Cycloaddition of Unactivated 2-Aza-1,3-dienes with Heterocumulenes:[1] A Convenient Route to the Synthesis of 1,3-Difunctionalized Compounds

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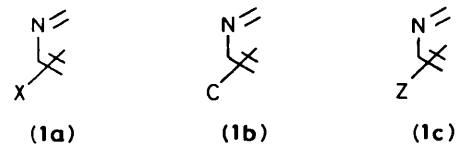
The cycloaddition of unactivated 2-aza-1,3-dienes (**2**) with isocyanates and isothiocyanates (**3**) gives with complete regio- and chemo-selectivity 1,2-dihydropyrimidin-4(3*H*)-ones and -thiones (**4**). This is the first example of a cycloaddition of unactivated 2-aza-1,3-dienes with heterocumulenes. Enamino amides and thioamides (**5**) were obtained by reduction with $LiAlH_4$ of (**4**). Also, 3-oxoamides and 3-oxothioamides (**6**) were prepared by acid hydrolysis of compound (**4**) or (**5**).

The Diels–Alder reaction is one of the most versatile methods for the synthesis of heterocyclic six-membered rings.[2] Cycloadditions with either heterodienophiles or heterodienes, or both, are the strategies usually used for this purpose.[3] Of the three, the cycloaddition with nitrogen-containing dienes, particularly 2-aza-1,3-dienes of the type (**1a**) (Figure 1), has been studied most during the last few years.[4]



(1a) (1b) (1c)

Figure 1.

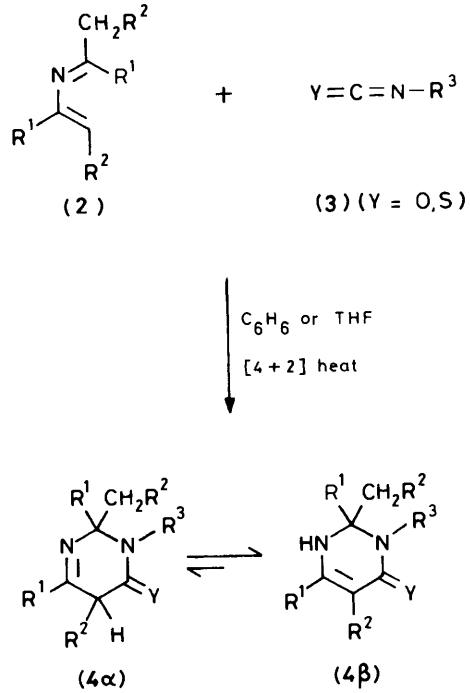
In previous papers,[5] we have indicated the participation of unactivated 2-aza-1,3-dienes of the type (**1b**) in [4 + 2] cycloadditions with different heterodienophiles.

Continuing our study of the reactivity of these systems, we now report an easy procedure for preparing 1,2-dihydropyrimidin-4(3*H*)-ones and -thiones (**4**) by reaction of the dienes (**2**) with heterocumulenes (**3**). In addition, we studied the utility of compounds (**4**) in the synthesis of 1,3-difunctionalized compounds (**5**) and (**6**).

Results and Discussion

Cycloaddition of Compounds (**2**) *and* (**3**).—The isocyanates and isothiocyanates have been frequently used as dienophiles in cycloadditions towards dienes[6] and heterodienes such as 1-oxa,[7] 1-aza,[8] and 1,3-diazadienes.[9] However, very little is known about their reactivity towards 2-aza-1,3-dienes (**1**). Gompper and Heinemann[10] have described the reaction of electron donor-substituted 2-aza-1,3-dienes with phenyl isocyanate and isothiocyanate. The results obtained by these authors have shown that the course of the reaction depends on the nature of the heterocumulene. Thus, whereas the reaction with phenyl isothiocyanate afforded the expected [4 + 2] cycloaddition product, a [2 + 2 + 2] process was observed with phenyl isocyanate. As far as we are aware this is the only example known in the literature.

The reaction of (**2**) with isocyanates and isothiocyanates (**3**) in refluxing benzene or THF for several hours (10—48 h) led with apparently complete regio- and chemo-selectivity, to the corresponding 1,2-dihydropyrimidin-4(3*H*)-ones and -thiones (**4**) in high yields (Scheme 1, Table 1). The resulting cycloaddition compounds (**4**) were isolated in the tautomeric form (**4β**). The most characteristic features of the ^1H n.m.r. (300 MHz) spectra of (**4**), for instance (**4g**), are two sets of signals centred at δ = 2.0 (3 H, s) and 5.0 (1 H, br s). These signals are assigned to the methyl substituent in the $CH_3C=$ grouping and the NH grouping [tautomeric form (**4β**), Scheme 1].



Scheme 1.

From Table 1 it can be seen that the course of this reaction is strongly influenced by the nature of the starting compounds (**2**) and (**3**). Thus, whereas in most cases the reaction works well in the absence of a catalyst, in some instances (see entries 12—14, Table 1) catalytic amounts of BF_3OEt_2 (molar ratio (**2**):(**3**):catalyst of 1:1.1:0.1) are necessary; and in others (entry 15, Table 1) the reaction did not take place, *i.e.* the reaction is slowed by increasing steric requirements in the diene, in the sequence R^2 = Me < Et < Pr^i.

Moreover, when the reaction was carried out with compounds (**3**;R^3 = alkyl and Y = O,S), both in the presence or absence of a catalyst, starting materials were recovered. This

Table 1. 1,2-Dihydropyrimidin-4(3*H*)-ones and -thiones (**4**) from (**2**) and (**3**)

Entry	Compd.	R^1	R^2	R^3	Y	Yield (%)	M.p. (°C)
1	(**4a**)	Ph	Me	Ph	O	80	163—165[a]
2	(**4b**)	Ph	Me	*p*-ClC_6H_4	O	75	210—212[a]
3	(**4c**)	*p*-MeC_6H_4	Me	Ph	O	70	122—124
4	(**4d**)	Ph	Me	*m*-ClC_6H_4	O	70	178—180
5	(**4e**)	*p*-MeC_6H_4	Me	Ph	S	82	197—199[a]
6	(**4f**)	Ph	Me	*p*-MeC_6H_4	S	70	194—196[a]
7	(**4g**)	Ph	Me	Ph	S	65	133—135
8	(**4h**)	Ph	Me	*p*-ClC_6H_4	S	75	191—193
9	(**4i**)	Ph	Me	H	O	50	193—195[b]
10	(**4j**)	Ph	Me	H	S	92	224—226[b]
11	(**4k**)	Ph	Me	*p*-$MeC_6H_4SO_2$	O	99	195—197
12	(**4l**)	Ph	Et	*p*-ClC_6H_4	O	75	143—145[c]
13	(**4m**)	Ph	Et	Ph	O	70	153—155[c]
14	(**4n**)	Ph	Et	*p*-ClC_6H_4	S	65	148—150[c]
15	—	Ph	Pr^i	Ph	O	—	—

[a] See ref. 4. [b] Me_3Si–N=C=Y (Y = O,S) were used as starting material (**3**). [c] In the presence of BF_3OEt_2 as catalyst.

Table 2. Enamino amides and thioamides (**5**) obtained by $LiAlH_4$ reduction from (**4**)

Entry	Compd.[a]	R^1	R^2	R^3	Y	Yield (%)	M.p. (°C)
1	(**5a**)	Ph	Me	Ph	O	85	96—98
2	(**5b**)	Ph	Me	*m*-ClC_6H_4	O	75	97—99
3	(**5c**)	Ph	Et	Ph	O	80	105—107
4	(**5d**)	*p*-MeC_6H_4	Me	Ph	S	88	Oil
5	(**5e**)	Ph	Me	*p*-ClC_6H_4	S	90	124—126
6	—	Ph	Me	H	O,S	—	—

[a] The enamino amide or thioamide form (**4β**) is shown. But in some instances there is a mixture of iminic and enaminic forms.

could be explained taking into account the lower reactivity of the aliphatic isocyanates and isothiocyanates compared with their aromatic analogues.[11]

Finally, the reaction of (**2**) and (**3**) (R^3 = $SiMe_3$) (entries 9—10, Table 1) led to interesting compounds (**4i—j**) which do not contain silicon and which are the equivalent of the [4 + 2] cycloaddition adduct resulting from the reaction between (**2**) and isocyanic or isothiocyanic acid.

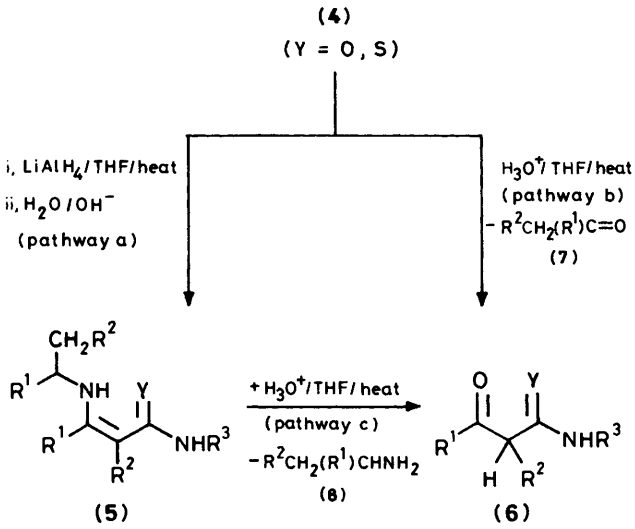
Reactivity of Compounds (**4**)*: Synthesis of the Enamino Amides and Thioamides* (**5**) *and 3-Oxoamides and 3-Oxothioamides* (**6**).—1,3-Difunctionalized compounds such as β-enamino and β-keto carboxylic acid derivatives, obtained in most instances by Claisen-type[12] condensation reactions, are important synthons in organic (*e.g.* heterocyclic,[13] asymmetric[14] or diastereoselective[15]) synthesis. We describe here a simple method for the preparation of this type of compound by reduction and/or acid hydrolysis of the cycloadducts (**4**).

Reduction of compounds (**4**;Y = O,S) with an excess of $LiAlH_4$ in refluxing THF for several hours, followed by basic hydrolysis, gave high yields of enamino amides or thioamides (**5**) (Scheme 2, pathway a, and Table 2).

The structure of compounds (**5**) was ascertained by ^1H and ^{13}C n.m.r. spectroscopy. For instance, the ^1H n.m.r (300 MHz) spectrum of (**5a**) shows signals at δ_H 0.85 (3 H, t, CH_3), 1.50 (3 H, s, CH_3), 1.66 (2 H, m, CH_2), 3.75 (1 H, q, CH) (+D_2O, 1 H, t), 6.55 (1 H, br s, NH), 6.9—7.5 (15 H, m, Ph), and 10.3 (1 H, br d, NH) which confirm the proposed structure.

We can observe that the net result of the reaction is the cleavage of the C–NR^3 bond. Very few examples are known in the literature of such reactions and only Yokoyama[16] has described a novel C–S hydrogenolysis of 3,4-dihydro-4-oxo-2*H*-1,3-thiazino derivatives by metal hydride complexes.

The formation of compounds (**5**) can be understood by assuming that the anion (**9**) initially formed suffers ring-opening to afford the intermediate (**10**). Further inter or intra hydride transfer led, through C=N reduction, to the desired compound (**5**) (Scheme 3).

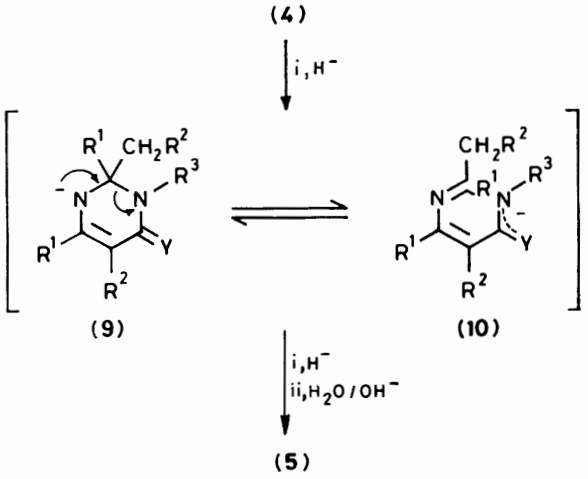


Scheme 2.

Furthermore, when the reduction was carried out with the compounds (**4i—j**) starting material was recovered. In this case, the dianion formed (**11**) (Figure 2) probably inhibits the process. This corroborates the proposed mechanism.

Moreover, treatment of (**4**) with 1M H_2SO_4 in THF at 60 °C for 2—6 h resulted in the formation of 3-oxoamides and 3-oxothioamides (**6**), along with almost quantitative yields of the corresponding ketone (**7**) (Scheme 2, pathway b, and Table 2).

Compounds (**6**) can alternatively be obtained through the



Scheme 3.

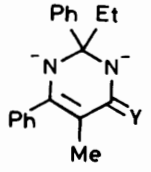


Figure 2.

sequence (4)→(5)→(6) by acid hydrolysis of (5) under the same conditions as for the direct hydrolysis of (4), with loss, in this case, of the amine (8) (Scheme 2, pathway c, Table 2).

Compounds (6) were characterized by their elemental analyses and spectroscopic data (see Experimental section). Of particular interest was the i.r. absorption at *ca.* 3 150 cm^{-1}, as well as the signal in the ^1H n.m.r. (300 MHz) spectra *e.g.* for (**6b**) at δ_H 4.35 (1 H, t, CH), corresponding to the R^2CH groups and the signals in ^{13}C n.m.r. spectra at δ_C 199.5 and 167.3 (singlets) which are assignable to carbonyl and amide groups respectively.

In conclusion, the versatility of 2-aza-1,3-dienes (**2**) in organic synthesis is shown once more by their use in the cycloadditions with isocyanates and isothiocyanates (**3**). Furthermore, a new and simple strategy for two-step synthesis of 1,3-difunctionalized compounds of the type (**5**) and (**6**) from unactivated 2-aza-1,3-dienes (**2**) is described.

Experimental

General.—I.r. spectra were recorded with a Perkin-Elmer 248 spectrometer. ^1H and ^{13}C N.m.r. spectra were recorded on a Varian FT-80 spectrometer and a Brucker AC-300 spectrometer. Elemental analyses were carried out with a Perkin-Elmer 240 elemental analyser. M.p.s are uncorrected. Mass spectra were taken on a Hewlett-Packard 5 930A spectrometer.

Isocyanates and isothiocyanates were of the best commercial grade available (Aldrich, Fluka, Merck) and were used without further purification. BF_3OEt_2 was distilled over CaH_2 and stored under argon. THF was dried with sodium, refluxed with $LiAlH_4$, distilled, and stored under argon. Ether refers to diethyl ether.

Reaction of 2-*Aza*-1,3-*dienes* (**2**) *with Heterocumulenes* (**3**). *Preparation of* 1,2-*Dihydropyrimidin*-4(3H)-*ones and* -*thiones* (**4**): *General Procedure.*— All reactions were carried out under argon. A small excess (16 mmol) of heterocumulene (**3**) was added to a benzene or THF solution (5 ml) of 2-aza-1,3-diene (**2**) (10 mmol). In three cases (**4l—n**) 1 mmol of BF_3OEt_2 was added. The reaction mixture was stirred at 80 °C (10—48 h). The solvents were then removed (0.1 mmHg) and the resulting residue washed with methanol, hexane, or hexane–chloroform (4:1) to give a white or yellow solid. The solid was recrystallized from hot methanol or hexane–chloroform (3:1). The yields are based on (**2**).

2-*Ethyl*-1,2-*dihydro*-5-*methyl*-2,3,6-*triphenylpyrimidin*-4(3H)-*one* (**4a**) (80% yield), m.p. 163—165 °C (Found: C, 81.40; H, 6.55; N, 7.65. $C_{25}H_{24}N_2O$ requires C, 81.48; H, 6.5; N, 7.60%); $\nu_{max.}$(KBr) 3 250 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.8 (3 H, s, CH_3), 2.3 (2 H, m, CH_2), 4.5 (1 H, br s, NH), and 7.7 (15 H, m, Ph); δ_C(20 MHz; [$^2H_6$]DMSO) 170.13 (s, CO), 152.88 (s), 148.93 (s), 142.92 (s), 138.67 (s), 132.78—129.25 (m), 100.36 (s, =*C*CH_3), 81.46 (s, C-2), 33.69 (t, *C*$H_2$$CH_3$), 15.79 (q, =C*C*$H_3$), and 11.70 (q, CH_2*C*H_3); *m/z* 368 (M^+).

3-p-*Chlorophenyl*-2-*ethyl*-1,2-*dihydro*-5-*methyl*-2,6-*diphenylpyrimidin*-4(3H)-*one* (**4b**) (75% yield), m.p. 210—212 °C (Found: C, 74.50; H, 5.7; N, 6.9. $C_{25}H_{23}ClN_2O$ requires C, 74.51; H, 5.76; N, 6.95%); $\nu_{max.}$(KBr) 3 210 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.8 (3 H, s, CH_3), 2.3 (2 H, m, CH_2), 4.5 (1 H, br s, NH), and 7.0 (14 H, m, Ph); δ_C(20 MHz; [$^2H_6$]DMSO) 170.54 (s, CO), 153.89 (s), 148.98 (s), 142.48 (s), 139.24 (s), 135.28 (s), 134.51—130.54 (m), 100.90 (s, =CMe), 82.19 (s, C-2), 34.82 (t, *C*$H_2$$CH_3$), 16.22 (q, =C*C*$H_3$), and 12.28 (q, CH_2*C*H_3); *m/z* 402 (M^+).

2-*Ethyl*-1,2-*dihydro*-5-*methyl*-3-*phenyl*-2,6-*bis*(p-*tolyl*)-*pyrimidin*-4(3H)-*one* (**4c**) (70% yield), m.p. 122—124 °C (Found: C, 81.75; H, 7.1; N, 7.0. $C_{27}H_{28}N_2O$ requires C, 81.77; H, 7.13; N, 7.06%); $\nu_{max.}$(Nujol) 3 320 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.6 (2 H, m, CH_2), 1.7 (3 H, s, CH_3), 2.3 (3 H, s, CH_3), 2.4 (3 H, s, CH_3), 4.5 (1 H, br s, NH), and 7.0 (13 H, m, Ph); δ_C(20 MHz; [$^2H_6$]DMSO) 170.78 (s, CO), 153.42 (s), 146.59 (s), 143.69 (s), 142,93 (s), 140.75 (s), 136.55 (s), 133.57—122.39 (m), 101.06 (s, =*C*CH_3), 81.85 (s, C-2), 34.36 (t, *C*$H_2$$CH_3$), 25.00 (q, CH_3-4), 24.67 (q, CH_3-4), 16.45 (q, =C*C*H_3), and 12.30 (q, CH_2*C*H_3); *m/z* 396 (M^+).

3-m-*Chlorophenyl*-2-*ethyl*-1,2-*dihydro*-5-*methyl*-2,6-*diphenyl*-

Table 3. 3-Oxoamides and 3-thioamides (**6**) obtained from (**4**) or (**5**)

Compd.	R^1	R^2	R^3	Y	Yield (%)	M.p. (°C)
(**6a**)	Ph	Me	Ph	O	75[a]	124—126
					85[b]	
(**6b**)	Ph	Et	Ph	O	90[a]	159—161
(**6c**)	Ph	Me	*p*-$MeC_6H_4SO_2$	O	97[a]	Oil
(**6d**)	Ph	Me	*p*-ClC_6H_4	S	80[a]	125—127
					90[b]	
(**6e**)	*p*-MeC_6H_4	Me	Ph	S	78[a]	128—130

[a] Obtained from the sequence (4)→(6). [b] Obtained from the sequence (4)→(5)→(6).

pyrimidin-4(3H)-*one* (**4d**) (70% yield), m.p. 178—180 °C (Found: C, 74.5; H, 5.7; N, 6.9. $C_{25}H_{23}ClN_2O$ requires C, 74.51; H, 5.76; N, 6.95%); $\nu_{max.}$(KBr) 3 250 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.7 (3 H, s, CH_3), 2.2 (2 H, m, CH_2), 4.5 (1 H, br s, NH), and 7.0 (14 H, m, Ph); δ_C(20 MHz; [$^2H_6$]DMSO) 170.55 (s, CO), 154.14 (s), 148.79 (s), 145.01 (s), 139.20 (s), 134.08 (s), 133.52—130.25 (m), 100.86 (s, =*C*CH_3), 82.27 (s, C-2), 34.00 (t, *C*H_2CH_3), 16.23 (q, =C*C*H_3), and 12.30 (q, CH_2CH_3).

2-*Ethyl*-1,2-*dihydro*-5-*methyl*-3-*phenyl*-2,6-*bis*(p-*tolyl*)-*pyrimidine*-4(3H)-*thione* (**4e**) (82% yield), m.p. 197—199 °C (Found: C, 72.55; H, 6.8; N, 6.8. $C_{27}H_{28}N_2S$ requires C, 78.58; H, 6.85; N, 6.79%); $\nu_{max.}$(KBr) 3 150 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.7 (3 H, t, CH_3), 1.5 (2 H, m, CH_2), 2.0 (3 H, s, CH_3), 2.2 (3 H, s, 4-CH_3), 2.3 (3 H, s, 4-CH_3), 4.8 (1 H, br s, NH), and 7.0 (13 H, m, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 191.53 (s, CS), 142.04 (s), 141.93 (s), 139.34 (s), 137.20 (s), 131.44—126.0 (m), 110.63 (s, =*C*CH_3), 77.8 (s, C-2), 28.97 (t, *C*H_2CH_3), 19.67 (q, CH_3-4), 19.64 (q, CH_3-4), 16.87 (q, =C*C*H_3), and 7.27 (q, CH_2CH_3); *m/z* 412 (M^+).

2-*Ethyl*-1,2-*dihydro*-5-*methyl*-2,6-*diphenyl*-3-(p-*tolyl*)-*pyrimidine*-4(3H)-*thione* (**4f**) (70% yield), m.p. 194—196 °C (Found: C, 78.3; H, 6.55; N, 7.0. $C_{26}H_{26}N_2S$ requires C, 78.33; H, 6.58; N, 7.02); $\nu_{max.}$(KBr) 3 110 cm^{-1} (NH); δ_H(80 MHz;$CDCl_3$, TMS as internal reference) 0.8 (3 H, t, CH_3), 2.0 (3 H, s, CH_3), 2.4 (5 H, br s, CH_2, 4-CH_3), 4.9 (1 H, br s, NH), and 7.0 (14 H, m, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 191.87 (s, CS), 141.75 (s), 140.83 (s), 139.35 (s), 136.12 (s), 134.35 (s), 129.76—125.98 (m), 111.44 (s, =*C*CH_3), 77.85 (s, C-2), 29.71 (t, *C*H_2CH_3), 20.19 (q, CH_3-4), 17.05 (q, =C*C*H_3), and 7.44 (q, CH_2CH_3); *m/z* 396 (M^+).

2-*Ethyl*-1,2-*dihydro*-5-*methyl*-2,3,6-*triphenylpyrimidine*-4-(3H)-*thione* (**4g**) (65% yield), m.p. 133—135 °C (Found: C, 78.0; H, 6.0; N, 7.1. $C_{25}H_{24}N_2S$ requires C, 78.07; H, 6.30; N, 7.28%); $\nu_{max.}$(KBr) 3 200 cm^{-1} (NH); δ_H(300 MHz; $CDCl_3$, TMS as internal reference) 0.8 (3 H, t, CH_3), 2.0 (3 H, s, CH_3), 2.2 (1 H, m, CH_2CH_3), 2.4 (1 H, m, CH_2CH_3), 5.0 (1 H, br s, NH), and 7.0—7.6 (15 H, complex, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 192.48 (s, CS), 142.72 (s), 141.15 (s), 135.11 (s), 130.87 (s), 129.94—126.87 (m), 111.93 (s, =*C*CH_3), 78.46 (s, C-2), 29.92 (t, *C*H_2CH_3), 17.83 (q, =C*C*H_3), and 8.21 (q, CH_2CH_3); *m/z* 384 (M^+).

3-p-*Chlorophenyl*-2-*ethyl*-1,2-*dihydro*-5-*methyl*-2,6-*diphenyl*-*pyrimidine*-4(3H)-*thione* (**4h**) (75% yield), m.p. 191—193 °C (Found: C, 71.55; H, 5.4; N, 6.6. $C_{25}H_{23}ClN_2S$ requires C, 71.65; H, 5.54; N, 6.68%); $\nu_{max.}$(KBr) 3 126 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 2.0 (3 H, s, CH_3), 2.3 (2 H, m, CH_2), 4.9 (1 H, br s, NH), and 7.0 (14 H, m, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 193.0 (s, CS), 142.41 (s), 140.45 (s), 140.0 (s), 134.23 (s), 132.03 (s), 131.5—126.01 (m), 110.01 (s, =*C*CH_3), 77.71 (s, C-2), 28.71 (t, *C*H_2CH_3), 16.91 (q, C*C*H_3), and 7.38 (q, CH_2CH_3); *m/z* 418 (M^+).

2-*Ethyl*-1,2-*dihydro*-5-*methyl*-2,6-*diphenylpyrimidin*-4(3H)-*one* (**4i**) (50% yield), m.p. 193—195 °C (Found: C, 78.0; H, 6.85; N, 9.5. $C_{19}H_{20}N_2O$ requires C, 78.04; H, 6.91; N, 9.58%); $\nu_{max.}$(KBr) 3 330 and 3 360 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.7 (3 H, s, CH_3), 2.0 (2 H, m, CH_2), 4.7 (1 H, br s, NH), 6.6 (1 H, br s, NH), and 7.2—7.7 (10 H, m, Ph); δ_C(20 MHz; [$^2H_6$]DMSO) 168.6 (s, CO), 151.0 (s), 148.9 (s), 136.5 (s), 133.5 (s), 133.0—125.0 (m), 96.2 (s, =*C*CH_3), 73.0 (s, C-2), 34.1 (t, *C*H_2CH_3), 11.0 (q, =C*C*H_3), and 8.5 (q, CH_2CH_3); *m/z* 292 (M^+).

2-*Ethyl*-1,2-*dihydro*-5-*methyl*-2,6-*diphenylpyrimidine*-4(3H)-*thione* (**4j**) (92% yield), m.p. 224—226 °C (Found: C, 73.95; H, 6.5; N, 9.0. $C_{19}H_{20}N_2S$ requires C, 73.97; H, 6.54; N, 9.08%); $\nu_{max.}$(KBr) 3 360 and 3 100 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$), TMS as internal reference) 0.9 (3 H, t, CH_3), 1.9 (3 H, s, CH_3), 2.0 (2 H, m, CH_2), 4.8 (1 H, br s, NH), 7.0 (10 H, m, Ph), and 7.6 (1 H, br s, NH); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 194.28 (s, CS), 151.60 (s), 150.86 (s), 139.34 (s), 133.63—129 (m), 108.53 (s, =*C*CH_3), 76.81 (s, C-2), 37.57 (t, *C*H_2CH_3), 20.40 (q, =C*C*H_3), and 13.35 (q, CH_2CH_3); *m/z* 308 (M^+).

2-*Ethyl*-1,2-*dihydro*-5-*methyl*-2,6-*diphenyl*-3-p-*tolylsulphonylpyrimidin*-4(3H)-*one* (**4k**) (99% yield), m.p. 195—197 °C (Found: C, 69.9; H, 5.8; N, 6.2. $C_{26}H_{26}N_2O_3S$ requires C, 69.95; H, 5.82; N, 6.28%); $\nu_{max.}$(KBr) 3 235 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.6 (3 H, s, CH_3), 2.0 (2 H, m, CH_2), 2.4 (3 H, s, CH_3), 5.5 (1 H, br s, NH), and 7.1—8.0 (14 H, m, Ph); δ_C(20 MHz; [$^2H_6$]DMSO) 163.90 (s, CO), 156.1 (s), 143.0 (s), 142.3 (s), 141.5 (s), 133.9—126.0 (m), 96.2 (s, =*C*CH_3), 92.3 (s, C-2), 33.7 (t, *C*H_2CH_3), 20.3 (q, =C*C*H_3), 12.0 (q, 4-*C*H_3), and 7.1 (q, CH_2CH_3); *m/z* 446 (M^+).

3-p-*Chlorophenyl*-5-*ethyl*-1,2-*dihydro*-2,6-*diphenyl*-2-*propyl*-*pyrimidin*-4(3H)-*one* (**4l**) (75% yield), m.p. 143—145 °C (Found: C, 75.2; H, 6.3; N, 6.5. $C_{27}H_{27}ClN_2O$ requires C, 75.23; H, 6.32; N, 6.50%); $\nu_{max.}$(KBr) 3 240 cm^{-1} (NH); δ_H(80 MHz; [$^2H_6$]DMSO) 1.0 (6 H, t, $2CH_3$), 1.4 (2 H, m, CH_2), 2.1 (2 H, m, CH_2), 2.4 (2 H, m, CH_2), 7.5—8.0 (14 H, m, Ph), and 9.3 (1 H, br s, NH); δ_C(20 MHz; [$^2H_6$]DMSO) 169.94 (s, CO), 154.04 (s), 149.08 (s), 142.69 (s), 142.50 (s), 139.34 (s), 135.25—124.04 (m), 108.72 (s, =*C*CH_3), 81.91 (s, C-2), 42.70 (t, *C*$H_2CH_2CH_3$), 23.08 (t, =C*C*H_2), 20.66 (t, *C*H_2CH_3), 19.12 (q, =CCH_2CH_3), and 17.93 (q, CH_2CH_3); *m/z* 430 (M^+).

5-*Ethyl*-1,2-*dihydro*-2,3,6-*triphenyl*-2-*propylpyrimidin*-4-(3H)-*one* (**4m**) (70% yield), m.p. 153—155 °C (Found: C, 81.7; H, 7.1; N, 7.0. $C_{27}H_{28}N_2O$ requires C, 81.76; H, 7.13; N, 7.06%); $\nu_{max.}$(KBr) 3 200 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.7 (3 H, t, CH_3) 1.1 (3 H, t, =CCHCH_3), 2.1 (6 H, m, $3CH_2$), 4.5 (1 H, br s, NH), and 7.0 (15 H, m, Ph); δ_C(20 MHz; [$^2H_6$]DMSO) 170.1 (s, CO), 153.62 (s), 149.57 (s), 143.62 (s), 139.48 (s), 133.62—122.41 (m), 109.23 (s, =*C*CH_3), 81.86 (s, C-2), 42.80 (t, *C*$H_2CH_2CH_3$), 23.16 (t, =C*C*H_2), 20.16 (t, *C*H_2CH_3), 19.14 (q, =CCH_2CH_3), and 17.93 (q, CH_2CH_3); *m/z* 396 (M^+).

3-p-*Chlorophenyl*-5-*ethyl*-1,2-*dihydro*-2,6-*diphenyl*-2-*propyl*-*pyrimidine*-4(3H)-*thione* (**4n**) (65% yield), m.p. 148—150 °C (Found: C, 72.5; H, 6.05; N, 6.2. $C_{27}H_{27}ClN_2S$ requires C, 72.53; H, 6.09; N, 6.26%); $\nu_{max.}$(KBr) 3 200 cm^{-1} (NH); δ_H(80 MHz; CCl_4, D_2O cap. as lock reference, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.2 (3 H, t, CH_3), 1.7 (2 H, m, CH_2), 2.5 (2 H, m, CH_2), 3.2 (2 H, m, CH_2), 5.3 (1 H, br s, NH), and 7.6—8.2 (14 H, m, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 190.73 (s, CS), 142.30 (s), 141.05 (s), 140.32 (s), 133.98 (s), 131.64—125.88 (m), 119.35 (s, =*C*CH_3), 77.47 (s, C-2), 39.14 (t, *C*$H_2CH_2CH_3$), 22.50 (t, =CCH_2CH_3), 16.31 (t, *C*H_2CH_3), and 13.07 (q, $2CH_3$); *m/z* 446 (M^+).

Reduction of Compounds (**4**) *with* $LiAlH_4$. *Preparation of Enamino Amides and Thioamides* (**5**); *General Procedure*.—All reactions were carried out under argon. A solution of (**4**) (5 mmol) in THF (20 ml) was slowly added to a stirred solution of $LiAlH_4$ (15 mmol) in THF (20 ml) at 0 °C. When the evolution of gas was complete the reaction mixture was stirred at 80 °C for 20 h. The solution was then cooled at 0 °C and the excess of $LiAlH_4$ destroyed with methanol–ether. The resulting mixture was treated with 3M NaOH (100 ml), extracted with ether, and the organic layer washed with water and dried (Na_2SO_4). The solvents were removed (15 mmHg) and the resulting residue was washed with hexane–chloroform (4:1) to give a solid. In one case (**5e**), a yellow oil was obtained. The yields are based on (**4**).

2-*Methyl*-3-(1-*phenylpropylamino*)-N,3-*diphenylprop*-2-*enamide* (**5a**) (85% yield), m.p. 96—98 °C (Found: C, 81.0; H, 7.05; N, 7.55. $C_{25}H_{26}N_2O$ requires C, 81.03; H, 7.08; N, 7.56%); $\nu_{max.}$(Nujol) 3 390 and 3 260 cm^{-1} (NH); δ_H(300 MHz; $CDCl_3$, TMS as internal reference) 0.85 (3 H, t, CH_3), 1.50 (3 H, s,

CH_3), 1.66 (2 H, m, CH_2), 3.75 (1 H, q, CH) (+D_2O, 1 H, t), 6.55 (1 H, br s, NH), 6.9—7.5 (15 H, m, Ph), and 10.3 (1 H, br s, NH); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 168.30 (s, CO), 159.29 (s, C-3), 142.98 (s), 137.17 (s), 134.53 (s), 127.1—121.65 (m), 119.01 (s, C-2), 58.8 (d, CHN), 29.99 (t, CH_2CH_3), 13.15 (q, $=CCH_3$), and 9.34 (q, CH_2CH_3); *m/z* 370 (M^+).

N-m-*Chlorophenyl*-2-*methyl*-3-*phenyl*-3-(1-*phenylpropylamino*)*prop*-2-*enamide* (**5b**) (75% yield), m.p. 97—99 °C (Found: C, 74.1; H, 6.2; N, 6.85. $C_{25}H_{25}ClN_2O$ requires C, 74.14; H, 6.23; N, 6.91%); $\nu_{max.}$(KBr) 3 225 and 3 040 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.5 (3 H, s, CH_3), 1.4—1.8 (2 H, m, CH_2), 3.6 (1 H, m, CH), 7.0 (14 H, m, Ph), and 10.0 (1 H, br s, NH); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 168.0 (s, CO), 160.61 (s, C-3), 143.44 (s), 134.99 (s), 128.7—127.59 (m), 117.32 (s, C-2), 59.5 (d, CHN), 30.60 (t, CH_2CH_3), 13.72 (q, $=CCH_3$), and 9.94 (q, CH_2CH_3); *m/z* 404 (M^+).

2-*Ethyl*-N,3-*diphenyl*-3-(1-*phenylbutylamino*)*prop*-2-*enamide* (**5c**) (80% yield), m.p. 105—107 °C (Found: C, 81.25; H, 7.5; N, 7.0. $C_{27}H_{30}N_2O$ requires C, 81.35; H, 7.60; N, 7.03%); $\nu_{max.}$(KBr) 3 280 and 3 043 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.7 (6 H, complex, $2CH_3$), 1.7 (6 H, complex, $3CH_2$), 3.4 (1 H, q, CH), 3.7 (1 H, m, CH), 4.4 (1 H, t, CH), and 6.8—7.7 (15 H, m, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 169.0 (s, CO), 160 (s, C-3), 144.0 (s), 139.0 (s), 135.10 (s), 128.0—118.6 (m), 96.5 (s, C-2), 57.1 (d, CHN), 40.2 (t, $CH_2CH_2CH_3$), 17.8 (t, $2CH_2$), and 12.1 (q, $2CH_3$); *m/z* 390 (M^+).

2-*Methyl*-N-*phenyl*-3-p-*tolyl*-3-(1-p-*tolylpropylamino*)*prop*-2-*enethioamide* (**5d**) (88% yield), oil (Found: C, 78.1; H, 7.25; N, 6.75. $C_{27}H_{30}N_2S$ requires C, 78.2; H, 7.3; N, 6.75); $\nu_{max.}$(Nujol) 3 240 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.8 (3 H, t, CH_3), 1.6 (3 H, s, CH_3), 1.4—1.7 (2 H, m, CH_2), 2.2 (3 H, s, 4-CH_3) 2.3 (3 H, s, 4-CH_3), 3.6 (1 H, m, CH), 7.0 (13 H, m, Ph), and 10.0 (1 H, br s, NH); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 186.75 (s, CS), 162.94 (s, C-3), 139. 57 (s), 138.77 (s), 137.12 (s), 135.09 (s), 132.79 (s), 128.45—121.39 (m), 97.82 (s, C-2), 60.78 (d, CHN), 30.64 (t, CH_2CH_3), 20.34 (q, CH_3-4), 20.07 (q, CH_3-4), 16.70 (q, $=CCH_3$), and 9.91 (q, CH_2CH_3); *m/z* 414 (M^+).

N-p-*Chlorophenyl*-2-*methyl*-3-*phenyl*-3-(1-*phenylpropylamino*)*prop*-2-*enethioamide* (**5e**) (90% yield), m.p. 124—126 °C (Found: C, 71.3; H, 5.95; N, 6.6. $C_{25}H_{25}ClN_2S$ requires C, 71.31; H, 5.99; N, 6.65%); $\nu_{max.}$(KBr) 3 210 and 3 025 cm^{-1} (NH); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 0.9 (3 H, t, CH_3), 1.6 (3 H, s, CH_3), 1.5—1.9 (2 H, m, CH_2), 3.8 (1 H, m, CH), 7.0 (14 H, m, Ph), and 9.4 (1 H, br s, NH); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 189.08 (s, CS), 166.98 (s, C-3), 144.78 (s), 139.67 (s), 137.85 (s), 132.53 (s), 132.34—127.61 (m), 98.0 (s, C-2), 63.47 (d, CHN), 32.96 (t, CH_2CH_3), 19.01 (q, $=CCH_3$), and 12.34 (q, CH_2CH_3); *m/z* 420 (M^+).

Hydrolysis of Compounds (**4**) *and* (**5**) *to give* 3-*Oxoamides and* 3-*Oxothioamides* (**6**): *General Procedure*.—1M H_2SO_4 (10ml) was added to a solution of (**4**) (5 mmol) in THF (15 ml) and the reaction mixture was stirred at 60 °C for 2—6 h. The solution was then cooled and extracted with CH_2Cl_2. The organic layer was washed with water, dried (Na_2SO_4), and evaporated and the resulting residue washed with hexane or hexane–ether (4:1) to give a white or yellow solid. In one case (**6c**), the resulting residue was dried under reduced pressure (0.1 mmHg) to give an oil. The hydrolysis of (**5**) was carried out in the same way. The yields are based on (**4**) or (**5**).

2-*Methyl*-3-*oxo*-N,3-*diphenylpropanamide* (**6a**) (75% yield), m.p. 124—126 °C (Found: C, 75.8; H, 5.95; N, 5.5. $C_{16}H_{15}NO_2$ requires C, 75.85; H, 5.98; N, 5.53%); $\nu_{max.}$(KBr) 3 200 (NH) and 1 680 cm^{-1} (CO); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 1.6 (3 H, d, CH_3), 5.3 (1 H, q, CH), 7.0 (10 H, m, Ph), and 8.4 (1 H, br s, NH); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 197.82 (s, CO), 166.98 (CON), 136 (s), 133.96 (s), 132.26—118.53 (m), 48.33 (d, CH), and 15.27 (q, CH_3); *m/z* 253 (M^+).

2-*Ethyl*-3-*oxo*-N,3-*diphenylpropanamide* (**6b**) (90% yield), m.p. 159—161 °C (Found: C, 76.3; H, 6.35; N, 5.25. $C_{17}H_{17}NO_2$ requires C, 76.37; H, 6.42; N, 5.24%); $\nu_{max.}$(KBr) 3 220 (NH) and 1 675 (CO) cm^{-1}; δ_H(300 MHz; $CDCl_3$, TMS as internal reference) 0.95 (3 H, t, CH_3), 2.05 (2 H, m, CH_2), 4.35 (1 H, t, CH), 6.9—8.1 (10 H, m, Ph), and 8.70 (1 H, br s, NH); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 199.49 (s, CO), 167.30 (s, CON), 134.09 (s), 132.30 (m), 132.17 (m), 126.90 (d), 122.75 (d), 55.09 (d, CH), 24.69 (t, CH_2), and 10.27 (q, CH_3); *m/z* 267 (M^+).

2-*Methyl*-3-*oxo*-3-*phenyl*-N-p-*tolylsulphonylpropanamide* (**6c**) (97% yield), oil (Found: C, 61.6; H, 5.1; N, 4.15. $C_{17}H_{17}NO_4S$ requires C, 61.59; H, 5.13; N, 4.15%); $\nu_{max.}$(Nujol) 3 230 (NH) and 1 690 cm^{-1} (CO); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 1.6 (3 H, t, CH_3), 2.5 (3 H, s, 4-CH_3), 4.5 (1 H, q, CH), and 7.2—8.1 (9 H, m, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 197.1 (s, CO), 169.3 (s, CON), 144.5 (s), 135.0—125.5 (m), 48.2 (d, CH), 20.0 (q, CH_3-4), and 13.1 (q, CH_3); *m/z* 331 (M^+).

N-p-*Chlorophenyl*-2-*methyl*-3-*oxo*-3-*phenylpropanethioamide* (**6d**) (80% yield), m.p. 125—127 °C (Found: C, 63.2; H, 4.6; N, 4.6. $C_{16}H_{14}ClNOS$ requires C, 63.24; H, 4.65; N, 4.61%); $\nu_{max.}$(KBr) 3 200 (NH) and 1 683 (CO) cm^{-1}; δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 1.3 (3 H, d, CH_3), 4.8 (1 H, q, CH), and 7.0 (9 H, m, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 199.93 (s, CO), 198.56 (s, CS), 133.26—123.48 (m), 57.16 (d, CH), and 20.03 (q, CH_3); *m/z* 303 (M^+).

2-*Methyl*-3-*oxo*-N-*phenyl*-3-p-*tolylpropanethioamide* (**6e**) (78% yield), m.p. 128—130 °C (Found: C, 72.0; H, 6.05; N, 4.9. $C_{17}H_{17}NSO$ requires C, 72.04; H, 6.05; N, 4.94%); $\nu_{max.}$(KBr) 3 150 (NH) and 1 660 cm^{-1} (CO); δ_H(80 MHz; $CDCl_3$, TMS as internal reference) 1.7 (3 H, d, CH_3), 2.4 (3 H, s, 4-CH_3), 5.2 (1 H, q, CH), and 7.0—8.0 (9 H, m, Ph); δ_C(20 MHz; $CDCl_3$, TMS as internal reference) 199.87 (s, CO), 198.35 (s, CS), 144.42 (s), 137.82 (s), 132.10 (s), 128.59—122.10 (m), 57.18 (d, CH), 20.64 (q, 4-CH_3), and 20.16 (q, CH_3); *m/z* 283 (M^+).

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Received 20*th July* 1987; *Paper* 7/1301