Metallation Studies with Pyrimidines

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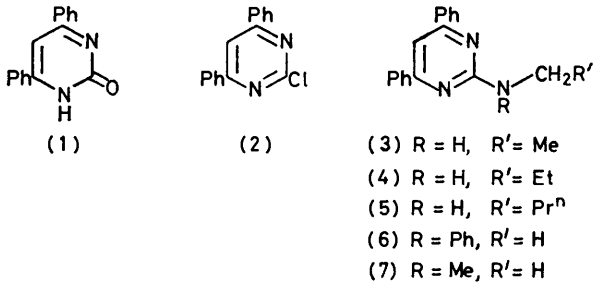
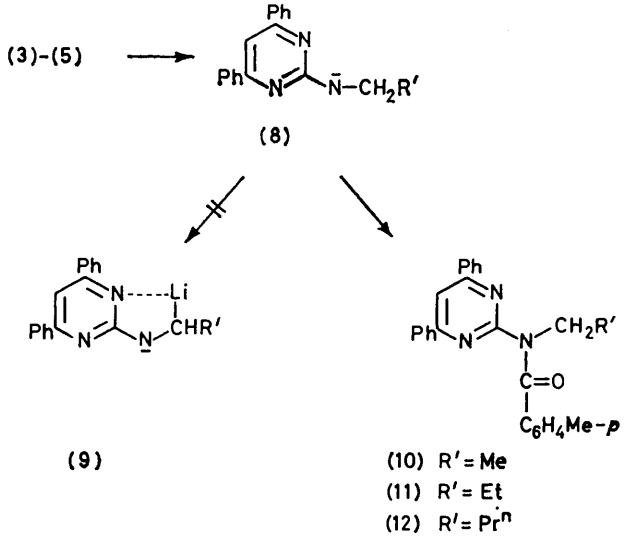
2-Alkylamino-4,6-diphenylpyrimidines are acylated only at nitrogen after treatment with lithium di-isopropylamide (LDA). 4,6-Diaryl-1-benzylpyrimidin-2(1*H*)-ones can be acylated and alkylated at the α-CH_2 group. 1-Methyl-4,6-di-*p*-tolylpyrimidin-2(1*H*)-one forms a carbanion which undergoes dimerisation.

As part of a larger study of heterocycle stabilised carbanions,[1] we have investigated pyrimidines: (a) 2-alkylamino-4,6-diphenylpyrimidines to attempt to generate carbanions of type (9), and (b) 1-substituted 4,6-diphenylpyrimidin-2(1*H*)-ones to examine carbanions of type (18).



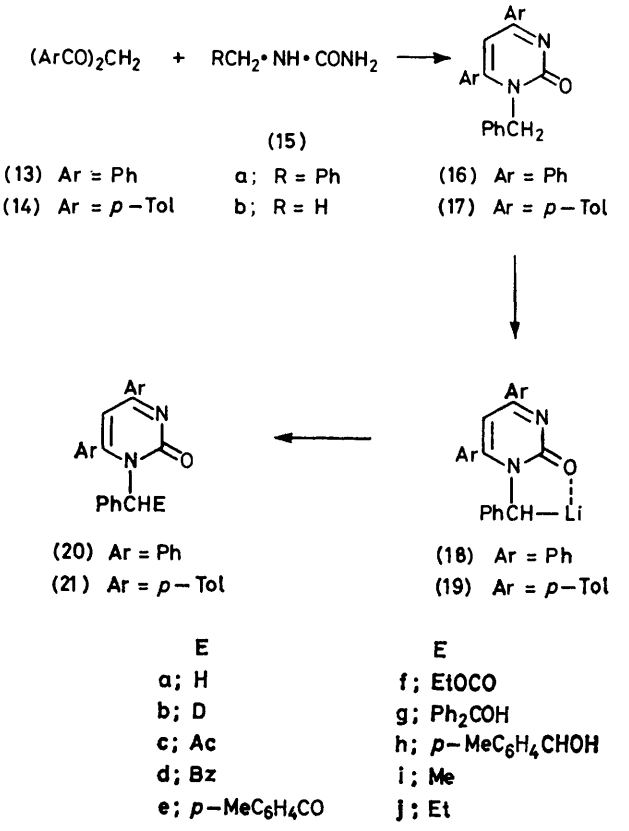
(1) (2) (3) R = H, R′ = Me; (4) R = H, R′ = Et; (5) R = H, R′ = Pr^n; (6) R = Ph, R′ = H; (7) R = Me, R′ = H



(8) (9) (10) R′ = Me; (11) R′ = Et; (12) R′ = Pr^n

SCHEME 1

2-*Alkylaminopyrimidines*.—4,6-Diphenylpyrimidin-2(1*H*)-one (1) is converted by phosphoryl chloride into 2-chloro-4,6-diphenylpyrimidine (2).[2] This reacts readily with primary and secondary amines (ethylamine, n-propylamine, n-butylamine, and *N*-methylaniline) to give the corresponding 2-alkylaminopyrimidines (3)—(6) (Table 1). The analogous 2-dimethylamino-derivative (7) was obtained by ring synthesis from dibenzoylmethane and *NN*-dimethylguanidine. Structures of all the compounds were confirmed by their spectral data (Table 2).



(13) Ar = Ph; (14) Ar = *p*-Tol; (15) a; R = Ph, b; R = H; (16) Ar = Ph; (17) Ar = *p*-Tol; (18) Ar = Ph; (19) Ar = *p*-Tol; (20) Ar = Ph; (21) Ar = *p*-Tol

E: a; H, b; D, c; Ac, d; Bz, e; *p*-MeC_6H_4CO; f; EtOCO, g; Ph_2COH, h; *p*-MeC_6H_4CHOH, i; Me, j; Et

SCHEME 2

Treatment of the 2-alkylamino-4,6-diphenylpyrimidines (3)—(5) with lithium di-isopropylamide (LDA) gave the mono-anion (8), but not the dianion (9): subsequent treatment with *p*-toluoyl chloride yielded amides (10)—(12) (Table 3). Structures were confirmed by their spectral data (Table 4): in particular the low ν(C=O) excludes the possibility that the acyl group is attached to a cyclic nitrogen atom. Use of excess LDA mainly gave the known [3] *NN*-di-isopropyl-*p*-toluamide.

4,6-*Diaryl*-1-*benzylpyrimidin*-2(1H)-*ones*.—The diaroylmethanes (13) and (14) reacted with benzylurea (15a) to give the 4,6-diaryl-1-benzylpyrimidin-2(1*H*)-

TABLE 1

Preparation of 2-alkylamino-4,6-diphenylpyrimidines (3)—(7)

No.	R	R′	M.p. (°C)	Yield (%)	Crystal form	Cryst. solvent	Found (%) C	H	N	Required (%) C	H	N
(3)	H	Me	66—68	49	Needles	EtOH	78.2	6.1	15.1	78.5	6.2	15.3
(4)	H	Et	96—99	51	Prisms	EtOH	78.7	6.7	14.5	78.9	6.6	14.5
(5)	H	Pr^n	58—61	58	Plates	EtOH	78.8	6.8	13.7	79.2	7.0	13.8
(6)	Ph	H	147—147.5	91	Fine needles	95% EtOH	81.8	5.8	12.4	81.9	5.7	12.5
(7)	Me	H	131.5—132.5	30	Prisms	EtOH	78.5	6.0	15.2	78.5	6.2	15.3

TABLE 2

I.r. [a] and ^{1}H n.m.r. (δ, 60 MHz) [b] spectral data of 2-alkylamino-4,6-diphenylpyrimidines (3)—(7)

No.	R	R′	I.r. NH (cm^{-1})	N.m.r. —N— R	—CH_2—	—R′		Aromatic
(3)	H	Me	3 280	5.35 (1 H, bm)	3.65 (2 H, qn)	1.33 (3 H, t)		7.8 (11 H, m)
(4)	H	Et	3 250	5.4 (1 H, bm)	3.5 (2 H, q)	1.5 (2 H, m)	1.0 (3 H, t)	7.8 (11 H, m)
(5)	H	Pr^n	3 280	5.9 (1 H, t)	centred at 3.35 (2 H, bm)	0.9 (3 H, d)	1.4 (4 H, m)	7.8 (11 H, m)
(6)	Ph	H			3.68 (3 H, m)			7.12—7.68 (12 H, m) 7.9—8.20 (4 H, m)
(7)	Me	H			3.34 (6 H, s)			7.36—7.66 (7 H, m) 8.17—8.2 (4 H, m)

[a] In $CHBr_3$. [b] In $CDCl_3$. s = singlet, bm = broad multiplet, t = triplet, q = quartet, qn = quintet, m = multiplet.

TABLE 3

Preparation of *N*-alkyl-*N*-(4,6-diphenylpyrimidinyl)-*p*-toluamides (10)—(12)

No.	R′	M.p. (°C)	Yield (%)	Cryst. form	Cryst. solvent	Found (%) C	H	N	Required (%) C	H	N
(10)	Me	128—132	60	Needles	Ether–light petroleum (b.p. 60—80 °C)	78.9	5.6	10.6	79.4	5.9	10.7
(11)	Et	135—138	55	Prisms	EtOH	79.4	6.4	10.3	79.6	6.2	10.3
(12)	Pr^n	91—94	37	Needles	95% EtOH	79.5	6.5	9.9	79.8	6.5	10.0

TABLE 4

I.r. [a] and ^{1}H n.m.r. (δ, 60 MHz) [b] spectral data of *N*-alkyl-*N*-(4,6-diphenylpyrimidinyl)-*p*-toluamides (10)—(12)

No.	R′	I.r. (cm^{-1}) >=O	N.m.r. *p*-Toluoyl	N-CH_2—	—R′		Aromatic
(10)	Me	1 655	2.27 (3 H, s)	4.42 (2 H, m)	1.4 (3 H, t)		7.4 (15 H, m)
(11)	Et	1 650	2.25 (3 H, s)	4.35 (2 H, t)	centred at 1.9 (2 H, m)	1.05 (3 H, t)	7.5 (15 H, m)
(12)	Pr^n	1 650	2.28 (3 H, s)	4.37 (2 H, t)	1.0 (3 H, t)	1.65 (4 H, m)	7.5 (15 H, m)

[a] In $CHBr_3$. [b] In $CDCl_3$. s = singlet, m = multiplet, t = triplet.

ones (16) and (17) (*cf.* ref. 4). We have shown previously that 1-benzyl-4,6-diphenyl-2(1*H*)-pyridone (22) is converted by LDA into the lithio-derivative (23) which reacts with electrophiles to form α-substituted products (24). We now find that lithio-derivatives (18) and (19) can be formed similarly; they show an intense blue colouration.

The diphenyl carbanions (18) and (19) react with D_2O to form the deuteriated pyrimidinones (20b) and (21b). Organolithium (18) adds to a variety of electrophiles to form products (20c—j); methyl and ethyl iodide gave the alkylated derivatives (20i) and (20j); ethyl chloroformate the ester (20f); acetyl, benzoyl, and *p*-toluoyl chloride the ketones (20c), (20d), and (20e); *p*-tolualdehyde and benzophenone the hydroxy-derivatives (20h) and (20g). Organolithium (19) reacted with methyl iodide to give the alkylated derivative (21i). All the compounds were characterised by their spectral data (Table 5).

1-*Methyl*-4,6-*di*-p-*tolylpyrimidin*-2(1H)-*one*.—Reaction

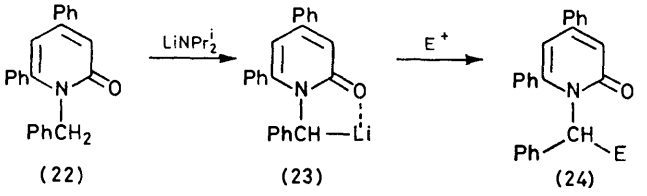
TABLE 5

I.r. [a] and ^{1}H n.m.r. (δ, 60 MHz) [b] spectral data of 4,6-diaryl-1-benzylpyrimidin-2-ones (20) and (21)

		I.r. (cm^{-1})			^{1}H N.m.r.				
			R						
No.	Alpha substituent	Pyridone C=O	OH	C=O	5-H (s)	1′-H	R		Aromatic (m)
(20a)	H	1 645			6.70	5.2 (s)			7.52—7.05 (15 H)
(20b)	D	1 650			6.70	5.2 (s) [c]			7.05—7.52 (15 H)
(20c)	MeCO	1 640		1 680	6.42	*d*		2.3 (s)	6.80—7.82 (16 H)
(20d)	PhCO	1 650		1 700	6.80	6.65 (s)			7.2—8.3 (20 H)
(20e)	*p*-MeC_6H_4CO	1 650		1 690	6.72	*d*		2.28 (s)	7.0—8.2 (20 H)
(20f)	EtOCO	1 650		1 740	6.40	6.30 (s)	4.0 (m)	1.1 (t)	6.98—7.9 (15 H)
(20g)	Ph_2COH	1 650	3 250		6.16	6.0 (s)			6.74—7.3 (25 H)
(20h)	*p*-MeC_6H_4CHOH	1 650	3 300		6.50	5.86 (d) [c]	5.45 (d) [c]	2.24 (s)	7.0—8.0 (14 H)
(20i)	Me	1 650			6.90	5.5 (q)		1.6 (d)	7.2—7.8 (15 H)
(20j)	Et	1 655			6.50	5.9 (m)	1.2 (m)	0.7 (t)	6.9—7.9 (15 H)
(21a) [f]	H	1 650			6.60	5.2 (s)			7.9—7.1 (13 H)
(21b) [f]	D	1 655			6.60	5.15 (s) [c]			7.0—8.0 (13 H)
(21i) [f]	Me	1 650			6.50	5.4 (q)		1.75 (d)	7.85—7.05 (13 H)

[a] In $CHBr_3$. [b] In $CDCl_3$. d = doublet, q = quartet, s = singlet, t = triplet, m = multiplet. [c] Integrates for 1 H. [d] Overlapped in the aromatic region. [e] CH, doublet (*J* 10 Hz). [f] In addition two singlets (3 H each) are shown at 2.3 and 2.4 p.p.m.

of *N*-methylurea (15b) with (14) yielded 1-methylpyrimidinone (25) which formed a deep red colouration with LDA; subsequent addition of electrophiles then merely gave recovered (25). Attempted use of n-butyllithium as base afforded the addition product (30), which shows ν(NH) 3 200 cm^{-1} and ν(C=O) 1 650 (broad).

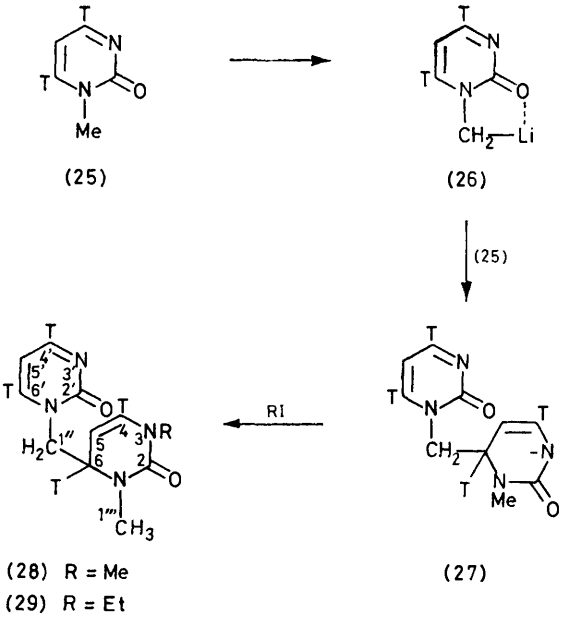


(22) (23) (24)

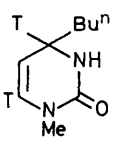
In the ^{1}H n.m.r., the n-butyl group signals occur at 0.84 (3 H, t), 1.3 (4 H, m), and 1.82 p.p.m. (2 H, m). The *C*-methyls resonate as two 3-H singlets near to 2.8 p.p.m. The heterocyclic ring olefinic hydrogens form a 2 Hz split doublet at 4.87 p.p.m. coupled (*J* 2 Hz) with the N–H proton (broad doublet at 5.74 p.p.m.). These spectral data appear to support a 1,2-addition to C=N to give (30) rather than 1,4-addition to C=C–C=N to give an isomer, but we have not rigorously excluded the isomeric structure. Sodium borohydride reduces pyrimidin-2-ones to dihydro- and tetrahydro-derivatives,[5] and this provides an analogy for the formation of (30).

However, reaction of (25) with 2,2,6,6-tetramethylpiperidyl-lithium (LTMP) followed by methyl iodide formed (28) by a 1,6-addition of the lithio-derivative (26) to a second molecule of (25) to give anion (27). Similarly addition of ethyl iodide produced (29).

The structures (28) and (29) are based on spectral evidence: both (28) and (29) showed ν(C=O) (pyrimidinone) at 1 650 cm^{-1} (broad). In the ^{1}H n.m.r. spectra, the ring proton of the undisturbed pyrimidinone ring in (28) gave a singlet at δ 6.56 (5′-H) and at δ 6.62 in (29) (5′-H). The corresponding signal in the pyrimidinone (25) was at δ 6.64. In the modified pyrimidinone ring of (28) and (29), the 5-H signal shifted upfield, resonating as a singlet at δ 4.54 and 4.56 respectively. The prochiral protons of the bridging methylene group were magnetically non-equivalent and gave an AB system in both compounds. In (28) the A-proton appeared at δ 4.75 and the B-proton at δ 5.34 with J_{gem} 12 Hz. Similarly in (29) the A-proton appeared at δ 4.76 and the B-proton at δ 5.41 with J_{gem} 14 Hz. In (28) and (29) the *N*-methyl group (1‴ protons) gave a singlet at δ 1.70; in (28) the incorporated methyl gave a singlet at δ 2.5 and in (29), the diastereotopic methylene protons of the incorporated



T = *p*—tolyl



(30)

SCHEME 3

ethyl formed two sextets at δ 3.10 and δ 3.90 with J_{vic} 7 Hz and J_{gem} 14 Hz. The methyl group displayed a triplet at δ 0.78 p.p.m. The aromatic protons in both (28) and (29) displayed a multiplet in the range δ 8.0—7.0.

In the ^{13}C n.m.r. spectra, with off-resonance C–H information, for both (28) and (29), the undisturbed pyrimidinone carbonyl carbon gave a singlet at δ 169.19 and at 169.23 respectively [*cf.* 169.31 in (25)] whilst the modified pyrimidinone carbonyl resonated at δ 160.27 and 160.12. The aromatic carbons displayed a series of lines in the range 159.68—126.55 (Table 6). The 5 and 5′ ring carbons gave doublets at δ 105.30 and δ 103.60 in (28) and at δ 105.20 and δ 103.84 in (29) [*cf.* 102.44 in (25)]. In the aliphatic region, the bridging methylene carbon gave a triplet at $\delta_{av.}$ 48, the 6-quaternary carbon a singlet at $\delta_{av.}$ 67, and the *N*-methyl, a quartet at $\delta_{av.}$ 30 (Table 6). The inserted methyl in (28) gave a quartet at δ 33.08 whilst in (29), the inserted ethyl gave a triplet at δ 39.27 and a quartet at 14.96. The *C*-methyl group gave 4 quartets in the range δ 21.50—20.90 (Table 6).

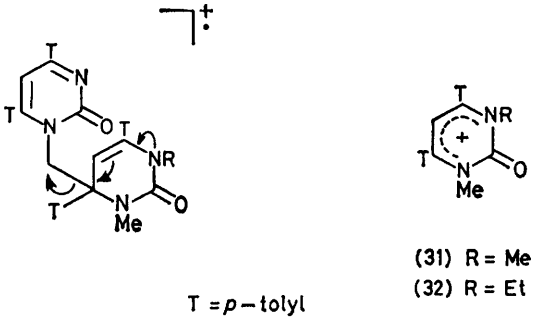
TABLE 6

^{13}C N.m.r. spectra [a] of 1,3-disubstituted 1,2,3,6-tetrahydro-6-(1,2-dihydro-2-oxo-4,6-di-*p*-tolylpyrimidinylmethyl)-4,6-di-*p*-tolylpyrimidin-2(1H)-ones (28) and (29)

Compd. no.	Carbonyl region (s) 2-CO	2′CO	Aromatic region Unassigned multiplet	Olefinic region 5-C (d)	5′-C (d)		Aliphatic region 6C (s)	1″-C (t)	1″′-C (q)	Aryl-CH_3 (q)				3-N-R	
(28)	169.19	160.27	159.68—126.64	105.30	103.60	(28)	67.15	48.53	30.35	21.48	21.38	21.28	20.91	33.08 (q)	
(29)	169.23	160.12	159.39—126.55	105.20	103.84	(29)	67.73	48.04	30.26	21.50	21.39	21.19	20.90	39.27 (t)	14.96 (q)

[a] In $CDCl_3$ with $SiMe_4$ as internal reference.

High-resolution mass spectroscopy showed the molecular ion peak at *m/e* 594.29 (0.12%) for (28) and at 608.31 (0.05%) for (29). Both (28) and (29) underwent a retrosynthetic expulsion of the oxopyrimidinylmethyl fragment to give the observed base peaks at *m/e* 305.16 (100%) (31) and 319.17 (100%) (32) respectively.



(31) R = Me
(32) R = Et

EXPERIMENTAL

M.p.s were measured on a Reichert hot-stage melting point apparatus and are uncorrected. I.r. spectra were recorded in $CHBr_3$ on a Perkin-Elmer 297 spectrophotometer, ^1H n.m.r. spectra on Perkin-Elmer R12 (60 MHz) and Varian HA-100 (100 MHz) n.m.r. spectrometers, ^{13}C n.m.r. spectra at 25.05 MHz on a Jeol FX-100 Fourier transform spectrophotometer, and high-resolution mass spectra on an AEI MS-9 spectrometer.

4,6-Diphenylpyrimidin-2-one (1).—Dibenzoylmethane (5 g, 22.3 mmol), urea (2.0 g, 33.4 mmol), toluene-*p*-sulphonic acid (5.75 g, 33.4 mmol), and glacial HOAc (15 ml) were heated under reflux for 48 h and neutralised with aqueous NaOH (12%). The product separated; it was collected, washed with water, dried, and crystallised (EtOH) (m.p. 237—239 °C) (4.20 g, 15%) [lit.,[2b] m.p. 237—239 °C].

2-Chloro-4,6-diphenylpyrimidine (2) (47%), had m.p. 113—113.5 °C [lit.,[2a] m.p. 115—116 °C].

General Procedure for the Preparation of 2-Amino-4,6-diphenylpyrimidines (3)—(6).—2-Chloro-4,6-diphenylpyrimidine (2) and the appropriate amine were heated under reflux in absolute EtOH for 2 h. [For the preparation of (3), dry $EtNH_2$ gas was bubbled through a solution of (2) in absolute EtOH and for (6), the reactants were heated in the absence of absolute EtOH]. Evaporation (100 °C/15 mmHg) gave the crude product, which was washed with water and crystallised (see Table 1).

2-Dimethylamino-4,6-diphenylpyrimidine (7).—Dibenzoylmethane (1 g, 4.46 mmol), *NN*-dimethylguanidine, HCl (1 g, 8.16 mmol), and K_2CO_3 (0.6 g, 4.3 mmol) were heated under reflux in EtOH (10 ml) for 2 h then extracted with CH_2Cl_2 (50 ml) and the extracts washed with H_2O (20 ml). The dried ($MgSO_4$) extracts on evaporation (100 °C/15 mmHg) furnished the product, which was crystallised (see Table 1).

General Procedure for the Preparation of Amides (10)—(12).—To LDA (1 mmol) in dry THF (5 ml) [prepared by adding dropwise n-butyl-lithium in hexane (1 mmol) to di-isopropylamine (1 mmol) at 0 to −5 °C under N_2] cooled to 0 to −5 °C was added 2-alkylaminopyrimidine (3)—(5) (0.5 mmol) in dry THF (2 ml). After 0.5 h at 0 to −5 °C, *p*-toluoyl chloride (1 mmol) in dry THF (2 ml) was added. Stirring was continued for a further 4 h at 20 °C, water (5 ml) was then added and the solution extracted with CH_2Cl_2 (30 ml); the extracts were washed with aqueous $NaHCO_3$ (10%, 10 ml) followed by H_2O (10 ml). The dried (Na_2SO_4) extracts on evaporation (100 °C/15 mmHg) gave the crude product as a yellowish oil which solidified slowly and crystallised from the appropriate solvent (Table 3). Purification of the mother-liquor afforded *NN*-di-isopropyl-*p*-toluamide as the by-product, m.p. 84 °C [lit.,[3] m.p. 85—86 °C] as colourless plates [toluene–light petroleum (b.p. 40—60 °C)].

1-Benzyl-4,6-diphenylpyrimidin-2(1H)-one (20a).—Dibenzoylmethane (5.0 g, 20 mmol), benzylurea (4.8 g, 32 mmol), and toluene-*p*-sulphonic acid (7.6 g, 40 mmol) in glacial HOAc (8 ml) were heated at reflux for 36 h. Cooling and treatment with aqueous (50%) EtOH gave the *pyrimidinone*

which crystallised from 95% EtOH as prisms (5.0 g, 68%), m.p. 164—165 °C (Found: C, 81.3; H, 5.4; N, 8.3. $C_{23}H_{18}N_2O$ requires C, 81.6; H, 5.3; N, 8.3%).

1-*Benzyl*-4,6-*di*-p-*tolylpyrimidin*-2(1H)-*one* (21a).—Di-*p*-toluoylmethane (1.0 g, 4 mmol), benzylurea (0.95 g, 6 mmol), and toluene-*p*-sulphonic acid (1.4 g, 7 mmol), in HOAc (1 ml) were heated at reflux for 36 h. Work-up as described for (20a) gave the *pyrimidinone* (21a) (0.9 g, 62%) as needles from 95% EtOH, m.p. 209—210 °C (Found: C, 81.9; H, 6.1; N, 7.6. $C_{25}H_{22}N_2O$ requires C, 82.0; H, 6.0; N, 7.6%).

1-*Methyl*-4,6-*di*-p-*tolylpyrimidin*-2(1H)-*one* (25).—Di-*p*-toluoylmethane (5.0 g, 19 mmol), methylurea (3.1 g, 40 mmol), and toluene-*p*-sulphonic acid (7.2 g, 37 mmol) in HOAc (9 ml) were heated at reflux for 36 h. Work-up as described for (20a) gave the *pyrimidinone* (25) (3.5 g, 61%) as needles from 95% EtOH, m.p. 197—199 °C (Found: C, 78.7; H, 6.3; N, 9.6. $C_{19}H_{18}N_2O$ requires C, 78.6; H, 6.2; N, 9.6%); $\nu_{max.}$ ($CHBr_3$) 1 645 cm^{-1} (C=O); δ ($CDCl_3$) 7.98—7.22 (8 H, m), 6.70 (1 H, s), 2.40 (3 H, s), 2.39 (3 H, s), and 3.40 (3 H, s).

General Procedure for the Lithiation and Alkylation of 4,6-*Diaryl*-1-*benzylpyrimidin*-2(1H)-*ones*.—LDA (3.0 mmol) was prepared by adding dropwise di-isopropylamine (0.3 g, 3.0 mmol) to n-butyl-lithium in hexane (3.1 ml, 3.0 mmol of 0.96M) at −20 °C under N_2. Stirring of the mixture was continued until it became cloudy when dry THF (6 ml) added; the whole was then cooled to −76 °C and 4,6-diaryl-1-benzylpyrimidin-2-one (3.0 mmol) in dry THF (20 ml) was added. After 40 min at −76 °C, the electrophile (3.0 mmol) in dry THF (5 ml) was added. Stirring was continued for 1 h at −76 °C and for a further 10 h at 20 °C. Water (1 ml) was then added and the solvent removed at 40—50 °C/20 mmHg. The residue in CH_2Cl_2 (70 ml) was washed with saturated aqueous NaCl (30 ml) and water (30 ml) and then dried (Na_2SO_4), and evaporated at 40—50 °C/20 mmHg. The product was separated by crystallisation [$CHCl_3$–light petroleum (b.p. 60—80 °C)], or prep. t.l.c. and further recrystallised from the appropriate solvent.

The following compounds were prepared according to the general procedure: 1-(α-*deuteriobenzyl*)-4,6-*diphenylpyrimidin*-2(1H)-*one* (20b) (90%), prisms from EtOH, m.p. 160—161 °C (Found: C, 81.5; N, 8.2. $C_{23}H_{17}DN_2O$ requires C, 81.4; N, 8.2%); 1-(α-*acetylbenzyl*)-4,6-*diphenylpyrimidin*-2(1H)-*one* (20c) (48%), plates from EtOH, m.p. 184—185 °C (Found: C, 78.7; H, 5.7; N, 7.4. $C_{25}H_{20}N_2O_2$ requires C, 78.9; H, 5.3; N, 7.4%); 1-(α-*benzoylbenzyl*)-4,6-*diphenylpyrimidin*-2(1H)-*one* (20d) (52%), plates from EtOH, m.p. 168—170 °C (Found: C, 81.4; H, 5.0; N, 6.3. $C_{30}H_{22}N_2O_2$ requires C, 81.4; H, 5.0; N, 6.3%); 4,6-*diphenyl*-1-[α-(4-*toluoyl*)*benzyl*]*pyrimidin*-2(1H)-*one* (20e) (54%), plates from EtOH, m.p. 140—142 °C (Found: C, 81.2; H, 5.6; N, 6.0. $C_{31}H_{24}N_2O_2$ requires C, 81.6; H, 5.3; N, 6.1%); 1-(α-*ethoxycarbonylbenzyl*)-4,6-*diphenylpyrimidin*-2(1H)-*one* (20f) (35%) (isolated by prep. t.l.c.), prisms from 95% EtOH, m.p. 228—230 °C (Found: C, 76.0; H, 6.8; N, 5.3. $C_{26}H_{22}N_2O_3$ requires C, 76.1; H, 6.8; N, 5.3%); 1-(2,2-*diphenyl*-2-*hydroxy*-1-*phenyl*)*ethyl*-4,6-*diphenylpyrimidin*-2(1H)-*one* (20g) (20%), prisms from 95% EtOH, m.p. 229 °C (decomp.) (Found: C, 82.7; H, 5.4; N, 5.3. $C_{36}H_{28}N_2O_2$ requires C, 83.0; H, 5.4; N, 5.4%); 1-[2-*hydroxy*-2-(4-*methylphenyl*)-1-*phenyl*]*ethyl*-4,6-*diphenylpyrimidin*-2(1H)-*one* (20h) (40%) (isolated by prep. t.l.c.), prisms from 95% EtOH, m.p. 230 °C (decomp.) (Found: C, 81.6; H, 5.7; N, 6.2. $C_{31}H_{26}N_2O_2$ requires C, 81.2; H, 5.7; N, 6.1%); 1-(α-*methylbenzyl*)-4,6-*diphenylpyrimidin*-2(1H)-*one* (20i) (40%), plates from toluene, m.p. 170—170.5 °C (Found: C, 81.7; H, 5.5; N, 7.9. $C_{24}H_{20}N_2O$ requires C, 81.8; H, 5.7; N, 7.9%); 1-(α-*ethylbenzyl*)-4,6-*diphenylpyrimidin*-2(1H)-*one* (20j) (33%) (isolated by prep. t.l.c.), prisms from 95% EtOH, m.p. 218 °C (decomp.) (Found: C, 81.8; H, 6.3; N, 7.6. $C_{25}H_{22}N_2O$ requires C, 81.9; H, 6.0; N, 7.6%): 1-(α-*deuteriobenzyl*)-4,6-*di*-p-*tolylpyrimidin*-2(1H)-*one* (21b) (85%), needles from 95% EtOH, m.p. 207—210 °C (Found: C, 81.5; N, 7.6. $C_{25}H_{21}DN_2O$ requires C, 81.7; N, 7.6%); 1-(α-*methylbenzyl*)-4,6-*di*-p-*tolylpyrimidin*-2(1H)-*one* (21i) (95%), prisms from 95% EtOH, m.p. 186.5—187 °C (Found: C, 81.9; H, 6.5; N, 7.3. $C_{26}H_{24}N_2O$ requires C, 81.7; H, 6.3; N, 7.3%).

4-*n*-*Butyl*-3,4-*dihydro*-4,6-*di*-p-*tolylpyrimidin*-2(1H)-*one* (30).—To 1-methyl-4,6-di-*p*-tolylpyrimidin-2(1H)-one (25) (1.0 g, 3.4 mmol) in dry THF (20 ml) at 0 °C, under N_2, n-butyl-lithium (0.22 g, 3.4 mmol) was added. Stirring was continued for 1 h at 0 °C and for a further 0.5 h at 20 °C. Water (1 ml) was added and the solvent removed at 30—40 °C/20 mmHg. The residue in EtOAc (50 ml) was washed with water (2 × 25 ml), dried (Na_2SO_4), and evaporated at 30—40 °C/20 mmHg. Prep. t.l.c. [EtOAc–light petroleum (b.p. 60—80 °C) (65 : 35)] gave the *title compound* (0.5 g, 42%) as needles (EtOH), m.p. 147—147.5 °C (Found: C, 79.1; H, 8.3; N, 8.1. $C_{23}H_{28}N_2O$ requires C, 79.3; H, 8.0; N, 8.0%); $\nu_{max.}$ ($CHBr_3$) 3 200 (N–H) and 1 650 cm^{-1} (C=O); δ ($CDCl_3$) 7.3—7.0 (8 H, m), 5.74 (1 H, d, *J* 2 Hz), 4.87 (1 H, d, *J* 5 Hz), 2.8 (3 H, s), 2.3 (3 H, s), 2.28 (3 H, s), 1.82 (2 H, m), 1.3 (2 H, m), and 0.84 (3 H, t, *J* 7 Hz).

3,6-*Dihydro*-1,3-*dimethyl*-6-(1,2-*dihydro*-2-*oxo*-4,6-*di*-p-*tolylpyrimidinylmethyl*)-4,6-*di*-p-*tolylpyrimidin*-2(1H)*one* (28).—LTMP (4.5 mmol) was prepared *in situ* from n-butyl-lithium (2.86 ml, 4.5 mmol of 1.0M) and 2,2,6,6-tetramethyl-piperidine (0.63 g, 4.5 mmol), under N_2 at −20 °C. Dry THF (6 ml) was added, the whole cooled to −76 °C, and 1-methyl-4,6-di-*p*-tolylpyrimidin-2(1*H*)-one (1.0 g, 3.5 mmol) in dry THF (25 ml) added. After 45 min, MeI (0.6 g, 4.9 mmol) was added, stirring continued for 1 h at −76 °C, and for a further 12 h at 20 °C. Water (1 ml) was then added, the solvent removed at 40—50 °C/20 mmHg, and the residue taken up in CH_2Cl_2 (60 ml), washed with H_2O (30 ml), and dried (anhydrous Na_2SO_4). The CH_2Cl_2 solution was evaporated at 40—50 °C/20 mmHg. Prep. t.l.c. [EtOAc–light petroleum (b.p. 60—80 °C) (55 : 45)] gave the *title compound* (0.11 g, 10%) as prisms, m.p. 286.5—289 °C (EtOH) (Found: C, 78.8; H, 6.5; N, 9.2. $C_{39}H_{38}N_4O_2$ requires C, 78.8; H, 6.4; N, 9.4%); $\nu_{max.}$ ($CHBr_3$) 1 650 cm^{-1} (C=O); δ ($CDCl_3$) 7.92—7.00 (16 H, m), 6.56 (1 H, s), 5.36 (1 H, d, *J* 12 Hz), 4.75 (1 H, d, *J* 12 Hz), 4.54 (1 H, s), 2.5 (3 H, s), 2.31 (3 H, s), 2.28 (3 H, s), 2.22 (3 H, s), 2.19 (3 H, s), and 1.68 (3 H, s); *m/e* 594.29 ($M^{+\bullet}$, 0.12), 305.16 (100), 261.15 (0.81), and 132.08 (12.48).

3-*Ethyl*-3,6-*dihydro*-1-*methyl*-2-*oxo*-6-(1,2-*dihydro*-2-*oxo*-4,6-*di*-p-*tolylpyrimidinylmethyl*)-4,6-*di*-p-*tolylpyrimidin*-2(1H)-*one* (29).—1-Methyl-4,6-di-*p*-tolylpyrimidin-2(1H)-one (1.0 g, 3.5 mmol) in THF (25 ml) was added to a solution [THF (10 ml)] of LTMP (4.5 mmol) (prepared as above) at −76 °C. After 45 min., EtI (0.75 g, 4.8 mmol) was added, stirring continued for 1 h at −76 °C and for a further 12 h at 20 °C. Work-up of the reaction was as above. Prep. t.l.c. separation [EtOAc–light petroleum (b.p. 60—80 °C) (55 : 45)] gave the *title compound* (0.163 g, 16%) as yellow prisms, m.p. 250—252 °C ($PhCH_3$) (Found: C, 78.8; H, 6.5; N, 9.2. $C_{40}H_{40}N_4O_2$ requires C, 78.9; H, 6.6; N,

9.2%); $\nu_{max.}$ ($CHBr_3$) 1 650 cm^{-1} (C=O); δ ($CDCl_3$) 8.0—7.0 (16 H, m), 6.64 (1 H, s), 5.34 (1 H, d, *J* 12 Hz), 4.76 (1 H, d, *J* 12 Hz), 4.56 (1 H, s), 3.90 (1 H, sextet), 3.10 (1 H, sextet), 2.36 (6 H, s), 2.26 (3 H, s), 2.24 (3 H, s), 1.70 (3 H, s), and 0.78 (3 H, t); *m/e* 608.31 (M^+, 0.05), 319.17 (100), 305.16 (2.22), and 132.08 (2.82).

We thank the Leverhulme Foundation for a Fellowship (to N. K. P.) and the Consejo Nacional de Ciencia y Tecnologia (Mexico) for a scholarship (to H. J. S. Z.).

[1/188 *Received*, 9*th February*, 1981]

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