Reactions of phenyl-substituted heterocyclic compounds. VII. Reagent-dependent orientation in the nitration of 4-phenylpyrimidine[1,2]

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In the nitration of 4-phenylpyrimidine, the nature of the reaction products is strongly dependent upon the nitrating reagent. Mixed nitric and sulfuric acids yield 4-*o*- and 4-*m*-nitrophenylpyrimidines in the ratio 2:3, whereas nitric acid – trifluoroacetic anhydride yields 4-*o*-, 4-*m*-, and 4-*p*-nitrophenylpyrimidines in the ratio 45:29:26, and nitric acid – acetic anhydride yields 2,4-diacetoxy-1,3,5-trinitro-6-phenyl-1,2,3,4-tetrahydropyrimidine.

An explanation of these findings involves the possibility of the addition of nitronium ion at the heterocyclic nitrogen, followed in some circumstances by nucleophilic addition.

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INTRODUCTION

In nitrations of aromatic compounds, there are several examples of reagent-dependent orientation; nitric acid – sulfuric acid and nitric acid – acetic anhydride give differing product distributions in the nitrations of anisole (1), acetanilide (2) and substituted acetanilides (3, 4), 1-arylpyrazoles (5, 6), 3-phenylisoxazole (7), and quinoline (8). Many, but not all, of these results may be rationalized if the aromatic substrate reacts as the conjugate acid species in strongly acidic nitrating media (cf. refs. 5 and 6). The present paper is concerned with some extreme examples of reagent-dependent orientation in the reactions of 4-phenylpyrimidine (I) with various nitrating agents.

Our study was prompted by a previous report of the nitrations of arylpyrimidines (9), in which it was found that mixed acid (i.e. nitric and sulfuric acid) nitration of 2-phenylpyrimidine at 100° yielded 2-*m*-nitrophenylpyrimidine; 4-phenylpyrimidine, when treated similarly, yielded a 4-nitrophenylpyrimidine, m.p. 121–121.5°, thought to be the meta isomer. The apparently selective deactivation of the ortho and para positions appeared somewhat surprising, since nitration of the analogously substituted 2,4-dinitrobiphenyl leads to ortho–para nitration of the unsubstituted phenyl ring (10).

In our investigation of the nitration of 4-phenylpyrimidine, we used three nitrating reagents: (*a*) mixed nitric and sulfuric acids, (*b*) nitric acid – trifluoroacetic anhydride, and (*c*) nitric acid – acetic anhydride. Adsorption chromatography and gas–liquid chromatography were employed in the separation and analyses of the reaction products.

RESULTS

Reagents *a* and *b* above gave mixtures of 4-*x*-nitrophenylpyrimidines in excellent yields at room temperature; thus it is evident that the reaction conditions employed by Lythgoe and Rayner (9) were unnecessarily severe. Nitric acid – acetic anhydride did *not* effect substitution in the phenyl ring; the *pyrimidine* ring was attacked preferentially.

Adsorption chromatography of the reaction mixtures obtained from the mixed acid nitrations effected the separation of two isomeric 4-*x*-nitrophenylpyrimidines, which were identified as the ortho and

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[1]For part VI in this series, see B. M. Lynch and L. Shiu, Can. J. Chem. 43, 2117 (1965).

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TABLE I

Hückel molecular orbital quantities for 4-phenylpyrimidine*

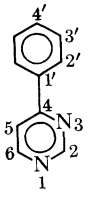
Position	π-Electron density	Localization energy†	Bond	Bond order
1	1.207	—	1–2	0.652
2	0.844	—	2–3	0.667
3	1.213	—	3–4	0.600
4	0.892	—	4–5	0.618
5	1.009	2.403	4–1′	0.375
6	0.879_5	—	5–6	0.679
1′	1.008	—	6–1	0.640
2′ (*o*)	0.981	2.458	1′–2′	0.617
3′ (*m*)	1.000_6	2.545	2′–3′	0.677
4′ (*p*)	0.984	2.507	3′–4′	0.660

*Energies of occupied orbitals (in β units): 2.366, 1.988, 1.440, 1.144, 1.000, and 0.807.
†For electrophilic substitution, in $-\beta$ units.

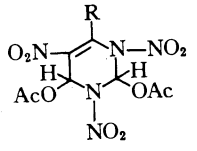
meta isomers, m.p. 67 and 123° (for evidence of structure, see the Discussion). Gas–liquid chromatographic analysis established the ratio of ortho to meta isomer as 40:60. No further products could be detected by adsorption chromatography or gas–liquid chromatography.

However, with the nitric acid – trifluoroacetic anhydride reagent, all three isomeric 4-*x*-nitrophenylpyrimidines were obtained; the para isomer had m.p. 190° (for evidence of structure, see the Discussion). Gas–liquid chromatography showed that the ratio of ortho to meta to para isomer was 45:29:26.

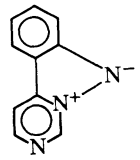
The treatment of 4-phenylpyrimidine with preformed acetyl nitrate (11) at room temperature yielded a compound, $C_{14}H_{13}N_5O_{10}$, m.p. 147°, which is formulated as 2,4-diacetoxy-1,3,5-trinitro-6-phenyl-1,2,3,4-tetrahydropyrimidine (II*a*) (for evidence of structure, see the Discussion). Similar treatment of 4-*o*-nitrophenyl- and 4-*m*-nitrophenyl-pyrimidine yielded the corresponding 6-*o*-nitrophenyl and 6-*m*-nitrophenyl derivatives II*b* and II*c*.



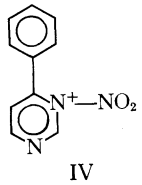
I



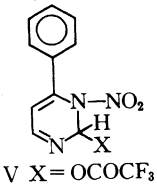
II*a* R = C_6H_5
II*b* R = *o*-$NO_2C_6H_4$
II*c* R = *m*-$NO_2C_6H_4$



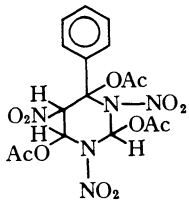
III



IV



V X = $OCOCF_3$ or OAc



VI

DISCUSSION

Evidence of Structure for the 4-x-Nitrophenyl-pyrimidines

Although it appeared likely that the three isomeric products obtained from the mononitration of 4-phenylpyrimidine were the expected ortho, meta, and para isomers, attack at the 5 position of the pyrimidine ring cannot be discounted. Hückel molecular orbital calculations, summarized in Table I, show that the 5 position is the carbon atom of highest π-electron density, and that the localization energy for electrophilic substitution is lowest for attack at the 5 position.

However, the proton magnetic resonance (p.m.r.) spectra of the isomers demonstrated that all three retained an intact 4-substituted pyrimidine fragment, although it was necessary to reduce the *m*-nitro compound to the corresponding amine, m.p. 131° (lit. m.p. 131° (9)), to resolve the signals from the pyrimidine 5 and 6 protons without interference from the aromatic protons in the meta-substituted phenyl group. The appropriate data are given in Table II, and it is evident that the pyrimidine ring proton chemical shifts are closely similar to those for the parent molecule, pyrimidine (12, 13).

TABLE II

Proton chemical shifts for pyrimidine ring protons in 4-phenylpyrimidine derivatives

4-Substituent	Solvent	Chemical shift (δ scale)			
		Proton 2	Proton 5	Proton 6	$J_{5,6}$ (Hz)
Phenyl	$CDCl_3$	9.22	7.36	8.62	5.2
	CF_3CO_2H	9.60	8.56	9.09	6.0
o-Nitrophenyl	$CDCl_3$	9.20	7.56	8.80	5.2
	CF_3CO_2H	9.67	8.36	9.31	6.0
m-Nitrophenyl	$CDCl_3$	9.32	ca. 7.7	ca. 8.8	
m-Aminophenyl	$CDCl_3$	9.23	7.62	8.70	5.0
	CF_3CO_2H	9.60	8.60	9.20	6.0
p-Nitrophenyl	CD_3COCD_3	8.97	7.85	8.58	5.0

Although the patterns observed for the chemical shifts of the nitrophenyl ring protons are too complex for first-order analysis, they are sufficiently characteristic to permit direct assignments of structure to each isomer. Thus, the four adjacent protons in 4-*o*-nitrophenylpyrimidine gave rise to a multiplet between 458 and 480 Hz downfield from tetramethylsilane in deuteriochloroform, whereas in trifluoroacetic acid a corresponding multiplet between 460 and 495 Hz, but showing maxima at 468.5, 472.5, 478.5, and 482.5 Hz, is found. We suggest that protonation of the pyrimidine ring renders the pyrimidine and nitro groups sufficiently similar in their magnetic effects to make the four protons form an A_2B_2 spin system. Since there are no discrete signals further downfield than ca. δ 8 from the nitrophenyl group protons, it appears highly likely that no protons are undergoing normal deshielding (ca. 1 p.p.m. (14)) by an *o*-nitro group. This is rationalized readily, since the adjacent nitro group and pyrimidine ring will suffer mutual displacements from coplanarity with the phenyl group, with resulting decreases in the deshielding effects normally associated with these substituents (for examples of shielding variations accompanying similar displacements of adjacent aryl and nitro groups, cf. ref. 6).

Unequivocal identification of the isomer of m.p. 67° as the ortho isomer was made by deoxygenation and ring closure effected by triethyl phosphite (cf. ref. 15), which yielded pyrimido(3,4-*b*)indazole (III). The structure of this product follows from the elemental analysis and molecular weight determination, from the absence of any NH absorption in its infrared spectrum, and from its p.m.r. spectrum in deuteriochloroform, which showed a one-proton singlet at δ 9.57 and a six-proton multiplet between 420 and 490 Hz. The low-field signal is assigned to the proton adjacent to the formal positive charge (compare the signals of the 2 proton for substituted 4-phenylpyrimidines in trifluoroacetic acid listed in Table II).

4-*p*-Nitrophenylpyrimidine, m.p. 190°, gave a four-proton p.m.r. signal at δ 8.07 (width at half-height, 6.0 Hz) (solvent acetone-d_6) from the nitrophenyl group. This behavior is to be expected if the chemical shifts induced by the nitro and 4-pyrimidyl substituents are of closely similar magnitudes, leading to virtual equivalence of all four protons; related examples showing similar behavior include 2-*p*-nitrophenyl-1,2,3(2*H*)-triazole (16) and 1,3-di(*p*-nitrophenyl)pyrazole (6).

The p.m.r. spectrum of 4-*m*-nitrophenylpyrimidine showed no readily resolvable pattern (solvent deuteriochloroform) in the region δ 7–9, but showed a multiplet from three protons between 525 and 535 Hz, a further multiplet from two protons between 493 and 507 Hz, and a further multiplet from one proton between 450 and 470 Hz. In addition, there is a one-proton singlet at δ 9.32. Of the seven protons in the molecule, the δ 9.32 signal is definitely from the 2 proton in the pyrimidine ring and, by analogy with the other 4-phenylpyrimidines in Table II, the 5 proton signal is to be expected around δ 7.50 and the 6 proton signal in the

δ 8.60–8.80 region. These expectations are confirmed from the p.m.r. spectrum of 4-*m*-aminophenylpyrimidine (Table II), and allow the conclusion that the three-proton multiplet between 525 and 535 Hz must contain a contribution from the 6 proton of the pyrimidine ring; the remaining two highly deshielded protons are those ortho to the nitro group. The two-proton multiplet between 493 and 507 Hz is then assigned to the protons meta and para to the nitro group, whereas the multiplet between 450 and 470 Hz is from the 5 proton of the pyrimidine ring.

Although further evidence is hardly necessary, the ultraviolet spectra of the three isomers show the expected (17) close resemblances to those of the correspondingly substituted 4-phenylpyridines. The spectrum of 4-*o*-nitrophenylpyridine shows λ_{max} 225 mμ (log ϵ 4.11), and of 4-*o*-nitrophenylpyrimidine λ_{max} 225 mμ (log ϵ 4.01). The spectrum of 4-*m*-nitrophenylpyridine gives λ_{max} 245 mμ (log ϵ 4.35), and of 4-*m*-nitrophenylpyrimidine λ_{max} 241 (log ϵ 4.00) and 267 mμ (log ϵ 4.11). The spectrum of 4-*p*-nitrophenylpyridine shows λ_{max} 282 mμ (log ϵ 4.21), and of 4-*p*-nitrophenylpyrimidine λ_{max} 287 mμ (log ϵ 4.26).

Evidence of Structure for the Tetrahydropyrimidine IIa

Structure II*a* for the compound $C_{14}H_{13}N_5O_{10}$ is assigned on the basis of the infrared and p.m.r. spectra. The p.m.r. spectrum in deuteriochloroform shows the following signals: two three-proton singlets at δ 2.10 and 2.16, a five-proton signal centered at δ 7.54 (peak width 8 Hz), and two one-proton singlets at δ 8.09 and 8.39. The two distinct three-proton signals fall in the region characteristic of acetyl methyl groups (cf. ref. 18), and the five-proton signal is assignable to a phenyl group. The compound shows strong infrared absorption at 1 750 and 1 775 cm^{-1}, and also at 1 270, 1 344, 1 520, and 1 590 cm^{-1}. The position of the high-frequency carbonyl peaks at 1 750 and 1 775 cm^{-1} is consistent with the assignment of the two acetyl methyl groups as *acetates*, and the presence of three nitro groups is evident from the elemental analysis data. The partial structure $C_6H_5C_4H_2N_2(NO_2)_3(OCOCH_3)_2$ follows, in which the nitro and acetate groups must occupy *five* sites on the pyrimidine portion of the molecule. This is accounted for by postulating the addition of acetyl nitrate as the species *nitronium acetate* across the 1,6 and 2,3 carbon–nitrogen bonds of the pyrimidine ring to yield *N*-nitro *C*-acetate species, consistent with the two different acetate signals in the p.m.r. spectrum and the two carbonyl stretching frequencies, and with the *N*-nitro infrared absorption at 1 270 and 1 590 cm^{-1} (cf. ref. 19). The remaining *C*-nitro group (infrared absorption at 1 344 and 1 520 cm^{-1}) is then assigned to the 5 position of the pyrimidine ring. (It is possible that the *C*-nitro group could be in the phenyl ring, but the position and sharpness of the five-proton peak in the p.m.r. spectrum rule against this; furthermore, analogues II*b* and II*c* of compound II*a* are obtained in an excellent yield by the acetyl nitrate treatment of 4-*o*- and 4-*m*-nitrophenylpyrimidines, and it seems improbable that these reactants would undergo substitution in the nitrophenyl rings.) The assignment of the two remaining proton signals is straightforward; the δ 8.09 signal corresponds to proton 6 and the δ 8.39 signal to proton 2 in the reactant (protons 4 and 2 in the product II*a*).

Interpretation of the Results

A consistent explanation of the results obtained with all three nitrating systems is possible if we propose that the initial act of a nitrating agent is the formation of an *N*-nitronium species IV (cf. refs. 20 and 21) at the nitrogen atom having the highest electron density (i.e. atom 3 (cf. Table I)). We suggest that this species is attacked by direct substitution at the meta position (a good analogy would be the nitration of benzyltrimethylammonium ion, which yields 88% of the meta isomer (22)). Although the localization energies of Table I indicate that the ortho and para positions will be favored, nitration proceeding through

species IV involves loss of the inter-ring conjugation assumed in the calculations; IV should be regarded as a benzene ring carrying a strongly electron attracting substituent, rather than as a modified 4-phenylpyrimidine. If species IV dissociates into nitronium ion and 4-phenylpyrimidine, then it would be most likely that the ortho position would be attacked, since this would be the most readily accessible sigma complex (compare Taylor's recent suggestion (23) postulating a related effect to account for predominant ortho substitution in biphenyl). In this way, we account for the observed ortho–meta orientation for the nitration of 4-phenylpyrimidine in sulfuric acid.

With nitric acid – trifluoroacetic anhydride, we suggest that species IV adds a trifluoroacetate ion to yield V, which now contains an aza-substituted phenylbutadiene residue (this should be an ortho–para orienting molecule (cf. ref. 24)). A combination of direct substitution in IV and attack on V explains the appreciable amounts of all three isomers formed with this reagent. Since the trifluoroacetate ion should be a good leaving group, it is suggested that the addition to give V is readily reversible.

A referee has suggested that the nitration in mixed acid will be more likely to proceed through the conjugate acid of 4-phenylpyrimidine than through species IV, and this possibility must be allowed. If 4-phenylpyrimidine is protonated at the 3 nitrogen (or at both the 1 and 3 nitrogens), and if the resultant solvation is sufficient to inhibit planarity and inter-ring conjugation, then the behavior of the protonated species should be similar to that postulated for IV. However, simple protonation *in itself* would not lead to a situation in which the localization energy would predict meta substitution, since, in the Hückel approximation, the order of localization energies (ortho < para < meta) does not change with increasing electronegativity. We consider that the formation of large amounts of the ortho isomer, with no detectable para isomer, is best explained by postulating species IV as the major precursor of 4-*o*-nitrophenylpyrimidine, although not necessarily of the meta isomer.

The referee also suggests that reaction in the nitric acid – trifluoroacetic anhydride medium may occur through the free base rather than by an addition–elimination route. Since this medium is effectively a solution of nitronium trifluoroacetate (trifluoroacetyl nitrate) in trifluoroacetic acid, it seems highly unlikely that nitronium ion would attack a ring carbon in preference to the pyrimidine nitrogen, and the p.m.r. spectra of 4-phenylpyrimidine in trifluoroacetic acid (Table II) indicate that the proportion of free base will be negligible under these reaction conditions.

An extension of this argument can be used to explain the results observed with acetyl nitrate (nitronium acetate in the present context). After the formation of V, further addition of nitronium acetate is proposed, leading to VI, which eliminates acetic acid on neutralization, to yield II*a*.

This interpretation is essentially the same as that used by Dewar and Maitlis (8) to explain reagent-dependent orientation in the nitration of quinoline; however, we have direct evidence of the addition of electrophilic species to heteroaromatic C—N bonds. Analogous addition products are to be expected from acetyl nitrate treatment of other diazines, and we are currently exploring this possibility.

EXPERIMENTAL

General

Microanalyses were carried out by the Schwarzkopf Microanalytical Laboratory, Woodside, New York. Melting points were measured on a Fisher–Johns apparatus, and are uncorrected. Infrared spectra were recorded on a Beckman IR-8 spectrophotometer; samples were examined as suspensions in potassium chloride disks. Ultraviolet absorption spectra refer to solutions in 95% ethanol, and were recorded on Hitachi Perkin–Elmer model 139 or Cary model 14 spectrophotometers. Proton magnetic resonance spectra were recorded with a Varian A-60A spectrometer. Signals are expressed in parts per million from tetramethylsilane, present as an internal reference (for singlets or completely analyzed multiplets), or in hertz (for multiplets which were not amenable to analysis). Gas–liquid chromatographic analyses were made on an Aero-

graph A-90P3 instrument with a thermal conductivity detector. Helium was used as the carrier gas, and the analytical column was 6 ft × ¼ in., 5% silicone SE-30 partitioning phase supported on 60–80 mesh Chromosorb P coated with dimethyldichlorosilane.

Starting and Reference Materials

4-Phenylpyrimidine, m.p. 64°, was a commercial sample (Aldrich Chemical Co.) which was homogeneous on gas–liquid chromatography at 190°. The various nitro-4-phenylpyridines were supplied by Miss G. Ho (25).

Nitrations

(a) With Nitric and Sulfuric Acids

4-Phenylpyrimidine (1.00 g) was dissolved in sulfuric acid (density 1.84, 3.3 ml) at 0°, a mixture of nitric acid (density 1.50, 1.6 ml) and sulfuric acid (density 1.84, 2.2 ml), cooled to 0°, was added, the reaction mixture was allowed to stand for 2 h and then poured into ice water, and the products were recovered by dichloromethane extraction of the resulting suspension. A typical sample of the resulting mixture of nitro-4-phenylpyrimidines weighed 1.20 g (93% yield). Several repetitions of this reaction sequence gave a series of mixtures which were treated as follows.

(*i*) The mixed nitro-4-phenylpyrimidines were crystallized from methanol. The first fraction obtained was 4-*m*-nitrophenylpyrimidine (0.32 g), m.p. 123° (lit. m.p. 121–121.5° (9)) (for the spectrometric data, see above).

Anal. Calcd. for $C_{10}H_7N_3O_2$: C, 59.70; H, 3.51. Found: C, 60.15; H, 3.92.

The second fraction (0.67 g) melted from 85 to 105°, and the mother liquor from this fraction was evaporated to dryness and extracted with dichloromethane. Concentration of the solvent yielded 4-*o*-nitrophenylpyrimidine (0.21 g), m.p. 67° (for the spectrometric data, see above).

Anal. Found: C, 60.09; H, 3.77.

(*ii*) The mixed nitro-4-phenylpyrimidines were dissolved in dichloromethane and chromatographed on a column of basic alumina with dichloromethane as eluent. The most readily eluted material was 4-*o*-nitrophenylpyrimidine, m.p. 67°.

(*iii*) The mixed nitro-4-phenylpyrimidines were dissolved in dichloromethane and analyzed by gas–liquid chromatography at a column temperature of 195° with a gas flow rate of 60 ml/min. Two peaks of area ratio 40:60 were observed at retention times of 3.0 and 5.0 min, and were identified as 4-*o*- and 4-*m*-nitrophenylpyrimidines by coincident retention times with the above samples and by trapping the material corresponding to each peak and comparing their infrared spectra with the above samples. Gas–liquid chromatography of synthetic mixtures of the two isomeric nitro-4-phenylpyrimidines showed that their molar responses were identical.

(b) With Nitric Acid – Trifluoroacetic Anhydride

4-Phenylpyrimidine (1.00 g) was dissolved in trifluoroacetic anhydride (12 ml) at 0°, nitric acid (density 1.50, 0.5 ml) was added, and the reaction mixture was set aside for 88 h. The solvent was removed under a reduced pressure and the residue was adjusted to pH 7 with dilute ammonia solution. The mixture of nitro-4-phenylpyrimidines was collected and dried (1.10 g), and was extracted with dichloromethane and chromatographed as in section *a* above. In addition to 4-*o*-nitrophenylpyrimidine, material with m.p. ca. 150° appeared in the most readily eluted material. Crystallization from methanol yielded 4-*p*-nitrophenylpyrimidine, m.p. 190° (lit. m.p. 184° (9)) (0.24 g) (for the spectrometric data, see above).

Anal. Found: C, 60.07; H, 4.04.

A further reaction mixture, obtained by dichloromethane extraction, was analyzed directly by gas–liquid chromatography at a column temperature of 200° with a gas flow rate of 60 ml/min. Three peaks were observed in the area ratio 45:29:26 (mean of several injections, deviation ±2%) with retention times of 2.2, 3.2, and 5.0 min, and were identified by trapping the material corresponding to each peak and comparing their infrared spectra, and by coincidence of retention times with 4-*o*-, 4-*m*-, and 4-*p*-nitrophenylpyrimidines. Gas–liquid chromatography of synthetic mixtures of the three isomers showed that the molar responses were identical.

(c) With Nitric Acid – Acetic Anhydride

4-Phenylpyrimidine (1.00 g) was dissolved in acetic anhydride (10 ml) at 0°, and treated with acetyl nitrate in acetic anhydride (generated from nitric acid (density 1.50, 3 ml) and acetic anhydride (8 ml) at 15–20°) at 0°. The reaction mixture was set aside for 24 h, poured onto ice, and neutralized with dilute ammonia solution. The mixture was extracted with dichloromethane, and the dichloromethane extract was concentrated and percolated through a basic alumina column, with dichloromethane as eluent. Evaporation of the eluate yielded 2,4-diacetoxy-6-phenyl-1,3,5-trinitro-1,2,3,4-tetrahydropyrimidine (1.05 g), which, after crystallization from methanol, had m.p. 147° (for the spectrometric data, see above).

Anal. Calcd. for $C_{14}H_{13}N_5O_{10}$: C, 40.88; H, 3.18; N, 17.03. Found: C, 40.74; H, 3.35; N, 16.94.

Similar treatment of 4-*o*-nitrophenylpyrimidine (0.4 g) yielded 2,4-diacetoxy-6-*o*-nitrophenyl-1,3,5-trinitro-1,2,3,4-tetrahydropyrimidine (0.3 g), m.p. 145–147° after crystallization from methanol.

Anal. Calcd. for $C_{14}H_{12}N_6O_{12}$: C, 36.85; H, 2.65; N, 18.42. Found: C, 37.65; H, 2.76; N, 18.10.

4-*m*-Nitrophenylpyrimidine (0.5 g) yielded 2,4-diacetoxy-6-*m*-nitrophenyl-1,3,5-trinitro-1,2,3,4-tetrahydropyrimidine (0.40 g), m.p. 161–162° after crystallization from methanol.

Anal. Found: C, 37.19; H, 3.00; N, 18.21.

Ring Closure of 4-o-Nitrophenylpyrimidine to Pyrimido(3,4-b)indazole

4-*o*-Nitrophenylpyrimidine (0.5 g) was heated under reflux with triethyl phosphite (10 ml) under a nitrogen atmosphere for 4 h, and triethyl phosphite and phosphate were removed under a reduced

pressure. The resulting mixture was chromatographed on neutral alumina, with benzene as eluent. Removal of the benzene left a pale-yellow solid, which was recrystallized from benzene to give almost colorless needles (0.18 g) of pyrimido(3,4-*b*)-indazole, m.p. 136–137°.

Anal. Calcd. for $C_{10}H_7N_3$: C, 70.99; H, 4.17; N, 24.84; mol. wt. 169. Found: C, 70.55; H, 4.04; N, 25.02; mol. wt. 180 (isothermal distillation method).

Molecular Orbital Calculations for 4-Phenylpyrimidine

The π-electron densities, bond orders, and orbital energies were evaluated on an IBM 1620 computer, with a Fortran II program modified from Klopfenstein (26). The localization energies for electrophilic substitution were evaluated by using an additional program which provided direct solutions of the secular polynomials for the residual conjugated systems (cf. ref. 27, p. 47). The input parameters were those of the simple Hückel method (27, p. 117), and the electronegativity parameter h for nitrogen was assigned a value of $+\frac{1}{2}$. Program listings and explanatory notes are available on request.

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