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Ketene-*S,N*-acetals as Synthetic Intermediates for Heterocycles.¹⁾ Reaction of Ketene-*S,N*-acetals with Aryl Isocyanates²⁾

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Reaction of ketene-*S,N*-acetals (**1**—**6**), which are useful synthetic intermediates for heterocycles, with aryl isocyanates (**7**) is described. Annulation of **1**—**3** and **4**—**6** with **7** in boiling toluene gave bicyclic (**8**—**10**) and monocyclic (**11**—**13**) uracil derivatives, respectively. Addition of **2**, **3**, and **4** to **7** under mild conditions afforded the 1:1 adducts (**18**, **19**, and **21**), respectively. Compounds **18** and **19** also reacted with **7** to give bicyclic uracil derivatives.

Keywords—ketene-*S,N*-acetal; enamine; aryl isocyanate; azacycloalka[2,3-*d*]pyrimidine; uracil; barbituric acid

Enamines are very important synthetic intermediates.³⁾ Semicyclic ketene-*S,N*-acetals (**1**, **2**, and **3**) and acyclic ketene-*S,N*-acetals (**4**, **5**, and **6**) derived from *N*-methylthiolactams and tertiary thioamides, respectively, may be regarded as α -methylthioenamines,⁴⁾ and are expected to serve as attractive synthetic intermediates for heterocycles. We report here a new synthesis of uracil derivatives of pharmacological interest by the reaction of ketene-*S,N*-acetals with aryl isocyanates as dipolarophiles.

Addition of 2 eq of aryl isocyanates (**7a**—**d**) to **1**, **2**, and **3** in boiling toluene gave azacycloalka[2,3-*d*] pyrimidines (**8a**—**d**, **9a**—**d**, and **10a**—**d**, respectively) (Chart 1). The

Chart 1

structures of **8a**—**d**, **9a**—**d**, and **10a**—**d** were supported by the spectral data. In the proton nuclear magnetic resonance (¹H-NMR) spectra, the proton signals of the *N*-methyl group were considerably shielded by the orthogonal aryl groups, an effect which can be attributed to the planarity of the fused pyrimidinediones. Mass spectra (MS) showed the fragmentation peaks $[\text{M} - \text{ArNCO}]^+$ due to retro Diels–Alder decomposition. Similarly, acyclic ketene-*S,N*-acetals (**4**, **5**, and **6**) were transformed into monocyclic 1,3-diarylpyrimidine-2,4-diones (**11a**—**c**, **12a**—**c**, and **13a**—**c**, respectively) (Tables I and II). Hydrolysis of **11a**—**c**, **12a**—**c**, and **13a**—**c** with 10% hydrochloric acid afforded barbituric acid derivatives (**14a**—**c**, **15a**, **c**, and **16a**—**c**, respectively) in good yields (Tables III and IV). However, the hydrolysis of **12b** gave

TABLE I. 1,3-Diaryl-2,4-dioxo-*N*-methylazacycloalka[2,3-*d*]pyrimidines (**8a—d**, **9d—d**, and **10a—d**) and 1,3-Diaryl-5-alkyl-6-dimethylamino-2,4-(1*H*,3*H*)-pyrimidinediones (**11a—c**, **12a—c**, and **13a—c**)

Compd. ^{a)}	Yield (%)	mp (°C)	Formula	Analysis (%)		
				Calcd (Found)		
				C	H	N
8a	43	234—235	C ₁₉ H ₁₇ N ₃ O ₂	71.45 (71.38)	5.37 5.26	13.16 12.66
8b	46	218—220	C ₂₁ H ₂₁ N ₃ O ₂	72.60 (72.86)	6.09 6.11	12.10 11.87
8c^{b)}	36	220—221	C ₁₉ H ₁₅ Cl ₂ N ₃ O ₂			
8d^{c)}	32	229—231	C ₁₉ H ₁₅ Br ₂ N ₃ O ₂			
9a	67	215—218	C ₂₀ H ₁₉ N ₃ O ₂	72.05 (71.84)	5.74 5.75	12.61 12.51
9b	67	211—213	C ₂₂ H ₂₃ N ₃ O ₂	73.10 (73.20)	6.41 6.44	11.63 11.51
9c	62	200—203	C ₂₀ H ₁₇ Cl ₂ N ₃ O ₂	59.71 (59.63)	4.26 4.31	10.45 10.27
9d	78	214—216	C ₂₀ H ₁₇ Br ₂ N ₃ O ₂	48.90 (48.90)	3.49 3.53	8.55 8.45
10a	62	273—276	C ₂₁ H ₂₁ N ₃ O ₂	72.60 (72.86)	6.09 6.08	12.10 12.07
10b	71	222—223	C ₂₃ H ₂₅ N ₃ O ₂	73.57 (73.48)	6.71 6.69	11.19 10.93
10c	70	227—229	C ₂₁ H ₁₉ Cl ₂ N ₃ O ₂	60.19 (60.47)	4.60 4.51	10.09 10.23
10d	54	206—209	C ₂₁ H ₁₉ Br ₂ N ₃ O ₂	49.92 (49.66)	3.79 3.87	8.32 8.15
11a	92	203—205	C ₁₈ H ₁₇ N ₃ O ₂	70.34 (70.23)	5.58 5.64	13.67 13.47
11b	73	205—207	C ₂₀ H ₂₁ N ₃ O ₂	71.62 (71.44)	6.31 6.31	12.53 12.40
11c	63	206—208	C ₁₈ H ₁₅ Cl ₂ N ₃ O ₂	57.46 (57.63)	4.02 4.16	11.17 10.77
12a	35	164—166	C ₁₉ H ₁₉ N ₃ O ₂	71.01 (70.72)	5.96 5.80	13.08 12.78
12b	40	168—170	C ₂₁ H ₂₃ N ₃ O ₂	72.18 (72.25)	6.63 6.67	12.03 11.87
12c	41	164—166	C ₁₉ H ₁₇ Cl ₂ N ₃ O ₂	58.47 (58.25)	4.39 4.40	10.77 10.93
13a	47	189—191	C ₂₀ H ₂₁ N ₃ O ₂	71.62 (71.25)	6.31 6.37	12.53 12.29
13b	37	220—222	C ₂₂ H ₂₅ N ₃ O ₂	72.70 (72.62)	6.93 6.93	11.56 11.37
13c	35	189—191	C ₂₀ H ₁₉ Cl ₂ N ₃ O ₂	59.41 (58.94)	4.74 4.75	10.39 10.38

^{a)} Compounds were recrystallized from CH₂Cl₂-diisopropyl ether except for **12c** (from ether). ^{b)} Exact mass: *m/z* 387.0494, 389.0561, 391.0547 (Calcd 387.0540, 389.0513, 391.0481). ^{c)} Exact mass: *m/z* 474.9504, 476.9545, 478.9579 (Calcd 474.9530, 476.9513, 478.9492).

an inseparable mixture of products (Chart 2).

When **1**, **2**, and **3** were treated with **7a—d** in ether at room temperature, **8a**, **b** and the lactams (**17a—d**) were obtained from **1**, whereas the 1 : 1 adducts (**18a—d** and **19a—d**) were obtained from **2** and **3**, respectively (Tables V and VI). The products formed were dependent

TABLE II. Spectroscopic Data for **8a—d**, **9a—d**, **10a—d**, **11a—c**, **12a—c**, and **13a—c**

Compd.	IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}	MS m/z	$^1\text{H-NMR } \delta$ (CDCl_3)
8a	1690, 1650, 1590	319 (M^+)	2.17 (3H, s, NMe)
8b	1700, 1660, 1600	347 (M^+)	2.13 (3H, s, NMe) 2.33 (3H, s, ArMe) 2.40 (3H, s, ArMe)
8c	1700, 1660, 1580	387 (M^+) 389 (M^+) 391 (M^+)	2.17 (3H, s, NMe)
8d	1700, 1660, 1590	475 (M^+) 477 (M^+) 479 (M^+)	2.20 (3H, s, NMe)
9a	1700, 1640, 1605	333 (M^+)	2.32 (3H, s, NMe)
9b	1705, 1645, 1610	361 (M^+)	2.27 (3H, s, NMe) 2.35 (6H, s, 2 ArMe)
9c	1705, 1640, 1605	401 (M^+) 403 (M^+) 405 (M^+)	2.33 (3H, s, NMe)
9d	1700, 1640, 1605	489 (M^+) 491 (M^+) 493 (M^+)	2.30 (3H, s, NMe)
10a	1700, 1650, 1610	347 (M^+)	2.27 (3H, s, NMe)
10b	1705, 1650, 1620	373 (M^+)	2.23 (3H, s, NMe) 2.40 (6H, s, 2 ArMe)
10c	1700, 1650, 1610	415 (M^+) 417 (M^+) 419 (M^+)	2.30 (3H, s, NMe)
10d	1700, 1640, 1605	503 (M^+) 505 (M^+) 507 (M^+)	2.23 (3H, s, NMe)
11a	1660	307 (M^+)	2.86 (6H, s, NMe_2) 5.33 (1H, s, 5-H)
11b	1660	335 (M^+)	2.47 (6H, s, NMe_2) 5.17 (1H, s, 5-H)
11c	1660	375 (M^+) 377 (M^+) 379 (M^+)	2.53 (6H, s, NMe_2) 5.30 (1H, s, 5-H)
12a	1640	321 (M^+)	2.00 (3H, s, 5-Me) 2.83 (6H, s, NMe_2)
12b	1640	349 (M^+)	2.00 (3H, s, 5-Me) 2.47 (6H, s, NMe_2)
12c	1640	389 (M^+) 391 (M^+) 393 (M^+)	2.06 (3H, s, 5-Me) 2.57 (6H, s, NMe_2)
13a	1640	335 (M^+)	1.17 (3H, t, $J=7.5$ Hz, 5- CH_2Me) 2.47 (6H, s, NMe_2)
13b	1660	363 (M^+)	1.17 (3H, t, $J=7.5$ Hz, 5- CH_2Me) 2.50 (6H, s, NMe_2)
13c	1660	403 (M^+) 405 (M^+) 407 (M^+)	1.17 (3H, t, $J=7.5$ Hz, 5- CH_2Me) 2.53 (6H, s, NMe_2)

on the ring size of the ketene-*S,N*-acetals. The ketene-*S,N*-acetal of a five-membered ring (**1**) was more reactive toward aryl isocyanates as compared with the ketene-*S,N*-acetals of six- and seven-membered rings (**2** and **3**). The lactams (**17a—d**) would be probably formed by hydrolysis of the 1:1 adducts (**20a—d**) during alumina column chromatography, though

TABLE III. 1,3-Diaryl-2,4,6-(1*H*,3*H*,5*H*)-pyrimidinetriones (**14a—c**, **15a, c**, and **16a—c**)

Compd. ^{a)}	Yield (%)	mp (°C)	Formula	Analysis (%)		
				Calcd (Found)		
				C	H	N
14a	86	253—254	C ₁₆ H ₁₂ N ₂ O ₃	68.56 (68.50)	4.32 4.36	10.00 9.85
14b	80	214—216 (213—214) ^{b)}				
14c	80	241—243	C ₁₆ H ₁₀ Cl ₂ N ₂ O ₃	55.03 (54.95)	2.89 3.08	8.02 8.09
15a	91	200—203 (201) ^{c)}				
15c	94	198—201	C ₁₇ H ₁₂ Cl ₂ N ₂ O ₃	56.21 (56.08)	3.33 3.52	7.71 7.52
16a	82	146—147	C ₁₈ H ₁₆ N ₂ O ₃	70.11 (70.17)	5.23 5.19	9.09 8.99
16b	85	149—151	C ₂₀ H ₂₀ N ₂ O ₃	71.41 (71.32)	5.99 5.94	8.33 8.25
16c	80	137—139	C ₁₈ H ₁₄ Cl ₂ N ₂ O ₃	57.27 (57.31)	3.74 3.78	7.42 7.37

a) Compounds were recrystallized from EtOH. b) Lit. 5. c) Lit. 6.

TABLE IV. Spectroscopic Data of **14a—c**, **15a, c** and **16a—c**

Compd.	IR $\nu_{\text{max}}^{\text{Nujol}}$ cm ⁻¹	¹ H-NMR δ (CDCl ₃)
14a	1695	3.95 (2H, s, 5-H ₂)
14b	1700	2.33 (6H, s, 2 ArMe) 3.77 (2H, s, 5-H ₂)
14c	1700	3.83 (2H, s, 5-H ₂)
15a	1695	1.66 (3H, d, <i>J</i> = 7.5 Hz, 5-Me) 3.70 (1H, q, <i>J</i> = 7.5 Hz, 5-H)
15c	1700	1.73 (3H, d, <i>J</i> = 8 Hz, 5-Me) 3.80 (1H, q, <i>J</i> = 8 Hz, 5-H)
16a	1690	1.13 (3H, t, <i>J</i> = 7 Hz, 5-CH ₂ Me) 3.70 (1H, t, <i>J</i> = 5.5 Hz, 5-H)
16b	1690	1.15 (3H, t, <i>J</i> = 6 Hz, CH ₂ Me) 2.30 (6H, s, 2 ArMe) 3.70 (1H, t, <i>J</i> = 5.5 Hz, 5-H)
16c	1700	1.13 (3H, t, <i>J</i> = 7 Hz, CH ₂ Me) 3.70 (1H, t, <i>J</i> = 5 Hz, 5-H)

Chart 2

TABLE V. Reaction of Ketene-S, N-acetals (1, 2, and 3) with 7a—d in Ether

Compd. ^{a)}	Yield (%)	mp (°C)	Formula	Analysis (%)		
				Calcd (Found)		
				C	H	N
8a	31					
17a	32	168—170	C ₁₂ H ₁₄ N ₂ O ₂	66.03 (65.80)	6.47 6.43	12.84 12.73
8b	26					
17b	33	189—195	C ₁₃ H ₁₆ N ₂ O ₂	67.22 (67.15)	6.94 6.95	12.06 11.81
17c	46	197—201	C ₁₂ H ₁₃ ClN ₂ O ₂	57.03 (56.41)	5.18 4.91	11.09 10.81
17d	53	207—213	C ₁₂ H ₁₃ BrN ₂ O ₂	48.50 (48.54)	4.41 4.40	9.43 9.38
18a	100	135—137	C ₁₄ H ₁₈ N ₂ OS	64.10 (63.60)	6.92 6.91	10.68 10.71
18b	95	134—136	C ₁₅ H ₂₀ N ₂ OS	65.19 (64.90)	7.30 7.43	10.14 10.14
18c	92	140—142	C ₁₄ H ₁₇ ClN ₂ OS	56.66 (56.71)	5.78 5.82	9.44 9.48
18d	93	146—147	C ₁₄ H ₁₇ BrN ₂ OS	49.27 (49.42)	5.02 5.06	8.21 8.24
19a	60	147—149	C ₁₅ H ₂₀ N ₂ OS	65.19 (65.31)	7.30 7.19	10.14 10.14
19b	66	144—146	C ₁₆ H ₂₂ N ₂ OS	66.16 (65.51)	7.64 7.71	9.65 9.60
19c	57	152—154	C ₁₅ H ₁₉ ClN ₂ OS	57.97 (57.68)	6.16 6.14	9.02 8.98
19d	53	157—159	C ₁₅ H ₁₉ BrN ₂ OS	50.71 (50.74)	5.39 5.41	7.89 7.78

a) Compounds were recrystallized from CH₂Cl₂-diisopropyl ether.

Chart 3

Chart 4

TABLE VI. Spectroscopic Data for **17a—d**, **18a—d**, and **19a—d**

Compd.	IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}	MS m/z	$^1\text{H-NMR } \delta$ (CDCl_3)
17a	3280, 1660, 1600	218 (M^+)	2.90 (3H, s, NMe), 9.87 (1H, br s, NH)
17b	3280, 1660, 1610	232 (M^+)	2.90 (3H, s, NMe), 9.67 (1H, br s, NH)
17c	3280, 1660, 1610	252 (M^+) 254 (M^+)	2.97 (3H, s, NMe), 9.95 (1H, br s, NH)
17d	3260, 1660, 1610	296 (M^+) 298 (M^+)	2.90 (3H, s, NMe), 9.87 (1H, br s, NH)
18a	3300, 1640	262 (M^+)	2.33 (3H, s, SMe), 3.00 (3H, s, NMe) 9.05 (1H, br s, NH)
18b	3350, 1620	276 (M^+)	2.25 (3H, s, SMe), 3.00 (3H, s, NMe) 9.05 (1H, br s, NH)
18c	3360, 1630	296 (M^+) 298 (M^+)	2.30 (3H, s, SMe), 3.03 (3H, s, NMe) 9.20 (1H, br s, NH)
18d	3360, 1630	340 (M^+) 342 (M^+)	2.30 (3H, s, SMe), 3.03 (3H, s, NMe) 9.20 (3H, br s, NH)
19a	3360, 1630	276 (M^+)	2.20 (3H, s, SMe), 3.03 (3H, s, NMe) 8.43 (1H, br s, NH)
19b	3340, 1635	290 (M^+)	2.27 (3H, s, SMe), 2.93 (3H, s, NMe) 8.33 (1H, br s, NH)
19c	3300, 1640	310 (M^+) 312 (M^+)	2.30 (3H, s, SMe), 3.03 (3H, s, NMe) 8.47 (1H, br s, NH)
19d	3300, 1640	354 (M^+) 356 (M^+)	2.30 (3H, s, SMe), 3.05 (3H, s, NMe) 8.47 (1H, br s, NH)

TABLE VII. *N*-Aryl-3-dimethylamino-3-methylthioacrylamides (**21a—c**)

Compd. ^{a)}	Yield (%)	mp ($^{\circ}\text{C}$)	Formula	Analysis (%)		
				Calcd	Found	
				C	H	N
21a	95	194—195	$\text{C}_{12}\text{H}_{16}\text{N}_2\text{OS}$	60.98 (60.96)	6.82 6.89	11.86 11.72
21b	93	194—195	$\text{C}_{13}\text{H}_{18}\text{N}_2\text{OS}$	62.26 (62.24)	7.25 7.14	11.19 11.09
21c	91	195—196	$\text{C}_{12}\text{H}_{15}\text{ClN}_2\text{OS}$	53.22 (53.29)	5.58 5.56	10.35 10.17

^{a)} Compounds were recrystallized from CH_2Cl_2 -diisopropyl ether.

TABLE VIII. Spectroscopic Data for **21a—c**

Compd.	IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}	$^1\text{H-NMR } \delta$ (CDCl_3)
21a	1630	<i>E</i> -Isomer: 2.27 (3H, s, SMe), 2.97 (6H, s, NMe_2), 4.90 (1H, s, 2-H) <i>Z</i> -Isomer: 2.33 (3H, s, SMe), 2.97 (6H, s, NMe_2), 5.00 (1H, s, 2-H)
21b	1620	<i>E</i> -Isomer: 2.30 (3H, s, SMe), 3.00 (6H, s, NMe_2), 4.95 (1H, s, 2-H) <i>Z</i> -Isomer: 2.37 (3H, s, SMe), 3.00 (6H, s, NMe_2), 5.05 (1H, s, 2-H)
21c	1620	<i>E</i> -Isomer: 2.33 (3H, s, SMe), 3.00 (6H, s, NMe_2), 4.92 (1H, s, 2-H) <i>Z</i> -Isomer: 2.83 (3H, s, SMe), 3.00 (6H, s, NMe_2), 5.00 (1H, s, 2-H)

20a—d could not be isolated (Chart 3). Treatment of **4** with **7a—c** in cyclohexane afforded (*E*) and (*Z*) mixtures of the 1 : 1 adducts (**21a—c**) (Table VII). A similar reaction in ether yielded no crystalline products. The ratio of (*E*) to (*Z*) isomers of **21a—c** was determined from the

TABLE IX. *N*-Aryl-*N'*, *N'*-dimethyl-2-methylmalonoamides (**23a–c**)

Compd. ^{a)}	Yield (%)	mp (°C)	Formula	Analysis (%)		
				Calcd (Found)		
				C	H	N
23a	34	139–141	C ₁₂ H ₁₆ N ₂ O ₃	65.43 (65.56)	7.32 7.35	12.72 12.94
23b	41	143–145	C ₁₃ H ₁₈ N ₂ O ₃	66.64 (66.54)	7.74 7.78	11.96 11.92
23c	33	169–171	C ₁₂ H ₁₅ ClN ₂ O ₃	56.58 (56.40)	5.94 5.94	11.00 10.96

a) Compounds were recrystallized from CH₂Cl₂–diisopropyl ether.

TABLE X. Spectroscopic Data for **23a–c**

Compd.	IR $\nu_{\max}^{\text{Nujol}}$ cm ⁻¹	¹ H-NMR δ (CDCl ₃)
23a	1670, 1620	1.53 (3H, d, <i>J</i> = 8 Hz, Me), 2.93, 3.07 (each 3H, s, NMe ₂) 3.60 (1H, q, <i>J</i> = 8 Hz, 2-H)
23b	1660, 1640	1.55 (3H, d, <i>J</i> = 8 Hz, Me), 2.30 (3H, s, ArMe) 3.02, 3.14 (each 3H, s, NMe ₂), 3.72 (1H, q, <i>J</i> = 8 Hz, 2-H)
23c	1660, 1640	1.53 (3H, d, <i>J</i> = 7 Hz, Me), 3.00, 3.10 (each 3H, s, NMe ₂) 3.63 (1H, q, <i>J</i> = 7 Hz, 2-H)

TABLE XI. Reaction of 1:1 Adducts (**18a,c** and **19a,c**) with Aryl Isocyanates (**7a,c**) and Phenyl Isothiocyanate

Compd. ^{a)}	Yield (%)	mp (°C)	Formula	Analysis (%)		
				Calcd (Found)		
				C	H	N
9a	55					
10a	74					
9c	36					
10c	42					
24	32	214–216	C ₂₀ H ₁₈ ClN ₃ O ₂	65.31 (65.63)	4.93 4.81	11.42 11.20
25	38	199–202	C ₂₁ H ₂₀ ClN ₃ O ₂	66.05 (66.20)	5.28 5.29	11.00 10.89
26	22	213–215	C ₂₀ H ₁₈ ClN ₃ O ₂	65.31 (65.20)	4.93 4.90	11.42 11.54
27	27	269–272	C ₂₁ H ₂₀ ClN ₃ O ₂	66.05 (66.43)	5.28 5.10	11.00 10.79
28	19	238–240	C ₂₀ H ₁₉ N ₃ OS	68.74 (68.45)	5.48 5.63	12.02 12.10
29	45	273–276	C ₂₁ H ₂₁ N ₃ OS	69.39 (69.24)	5.82 5.68	11.56 11.70

a) Compounds were recrystallized from CH₂Cl₂–diisopropyl ether.

integral ratio of vinyl protons to be about 1:2. The chemical shifts of trisubstituted vinyl protons such as those in **21a–c** appear at higher field in the (*E*) isomer than in the (*Z*) isomer⁷⁾ (Table VIII). A similar reaction using a methyl-substituted ketene-*S,N*-acetal (**5**) re-

TABLE XII. Spectroscopic Data for 24–29

Compd.	IR $\nu_{\text{max}}^{\text{Nujol}}$ cm^{-1}	MS m/z	$^1\text{H-NMR } \delta$ (CDCl_3)
24	1710, 1640, 1610	368 (M^+), 370 (M^+)	2.20 (3H, s, NMe)
25	1710, 1660, 1620	382 (M^+), 384 (M^+)	2.33 (3H, s, NMe)
26	1715, 1640, 1615	368 (M^+), 370 (M^+)	2.20 (3H, s, NMe)
27	1700, 1650, 1625	382 (M^+), 384 (M^+)	2.30 (3H, s, NMe)
28	1690, 1640, 1620	349 (M^+)	2.15 (3H, s, NMe)
29	1690, 1640, 1610	363 (M^+)	2.20 (3H, s, NMe)

Chart 5

Chart 6

quired stronger conditions (cyclohexane-reflux). Therefore, the addition of 5 to 4a–c followed by column chromatography on alumina gave the corresponding amides (23a–c) (Tables IX and X, and Chart 4).

We found that the reaction of the 1:1 adducts (18a and 19a) with 7a in boiling toluene afforded the corresponding annulation products 9a and 10a, respectively. In a similar manner, 9c and 10c were also prepared from the reactions of 18c and 19c with 7c, respectively. Next, we attempted the reaction of the 1:1 adducts with various aryl isocyanates (Ar'NCO). The annulation reaction of 18a with 7c in boiling toluene yielded the fused pyrimidine derivative (24). Similarly, 25, 26, and 27 were synthesized. Further, the reactions of 18a and 19a with phenyl isothiocyanate were carried out to give the monothiones (28 and 29, respectively) (Table XI and XII, and Chart 5). However, the treatment of 21a with 7c gave an inseparable mixture of pyrimidines, the MS which showed peaks corresponding to the molecular ion peaks of 11a, 11c, 30, and 31. This result suggested that thermal dissociation of the 1:1

adducts (21) into ketene-*S,N*-acetal (4) and aryl isocyanates (7) had occurred. Reaction of the 1:1 adducts (21a, c) alone in boiling toluene gave the corresponding pyrimidinediones (11a, c), as expected, in good yields (Chart 6). On the other hand, similar reactions of the semicyclic 1:1 adducts (18a and 19a) resulted in recovery of the starting materials.

Experimental

Melting points were determined on a Yanagimoto melting point apparatus and are uncorrected. Infrared (IR) spectra were obtained on a JASCO IRA-1 spectrometer. ¹H-NMR spectra were recorded on a JEOL PMX-60 instrument at 60 MHz. Chemical shifts are reported in ppm (δ) relative to tetramethylsilane as an internal standard. MS were measured with a JEOL D-200 instrument.

1,3-Diaryl-7-methyl-2,4-dioxo-1,2,3,4,5,6-hexahydro-7H-pyrrolo[2,3-*d*]pyrimidines (8a—d), 1,3-Diaryl-8-methyl-2,4-dioxo-1,2,3,4,5,6,7,8-octahydropyrido[2,3-*d*]pyrimidines (9a—d), 1,3-Diaryl-9-methyl-2,4-dioxo-1,2,3,4,5,6,7,8-octahydro-9H-pyrimido[4,5-*b*]azepines (10a—d), and 1,3-Diaryl-6-dimethylamino-5-alkyl-2,4-dioxo-1,2,3,4-tetrahydropyrimidines (11a—c, 12a—c, and 13a—c). **General Procedure**—A ketene-*S,N*-acetal (1, 2, 3, 4, 5, or 6) (2 mmol) was added to a solution of an aryl isocyanate (7a—d) (4 mmol) in toluene (20 ml) and the mixture was refluxed for 15 h with stirring. The solvent was evaporated and the resultant oil was recrystallized from diisopropyl ether to afford 8a—d, 9a—d, 10a—d, 11a—c, 12a—c, or 13a—c, respectively.

1,3-Diaryl-5-alkyl-2,4,6(1*H*,3*H*,5*H*)-pyrimidinetriones (14a—c, 15a, c, and 16a—c). **General Procedure**—A solution of 11a—c, 12a, c, or 13a—c (0.5 mmol) in 10% hydrochloric acid (10 ml) was refluxed for 2 h. The mixture was extracted with dichloromethane three times. The extracts were washed with brine, dried over anhyd. magnesium sulfate, and evaporated to give a solid, which was recrystallized to afford 14a—c, 15a, c, or 16a—c, respectively.

1-Methyl-3-(*N*-arylcarbamoyl-2-pyrrolidinones (17a—d). **General Procedure**—1 (1 mmol) was added to a stirred solution of 7a—d (1 mmol) in ether (10 ml) and stirring was continued for 4 h at room temperature. The solvent was evaporated off and the residual oil was separated by column chromatography on alumina using benzene–dichloromethane (1:1) as an eluant to give 8a, b and 17a—d.

1-Methyl-2-methylthio-1,4,5,6-tetrahydropyridine-3-(*N*-arylcarboxamides) (18a—d) and 1-Methyl-2-methylthio-4,5,6,7-tetrahydro-1*H*-azepine-3-(*N*-arylcarboxamides) (19a—d). **General Procedure**—2 or 3 (1 mmol) was added to a stirred solution of 7a—d (1 mmol) in ether (10 ml) and stirring was continued for 4 or 15 h, respectively, at room temperature. The precipitate was isolated by suction and recrystallized to afford 18a—d or 19a—d, respectively.

***N*-Aryl-3-dimethylamino-3-methylthioacrylamides (21a—c).** **General Procedure**—4 (1 mmol) was added to a stirred solution of 7a—c (1 mmol) in cyclohexane (10 ml) and stirring was continued for 4 h at room temperature. The precipitate was isolated by suction and recrystallized to afford 21a—c.

***N*-Aryl-*N*',*N*'-dimethyl-2-methylmalonamides (23a—c).** **General Procedure**—5 (1 mmol) was added to a solution of 7a—c (1 mmol) in cyclohexane (10 ml) and the mixture was refluxed for 15 h. The solvent was evaporated off and the residual oil was purified by column chromatography on alumina using benzene–dichloromethane (1:1) as an eluant to give 23a—c.

1-4'-Chlorophenyl-8-methyl-2,4-dioxo-3-phenyl-1,2,3,4,5,6,7,8-octahydropyrido[2,3-*d*]pyrimidine (24), 1-4'-Chlorophenyl-9-methyl-2,4-dioxo-3-phenyl-1,2,3,4,5,6,7,8-octahydro-9H-pyrimido[4,5-*b*]azepine (25), 3-4'-Chlorophenyl-8-methyl-2,4-dioxo-1-phenyl-1,2,3,4,5,6,7,8-octahydropyrido[2,3-*d*]pyrimidine (26), 3-4'-Chlorophenyl-9-methyl-2,4-dioxo-1-phenyl-1,2,3,4,5,6,7,8-octahydro-9H-pyrimido[4,5-*b*]azepine (27), 8-Methyl-4-oxo-1,3-diphenyl-2-thioxo-1,2,3,4,5,6,7,8-octahydropyrido[2,3-*d*]pyrimidine (28), and 9-Methyl-4-oxo-1,3-diphenyl-4-thioxo-1,2,3,4,5,6,7,8-octahydro-9H-pyrimido[4,5-*b*]azepine (29)—A mixture of 18a (1 mmol) and 7c (1 mmol) in toluene (10 ml) was refluxed for 15 h. The solvent was evaporated off and the residual oil was purified by column chromatography on alumina using benzene–dichloromethane (1:1) as an eluant to give 24. In a similar manner, 25, 26, 27, 28, and 29 were prepared from 19a and 7c, 18c and 7a, 19c and 7a, 18a and phenyl isothiocyanate, and 19a and phenyl isothiocyanate, respectively. 9a, c and 10a, c were similarly obtained from 18a and 7a, 18c and 7c, 19a and 7a, and 19c and 7c, respectively, without purification by chromatography.

Reaction of 21a, c, 18a or 19a in Toluene—A solution of 21a, c (1 mmol) in toluene (10 ml) was refluxed for 15 h. The solvent was evaporated off to give 11a, c in 95% and 76% yields, respectively. These products were identical with the samples prepared by the reaction of 4 with 7a, c in terms of melting points, IR, and ¹H-NMR data. Reflux of 18a (1 mmol) or 19a (1 mmol) in toluene (10 ml) for 15 h resulted in the recovery of 18a or 19a, respectively.

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