Substituted 1,4-Dihydropyrimidines. 3.[1] Synthesis of Selectively Functionalized 2-Hetero-1,4-dihydropyrimidines

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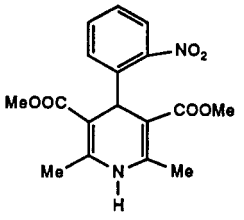
Received June 12, 1989

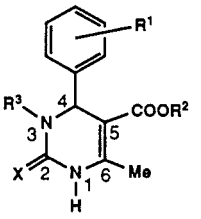
The utility of 2-[[(4-methoxyphenyl)methyl]thio]- and 2-methoxy-1,4-dihydropyrimidines **9** and **10** for the preparation of 3-substituted 1,4-dihydropyrimidines **1–3** is described. The pyrimidines **9** and **10**, which were prepared in high yield by the reaction of benzylidene **11** with 2-[(4-methoxyphenyl)methyl]-2-thiopseudourea (**12**) and *O*-methylisourea (**13**), respectively, underwent reaction with various electrophiles in a selective manner. The fully functionalized intermediates **15** and **16** were deprotected to yield the desired products **1** and **2** in high overall yield. The methoxy group in intermediate **16** could also be exchanged with an amine to provide the selectively functionalized aminopyrimidines **3**.

Introduction

In addition to being essential components of naturally occurring nucleic acids, pyrimidines are integral parts of such biologically important compounds as antiviral agents,[2] antitumor agents,[3] and cardiovascular agents.[4] Because of their biological importance, these compounds have been the subject of considerable synthetic activity during the past several years.[5] A sizeable portion of this work is directed toward the selective functionalization of the pyrimidine nitrogens.[6] Because of their structural relationship to the clinically important dihydropyridine calcium channel blockers[7] (e.g. nifedipine), we were interested in the synthesis of 3-substituted 1,4-dihydropyrimidines **1–3**.[8] Attempted functionalization of the unsubstituted

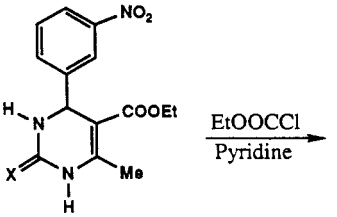


Nifedipine

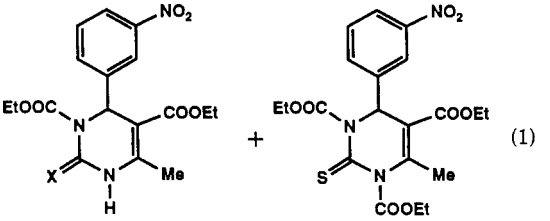


1 X = S
2 X = O
3 X = NH

pyrimidinethione (**1**, R^3 = H), pyrimidinone (**2**, R^3 = H), and aminopyrimidine (**3**, R^3 = H) was either unsuccessful or gave a mixture of products. For example, the reaction of pyrimidinethione **4** with ethyl chloroformate gave, in addition to the desired product **1a**, varying amounts of the diethoxycarbonylated product **6** (eq 1). The corresponding reaction involving the unsubstituted pyrimidinone **5** was



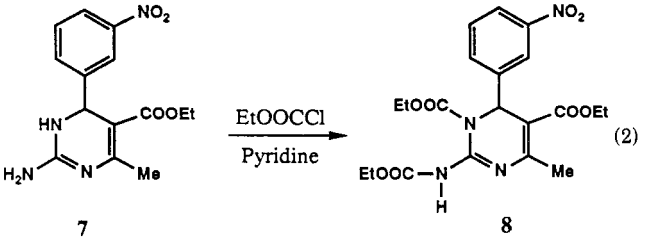
4 X = S
5 X = O



1a X = S
2a X = O

6 (1)

sluggish and required the use of a strong base such as sodium hydride. The regiochemistry of this alkoxycarbonylation is highly dependent on the position of the substituent on the aromatic ring, with ortho-substituted compounds usually leading to N1 alkoxycarbonylation.[6d] In order to achieve a meaningful yield of ortho-substituted N3-alkoxycarbonylated products via this route, Cho et al. had to protect N1.[6d] Functionalization of the 2-aminodihydropyrimidine **7** offers essentially no selectivity between the exo- and the endocyclic nitrogens (eq 2).[6a]



7 **8** (2)

In recent papers, we reported the utility of 1,4-dihydropyrimidines **9** and **10** for the synthesis of dihydropyrimidinethiones **1** (R^3 = H) and pyrimidinones **2** (R^3 = H), respectively.[1] Realizing the difficulty attending the selective ethoxycarbonylation of pyrimidines **4** and **5**, we explored the reaction of 1,4-dihydropyrimidines **9** and **10** with various electrophiles. These studies have resulted in the synthesis of 1,4-dihydropyrimidines (**1–3**) selectively

(1) For previous papers in this series, see: (a) O'Reilly, B. C.; Atwal, K. S. *Heterocycles* **1987**, *26*, 1185. (b) Atwal, K. S.; O'Reilly, B. C.; Gougoutass, J. Z.; Malley, M. F. *Heterocycles* **1987**, *26*, 1189.

(2) (a) Hull, R.; Swain, G. British Patent 1961, 868,030. (b) McKinstry, D.; Reading, E. H. *J. Franklin Inst.* **1944**, *237*, 203.

(3) Hurst, E. W.; Hull, R. *J. Med. Pharm. Chem.* **1961**, *3*, 215.

(4) Khania, E. L.; Sillinietse, G. O.; Ozol, Ya. Ya.; Dabur, G. Ya.; Kimenis, A. A. *Khim. Pharm. Zh.* **1978**, *78*, 1321.

(5) (a) Weis, A. L.; van der Plas, H. C. *Heterocycles* **1986**, *24*, 1433. (b) Weis, A. L. *Synthesis* **1985**, 528.

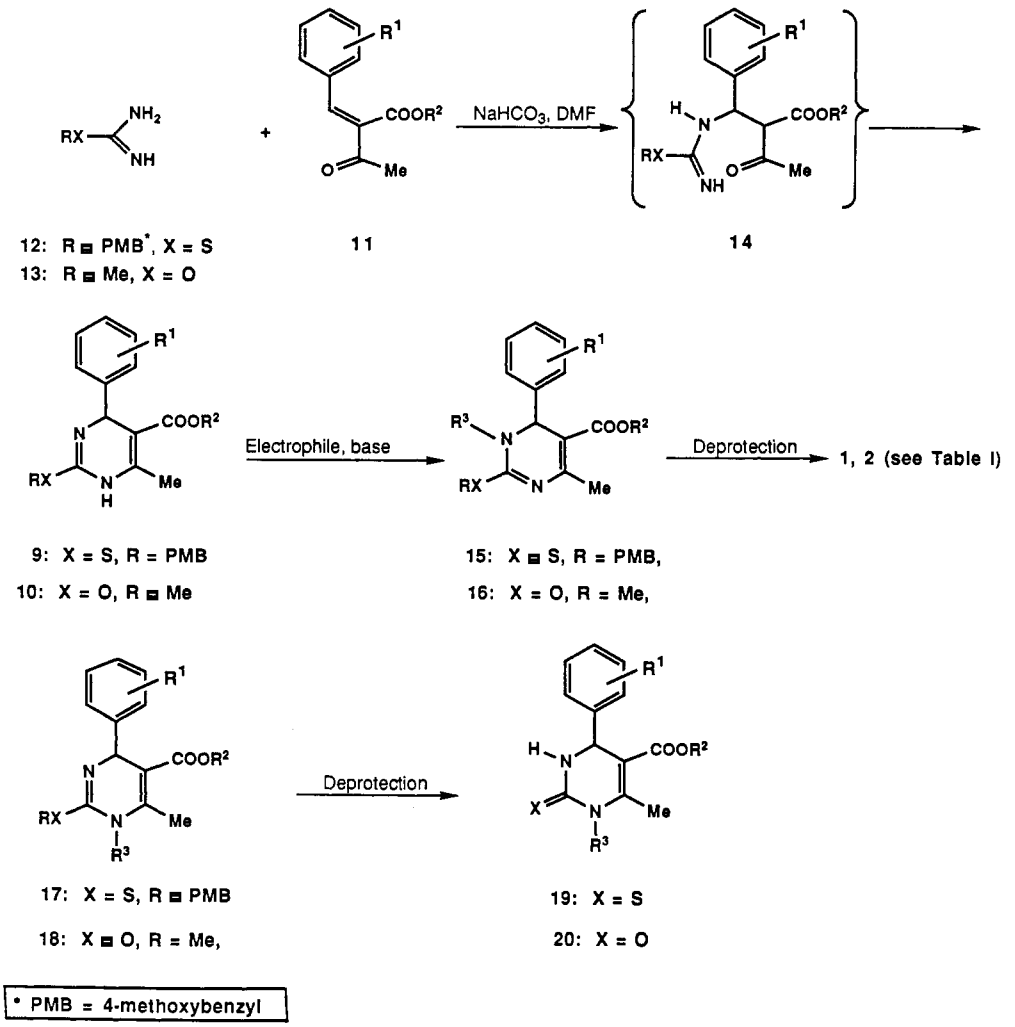
(6) (a) Cho, H.; Shima, K.; Hayashimatsu, M.; Ohnaka, Y.; Mizuno, A.; Takeuchi, Y. *J. Org. Chem.* **1985**, *50*, 4227. (b) Cho, H.; Mizuno, A.; Shima, K.; Ueda, M.; Takeuchi, Y.l; Hamaguchi, M.; Taniguchi, N. *Heterocycles* **1988**, *27*, 769. (c) Cho, H.; Ohnaka, Y.; Hayashimatsu, M.; Ueda, M.; Shima, K. *Tetrahedron Lett.* **1986**, *27*, 6377. (d) Cho, H.; Takeuchi, Y.; Ueda, M.; Mizuno, A. *Tetrahedron Lett.* **1988**, *29*, 5405.

(7) (a) Fossheim, R.; Svarteng, K.; Mostad, A.; Romming, C.; Shefter, E. Triggle, D. J. *J. Med. Chem.* **1982**, *25*, 126. (b) Loev, B.; Goodman, M. M.; Snader, K. M.; Tedeschi, R.; Macko, E. *J. Med. Chem.* **1974**, *17*, 956.

(8) In order to simplify discussion of results, the numbering system as indicated in formula **1** is used throughout; however, proper nomenclature is assigned to each compound as it appears in the Experimental Section.

0022-3263/89/1954-5898$01.50/0

Scheme I



functionalized at N3 and is the subject of this publication.

Results and Discussion

The synthesis of ethoxycarbonylated product **1a** from **4** is complicated not only by the low yield for the preparation of pyrimidinethione **4** using the Biginelli condensation[1] but also by the lack of regioselectivity in the reaction of **4** with ethylchloroformate (eq 1). We envisaged that use of 2-heterosubstituted 1,4-dihydropyrimidines **9** and **10** could circumvent these problems, anticipating the difference in reactivity between the pyrimidine nitrogens of **9** and **10** would increase the selectivity of their reaction with an incoming electrophile (**9**/**10** → **15**/**16**) (Scheme I).[6a] Deprotection of the fully functionalized intermediates **15** and **16** would lead to the desired products **1** and **2**, respectively.

2-[[(4-Methoxyphenyl)methyl]thio]- and 2-methoxy-1,4-dihydropyrimidines **9** and **10** were prepared by the condensation of benzylidene **11**[9] with 2-((4-methoxyphenyl)methyl)-2-thiopseudourea (**12**) and *O*-methylisourea (**13**), respectively (Scheme I).[1] This reaction presumably proceeds through the Michael addition product **14**, giving 1,4-dihydropyrimidines **9** and **10** in excellent yields. Both 2-(alkylthio)pyrimidine **9** and 2-methoxypyrimidine **10** exist in solution as a mixture of tautomers (variable ratio) as demonstrated by ^1H and ^{13}C NMR spectroscopy.[10] Nevertheless, reaction with electrophiles led to a single product (**9**/**10** → **15**/**16**).

Treatment of **9a** with ethyl chloroformate gave **15a** (R^1 = 3-NO_2, R^2 = Et, R^3 = COOEt). Removal of the 4-methoxybenzyl group (trifluoroacetic acid, ethanethiol) furnished **1a** (Table I), the product of exclusive ethoxycarbonylation at N3.[11] In the ^1H NMR spectrum the C4 methine and the C6 methyl group of **1a** are singlets at 6.4 and 2.4 ppm, respectively. The ^{13}C NMR spectrum shows characteristic signals at 141, 106 (double bond of the enamino ester), and 176 ppm (thiocarbonyl). As illustrated by the preparation of **1b**, ortho substitution does not change the outcome of this reaction.

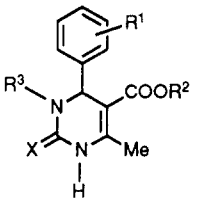
When the appropriate chloroformate was unavailable for reaction with **9** (e.g. as in **1c**), a convenient alternate method was employed.[6b] Treatment of the 1,4-dihydropyrimidine **9b** with phosgene followed by appropriate alcohol gave intermediate **15c** (R^1 = CF_3, R^2 = Et, R^3 = COO-4-benzylpiperidine). Although **15c** could be isolated, it was most convenient to remove the protecting group and isolate the final product **1c**. Both methods gave good yields of products. Furthermore, selective N3 functionalization of **9** is not restricted to alkoxycarbonylation, as

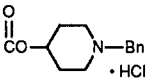
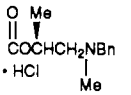
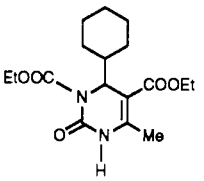
(9) The unsaturated keto ester **11** is prepared in high yield from an aldehyde and acetoacetic ester by the standard Knoevenagel condensation.

(10) For a discussion of the ratio of tautomers in substituted dihydropyrimidines, see, for example: Cho, H.; Iwashita, T.; Ueda, M.; Mizuno, A.; Mizukawa, K.; Hamaguchi, M. *J. Am. Chem. Soc.* **1988**, *110*, 4832.

(11) All compounds were characterized by ^1H and ^{13}C NMR, IR, and mass spectra. Satisfactory elemental analysis was obtained for all crystalline compounds.

Table I. Preparation of 1,4-Dihydropyrimidinethiones 1 and 1,4-Dihydropyrimidinones 2



substrate	product	X	R^1	R^2	R^3	% yield[a]	mp, °C
9a	**1a**	S	3-NO_2	Et	C(O)OEt	82	126–128
9b	**1b**	S	2-CF_3	Et	C(O)OEt	58	104–106
9b	**1c**	S	2-CF_3	Et		60	202–204
9c	**1d**	S	3-NO_2	Me	C(O)Et	74	167–171
9a	**1e**	S	3-NO_2	Et	$C(O)NMe_2$	78	168–170
9a	**1f**	S	3-NO_2	Et	$C(S)NMe_2$	54	179.5–181
9a	**1g**	S	3-NO_2	Et	SO_2Me	59	161–163
9a	**1h**	S	3-NO_2	Et	$CH_2CH_2CH_3$	60[b]	159–162
9b	**1i**	S	2-CF_3	Et	$CH_2CH_2CH_3$	36[b]	139–141
10a	**2a**	O	3-NO_2	Et	C(O)OEt	92	107–109
10a	**2b**	O	3-NO_2	Et	C(O)Ot-Bu	65	139–140
10b	**2c**	O	2-NO_2	Et	C(O)OEt	76	151–152
10a	**2d**	O	3-NO_2	Et	C(O)Et	64	152–154
10c	**2e**	O	3-NO_2	i-Pr	$C(O)NMe_2$	84	165–166
10a	**2f**	O	3-NO_2	Et	SO_2Ph	41	187–188
10c	**2g**	O	3-NO_2	i-Pr	$C(O)NH_2$	91	206–207
10c	**2h**	O	3-NO_2	i-Pr		73	109–119[c]
10c	**2i**	O	3-NO_2	i-Pr	$CH_2CH{=}CH_2$	42[b]	172–174
10d	**2j**					91	152–153

[a] Yield is based on the crystalline product isolated and is unoptimized. [b] Accompanied by the regioisomer, see the Experimental Section. [c] Mixture of diastereomers.

illustrated by the preparation of acylated (**1d**), ureido (**1e**), thioureido (**1f**), and sulfonylated (**1g**) pyrimidinethiones (Table I).

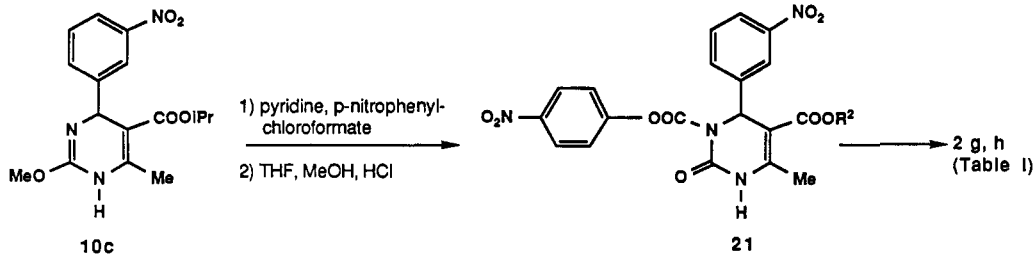
The regioselectivity for alkylation of 1,4-dihydropyrimidinethione **9** depends on the substrate as well as on the alkylating agent used. We have recently reported the alkylation of **9a** (R^1 = 3-nitro, R^2 = Et) with benzyl bromide followed by deprotection gives exclusively the product of N3 alkylation.[1b] In contrast, reaction of **9a** with less reactive electrophile 1-bromopropane and removal of the protecting group gave a 5:1 mixture of N3 (**1h**) and N1 (**19a**) alkylated product. Moreover, in a similar reaction of **9b** with propyl bromide, we obtained a 1:1 mixture of the N3 (**1i**) and N1 (**19b**) alkylated products, presumably a result of steric hindrance at N3 by the ortho-substituted aromatic ring. Regardless of the lack of regioselectivity of alkylation in certain cases, the methodology reported here does make available the N3 alkylated pyrimidinethiones (**1**), which are not accessible by the previous methodology.[1]

The regioisomers were readily distinguished by ^1H NMR spectroscopy. The N3 substituted compound **1i** shows the C4 methine as a singlet at 6.0 ppm, and the N1 substituted compound **19b** shows the same proton as a narrow doublet (J = 3.0 Hz) at 5.75 ppm. The doublet becomes a singlet on deuteration, which confirms that the coupling is due to the neighboring N3-H. These products can also be distinguished at the intermediate stage (**15**, **17**) by ^{13}C NMR spectroscopy. The most diagnostic signal is due to the vinylic methyl in the ^{13}C NMR spectrum. The conjugated diene **15** shows this methyl group at 21–22 ppm whereas the cross conjugated diene **17** displays the same methyl at 15–17 ppm.

When the methoxypyrimidine **10**, prepared from *O*-methylisourea (**13**) and benzylidene **11**,[9] was treated with a variety of electrophiles under the reaction conditions described for **9** (Scheme I), we obtained the N3-substituted 1,4-dihydropyrimidinones **2a–j** in good yields (see Table I). By monitoring the hydrolysis (**16b** → **2b**) carefully, we were able to obtain the acid compound **2b**. The N3 functionalization reaction is not restricted to pyrimidines substituted with a phenyl group at C4 as the bulky cyclohexyl-substituted pyrimidinone **2j** was obtained from **10d** in excellent yield. Ureido derivative **2e** was obtained by the reaction of methoxypyrimidine **10c** with phosgene followed by dimethylamine and deprotection. As an alternative to the use of phosgene, methoxypyrimidine **10c** was converted to the crystalline 4-nitrophenyl carbamate **21**, which on treatment with ammonia provided the desired product **2g** in good yield (Scheme II). This alternate procedure is useful for the synthesis of branched carbamate **2h**, which was obtained in poor yield via phosgene method.

Alkylation (K_2CO_3, allyl bromide) of methoxypyrimidine **10c** followed by removal of the protecting group gave a 6:4 mixture of N3 (**2j**) and N1 (**20**) alkylated products. The structure assignments were confirmed by ^1H and ^{13}C NMR

Scheme II



Scheme III

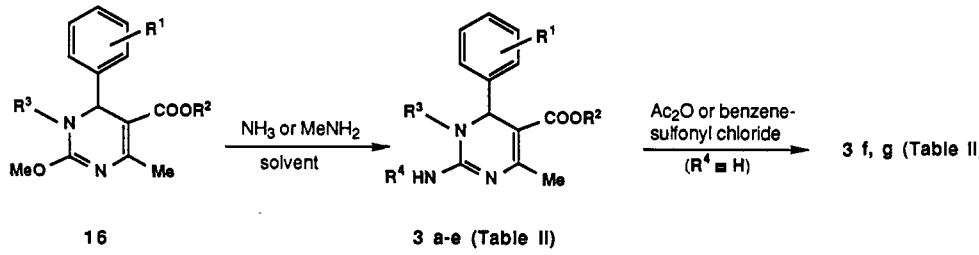
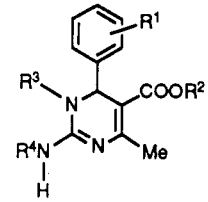


Table II. Preparation of Substituted 2-Aminopyrimidines (3)



substrate	product	R^1	R^2	R^3	R^4	% yield[a]	mp, °C
16c	**3a**	3-NO_2	Et	C(O)OEt	H	54	166–168
16a	**3b**	3-NO_2	Et	C(O)OEt	Me	49	112–114
16c	**3c**	3-NO_2	i-Pr	$C(O)NMe_2$	H	40	202–203
16c	**3d**	3-NO_2	Et	SO_2Ph	H	30	200–201
16c	**3e**	3-NO_2	i-Pr	$CH_2CH{=}CH_2{\cdot}HCl$	H	47	208–210
3a	**3f**	3-NO_2	Et	C(O)OEt	Ac	87[b]	154–156
3a	**3g**	3-NO_2	Et	C(O)OEt	SO_2Me	90[c]	139–141

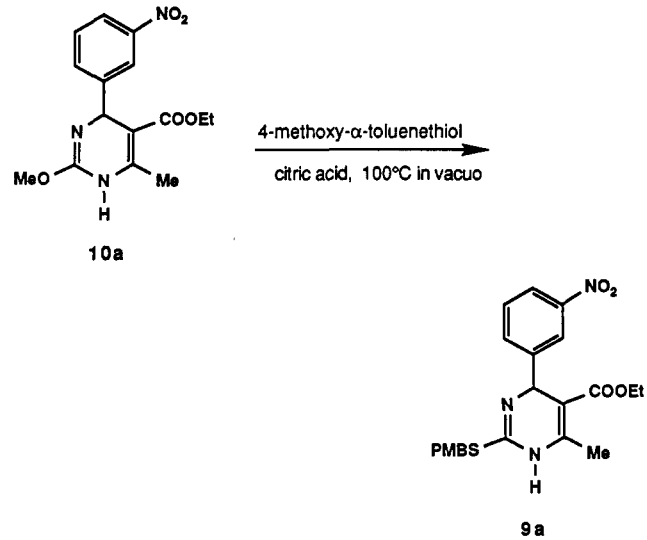
[a] Yield is based on the crystalline product isolated and is unoptimized. [b] Mixture of tautomers. [c] Double bond in the exocyclic position.

spectroscopy in a manner as described for dihydropyrimidinethiones (vide supra).

We next investigated the utility of 2-methoxy-1,4-dihydropyrimidine **10** for the preparation of aminopyrimidines **3**. Our strategy was to introduce the amine into the functionalized intermediate **16** via an exchange reaction. We assumed this would allow the selective functionalization of either the exo- or the endocyclic nitrogens. As shown in Scheme III, **16a** (R^1 = 3-NO_2, R^2 = Et, R^3 = COOEt) undergoes smooth exchange with ammonia to provide the aminopyrimidine **3a**. The reaction with methylamine proceeded equally well, providing 2-(methylamino)pyrimidine **3b** in good yield. This reaction was also successful with a variety of substituents present on the pyrimidine nitrogen (**3c–e**, Table II). The advantange of this process is further illustrated by the preparation of pyrimidines **3f** and **3g**, where the exocyclic nitrogen is distinguished from the ring nitrogens (Scheme III).

The utility of 2-methoxy-1,4-dihydropyrimidine **10** for the preparation of 2-[[(4-methoxyphenyl)methyl]thio]-1,4-dihydropyrimidine **9** was also examined. Thus heating methoxypyrimidine **10a** with 4-methoxybenzyl mercaptan in the presence of an acid catalyst provided 2-mercaptopyrimidine **9a** (Scheme IV). Our combined results demonstrate that 2-methoxypyrimidine **10** is an excellent source of 2-hetero-1,4-dihydropyrimidines (**1–3**).

Scheme IV



Conclusion

We have shown that 2-hetero-1,4-dihydropyrimidines **1–3** can be prepared in a selective manner from the readily available 1,4-dihydropyrimidines **9** and **10**. With the exception of alkylation, the reactions of **9** and **10** with various

electrophiles takes place at N3 with complete selectivity. We believe this selectivity is due to a difference in the electron density at N3 and N1.[6a] The former, being richer in electron density, is more reactive and produces products of exclusive functionalization at N3. The methodology described here avoids use of pyrimidinethiones (e.g. **4**) and pyrimidinones (e.g. **5**) as starting materials and consequently, it does not rely on the unpredictable Biginelli condensation.[1] Also, the ortho-substituted compounds (**1b,c**, **2c**), otherwise difficulty accessible, are available by this method. A particularly attractive feature of this method is its utility for the preparation of functionalized 2-amino-1,4-dihydropyrimidines (Table II), which are unavailable by previous methods.[6a]

Experimental Section

All melting points were taken on a capillary melting point apparatus and are uncorrected. The infrared spectra were recorded with a Perkin-Elmer 983 spectrophotometer in KBr pellets. ^{1}H NMR and ^{13}C NMR spectra were measured on JEOL GX-400 and FX-270 spectrometers with Me_4Si as an internal standard. Mass spectra were obtained with a Finnigan TSQ-4600 spectrometer. Flash chromatography was run with Whatman LPS-1 silica gel and Merck kieselgel 60 (230–400 mesh ASTM).

1,4-Dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic Acid Ethyl Ester (9a). The reaction mixture containing 2-[(3-nitrophenyl)methylene]-3-oxobutanoic acid ethyl ester (**11a**)[9] (13.58 g, 51.0 mmol), 2-((4-methoxyphenyl)methyl)-2-thiopseudourea hydrochloride (**12**)[1b] (4.18 g, 51.0 mmol), and sodium acetate (4.92 g, 60 mmol) in dimethylformamide (75 mL) was heated at 70 °C for 4 h. The reaction was cooled to room temperature, diluted with ether, and filtered. The filtrate was washed with water, sodium bicarbonate, and brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was crystallized from isopropyl ether to yield a colorless solid **9a** (18.8 g, 83%): mp 95–97 °C; IR (KBr) 1674, 1648, 1610, 1525, 1512, 1480, 1348, 1282, 1250, 1178, and 1105 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.12 (s, 1 H), 8.07 (d, J = 8 Hz, 1 H), 7.52 (d, J = 8 Hz, 1 H), 7.4 (t, J = 8.0 Hz, 1 H), 7.12 (d, J = 10 Hz, 2 H), 6.67 (d, J = 10 Hz, 2 H), 6.32 (s, 1 H), 5.83 (s, 1 H), 4.15, 4.1 (AB q, J = 12 Hz, 2 H), 4.12 (q, J = 7 Hz, 2 H), 3.76 (s, 3 H), 2.32 (s, 3 H), 1.22 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.3, 158.9, 150.0, 148.3, 146.9, 145.0, 133.5, 130.1, 129.1, 128.9, 122.1, 121.9, 113.8, 100.0, 60.1, 59.5, 55.2, 34.8, 18.8, 14.2. Anal. Calcd for $C_{22}H_{23}N_3O_5S$: C, 59.84; H, 5.25; N, 9.51; S, 7.26. Found: C, 59.90; H, 5.26; N, 9.58; S, 7.34.

1,4-Dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-[2-(trifluoromethyl)phenyl]-5-pyrimidinecarboxylic Acid Ethyl Ester Monohydrochloride (9b). This compound was prepared in 64% yield by the same procedure as described for **9a**: mp 99–100 °C; IR (KBr) 1717, 1609, 1513, 1314, 1253, 1220, 1162, 1126, 1100 cm^{-1}; ^{1}H NMR (DMSO-d_6) δ 7.76 (d, J = 7 Hz, 1 H), 7.62 (t, J = 7.0 Hz, 1 H), 7.55 (t, J = 7 Hz, 1 H), 7.34 (d, J = 7.0 Hz, 1 H), 7.04 (d, J = 10 Hz, 2 H), 6.57 (d, J = 10 Hz, 2 H), 5.91 (s, 1 H), 4.8–4.6 (m, 1 H), 4.4–4.2 (m, 1H), 3.93 (q, J = 6 Hz, 2 H), 3.7 (s, 3 H), 2.45 (s, 3 H), 0.96 (t, J = 6 Hz, 3 H); ^{13}C NMR (DMSO-d_6) δ 164.7, 160.6, 145.1, 134.7, 131.1, 131.0, 130.8, 127.8, 127.3, 115.2, 107.4, 61.9, 55.9, 52.4, 37.4, 17.4, 14.3. Anal. Calcd for $C_{23}H_{23}F_3N_2O_3S$·HCl: C, 55.14; H, 4.82; N, 5.59; Cl, 7.07; F, 11.37; S, 6.39. Found: C, 55.28; H, 4.83; N, 5.86; Cl, 6.83; F, 11.32; S, 6.27.

1,4-Dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic Acid Methyl Ester (9c). This compound was prepared in 80% yield by the same procedure as described for **9a**: mp 125–127.5 °C; IR (KBr) 1649, 1610, 1527, 1511, 1477, 1432, 1347, 1162, 1109 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.1 (s, 1 H), 8.08 (d, J = 8 Hz, 1 H), 7.63 (d, J = 8 Hz, 1 H), 7.43 (t, J = 8.0 Hz, 1 H), 7.12 (d, J = 9 Hz, 2 H), 6.67 (d, J = 9 Hz, 2 H), 6.24 (s, 1 H), 5.82 (s, 1 H), 3.77 (s, 3 H), 3.67 (s, 3 H), 2.33 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.8, 158.8, 150.3, 148.3, 146.7, 145.6, 133.4, 129.3, 129.0, 121.9, 113.7, 99.4, 59.3, 55.1, 51.5, 34.6, 18.5. Anal. Calcd for $C_{21}H_{21}N_3O_5S$: C, 59.00; H, 4.95; N, 9.83; S, 7.50. Found: C, 58.86; H, 4.82, N, 9.51; S, 7.25.

1,4-Dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic Acid 1-Methylethyl Ester (10c). The reaction mixture containing 2-[(3-nitrophenyl)methylene]-3-oxobutanoic acid 1-methylethyl ester (**11d**)[9] (41.3 g, 149.0 mmol), *O*-methylisourea hydrogen sulfate **13** (33.35 g, 194.0 mmol), and sodium bicarbonate (50.07 g, 596 mmol) in dimethylformamide (150 mL) was heated at 70 °C for 24 h.[1a] The reaction was cooled to room temperature, diluted with ether, and filtered. The filtrate was washed with water, sodium bicarbonate, and brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was crystallized from isopropyl ether to yield a colorless solid **10c** (43.84 g, 88%): mp 130–132 °C; IR (KBr) 1685, 1524, 1489, 1345, 1232, 1102 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.17 (s, 1 H), 8.09 (d, J = 7.9 Hz, 1 H), 7.68 (d, J = 7.9 Hz, 1 H), 7.45 (t, J = 7.9 Hz, 1 H), 6.2 (br, 1 H), 5.67 (s, 1 H), 4.95 (q, J = 6.33 Hz, 2 H), 3.75 (s, 3 H), 2.35 (s, 3 H), 1.22, 1.07 (d, J = 6.33 Hz, 3 H each); ^{13}C NMR ($CDCl_3$) δ 165.93, 148.22, 133.35, 129.88, 122.05, 67.26, 53.95, 21.98, 21.67 (some signals were of low intensity due to tautomeric equilibrium). Anal. Calcd for $C_{16}H_{19}N_3O_5$: C, 57.65; H, 5.74; N, 12.61. Found: C, 57.72; H, 5.93; N, 12.66.

1,4-Dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic Acid Ethyl Ester (10a). This compound was prepared in 82% yield by the same procedure as described for **10c**: mp 103–105 °C; IR (KBr) 1691, 1647, and 1529 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.16, 8.11 (s, 1 H), 8.07 (dd, J = 8.0 and 1.0 Hz, 1 H), 7.7 (d, J = 7.4 Hz, 1 H), 7.4 (t, J = 8.0 Hz, 1 H), 6.5, 6.0 (s, 1 H), 5.7, 5.55 (s and d respectively, J = 2.7 Hz, 1 H), 4.1 (dq, J = 6.9 and 1.0 Hz, 2 H), 3.85, 3.7 (s, 3 H), 2.4, 2.3 (s, 3 H), 1.2 (t, J = 6.9 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.25, 150.6 (159), 148.2, 148.1, 146.3 (146.9), 133.4 (132.8), 122.1 (122.6), 121.8 (121.6), 100.1 (102.6), 59.8 (59.75), 58.5 (54.9), 53.8 (54.3), 18.6 (22.8); the values in parenthesis indicate the signals due to the minor 3,4-dihydropyrimidine tautomer. Anal. Calcd for $C_{15}H_{17}N_3O_5$: C, 56.40; H, 5.37; N, 13.16. Found: C, 56.52; H, 5.35; N, 13.03.

1,4-Dihydro-2-methoxy-6-methyl-4-(2-nitrophenyl)-5-pyrimidinecarboxylic Acid Ethyl Ester (10b). This compound, prepared in 78% yield by the same procedure as described for **10c**, was obtained as a yellow gum: IR (KBr) 1710, 1675, and 1625 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.87 (d, J = 8.5 Hz, 1 H), 7.7–7.3 (m, 3 H), 3.9 (m, 2 H), 3.82, 3.64 (s, 3 H), 2.5, 2.36 (s, 3 H), 1.05, 0.95 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.7, 160.7, 157.0 (149.7), 147.9 (139.8), 138.0, 134.1 (132.24), 129.8, 128.9, 128.6, 124.2, 123.8, 101.1 (99.2) (59.7), 59.5, 54.2 (54.1) (53.73), 50.1, 23.3 (18.5) (14.03), 13.9; the values in parentheses indicate the signals due to the minor 3,4-dihydropyrimidine tautomer. Anal. Calcd for $C_{15}H_{17}N_3O_5$: C, 56.42; H, 5.39; N, 13.16. Found: C, 56.21; H, 5.44; N, 12.84.

4-Cyclohexyl-1,4-dihydro-2-methoxy-6-methyl-5-pyrimidinecarboxylic Acid Ethyl Ester (10d). This compound, prepared in 79% yield by the same method as described for **10c**, was obtained as a colorless foam; IR (KBr) 1693, 1530 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 6.1, 5.2 (s, 1 H), 4.43 (d, J = 4.2 Hz, 0.6 H), 4.25 (t, J = 3.67 Hz, 0.4 H), 4.15 (q, J = 6.9 Hz, 3 H), 3.8, 3.75 (s, 3 H), 2.3, 2.25 (s, 3 H), 1.8–0.9 (complex m, 11 H), 1.25 (t, J = 6.9 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 167.45 (167.36), 158.27 (158.16), 150.12 (145.4), 102.25 (100.2), 59.5 (56.05), 59.4, 54.0 (53.45), 45.6 (44.8), 28.9 (28.23), 27.34 (26.58), 26.33, 26.22, 25.9, 23.4 (18.43), 14.30; the values in parentheses indicate the signals due to the minor 3,4-dihydropyrimidine tautomer; mass spectrum (CI), m/z 281.

3,6-Dihydro-4-methyl-6-(3-nitrophenyl)-2-thioxo-1,5-(2*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (1a). The solution of 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**9a**) (3.0 g, 6.8 mmol) in dichloromethane (15 mL) and pyridine (1.5 mL) was treated with ethyl chloroformate (0.87 mL, 8.84 mmol) at 0 °C under argon. After the addition was finished, the reaction was stirred at room temperature for 2 h and then diluted with more dichloromethane. The resulting solution was washed with 1 N hydrochloric acid, water, sodium bicarbonate, and brine. After drying over magnesium sulfate, the solvent was evaporated to yield a light yellow oil (3.4 g). This was dissolved in dichloromethane (20 mL) and treated with trifluoroacetic acid (2.0 mL) and ethanethiol (1.0 mL). The reaction was stirred at room temperature overnight, and the solvent was evaporated. The

residue was purified by flash chromatography (3% ethyl acetate in dichloromethane), and the product was crystallized from ether–hexanes to yield 3,6-dihydro-4-methyl-6-(3-nitrophenyl)-2-thioxo-1,5(2*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**1a**) as a light yellow solid (2.2 g): IR (KBr) 1763, 1713, 1619, 1660 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.6 (s, 1 H), 8.21 (s, 1 H), 8.14 (d, J = 9.0 Hz, 1 H), 7.7 (d, J = 7.9 Hz, 1 H), 7.5 (t, J = 7.9 Hz, 1 H), 6.4 (s, 1 H), 4.4 (q, J = 6.9 Hz, 2 H), 4.25 (q, J = 7.4 Hz, 2 H), 2.4 (s, 3 H), 1.4 (t, J = 6.9 Hz, 3 H), 1.3 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 176.2, 164.7, 153.8, 148.5, 143.6, 141.4, 132.6, 129.8, 123.2, 121.8, 106.4, 64.7, 61.2, 56.1, 17.7, 14.2, 14.0. Anal. Calcd for $C_{17}H_{19}N_3O_6S$: C, 51.90; H, 4.87; N, 10.68; S, 8.15. Found: C, 51.73; H, 4.80; N, 10.44; S, 7.93.

3,6-Dihydro-4-methyl-6-[2-(trifluoromethyl)phenyl]-2-thioxo-1,5(2*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (1b). This compound was prepared from 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-[2-(trifluoromethyl)-phenyl]-5-pyrimidinecarboxylic acid ethyl ester (**9b**) in a manner as described for **1a**: IR (KBr) 1716, 1646, 1305, 1233, 1217 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.7 (s, 1 H), 7.3–7.8 (m, 4 H), 6.6 (s, 1 H), 4.3 (q, J = 6.5 Hz, 2 H), 4.1 (q, J = 6.5 Hz, 2 H), 2.42 (s, 3 H), 1.3 (t, J = 6.5 Hz, 3 H), 1.16 (t, J = 6.5 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 175.0, 164.3, 152.7, 142.5, 138.3, 132.7, 129.1, 128.8, 127.8, 126.9, 106.2, 64.6, 60.6, 54.0, 17.5, 13.8, 13.6. Anal. Calcd for $C_{18}H_{19}F_3N_2O_4S$: C, 51.91; H, 4.59; N, 6.72; F, 13.68; S, 7.69. Found: C, 51.94; H, 4.53; N, 6.72; F, 13.40; S, 7.82.

3,6-Dihydro-4-methyl-2-thioxo-6-[2-(trifluoromethyl)-phenyl]-1,5(2*H*)-pyrimidinedicarboxylic Acid 5-Ethyl 1-[1-(Phenylmethyl)-4-piperidinyl] Diester Monohydrochloride (1c). A solution of 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-[2-(trifluoromethyl)phenyl]-5-pyrimidinecarboxylic acid ethyl ester (**9b**) (4.8 g, 103 mmol) in acetonitrile (100 mL) and pyridine (60 mL) at room temperature under argon was treated dropwise with phosgene (16 mL of 12.5% solution in toluene). After stirring for 6 h, the reaction mixture was treated with a solution of 1-benzyl-4-hydroxypiperidine hydrochloride in acetonitrile (9.1 g, 0.04M) and allowed to stir at room temperature for 16 h. Water (10 mL) was added, and solvent was evaporated in vacuo. The oily residue in ethyl acetate was washed with 1 N hydrochloric acid, water, sodium bicarbonate, and brine. The dried (magnesium sulfate) organic solution was concentrated in vacuo to give a dark oil (6.4 g). This was dissolve in dichloromethane (100 mL) and treated with trifluoroacetic acid (3.6 mL) and ethanethiol (1.8 mL) and stirred at room temperature for 6 h. Volatiles were evaporated, and the residue, dissolved in ethyl acetate, was washed with sodium bicarbonate and brine, dried (magnesium sulfate), and concentrated in vacuo. The resulting dark oil was converted to its hydrochloride salt and crystallized from acetonitrile to give 3,6-dihydro-4-methyl-2-thioxo-6-[2-(trifluoromethyl)phenyl]-1,5(2*H*)-pyrimidinedicarboxylic acid 5-ethyl 1-[1-(phenylmethyl)-4-piperidinyl] diester monohydrochloride (**1c**) (3.7 g) as a yellow solid: IR (KBr) 1713, 1644, 1503, 1454, 1233 cm^{-1}; ^1H NMR (DMSO-d_6) δ 11.6, 11.7 (2 s, 1 H), 10.7, 10.9 (2 br s, 1 H), 7.3–7.8 (m, 9 H), 6.44, 6.55 (2 s, 1 H), 4.87, 5.03 (2 br s, 1 H), 4.24 (m, 2 H), 4.0 (q, J = 6.0 Hz, 2 H), 2.8–3.4 (m, 4 H), 2.38 (s, 3 H), 1.8–2.3 (m, 4 H), 1.06 (t, J = 6.0 Hz, 3 H); ^{13}C NMR (free base) ($CDCl_3$) δ 174.7, 164.2, 152.2, 142.7, 138.2, 132.5, 129.1, 128.8, 127.9, 126.7, 105.7, 75.3, 62.6, 60.4, 53.9, 50.0, 29.9, 17.3, 13.7. Anal. Calcd for $C_{28}H_{30}F_3N_3O_4S$·HCl: C, 56.23; H, 5.22; N, 7.02; Cl, 5.92; S, 5.36. Found: C, 56.35; H, 5.21; N, 7.47; Cl, 6.01; S, 5.36.

1,2,3,4-Tetrahydro-6-methyl-4-(3-nitrophenyl)-3-(1-oxopropyl)-2-thioxo-5-pyrimidinecarboxylic Acid Methyl Ester (1d). A solution of 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]-thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid methyl ester (**9c**) (1.52 g, 3.5 mmol) in dichloromethane (15 mL) was cooled under argon to 0–5 °C and treated with pyridine (0.55 g, 7.0 mmol) and propionyl chloride (0.43 g, 4.7 mmol). The mixture was allowed to stir at room temperature for 3 h, diluted with ether, and washed with 1 N hydrochloric acid, water, sodium bicarbonate, and brine. The dried (magnesium sulfate) solution was concentrated in vacuo to give a viscous oil (1.6 g). This material was deprotected (as described for **1a**), and the product was crystallized from isopropyl ether to give 1,2,3,4-tetrahydro-6-methyl-4-(3-nitrophenyl)-3-(1-oxopropyl)-2-thioxo-5-pyrimidinecarboxylic acid methyl ester (**1d**) (0.95 g) as a pale yellow powder: IR (KBr) 1711, 1670, 1644, 1533, 1503, 1391, 1368, 1352 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.24 (s, 1 H), 8.14 (d, J = 6.0 Hz, 1 H), 8.13 (s, 1 H), 7.68 (d, J = 6.0 Hz, 1 H), 7.5 (t, J = 6.0 Hz, 1 H), 6.69 (s, 1 H), 3.81 (s, 3 H), 3.4–3.6 (m, 1 H), 2.85–3.05 (m, 1 H), 2.48 (s, 3 H), 1.26 (t, J = 6.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 177.9, 165.3, 145.3, 140.8, 132.7, 129.3, 122.5, 121.2, 106.0, 53.0, 51.3, 32.2, 16.1, 9.5. Anal. Calcd for $C_{16}H_{17}N_3O_5S$: C, 52.88; H, 4.72; N, 11.56; S, 8.82. Found: C, 52.83; H, 4.74; N, 11.45; S, 8.71.

1-[(Dimethylamino)carbonyl]-1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-thioxo-5-pyrimidinecarboxylic Acid Ethyl Ester (1e). A solution of 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**9a**) (0.5 g, 11 mmol) in tetrahydrofuran (10 mL) and pyridine (1 mL) under argon at 0–5 °C was treated with phosgene (1.16 mL of 12.5% sol in toluene). After 0.5 h, dimethylamine (1 mL of 40% aqueous solution) was added, and the reaction continued for 0.5 h, after which the mixture was diluted with ethyl acetate and washed with 1 N hydrochloric acid, water, and brine. The dried (magnesium sulfate) organic fraction was concentrated in vacuo to give an oil (0.6 g). This material was deprotected (as described for **1a**), and the product was triturated with isopropyl ether to give 1-[(dimethylamino)-carbonyl]-1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-thioxo-5-pyrimidinecarboxylic acid ethyl ester (**1e**) as an off-white powder: IR (KBr) 1711, 1674, 1532, 1383, 1220, 1091 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.4–8.3 (m, 5 H), 5.75, 6.05 (2 s, 1 H), 3.99, 4.28 (2 q, J = 6.0 Hz, 2 H), 3.06, 2.9 (2 s, 6 H), 2.33, 2.42, 2.45 (3 s, 4 H), 1.05, 1.35 (2 t, J = 6.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 174.7, 164.5, 154.7, 148.0, 144.5, 143.0, 132.7, 129.3, 122.6, 121.6, 104.3, 60.9, 57.8, 38.0, 36.5, 17.7, 13.9. Anal. Calcd for $C_{17}H_{20}N_4O_5S$: C, 52.03; H, 5.14; N, 14.28; S, 8.17. Found: C, 52.01; H, 5.19; N, 14.23; S, 7.93.

1-[[(Dimethylamino)thioxo]methyl]-1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-thioxo-5-pyrimidinecarboxylic Acid Ethyl Ester (1f). This compound was prepared from 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**9a**) in a manner as described for **1e** except that phosgene was replaced with thiophosgene. Following deprotection (as described for **1a**), the residue was flash chromatographed on silica gel, eluting with ethyl acetate/hexane (3:7). Trituration with isopropyl ether afforded 1-[[(dimethylamino)thioxo]methyl]-1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-thioxo-5-pyrimidinecarboxylic acid ethyl ester (**1f**) (0.5 g) as an off-white powder: IR (KBr) 1720, 1660, 1530, 1511, 1351, 1230 cm^{-1}; ^1H NMR (DMSO-d_6) δ 8.15–8.30 (m, 1 H), 8.11, 7.99 (d, J = 6.0 Hz, s, 1 H), 7.55–7.8 (m, 2 H), 5.81, 6.24 (2 s, 1 H), 3.8–4.0, 4.05–4.3 (2 m, 2 H), 3.31, 3.35 (2 s, 3 H), 3.14, 3.18 (2 s, 3 H), 2.41, 2.43 (2 s, 3 H), 0.92, 1.26 (2 t, J = 6.0 Hz, 3 H); ^{13}C NMR (DMSO-d_6) δ 183.7, 179.9, 173.8, 170.1, 164.5, 164.1, 148.3, 147.8, 144.5, 142.9, 142.1, 134.1, 132.9, 129.8, 129.0, 123.6, 122.5, 121.8, 104.5, 101.4, 63.5, 61.0, 60.3, 43.4, 42.0, 17.8, 14.0, 13.7. Anal. Calcd for $C_{17}H_{20}N_4O_4S_2$: C, 49.88; H, 4.94; N, 13.72; S, 15.70. Found: C, 50.17; H, 4.98; N, 13.64, S, 15.72.

1,2,3,4-Tetrahydro-6-methyl-3-(methylsulfonyl)-4-(3-nitrophenyl)-2-thioxo-5-pyrimidinecarboxylic Acid Ethyl Ester (1g). A solution of 1,4-dihydro-2-[[(4-methoxyphenyl)-methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**9a**) (2.0 g, 4.5 mmol) in dichloromethane (15 mL) and pyridine (0.72 mL) under argon at −10 °C was treated dropwise with a solution of methanesulfonyl chloride (0.62 g, 5.4 mmol) in dichloromethane (5 mL). After the mixture was stirred at room temperature overnight, additional dichloromethane was added, and the mixture was washed with water, 1 N hydrochloric acid, and brine. The dried (magnesium sulfate) solution was concentrated in vacuo, and the residue flash was chromatographed (dichloromethane) to give an oil (2.0 g). This was deprotected (as described for **1a**) to give 1,2,3,4-tetrahydro-6-methyl-3-(methylsulfonyl)-4-(3-nitrophenyl)-2-thioxo-5-pyrimidinecarboxylic acid ethyl ester (**1g**) as a colorless solid (1.05 g): IR (KBr) 1724, 1530, 1507, 1352, 1245, 1221, 1162 cm^{-1}; ^1H NMR (DMSO-d_6) δ 11.75 (s, 1 H), 8.15–8.25 (m, 1 H), 8.07 (s, 1 H), 7.65–7.8 (m, 2 H), 6.55 (s, 1 H), 4.05–4.25 (m, 2 H), 3.62 (s, 3 H), 2.37 (s, 3 H), 1.23 (t, J = 7.0 Hz, 3 H); ^{13}C NMR (DMSO-d_6) δ 175.2, 164.1, 148.0, 145.0, 141.2, 132.6, 130.8, 123.4, 120.7, 105.3, 60.5, 55.5, 43.0, 16.5, 13.8. Anal. Calcd for $C_{15}H_{17}N_3O_6S_2$: C, 45.10; H, 4.28; N, 10.51; S, 16.05. Found: C, 45.03; H, 4.17; N, 10.42; S, 16.04.

1,2,3,6-Tetrahydro-4-methyl-6-(3-nitrophenyl)-1-propyl-2-thioxo-5-pyrimidinecarboxylic Acid Ethyl Ester (1h). A solution of 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ether ester (**9a**) (1.11 g, 2.5 mmol) in dimethylformamide (8 mL) under argon at room temperature was treated with 1-bromopropane (0.5 mL, 5.4 mmol) and powdered potassium carbonate (0.69 g, 5.0 mmol) and stirred at 80 °C overnight. The reaction was diluted with ethyl acetate and washed with water and brine. The dried (magnesium sulfate) solution was concentrated to give a brown oil (1.25 g). Flash chromatography on LPS-1 silica gel and elution with ethyl acetate/hexanes (1:10) gave 1,6-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-4-methyl-6-(3-nitrophenyl)-1-propyl-5-pyrimidinecarboxylic acid ethyl ester (**15h**) (1.01 g, 83%) as an oil: ^{1}H NMR ($CDCl_3$) δ 8.15 (s, 1 H), 8.1 (d, J = 8.5 Hz, 1 H), 7.65 (d, J = 8.0 Hz, 1 H), 7.45 (t, J = 7.9 Hz, 1 H), 7.3 (d, J = 8.1 Hz, 2 H), 6.8 (d, J = 8.1 Hz, 2 H), 5.45 (s, 1 H), 4.4 (AB q, J = 11.0 Hz, 2 H), 4.15 (m, 2 H), 3.8 (s, 3 H), 3.45 (m, 1 H), 3.1 (m, 1 H), 2.4 (s, 3 H), 1.55 (m, 2 H), 1.3 (t, J = 7.5 Hz, 3 H), 0.9 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.2, 161.9, 158.7, 155.3, 148.1, 144.9, 132.7, 130.5, 130.1, 129.80, 129.5, 128.9, 122.6, 121.5, 113.7, 103.2, 59.9, 59.7, 55.0, 51.7, 35.2, 22.9, 21.3, 14.13, 10.8. Further elution of the column provided the more polar component, 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-1-propyl-5-pyrimidinecarboxylic acid ethyl ester (**17a**) (0.18 g, 15%) as an oil: ^{1}H NMR ($CDCl_3$) δ 8.15 (s, 1 H), 8.05 (d, J = 8.5 Hz, 1 H), 7.60 (d, J = 8.0 Hz, 1 H), 7.40 (t, J = 8.0 Hz, 1 H), 7.2 (d, J = 8.1 Hz, 2 H), 6.75 (d, J = 8.1 Hz, 2 H), 5.85 (s, 1 H), 4.25–4.15 (m, 4 H), 3.8 (s, 3 H), 3.6 (m, 2 H), 2.45 (s, 3 H), 1.45 (m, 2 H), 1.25 (t, J = 7.5 Hz, 3 H), 0.85 (t, J = 7.2 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.5, 158.6, 154.3, 148.4, 148.0, 146.5, 132.8, 130.0, 128.7, 121.5, 113.6, 102.3, 59.9, 57.6, 55.0, 47.0, 35.9, 23.8, 15.2, 14.1, 10.5.

The 1,6-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-4-methyl-6-(3-nitrophenyl)-1-propyl-5-pyrimidinecarboxylic acid ethyl ester (**15h**) (1.0 g, 2.0 mmol) was deprotected (trifluoroacetic acid, ethanethiol), and the residue, after workup, was crystallized from isopropyl ether to yield 1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-1-propyl-2-thioxo-5-pyrimidinecarboxylic acid ethyl ester (**1h**) (0.65 g): IR (KBr) 1653, 1528, 1461, 1382, 1374, 1349, 1254, 1130 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.10–8.25 (m, 2 H), 8.0 (s, 1 H), 7.64 (d, J = 6.3 Hz, 1 H), 7.52 (t, J = 8.0 Hz, 1 H), 5.6 (s, 1 H), 4.1–4.5 (m, 3 H), 3.05–3.3 (m, 1 H), 2.34 (s, 3 H), 1.6–1.9 (m, 2 H), 1.31 (t, J = 7.0 Hz, 3 H), 0.93 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 175.1, 164.9, 148.1, 144.0, 143.1, 132.5, 129.9, 122.9, 121.8, 101.4, 60.5, 59.9, 53.8, 19.8, 17.8, 14.0, 10.8. Anal. Calcd for $C_{17}H_{21}N_3O_4S$: C, 56.18; H, 5.83; N, 11.56; S, 8.82. Found: C, 56.51; H, 5.79; N, 11.40; S, 8.78.

1,2,3,6-Tetrahydro-4-methyl-1-propyl-2-thioxo-6-[2-(trifluoromethyl)phenyl]-5-pyrimidinecarboxylic Acid Ethyl Ester (1i) and 1,2,3,4-Tetrahydro-6-methyl-1-propyl-2-thioxo-4-[2-(trifluoromethyl)phenyl]-5-pyrimidinecarboxylic Acid Ethyl Ester (19b). A solution of 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-[2-(trifluoromethyl)-phenyl]-5-pyrimidinecarboxylic acid ethyl ester (**9b**) (2.0 g, 4.3 mmol) in dimethylformamide (8 mL) under argon at room temperature was treated with 1-bromopropane (1.0 mL, 1.35 g, 10.9 mmol) and powdered potassium carbonate (1.18 g, 8.6 mmol) and stirred at 70 °C overnight. The reaction mixture was diluted with ethyl acetate and washed with water and brine. The dried (magnesium sulfate) solution was concentrated in vacuo to give a tan oil (2.27 g). Flash chromatography on silica gel and elution with ethyl acetate/hexane (1:10) gave 1,6-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-4-methyl-6-[2-(trifluoromethyl)-phenyl]-1-propyl-5-pyrimidinecarboxylic acid ethyl ester **15i** (1.02 g) as a thick oil. Further elution with the same solvent system provided the more polar component, 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-[2-(trifluoromethyl)-phenyl]-1-propyl-5-pyrimidinecarboxylic acid ethyl ester (**17b**) (0.88 g), also an oil.

The 1,6-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-4-methyl-6-[2-(trifluoromethyl)phenyl]-1-propyl-5-pyrimidinecarboxylic acid ethyl ester (**15i**) (1.02 g, 0.002 mol) was deprotected with trifluoroacetic acid and ethanethiol, and the resulting oil after workup was crystallized from isopropyl ether/hexane and then from dichloromethane/hexane to give 1,2,3,6-tetrahydro-4-methyl-1-propyl-2-thioxo-6-[2-(trifluoromethyl)phenyl]-5-pyrimidinecarboxylic acid ethyl ester (**1i**) as an off-white powder (0.57 g): IR (KBr) 1716, 1651, 1549, 1479, 1307, 1220 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.84 (s, 1 H), 7.67 (d, J = 8.0 Hz, 1 H), 7.63 (d, J = 9.0 Hz, 1 H), 5.98 (s, 1 H), 3.95–4.3 (m, 3 H), 3.05–3.25 (m, 1 H), 2.38 (s, 3 H), 1.45–1.85 (m, 2 H), 1.15 (s, 3 H), 0.1 (s, 3 H); ^{13}C NMR ($CDCl_3$) δ 174.4, 164.8, 142.8, 140.8, 133.1, 130.1, 128.6, 126.4 (d, J = 5 Hz), 102.8, 60.1, 55.8 (d, J = 3 Hz), 52.6, 19.3, 17.6, 13.8, 10.6. Anal. Calcd for $C_{18}H_{21}F_3N_2O_2S$: C, 55.95; H, 5.48; N, 7.25, F, 14.75; S, 8.30. Found: C, 56.17; H, 5.56; N, 7.21; F, 14.97; S, 8.47.

1,4-Dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-[2-(trifluoromethyl)phenyl]-1-propyl-5-pyrimidinecarboxylic acid ethyl ester **17b** (0.8 g, 0.0016 mol) was similarly deprotected and the oily residue (0.8 g) was flash chromatographed on 300 mL of LSP-1 silica gel and eluted with dichloromethane/hexane to give an oil that slowly solidified to yield 1,2,3,4-tetrahydro-6-methyl-1-propyl-2-thioxo-4-[2-(trifluoromethyl)phenyl]-5-pyrimidinecarboxylic acid ethyl ester (**19b**) (0.41 g, 21% from **9b**): mp 127–129.5 °C; IR (KBr) 1706, 1636, 1404, 1313, 1200, 1157, 1118 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 7.69 (d, J = 8 Hz, 1 H), 7.54 (t, J = 8 Hz, 1 H), 7.42 (t, J = 8 Hz, 1 H), 7.35 (d, J = 8 Hz, 1 H), 6.96 (br s, 1 H), 5.75 (d, J = 3 Hz, 1 H), 4.54–4.74 (m, 1 H), 3.98–4.10 (m, 3 H), 2.70 (s, 3 H), 1.60–1.95 (m, 2 H), 0.98 (t, J = 7 Hz, 6 H); ^{13}C NMR ($CDCl_3$) δ 177.7, 164.7, 147.3, 139.0, 132.7, 128.2, 128.1, 126.2 (d, J = 6 Hz), 105.5, 60.2, 49.7, 22.4, 16.0, 13.4, 10.7. Anal. Calcd for $C_{18}H_{21}F_3N_2O_2S$: C, 55.95; H, 5.48; N, 7.25; S, 8.30. Found: C, 55.99; H, 5.44; N, 7.19; S, 8.07.

3,6-Dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (2a). The solution of 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**10a**) (1.5 g, 4.7 mmol) in dichloromethane (15 mL) and pyridine (0.4 mL) was cooled to 0 °C and treated with ethyl chloroformate (540 mg, 4.8 mmol). After the addition, the cooling bath was removed, and the reaction was stirred at room temperature for 30 min. The solvent was removed, and the residue was dissolved in methanol (10 mL) and treated with 2 N hydrochloric acid (2 mL). After 30 min at room temperature, the solvent was removed, and the residue in ethyl acetate was washed with sodium bicarbonate and brine. It was dried over magnesium sulfate and evaporated. The residue was crystallized from isopropyl ether–hexanes to yield 3,6-dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**2a**) (1.64 g): IR (KBr) 1732, 1710, 1645 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 8.22 (s, 1 H), 8.14 (d, J = 7.9 Hz, 1 H), 8.1 (br s, 1 H), 7.73 (d, J = 7.9 Hz, 1 H), 7.49 (t, J = 7.9 Hz, 1 H), 6.4 (s, 1 H), 4.34 (dq, J = 7.4 and 2.6 Hz, 2 H), 4.2 (dq, J = 7.4 and 4.75 Hz, 2 H), 2.42 (s, 3 H), 1.35 (t, J = 7.4 Hz, 3 H), 1.27 (t, J = 7.9 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 164.6, 152.8, 150.2, 148.3, 146.6, 142.1, 132.7, 129.6, 123.0, 121.9, 103.9, 64.0, 60.7, 55.9, 17.7, 14.1, 14.0. Anal. Calcd for $C_{17}H_{19}N_3O_7$: C, 54.11; H, 5.08; N, 11.14. Found: C, 54.10; H, 5.06; N, 10.93.

3,6-Dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5-pyrimidinedicarboxylic Acid 1-(1,1-Dimethylethyl) 5-Ethyl Diester (2b). A solution of 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**10a**) (960 mg, 3.0 mmol) and 4-(dimethylamino)pyridine (36 mg, 0.3 mmol) in acetonitrile (6.0 ml) was treated with di-*tert*-butyl dicarbonate (0.75 mL, 3.6 mmol), and the reaction was stirred at room temperature for 1 h. The reaction was evaporated, and the residue was hydrolyzed in a manner as described for **2a**. The product was purified by flash chromatography (ethyl acetate/hexanes, 1:1) and crystallized from dichloromethane–isopropyl ether to provide 3,6-dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5-pyrimidinedicarboxylic acid 1-(1,1-dimethylethyl) 5-ethyl diester (**2b**) (792 mg): ^{1}H NMR ($CDCl_3$) δ 8.79 (br s, 1 H), 8.24 (s, 1 H), 9.14 (d, J = 8 Hz, 1 H), 7.7 (d, J = 8 Hz, 1 H), 7.5 (m, 1 H), 6.33 (s, 1 H), 4.2 (m, 2 H), 2.4 (s, 3 H), 1.53 (s, 3 H), 1.3 (s, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 164.8, 151.2, 150.7, 148.3, 146.7, 142.6, 132.7, 129.6, 123.0, 122.0, 103.9, 84.5, 60.7, 55.7, 28.0, 17.9, 14.2. Anal. Calcd for $C_{19}H_{23}N_3O_7$: C, 56.29; H, 5.72; N, 10.36. Found: C, 56.36; H, 5.62; N, 10.03.

3,6-Dihydro-4-methyl-2-oxo-6-(2-nitrophenyl)-1,5(2*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (2c). This compound was prepared from 1,4-dihydro-2-methoxy-6-methyl-4-(2-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester

(**10b**) by the same procedure as described for **2a**. The product was crystallized from dichloromethane–isopropyl ether to yield a light yellow solid: IR (KBr) 1728, 1712, and 1643 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.8 (s, 1 H), 7.83 (dd, J = 8.0 and 1.0 Hz, 1 H), 7.62–7.52 (m, 2 H), 7.43 (dt, J = 8.5 and 2.1 Hz, 1 H), 7.0 (s, 1 H), 4.35–4.0 (m, 4 H), 2.4 (s, 1 H), 1.3 (t, J = 7.4 Hz, 1.2 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 164.5, 152.4, 150.3, 148.5, 145.7, 134.9, 133.3, 128.7, 124.9, 104.1, 64.0, 60.7, 52.0, 17.9, 14.0. Anal. Calcd for $C_{17}H_{19}N_3O_7$: C, 54.11; H, 5.08; N, 11.14. Found: C, 54.00; H, 5.09; N, 11.08.

1,2,3,4-Tetrahydro-6-methyl-4-(3-nitrophenyl)-2-oxo-3-(1-oxopropyl)-5-pyrimidinecarboxylic Acid Ethyl Ester (2d). The solution of 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**10a**) (750 mg, 2.35 mmol) in dichloromethane (5.0 mL) and pyridine (0.6 mL) was cooled to −20 °C under argon and treated with propionyl chloride (0.26 mL, 2.82 mmol). The reaction was allowed to stir for 2 h and evaporated. The resulting solid was hydrolyzed with 5 N hydrochloric acid (6.0 mL) in a manner as described for **2a**. The residue was purified by flash chromatography (ethyl acetate/hexanes, 1:3), and the product was crystallized from dichloromethane–isopropyl ether to yield a colorless solid **2d** (567 mg): IR (KBr) 1782, 1706, and 1536 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2–8.1 (m, 2 H), 7.95 (br s, 1 H), 7.7 (d, J = 8 Hz, 1 H), 7.5 (m, 1 H), 6.6 (s, 1 H), 4.2 (dq, J = 2 and 7 Hz, 2 H), 3.2–2.7 (m, 2 H), 2.45 (s, 3 H), 1.3, 1.17 (t, J = 7 Hz, 3 H each); ^{13}C NMR ($CDCl_3$) δ 175.5, 164.5, 151.6, 148.5, 146.0, 142.3, 133.4, 129.6, 123.1, 121.9, 104.6, 60.8, 53.5, 31.9, 18.0, 14.2, 9.1. Anal. Cacld for $C_{17}H_{19}N_3O_6$: C, 56.50; H, 5.30; N, 11.63. Found: C, 56.59; H, 5.25; N, 11.57.

1-[(Dimethylamino)carbonyl]-1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-oxo-5-pyrimidinecarboxylic Acid 1-Methylethyl Ester (2e). A solution of 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid 1-methylethyl ester (**10c**) (3.34 g, 10.0 mmol) and triethylamine (6.3 mL) in dichloromethane (10 mL) was cooled to 0 °C under argon and treated slowly with 1.3 M phosgene solution in benzene (9.2 mL, 12.0 mmol). After stirring at 0 °C for 1.5 h, the reaction was treated with 40% aqueous dimethylamine (3.3 mL, 15 mmol). The cooling bath was removed, and the reaction was stirred at room temperature for 16 h. It was evaporated, and the residue in methanol (15 mL) and tetrahydrofuran (15 mL) was hydrolyzed with hydrochloric acid by the same procedure as described for **2a**. The product was crystallized from dichloromethane–isopropyl ether to provide a colorless solid **2e** (1.55 g): IR (KBr) 1708, 1643, 1530 cm^{-1}; ^1H NMR (CD_3OD) δ 8.2 (s, 1 H), 8.13 (d, J = 8.4 Hz, 1 H), 7.75 (d, J = 7.9 Hz, 1 H), 7.6 (t, J = 7.9 Hz, 1 H), 5.8 (s, 1 H), 4.95 (m, 1 H), 2.85 (s, 6 H), 2.35 (s, 3 H), 1.25, 1.1 (d, J = 6.3 Hz, 3 H each); ^{13}C NMR (DMSO-d_6) δ 163.9, 154.6, 149.5, 148.1, 147.5, 144.4, 132.8, 129.9, 122.3, 121.0, 67.2, 56.7, 38.5, 21.6, 21.4, 17.3. Anal. Calcd for $C_{18}H_{22}N_4O_6$: C, 55.38; H, 5.68; N, 14.35. Found: C, 55.44; H, 5.70; N, 14.27.

1,2,3,4-Tetrahydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1-(phenylsulfonyl)-5-pyrimidinecarboxylic Acid Ethyl Ester (2f). A solution of 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**10a**) (3.19 g, 10 mmol) and triethylamine (4.2 mL) in dichloromethane (20 mL) was cooled to 0 °C under argon and treated with benzensulfonyl chloride (1.5 mL, 12.0 mmol). The reaction was stirred at room temperature for 24 h, and the product was hydrolyzed to provide 1,2,3,4-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1-(phenylsulfonyl)-5-pyrimidinecarboxylic acid ethyl ester (**2f**) (1.8 g): ^1H NMR ($CDCl_3$) δ 8.35 (br s, 1 H), 8.15 (m, 2 H), 7.7 (d, J = 8 Hz, 1 H), 7.65–7.25 (m, 6 H), 6.6 (s, 1 H), 4.2 (dq, J = 7 and 2 Hz, 2 H), 2.35 (s, 3 H), 1.3 (t, J = 7 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 164.1, 150.0, 148.3, 145.9, 142.3, 138.2, 134.1, 133.4, 129.8, 128.9, 128.5, 123.3, 104.3, 61.0, 57.8, 18.1, 14.2. Anal. Calcd for $C_{20}H_{19}N_3O_7S$: C, 53.93; H, 4.30; N, 9.43; S, 7.20. Found: C, 53.71; H, 4.19; N, 9.27; S, 7.13.

1-(Aminocarbonyl)-1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-oxo-5-pyrimidinecarboxylic Acid 1-Methylethyl Ester (2g). (a) A solution of 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid 1-methylethyl ester (**10c**) (15.5 g, 46.5 mmol) in dichloromethane (100 mL) and pyridine (20 mL) was cooled to 0 °C under argon and was treated dropwise with a solution of 4-nitrophenyl chloroformate (10.5 g, 52.0 mmol) in dichloromethane (40 mL). After the addition was finished, the cooling bath was removed and the reaction was allowed to stir at room temperature for 2 h. The solvent was removed under reduced pressure, and the resulting solid was suspended in tetrahydrofuran (75 mL) and methanol (75 mL) and treated with 2.5 N hydrochloric acid until pH ~2.0. The reaction was allowed to stir at room temperature overnight (became a homogeneous light yellow solution), and most of the solvent was evaporated under reduced pressure. The residue was diluted with water and extracted with ethyl acetate. The combined extracts were washed with water, 5% sodium carbonate, and brine. After drying over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was passed through a short column of silica gel (10% ethyl acetate in dichloromethane). The product was crystallized from dichloromethane–isopropyl ether to provide 3,6-dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic acid 5-(1-methylethyl) 1-(4-nitrophenyl)diester (**21**) (16.61 g, 73.6%): mp 118–120 °C; IR (KBr) 1740, 1730, 1710, 1660, 1650, 1530, 1520 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.28 (d, J = 8.9 Hz, 2 H), 8.26 (s, 1 H), 8.18 (d, J = 7.9 Hz, 1 H), 8.0 (s, 1 H), 7.78 (d, J = 7.9 Hz, 2 H), 7.54 (t, J = 7.9 Hz, 2 H), 7.38 (d, J = 8.9 Hz, 2 H), 6.43 (s, 2 H), 5.1 (m, 1 H), 2.45 (s, 3 H), 1.30, 1.20 (d, J = 6.3 Hz, 3 H each); ^{13}C NMR ($CDCl_3$) δ 163.8, 154.8, 150.9, 149.1, 148.5, 145.7, 141.3, 133.1, 129.9, 125.3, 122.2, 121.9, 104.9, 68.9, 56.8, 21.9, 21.8, 18.0. Anal. Calcd for $C_{22}H_{20}N_4O_9$: C, 54.54; H, 4.16; N, 11.57. Found: C, 54.24; H, 3.97; N, 11.46.

(b) The solution of 3,6-dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic acid 5-(1-methylethyl) 1-(4-nitrophenyl) diester (**21**) (3.0 g, 6.43 mmol) in acetonitrile (10 mL) was treated with excess ammonia at room temperature. The reaction turned yellow instantaneously. After 30 min at room temperature, the solvent was evaporated, and the residue in ethyl acetate was washed with water, 5% potassium carbonate, and brine. After drying over anhydrous magnesium sulfate, the solvent was evaporated and the residue was crystallized from ether to yield 1-(aminocarbonyl)-1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-oxo-5-pyrimidinecarboxylic acid 1-methylethyl ester (**2g**) (2.03 g) as a coloress solid: IR (KBr) 1648, 1716 cm^{-1}; ^1H NMR ($CDCl_3$ + DMSO-d_6) δ 9.75 (s, 1 H), 8.5 (br s, 1 H), 8.2 (s, 1 H), 8.10 (d, J = 8.4 Hz, 1 H), 7.72 (d, J = 7.4 Hz, 1 H), 7.48 (t, J = 7.91 Hz, 1 H), 6.7 (s, 1 H), 6.4 (br s, 1 H), 5.05 (qn, J = 6.3 Hz, 1 H), 2.4 (s, 3 H), 1.29 (d, J = 5.8 Hz, 3 H), 1.16 (d, J = 6.3 Hz, 3 H); ^{13}C NMR ($CDCl_3$ + DMSO-d_6) δ 163.8, 153.5, 152.4, 148.0, 146.7, 143.3, 132.63, 128.8, 122.00, 121.5, 102.5, 67.3, 52.64, 21.4, 21.2, 16.95. Anal. Calcd for $C_{16}H_{18}N_4O_6$: C, 53.04; H, 50.1; N, 15.46. Found: C, 52.78; H, 4.90; N, 15.24.

3,6-Dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic Acid 5-(1-Methylethyl) 1-[(*S*)-1-Methyl-2-[methyl(phenylmethyl)amino]ethyl] Diester Monohydrochloride (2h). A mixture of 3,6-dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic acid 5-(1-methylethyl) 1-(4-nitrophenyl) diester (**21**) (1.27 g, 2.64 mmol) and (*S*)-1-methyl-2-[methyl(phenylmethyl)amino]ethyl alcohol[12] (472 mg, 2.64 mmol) in acetonitrile (3 mL) was heated at 50 °C under argon for 15 h. The solvent was evaporated, and the residue was dissolved in ethyl acetate. The resulting solution was washed with 5% potassium carbonate, water, and brine and dried over magnesium sulfate. The solvent was evaporated, and the residue was purified by flash chromatography (25% acetone in hexanes). The product was dissolved in ether and converted to its hydrochloride salt by treatment with ethereal hydrochloric acid. The precipitate formed was filtered to give 3,6-dihydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic acid 5-(1-methylethyl) 1-[(*S*)-1-methyl-2-[methyl(phenylmethyl)amino]-ethyl] diester monohydrochloride (**2h**) (1.1 g) as a colorless solid: IR (KBr) 1779, 1730, 1532 cm^{-1}; ^1H NMR (free amine, $CDCl_3$) δ 8.2 (br s, 1 H), 8.14 (m, 1 H), 7.6 (br s, 1 H), 7.45 (m, 1 H), 7.24 (m, 5 H), 6.38, 6.36 (s, 1 H), 5.17 (m, 1 H), 5.07 (m, 1 H), 3.55 (s, 1 H), 3.50 (d, J = 2 Hz, 1 H), 2.7–2.4 (m, 2 H), 2.4, 2.38 (s, 3 H), 2.24, 2.2 (s, 3 H), 1.35–1.18 (m, 9 H); ^{13}C NMR (free amine, $CDCl_3$) δ 164.1, 152.5 (152.4), 149.6 (149.5), 148.3, 146.0 (145.9), 142.4

(12) (*S*)-1-Methyl-2-[methyl(phenylmethyl)amino]ethyl alcohol was prepared by trimethylaluminum catalyzed reaction[13] of *N*-(methylbenzyl)amine with (*S*)-(−)-propylene oxide.

(13) Overman, L. E.; Flippin, L. A. *Tetrahedron Lett.* **1981**, *22*, 195.

(142.3), 138.8, 132.8 (132.6), 129.6, 128.9 (128.8), 128.1, 126.9, 123.0, 122.1 (122.0), 104.5, 73.3 (73.2), 68.5, 62.8 (62.7), 62.0 (61.9), 56.0, 42.8 (42.7), 22.0 (21.8), 18.2, 18.1 (chemical shifts in parentheses result from diastereomeric mixture). Anal. Calcd for $C_{27}H_{32}N_4O_7$·HCl: C, 57.80; H, 5.93; N, 9.99; Cl, 6.32. Found: C, 57.58; H, 6.04; N, 9.77; Cl, 6.62.

1,2,3,6-Tetrahydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1-(2-propenyl)-5-pyrimidinecarboxylic Acid 1-Methylethyl Ester (2i) and 1,2,3,4-Tetrahydro-6-methyl-4-(3-nitrophenyl)-2-oxo-1-(2-propenyl)-5-pyrimidinecarboxylic Acid 1-Methylethyl Ester (20). The reaction mixture containing 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid 1-methylethyl ester (**10c**) (170 mg, 0.5 mmol), allyl bromide (100 μL), and finely ground potassium carbonate (280 mg, 2.0 mmol) in dimethylformamide (2 mL) was stirred at room temperature for 16 h. The solid was filtered off, and the filtrate was diluted with ethyl acetate and washed with water and brine. After drying over magnesium sulfate, the solvent was evaporated and the residue was purified by preparative TLC (ethyl acetate/hexanes, 40:60) to yield two products: 100 mg (A), 65 mg (B). The major product (A), on deprotection with acid, provided 1,2,3,6-tetrahydro-4-methyl-6-(3-nitrophenyl)-2-oxo-1-(2-propenyl)-5-pyrimidinecarboxylic acid 1-methylethyl ester (**2i**) (87 mg): IR (KBr) 1703, 1686, 1636, 1525, 1346 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.4 (s, 1 H), 8.2 (d, J = 1.6 Hz, 1 H), 8.15 (dd, J = 7.9 and 1.1 Hz, 1 H), 7.8 (dd, J = 7.4 and 1.1 Hz, 1 H), 5.2 (d, J = 13.7 Hz, 1 H), 5.0 (m, 1 H), 4.55 (m, 1 H), 3.25 (dd, J = 15.3 (and 7.4 Hz, 1 H), 2.35 (s, 3 H), 1.25 and 1.1 (d, J = 6.3 Hz, 3 H each); ^{13}C NMR ($CDCl_3$) δ 164.6, 152.8, 150.7, 148.2, 147.4, 144.1, 133.3, 131.9, 129.6, 122.9, 122.6, 118.5, 67.7, 58.7, 47.1, 22.0, 21.8, 18.4. Anal. Calcd for $C_{18}H_{21}N_3O_5$: C, 60.16; H, 5.89; N, 11.69. Found: C, 60.08; H, 5.83; N, 11.65. The minor product was deprotected to provide 1,2,3,4-tetrahydro-6-methyl-4-(3-nitrophenyl)-2-oxo-1-(2-propenyl)-5-pyrimidinecarboxylic acid 1-methylethyl ester (**20**) (61 mg, 33.3%) as a colorless foam: IR ($CHCl_3$) 1684, 1530, 1348, 1099 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.1 (s, 1 H), 8.0 (d, J = 7.4 Hz, 1 H), 7.5 (d, J = 7.9 Hz, 1 H), 7.35 (t, J = 7.9 Hz, 1 H), 7.0 (br s, 1 H), 5.75 (m, 1 H), 5.4 (d, J = 3.7 Hz, 1 H), 5.1 (d, J = 10.0 Hz, 1 H), 5.0 (d, J = 17.4 Hz, 1 H), 4.9 (m, 1 H), 4.33 (d of AB q, J = 17.4 and 4.75 Hz, 2 H), 2.46 (s, 3 H), 1.15 and 1.0 (d, J = 6.3 Hz, 3 H each); ^{13}C NMR ($CDCl_3$) δ 165.0, 153.44, 149.87, 148.25, 145.66, 133.66, 132.26, 129.45, 122.53, 121.66, 116.28, 103.44, 67.9, 53.2, 44.8, 21.9, 21.6, 16.0; mass spectrum (CI), m/z (relative intensity) 360 (100), 318 (10).

6-Cyclohexyl-3,6-dihydro-4-methyl-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (2j). By use of the procedure described for **2a**, 4-cyclohexyl-1,4-dihydro-2-methoxy-6-methyl-5-pyrimidinecarboxylic acid ethyl ester (**10d**) was converted to 6-cyclohexyl-3,6-dihydro-4-methyl-2-oxo-1,5(2*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**2j**): IR (KBr) 1711, 1646 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.64 (br s, 1 H), 5.2 (d, J = 8 Hz, 1 H), 4.3 (q, J = 7.0 Hz, 2 H), 4.2 (dq, J = 7 and 1.6 Hz, 2 H), 2.35 (s, 3 H), 1.66 (m, 5 H), 1.34, 1.30 (d, J = 7.0 Hz, 3 H each), 1.13 (m, 5 H); ^{13}C NMR ($CDCl_3$) δ 165.6, 153.2, 151.5, 145.2, 104.9, 63.3, 60.2, 57.4, 42.7, 29.2, 28.4, 26.1, 17.7, 14.2, 14.1. Anal. Calcd for $C_{17}H_{26}N_2O_5$: C, 60.34; H, 7.74; N, 8.23. Found: C, 60.29; H, 7.89; N, 8.11.

2-Amino-4-methyl-6-(3-nitrophenyl)-1,5(6*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (3a). The reaction mixture containing 2-methoxy-4-methyl-6-(3-nitrophenyl)-1,5(6*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**16a**) (3.78 g, 9.66 mmol), obtained during the preparation of **2a**, and ammonium acetate (385 mg, 5.0 mmol) in tetrahydrofuran (20 mL) was cooled to 0 °C, and ammonia was bubbled through for 5 min. The flask was tightly stoppered, and the reaction mixture was allowed to stir at room temperature for 72 h. Some solid precipitated out of the reaction. The solvent was removed, and the residue was dissolved in dichloromethane. The insoluble material was filtered off, and the solvent was evaporated. The residue was purified by flash chromatography (30% ethyl acetate in dichloromethane) to provide 2-amino-4-methyl-6-(3-nitrophenyl)-1,5(6*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**3a**) (2.03 g): IR (KBr) 1727, 1660, 1613, 1596, 1530, 1295 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.2 (d, J = 2.0 Hz, 1 H), 8.1 (d, J = 7.9 Hz, 1 H), 7.7 (d, J = 7.9 Hz, 1 H), 7.5 (d, J = 7.9 Hz, 1 H), 7.4 (br s, 2 H), 6.3 (s, 1 H), 4.3 (dd, J = 7.4 Hz, 3 H), 1.25 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.8, 156.5, 153.75, 150.5, 148.2, 148.2, 143.6, 133.0, 129.7, 123.0, 122.4, 103.7, 64.2, 60.0, 54.9, 22.2, 14.0, 14.1. Anal. Calcd for $C_{17}H_{20}N_4O_6$: C, 54.25; H, 5.36; N, 14.89. Found: C, 54.19, H, 5.19, N, 14.84.

4-Methyl-2-(methylamino)-6-(3-nitrophenyl)-1,5(6*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (3b). The solution of 2-methoxy-4-methyl-6(3-nitrophenyl)-1,5(6*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**16a**) (3.7 g, 9.46 mmol), obtained during the preparation of **2a**, in dimethylformamide (15 mL) was treated with methylamine hydrochloride (1.01 g, 15.0 mmol) and sodium acetate (1.49 g, 17 mmol), and the resulting reaction mixture was stirred at room temperature for 24 h. It was diluted with ethyl acetate, the solid was filtered off, and the filtrate was washed with water, sodium bicarbonate, and brine. After drying over magnesium sulfate, the solvent was evaporated, and the residue was purified by flash chromatography (5% ethyl acetate in dichloromethane). The product was crystallized from isopropyl ether–hexanes to yield a yellow solid **3b** (1.91 g): IR (KBr) 1714, 1697, 1570, 1525, 1351, 1295, 1220 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (d, J = 1.6 Hz, 1 H), 7.45 (d, J = 7.9 Hz, 1 H), 6.3 (s, 1 H), 4.3 (m, 2 H), 4.15 (m, 2 H), 3.0 (d, J = 3.7 Hz, 3 H), 2.4 (s, 3 H), 1.35 (t, J = 6.85 Hz, 3 H), 1.25 (d, J = 6.85 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 166.1, 157.7, 154.1, 149.0, 148.2, 143.5, 133.0, 129.6, 122.8, 122.2, 103.3, 63.8, 59.8, 54.6, 28.5, 23.1, 14.3, 14.1. Anal. Calcd for $C_{18}H_{22}N_4O_6$: C, 55.38; H, 5.68; N, 14.35. Found: C, 55.19; H, 5.59; N, 14.24.

2-Amino-1,6-dihydro-4-methyl-1-[(dimethylamino)carbonyl]-6-(3-nitrophenyl)-5-pyrimidinecarboxylic Acid 1-Methylethyl Ester (3c). The solution of intermediate **16e** (2.09 g, 5.17 mmol), obtained during the preparation of **2e**, in ethanol (50 mL) was saturated at 0 °C with ammonia and heated at 75 °C in a sealed tube for 72 h. The solvent was removed, the residue was purified by flash chromatography, and the product crystallized from dichloromethane–isopropyl ether to yield 2-amino-1,6-dihydro-4-methyl-1-[(dimethylamino)carbonyl]-6-(3-nitrophenyl)-5-pyrimidinecarboxylic acid 1-methylethyl ester (**3c**) (810 mg): IR (KBr) 1668, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.53 (d, J = 1.6 Hz, 1 H), 8.4 (dd, J = 7 and 1.6 Hz, 1 H), 3.2 (s, 6 H), 2.6 (s, 3 H), 1.55, 1.50 (d, J = 6.0 Hz, 3 H each); ^{13}C NMR ($CDCl_3$) δ 166.8, 157.9, 153.1, 149.4, 145.5, 134.3, 130.6, 123.5, 122.9, 105.4, 68.4, 56.9, 38.3, 22.6, 22.5. Anal. Calcd for $C_{18}H_{23}N_5O_5$: C, 55.52; H, 5.95; N, 17.98. Found: C, 55.35; H, 5.85; N, 17.80.

2-Amino-1,6-dihydro-4-methyl-6-(3-nitrophenyl)-1-(phenylsulfonyl)-5-pyrimidinecarboxylic Acid Ethyl Ester (3d). The solution of intermediate **16f** (1.45 g, 3.16 mmol), obtained during the preparation of **2f**, in tetrahydrofuran (20 mL) was saturated at 0 °C with ammonia. The reaction was tightly stoppered and allowed to stand at room temperature for 48 h. The solvent was evaporated, and the residue was purified by flash chromatography (10% methanol in dichloromethane). The product was crystallized from dichloromethane–isopropyl ether to yield 2-amino-1,6-dihydro-4-methyl-6-(3-nitrophenyl)-1-(phenylsulfonyl)-5-pyrimidinecarboxylic acid ethyl ester (**3d**) (445 mg): IR (KBr) 1700, 1656, 1600 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (m, 2 H), 7.8–7.3 (complex m, 7 H), 6.40 (s, 1 H), 6.2 (br s, 2 H), 4.15 (q, J = 7.0 Hz, 2 H), 2.15 (s, 3 H), 1.24 (t, J = 7.0 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 165.2, 157.0, 148.5, 147.3, 141.6, 138.4, 134.2, 133.1, 129.7, 129.4, 127.0, 123.3, 121.9, 104.8, 60.3, 56.0, 21.3, 14.4. Anal. Calcd for $C_{20}H_{20}N_4O_6S$: C, 54.05; H, 4.54; N, 12.61; S, 7.21. Found: C, 54.19; H, 4.53; N, 12.73; S, 7.18.

1,2,3,6-Tetrahydro-2-imino-4-methyl-6-(3-nitrophenyl)-1-(2-propenyl)-5-pyrimidinecarboxylic Acid 1-Methylethyl Ester Monohydrochloride (3e). The solution of intermediate **16i** (1.06 g, 2.84 mmol), obtained during the preparation of **2i**, in methanol (10 mL) was cooled to 0 °C and saturated with ammonia. The reaction was treated with ammonium acetate (220 mg) and heated at 90–100 °C for 18 h. The residue, after evaporation of the solvent, was purified by flash chromatography (dichloromethane/methanol/acetic acid, 18:1:1) to yield a colorless solid, which was converted to its hydrochloride salt and crystallized from acetonitrile–ether to provide 1,2,3,6-tetrahydro-2-imino-4-methyl-6-(3-nitrophenyl)-1-(2-propenyl)-5-pyrimidinecarboxylic acid 1-methylethyl ester monohydrochloride (**3e**) (480 mg): IR (KBr) 3080, 1710, 1669, 1530 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.7 (br s, 1 H), 8.2 (d, J = 7.9 Hz, 1 H), 8.15 (d, J = 7.9 Hz, 1 H), 7.7 (d, J = 7.4 Hz, 1 H), 7.6 (d, J = 7.9 Hz, 1 H), 5.7 (m, 1 H), 5.44 (s, 1 H), 5.4 (d, J = 7.9 Hz, 1 H), 5.32 (d, J = 16.9 Hz, 1 H), 5.0 (m,

1 H), 4.4 (dd, J = 16.9 and 4.75 Hz, 1 H), 3.7 (dd, J = 16.4 and 6.3 Hz, 1 H), 2.5 (s, 3 H), 1.25, 1.15 (d, J = 6.3 Hz, 3 H each); ^{13}C NMR ($CDCl_3$) δ 162.4, 150.4, 147.2, 143.2, 140.8, 132.2, 129.5, 128.1, 122.7, 121.4, 118.8, 101.9, 67.5, 57.8, 49.0, 20.9, 20.7, 16.9. Anal. Calcd for $C_{18}H_{22}N_4O_4$·HCl: C, 54.75; H, 5.87; N, 14.19; Cl, 8.98. Found: C, 54.38; H, 5.80; H, 14.00; Cl, 9.03.

2-(Acetylamino)-3,6-dihydro-4-methyl-6-(3-nitrophenyl)-1,5(2*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (3f). The suspension of 2-amino-4-methyl-6-(3-nitrophenyl)-1,5(6*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**3a**) (550 mg, 1.46 mmol) in dichloromethane (5.0 mL) and pyridine (0.5 mL) was treated with acetic anhydride (0.3 mL), and the reaction was stirred at room temperature for 1 h. The reaction was diluted with water and washed with 5% citric acid, sodium bicarbonate, and brine and dried over anhydrous magnesium sulfate. The solvent was evaporated, and the residue was crystallized from ether–hexanes to give 2-(acetylamino)-3,6-dihydro-4-methyl-6-(3-nitrophenyl)-1,5(2*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**3f**) (530 mg): IR (KBr) 1746, 1711, 1692, 1562, 1532 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.15 (d, J = 1.6 Hz, 1 H), 8.1 (d, J = 9.0 Hz, 1 H), 7.7 (d, J = 7.4 Hz, 1 H), 7.5 (d, J = 7.9 Hz, 1 H), 6.4 (s, 1 H), 4.35 (q, J = 7.4 Hz, 2 H), 4.2 (m, 2 H), 2.45 (s, 3 H), 2.2 (s, 3 H), 1.35 (t, J = 7.4 Hz, 3 H), 1.3 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 164.8, 152.8, 148.3, 140.7, 133.4, 129.6, 123.3, 122.0, 109.1, 60.8, 54.2, 26.0, 20.3, 14.2, 14.1. Anal. Calcd for $C_{19}H_{22}N_4O_7$: C, 54.54; H, 5.30; N, 13.39. Found: C, 54.61; H, 5.40; N, 13.29.

3,6-Dihydro-4-methyl-2-[(methylsulfonyl)imino]-6-(3-nitrophenyl)-1,5(2*H*)-pyrimidinedicarboxylic Acid Bis(ethyl ester) (3g). The suspension of **3a** (600 mg, 1.6 mmol) in dichloromethane (5.0 mL) and pyridine (1.0 mL) was treated at 0 °C with methanesulfonyl chloride (0.42 mL, 5.25 mmol) and 4-(dimethylamino)pyridine (10 mg). The reaction was stirred at room temperature for 16 h and diluted with ethyl acetate. The solution was washed with 1 N hydrochloric acid, sodium bicarbonate, and brine. After drying over anhydrous magnesium sulfate, the solvent was evaporated, and the residue was crystallized from ether–hexanes to yield 3,6-dihydro-4-methyl-2-[(methylsulfonyl)imino]-6-(3-nitrophenyl)-1,5(2*H*)-pyrimidinedicarboxylic acid bis(ethyl ester) (**3g**) (650 mg) as a colorless solid: IR (KBr) 1728, 1712, 1620, 1529 cm^{-1}; ^1H NMR ($CDCl_3$) δ 9.6 (s, 1 H), 8.2 (s, 1 H), 8.15 (d, J = 8.4 Hz, 1 H), 7.7 (d, J = 7.4 Hz, 1 H), 7.5 (t, J = 7.4 Hz, 1 H), 6.4 (s, 1 H), 4.35 (m, 2 H), 4.25 (m, 2 H), 3.05 (s, 3 H), 2.5 (s, 3 H), 1.4 (t, J = 6.9 Hz, 3 H), 1.3 (t, J = 7.4 Hz, 3 H); ^{13}C NMR ($CDCl_3$) δ 164.1, 152.5, 148.45, 147.35, 143.8, 140.5, 132.5, 130.0, 123.4, 121.9, 107.2, 64.7, 61.23, 54.6, 42.6, 18.35, 14.15, 14.1. Anal. Calcd for $C_{18}H_{22}N_4O_8S$: C, 47.57; H, 4.88; N, 12.33; S, 7.05. Found: C, 47.52; H, 4.94; N, 12.17; S, 7.12.

Preparation of 1,4-Dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic Acid Ethyl Ester (9a) from 1,4-Dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic Acid Ethyl Ester (10a). The reaction mixture containing 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**10a**) (180 mg, 0.54 mmol) and 4-methoxybenzyl mercaptan (0.3 mL, 2.0 mmol)) was treated with citric acid (5 mg, 0.026 mmol) and heated at 100 °C in vacuo for 8 h. Upon cooling, the reaction mixture was diluted with ethyl acetate and washed with sodium bicarbonate, water, and brine. It was dried over magnesium sulfate and evaporated, and the residue was purified by flash chromatography on silica gel (ethyl acetate/hexanes, 1:3) to give 1,4-dihydro-2-[[(4-methoxyphenyl)methyl]thio]-6-methyl-4-(3-nitrophenyl)-5-pyrimidinecarboxylic acid ethyl ester (**9a**) (103 mg, 41%), which was identical with the previously prepared material.

Acknowledgment. We wish to thank Squibb's analytical chemistry department for microanalysis, Dr. Michael Porubcan for helping with NMR analysis, and Dr. David M. Floyd for helpful discussions.

Registry No. **1a**, 108930-57-0; **1b**, 108930-93-4; **1c**, 108931-33-5; **1d**, 108931-41-5; **1e**, 112795-80-9; **1f**, 123485-97-2; **1g**, 110926-35-7; **1h**, 123485-98-3; **1i**, 123485-99-4; **2a**, 108930-58-1; **2b**, 108930-65-0; **2c**, 108930-61-6; **2d**, 108931-46-0; **2e**, 112795-79-6; **2f**, 110926-37-9; **2g**, 112795-83-2; **2h** (diastereomer 1), 123505-61-3; **2h** (diasteromer 2), 123486-16-8; **2h**·HCl (diastereomer 1), 123486-00-0; **2h**·HCl (diastereomer 2), 123486-17-9; **2i**, 110887-87-1; **2j**, 123486-01-1; **3a**, 111199-70-3; **3b**, 111199-75-8; **3c**, 119126-23-7; **3d**, 119144-83-1; **3e**, 123486-15-7; **3e**·HCl, 119126-21-5; **3f**, 123486-02-2; **3g**, 111199-72-5; **9a**, 108931-96-0; **9b**, 123486-03-3; **9c**, 106720-64-3; **10a**, 106720-60-9; **10b**, 108931-50-6; **10c**, 108931-52-8; **10d**, 123486-05-5; **11a**, 39562-16-8; **11d**, 39562-25-9; **11** (R^1 = 2-CF_3, R^2 = Et), 39561-91-6; **11** (R^1 = 2-NO_2, R^2 = Et), 67593-37-7; **11** (R^1 = 3-NO_2, R^2 = Me), 39562-17-9; **12**·HCl, 25985-08-4; **13**·H_2SO_4, 52328-05-9; **15h**, 123486-08-8; **15i**, 123486-09-9; **15** (R^1 = 3-NO_2, R^2 = Et, R^3 = CO_2Et), 123485-93-8; **15** (R^1 = 3-NO_2, R^2 = Me, R^3 = COEt), 108932-31-6; **15** (R^1 = 3-NO_2, R^2 = Et, R^3 = $CONMe_2$), 123486-07-7; **15** (R^1 = 3-NO_2, R^2 = Et, R^3 = SO_2Me), 110926-42-6; **16a**, 111199-77-0; **16e**, 119126-26-0; **16f**, 119126-25-9; **16i**, 110887-93-9; **16** (R^1 = 3-NO_2, R^2 = Et, R^3 = CO_2Bu-t), 123486-10-2; **16** (R^1 = 3-NO_2, R^2 = Et, R^3 = COEt), 123486-11-3; **16** (R^1 = 3-NO_2, R^2 = Pr-i, R^3 = $CO_2C_6H_4NO_2$-*p*), 123486-12-4; **17a**, 123485-94-9; **17b**, 123486-04-4; **19b**, 123485-95-0; **20**, 123505-60-2; **21**, 123485-96-1; 2-(cyclohexanylmethylene)-3-oxobutanoic acid ethyl ester, 89082-76-8; 1-benzyl-4-hydroxypiperidine hydrochloride, 123486-06-6; 4-methyl-2-[[(4-methoxyphenyl)methyl]thio]-6-[2-(trifluoromethyl)phenyl]-1,5(6*H*)-pyrimidinedicarboxylic acid 5-ethyl 1-[1-(phenylmethyl)-4-piperidinyl] diester, 108932-21-4; 4-nitrophenyl chloroformate, 7693-46-1; (*S*)-1-methyl-2-[methyl(phenylmethyl)amino]ethyl alcohol, 123486-13-5; 1,4-dihydro-2-methoxy-6-methyl-4-(3-nitrophenyl)-1-(2-propenyl)-5-pyrimidinecarboxylic acid 1-methylethyl ester, 123486-14-6; 4-methoxybenzyl mercaptan, 6258-60-2.