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Ketene-*S*,*N*-acetals as Synthetic Intermediates for Heterocycles.[1] Reaction of Ketene-*S*,*N*-acetals with Aryl Isocyanates[2]

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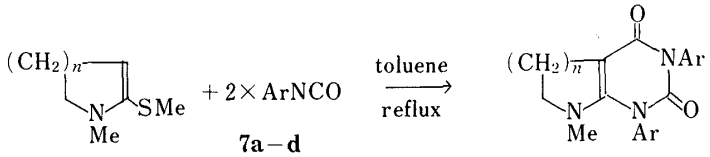
Reaction of ketene-*S*,*N*-acetals (**1**—**6**), which are useful synthetic intermediates for heterocycles, with aryl isocyanates (**7**) is described. Annulation of **1**—**3** and **4**—**6** with **7** in boiling toluene gave bicyclic (**8**—**10**) and monocyclic (**11**—**13**) uracil derivatives, 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



7a—**d**

a: Ar = Ph
b: Ar = 4-MeC_6H_4
c: Ar = 4-ClC_6H_4
d: Ar = 4-BrC_6H_4

1: $n=1$ **2**: $n=2$ **3**: $n=3$

8a—**d**: $n=1$ **9a**—**d**: $n=2$ **10a**—**d**: $n=3$

Chart 1

structures of **8a**—**d**, **9a**—**d**, and **10a**—**d** were supported by the spectral data. In the proton nuclear magnetic resonance (^{1}H-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 $[M-ArNCO]^+$ 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	$C_{19}H_{17}N_3O_2$	71.45	5.37	13.16
				(71.38	5.26	12.66)
8b	46	218—220	$C_{21}H_{21}N_3O_2$	72.60	6.09	12.10
				(72.86	6.11	11.87)
8c[b]	36	220—221	$C_{19}H_{15}Cl_2N_3O_2$			
8d[c]	32	229—231	$C_{19}H_{15}Br_2N_3O_2$			
9a	67	215—218	$C_{20}H_{19}N_3O_2$	72.05	5.74	12.61
				(71.84	5.75	12.51)
9b	67	211—213	$C_{22}H_{23}N_3O_2$	73.10	6.41	11.63
				(73.20	6.44	11.51)
9c	62	200—203	$C_{20}H_{17}Cl_2N_3O_2$	59.71	4.26	10.45
				(59.63	4.31	10.27)
9d	78	214—216	$C_{20}H_{17}Br_2N_3O_2$	48.90	3.49	8.55
				(48.90	3.53	8.45)
10a	62	273—276	$C_{21}H_{21}N_3O_2$	72.60	6.09	12.10
				(72.86	6.08	12.07)
10b	71	222—223	$C_{23}H_{25}N_3O_2$	73.57	6.71	11.19
				(73.48	6.69	10.93)
10c	70	227—229	$C_{21}H_{19}Cl_2N_3O_2$	60.19	4.60	10.09
				(60.47	4.51	10.23)
10d	54	206—209	$C_{21}H_{19}Br_2N_3O_2$	49.92	3.79	8.32
				(49.66	3.87	8.15)
11a	92	203—205	$C_{18}H_{17}N_3O_2$	70.34	5.58	13.67
				(70.23	5.64	13.47)
11b	73	205—207	$C_{20}H_{21}N_3O_2$	71.62	6.31	12.53
				(71.44	6.31	12.40)
11c	63	206—208	$C_{18}H_{15}Cl_2N_3O_2$	57.46	4.02	11.17
				(57.63	4.16	10.77)
12a	35	164—166	$C_{19}H_{19}N_3O_2$	71.01	5.96	13.08
				(70.72	5.80	12.78)
12b	40	168—170	$C_{21}H_{23}N_3O_2$	72.18	6.63	12.03
				(72.25	6.67	11.87)
12c	41	164—166	$C_{19}H_{17}Cl_2N_3O_2$	58.47	4.39	10.77
				(58.25	4.40	10.93)
13a	47	189—191	$C_{20}H_{21}N_3O_2$	71.62	6.31	12.53
				(71.25	6.37	12.29)
13b	37	220—222	$C_{22}H_{25}N_3O_2$	72.70	6.93	11.56
				(72.62	6.93	11.37)
13c	35	189—191	$C_{20}H_{19}Cl_2N_3O_2$	59.41	4.74	10.39
				(58.94	4.75	10.38)

a) Compounds were recrystallized from CH_2Cl_2–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 ν_{max}^{Nujol} cm^{-1}	MS m/z	^{1}H-NMR δ ($CDCl_3$)
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^+)	2.17 (3H, s, NMe)
		389 (M^+)	
		391 (M^+)	
8d	1700, 1660, 1590	475 (M^+)	2.20 (3H, s, NMe)
		477 (M^+)	
		479 (M^+)	
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^+)	2.33 (3H, s, NMe)
		403 (M^+)	
		405 (M^+)	
9d	1700, 1640, 1605	489 (M^+)	2.30 (3H, s, NMe)
		491 (M^+)	
		493 (M^+)	
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^+)	2.30 (3H, s, NMe)
		417 (M^+)	
		419 (M^+)	
10d	1700, 1640, 1605	503 (M^+)	2.23 (3H, s, NMe)
		505 (M^+)	
		507 (M^+)	
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^+)	2.53 (6H, s, NMe_2)
		377 (M^+)	5.30 (1H, s, 5-H)
		379 (M^+)	
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^+)	2.06 (3H, s, 5-Me)
		391 (M^+)	2.57 (6H, s, NMe_2)
		393 (M^+)	
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^+)	1.17 (3H, t, J=7.5 Hz, 5-CH_2Me)
		405 (M^+)	2.53 (6H, s, NMe_2)
		407 (M^+)	

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

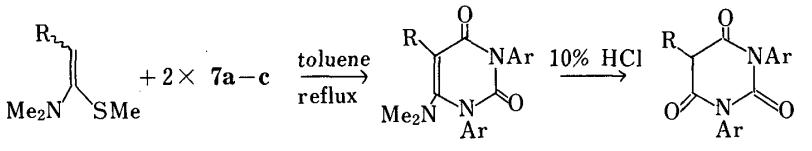
TABLE III. 1,3-Diaryl-2,4,6-(1*H*,3*H*,5*H*)-pyrimidinetriones (**14a—c**, **15a, c**, and **16a—c**)

Compd.[a]	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found)		
				C	H	N
14a	86	253—254	$C_{16}H_{12}N_2O_3$	68.56 (68.50	4.32 4.36	10.00 9.85)
14b	80	214—216 (213—214)[b]				
14c	80	241—243	$C_{16}H_{10}Cl_2N_2O_3$	55.03 (54.95	2.89 3.08	8.02 8.09)
15a	91	200—203 (201)[c]				
15c	94	198—201	$C_{17}H_{12}Cl_2N_2O_3$	56.21 (56.08	3.33 3.52	7.71 7.52)
16a	82	146—147	$C_{18}H_{16}N_2O_3$	70.11 (70.17	5.23 5.19	9.09 8.99)
16b	85	149—151	$C_{20}H_{20}N_2O_3$	71.41 (71.32	5.99 5.94	8.33 8.25)
16c	80	137—139	$C_{18}H_{14}Cl_2N_2O_3$	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 ν_{max}^{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, J=7.5 Hz, 5-Me) 3.70 (1H, q, J=7.5 Hz, 5-H)
15c	1700	1.73 (3H, d, J=8 Hz, 5-Me) 3.80 (1H, q, J=8 Hz, 5-H)
16a	1690	1.13 (3H, t, J=7 Hz, 5-CH_2Me) 3.70 (1H, t, J=5.5 Hz, 5-H)
16b	1690	1.15 (3H, t, J=6 Hz, CH_2Me) 2.30 (6H, s, 2 ArMe) 3.70 (1H, t, J=5.5 Hz, 5-H)
16c	1700	1.13 (3H, t, J=7 Hz, CH_2Me) 3.70 (1H, t, J=5 Hz, 5-H)



4: R=H
5: R=Me
6: R=Et

11a—c: R=H
12a—c: R=Me
13a—c: R=Et

14a—c: R=H
15a, c: R=Me
16a—c: R=Et

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	$C_{12}H_{14}N_2O_2$	66.03	6.47	12.84
				(65.80	6.43	12.73)
8b	26					
17b	33	189—195	$C_{13}H_{16}N_2O_2$	67.22	6.94	12.06
				(67.15	6.95	11.81)
17c	46	197—201	$C_{12}H_{13}ClN_2O_2$	57.03	5.18	11.09
				(56.41	4.91	10.81)
17d	53	207—213	$C_{12}H_{13}BrN_2O_2$	48.50	4.41	9.43
				(48.54	4.40	9.38)
18a	100	135—137	$C_{14}H_{18}N_2OS$	64.10	6.92	10.68
				(63.60	6.91	10.71)
18b	95	134—136	$C_{15}H_{20}N_2OS$	65.19	7.30	10.14
				(64.90	7.43	10.14)
18c	92	140—142	$C_{14}H_{17}ClN_2OS$	56.66	5.78	9.44
				(56.71	5.82	9.48)
18d	93	146—147	$C_{14}H_{17}BrN_2OS$	49.27	5.02	8.21
				(49.42	5.06	8.24)
19a	60	147—149	$C_{15}H_{20}N_2OS$	65.19	7.30	10.14
				(65.31	7.19	10.14)
19b	66	144—146	$C_{16}H_{22}N_2OS$	66.16	7.64	9.65
				(65.51	7.71	9.60)
19c	57	152—154	$C_{15}H_{19}ClN_2OS$	57.97	6.16	9.02
				(57.68	6.14	8.98)
19d	53	157—159	$C_{15}H_{19}BrN_2OS$	50.71	5.39	7.89
				(50.74	5.41	7.78)

a) Compounds were recrystallized from CH_2Cl_2–diisopropyl ether.

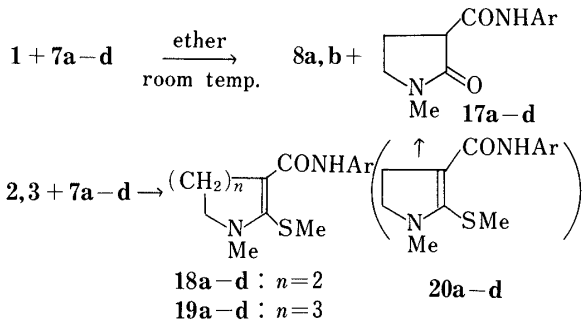


Chart 3

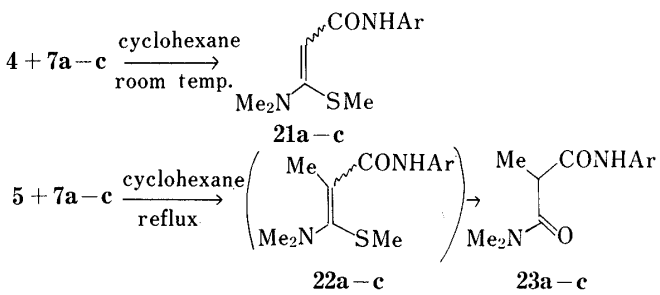


Chart 4

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

Compd.	IR ν_{max}^{Nujol} cm^{-1}	MS *m/z*	^{1}H-NMR δ ($CDCl_3$)
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 (°C)	Formula	Analysis (%) Calcd (Found)		
				C	H	N
21a	95	194—195	$C_{12}H_{16}N_2OS$	60.98 (60.96	6.82 6.89	11.86 11.72)
21b	93	194—195	$C_{13}H_{18}N_2OS$	62.26 (62.24	7.25 7.14	11.19 11.09)
21c	91	195—196	$C_{12}H_{15}ClN_2OS$	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 ν_{max}^{Nujol} cm^{-1}	^{1}H-NMR δ ($CDCl_3$)
21a	1630	*E*-Isomer: 2.27 (3H, s, SMe), 2.97 (6H, s, NMe_2), 4.90 (1H, s, 2-H) *Z*-Isomer: 2.33 (3H, s, SMe), 2.97 (6H, s, NMe_2), 5.00 (1H, s, 2-H)
21b	1620	*E*-Isomer: 2.30 (3H, s, SMe), 3.00 (6H, s, NMe_2), 4.95 (1H, s, 2-H) *Z*-Isomer: 2.37 (3H, s, SMe), 3.00 (6H, s, NMe_2), 5.05 (1H, s, 2-H)
21c	1620	*E*-Isomer: 2.33 (3H, s, SMe), 3.00 (6H, s, NMe_2), 4.92 (1H, s, 2-H) *Z*-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	$C_{12}H_{16}N_2O_3$	65.43	7.32	12.72
				(65.56	7.35	12.94)
23b	41	143—145	$C_{13}H_{18}N_2O_3$	66.64	7.74	11.96
				(66.54	7.78	11.92)
23c	33	169—171	$C_{12}H_{15}ClN_2O_3$	56.58	5.94	11.00
				(56.40	5.94	10.96)

a) Compounds were recrystallized from CH_2Cl_2–diisopropyl ether.

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

Compd.	IR ν_{max}^{Nujol} cm^{-1}	^{1}H-NMR δ ($CDCl_3$)
23a	1670, 1620	1.53 (3H, d, J=8 Hz, Me), 2.93, 3.07 (each 3H, s, NMe_2) 3.60 (1H, q, J=8 Hz, 2-H)
23b	1660, 1640	1.55 (3H, d, J=8 Hz, Me), 2.30 (3H, s, ArMe) 3.02, 3.14 (each 3H, s, NMe_2), 3.72 (1H, q, J=8 Hz, 2-H)
23c	1660, 1640	1.53 (3H, d, J=7 Hz, Me), 3.00, 3.10 (each 3H, s, NMe_2) 3.63 (1H, q, J=7 Hz, 2-H)

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

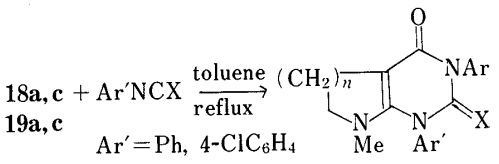
Compd.[a]	Yield (%)	mp (°C)	Formula	Analysis (%) Calcd (Found)		
				C	H	N
9a	55					
10a	74					
9c	36					
10c	42					
24	32	214—216	$C_{20}H_{18}ClN_3O_2$	65.31	4.93	11.42
				(65.63	4.81	11.20)
25	38	199—202	$C_{21}H_{20}ClN_3O_2$	66.05	5.28	11.00
				(66.20	5.29	10.89)
26	22	213—215	$C_{20}H_{18}ClN_3O_2$	65.31	4.93	11.42
				(65.20	4.90	11.54)
27	27	269—272	$C_{21}H_{20}ClN_3O_2$	66.05	5.28	11.00
				(66.43	5.10	10.79)
28	19	238—240	$C_{20}H_{19}N_3OS$	68.74	5.48	12.02
				(68.45	5.63	12.10)
29	45	273—276	$C_{21}H_{21}N_3OS$	69.39	5.82	11.56
				(69.24	5.68	11.70)

a) Compounds were recrystallized from CH_2Cl_2–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*) isomer[7] (Table VIII). A similar reaction using a methyl-substituted ketene-*S*,*N*-acetal (**5**) re-

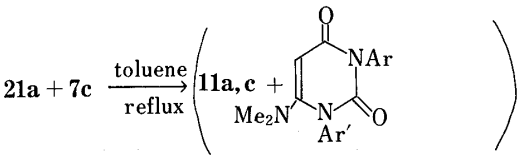
TABLE XII. Spectroscopic Data for **24**—**29**

Compd.	IR ν_{max}^{Nujol} cm^{-1}	MS *m/z*	^{1}H-NMR δ ($CDCl_3$)
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)



9a, **10a**
9c, **10c**
24: n=2, Ar=Ph, Ar'=4-ClC_6H_4, X=O
25: n=3, Ar=Ph, Ar'=4-ClC_6H_4, X=O
26: n=2, Ar=4-ClC_6H_5, Ar'=Ph, X=O
27: n=3, Ar=4-ClC_6H_5, Ar'=Ph, X=O
28: n=2, Ar=Ar'=Ph, X=S
29: n=3, Ar=Ar'=Ph, X=S

Chart 5



30 : Ar=Ph, Ar'=4-ClC_6H_4
31 : Ar=4-ClC_6H_4, Ar'=Ph

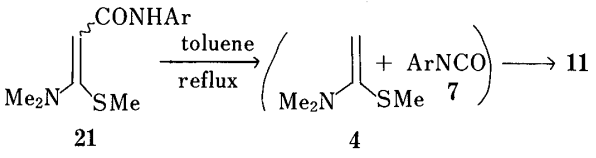


Chart 6

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. ^{1}H-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-7*H*-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-9*H*-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 to 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-9*H*-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-9*H*-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-9*H*-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 ^{1}H-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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