14.20	14.58	290 (4.46), 253 (4.54)	3200	1670
XVIIId	*p*-ClC_6H_4	305	$C_{23}H_{15}ClN_4O$	69.26	68.77	3.79	3.89	14.04	14.16	300 (4.15), 250 (4.43)	3190	1675
			2-Aryl-3,4,6-triphenyl-2*H*-pyrazolo[3,4-*d*]pyridazin-7(6*H*)ones, XIX									
XIXa	C_6H_5	215	$C_{29}H_{20}N_4O$	79.07	78.90	4.57	4.50	12.72	12.67	300 (4.10) sh; 250 (4.42) sh		1690
			2-Aryl-3-phenyl-4-amino-2*H*-pyrazolo[3,4-*d*]pyridazin-7(6*H*)ones, XX									
XXa	C_6H_5	255	$C_{17}H_{13}N_5O$	67.09	66.68	4.30	4.22	23.01	22.97	315 (3.76), 250 (4.25)	3480, 3300 3200	1670
XXc	*p*-$CH_3OC_6H_4$	268-270	$C_{18}H_{15}N_5O_2$	64.85	64.56	4.53	4.50	21.09	21.00	325 (3.80), 260 (4.30)	3480, 3300 3200	1670
XXd	*p*-ClC_6H_4	298-301	$C_{17}H_{12}ClN_5O$	60.44	60.19	3.58	4.60	20.76	20.24	325 (3.72), 252 (4.30)	3480, 3240 3200	1680
			2-Aryl-3-phenyl-2*H*-pyrazolo[3,4-*d*]pyridazin-4,7(5*H*,6*H*)diones, XXI									
XXIa	C_6H_5	310	$C_{17}H_{12}N_4O_2$	67.09	67.08	3.97	4.18	18.41	18.74	315 (3.32) sh, 248 (4.32)	3200, 3050 2900	1640
XXIb	*p*-$CH_3C_6H_4$	303	$C_{18}H_{14}N_4O_2$	67.91	68.25	4.43	4.75	17.59	17.95	315 (3.66) sh, 250 (4.39)	3200-2500	1640
XXId	*p*-ClC_6H_4	314	$C_{17}H_{11}ClN_4O_2$	60.27	60.49	3.27	3.47	16.53	16.88	315 (3.79) sh, 251 (4.38)	3200, 3050 2900	1650

form in solution phase. The correctness of this monolactim form is also substantiated by the pmr data. Thus the spectra of XXIa and XXIb in deuterated dimethylsulfoxide revealed a broad signal near 11.07 ppm (1H), which disappeared upon shaking the solution with deuterium oxide and a new signal at δ 4.50 ppm due to DOH proton resonance appeared. The signal for an intramolecularly hydrogen bonded OH proton, as in structures of type XXI-C, usually appears at δ> 11.0 ppm (9). Judging from these results, it is not unreasonable to conclude that the pyrazolopyridazinediones prepared exist in the hydroxyoxo form XXI-B in solution phase. That the latter monolactim form is preferred is perhaps not surprising, this structure permits resonance stabilization in the way that Elvidge and Redman (10) has indicated for the related phthalhydrazide, assumption of the dilactim form XXI-D being unnecessary for attainment of aromaticity.

On the basis of the foregoing evidence the present author disagrees with the dihydroxy structure assigned earlier for the hydrazinolysis product of 1-phenyl-3,4-dicarbethoxypyrazole (2).

EXPERIMENTAL

Melting points were determined with an electrothermal melting point apparatus (Gallenkamp MF 550, England) and are uncorrected. The ir spectra (potassium bromide) were measured on a Pye-Unicam SP1000 spectrophotometer. Pmr spectra were recorded on a Varian T60-A spectrometer using tetramethylsilane as internal reference. Uv spectra were run on a Pye-Unicam SP8000 spectrophotometer. Elemental analyses were performed by Alfred Bernhardt Mikroanalytisches Laboratorium, West Germany.

The hydrazonoyl halides (III) used in the synthesis of the pyrazole derivatives (V to XII) were prepared by literature methods, their properties corresponded to data reported (8,11). The synthesis of 1-aryl-3,4-diacylpyrazoles V to VII has been described by the author in a recent report (8b).

Synthesis of Pyrazoles VIII to XII. General Procedure.

To an ethanolic solution of sodium ethoxide (prepared from sodium metal 0.11 g. (0.005 g.-atom) and 20 ml. of absolute ethanol) was added 0.005 mole of the appropriate active methylene compound. After stirring for 15 minutes at room temperature, the appropriate hydrazonoyl halide (0.005 mole) was added and stirring continued for 4-6 hours during which the hydrazonoyl halide dissolved and the product precipitated. The reaction mixture was left overnight at room temperature. In some cases dilution of the reaction mixture with water was necessary to precipitate the product. The crude product was collected, washed with water, dried and finally purified by crystallization from ethanol or acetic acid. The results are summarized in Table 1.

2*H*-Pyrazolo[3,4-*d*]pyridazines, XIII-XVI. General Procedure.

The appropriate pyrazole derivative (0.005 mole), ethanol (20 ml.) and hydrazine hydrate (0.015 mole) were refluxed for 6 hours, during which time the pyrazole dissolved and pyrazolopyridazine precipitated. The latter was collected, washed with water and purified by crystallization from acetic acid or dimethylformamide. The compounds prepared together with their physidal constants are listed in Table 3.

2*H*-Pyrazolo[3,4-*d*]pyridazinones, XVII-XXI.

These were prepared by the same general procedure described above without using ethanol; only the appropriate pyrazole derivative was refluxed in excess hydrazine hydrate.

2,3,4,6-Tetraphenyl-2*H*-pyrazolo[3,4-*d*]pyridazin-7(6*H*)one, XIXa, was prepared similarly from IXa and phenylhydrazine. Table 4 lists the compounds prepared and their physical properties.

EXPERIMENTAL AND NOTES

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