Reaction of Enaminonitriles with Isocyanates. Synthesis of New 2-Oxo- and 6-Oxopyrimidines

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The reaction of enaminonitriles **1** with aryl or benzyl isocyanates afforded C- **3-5** or N-adducts **6-8** or a mixture of both depending on the substitution pattern of the considered enaminonitrile. The one-step synthesis of 6-oxopyrimidines **9-11** and 2-oxopyrimidines **12-14** by cyclization of compounds **3-5** and **6-8** respectively is also described.

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Enamines are ambidentate conjugated systems with high, but variable, nucleophilicity at both the nitrogen and β-carbon atoms. It is therefore difficult to foresee their reactivity towards the electrophilic reagents, in spite of the amount of available information [1]. The preferential site for the electrophilic attack depends both on the kind of electrophile and on the experimental conditions. The same electrophiles can yield totally different products if the reaction conditions are changed slightly. Moreover the nature of the substitutents in α- and β-position play a fundamental role in the reactivity of the enamines.

Thus enamino compounds with a primary or secondary amino group such as the alkyl 3-aminocrotonates and the 3-alkoxy-3-aminopropenoic esters are additioned to the organic isocyanates to give *N*-adducts [2,3]. Similarly the reaction of ethyl 3,3-diaminopropenoate with the isocyanates leads to *N*-monoadducts, while with the isothiocyanates it gives the *C*-monoadducts in low yields [4]. In this paper we examine the reactivity of some 3-amino-3-(dialkylamino)propenenitriles **1** towards the aryl (or benzyl) isocyanates **2**.

The reaction of enaminonitriles **1** with the isocyanates **2** in a 1:1 molar ratio was carried out in acetonitrile at room temperature. While in previous reactions between enaminonitriles **1** and electrophilic reagents we only isolated *C*-adducts [5-8], in this case we obtained *C*- or *N*-adducts or mixtures of both depending on the enaminonitrile considered (Table 1).

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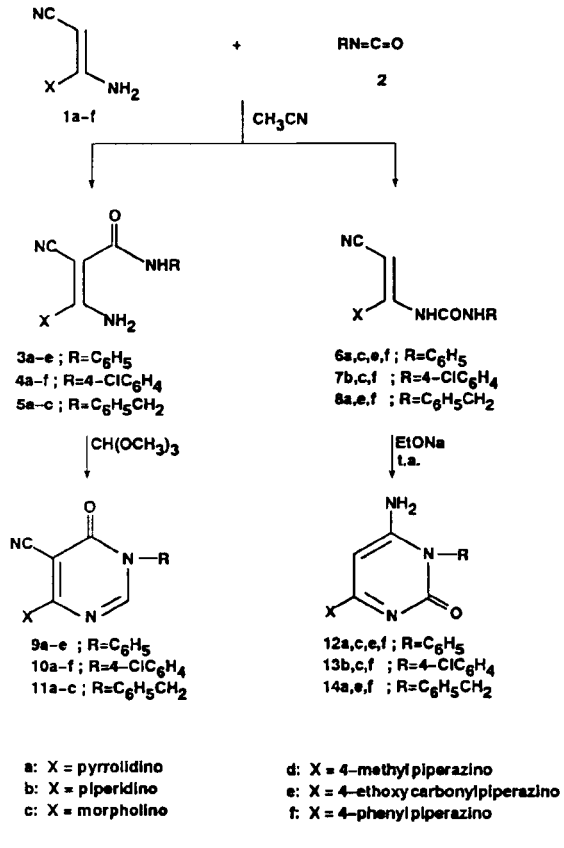


Table 1
Reaction of Amidines with Isocyanates

Amidines	Isocyanates	Time hours	Products (yield, %)	
1a	C_6H_5NCO	4	**3a** (55)	**6a** (27)
1b	C_6H_5NCO	4	**3b** (63)	
1c	C_6H_5NCO	4	**3c** (40)	**6c** (38)
1d	C_6H_5NCO	4	**3d** (52)	
1e	C_6H_5NCO	6	**3e** (44)	**6e** (33)
1f	C_6H_5NCO	8		**6f** (93)
1a	$4\text{-}ClC_6H_4NCO$	4	**4a** (83)	
1b	$4\text{-}ClC_6H_4NCO$	4	**4b** (70)	**7b** (25)
1c	$4\text{-}ClC_6H_4NCO$	4	**4c** (59)	**7c** (25)
1d	$4\text{-}ClC_6H_4NCO$	4	**4d** (58)	
1e	$4\text{-}ClC_6H_4NCO$	8	**4e** (70)	
1f	$4\text{-}ClC_6H_4NCO$	10	**4f** (6)	**7f** (78)
1a	$C_6H_5CH_2NCO$	1	**5a** (72)	**8a** (12)
1b	$C_6H_5CH_2NCO$	1	**5b** (55)	
1c	$C_6H_5CH_2NCO$	2	**5c** (95)	
1e	$C_6H_5CH_2NCO$	5		**8e** (73)
1f	$C_6H_5CH_2NCO$	6		**8f** (97)

The reaction of the enaminonitriles **1b** and **1d** with phenyl isocyanate led only to the *C*-adducts **3b** and **3d** respectively, while **1a**, **1c** and **1e** led to mixtures of *C*- and *N*-adducts. Analogously, the reaction of **1** with 4-chlorophenyl isocyanate prevalently led to the formation

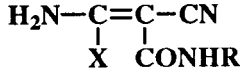
of C-adducts **4** and, only in the cases of **1b** and **1c**, also the respective *N*-adduct **7** was isolated in 25% yield. The enaminonitriles **1a-c** react with benzyl isocyanate to form the *C*-adducts **5** as main product, while **1e-f** formed only the *N*-adducts **8**. Addition of **1f** to the isocyanates **2** led to *N*-adducts, however, in the reaction with 4-chlorophenyl isocyanate, **4f** (6%) was isolated as a minor product. Separation of the mixtures of *C*- and *N*-adducts (Table 2,4) was simplified by the fact that *C*-adducts crystallize from the reaction medium.

The same results were obtained when the reaction was carried out in chloroform, but separation of the mixtures is more complex. Only monoaddition products were obtained when **1** was additioned to the isocyanates in a 1:2 molar ratio under the same conditions. This is supported by the fact that the reaction between equimolecular amounts of **3** and phenyl isocyanate failed.

The ^{1}H nmr spectra of the *C*-adducts **3-5** (Table 3) show downfield signals that disappear on addition of deuterium oxide. One of these signals integrates for two protons, the

Table 2

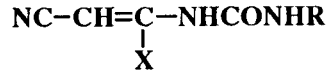
Physical and Analytical Data of Compounds **3**, **4** and **5**



Compound	Mp (°C)	Crystallization solvent	Formula	Analysis % Calcd. C	H	N	Found C	H	N
3a	186-187	Acetonitrile	$C_{14}H_{16}N_4O$	65.60	6.29	21.86	65.55	6.27	21.83
3b	177-178	Acetonitrile	$C_{15}H_{18}N_4O$	66.66	6.71	20.73	66.61	6.73	20.70
3c	219-220	Acetonitrile	$C_{14}H_{16}N_4O_2$	61.75	5.92	20.58	61.81	5.90	20.50
3d	185-186	Acetonitrile	$C_{15}H_{19}N_5O$	63.14	6.71	24.55	63.10	6.69	24.52
3e	190-191	Acetonitrile	$C_{17}H_{21}N_5O_3$	59.46	6.16	20.40	59.40	6.18	20.37
4a	244-245	Diethylene glycol	$C_{14}H_{15}ClN_4O$	57.82	5.20	19.27	57.78	5.23	19.24
4b	204-205	Acetonitrile	$C_{15}H_{17}ClN_4O$	59.10	5.62	18.38	59.15	5.60	18.35
4c	224-225	Acetonitrile	$C_{14}H_{15}ClN_4O_2$	54.82	4.93	18.26	55.03	4.95	18.30
4d	204-205	Acetonitrile	$C_{15}H_{18}ClN_5O$	56.33	5.67	21.90	56.30	5.65	21.87
4e	214-215	Acetonitrile	$C_{17}H_{20}ClN_5O_3$	54.03	5.33	18.54	54.18	5.31	18.64
4f	219-220	Acetonitrile	$C_{20}H_{20}ClN_5O$	62.90	5.27	18.34	62.79	5.25	18.27
5a	179-180	2-Propanol	$C_{15}H_{18}N_4O$	66.66	6.71	20.73	66.61	6.69	20.70
5b	159-160	2-Propanol	$C_{16}H_{20}N_4O$	67.58	7.09	19.71	67.50	7.11	19.76
5c	114-115	2-Propanol	$C_{15}H_{18}N_4O_2$	62.92	6.34	19.57	62.87	6.36	19.54

Table 4

Physical and Analytical Data of Compounds **6**, **7** and **8**



Compound	Mp (°C)	Crystallization solvent	Formula	Analysis % Calcd. C	H	N	Found C	H	N
6a	134-135	Benzene	$C_{14}H_{16}N_4O$	65.60	6.29	21.86	65.55	6.31	21.83
6c	159-160	Benzene	$C_{14}H_{16}N_4O_2$	61.75	5.92	20.58	61.70	5.94	20.63
6e	155-156	Benzene	$C_{17}H_{21}N_5O_3$	59.46	6.16	20.40	59.41	6.14	20.43
6f	160-161	Benzene	$C_{20}H_{21}N_5O$	69.14	6.09	20.16	69.10	6.07	20.13
7b	129-130	Benzene	$C_{15}H_{17}ClN_4O$	59.10	5.62	18.38	59.06	5.60	18.35
7c	215-216	Benzene	$C_{14}H_{15}ClN_4O_2$	54.82	4.93	18.26	54.89	4.91	18.30
7f	179-180	Acetonitrile	$C_{20}H_{20}ClN_5O$	62.90	5.27	18.34	62.79	5.30	18.27
8a	104-105	Benzene	$C_{15}H_{18}N_4O$	66.66	6.71	20.73	66.59	6.69	20.70
8e	129-130	2-Propanol	$C_{18}H_{23}N_5O_3$	60.49	6.49	19.60	60.45	6.51	19.57
8f	134-135	2-Propanol	$C_{21}H_{23}N_5O$	69.78	6.41	19.38	69.73	6.39	19.35

Table 3

Spectroscopic Data of Compounds **3**, **4** and **5**

Compound No.	IR cm^{-1}	^{1}H-NMR (ppm)			
		X	R	NH	NH_2
3a	3460, 3330, 3120 2170, 1630, 1590	1.83, 3.86 (m)	6.90, 7.17, 7.38 (m)	8.55 (s)	9.20 (br s)
3b	3420, 3380, 3200 2220, 1670, 1640 1620	1.53, 3.35 (m)	6.90, 7.18, 7.44 (m)	8.71 (s)	9.18 (br s)
3c	3410, 3280, 3220 2240, 1630, 1595	3.39, 3.61 (m)	6.92, 7.19, 7.45 (m)	8.80 (s)	9.20 (br s)
3d	3420, 3300, 3250 3200, 2180, 1640 1625, 1600	2.14 (s), 2.32, 3.37 (m)	6.90, 7.17, 7.43 (m)	8.75 (s)	9.22 (br s)
3e	3400, 3300, 2190 1690, 1615, 1585	1.30 (t), 4.00 (q) 3.39 (m)	6.89, 7.16, 7.45 (m)	8.79 (s)	9.21 (br s)
4a	3380, 3160, 2160 1635, 1610, 1590	1.83, 3.43 (m)	7.22, 7.47 (m)	8.77 (s)	9.20 (br s)
4b	3450, 3270, 2180 1620, 1580	1.53, 3.34 (m)	7.23, 7.47 (m)	8.91 (s)	9.07 (br s)
4c	3440, 3260, 2160 1615, 1580	3.38, 3.60 (m)	7.22, 7.50 (m)	8.97 (s)	9.17 (br s)
4d	3430, 3300, 3260 2170, 1625, 1600	2.14 (s), 2.32, 3.37 (m)	7.23, 7.47 (m)	8.94 (s)	9.10 (br s)
4e	3350, 3130, 2160 1700, 1630, 1610	1.11 (t), 3.98 (q) 3.38 (m)	7.20, 7.48 (m)	8.97 (s)	9.10 (br s)
4f	3340, 3280, 3200 2180, 1620, 1600	3.17, 3.54, 6.76 6.91, 7.17 (m)	7.23, 7.50 (m)	8.98 (s)	9.15 (br s)
5a	3350, 3340, 3150 2170, 1635, 1610	1.82, 3.41 (m)	4.23 (d), 7.22 (m)	7.27 (t)	9.54 (br s)
5b	3350, 3290, 3120 2180, 1640, 1590	1.52, 3.29 (m)	4.22 (d), 7.19 (m)	7.31 (t)	9.42 (br s)
5c	3320, 3170, 2190 1595	3.34, 3.58 (m)	4.23 (d), 7.21 (m)	7.41 (t)	9.48 (br s)

Table 5

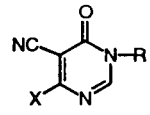
Spectroscopic Data of Compounds **6**, **7** and **8**

Compound No.	IR cm^{-1}	^{1}H-NMR (ppm)			
		X	R	NHCONH	CH_2, = CH (E/Z)
6a	3430, 3280, 2170 2150, 1680, 1640 1620	1.79, 3.17, 3.43, 3.55 (m)	6.92, 7.20, 7.38, 7.55 (m)	8.37, 8.55, 8.78, 9.18 (s)	3.60, 4.10 (s)
6c	3310, 3270, 2240 2170, 1680, 1650 1585	3.12, 3.39, 3.55, 3.61 (m)	6.93, 7.23, 7.40, 7.56 (m)	8.42, 8.80, 8.84, 9.38 (s)	4.02, 4.18 (s)
6e	3280, 3180, 3060 2190, 2160, 1700 1660, 1615, 1600	1.04, 1.33 (t), 3.16, 3.35, 3.43, 3.63, 4.01 (m)	6.93, 7.24, 7.38, 7.55 (m)	8.43, 8.84, 9.38 (s)	3.26, 4.04, 4.18 (s)
6f	3280, 3200, 3100 2180, 2170, 1680 1600, 1580	[a] 3.13, 3.20, 3.54, 3.56, 3.76 (m)	6.76, 6.92, 7.23, 7.41, 7.57 (m)	8.50, 8.82, 8.92, 9.40 (s)	3.29, 4.07, 4.24 (s)
7b	3290, 2180, 1640 1610, 1580	1.54, 3.12, 3.34, 3.58 (m)	7.23, 7.40, 7.47, 7.57 (m)	8.36, 8.79, 8.91, 9.40 (s)	3.25, 3.94, 4.17 (s)
7c	3320, 2240, 1650 1595, 1580	3.10, 3.38, 3.53 3.59 (m)	7.24, 7.43, 7.56 (m)	8.44, 8.94, 9.50 (s)	4.02, 4.16 (s)
7f	3250, 3190, 2180 1680, 1610, 1590	[a] 3.14, 3.20, 3.30, 3.40, 3.78 (m)	6.77, 6.93, 7.23, 7.44, 7.60 (m)	8.52, 8.99, 9.55 (s)	3.27, 4.11, 4.24 (s)
8a	3310, 2190, 1690 1650, 1620	[b] 1.85, 1.95, 3.24, 3.41, 3.54 (m)	4.30, 4.36 (d), 7.25 (m)	5.54, 7.71, 8.42, 10.60 (s)	3.33, 3.92, 4.06 (s)
8e	3340, 2210, 1700 1660, 1620, 1570	1.14, 1.17 (t), 3.13, 3.25, 3.33, 3.55, 4.01 (m)	4.19, 4.24 (d), 6.91, 7.26 (m)	7.68, 8.30, 8.38 (s)	3.31, 3.91, 4.11 (s)
8f	3430, 3320, 3180 2200, 2180, 2160 1660, 1615	[a] 3.10, 3.28, 3.41, 3.51, 3.68 (m) 7.43 (m)	4.20, 4.25 (d), 6.76, 6.90, 7.22,	7.70, 8.30, 8.38 (m)	3.17, 3.97, 4.15 (s)

[a] Aromatic protons not distinguishable for X and R groups. [b] Taken in deuteriochloroform.

Table 6

Physical and Analytical Data of Compounds **9, 10** and **11**



Compound	Mp (°C)	Yield (%)	Crystallization solvent	Formula	Analysis % Calcd. C	H	N	Found C	H	N
9a	180-181	85	Benzene	$C_{15}H_{14}N_4O$	67.65	5.30	21.04	67.60	5.32	21.00
9b	217-218	98	Ethanol	$C_{16}H_{16}N_4O$	68.55	5.75	19.99	68.51	5.78	20.03
9c	114-115	96	Cyclohexane	$C_{15}H_{14}N_4O_2$	63.82	5.00	19.85	63.80	4.98	19.82
9d	144-145	98	Cyclohexane	$C_{16}H_{17}N_5O$	65.06	5.80	23.72	64.99	5.82	23.75
9e	162-163	98	Ethanol	$C_{18}H_{19}N_5O_3$	61.18	5.42	19.82	61.21	5.40	19.80
10a	258-259	97	2-Ethoxyethanol	$C_{15}H_{13}ClN_4O$	59.90	4.35	18.63	60.01	4.37	18.60
10b	179-180	90	Ethanol	$C_{16}H_{15}ClN_4O$	61.05	4.80	17.80	61.00	4.82	17.77
10c	240-241	90	Acetonitrile	$C_{15}H_{13}ClN_4O_2$	56.87	4.13	17.69	56.93	4.11	17.66
10d	209-210	98	Acetonitrile	$C_{16}H_{16}ClN_5O$	58.27	4.89	21.24	58.32	4.91	21.20
10e	194-195	93	Ethanol	$C_{18}H_{18}ClN_5O_3$	55.74	4.68	18.06	55.83	4.65	18.04
10f	258-259	98	2-Ethoxyethanol	$C_{21}H_{18}ClN_5O$	64.36	4.63	17.87	64.30	4.66	17.84
11a	214-215	95	Acetonitrile	$C_{16}H_{16}N_4O$	68.55	5.75	19.99	68.50	5.73	19.96
11b	140-141	98	Benzene	$C_{17}H_{18}N_4O$	69.37	6.16	19.04	69.45	6.18	19.08
11c	165-166	80	2-Propanol	$C_{16}H_{16}N_4O_2$	64.85	5.44	18.91	64.80	5.41	18.87

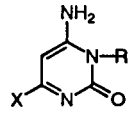
Table 7

Spectroscopic Data of Compounds **9, 10 and 11**

Compound No.	IR cm^{-1}	^{1}H-NMR (ppm) X	R	H-2
9a	2200, 1660, 1615, 1590, 1550	1.88, 3.73 (m)	7.39, 7.46 (m)	8.30 (s)
9b	2200, 1665, 1610 1585, 1540	1.63, 3.89 (m)	7.41, 7.46 (m)	8.30 (s)
9c	2200, 1660, 1610 1590, 1540	3.67, 3.92 (m)	7.41, 7.49 (m)	8.35 (s)
9d	2210, 1660, 1615 1530	2.18 (s), 2.40 3.91 (m)	7.42, 7.48 (m)	8.33 (s)
9e	2210, 1700, 1670 1590, 1530	1.16 (t), 4.03 (q) 3.50, 3.93 (m)	7.41, 7.47 (m)	8.37 (s)
10a	2200, 1665, 1620 1580, 1545	1.89, 3.74 (m)	7.45, 7.54 (m)	8.30 (s)
10b	2200, 1650, 1615 1580	1.62, 3.89 (m)	7.45, 7.55 (m)	8.29 (s)
10c	2210, 1660, 1615 1585, 1540	3.68, 3.92 (m)	7.47, 7.55 (m)	8.36 (s)
10d	2210, 1660, 1610 1585, 1530	2.17 (s), 3.29, 3.90 (m)	7.45, 7.52 (m)	8.33 (s)
10e	2200, 1710, 1690, 1650, 1610, 1570	1.16 (t), 4.04 (q), 3.50, 3.93 (m)	7.44, 7.55 (m)	8.37 (s)
10f	2200, 1650, 1610 1595, 1575	3.25, 4.08, 6.77 6.94, 7.19 (m)	7.47, 7.54 (m)	8.36 (s)
11a	2200, 1645, 1605 1545	1.84, 3.66 (m)	4.94 (s), 7.27 (m)	8.46 (s)
11b	2200, 1640, 1605 1550	1.56, 3.81 (m)	4.95 (s), 7.28 (m)	8.48 (s)
11c	2200, 1640, 1600 1535	3.64, 3.86 (m)	4.96 (s), 7.30 (m)	8.54 (s)

Table 8

Physical and Analytical Data of Compounds **12, 13** and **14**



Compound	Mp (°C)	Yield (%)	Crystallization solvent	Formula	Analysis % Calcd. C	H	N	Found C	H	N
12a	284-285	98	Acetonitrile	$C_{14}H_{16}N_4O$	65.60	6.29	21.86	65.67	6.27	21.83
12c	259-260	98	Acetonitrile	$C_{14}H_{16}N_4O_2$	61.75	5.92	20.58	61.70	5.90	20.55
12f	260-261	95	Ethanol	$C_{20}H_{21}N_5O$	69.14	6.09	20.16	69.19	6.11	20.12
13b	264-265	50	Ethanol	$C_{15}H_{17}ClN_4O$	59.10	5.62	18.38	59.18	5.60	18.35
13c	284-285	91	Ethanol	$C_{14}H_{15}ClN_4O_2$	54.82	4.93	18.26	54.77	4.91	18.29
13f	278-279	93	2-Ethoxyethanol	$C_{20}H_{20}ClN_5O$	62.90	5.27	18.34	62.88	5.25	18.31
14a	280-281	82	Acetonitrile	$C_{15}H_{18}N_4O$	66.66	6.71	20.73	66.60	6.73	20.70
14e	280-281	98	Acetonitrile	$C_{18}H_{23}N_5O_3$	60.49	6.49	19.60	60.41	6.73	19.58
14f	290-291	90	2-Ethoxyethanol	$C_{21}H_{23}N_5O$	69.78	6.41	19.38	69.70	6.43	19.34

Table 9

Spectroscopic Data of Compounds **12, 13** and **14**

Compound No.	IR cm^{-1}	^{1}H-NMR (ppm) X	R	NH_2	H-5
12a	3400, 3270, 3210 3160, 1675, 1605, 1585	1.83, 3.23 (m)	7.10, 7.44 (m)	5.90 (s)	4.89 (s)
12c	3420, 3260, 1660 1620, 1570	3.40, 3.57 (m)	7.13, 7.44 (m)	6.06 (s)	5.12 (s)
12f	3480, 3280, 3160 1665, 1620, 1590 1570	3.14, 3.60, 6.76, 6.94, 7.38 (m)	7.15, 7.45 (m)	6.06 (s)	5.20 (s)
13b	3550, 3460, 3380 1660, 1615, 1590 1570	1.43, 1.56, 3.43 (m)	7.15, 7.47 (m)	6.07 (s)	5.12 (s)
13c	3540, 3460, 3280 3180, 1670, 1620 1570	3.40, 3.57 (m)	7.16, 7.49 (m)	6.23 (s)	5.06 (s)
13f	3470, 3300, 3120 1670, 1630, 1600 1575	3.14, 3.59, 6.74, 6.94, 7.17 (m)	7.18, 7.48 (m)	6.21 (s)	5.17 (s)
14a	3420, 3340, 3100 1670, 1625, 1580	1.81, 3.23 (m)	5.01 (s), 7.20 (m)	6.56 (s)	4.80 (s)
14e	3480, 3120, 1700 1680, 1630, 1610	1.15 (t), 4.02 (q) 3.36, 3.41 (m)	5.02 (s), 7.19 (m)	6.73 (s)	5.06 (s)
14f	3380, 3120, 1680 1605, 1575	3.14, 3.58, 6.75, 6.95, 7.28 (m)	5.05 (s), 7.19 (m)	6.73 (s)	5.13 (s)

other for only one. They can be attributed to the NH_2 and NHCOR groups respectively. No signals relating to the iminic form are observed. The ^{1}H nmr spectra of the *N*-adducts **6-8** (Table 5) are complicated by an equilibrium between π-diastereoisomeric and tautomeric forms. In these spectra particularly a (deuterium oxide exchangeable) singlet is observed at 3.17-3.33 ppm due to the methylene protons of the imino form, and two signals at lower fields for the olefinic proton (H-2) of the enamino form. This splitting is due to an equilibrium mixture of the isomers with the *Z* and *E*-configuration. Moreover several exchangeable signals are present at low fields with a total intensity of two NH protons.

Adducts **3-5** are excellent synthons for the preparation

of 6-pyrimidone derivatives. When heating **3-5** under reflux with an excess of methyl orthoformate in the presence of catalytic amounts of *p*-toluenesulfonic acid, good yields of the cyclization compounds **9-11** were obtained (Table 6). Under these conditions the cyclization of **3d** and **4d** failed. In fact complex mixtures of decomposition products were obtained. Conversion of the above adducts into compounds **9d** and **10d** was therefore carried out by heating in toluene with *N,N*-dimethylformamide dimethyl acetal (DMF-DMA).

The *N*-adducts **6-8** were transformed into the 6-amino-2-pyrimidone derivatives **12-14** (Table 8) by treatment with sodium ethoxide in ethanol at room temperature.

The spectral data to allow a complete characterization of the cyclization products are summarized in Tables 7 and 9. Besides the signals of the X and R groups. the ^1H nmr spectra of the compounds **9-11**, moreover, show a singlet at 8.29-8.54 ppm due to H-2, while in the spectra of the compounds **12-14**, the H-5 proton resonates between 4.80 and 5.20 and the NH_2 group between 5.90 and 6.73 ppm.

EXPERIMENTAL

Melting points were determined on Köfler hot stage and are uncorrected. The ir spectra were obtained in Nujol with a Perkin-Elmer 398 spectrophotometer. The ^1H nmr spectra were recorded in hexadeuteriodimethyl sulfoxide solution unless otherwise specified with a Varian Unity 300 spectrometer; chemical shifts are reported in ppm from hexamethyldisiloxane as an internal standard and are given in δ units. The elemental analyses (C, H, N) were carried out with a Carlo Erba model 1106 Elemental Analyzer. The enaminonitriles **1** were obtained with a previously described procedure [9].

Reaction of Enaminonitriles 1 with Isocyanates

A solution of compound **1** (10 mmoles) and the appropriate isocyanate **2** (10 mmoles) in anhydrous acetonitrile (20 ml) was stirred at room temperature for the time reported in Table 1. The formed precipitate was collected by suction and recrystallized from a suitable solvent to give the 3-amino-3-(dialkylamino)-2-[(aryl or benzylamino)carbonyl]-2-propenenitriles **3a-e**, **4a-f**, **5a-c**. In the relevant cases, the mother liquors contained the soluble 3-amino-3-[(aryl or benzylaminocarbonyl)amino]-2-propenenitriles **6-8**. It was concentrated *in vacuo* and the residue triturated with ethyl acetate and then recrystallized from the appropriate solvent to give the compounds **6a,c,e,f**, **7b,c,f**, and **8a,e,f**. When the reaction was performed in chloroform, after evaporation *in vacuo*, the residue was chromatographed on silica gel and eluted with ethyl acetate/petroleum ether (2:1) to give *N*- and *C*-adducts.

General Procedure for the Preparation of 6-Oxopyrimidines 9a-e, 10a-f, 11a-c.

A mixture of compounds **3-5** (5 mmoles) in 10 ml of trimethyl orthoformate and in the presence of a catalytic amount of *p*-toluenesulfonic acid was heated under reflux. In the case of compounds **3** and **4** the mixture was refluxed for 24 hours while in the case of **5** for 1 hour. After cooling the formed precipitate was filtered off, washed with water, dried and recrystallized to give compounds **9-11**.

General Procedure for the Preparation of 1-Aryl-1,6-dihydro-4-(4-methylpiperazino)-6-oxopyrimidine-5-carbonitriles 9d, 10d.

N,N-Dimethylformamide dimethyl acetal (1 ml) was added to a suspension of **3d**, **4d** (2.5 mmoles) in 10 ml of anhydrous toluene. The resulting mixture was heated at 70-80° for 8 hours. After removal of the solvent the residue was recrystallized from a suitable solvent and identified as compounds **9d** and **10d**.

Cyclization of Compounds 6-8 in Sodium Ethoxide Solution.

The appropriate 3-amino-3-[(aryl or benzylaminocarbonyl)-amino]-2-propenenitrile **6-8** (2.5 mmoles) was added with stirring to a solution of sodium ethoxide (2.5 mmoles) obtained from metallic sodium (57.5 mg) in anhydrous ethanol (10 ml). The resulting solution was stirred at room temperature for 5 hours. The formed precipitate was filtered off, washed with water and recrystallized from the appropriate solvent to give the 6-amino-1,2-dihydro-2-oxopyrimidine derivatives **12-14**.

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