1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.26 (3 H, t, J = 7 Hz), 2.70–3.02 (2 H, m), 2.92 (3 H, s), 3.85 (3 H, s), 4.18 (2 H, q, J = 7 Hz), 4.46 (1 H, d, J = 8 Hz), 4.77 (1 H, s), 5.79 (1 H, dd, J = 8,2 Hz), 6.03 (1 H, br s), 6.64–6.99 (3 H, m), 11.81 (1 H, s, OH); calcd for $C_{20}H_{21}NO_5$ mol wt 355.142, found mol wt 355.144.

Ethyl 9-Methoxy-3-methyl-7-oxo-2,3,4,4a,5,6,7,7a-octahydro-1*H*-benzofuro[3,2-*e*]isoquinoline-6-carboxylate (22b). A mixture of **5b** (18.0 mg, 0.051 mmol) and PtO_2 (3.0 mg) in EtOH (20 mL) was hydrogenated to give **22b**: 18.2 mg (100%); oil; MS, m/z (relative intensity) 359 (M^+, 100), 313, 71, 70; IR (thin film) 1730, 1650, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.24 (t, J = 7 Hz, total intensity 3 H), 1.85–3.07 (m) and 2.47 (s) (total intensity 13 H), (s, total intensity 3 H), 4.16 (q, J = 7 Hz, total intensity 2 H), 4.83 and 4.99 (each s, total intensity 1 H, relative intensity 88:12), 6.72–7.17 (m, total intensity 3 H); calcd for $C_{20}H_{25}NO_5$ mol wt 359.173, found mol wt 359.171.

9-Methoxy-3-methyl-2,3,4,4a,5,6-hexahydro-1*H*-benzofuro[3,2-*e*]isoquinolin-7(7a*H*)-one (24). A solution of **22b** (323.4 mg, 0.901 mmol) in 6 N HCl (10.0 mL) was heated at reflux for 4 h. When cool, the reaction mixture was basified with 4 N NaOH and extracted with benzene. The extracts were washed once with brine, dried (Na_2SO_4), and evaporated to give **24** (175.1 mg, 68%) as an oil which solidified upon standing. The product is an 88:12 mixture of trans/cis ring junction stereoisomers.

The trans isomer (**24a**) was isolated by recrystallization from benzene/hexane, and an analytical sample was then sublimed: mp 139.5-140.0 °C; MS, m/z (relative intensity) 287 (M^+, 100); IR (KBr) 1720 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.49–2.99 (11 H, m), 2.43 (3 H, s), 3.89 (3 H, s), 4.42 (1 H, s), 6.78–7.09 (3 H, m). Anal. Calcd for $C_{17}H_{21}NO_3$: C, 71.03; H, 7.39; N, 4.88. Found: C, 70.97; H, 7.70; N, 4.84.

An analytical sample of the cis isomer (**24b**) was obtained by preparative TLC (5% MeOH/$CHCl_3$): MS, m/z (relative intensity) 287 (M^+, 100); IR (thin film) 1720, 1620 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.67–2.94 (11 H, m), 2.33 (3 H, s), 3.89 (3 H, s), 4.60 (1 H, s), 6.62–7.00 (3 H, m); calcd for $C_{17}H_{21}NO_3$ mol wt 287.152, found mol wt 287.153.

3-Methyl-5,6-dihydro-3*H*-benzofuro[3,2-*e*]isoquinolin-7(7a*H*)-one (30a). A solution of **5a** (65.5 mg, 0.202 mmol) in 6 N HCl (2.0 mL) was refluxed for 4 h. When cool, the reaction mixture was basified with 4 N NaOH and extracted with benzene. The extracts were washed once with 4 N NaOH/brine (1:1), dried (Na_2SO_4), and evaporated to give **30a**: 36.3 mg (71%); oil; MS, m/z (relative intensity) 253 (M^+), 197 (100), 196, 169; IR (thin film) 1720, 1680, 1610, 1600 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.22–2.87 (4 H, m), 2.97 (3 H, s), 4.43 (1 H, s), 4.50 (1 H, d, J = 8 Hz), 5.87 (1 H, dd, J = 8,2 Hz), 6.02 (1 H, br s), 6.82–7.17 (4 H, m); calcd for $C_{16}H_{15}NO_2$ mol wt 253.110, found mol wt 253.110.

9-Methoxy-3-methyl-5,6-dihydro-3*H*-benzofuro[3,2-*e*]isoquinolin-7(7a*H*)-one (30b). A solution of **5b** (111.2 mg, 0.313 mmol) in 6 N HCl (4.0 mL) was heated at reflux for 4 h. When cool, the solution was basified with 4 N NaOH and extracted with benzene. The extracts were washed once with 4 N NaOH/brine (1:1), dried (Na_2SO_4), and evaporated to give **30b**: 53.4 mg (60%); solid; mp 137–139 °C dec; MS, m/z (relative intensity) 283 (M^+), 227, 226 (100), 198; IR (KBr) 1720, 1680, 1610 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 2.10–2.77 (4 H, m), 2.95 (3 H, s), 3.89 (3 H, s), 4.42 (1 H, s), 4.45 (1 H, d, J = 8 Hz), 5.86 (1 H, dd, J = 8, 2 Hz), 5.92 (1 H, s), 6.56–6.97 (3 H, m); calcd for $C_{17}H_{17}NO_3$ mol wt 283.121, found mol wt 283.121.

Acknowledgment. This research was supported by funds from the National Institutes of Health (Grant No. DA-02708) and the N. L. Tartar Fund.

Registry No. 3b, 85891-87-8; **3c**, 87307-96-8; *syn*-**4b**, 85891-90-3; *anti*-**4b**, 85891-89-0; *syn*-**4c**, 87307-97-9; *anti*-**4c**, 87308-12-1; **5a**, 85891-88-9; **5b**, 87307-98-0; **6**, 118-93-4; **7a**, 31165-67-0; **7b**, 87307-77-5; **7b**-ol, 87307-78-6; **8a**, 87307-75-3; **8b**, 87307-80-0; **9a**, 85891-82-3; **9b**, 87307-79-7; **9b**-ol, 87307-81-1; **10a**, 85891-84-5; **10b**, 87307-82-2; **11a**, 85891-85-6; **11b**, 87307-83-3; **12a**, 87307-76-4; **13a**, 85891-86-7; **13b**, 87307-84-4; **14**, 87308-11-0; **15a**, 79263-63-1; **15b**, 87307-86-6; **16a**, 63755-30-6; **16b**, 87307-89-9; **16c**, 87307-92-4; **17a**, 64107-54-6; **17b**, 28447-17-8; **18a**, 87307-87-7; **18b**, 87307-90-2; **18c**, 87307-91-3; **19a**, 87307-85-5; **19b**, 87307-88-8; **19c**, 87307-93-5; **20a**, 87307-94-6; **20b**, 87307-95-7; **21** (isomer 1), 87335-02-2; **21** (isomer 2), 87335-03-3; **21** (isomer 3), 87335-04-4; **21** (isomer 4), 87335-05-5; *cis*-**22a**, 85923-12-2; *trans*-**22a**, 85891-92-5; *cis*-**22b**, 87307-99-1; *trans*-**22b**, 87335-06-6; **23a**, 85891-93-6; **23b**, 85923-13-3; **24a**, 79619-24-2; **24b**, 79647-01-1; **25**, 87308-01-8; **27**, 81115-40-4; **29b**, 87308-02-9; **30a**, 85891-94-7; **30b**, 87308-00-7; **31a**, 87308-04-1; **31b**, 87308-05-2; **31d**, 86610-21-1; **31d**·BH_3, 87307-74-2; **31e**, 87308-06-3; **31f**, 87308-07-4; **31g**, 87308-08-5; **31g**·MeI, 87308-09-6; **32**, 87308-10-9; **33**, 2011-06-5; $PhCH_2I$, 620-05-3; $CH_2(CO_2H)CO_2Et$, 1071-46-1; $BrCH_2CO_2Et$, 105-36-2; $ClCH_2CN$, 107-14-2; CH_2=C-HLi, 917-57-7; CH_2=CHMgBr, 1826-67-1; *o*-vanillin, 148-53-8; guaiacol, 90-05-1; chloromethyl ethyl ether, 3188-13-4; pyridine-3-carboxaldehyde, 500-22-1; malonic acid, 141-82-2; 3-(3-pyridyl)propenoic acid, 1126-74-5; 1-chloro-4-methoxy-2-butanone, 87308-03-0; 4-(2-hydroxyphenyl)pyridine, 86610-20-0; piperidine, 110-89-4; chloroacetyl chloride, 79-04-9; *N*-(chloroacetyl)piperidine, 1440-60-4; allyl bromide, 106-95-6.

Supplementary Material Available: Attempted preparation of and experimental data for **26**, **28a**, **29a**, and **30a** (7 pages). Ordering information is given on any current masthead page.

Aryl Coupling Reactions of Pyrazolo[3,4-*d*]pyrimidin-4-yl Radicals

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4-Arylpyrazolo[3,4-*d*]pyrimidines (**4**) were the subjects of a synthetic investigation in order to evaluate their biological activity. Attempts to prepare **4** from 4-aminopyrazolo[3,4-*d*]pyrimidines (**5**) via classical Gomberg–Bachmann–Hey aryl coupling conditions failed. Conversion of **5** to **4** was accomplished by diazotiazation of **5** using alkyl nitrites with an acid catalyst in aromatic solvents. Isomer distribution of the aryl-coupled products **4** was that predicted for a radical intermediate (ortho > meta ≃ para); isomer structures were assigned by a detailed ^{1}H NMR analysis. Unusual fragmentation products **17** and **18** were isolated during the course of investigations. These oxadiazoles probably arise from collapse of intermediate pyrazolo[3,4-*d*]pyrimidin-4-yl radicals **15**.

Recent reports of the interesting anxiolytic properties of compounds such as **1**,[1] **2**,[2] and **3**[3] led us to investigate preparation of related 4-arylpyrazolo[3,4-*d*]pyrimidines (**4**) as potentially active pharmaceutical agents. A straight-

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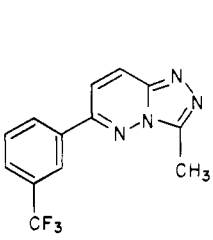
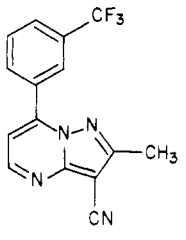


1



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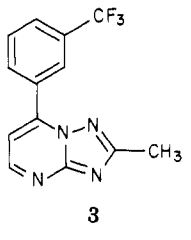
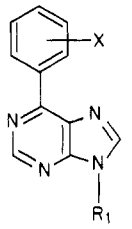


3

forward synthesis of **4** could be envisioned as a one-step Gomberg–Bachmann–Hey aryl coupling reaction[3] between readily available 4-aminopyrazolo[3,4-*d*]pyrimidines (**5**)[4] and a variety of aromatic solvents. This method would allow for specific control of the site for arylation as well as for the preparation of numerous analogues from only a few common radical intermediates. A similar approach to the preparation of **6**, the purine analogue of **4**, was recently reported.[5,6]

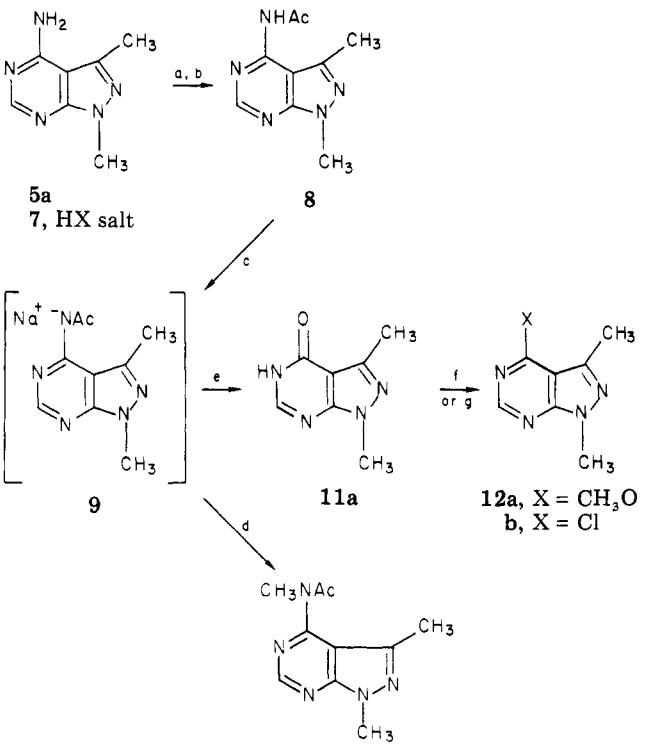


6

The difficulty of diazotization of amine derivatives of electron-deficient heterocyclic systems is well-documented,[7] but numerous examples of the nitrous acid hydrolysis of **5** to allopurinol derivatives exist.[8] Hydrolysis of **5** under these conditions is presumptive of the intermediacy of a short-lived diazonium salt. In our hands, however, attempts to diazotize **5a** by using aqueous nitrous acid, nitrosylsulfuric acid, or nitrosofluoroborate led to the immediate precipitation of **7** from the reaction medium with no subsequent reaction (Scheme I). Attempted diazotization of **5a** with *tert*-butyl thionitrate[9] also failed.

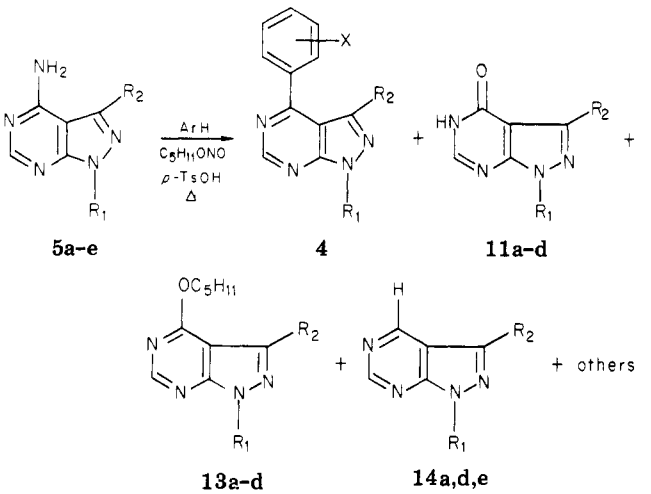
Since acetamides may be nitrosated/diazotized as an alternative to amines,[10] amine **5a** was converted to acetamide **8** via mild hydrolysis of an intermediate diacyl derivative (Scheme I). Although **8** did not react with nitrosyl chloride directly, lactam **11a** was formed in 80% yield when **8** was treated with sodium hydride in dimethylformamide and subsequently reacted with nitrosyl chloride (Scheme I). The intermediacy of anion **9** in this reaction was demonstrated by the addition of methyl iodide rather than nitrosyl chloride with the consequent formation of *N*-methylacetamide **10**. Methyl ether **12a** and chloro derivative **12b** were prepared from **11a** to confirm structural assignments. Since **11a** probably results from

Scheme I[a]



[a] (a) Ac_2O/pyr/Δ, (b) $NaHCO_3/H_2O$/EtOH, (c) NaH/DMF, (d) CH_3I/DMF, (e) NOCl/DMF or $PhCH_3$, (f) NaH/CH_3I/DMF, (g) $POCl_3$.

Scheme II[a]



[a] a, $R_1 = R_2 = CH_3$; b, $R_1 = CH_3$, $R_2 = H$; c, $R_1 = Ph$, $R_2 = H$; d, $R_1 = Ph$, $R_2 = CH_3$; e, $R_1 = PhCH_2$, $R_2 = CH_3$.

decomposition of an intermediate diazonium ion, reaction of anion **9** with nitrosyl chloride was repeated in toluene in an attempt to trap the intermediate via the desired aryl coupling reaction to give **4**. Unfortunately, lactam **11a** was the only isolable product under these conditions, albeit in slightly lower yield than in the previous experiment.

Aryl radicals may also be prepared from arylamines by the action of alkyl nitrites. The use of these diazotizing reagents to effect Gomberg-type arylations was reported more than 20 years ago.[11] More recently alkyl nitrites have been used to diazotize electron-deficient 6-aminopurines in order to prepare 6-deaminated-,[12a] 6-halo-,[12b] and 6-

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(3) For a recent review of aryl–aryl bond forming reactions see: Sainsbury, M. *Tetrahedron* **1980**, *36*, 3327.
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(8) See for example: Tang, K. V.; Delbarre, F. *C. R. Hebd. Seances Acad. Sci., Ser. C* **1969**, *268*, 525.
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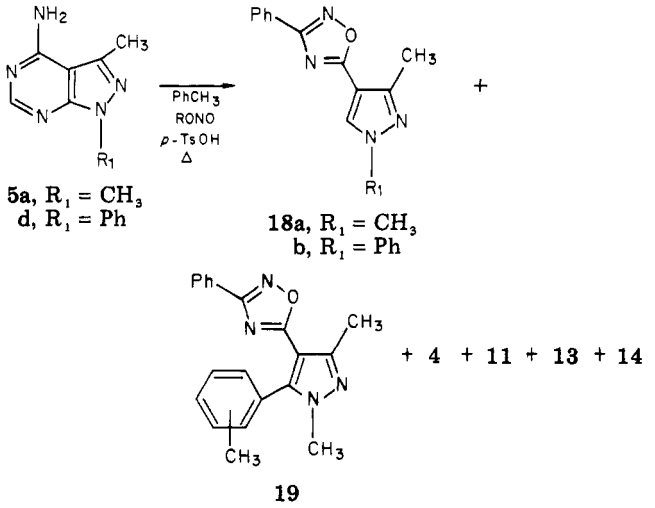
Table I. Isolated Products[a] from Diazotization of 5 (Scheme II)

expt	starting amine	aromatic solvent	% yield 4 (*o*/*m*/*p* ratio[b])	11	13	14	other	total yield, %
1	5a	$PhCH_3$	9 (2.5:1[c]:1.5)	22	0.3	6	11.5	49
2	5a	$Ph^{13}CH_3$	17 (2.25:1:1.75)	21			19	57
3	5a	$PhOCH_3$		6				6
4	5a	PhH	14	9	9			32
5	5a	PhCl	14 (3.5[d]:0:1)	42	2			58
6	5b	$PhCH_3$	39 (4[d]:2:1)	34				73
7	5b	$PhOCH_3$	37 (3.5:2:1)	43				80
8	5b	PhH	14	58	3			75
9	5b	PhCl	38 (3:2:0)	41				79
10	5c	$PhCH_3$	41 (3:2:0)	40	1.5			83
11	5c	$PhOCH_3$	27 (2:1:1)	42				69
12	5c	PhH	21	48				69
13	5c	PhCl	29 (3[d]:2:1)	51				80
14	5d	$PhCH_3$		15	2	17[e]	6	40
15	5d	$PhOCH_3$	17[f] (4:1:0)	16	2	12		47
16	5e	$PhOCH_3$	7 (1:0:0)			7[g]		18[h]
17	5e	PhH	16					20[h]

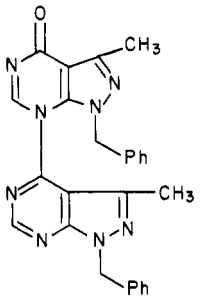
[a] Yields are reported for compounds isolated by chromatographic separations prior to the preparation of analytical samples. [b] Isomer structures were determined by ^1H NMR analysis (see Table II). [c] Unisolated isomer observed by ^1H NMR analysis of total isolated 4-arylation product. [d] Ratio of ortho product includes the expected substituted aryl product combined with product which further reacted to give 4'-nitrated byproduct (see Table II and Experimental Section). [e] See ref 13. [f] Isomeric product mixture could not be separated or further purified. [g] Product identified by ^1H NMR analysis without isolation. [h] See text and ref 14.

Scheme III



arylpurine[5] derivatives. When amines **5** were treated with isoamyl nitrite in refluxing aromatic solvents such as benzene, toluene, chlorobenzene, and anisole, a gradual disappearance of **5** with concomitant formation of several new products was observed (Scheme II). Because of the slow rates of reaction as well as the instability of isoamyl nitrite at these elevated reaction temperatures (85–140 °C), the reaction mixtures were periodically recharged with diazotizing reagent until amine **5** was completely consumed. While methanesulfonic and trifluoroacetic acids effectively catalyzed the reactions, *p*-toluenesulfonic acid produced the cleanest results and simplified product separation by dry column silica gel chromatography. The results of the diazotiazation of **5a–e** are summarized in Table I.

Some general observations concerning these results may be made. In almost all cases, lactam **11** formation was a significant side reaction which could not be prevented by scrupulous drying of solvents and reagents, by using an inert atmosphere, or by varying the catalysts. Consequently, most of the reactions reported were performed by using commercial solvents and reagents with no additional purifications. Because lactam **11** precipitated from the reaction mixtures upon cooling, it was easily separated from the crude reaction product prior to column chromatography. In experiments 16 and 17, the more soluble lactam product was not isolated. Ether **13** probably arose via trapping of the intermediate pyrazolo[3,4-*d*]pyrimidin-4-yl radical (**15**) by isoamyl alcohol. Deaminated



15

products **14** resulted from hydrogen radical abstraction by **15** in a manner analogous to the process reported for purines.[12a] As may be seen from Table I, **13** and **14** were formed in minor amounts and could be ignored for preparative purposes.

The desired arylation products **4** were isolated in moderate yields. The highest yields of these products were obtained from amines **5b** and **5c** (experiments 6–13) with a 3-hydrogen as compared to the 3-methyl derivatives **5a,d,e**. (experiments 1–5, 14–17). The lower yield of arylated products **4** in the latter cases was probably due to steric hindrance to the approach of the bulky aromatic reactants by the 3-CH_3 group. The effects of the 3-CH_3 substituent were evidenced in other ways. The total yields from reactions performed on **5a,d,e** were significantly lower than those for **5b,c**. In several of the these cases, "dimeric" products as measured by mass spectrometry were isolated in small amounts; in experiments 16 and 17, for example, compound **15** was isolated.[14] Lastly, in experiments 1, 2,

(12) (a) Nair, V.; Richardson, S. G. *Tetrahedron Lett.* **1979**, 1181. (b) Nair, V.; Richardson, S. G. *J. Org. Chem.* **1980**, *45*, 3969.

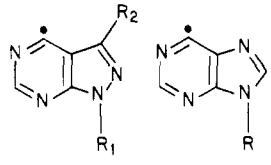
(13) Physical properties of 3-methyl-1-phenylpyrazolo[3,4-*d*]pyrimidine (**14d**): mp 73–74 °C; mass spectrum, *m*/*z* calcd for $C_{12}H_{10}N_4$ 210.0905, found 210.0910. Anal. Calcd C, 68.56; H, 4.79; N, 26.65. Found: C, 27.82; H, 4.97; N, 26.12.

and 14, compounds of vastly different structure were isolated (Table I, "other") which will be discussed later.

While mechanistic studies have not been attempted, several results support the radical character of this reaction. First, the yields of **4** were generally greater from substituted benzenes as compared to benzene itself (see experiments 6, 7, and 9 vs. 8). Second, isomer distribution of isolated 4-arylated products **4** (ortho > meta ≃ para) reflected the expected results for aryl radical coupling[15] (Table I). Isomer structural assignments for **4** were determined by ^{1}H NMR spectral properties, and selected chemical shifts are reported in Table II.

^{1}H NMR spectral features of **4** may be summarized as follows. When R_2 = H, the H_3 absorption appears between δ 8.00 and 8.40 when R_1 = alkyl and between δ 8.25 and 8.60 when R_1 = aryl. When R_2 = CH_3, this methyl signal occurs between δ 2.10 and 2.50 for R_1 = alkyl and between δ 2.30 and 2.50 for R_1 = aryl. The 4-aryl absorptions of **4** were difficult to analyze for several derivatives due to considerable overlap with other protons and could not be analyzed when R_1 = aryl (see 4-10*o*, 4-10*m*, and 4-11*o*). All 2′-substituted isomers had an upfield shift for H_3 or the 3-CH_3 (R_2) as compared to the 3′- or 4′-substituted derivatives (for example, see R_2 (δ) in Table III for 4-1*o* vs. 4-1*m* and 4-1*p*. This upfield shift also appeared for the 2′-CH_3 or the 2′-CH_3O signals for 4-1*o*, 4-6*o*, 4-7*o*, 4-10*o*, and 4-11*o* as compared to the 3′- and 4′-isomers. These upfield shifts presumably result from steric compression. It is also interesting to note that when R_2 = CH_3, the aromatic ring twists significantly out of planarity, with H_2′ and H_6′ shifted upfield as compared to similar compounds with R_2 = H (see 4-1*p* vs. 4-6*p*). The meta and para isomers were easily identified as a result of obvious symmetry differences. ^{13}C NMR spectral analysis of ^{13}C-enriched products 4-2 (experiment 2) confirmed the above product assignments.

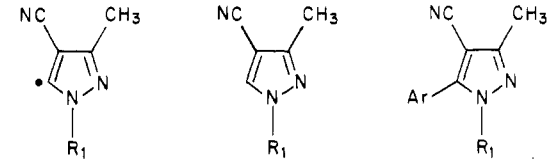
It may be concluded from this analysis that aryl coupling of in situ generated pyrazolo[3,4-*d*]pyrimidin-4-yl radical (**16**) with aromatic molecules occurs in the predicted



16 **17**

manner (ortho isomer predominant) regardless of steric constraints imposed by 3-substitution of the heterocycle. Thus, despite lower yields of 4-arylated products **4** for the 3-methyl vis-à-vis the 3-hydrogen systems, the ortho isomer remains the major product. This result is in stark contrast to that recently reported for the analogous purinyl radical **17** where no ortho-substituted aryl products were obtained.[5] The reason for these differences is obscure, but it is a priori difficult to believe that "steric effects" are more severe for **17** than for **16**.

We previously reported a remarkable fragmentation of **16** (R_1 = R_2 = CH_3) that occurred during the attempted aryl coupling of amine **5a** with toluene. (Scheme III; Table I, "other").[16] Oxadiazole fragmentation products **18a** and **19** represent a large portion of the isolated product (experiments 1 and 2).[16] These unusual products probably formed via fragmentation of radical **16** (R_1 = R_2 = CH_3) to radical **20a** and HCN. Reaction of **20a** either by hydrogen radical abstraction or by aryl coupling in the reaction medium would give either **21a** or **22a**, respectively. Long exposure of the solvent toluene to the oxidative reaction conditions could cause the formation of benzonitrile *N*-oxide which would react with **21a** or **22a** to give **18a** and **19**, respectively. A similar fragmentation product **18b** was isolated when amine **5d** was diazotized in toluene (experiment 14). In this case, no analogue of **19** was found, probably as a result of the steric bulk of the *N*-phenyl moiety of radical **20b** which could prevent the formation of **22b**. The structure of **18b**, was confirmed by comparison of its ^{13}C NMR spectrum with that of the previously reported[16] **18a** (Table III). This fragmentation presumably occurred during all the reactions in this report but was only observable in the cases where the toluene solvent allowed the trapping of **21** or **22** to give easily isolable oxadiazole products. In other cases, the 4-cyanopyrazoles may either have decomposed or were lost during the workup procedures.



20a, R_1 = CH_3 **21a**, R_1 = CH_3 **22a**, R_1 = CH_3
b, R_1 = Ph **b**, R_1 = Ph **b**, R_1 = Ph

A number of conclusions concerning the preparation of **4** and oxadiazole fragmentation products **18** and **19** may be drawn. Clearly, 3-methyl substitution (R_2 = CH_3) lowers the yield of **4** as compared to the results for 3-hydrogen substitution (see amines **5a** and **5d** vs. demethyl amines **5c** and **5d**). Presumably this is a consequence of steric hindrance to the approach of the aromatic solvent molecules to **15** by the 3-methyl moiety. Notice that formation of ether **13** and deaminated **14** is enhanced by these "hindered" radicals. Further, the unusual fragmentation products formed only from amines **5a** and **5d**.[18] This again is presumably the consequence of steric hindrance toward reaction of radical **16** which extends the lifetime of **16** and hence allows other modes of reaction to occur.

Finally, it is important to note that the purpose of these investigations was to prepare 4-arylpyrazolo[3,4-*d*]pyrimidines (**4**). In this regard we found a simple procedure to form and isolate the desired **4** (albeit as a difficultly separable mixture of isomers). Thus an easy one-step conversion of the readily available amines **5** to the 4-aryl derivatives **4** has allowed the preparation of a number of these derivatives for biological evaluation.

Experimental Section

Melting points were determined on a Mel-Temp capillary block apparatus and are uncorrected. All compounds are homogeneous

(14) A small amount (<4%) of **15** was collected: mp 265–266 °C; mass spectrum, *m/z* 462 (M^+); IR (KBr) 1715 cm^{-1}. Anal. Calcd for $C_{26}H_{22}N_8O$: C, 67.52; H, 4.79; N, 24.23. Found: C, 67.35; H, 5.02; N, 24.39.

(15) For discussions of isomer distribution as a result of radical attacks on aromatic systems see: (a) Fleming, I. "Frontiers Orbitals and Organic Chemical Reactions"; Wiley: New York, 1976; pp 191–194. (b) Augood, D. R.; Williams, G. H. *Chem. Rev.* **1957**, *57*, 123.

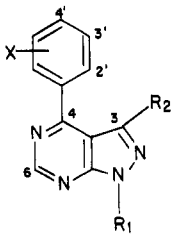
(16) Press, J. B.; Eudy, N. H.; Lovell, F. M.; Morton, G. O.; Siegel, M. M. *J. Am. Chem. Soc.* **1982**, *104*, 4013.

(17) Physical properties of 5-(3-methyl-1-phenyl-4-pyrazolyl)-3-phenyl-1,2,4-oxadiazole (**18b**): mp 119–120 °C. Mass spectrum, *m/z* calcd for $C_{18}H_{14}N_4O$, 302.1168, found 302.1168. Anal. Calcd C, 71.50; H, 4.68; N, 18.53. Found: C, 71.86; H, 4.61; N, 18.39.

(18) Oxadiazole products **18** and **19** may only form if benzonitrile *N*-oxide is present. As a consequence, these products may only arise when toluene (which is the precursor of benzonitrile *N*-oxide as shown by ^{13}C-enriched toluene experiments[16]) is used as the solvent.

(19) Higashino, T.; Iwai, Y.; Hayashi, E. *Yakugaku Zasshi* **1974**, *94*, 666.

Table II. Melting Points and Selected ^{1}H NMR Chemical Shifts for 4-Arylpyrazolo[3,4-*d*]pyrimidines (4)



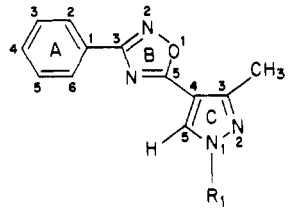
4

compd[a]	mp °C	R_1	R_2 (δ)[b]	X (δ)[b]	aromatic[b,c] H, shift, δ
4-1*o* (4-2*o*)	54-55[d]	CH_3	CH_3 (2.11)	2'-CH_3 (2.18)	7.32 (m)
4-1*m* (4-2*m*)		CH_3	CH_3 (2.43)	3'-CH_3 (2.43)	7.32 (m)
4-1*p* (4-2*p*)	96-98[d]	CH_3	CH_3 (2.41)	4'-CH_3 (2.45)	$H_{2',6'}$, 7.62 (d); $H_{3',5'}$, 7.36 (d)
4-4	100-102[d,e]	CH_3	CH_3 (2.48)	H (7.7)	7.7 (m)
4-5*o*	79-82[e]	CH_3	CH_3 (2.18)	2'-Cl	7.7 (m)
4-5*p*	99-102[e]	CH_3	CH_3 (2.42)	4'-Cl	7.5 (m)
4-5*o*-NO_2	146-150[d]	CH_3	CH_3 (2.20)	2'-Cl,4'-NO_2	$H_{6'}$, 7.64 (d); $H_{5'}$, 8.30 (dd); $H_{3'}$, 8.44 (d)
4-6*o*	80-81[e]	CH_3	H (8.00)	2'-CH_3 (2.40)	$H_{6'}$, 7.50 (m); $H_{3',4',5'}$, 7.37 (m)
4-6*m*		CH_3	H (8.35)	3'-CH_3 (2.47)	$H_{2'}$, 8.02 (d); $H_{6'}$, 7.95 (m); $H_{4',5'}$, 7.45 (m)
4-6*p*	95-96[d,e]	CH_3	H (8.35)	4'-CH_3 (2.49)	$H_{2',6'}$, 8.03 (d); $H_{3',5'}$, 7.39 (d)
4-6*o*-NO_2	160-161[e]	CH_3	H (8.00)	2'-CH_3 (2.52), 4'-NO_2	$H_{6'}$, 7.70 (d); $H_{5'}$, 8.23 (m); $H_{3'}$, 8.28 (m)
4-7*o*	66-68[e]	CH_3	H (8.09)	2'-CH_3O (3.90)	$H_{6'}$, 7.80 (d); $H_{3'}$, 7.10 (d); $H_{4'}$, 7.50 (m); $H_{5'}$, 7.15 (t)
4-7*m*	109-112[d,e]	CH_3	H (8.40)	3'-CH_3O (3.98)	$H_{2'}$, 7.75 (s); $H_{6'}$, 7.80 (m); $H_{4'}$, 7.17 (m); $H_{5'}$, 7.55 (t)
4-7*p*	112-114[d]	CH_3	H (8.36)	4'-CH_3O (3.95)	$H_{2',6'}$, 8.23 (d); $H_{3',5'}$, 7.10 (d)
4-8	116-118[e,f]	CH_3	H (8.34)	H (7.55)	$H_{2',6'}$, 8.15 (m); $H_{3',4',5'}$, 7.55 (m)
4-9*o*	86-88[e]	CH_3	H (8.07)	2'-Cl	7.5 (m)
4-9*m*	113-116[e]	CH_3	H (8.33)	3'-Cl	$H_{2'}$, 8.20 (d); $H_{6'}$, 8.06 (d); $H_{4',5'}$, 7.55 (m)
4-10*o*	95-98[e]	Ph	H (8.24)	2'-CH_3 (2.47)	*
4-10*m*		Ph	H (8.57)	3'-CH_3 (2.50)	*
4-11*o*	102-104[e]	Ph	H (8.30)	2'-CH_3O (3.96)	$H_{4',6'}$, 7.55 (m); $H_{3',5'}$, 7.16 (d)
4-11*m*	133-134[e]	Ph	H (8.59)	3'-CH_3O (4.01)	*
4-12	121-122[d,e,g]	Ph	H (8.60)	H (7.70)	$H_{2',6'}$, 8.30 (m); $H_{3',4',5'}$, 7.70 (m)
4-13*o*	90-95[d,e]	Ph	H (8.25)	2'-Cl	7.5 (m)
4-13*m*	127-128[e]	Ph	H (8.50)	3'-Cl	$H_{2'}$, 8.26 (d); $H_{6'}$, 8.05 (m); $H_{4',5'}$, 7.55 (m)
4-13*p*		Ph	H (8.46)	4'-Cl	*
4-13*o*-NO_2	114-117[d,e]	Ph	H (8.20)	2'-Cl,4'-NO_2	$H_{6'}$, 7.83 (d); $H_{3',4'}$, 8.40 (m)
4-15*o*		Ph	CH_3 (2.32)	2'-CH_3O (3.85)	$H_{3'}$, 7.12 (m); $H_{4'}$, 7.50 (m); $H_{5'}$, 7.17 (m); $H_{6'}$, 7.60 (m)
4-15*m*		Ph	CH_3 (2.50)	3'-CH_3O (3.90)	*
4-16*o*	85-86[e]	$PhCH_2$	CH_3 (2.19)	2'-CH_3O (3.76)	$H_{4',6'}$, 7.34 (d); $H_{3',5'}$, 7.04 (d)
4-17	102-103[e]	$PhCH_2$	CH_3 (2.40)	H (7.55)	$H_{2',6'}$, 7.75 (m); $H_{3',4',5'}$, 7.55 (m)

[a] Compound numbers were derived from compound 4 and the appropriate experiment number coupled with the *o*, *m*, or *p* designation for the proper isomeric assignment. Compounds 4-5*o*-NO_2, 4-6*o*-NO_2, and 4-13*o*-NO_2 all were formed as nitrated byproducts of 4-5*o*, 4-6*o*, and 4-13*o*, respectively. [b] Chemical shifts are in δ downfield from internal Me_4Si. [c] Proton assignments for 4-aryl substituent. Assignments for aryl protons for R_1 = phenyl or R_1 = benzyl are ignored. In some of these cases the aryl absorptions are ambiguous; specific data could not be derived, and these cases are marked with an asterisk. [d] Exact mass spectral analysis. [e] Combustion analysis for C, H, and N. [f] Lit.[19] mp 116-117 °C. [g] Lit.[19] mp 126-128 °C.

by thin-layer chromatographic analysis with Whatman K-5F or K-6F (5 × 10 cm) silica gel plates or Analtech alumina (5 × 20 cm) plates. ^{1}H and ^{13}C NMR measurements were determined by a Varian Associates CFT-20 spectrometer in deuteriochloroform with tetramethylsilane as an internal standard. The several procedures for the preparation of and isolation of 4-arylpyrazolo[3,4-*d*]pyrimidines (4) should be considered representative; the physical properties of compounds 4 not mentioned

Table III. ^{13}C NMR Chemical Shifts for 18a,b



18a, $R_1 = CH_3$

b, R_1 = 

ring carbon no.	shift[a] 18a[b]	18b[c]
A-1	127.1	127.0
A-2	128.8	128.8
A-3	127.5	127.5
A-4	131.0	131.1
A-5	127.5	127.5
A-6	128.8	128.8
B-3	168.3	168.4
B-5	171.5	171.3
C-3	149.6	150.8
C-4	106.1	108.2
C-5	132.8	129.2
D-1		139.1
D-2		119.4
D-3		129.6
D-4		127.4
D-5		129.6
D-6		119.4
C-CH_3	13.4	13.7
N-CH_3	39.1	

[a] Chemical shifts are in δ downfield from internal Me_4Si. [b] See ref 16. [c] See ref 17.

specifically in these examples are summarized in Table II.

4-Aminopyrazolo[3,4-*d*]pyrimidines (5). These compounds were prepared according to the procedures of Southwick et al.[4a] Compounds **5a–c** were identical with the literature materials.[20] 4-Amino-3-methyl-1-phenylpyrazolo[3,4-*d*]pyrimidine (**5d**) melted at 178–179 °C after recrystallization from methanol. Anal. Calcd for $C_{12}H_{11}N_5$: C, 63.98; H, 4.92; N, 31.09. Found: C, 63.69; H, 5.03; N, 31.20.

4-Amino-1-benzyl-3-methylpyrazolo[3,4-*d*]pyrimidine (**5e**) was recrystallized from ethanol; mp 182–183 °C. Anal. Calcd for $C_{13}H_{13}N_5$: C, 65.25; H, 5.47; N, 29.27. Found: C, 65.32; H, 5.48; N, 29.40.

***N*-(1,3-Dimethylpyrazolo[3,4-*d*]pyrimidin-4-yl)acetamide (8).** A solution of 4-amino-1,3-dimethyl-1*H*-pyrazolo[3,4-*d*]pyrmidine (**5a**; 15.0 g, 0.092 mol) in acetic anhydride/pyridine (2:1, 175 mL) was stirred for 18 h. The mixture was concentrated and extracted with methylene chloride (3 × 100 mL) and water (50 mL), and the combined organic layer was washed with 3 N hydrochloric acid (3 × 25 mL) and water (25 mL). Concentration of the dried (sodium sulfate) organic layer provided *N*-(1,3-dimethylpyrazolo[3,4-*d*]pyrimidin-4-yl)diacetamide, 15.52 g (68%). The analytical sample was prepared from methylene chloride–hexanes: mp 87–88 °C; IR (KBr) 1722, 1705 cm^{-1}; UV (EtOH) 210, 264, 300 nm; mass spectrum, *m/z* 247 (M^+); ^1H NMR δ 8.96 (s, 1 H, H-6), 4.12 (s, 3 H, NCH_3), 2.48 (s, 3 H, CCH_3), 2.34 (s, 6 H, $COCH_3$). Anal. Calcd for $C_{11}H_{13}N_5O_2$: C, 53.43; H, 5.30; N, 28.33. Found C, 53.22; H, 5.23; N, 28.71. A sample of this diacetate (7.75 g, 0.0314 mol) was dissolved in ethanol (310 mL) and treated with saturated sodium bicarbonate (78 mL). Water (200 mL) was added to redissolve inorganic precipitate, and the resultant solution was warmed to 41 °C overnight. Concentration (no heat) and extraction with methylene chloride (3 × 100 mL), drying of the organic layer (sodium sulfate), and evaporation gave 8 as a white solid, 3.87 g (60%). Recrystallization of the material from chloroform–hexanes gave purified product: 3.49 g (54%); mp 163–165 °C; IR (KBr) 1700 cm^{-1}; UV (EtOH) 213, 232 (sh), 262, 268, 294 nm; mass spectrum, *m/z* 205 (M^+); ^1H NMR δ 8.60 (br s, 1 H, NH), 8.58 (s, 1 H, H-6), 4.04 (s, 3 H, NCH_3), 2.64 (s, 3 H, CCH_3), 2.56 (s, 3 H, $COCH_3$). Anal. Calcd for $C_9H_{11}N_5O$: C, 52.67; H, 5.40; N, 34.13. Found: C, 52.47; H, 5.47; N, 34.38.

***N*-(1,3-Dimethylpyrazolo[3,4-*d*]pyrimidin-4-yl)-*N*-methylacetamide (10).** A solution of acetamide 8 (0.41 g, 0.002 mol) in dimethylformamide (5 mL) was treated with sodium hydride (0.096 g of a 50% suspension in mineral oil, 0.002 mol, prewashed with petroleum ether to remove the residual oil), and the suspension was stirred for 0.5 h. Methyl iodide (0.21 mL, 0.003 mol) was added, and the mixture was stirred 18 h. The reaction was quenched with water (5 mL) and extracted with chloroform (3 × 25 mL), and the organic layers were dried. Concentration gave the product as a white solid (0.40 g, 91%) which was recrystallized from chloroform–petroleum ether to give the analytical sample of **10**: 0.275 g (63%); mp 102–104 °C; IR (KBr) 1680 cm^{-1}; UV (EtOH) 215, 256, 271, 302 (sh) nm; mass spectrum, *m/z* 219 (M^+); ^1H NMR δ 8.83 (s, 1 H, H-6), 4.10 (s, 3 H, NCH_3), 3.45 (s, 3 H, N(Ac)CH_3), 2.56 (s, 3 H, CCH_3), 2.10 (s, 3 H, $COCH_3$). Anal. Calcd for $C_{10}H_{13}N_5O$: C, 54.78; H, 5.98; N, 31.95. Found: C, 54.68; H, 5.94; N, 32.00.

1,5-Dihydro-1,3-dimethyl-4*H*-pyrazolo[3,4-*d*]pyrimidin-4-one (11a). Acetamide 8 (0.82 g, 0.004 mol) was dissolved in dimethylformamide (10 mL) and treated with sodium hydride (1.0 g of 50% suspension, 0.021 mol, prewashed with petroleum ether) for 0.5 h. The resulting suspension was cooled to 0 °C and treated dropwise with a solution of nitrosyl chloride (1.44 g, 0.022 mol) in dimethylformamide (5 mL). After the mixture was stirred overnight, 5 N sodium hydroxide was added dropwise to pH 6–7, and the mixture was concentrated to dryness. The residue was dissolved in chloroform, dried, and crystallized by addition of petroleum ether to give **11a**: 0.58 g (81%); mp 253–254 °C. Recrystallization of the sample from ethanol gave white crystals, mp 268–270 °C (lit.[20] mp 276.5 °C).

4-Methoxy-1,3-dimethylpyrazolo[3,4-*d*]pyrimidine (12a). Compound **11a** (0.50 g, 0.0031 mol) in dimethylformamide (50 mL) was treated with sodium hydride (0.164 g of a 50% suspension, 0.0034 mol, prewashed with petroleum ether) and allowed to react 0.5 h. Methyl iodide (0.5 mL, excess) was added, and the reaction mixture was stirred for 1 h. Water (0.1 mL) was added, the reaction mixture was concentrated, and the residue was dissolved in chloroform. Ether **12** (0.42 g, 60%) was obtained after concentration. The analytical sample was prepared from chloroform–petroleum ether: mp 152–153 °C; UV (EtOH) 213, 254, 266 nm; mass spectrum, *m/z* 178 (M^+); ^1H NMR δ 7.88 (s, 1 H, H-6), 3.90 (s, 3 H, OCH_3), 3.54 (s, 3 H, NCH_3), 2.57 (s, 3 H, CCH_3). Anal. Calcd for $C_8H_{10}N_4O$: C, 53.92; H, 5.66; N, 31.44. Found: C, 53.96; H, 5.67; N. 31.13

4-Chloro-1,3-dimethylpyrazolo[3,4-*d*]pyrimidine. (12b). Compound **11a** (1.0 g, 0.0061 mol) was treated with phosphorus oxychloride (31 mL), and the mixture was refluxed for 3 h. Excess reagent was removed by distillation and the residue was cautiously quenched with ice–water. The product was collected by filtration and air-dried. This solid was dissolved in methylene chloride, passed through magnesium silicate, and concentrated to give a white solid, 0.77 g (69%). The analytical sample of **12b** was prepared from chloroform–petroleum ether: mp 105–106 °C; UV(EtOH) 217, 260, 291 nm; mass spectrum, *m/z* 182 (M^+); ^1H NMR ($CDCl_3$) δ 8.70 (s, 1 H, H-6), 4.06 (s, 3 H, NCH_3), 2.70 (s, 3 H, CCH_3). Anal. Calcd for $C_7H_7H_4Cl$: C, 46.04; H, 3.87; N, 30.68; Cl, 19.42. Found: C, 45.93; H, 3.97; N, 30.50; Cl, 19.40.

Diazotiazation of 4-Amino-1,3-dimethylpyrazolo[3,4-*d*]-pyrimidine (5a) in Toluene (Experiment 1). The following procedure is representative of reactions in this report. Amine **5a** (5.0 g, 0.031 mol) dissolved in toluene (75 mL, dried over 4-Å molecular sieves) was treated with *p*-toluenesulfonic acid (0.6 g, 0.0031 mol) and amyl nitrite (4.2 mL, 0.035 mol) and refluxed. Amyl nitrite (4.2 mL) was added every 2 h until TLC analysis revealed complete disappearance of **5a** (a total of 37.8 mL, 0.28 mol, of amyl nitrite was added).

The reaction mixture was cooled to 0 °C and filtered to collect lactam **11a** (1.1 g, 22%) which was identical with that prepared above. The filtrate was concentrated to an oil (10 g) which was

(20) Cheng, C. C.; Robins, R. K. *J. Org. Chem.* **1956**, *21*, 1240.

chromatographed on a silica gel dry column by using 50% ethyl acetate in hexanes containing ammonia as the eluant. Products isolated from this column in order of increasing polarity were as follows.

5-[1,3-Dimethyl-5-(methylphenyl)-1*H*-pyrazol-4-yl]-3-phenyl-1,2,4-oxadiazole (19). Oxadiazole **19** was collected as a mixture of ortho and meta isomers as previously reported;[16] 0.70 g (6.9%).

1,3-Dimethyl-4-(pentyloxy)-1*H*-pyrazolo[3,4-*d*]pyrimidine (13a). Ether **13a** was isolated and recrystallized from petroleum ether at −78 °C: 0.021 g (0.3%); white solid; mp 30–32 °C; UV (EtOH) 206, 245, 273 nm; mass spectrum, m/z calcd for $C_{12}H_{18}N_4O$ 234.1481, found 234.1476; ^1H NMR δ 8.50 (s, 1 H, H-6), 4.57 (m, 2 H, CH_2O), 4.05 (s, 3 H, CH_3N), 2.62 (s, 3 H, CH_3C), 1.7 (m, 6 H, CH_2), 0.95 (t, 3 H, CH_3). Anal. Calcd for $C_{12}H_{18}N_4O$: C, 61.51; H, 7.74; N, 23.91. Found: C, 61.31; H, 7.29; N, 23.37.

1,3-Dimethyl-4-(methylphenyl)pyrazolo[3,4-*d*]pyrimidine (4-1). The mixture of ortho, meta, and para isomers of (**4-1**) was isolated (0.65 g, 9%) and was further separated on alumina (activity grade II) with 5% acetone in hexanes as the eluant.

5-(1,3-Dimethyl-1*H*-pyrazol-4-yl)-3-phenyl-1,2,4-oxadiazole (18). Oxadiazole **18a** was collected as reported;[16] 0.35 g (4.7%).

1,3-Dimethylpyrazolo[3,4-*d*]pyrimidine (14a). Compound **14a** was obtained as a plae yellow oil: 0.27 g (6%); UV (EtOH) 215, 254, 283 nm; ^1H NMR δ 9.07 (s, 1 H, H-6), 9.00 (s, 1 H, H-4), 4.05 (s, 3 H, NCH_3), 2.37 (s, 3 H, CCH_3), mass spectrum, m/z calcd for $C_7H_8N_4$ 148.0750, found 148.0749.

Diazotization of 5a in ^{13}C-Enriched Toluene (Experiment 2). The above procedure was performed in 18% enriched toluene-^{13}C (prepared by diluting 1.15 mL of 90% toluene-*methyl*-^{13}C (KOR Isotopes) with 4.62 mL of toluene dried over 4-Å molecular sieves) by using 0.385 g (2.36 mmol) of **5a** and a 1.6 mL total volume of amyl nitrite added portionwise. Lactam **11a** (0.074 g, 21%) precipitated upon cooling. The filtrate was concentrated and chromatographed on 2-mm silica gel thick-layer plates with 50% ethyl acetate in hexanes as the eluant. ^{13}C-enriched **18** was the least polar compound: 0.0905 g (12%); mp 136–137 °C; spectral properties of the isomeric mixture were previously reported.[20] ^{13}C-enriched **14-1** (isolated as a 2.25:1:1.75 mixture of ortho/meta/para isomers) was isolated as a white solid, 0.095 g (17%). ^{13}C-enriched **18a** was the most polar material recovered from the silica gel and weighed 0.040 g (7%).

Diazotization of 5b in Chlorobenzene (Experiment 9). Amine **5b** (6.0 g, 0.040 mol), *p*-toluenesulfonic acid (0.77 g, 0.0040 mol), and isoamyl nitrite (5.5 mL, 0.041 mol) were refluxed in chlorobenzene (100 mL) for 24 h. Additional isoamyl nitrite (3 × 5.5 mL) was added portionwise every 4 h until TLC analysis revealed complete consumption of **5a** (total isoamyl nitrite added 0.164 mol).

Lactam **11b** precipitated from the reaction mixture upon cooling: 2.45 g (41%); mp 290–291 °C; UV (EtOH) 206, 250 nm; IR (KBr) 1680 cm^{-1}; mass spectrum, m/z 150 (M^+); ^1H NMR δ 12.11 (br s, 1 H, NH), 8.00 (s, 2 H, H-3, H-6), 3.95 (s, 3 H, NCH_3). Anal. Calcd for $C_6H_6N_4O$: C, 47.99; H, 4.03; N, 37.32. Found: C, 47.68; H, 4.09; N, 37.29. The filtrate was concentrated to a thick oil (7.66 g) and purified by using dry column silica gel chromatography as above. Only the bands corresponding to the aryl products **4-9** were analyzed. The least polar was **4-9*m***: 0.67 g (7%) (recrystallized from hexanes); UV (EtOH) 216, 257, 280 nm; mass spectrum, m/z calcd for $C_{12}H_9N_4Cl$ 244.0516, found 244.0524.

The ortho and meta isomers **4-9*o*** and **4-9*m*** were isolated as a 3:1 mixture from the silica gel (3.00 g, 30%) which was not further separated but crystallized from chloroform–hexanes: UV 213, 248, 277 nm.

Diazotization of 5c in Benzene (Experiment 12). Amine **5c** (6.55 g, 0.031 mol) dissolved in benzene (75 mL) was treated as before with *p*-toluenesulfonic acid (0.6 g, 0.0031 mol) and amyl nitrite (17 × 4.2 mL, 67.2 mL total) over a total of 3 days.

Lactam **11c** precipitated upon cooling (3.17 g, 48%) and was recrystallized from glacial acetic acid; mp 301–304 °C (lit.[14] mp 299 °C). The filtrate was concentrated to an oil and purified by silica gel dry column chromatography (20% ethyl acetate in hexanes containing ammonia as the eluant). The band corresponding to the desired arylation product **4-12** was extracted to give the product: 1.73 g (21%); mp 121–122 °C (recrystallized from chloroform–hexanes) (lit.[19] mp 126–128 °C; UV (EtOH) 204, 250 (sh), 263, 320 nm.

Isolation of Nitration Products. In several experiments (no. 5, 6, 13), the desired 4-arylpyrazolo[3,4-*d*]pyrimidines **4** reacted in the nitrating reaction medium to form nitration byproducts **4-5*o*-NO$_2$**, **4-6*o*-NO$_2$** and **4-13*o*-NO$_2$** in 2.1%, 2.6% and 1.8% yields, respectively. These products were isolated by silica gel dry column chromatography as more polar materials than the expected 4-aryl products.

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Registry No. **4-1*m***, 87412-56-4; **4-1*o***, 87412-57-5; **4-1*p***, 87412-58-6; **4-2*m***, 87412-59-7; **4-2*o***, 87412-60-0; **4-2*p***, 87412-61-1; **4-4**, 87412-62-2; **4-5*o***, 87412-63-3; **4-5*p***, 87412-64-4; **4-6*m***, 87412-65-5; **4-6*o***, 87412-66-6; **4-6*p***, 87412-67-7; **4-7*m***, 87412-68-8; **4-7*o***, 87412-69-9; **4-7*p***, 87412-70-2; **4-8**, 53645-68-4; **4-9*m***, 87412-71-3; **4-9*o***, 87432-47-1; **4-10*m***, 87412-72-4; **4-10*o***, 87412-73-5; **4-11*m***, 87412-74-6; **4-11*o***, 87412-75-7; **4-11*p***, 87412-76-8; **4-12**, 53645-78-6; **4-13*m***, 87412-77-9; **4-13*o***, 87412-78-0; **4-13*p***, 87412-79-1; **4-15*m***, 87412-80-4; **4-15*o***, 87412-81-5; **4-16**, 87412-82-6; **4-17**, 87412-83-7; **5a**, 5346-58-7; **5b**, 5334-99-6; **5c**, 5334-30-5; **5d**, 87412-84-8; **5e**, 87432-48-2; **8**, 87412-85-9; **10**, 87432-49-3; **11a**, 87412-86-0; **11b**, 5334-56-5; **11c**, 21314-17-0; **11d**, 87412-87-1; **12a**, 87412-88-2; **12b**, 87412-89-3; **13a**, 87432-50-6; **13b**, 87412-90-6; **13c**, 87432-51-7; **13d**, 87412-91-7; **14a**, 87412-92-8; **14d**, 52217-39-7; **14e**, 87412-93-9; **15**, 87412-94-0; **18a**, 82044-28-8; **18b**, 87412-95-1; **19*m***, 82044-27-7; **19*o***, 82044-26-6; **21a**, 87412-96-2; **21b**, 18093-92-0; **22a**, 87412-54-2; **22b**, 87412-55-3.