needles. Recrystallization gave material identical with the *cis* bis adduct.

Reaction of *cis,cis*-1,5-Cyclooctadiene with Dichlorocarbene from Chloroform.—A suspension of 10 g. of potassium *t*-butoxide in 50 ml. of dry ether was stirred magnetically in an ice bath, 2 g. of the diene was introduced, and then 5 ml. of chloroform was added dropwise in the course of 10 min. Stirring was continued for 1 hr., 50 ml. more ether was added, and the mixture was filtered by suction. After washing the filter cake thoroughly with ether, the filtrate was evaporated to dryness. Crystallization of the residual solid from ethyl acetate yielded 1.5 g. of colorless needles of nearly pure (m.p. 172–174°) *cis* bis adduct (mixture melting point determination).

***cis*-Tricyclo[7.1.0.0^{1,8}]decane.**—A solution of 2 g. of the *cis* bis adduct 2 in 20 ml. of tetrahydrofuran was stirred mechanically in a 125-ml. erlenmeyer flask mounted above an ice bath which could be raised for cooling when required to prevent boiling. Two grams of lithium wire which had been flaked with a hammer was added in portions along with enough *t*-butyl alcohol to dissolve the metal. After disappearance of all but a few small particles of lithium, the mixture was diluted with water and extracted with ether. Evaporation gave a yellow oil which was distilled at the pressure of the water pump (b.p. 135–140°). The n.m.r. spectrum in carbon tetrachloride clearly showed the presence of cyclopropyl hydrogens in a multiplet centering at τ 10.2 relative to tetramethylsilane.

Improved Procedure (L.F.F.).—A 250-ml. round-bottomed flask containing 5 ml. (4.4 g.) of *cis,cis*-1,5-cyclodecadiene, 14.5 g. (2 equiv.) of sodium trichloroacetate, 20 ml. of tetrachloroethylene, and 5 ml. of diglyme was fitted with a condenser connected to a gas bubbler containing a little tetrachloroethylene and heated over a microburner. Gas evolution continued at a steady rate for 75 min. and then stopped. Lumps of sodium trichloroacetate visible at the bottom of the flask gradually gave way completely to finely divided sodium chloride. The mixture acquired no more than a light tan color. At the end of the reaction, 75 ml. of water was added, the flask was fitted with a distillation adapter carrying a steam inlet tube, and the tetrachloroethylene was removed by distillation. The reaction product separating as a tan solid was extracted with methylene chloride; evaporation of the dried extract gave 8 g. of tan solid. The cake was covered with methanol, the lumps were crushed with a flattened stirring rod, the mixture was cooled, and the product was collected and washed free of brown mother liquor. The nearly colorless solid (3.3 g., m.p. 174–176°) consisting almost entirely of the *cis* bis adduct on crystallization from ethyl acetate (15 ml.) gave 2.9 g. (27%) of large needles of pure material, m.p. 175–176°.

In another run in which the amount of sodium trichloroacetate was increased to double the theoretical amount, gas evolution stopped after 1 hr. and 50 min. Evaporation of the dried extract gave 15.4 g. of tan product which, when washed with methanol, afforded 7.1 g. of material, m.p. 173–175°. Concentration of the methanol washings and recrystallization of the main product afforded a total of 6.6 g. (62%) of pure *cis* bis adduct, m.p. 175–176°.

7,7,8,8-Tetrachlorotricyclo[5.1.0.0^{1,6}]hexane (5).—A mixture of 3.5 ml. of 1,4-cyclohexadiene, 14.5 g. of sodium trichloroacetate, 20 ml. of tetrachloroethylene, and 5 ml. of triglyme was refluxed for 75 min., when bubbling stopped. After steam distillation for removal of solvent, further steam distillation afforded 0.53 g. of colorless solid, m.p. 169°. The substance crystallized from about 20 ml. of 95% ethanol in heavy prismatic crystals, m.p. 170–171°.

Anal. Calcd. for $C_8H_8Cl_4$ (245.97): C, 39.06; H, 3.28; Cl, 57.66. Found: C, 39.14; H, 3.39; Cl, 57.33.

X-Ray Analysis.—X-Ray photographs of a crystal of the lower melting isomer demonstrated C2h lattice symmetry, that is, a twofold axis perpendicular to a mirror plane, and hence showed that the crystal lattice is monoclinic. Measurement and calculation established the following dimensions of the unit cell: a = 14.8, b = 7.62, c = 12.1 Å.; β = 58°. Calculation from the molecular weight of 274 and the observed density of 1.49 g./ml. indicates the presence of four molecules per unit cell.

Crystals of the higher melting isomer have lattice symmetry D2h (three mutually perpendicular mirror planes) and, therefore, are orthorhombic. The units cell dimensions are a = 12.0, b = 6.11, c = 7.89 Å. On the assumption that the molecular weight is 274 and the density is the same as observed for the iso mer, calculation shows the presence of two molecules per unit cell.

The precise space group for the monoclinic crystal is C2, Cc, C2/m, or C2/c and that for the orthorhombic crystal is either Pnnm or Pnn2, but these possibilities in themselves do not distinguish between the two configurations. However, measurement of the molecular dimensions of models on the assumption of an intramolecular H–H distance of 2.4 Å. indicated that the *cis* isomer cannot preserve the symmetry of the space group Pnn2 and fit into this unit cell, whereas the *trans* isomer does fit in this space group. Furthermore, symmetry requirements show that the *cis* isomer cannot yield crystals of the Pnnm space group. Therefore, the higher melting bis adduct forming orthorhombic crystals must be the *trans* isomer.

Investigations in Heterocycles. XVI.[1] A New Synthesis of 1,2-Disubstituted 4-Thiopyrimidines *via* Enamines

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A simple one-step synthesis has been developed for the preparation of 1,2-disubstituted 4-thiopyrimidines by condensing an α,β-unsaturated amino ester (enamine) with an acyl isothiocyanate. The general structure of these compounds has been confirmed by chemical and spectral methods. The spectral properties of these compounds are described.

The recent monograph on pyrimidines by Brown[2] has outlined comprehensively the principal methods of synthesis and the chemical and physical properties of pyrimidines. It has been tacitly implied herein that, although a great variety of mercaptopyrimidines have been prepared, only the 2-mercaptopyrimidines have been synthesized directly from a 3-carbon intermediate and an appropriate condensing agent (*e.g.*, thiourea). However, the usual procedure employed to arrive at the 4-mercaptopyrimidines involves the synthesis of the 4-hydroxy- or 4-chloropyrimidines, which then are allowed to react with phosphorus pentasulfide or sodium hydrosulfide, respectively. This method is limited in that it permits substitution at position 1 only after a 4-aminopyrimidine derivative has been alkylated and the resulting alkyl 4-imino intermediate has been hydrolyzed to the corresponding 4-oxo derivative.[3] Thus, a minimum of four steps is required in the preparation of a 1-alkyl 1,4-dihydro-4-thiopyrimidine from the appro-

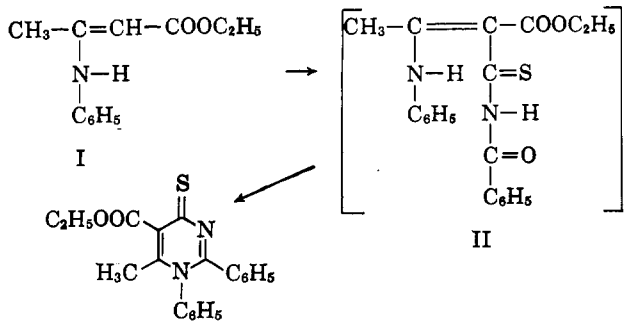
(1) Presented in part before the Organic Division at the 145th National Meeting of the American Chemical Society, New York, N. Y., Sept., 1963.

(2) D. J. Brown, "The Pyrimidines," John Wiley and Sons, Inc., New York, N. Y., 1962.

(3) D. J. Brown, E. Hoerger, and S. F. Mason, *J. Chem. Soc.*, 211 (1955); see also pp. 373–382 of ref. 2.

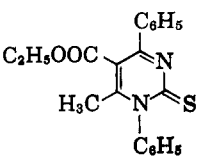
priate 3-carbon intermediate. The problem becomes even more acute if one considers the synthesis of the heretofore unknown 1,2-disubstituted 4-thiopyrimidines and especially the 1,2-diaryl substituted compounds which are unavailable by conventional routes. The synthesis of such substances serves as the subject of this report.

Behrend[4,5] found that ethyl β-aminocrotonate on condensation with phenyl isothiocyanate affords only a low yield of 6-methyl-3-phenyl-2-thiouracil along with a by-product, ethyl β-amino-α-phenylthiocarbamoylcrotonate. The identification of this ester was the first suggestion of the enamine character of ethyl β-aminocrotonate. It was with this observation in mind that we considered the condensation of ethyl β-anilinocrotonate (I) with benzoyl isothiocyanate. It was anticipated that the primary product of this condensation reaction would be ethyl β-anilino-α-benzoylthiocarbamoylcrotonate (II). However, when these intermediates were allowed to react in ethyl ether or tetrahydrofuran under mild reflux, a bright yellow copious precipitate was obtained in 60% yield. The elemental analysis of this compound indicated that the elements of water had been eliminated through condensation of the intermediates described. This substance dissolved



I II III

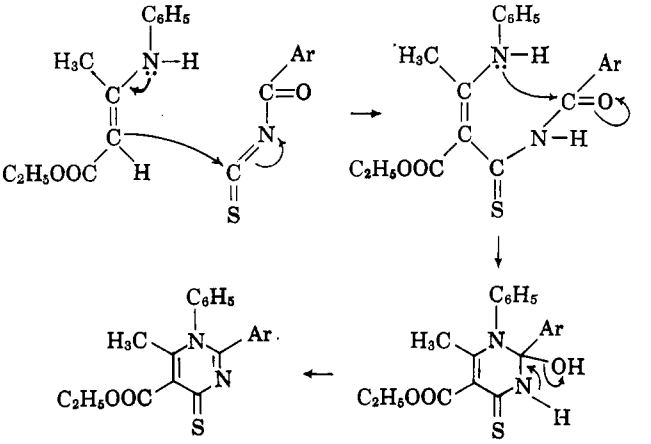
in ethyl alcohol gave maxima in the ultraviolet at 247 and 341 mμ. No bands were observed in the –NH or –OH region of the infrared, but the carbonyl region had three strong bands: 1732 cm.$^{-1}$ for the ester group, 1630 cm.$^{-1}$ for –C=N, and 1600 cm.$^{-1}$ for the phenyl group. The n.m.r. spectrum contained signals for ten aromatic protons from τ 3.12 to 2.67. The singlet at τ 8.08 corresponded to the methyl group linked to unsaturated carbon, and the triplet at τ 8.63 and the quartet at τ 5.67 are characteristic for carbethoxy protons. These data support the assignment of structure III to this compound. The alternative structure IV was not considered feasible since it required an amide carbonyl interaction with the carbon bearing the vinyl proton, a reaction which is not favored for the elimination of water under the mild reaction conditions described.



IV

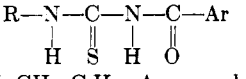
(4) R. Behrend, F. Meyer, and Y. Buchholz, *Ann.*, **314**, 200 (1901).
(5) R. Behrend and P. Hesse, *ibid.*, **329**, 341 (1903).

This reaction has been applied to a variety of α,β-unsaturated amino esters and acyl isothiocyanates, and the results of this work are recorded in Table I. Several interesting factors are worthy of note. The reaction seems to be quite general, although higher yields of 4-thiopyrimidines were obtained if the acyl isothiocyanate were substituted with an electron-withdrawing group. On the other hand, the condensation with *o*-methoxybenzoyl isothiocyanate gave a very poor yield of product and a number of different by-products were formed. These facts then suggest the following mechanism which



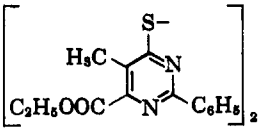
requires an electron-deficient carbonyl to facilitate the ring closure and subsequent dehydration. It was also observed that the isothiocyanate derivatives of aliphatic acids gave good yields of product. Variations in the structure of the crotonic ester did not significantly affect the course of the reaction. Ethyl β-methylaminocrotonate and ethyl β-aminocrotonate in general similarly gave good yields of the corresponding pyrimidines.

It was also observed that, in all cases, a small amount (2–5%) of the acylthiourea derivative was formed. This could usually be avoided by using freshly distilled crotonic acid ester.



R = H, CH_3, C_6H_5; Ar = aryl group

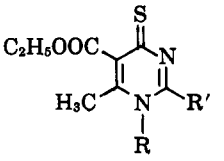
Recently, Goerdeler and Pohland[6] have reported that ethyl β-amino-α-benzoylthiocarbamoylcrotonate can be converted to the corresponding 4-thiopyrimidine in a 25% ammonium hydroxide solution. We have studied this also, but have found that the ring closure is easily accomplished merely by carrying out the reaction in refluxing tetrahydrofuran. Condensation of ethyl β-aminocrotonate with acyl isothiocyanates in refluxing tetrahydrofuran in the absence of base also affords the desired product. However, allowing III, dissolved in ammonium hydroxide solution, to stand at room temperature for 2 days gave rise to a colorless substance which was determined to have the following dimeric structure.



(6) J. Goerdeler and H. W. Pohland, *Chem. Ber.*, **96**, 526 (1963).

TABLE I

4-THIOPYRIMIDINES

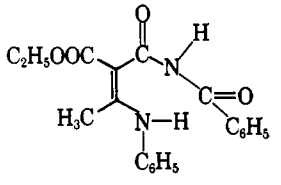


Compound	R	R′	M.p., °C.	Yield, %	Empirical formula	Calcd., % C	Calcd., % H	Calcd., % N	Found, % C	Found, % H	Found, % N
1	H	C_6H_5	130	42	$C_{14}H_{14}N_2O_2S$	61.30	5.14	10.21	61.04	5.15	10.60
2	H	*p*-Br-C_6H_4	174–176	45	$C_{14}H_{13}BrN_2O_2S$	47.63	3.71	7.94	47.35	3.71	7.90
3	H	$C_6H_5CH_2$	162–164	57	$C_{15}H_{16}N_2O_2S$	62.48	5.59	9.72	62.69	5.59	9.75
4	CH_3	CH_3	164–165	65	$C_{10}H_{14}N_2O_2S$	53.14	6.24	12.38	53.47	6.16	12.01
5	CH_3	C_6H_5	152	50	$C_{15}H_{16}N_2O_2S$	62.48	5.59	9.72	62.58	5.53	9.55
6	CH_3	*p*-Br-C_6H_4	230	47	$C_{15}H_{15}BrN_2O_2S$	49.09	4.12	7.63	49.18	4.12	7.32
7	C_6H_5	CH_3	207–209	70	$C_{15}H_{16}N_2O_2S$	62.48	5.59	9.72	62.60	5.58	9.42
8	C_6H_5	$ClCH_2$	130	73	$C_{15}H_{15}ClN_2O_2S$	55.95	4.70	8.70	55.97	4.81	8.53
9	C_6H_5	$C_6H_5CH_2$	182–183	65	$C_{21}H_{20}N_2O_2S$	69.15	5.53	7.69	69.05	5.50	7.46
10	C_6H_5	$C_6H_5C_3H_4$[a]	229–230	48	$C_{22}H_{22}N_2O_2S$	70.83	5.69	7.18	71.19	5.54	7.02
11	C_6H_5	C_6H_5	215	60	$C_{20}H_{18}N_2O_2S$	68.57	5.14	8.00	68.60	5.26	7.95
12	C_6H_5	*p*-Br-C_6H_4	190	45	$C_{20}H_{17}BrN_2O_2S$	55.99	3.99	6.53	60.01	3.89	6.27
13	C_6H_5	2,4-$Cl_2C_4H_3$	183–184	75	$C_{20}H_{16}Cl_2N_2O_2S \cdot C_2H_5OH$	56.89	4.73	6.03	57.04	4.73	6.03
14	C_6H_5	*o*-$(OCH_3)C_6H_4$	184–185	15	$C_{21}H_{20}N_2O_3S$	66.28	5.31	7.36	66.12	5.20	7.14
15	C_6H_5	3,4,5-$(OCH_3)_3C_6H_2$	232–233	12	$C_{23}H_{24}N_2O_5S$	62.64	5.71	6.35	62.26	5.49	6.26
16	C_6H_5	*p*-$NO_2C_6H_4$	250 dec.	77	$C_{20}H_{17}N_3O_4S$	60.81	4.34	10.64	60.72	4.30	10.25
17	C_6H_5	*m*-$NO_2C_6H_4$	240 dec.	65	$C_{20}H_{17}N_3O_4S$	60.81	4.34	10.64	60.92	4.52	10.67
18	C_6H_5	2-C_5H_4N	226–227	40	$C_{19}H_{17}N_3O_2S$	65.01	4.88	11.97	64.90	4.74	11.61

[a] Cyclopropyl.

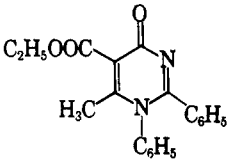
In this case the stronger base ammonia replaces the anilino group and the resulting 4-mercaptopyrimidine can undergo air oxidation to give the disulfide.

Finally, ethyl β-anilinocrotonate was allowed to react in refluxing tetrahydrofuran with benzoyl isocyanate. Surprisingly, even after long periods of reflux, only ethyl β-anilino-α-benzoylcarbamoyl crotonate (VI) could be isolated. The absence of a vinyl proton signal in the n.m.r. served to confirm the structural assignment. Attempted ring closure in higher boiling sol-



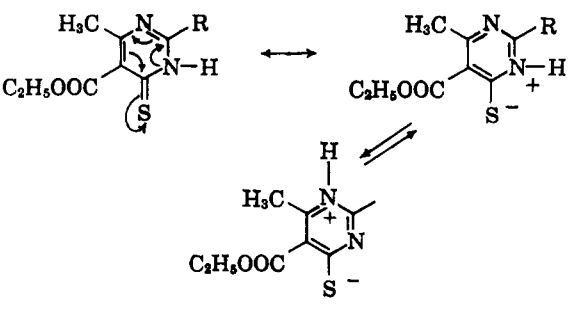
VI

vents, *e.g.*, toluene, xylene, or in the presence of dehydrating agents (*e.g.*, carbodiimide), was to no avail. Heating VI for a short time at a temperature slightly above its melting point yielded only N-benzoyl-N′-phenylurea. Condensation of I with *p*-nitrobenzoyl isocyanate also gave only the carbamoyl derivative. It, therefore, appears that the greater electronegativity of the carbamoyl oxygen as compared to sulfur[7] is instrumental in overcoming the tendency for cyclization followed by dehydration. The synthesis of ethyl 6-methyl-4-oxo-1,2-diphenylpyrimidine carboxylate (VII) was achieved through mercuric acetate in acetic acid oxidation of III.. In addition to the 1735-cm.$^{-1}$ absorption band for the carbethoxy group, VIII also gave a strong band at 1648 cm.$^{-1}$, which is characteristic of the 1-substituted pyrimidin-4-ones.[8]



VII

Spectral Data Interpretation.—The ultraviolet absorption data for the compounds prepared are listed in Table II. Several correlations can be derived therefrom. Substitution of the 2-position with an aromatic group is responsible for the absorption band at 250 to 260 mμ, since with 2-alkyl substituted derivatives this absorption maximum is shifted to approximately 230 mμ. It would appear that the 260-mμ absorption is due to the resonance contribution of the 2-phenyl group in conjugation with the 4-thione grouping through the C=N. It was also observed that the 1-unsubstituted compounds (1, 2, and 3 in Tables I and II) contain an additional absorption maximum at 305–310 mμ. Since this band is absent from the N-methyl and N-phenyl derivatives, it seems reasonable to assume that it arises mainly from this type resonance contribution.



Moreover, this indicates the difficulty of assigning a predominant tautomeric form to the -N–H compounds.

(7) L. Pauling, "Nature of the Chemical Bond," Cornell University Press, Ithaca, N. Y., 1951, p. 59.

(8) E. D. Bergmann, S. Cohen, and I. Shakak, *J. Chem. Soc.* 3278 (1959).

TABLE II

1,2-DISUBSTITUTED PYRIMIDINES

Compound no.[a]	λ_{max}, mμ	ε
1	240	14,540
	308	13,770
	352	4780
2	267	15,730
	308	13,940
	356	4790
3	300	12,950
	345	5920
4	228	5680
	337	21,270
5	250	10,310
	340	20,650
6	259	12,370
	340	19,190
7	228	6350
	337	22,740
8	234	11,810
	326	15,040
9	234	7920
	339	21,990
10	249	11,810
	338	25,820
11	248	8890
	341	23,420
12	254	11,670
	341	25,100
13	230	16,560
	340	24,690
14		
15	230	17,980
	340	24,940
16	262	13,350
	340	20,350
17	243	17,860
	342	22,520
18	340	10,990
	272 (shoulder)	6470
	341	24,040

[a] See Table I.

Furthermore, the absence of absorption bands at the 2600-cm.$^{-1}$ region of the infrared and the presence of only –N–H signals in the n.m.r. precluded the presence of appreciable amounts of a 4-thiol tautomer in this series of heterocycles.

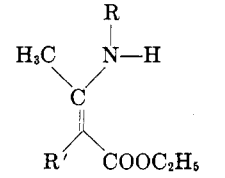
Finally, all of the 4-thiopyrimidines exhibited a maximum at 345–350 mμ, regardless of the substituents in the 1- or 2-position. This absorption maximum was found to be conspicuously absent in the spectrum of VIII. Thus, this long wave-length absorption can be attributed to the influence of the sulfur with its expanded valence shell on the resonating pyrimidine system.

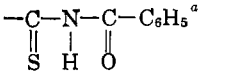
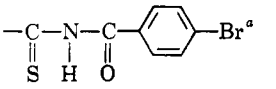
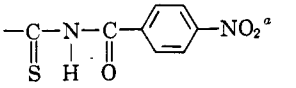
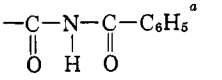
The infrared absorption spectra of these substances have already been discussed in connection with the structure proof of III. However, the ester group for the 1-unsubstituted compounds in Nujol mull absorbs at 1710 cm.$^{-1}$, whereas the 1-substituted compounds give a strong band at 1735 cm.$^{-1}$ in Nujol mull. When the infrared absorption of the former compounds was determined in chloroform, the ester absorption was shifted to 1732 cm.$^{-1}$. Thus, the shift to higher wave lengths in Nujol mull for the –N–H containing compounds can be associated with hydrogen bonding effects.

Infrared and n.m.r. spectroscopy were very useful in determining the stereochemical relationship of ethyl

TABLE III

INFRARED ABSORPTION IN THE CARBONYL REGION



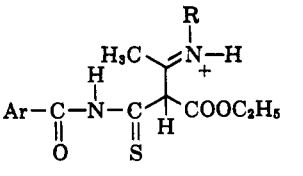
R	R′	ν, cm.$^{-1}$
H	H	1665 (s), 1624 (vs)
C_6H_5	H	1655 (s), 1620 (vs), 1600 (s)
H		1698 (s), 1665 (vs), 1618 (s)
H		1695 (s), 1665 (vs), 1615 (s)
H		1700 (s), 1672 (vs), 1610 (S)
C_6H_5		1713 (s), 1657 (vs), 1620 (s)

[a] In Nujol mull.

α-benzoylthiocarbamoyl-β-aminocrotonate and related compounds. The principal absorption bands in the carbonyl region of the infrared for these substances are listed in Table III.

The 1665-cm.$^{-1}$ band for ethyl β-aminocrotonate is assigned to the ester grouping and, in the β-anilino derivative, the carbethoxy group absorbs at 1655 cm.$^{-1}$. This shift to a lower wave length has been ascribed to intramolecular hydrogen bonding effect, thus suggesting a *cis* relationship between the amino and the ester groups. This was supported by the chemical shifts observed in the n.m.r.[9] In addition, ethyl β-diethylaminocrotonate[9] gives two carbonyl bands, 1677 (strong) and 1655 cm.$^{-1}$ (very weak), in the infrared. This consists of a mixture of *cis* and *trans* isomers, with *trans* predominating as evidenced by the strength of the absorption bands.

The *cis* stereochemical relationship (*i.e.*, the *cis* orientation of the amino and ester groups) holds for the aroylthiocarbamoyl and carbamoyl derivatives, since the ester group absorption is found at 1665–1672 cm.$^{-1}$, when the amino group is unsubstituted, and at 1657 cm.$^{-1}$ with the β-anilino derivative. However, this stereochemical assignment has little if any influence on the ring closure reaction since the driving force for this reaction appears to be the unshared pair of electrons of the amino group, thus leading to a transition state in which free rotation about the α-carbon is possible.



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Experimental

The n.m.r. spectra were run in deuteriochloroform solutions at 60 Mc. using trimethylsilane as an internal standard. The infrared spectra were obtained from Nujol mulls or chloroform using a Perkin-Elmer Model 21 grating spectrophotometer. The ultraviolet absorption spectra were obtained from ethyl alcohol solutions using a Beckman recording spectrophotometer, Model DK. The melting points are corrected.

All acyl isothiocyanates were prepared by allowing equimolar amounts of acid chloride and lead isothiocyanate to react in benzene solution under mild reflux for 1 hr. The lead salts then were removed by filtration, and the filtrate was concentrated to an oily residue which then was purified by vacuum distillation. As outlined by Assony[10] acid chlorides as a rule react with isothiocyanate salts to form the isothiocyanate derivatives rather than the thiocyanate. Infrared absorption spectroscopy supported this, since the acyl isothiocyanates prepared exhibited a broad strong band at 2000–2050 cm.$^{-1}$, typical of the isothiocyanate group, whereas the thiocyanate group shows a sharp medium band at 2150 cm.$^{-1}$.

General Method for the Preparation of Thiocarbamoyl Derivatives. Ethyl β-Amino-α-benzoylthiocarbamoylcrotonate.—Ethyl β-aminocrotonate (5.5 g., 0.043 mole) dissolved in 50 ml. of ethyl ether was treated with vigorous stirring at 5–10° with 7.0 g. (0.043 mole) of benzoyl isothiocyanate. An immediate reaction occurred resulting in the formation of a copious orange precipitate, m.p. 115°. This was found to be identical with the compound prepared by Goerdeler and Pohland.[11]

Anal. Calcd. for $C_{14}H_{16}N_2O_3S$. N, 9.58; S, 10.97. Found: N, 9.32; S, 10.62.

Ethyl β-amino-α-(p-bromobenzoylthiocarbamoyl)crotonate had m.p. 106°.

Anal. Calcd. for $C_{14}H_{15}BrN_2O_3S$: C, 45.45; H, 4.06; N, 7.50. Found: C, 45.71; H, 4.07; N, 7.31.

Ethyl β-amino-α-(p-nitrobenzoylthiocarbamoyl)crotonate had m.p. 112°.

Anal. Calcd. for $C_{14}H_{15}N_3O_5S$: C, 49.80; H, 4.47; N, 12.45. Found: C, 49.72; H, 4.36; N, 12.29.

The above described esters could be recrystallized from glacial acetic acid.

Conversion of Crotonate Derivatives to Pyrimidines. Ethyl 4-Mercapto-6-methyl-2-phenyl-5-pyrimidinecarboxylate.—Ethyl β-amino-α-benzoylthiocarbamoylcrotonate (5.0 g., 0.017 mole) was dissolved in 25 ml. of ethyl alcohol and refluxed on the steam bath for 6 hr. The color of the solution turned from orange to bright yellow. The solvent then was removed *in vacuo*, and the resulting bright yellow residue was crystallized from ethyl alcohol to give the product, m.p. 140°.

Anal. Calcd. for $C_{14}H_{14}N_2O_2S$: C, 61.30; H, 5.14; N, 10.21. Found: C, 61.14; H, 5.15; N, 10.23.

This compound could be obtained also by allowing ethyl β-aminocrotonate to react with benzoyl isothiocyanate in refluxing tetrahydrofuran for 2 hr. After chilling the reaction mixture overnight, the yellow precipitate was collected on a filter and crystallized from ethyl alcohol. The yield of product was usually higher by this direct method.

Bis(6-methyl-2-phenyl-5-carbethoxypyrimidyl) Disulfide (V).—Six grams (0.017 mole) of ethyl 4-mercapto-6-methyl-2-phenyl-5-pyrimidinecarboxylate was dissolved in 100 ml. of 28% ammonium hydroxide solution. The solution was allowed to stand at room temperature for 24 hr. A white precipitate formed which was collected and recrystallized from methylene chloride–ethyl alcohol (1:1). The white crystalline substance melted at 174–175°. Molecular weight determination by osmometry gave a value of 548. Thus, a dimeric compound (molecular weight of 546.7) was indicated; it showed $\lambda_{max}^{C_2H_5OH}$ 273 mμ (ε 59,568).

Anal. Calcd. for $C_{28}H_{26}N_4O_4S_2$: C, 61.59; H, 4.80; N, 10.26; S, 11.77. Found: C, 61.73; H, 4.96; N, 10.05; S, 11.49.

Goerdeler and Pohland have reported a melting point of 137° for their bis compound. We are at a loss to explain this discrepancy; however, these investigators did not determine the molecular weight of their substance.

General Method for Preparation of 1,2-Disubstituted Pyrimidines. Ethyl 6-Methyl-1,2-diphenyl-4-thiono-5-pyrimidinecarboxylate (III).—Ethyl β-anilinocrotonate (4.01 g.) dissolved in 25 ml. of ethyl ether was allowed to react at room temperature with stirring for 2 hr. with 3.6 g. of benzoyl isothiocyanate. A copious yellow orange precipitate formed which was collected on a filter and washed with a small amount of ether. The weight of this substance, m.p. 210°, was 2.0 g. Work-up of the mother liquors gave an additional 1.8 g. of product plus a small amount (0.3 g.) of N-benzoyl-N′-phenylthiourea, m.p. 148–150°, lit.[12] m.p. 150°.

Ethyl β-Anilino-α-benzoylcarbamoylcrotonate (VI).—Ethyl β-anilinocrotonate (10 g., 0.05 mole) was dissolved in 25 ml. of ethyl ether and then treated at 5–10° with 7.4 g. (0.05 mole) of benzoyl isocyanate. An immediate reaction occurred and a white precipitate was formed. This was collected and crystallized from ethyl alcohol to give 4.0 g. of white crystals, m.p. 120°. In the n.m.r. spectrum, the absence of a signal at τ 3–4 characteristic of a vinyl proton confirmed the structural assignment.

Anal. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.25; H, 5.68; N, 7.97. Found: C, 68.23; H, 5.75; N, 7.94.

Several attempts were made to convert VII to the corresponding pyrimidine. Compound VII was refluxed in benzene with carbodiimide or in toluene or xylene, but only starting material was recovered. Compound VII also was heated at its melting point for 10 min. Under these conditions only N-benzoyl-N′-phenylurea, m.p. 209° (lit.[13] m.p. 210°), was identified.

Ethyl β-methylamino-2-(benzoylcarbamoyl)crotonate was crystallized from ethyl alcohol to give 60% yield of product, m.p. 134–135°.

Anal. Calcd. for $C_{15}H_{18}N_2O_4$: C, 62.12; H, 6.26; N, 9.66. Found: C, 62.23; H, 6.40; N, 9.63.

Ethyl β-anilino-2-(p-nitrobenzoylcarbamoyl)crotonate was crystallized from ethyl alcohol to afford a 45% yield of product, m.p. 157–159°.

Anal. Calcd. for $C_{20}H_{19}N_3O_6$: C, 60.61; H, 4.82; N, 10.59. Found: C, 61.00; H, 4.77; N, 10.87.

Ethyl 6-Methyl-1,2-diphenyl-4-oxopyrimidinecarboxylate (VII).—Compound III (2.7 g.) dissolved in 100 ml. of glacial acetic acid was treated with 2.7 g. of mercuric acetate. The resulting pale yellow solution was heated at reflux temperature for 5 hr. The dark brown mixture was filtered, and the filtrate was concentrated *in vacuo* on the steam bath. A yellow oil was obtained which was triturated with ether. The white solid which formed was collected and triturated with chloroform. The chloroform extract was concentrated *in vacuo* to afford a powder which was crystallized from isopropyl alcohol–ether (1:2). The product was obtained as tiny white crystals, m.p. 155–157°, in 34% yield; $\lambda_{max}^{C_2H_5OH}$ 244 mμ (ε 22,230), 274 shoulder (8100); infrared absorption 1735 (ester), 1648 cm.$^{-1}$ (–C=O of ring system).

Anal. Calcd. for $C_{20}H_{18}N_2O_3$: C, 71.92; H, 5.43; N, 8.39. Found: C, 71.52; H, 5.41; N, 8.45.

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