Stereochemical Studies. Part 103.[1] Saturated Heterocycles Part 107.[1] Preparation of 3-Mono- and 2,3-Di-substituted Pyrimidin-4(3*H*)-ones in Retro-Diels–Alder Reactions. The Correct 1,2-Disubstituted Structure of the Compounds previously described as 2,3-Disubstituted Derivatives

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The orthoformate cyclization of carboxamides (**4**) obtained from 3-*exo*-aminobicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylic acid (**1**) yielded intermediate 8,9,10-trinorbornene-fused pyrimidinones (**5**) and hence 3-substituted pyrimidin-4(3 H)-ones (**6**) through the splitting off of cyclopentadiene. Analogously, the reaction of carboxamides (**4**) with orthoacetate or orthopropionate led to the formation of 2,3-disubstituted pyrimidin-4(3*H*)-ones (**8**). A comparative i.r. and n.m.r. study of compounds (**8**) and of the previously described derivatives (**9**) gave unambiguous evidence for the structure of the new compounds. It was also established unequivocally that the products obtained from propiolate with amidines are not the previously assumed 2,3-disubstituted 4(3*H*)-ones (**8**), but are in fact the 1,2-disubstituted pyrimidin-4(1*H*)-ones (**9**).

Relatively few cycloreversion methods are suitable for the synthesis of heterocycles on a preparative scale under mild conditions.[2] In most of these methods the target molecules are obtained by vacuum pyrolysis of an adduct which contains the preformed heterocycle.

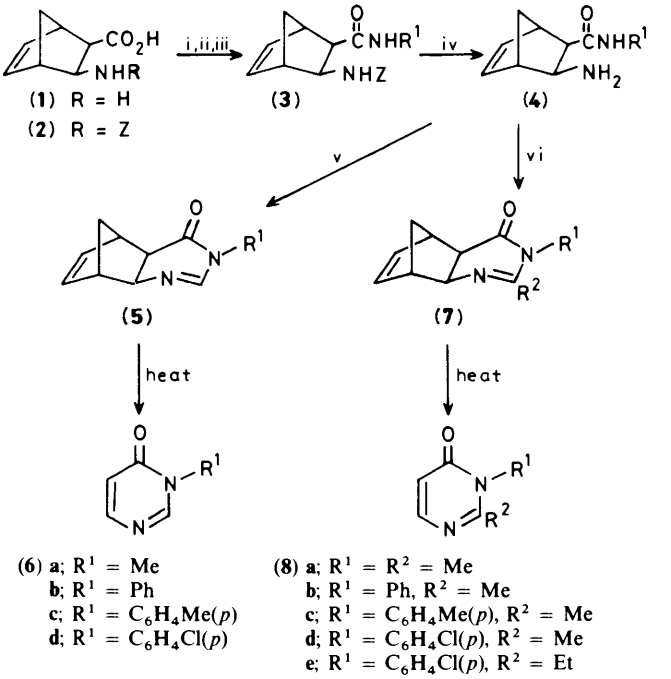
In the synthesis of 6*H*-1,3-oxazin-6-ones,[3a,b] 3-substituted thiouracils,[3c] and 2-substituted pyrimidin-4-ones,[3d] we have observed that heteromonocycles which are difficult to obtain by other means can easily be synthesized in one or more steps from di*exo*- and di*endo*-norbornene β-amino acids or from norbornene-fused azetidinone. In our process the condensed 1,3-heterocycles containing one fewer double bond are built up on cyclopentadiene, which is split off in the last step by heating the compound to its m.p., or even at lower temperature by boiling it in a solvent.

Continuing this research, we now report the retrodiene synthesis of 3-mono- and 2,3-di-substituted pyrimidin-4(3*H*)-ones from the di*exo*-trinorbornene β-amino acid (**1**) and, on the basis of evidence obtained in the course of the present synthetic and spectroscopic studies, we correct the proposed structures of a series of disubstituted compounds described previously.[4a,c]

Results and Discussion

The amino group of 3-*exo*-aminobicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylic acid [3b] (**1**) was protected by benzyloxycarbonylation; then, from reaction of the product (**2**) with isobutyl chloroformate, a mixed anhydride was prepared which on aminolysis gave carboxamides (**3**) (Scheme 1). After removal of the protecting group with hydrogen bromide in glacial acetic acid, the 3-*exo*-aminobicyclo[2.2.1]hept-5-ene-2-*exo*-carboxamides (**4b—d**) were cyclized with triethyl orthoformate to 3-aryl-*r*-4a,*c*-5,*c*-8,*c*-8a-tetrahydro-5,8-methano-quinazolin-4(3*H*)-ones (**5**), which under the applied reaction conditions underwent decomposition by splitting off cyclopentadiene and furnished 3-substituted pryimidin-4-(3*H*)-ones (**6**) in 54—60% yield calculated from compound (**4**) consumed.

By cyclization with triethyl orthoacetate or triethyl orthopropionate, through compound (**7**) the 2,3-disubstituted pyrimidin-4(3*H*)-ones (**8**) were formed in an analogous process (yield 42—52%).



Scheme 1. *Reagents:* i, $PhCH_2OC(O)Cl$; ii, $Me_2CHCH_2OC(O)Cl$; iii, R^1NH_2; iv, HBr–AcOH; v, $HC(OEt)_3$; vi, $R^2C(OEt)_3$. Z = $PhCH_2OC(O)$-

The *N*-methylcarboxamide (**4a**) was obtained from the ethyl ester of the amino acid (**1**) with methylamine, and was cyclized in a similar manner as for compounds (**4b—d**).

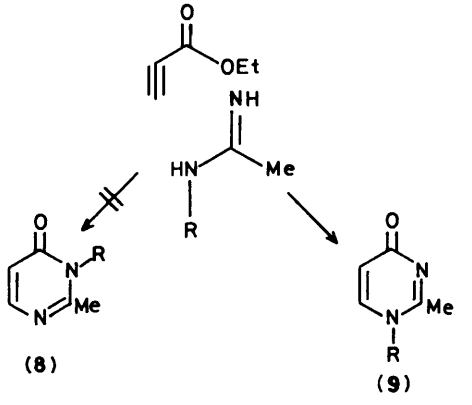
The importance of the present method is that it provides an unambiguous synthetic pathway for 3-substituted [5] (**6**) and 2,3-disubstituted [5a,d] (**8**) pyrimidin-4(3*H*)-ones, while our results demonstrated that the general method [4] described for the preparation of compounds (**8a—e**) does not give the previously reported products.

3-Alkylpyrimidin-4(3*H*)-ones (**6**) have previously been prepared by the alkylation of pyrimidin-4(3*H*)-one with methyl,

ethyl, or isopropyl iodide.[5a,d] Of the 3-arylpyrimidin-4(3*H*)-ones, only the phenyl derivative (**6b**) was known; this was synthesized from azetidinone by imidate ring transformation.[5e] The few known 2,3-disubstituted (2,3-diethyl, 2,3-dimethyl (**8a**), 2-methyl-3-ethyl, *etc.*) pyrimidin-4(3*H*)-ones (**8**) were also obtained by the alkylation of pyrimidin-4(3*H*)-one or 2-substituted pyrimidin-4(3*H*)-ones.

From 1981—1983, Indian authors reported the synthesis of numerous 2,3-disubstituted (dialkyl, diaryl, alkyl–aryl) pyrimidin-4(3*H*)-ones from reaction of ethyl propiolate with amidines,[4] and they examined the structures of the compounds by ^{1}H n.m.r. spectroscopy at 60 MHz. However, the m.p.s of these products, having the presumed structures (**8b—d**), but which were in fact compounds (**9b—d**), were 40—90 °C higher than those of the compounds we obtained by cycloreversion in an unambiguous way; furthermore, the ^{1}H (250 MHz) and ^{13}C n.m.r. investigations also supported the correctness of the structures of our compounds. The m.p.s (°C) of our compounds were as follows: 118—120 (**8b**) (lit.,[4a] 210—211); 137—139 (**8c**) (lit.,[4c] 198); and 135—136 (**8d**) (lit.,[4d] 180).

To find the reasons for this discrepancy, we reproduced the literature synthesis[4a,c] of the postulated compounds (**8b—d**) (Scheme 2). The m.p.s (uncorrected) of the compounds (**9b—d**)



(*b*) R = Ph; (*c*) R = $C_6H_4Me(p)$; (*d*) R = $C_6H_4Cl(p)$

Scheme 2.

obtained from ethylpropiolate with *N*-arylacetamidines[6] differed only slightly (6—18 °C) from the literature values.[4a,c] A comparative spectroscopic study of the compounds obtained in the retro-Diels–Alder reactions and those synthesized from amidines indicated that the literature compounds[4a,c] were not the suggested 2,3-disubstituted derivatives (**8**), but were in fact 1,2-disubstituted pyrimidin-4(1*H*)-ones (**9**) having a substituent in position 1 instead of the assumed position 3.

By systematic study[7a] we showed previously that in the i.r. spectra of *N*-acylimino compounds (>C=N–CO–) the amide-I bands appeared at considerably lower frequencies than those of the analogous α,β-unsaturated amides substituted on the amide nitrogen (*e.g.*, –N=C–N–CO–, –CO–N–CO–, =N–N–C=O, *etc.*) This finding was applied successfully in the structure elucidation of, for example, isomeric triazolones,[7b] pyrimidines,[7c] thiohydantoins,[7d,e] and pyrimidopyridazines,[7f] its validity being verified for a great variety of compounds with known structures. The difference in frequencies can be explained by the change occurring in the mesomeric structure of the amides >N–C=Ö ⟷ N̈=C–Ö:$^-$ [7a] The importance of the dipolar canonical form is higher in the acylimino derivatives, and therefore both the bond order and hence the frequency of the carbonyl group decrease. In the compounds having an unsaturated substituent on the nitrogen atom, the $-I$ effect of the substituent hinders the electron flux from the nitrogen towards the oxygen atom (the basicity of the nitrogen is reduced), with a resulting decrease in the bond order of the carbonyl group.

The relatively high amide-I frequencies (1 674—1 690 cm^{-1}, Table 1) of our compounds (**6a—d**) and (**8a—d**) indicated that these are not acylimino derivatives of type (**9**). Since the n.m.r. data (Tables 1 and 2) unambiguously point to the pyrimidone structure, and the different m.p.s and the published i.r. and n.m.r. data precluded identity with the compounds prepared by the Indian authors, we concluded that the proposed structures[4a,c] were erroneous, and that in fact the 1-substituted acylimino analogues of type (**9**) had been synthesized instead of compounds (**8**). The amide-I frequencies of the compounds (**9b—d**) we obtained using the literature procedure (the m.p., i.r., and ^{1}H n.m.r. data of which were identical with those given in the literature) are much lower (1 651—1 658 cm^{-1}) than those of the compounds (**8b—d**) prepared by cycloreversion.

Our assumptions are supported by the ^{1}H and ^{13}C n.m.r. data (Tables 1 and 2). For compounds (**9b—d**) the chemical shifts of 5-H and 6-H are markedly lower (δ_H 6.18—6.20 and 7.26—7.35) than those in the structural isomers (**6**) and (**8**) (6.34—6.55 and 7.44—7.94). The *ca.* 0.25 and 0.4 p.p.m. downfield shifts in the latter are attributed to the fact that 5-H and 6-H in compounds (**6**) and (**8**) are 'inner' protons of a conjugated chain.[8a] Owing to the lower electron density around the C-5,C-6 double bond,[8b] the vicinal proton–proton coupling constant $^3J(5,6)$ is smaller (*ca.* 6—7 Hz) than that (7.6 Hz) in the analogues (**9**).

In accord with the higher electron density around the C-5,C-6 double bond,[8c] upfield shifts (4.5 and 9.0 p.p.m.) were observed for the C-5 and C-6 signals in the ^{13}C n.m.r. spectra of compounds (**9**) as compared with those of compounds (**6**) and (**8**).

The increased contribution of the dipolar mesomeric structure, and hence of the lower electron density around the carbonyl carbon atom, is manifested by a considerable downfield shift of the carbonyl signal in the ^{13}C n.m.r. spectra of compounds (**9**) as compared with those of the analogous pyrimidinones (**6**) and (**8**) (the mean shifts for the two types are δ_C 169.5 and 161.4 p.p.m., respectively).

All these results indicate that ethyl propiolate does not react in the manner suggested by Gupta *et al.*; instead, the aryl-substituted amino group of the acetamidine undergoes addition at the acetylenic bond and the intermediates lead to the heteromonocycles (**9**) ruled out by the Indian authors.[4a–d]

In view of the above data, our method is the first generally applicable synthesis for the 2,3-disubstituted pyrimidin-4-ones (**8**).

It should be noted that the 1,2-disubstituted compounds (**9**) previously thought (erroneously) to be the 2,3-disubstituted derivatives are not otherwise known in the literature.

Besides the spectroscopic data, the structures of our compounds (**8a—d**) are supported by the clear-cut synthetic route. Furthermore, the m.p. of compound (**8a**) was found to be identical with the m.p. reported for the derivative obtained by methylation.[5a,d]

Experimental

I.r. spectra were run in KBr discs on a Bruker IFS-113v FT spectrometer equipped with an Aspect 2000 computer. ^{1}H and ^{13}C n.m.r. spectra were recorded at room temperature in $CDCl_3$ solution in 5 mm tubes, on Bruker WM-250 and WP-80-SY FT spectrometers controlled by an Aspect 2000 computer, at

Table 1. Characteristic i.r. frequencies[a] and ^{1}H n.m.r. data[b] for compounds (**6a—d**), (**8a—e**), and (**9b—d**)

		Chemical shifts δ_H				
Compound	Amide-I bands	2-H/R^2 s (1 H/3 H)[c]	5-H d (1 H)	6-H d (1 H)	Signals of substituents R^1 (**8a—e**) or R (**9b—d**)	^3J(5,6) (Hz)
(**6a**)	1 678	8.14	6.46	7.89	Me 3.55s (3 H)	6.6
(**6b**)	1 684	8.15	6.55	7.92	ArH-2′,6′ 7.35; ArH-3′—5′ ~7.5m (3 H)	6.7
(**6c**)	1 684	8.16	6.54[d]	7.92	Me 2.42s (3 H); ArH-2′,6′ 7.32;[e] ArH-3′,5′ 7.24[e]	6.7
(**6d**)	1 684	8.13	6.55[d]	7.94	ArH-2′,6′ 7.51;[e] ArH-3′,5′ 7.32[e]	6.6
(**8a**)	1 674	2.55	6.34	7.74	Me 3.54s (3 H)	6.6
(**8b**)	1 680	2.18	6.45	7.86	ArH-2′,6′ 7.21m (2 H); ArH-3′—5′ ~7.55m (3 H)	6.8
(**8c**)	1 688	2.17	6.42	7.84	Me 2.42s (3 H); ArH-2′,6′ 7.33,[e] ArH-3′,5′ 7.08[e]	6.9
(**8d**)	1 686	2.19	6.43	7.85	ArH-2′,6′ 7.52;[e] ArH-3′,5′ 7.17[e]	6.8
(**8e**)	1 690	1.17[f]	6.43	7.92	ArH-2′,6′ 7.52;[e] ArH-3′,5′ 7.14[e]	6.7
(**9b**)	1 653	2.21	6.18	~7.35[g]	ArH-2′,6′ ~7.35m (3 H);[g] ArH-3′,5′ ~7.6m (3 H)	7.5
(**9c**)	1 651	2.21	6.20	7.26	Me 2.45s (3 H); ArH-2′,6′ 7.18;[e] ArH-3′,5′ 7.36[e]	7.6
(**9d**)	1 672,[h] 1 643[h]	2.21	6.19	7.26	ArH-2′,6′ ~7.33m (2 H);[e] ArH-3′,5′ ~7.55m (2 H)[e]	7.7

[a] KBr disc, cm^{-1}. [b] In $CDCl_3$, $\delta(SiMe_4)$ 0 p.p.m. Chemical shifts in p.p.m., coupling constants in Hz at 250 MHz. [c] 1 H (**6a—d**) or 3 H (**8a—d**; **9b—d**). [d] dd due to 5-H,6-H and 2-H,5-H interactions, ^3J(2,5) 0.8 Hz. [e] AA′BB′ type m-pair, J(A,B) ~8.5 Hz. [f] Ethyl group: Me t (^3J 7.5 Hz); CH_2 2.36 q (2 H). [g] Overlapping signals. [h] Split bands, probably due to Fermi resonance with the first overtone of the strong band at 830 cm^{-1} (mean frequency 1 685 cm^{-1}).

Table 2. ^{13}C N.m.r. data on compounds (**6a—d**), (**8a—e**), and (**9b—d**)[a]

	Chemical shifts δ_C/p.p.m.									
Compound	C-2	C=O(4)	C-5	C-6	2-Me[b]	Me (R^1)	C-1′[c]	C-2′,6′[c]	C-3′,5′[c]	C-4′[c]
(**6a**)	153.5[d]	161.4	115.7	151.6[d]		34.1				
(**6b**)	153.1[d]	160.4	116.6	151.0[d]			137.1	126.7	129.6	129.4
(**6c**)	153.0[d]	160.6	116.7	151.1[d]		21.1	134.5	126.4	130.3	139.7
(**6d**)	153.1[d]	160.0	116.5	150.4[d]			135.4[e]	127.9	129.7	135.4[e]
(**8a**)	159.9	162.1	112.7	152.0	23.0	30.8				
(**8b**)	159.6	161.6	113.3	152.2	23.5		137.1	127.1	129.6	129.0
(**8c**)	160.3	162.2	113.7	152.5	23.9	21.1	134.8	127.2	130.7	139.5
(**8d**)	159.7	161.9	113.8	152.7	23.9		135.7[d]	129.1	130.4	135.9[d]
(**8e**)	161.1[d]	162.5[d]	112.7	152.0	10.1[f]		134.4[d]	128.7	129.4	134.8[d]
(**9b**)	159.3	169.6	110.0	142.7	22.7		140.5	126.1	130.0	129.6
(**9c**)	159.4	169.5	109.8	142.9	22.5	20.5[g]	137.8	125.7	130.3	139.7
(**9d**)	159.3	169.5	110.4	142.7	22.9		139.1	127.9	130.3	136.0

[a] In $CDCl_3$ at 20.15 MHz. [b] R^2 For compounds (**8a—e**). [c] *N*-Aryl group in pos. 3 [R^1 for (**6a—d**) and (**8a—e**)] or at C-1 [R for (**9b—d**)]. [d] Reversed assignment may also be possible. [e] Two overlapping lines. [f] Ethyl group Me; CH_2 28.3 p.p.m. [g] At pos. 1 (R).

250.13 (^{1}H), and 20.14 (^{13}C) MHz, respectively, using the deuterium signal of the solvent as lock and $SiMe_4$ as internal standard. The most important measurement parameters were as follows: sweep width 5 kHz, pulse width 1 and 3.5 μs (*ca.* 20° and *ca.* 30° flip angle), acquisition time 1.64 s, number of scans: 16 and 2^9—2^{15}, computer memory 16 K. Complete proton-noise decoupling (*ca.* 1.5 W) for signal-to-noise enhancement were used (line width 0.7 and 1.0 Hz).

Preparation of 3-exo-*Benzyloxycarbonylaminobicyclo*[2.2.1]-*hept*-5-*ene*-2-exo-*carboxylic acid* (**2**).—To a solution of 3-*exo*-aminobicyclo[2.2.1]hept-5-ene-2-*exo*-carboxylic acid[3b] (**1**) (6.1 g, 0.04 mol) and sodium hydroxide (1.6 g, 0.04 mol) in water (20 ml) at 0 °C were added dropwise benzyl chloroformate (7.5 g, 0.044 mol) and aqueous (20 ml) sodium hydroxide (1.6 g, 0.04 mol) simultaneously during 30 min, the solution being maintained alkaline. The mixture was stirred for an additional 1 h under ice-cooling, and then for 4 h at room temperature. The excess of the acid chloride was removed by extraction with ether (4 × 50 ml), the aqueous phase was cooled to 0 °C, and the pH was adjusted to 2 with 20% hydrochloric acid. The solid which precipitated out was filtered off and washed with water (10.8 g, 93%), m.p. 93—99 °C. After crystallization from ethanol, the *title product* had m.p. 104—105 °C (Found: C, 66.7; H, 6.05; N, 5.0. $C_{16}H_{17}NO_4$ requires C, 66.89; H, 5.96; N, 4.87%).

Preparation of 3-exo-*Benzyloxycarbonylaminobicyclo*[2.2.1]-*hept*-5-*ene*-2-exo-*carboxamides* (**3b—d**).—To a stirred solution of acid (**2**) (5.70 g, 0.02 mol) in dry tetrahydrofuran (THF) (70 ml) at −10 °C were added dropwise triethylamine (2.0 g, 0.02 mol) and then isobutyl chloroformate (2.73 g, 0.02 mol). This was followed by dropwise addition of a solution of the appropriate amine (0.02 mol) [aniline (1.95 g), *p*-toluidine (2.14 g), or *p*-chloroaniline (2.55 g)] dissolved in dry THF (20 ml), after which the mixture was stirred for 5 h at −10 °C, kept overnight at room temperature, and then evaporated to dryness. The residue was washed with water and the product was crystallized from ethanol. Data on the compounds prepared (**3b—d**) are shown in Table 3.

Preparation of Ethyl 3-exo-*Aminobicyclo*[2.2.1]*hept*-5-*ene*-2-exo-*carboxylate*.—To stirred, dry ethanol (90 ml) cooled to −10 °C was added dropwise thionyl chloride (8 ml), and amino acid (**1**) (15.3 g, 0.1 mol) was then added in small portions. The

Table 3. Physical and analytical data on compounds (**3b—d**) and (**4a—d**)

Compound (Formula)	M.p. (°C)	Yield (%)	Found (%) (Required) C	H	N
(**3b**) ($C_{22}H_{22}N_2O_3$)	227—229	74	73.1 (72.91)	6.0 (6.12)	7.75 (7.73)
(**3c**) ($C_{23}H_{24}N_2O_3$)	195—196	86	73.3 (73.38)	6.5 (6.43)	7.2 (7.44)
(**3d**) ($C_{22}H_{21}ClN_2O_3$)	198—200	75	66.7 (66.58)	5.4 (5.33)	6.9 (7.06)
(**4a**) ($C_9H_{14}N_2O$)	102—104[a]	82	65.1 (65.03)	8.4 (8.49)	16.9 (16.85)
(**4b**) ($C_{14}H_{16}N_2O$)	163—165[b]	64	73.5 (73.66)	7.1 (7.06)	12.1 (12.27)
(**4c**) ($C_{15}H_{18}N_2O$)	146—148[b]	58	73.4 (74.35)	7.5 (7.49)	11.5 (11.56)
(**4d**) ($C_{14}H_{15}ClN_2O$)	162—163[b]	65	63.9 (64.00)	5.75 (5.75)	10.8 (10.66)

[a] B.p./520 Pa. [b] M.p. of HBr salt (decomp.): (**4b**) 266—268, (**4c**) 245—248, and (**4d**) 258—260.

mixture was subsequently stirred for 30 min at 0 °C, kept at room temperature for 3 h, refluxed for 1 h, and then evaporated to dryness. The solid residue was crystallized from ethanol, to afford a product with m.p. 142—144 °C.

To a solution of the above hydrochloride salt (2.18 g, 0.01 mol) in acetone (20 ml) was added triethylamine (1.0 g, 0.01 mol). The mixture was cooled to 0 °C and the triethylammonium hydrochloride was removed by filtration. After evaporation of the solvent, the residue was distilled. Colourless oil (1.0 g, 55%), b.p. 99—100 °C/530 Pa.

Preparation of 3-exo-*Amino*-N-*methylbicyclo*[2.2.1]*hept*-5-*ene*-2-exo-*carboxamide* (**4a**).—A mixture of the above amino acid ester (3.6 g, 0.02 mol) and a 25% methylamine–methanol solution (30 ml) was kept for 6 days at room temperature. After removal of the solvent, the oily residue was transferred to a silica gel column and eluted first with benzene and then with ethyl acetate. The crystalline product (1.46 g, 44%), m.p. 99—103 °C, obtained from the latter eluate by evaporation was crystallized from benzene–light petroleum (1:1), and the *title product* had m.p. 104—106 °C (Found: C, 65.2; H, 8.6; N, 16.9. $C_9H_{14}N_2O$ requires C, 65.03; H, 8.49; N, 16.85%).

Preparation of 3-exo-*Amino*-N-*arylbicyclo*[2.2.1]*hept*-5-*ene*-2-exo-*carboxamides* (**4b—d**).—The appropriate carboxamide (0.02 mol) [(**3b**) (7.23 g), (**3c**) (7.52 g), (**3d**) (7.93 g] was dissolved in portions in 25% hydrogen bromide–glacial acetic acid (35 ml). After the addition of dry ether (50 ml), the mixture was left for 1 h at room temperature, and the deposited solid was separated.

To the product obtained were added water (50 ml) and chloroform (30 ml). The stirred mixture was made alkaline with aqueous sodium carbonate (10%), added portionwise, and was extracted with chloroform (3 × 20 ml). After being dried (Na_2SO_4) the chloroform was evaporated off and the product was crystallized from an ethanol–ether (1:1) mixture. Data on compounds (**4b—d**) are shown in Table 3.

Preparation of 3-*Substituted* (**6a—d**) *and* 2,3-*Disubstituted Pyrimidin*-4(3H)-*ones* (**8a—e**).—A mixture of the appropriate carboxamide (0.01 mol) [(**4a**) (1.66 g), (**4b**) (2.28 g), (**4c**) (2.42 g), or (**4d**) (2.62 g)] and triethylorthoformate (4.45 g, 0.03 mol), orthoacetate (4.87 g), or orthopropionate (5.29 g) was refluxed for the time given in Table 2. The mixture was evaporated and

Table 4. Physical and analytical data on compounds (**6a—d**) and (**8a—e**)

Compound (Formula)	M.p. (°C)	Refluxing time (h)	Yield (%)	Found (%) (Required) C	H	N
(**6a**) ($C_5H_6N_2O$)	125—127[a]	15	62	54.6 (54.54)	5.6 (5.49)	25.6 (25.44)
(**6b**) ($C_{10}H_8N_2O$)	147—149[b]	6	57	69.8 (69.76)	4.8 (4.68)	16.4 (16.27)
(**6c**) ($C_{11}H_{10}N_2O$)	152—153	6	54	70.8 (70.95)	5.35 (5.41)	15.1 (15.04)
(**6d**) ($C_{10}H_7ClN_2O$)	131—133	13	60	58.3 (58.13)	3.5 (3.41)	13.4 (13.56)
(**8a**) ($C_6H_8N_2O$)	65—66[c]	15	48	58.2 (58.05)	6.6 (6.50)	22.6 (22.57)
(**8b**) ($C_{11}H_{10}N_2O$)	118—120	12	46	70.8 (70.95)	5.3 (5.41)	15.1 (15.04)
(**8c**) ($C_{12}H_{12}N_2O$)	137—139	10	52	71.8 (71.98)	5.9 (6.04)	14.15 (13.99)
(**8d**) ($C_{11}H_9ClN_2O$)	135—136	10	50	60.0 (59.88)	4.2 (4.11)	12.7 (12.70)
(**8e**) ($C_{12}H_{11}ClN_2O$)	112—114	8	42	61.25 (61.42)	4.5 (4.72)	11.9 (11.94)

[a] Lit.,[5a] m.p. 122 °C,[5c] 123—124 °C. [b] Lit.,[5e] m.p. 144—145 °C. [c] Lit.,[5a] m.p. 63—65 °C,[5d] 65 °C.

the residue was transferred to a silical gel column and eluted first with benzene and then with ethyl acetate. The latter eluate was evaporated and the residue was crystallized from an ethyl acetate–ether (1:1) mixture. Data on the obtained compounds (**6a—d**) and (**8a—e**) are shown in Table 4.

References

1 Part 102/106: G. Stájer, A. E. Szabó, G. Bernáth, and P. Sohár, submitted for publication in *Pharmazie*.

2 (*a*) R. Huisgen, M. Seidel, G. Wallbillich, and H. Knupfer, *Tetrahedron*, 1962, **17**, 3; (*b*) M. C. Lasne and J. L. Ripoll, *Synthesis*, 1985, 121.

3 (*a*) G. Stájer, A. E. Szabó, F. Fülöp, and G. Bernáth, *Synthesis*, 1984, 345; (*b*) G. Stájer, L. Mód, A. E. Szabó, F. Fülöp, G. Bernáth, and P. Sohár, *Tetrahedron*, 1984, **40**, 2385; (*c*) G. Stájer, A. E. Szabó, J. Pintye, G. Bernáth, and P. Sohár, *J. Chem. Soc., Perkin Trans. 1*, 1985, 2483; (*d*) G. Stájer, A. E. Szabó, G. Bernáth, and P. Sohár, *Synthesis*, in the press.

4 K. A. Gupta, A. K. Saxena, and P. C. Jain, (*a*) *Synthesis*, 1981, 905; (*b*) *Indian J. Chem., Sect. B*, 1982, **21**, 228; (*c*) K. A. Gupta, A. K. Saxena, P. C. Jain, R. C. Srimal, K. Kar, and N. Anand, *ibid.*, 1983, **22**, 384; (*d*) K. A. Gupta, A. K. Saxena, P. C. Jain, P. R. Dua, C. R. Prasad, and N. Anand, *ibid.*, p. 789.

5 (*a*) J. P. Jonak, G. C. Hopkins, H. J. Minnemeyer, and H. Trieckelmann, *J. Org. Chem.*, 1970, **35**, 2512; (*b*) O. Kasende and T. Zeegers-Huyskens, *J. Phys. Chem.*, 1984, **88**, 2636; (*c*) D. J. Brown, E. Hoeger, and S. F. Mason, *J. Chem. Soc.*, 1955, 211; (*d*) F. H. Curd and D. N. Richardson, *ibid.*, p. 1853; (*e*) D. Bormann, *Chem. Ber.*, 1974, **107**, 270.

6 P. Oxley, M. W. Partridge, and W. F. Short, *J. Chem. Soc.*, 1947, 1110.

7 (*a*) P. Sohár, *Magy. Kém. Foly.*, 1968, **74**, 298 (*Chem. Abstr.*, 1968, **69**, 111675t); (*b*) S. Holly and P. Sohár, 'Infrared Spectroscopy,' Müszaki Kiadó, Budapest, 1968, p. 201 (in Hungarian); (*c*) J. Reiter, P. Sohár, J. Lipták, and L. Toldy, *Tetrahedron Lett.*, 1970, 1417; (*d*) K. Lempert, J. Nyitrai, P. Sohár, and K. Zauer, *ibid.*, 1964, 2679; (*e*) K. Lempert, J. Nyitrai, and P. Sohár, *ibid.*, 1965, 1795; (*f*) P. Mátyus, E. Kasztreiner, G. Szilágyi, M. Sóti, and P. Sohár, *Heterocycles*, 1983, **20**, 2225.

8 P. Sohár, 'Nuclear Magnetic Resonance Spectroscopy,' CRC Press, Boca Raton, Florida, 1984, (*a*) vol. 2, p. 54; (*b*) vol. 1, p. 61; (*c*) vol. 2, pp. 150—153.

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