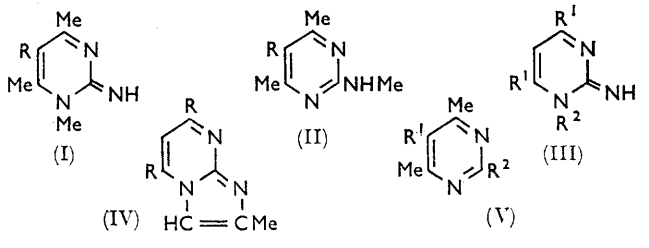
The Dimroth Rearrangement. Part IX.[1] The Formation and Isomerisations of Propynyl (and Related)-iminopyrimidines

By **D. J. Brown** and **B. T. England**, Department of Medical Chemistry, John Curtin School of Medical Research, Australian National University, Canberra

The insertion of a 5-allyl, a prop-2-ynyl, or a prop-1-ynyl substituent into 1,2-dihydro-2-imino-1,4,6-trimethylpyrimidine progressively decreases the basic strength and increases the rate of Dimroth rearrangement into the corresponding 4,6-dimethyl-2-methylaminopyrimidine; similar effects follow replacement of the 1-methyl group in the same imine by such substituents. Condensation of 3-(prop-2-ynyl)acetylacetone with guanidine gives the expected 2-amino-4,6-dimethyl-5-(prop-2-ynyl)pyrimidine, but also the isomeric 5-(prop-1-ynyl)- and 5-allenyl-pyrimidines; other prop-2-ynylpyrimidines also suffer such prototropic changes which are unprecedented in the series. An alkaline solution of 1,2-dihydro-2-imino-4,6-dimethyl 1-(prop-2-ynyl)pyrimidine undergoes two parallel isomerisations at comparable rates; one is a normal Dimroth rearrangement, and the other a cyclisation to 2,4,6-trimethyl-1,3a,7-triazaindene. Evidence for some of the structures was obtained from ^{1}H n.m.r. and ultraviolet spectra, which were also used to measure rates of rearrangement.

ALTHOUGH the Dimroth rearrangement [*e.g.*,(I) ⟶ (II)] may be accelerated by a variety of electron-withdrawing substituents,[1,2] unsaturated aliphatic groups have been little used for this purpose. We now report the preparation of 1-and 5-(prop-2-ynyl), and 5-allyl derivatives of 1,2-dihydro-2-imino-4,6-dimethylpyrimidines; the alkali-induced isomerisation of some of the prop-2-ynylpyrimidine intermediates into their corresponding allenyl and prop-1-ynyl iosomers (new reactions in this series); the rates for Dimroth rearrangement of the imines so derived; and some observations on the previously noted[3] cyclisation of 1,2-dihydro- 2-imino-1-(prop-2-ynyl)pyrimidines (III; R = $CH_2C{:}CH$) into 2-methyltriazaindenes (IV).



Preparations.—The imines (I) were made from appropriate derivatives of acetylacetone, *e.g.*, 3-allylacetylacetone was condensed with guanidine carbonate to give 5-allyl-2-amino-4,6-dimethylpyrimidine (V; $R^1 = CH_2{\cdot}CH{:}CH_2$, $R^2 = NH_2$) which was methylated to give the imine (I; R = $CH_2CH{:}CH_2$). During the analogous formation of 2-amino-4,6-dimethyl-5-(prop-2-ynyl)pyrimidine (V; $R^1 = CH_2{\cdot}C{:}CH$, $R^2 = NH_2$), two isomeric products were also formed: the prop-1-ynyl derivative (V; $R^1 = C{:}CMe$, $R^2 = NH_2$), in which the triple bond had moved into conjugation with the pyrimidine ring, and an allenylpyrimidine (V; $R^1 = CH{:}C{:}CH_2$, $R^2 = NH_2$). The three isomers were identified by their characteristic ^{1}H n.m.r. spectra (Table 1). The first two were converted into the corresponding imines (I), but there was too little of the allene for this. For comparison, the n-propylimine (I; R = Pr) was made by a similar route.

Three typical imines (I; R = Pr, $CH_2{\cdot}CH{:}CH_2$, or $C{:}CMe$) were rearranged preparatively by warming the hydrohalides for 10 minutes in 2N-alkali. Each of the resulting methylamino-derivatives (II) was precipitated (>80%). These and the potential products from other imines were made unambiguously, also from acetylacetone derivatives. Condensation with urea under acidic conditions gave the hydroxypyrimidines (V; R^1 = Pr, $CH_2{\cdot}CH{:}CH_2$, or $CH_2{\cdot}C{:}CH$, R^2 = OH). Treatment of each with phosphoryl chloride gave the corresponding 2-chloropyrimidine which when treated with methylamine gave the amine (II; R = Pr, $CH_2{\cdot}CH{:}CH_2$,

[1] Part VIII, D. J. Brown and M. N. Paddon-Row, *J. Chem. Soc.* (*C*), 1967, 903.
[2] D. J. Brown and J. S. Harper, *J. Chem. Soc.*, 1963, 1276; 1965, 5542; D. J. Brown and M. N. Paddon-Row, *J. Chem. Soc.* (*C*), 1966, 164.
[3] I. Iwai and T. Hiraoka, *Chem. Pharm. Bull.* (*Japan*), 1964, **12**, 813.
[4] A. T. Bottini and E. F. Böttner, *J. Org. Chem.*, 1966, **31**, 385 and 389.

or CH_2·C:CH). The last of these was accompanied by an isomer (II; R = CH:C:CH_2), separated chromatographically and identified as an allene [4] by its strong i.r. absorption at 1950 cm.$^{-1}$ and ^{1}H n.m.r. spectrum. Under less strongly basic conditions, with aqueous methylamine acetate in place of the free base, much less of the allene was formed. The prop-1-ynylpyrimidine R^1 = H, R^2 = CH_2·C:CH),[3] the acetylenic derivative cyclised in ethanolic sodium ethoxide to yield (in this case) the triazaindene (IV; R = Me), but in aqueous potassium hydroxide, the same product was mixed with the normal rearranged material (V; R^1 = H, R^2 = NH·CH_2·C:CH); both structural assignments were confirmed by ultraviolet (Table 2) and ^{1}H n.m.r. spectra.

TABLE 1

Proton magnetic resonance spectra

	Compound [a] and medium	τ-Values; J in c./sec.
1	$CDCl_3$	4- and 6-Me: 7·72s; α-CH_2: 5·83m (J = 11); γ-CH_2: 4·78m; NH: 4·1s(broad); β-CH: 4·05m; 5-H: 3·60s
2	$CDCl_3$	γ-CH: 7·80t; 4- and 6-Me: 7·68s; α-CH_2: 5·68q ($J_{NH,\alpha}$ = 6; $J_{\alpha,\gamma}$ = 3); NH: 4·4s(broad); 5-H: 3·57s
4	$CDCl_3$	γ-CH: 7·78t; α-CH_2: 5·72q ($J_{\alpha,NH}$ = 6; $J_{\alpha,\gamma}$ = 3); NH: 3·8s(broad); 5-H: 3·37t (J = 5); 4- and 6-H: 1·58d (J = 5)
5	$CDCl_3$	4- and 6-Me: 7·58s; γ-CH_2: 4·92d; NH: 4·84s(broad); α-CH: 3·80t ($J_{\alpha,\gamma}$ = 7·1)
6	CCl_4	4- and 6-Me: 7·75s; α-CH_2: 6·78m ($J_{\alpha,\beta}$ = 5); γ-CH_2: 5·0m; NH_2: 4·9s(broad); β-CH: 4·1m ($J_{\beta,\gamma\ trans}$ = 16; $J_{\beta,\gamma\ cis}$ = 12)
7	CCl_4	γ-Me: 8·95t ($J_{\beta,\gamma}$ = 7); β-CH_2: 8·35m; 4- and 6-Me: 7·73s; α-CH_2: 7·4t ($J_{\alpha,\beta}$ = 6·3)
8	$CDCl_3$	γ-Me: 7·88s; 4- and 6-Me: 7·57s; NH: 4·8s(broad)
9	$CDCl_3$	γ-CH: 7·90t; 4- and 6-Me: 7·35s; α-CH_2: 6·46d ($J_{\alpha,\gamma}$ = 3)
11	$CDCl_3$	4- and 6-Me: 7·5s; α-CH_2: 6·51m ($J_{\alpha,\beta}$ = 5); γ-CH_2: 5·0m; β-CH: 4·1m ($J_{\beta,\gamma\ trans}$ = 16; $J_{\beta,\gamma\ cis}$ = 12)
12	$CDCl_3$	γ-Me: 9·02t ($J_{\beta,\gamma}$ = 7); β-CH_2: 8·5m; 4- and 6-Me: 7·62s; α-CH_2: 7·42t ($J_{\alpha,\beta}$ = 6·5)
13	$CDCl_3$	γ-Me: 7·81s; 4- and 6-Me: 7·38s
14	$CDCl_3$	γ-CH: 7·90t; 4- and 6-Me: 7·36s; α-CH_2: 6·45d ($J_{\alpha,\gamma}$ = 3)
15	N-DCl	4-Me: 7·51s; 6-Me: 7·41s; γ-CH_2: 5·15m; β-CH: 4·08m; α-CH_2: —
16	0·1N-DCl	4-Me: 7·48s; 6-Me: 7·43s; α-CH_2: 6·55m; 1-Me: 6·25s; γ-CH_2: 4·83m; β-CH: 4·08m
17	N-DCl	4-Me: 7·46s; 6-Me: 7·27s; γ-CH: 6·94t; α-CH_2: 4·90d ($J_{\alpha,\gamma}$ = 3); 5-H: 2·91s
18	0·1N-DCl	γ-CH: 6·75t; α-CH_2: 4·90d ($J_{\alpha,\gamma}$ = 3); 5-H: 2·76m; 4- and 6-H: 1·18m
19	0·1N-DCl	γ-Me: 9·02t ($J_{\beta,\gamma}$ = 6·5); β-CH_2: 8·35m; 4-Me: 7·45s; 6-Me: 7·41s; α-CH_2: 7·30m; 1-Me: 6·27s
20	0·1N-DCl	γ-Me: 7·81s; 4-Me: 7·37s; 6-Me: 7·20s; 1-Me: 6·21s
21	0·1N-DCl	4-Me: 7·28s; 6-Me: 7·22s; α-CH_2: 6·30d ($J_{\alpha,\gamma}$ = 3); 1-Me: 6·12s; γ-CH: —
23	0·1N-DCl	4- and 6-Me: 7·38s; α-CH_2: 6·60m ($J_{\alpha,\beta}$ = 5); β-CH: 4·1m; γ-CH_2: —
24	0·1N-DCl	γ-Me: 8·98t ($J_{\beta,\gamma}$ = 7); β-CH_2: 8·4m; 4- and 6-Me: 7·37s; α-CH_2: 7·2t ($J_{\alpha,\gamma}$ = 6·3)
25	0·1N-DCl	γ-Me: 7·83s; 4- and 6-Me: 7·28s
26	0·1N-DCl	γ-CH: 7·42t; 4- and 6-Me: 7·28s; α-CH_2: 6·40d ($J_{\alpha,\gamma}$ = 3)
	$CDCl_3$	γ-CH: 7·96t; 4- and 6-Me: 7·48s; α-CH_2: 6·65d
27	$CDCl_3$	4- and 6-Me: 7·60s; *N*-Me: 6·97d (J = 5·6); γ-CH_2: 5·0d; α-CH: 4·82t ($J_{\alpha,\gamma}$ = 7·1)
28	$CDCl_3$	4- and 6-Me: 7·66s; *N*-Me: 9·8d (J = 5·6); α-CH_2: 6·72m ($J_{\alpha,\beta}$ = 5); γ-CH_2: 4·96m; NH: 4·4s(broad); β-CH: 4·1m
29	$CDCl_3$	γ-Me: 9·04t (J = 7); β-CH_2: 8·53m; 4- and 6-Me: 7·65s; α-CH_2: 7·38t (J = 6·5); *N*-Me: 7·0d (J = 5·6); NH: 4·9s(broad)
30	$CDCl_3$	γ-Me: 7·85s; 4- and 6-Me: 7·53s; *N*-Me: 6·97d (J = 5·6); NH: 4·7s(broad)
31	$CDCl_3$	γ-CH: 7·98t; 4- and 6-Me: 7·60s; *N*-Me: 6·96d (J = 5·6); α-CH_2: 6·62d ($J_{\alpha,\gamma}$ = 3); NH: 4·9s(broad)
32	$CDCl_3$	2-Me: 7·52s; 5-H: 3·1m; 3-H: 2·6m; 4- and 6-H: 1·44m
33	$CDCl_3$	2-Me: 7·53s; 4- and 6-Me: 7·46s; 5-H: 3·42s; 3-H: 2·83s
34 [b]	$CDCl_3$	4- and 6-Me: 7·71s; NH_2: 4·05s(broad); 5-H: 3·59s
35 [c]	0·1N-DCl	γ-CH: 7·78t; 6-Me: 7·48s; 2-Me: 7·25s; α-CH_2: 6·50d (J = 3)
36 [d]	Dioxan	γ-CH: 8·90t; α-CH_2: 7·24d (J = 3)

[a] Numbers as Table 2. [b] 2-Amino-4,6-dimethylpyrimidine. [c] 4-Hydroxy-2,6-dimethyl-5-(prop-2-ynyl)pyrimidine. [d] 2,4,6-Trihydroxy-5-(prop-2-ynyl)pyrimidine.

s = Singlet, d = doublet, t = triplet, q = quartet, m = multiplet.

(II; R = C:CMe) was prepared by alkaline hydrolysis and isomerisation of the chloro-compound (V; R^1 = CH_2·C:CH, R^2 = Cl) to the hydroxypyrimidine (V; R^1 = C:CMe, R^2 = OH) followed by rechlorination and aminolysis.

The 1-prop-2-ynylimine (III; R^1 = Me, R^2 = CH_2·C:CH) and its 1-allyl analogue (III; R^1 = Me, R^2 = CH_2·CH:CH_2) were made from the reaction of 2-amino-4,6-dimethylpyrimidine with prop-2-ynyl bromide and allyl iodide, respectively; analogous propylation was unsuccessful. Like its lower homologue (III; The remote possibility (cf. ref. 5) that the 2-methyltriazaindenes (IV) underwent Dimroth rearrangement to their 3-methyl isomers was excluded by comparison with salts of 2-methyl-1,3a,7-triazaindene, prepared by a known synthesis [6] rendered unambiguous by avoidance of alkaline conditions. 2-Allylamino-4,6-dimethylpyrimidine was made from its 2-chloro-analogue and allylamine.

The isomerisations of prop-2-ynyl- into allenylpyrimidines occurred under relatively mild alkaline conditions probably because the attached pyrimidine ring acted as an electron-withdrawing centre.[7] The

[5] K. T. Potts and H. R. Burton, *Proc. Chem. Soc.*, 1964, 420.
[6] N. P. Buu-Hoï, L. Petit, and N. D. Xuong, *Compt. rend.*, 1959, **248**, 1832.
[7] H. Fischer, "The Chemistry of Alkenes," ed. S. Patai, Interscience, New York, 1964, pp. 1048—1051.

TABLE 2

Ionisation and ultraviolet spectra

		pK_a [a]	λ_{max} ($m\mu$) [b]	pH [c]
Pyrimidine				
1	2-Allylamino-4,6-dimethyl [d]		298 (3·60), 237 (4·18)	8·0
	cation	5·02 ± 0·02 (310)	307 (3·76), 229 (4·20)	2·0
2	4,6-Dimethyl-2-(prop-2-ynylamino)-		292 (3·62), 233 (4·15)	7·0
	cation	4·42 ± 0·04 (310)	302 (3·79), 226 (4·17)	1·0
3	4-Hydroxy-2,6-dimethyl		253 (3·76), 227 (3·90)	6·0
	cation	3·06 ± 0·04 (280)	*260* (*3·61*), 229 (4·02)	1·0
	anion	9·77 ± 0·05 (280)	262 (3·68), 230 (3·98)	12·0
4	2-(Prop-2-ynylamino) [d]		298 (3·46), 230 (4·21)	6·0
	cation	2·90 ± 0·02 (320)	309 (3·59), 225 (4·21)	0·0
2-*Amino*-4,6-*dimethylpyrimidine*				
5	5-Allenyl [e]	—	304 (—), 256 (—)	8·0
6	5-Allyl		293 (3·64), 230 (4·14)	8·0
	cation	5·15 ± 0·03 (310)	304 (3·79), 226 (4·19)	1·0
7	5-Propyl		294 (3·65), 229 (4·12)	8·0
	cation	5·47 ± 0·03 (305)	306 (3·78), 227 (4·16)	1·0
8	5-(Prop-1-ynyl)		308 (3·63), 258 (4·31)	8·0
	cation	4·04 ± 0·03 (335)	325 (3·69), 254 (4·32)	1·0
9	5-(Prop-2-ynyl)		291 (3·62), 230 (4·14)	7·0
	cation	4·54 ± 0·01 (310)	302 (3·76), 227 (4·18)	1·0
2-*Chloro*-4,6-*dimethylpyrimidine*				
10	Unsubstituted [f]		255 (3·65), *263* (*3·49*)	2·0
	cation	−0·68 ± 0·03 (261)	261 (3·87)	−3·0
11	5-Allyl		*270* (*3·46*), 261 (3·66), 218 (3·94)	2·0
	cation	−0·46 ± 0·03 (270)	270 (3·87), 224 (3·91)	−3·0
12	5-Propyl		*271* (*3·57*), 263 (3·68), 218 (3·92)	2·0
	cation	−0·34 ± 0·04 (280)	274 (3·86), 225 (3·90)	−3·0
13	5-(Prop-1-ynyl) [g]	—	*290* (*3·47*), 253 (4·16)	2·0
14	5-(Prop-2-ynyl) [g]	—	*268* (*3·46*), 259 (3·64), 217 (3·92)	2·0
1,2-*Dihydro*-2-*iminopyrimidine* [h]				
15	1-Allyl-4,6-dimethyl		337 (3·55), 241 (4·11)	14·0
	cation	11·16 ± 0·01 (337)	298 (3·78)	8·0
16	5-Allyl-1,4,6-trimethyl		345 (3·55), 243 (4·24)	14·0
	cation	11·99 ± 0·02 (345)	305 (3·79), 227 (4·14)	9·0
17	4,6-Dimethyl-1-(prop-2-ynyl)		347 (3·58), 238 (4·13)	13·0
	cation	10·41 ± 0·01 (347)	298 (3·82), 225 (3·91)	8·0
18	1-(Prop-2-ynyl)		345 (3·43), 234 (4·15)	12·5
	cation	10·04 ± 0·02 (345)	305 (3·62), 222 (4·06)	7·0
19	1,4,6-Trimethyl-5-propyl		348 (3·58), 244 (4·23)	14·3
	cation	12·21 ± 0·04 (350)	307 (3·80), 229 (4·11)	9·0
20	1,4,6-Trimethyl-5-(prop-1-ynyl)		360 (3·54), 268 (4·40)	14·0
	cation	10·97 ± 0·05 (360)	327 (3·70), 255 (4·33)	8·0
21	1,4,6-Trimethyl-5-(prop-2-ynyl)		343 (3·52), 243 (4·22)	14·0
	cation	11·55 ± 0·05 (343)	303 (3·76), 232 (4·08)	8·0
4,6-*Dimethyl*-2-*hydroxypyrimidine*				
22	Unsubstituted		296 (3·80), <220	6·0
	cation	3·82 ± 0·02 (315)	303 (3·91), <220	1·0
	anion	10·45 ± 0·05 (305)	295 (3·75), 222 (3·93)	13·0
23	5-Allyl		302 (3·83), 220 (4·11)	7·0
	cation	3·96 ± 0·03 (314)	314 (3·93), 214 (4·11)	1·0
	anion	10·69 ± 0·02 (310)	296 (3·78), 225 (4·10)	13·0
24	5-Propyl		305 (3·84), 220 (4·07)	8·0
	cation	4·22 ± 0·01 (325)	316 (3·94), 212 (4·10)	1·0
	anion	10·84 ± 0·03 (315)	298 (3·79), 224 (4·08)	13·0
25	5-(Prop-1-ynyl)		319 (3·67), 247 (4·22)	6·0
	cation	2·72 ± 0·05 (355)	345 (3·77), 244 (4·28)	1·0
	anion	9·44 ± 0·02 (330)	306 (3·73), 255 (4·29)	12·0
26	5-(Prop-2-ynyl)		300 (3·81), 220 (4·09)	7·0
	cation	3·56 ± 0·02 (320)	311 (3·91), 212 (4·09)	1·0
	anion	10·20 ± 0·03 (310)	293 (3·76), 225 (4·11)	13·0
4,6-*Dimethyl*-2-*methylaminopyrimidine*				
27	5-Allenyl		312 (3·56), 259 (4·21)	8·0
	cation	4·90 ± 0·04 (340)	326 (3·64), 253 (4·21)	2·0
28	5-Allyl		307 (3·59), 239 (4·24)	8·0
	cation	5·36 ± 0·03 (330)	317 (3·74), 233 (4·27)	2·0
29	5-Propyl		308 (3·58), 238 (4·20)	8·0
	cation	5·63 ± 0·04 (330)	318 (3·74), 233 (4·26)	2·0
30	5-(Prop-1-ynyl)		319 (3·56), 265 (4·36)	8·0
	cation	4·13 ± 0·02 (345)	337 (3·66), 258 (4·38)	1·0
31	5-(Prop-2-ynyl)		307 (3·55), 239 (4·24)	8·0
	cation	4·92 ± 0·02 (320)	316 (3·70), 233 (4·26)	2·0

TABLE 2. (*Continued*)

		pK_a [a]	λ_{max} (mμ) [b]	pH [c]
1,3a,7-*Triazaindene* [i]				
32	2-Methyl		322 (3·59), 290 (3·46), 229 (4·21)	8·0
	cation	5·15 ± 0·03 (298)	295 (3·74), 281 (3·74), *235* (*3·73*), 219 (4·21)	3·0
33	2,4,6-Trimethyl		310 (3·64), 285 (3·67), *275* (*3·61*), 230 (4·34)	8·5
	cation	6·12 ± 0·01 (330)	*294* (*3·77*), 278 (3·88)	3·0

[a] Measured spectrometrically at 20° by methods of A. Albert and E. P. Serjeant, "Ionisation Constants of Acids and Bases," Methuen, London, 1962. [b] Inflexions in italics. [c] Buffers as D. D. Perrin, *Austral. J. Chem.*, 1963, **16**, 572. [d] Cf. 2-allylaminopyrimidine, pK_a 3·57 [D. J. Brown, B. T. England, and J. M. Lyall, *J. Chem. Soc.* (*C*), 1966, 226.] [e] Insufficient material to complete measurements. [f] Cf. 2-chloropyrimidine at pH 2·0: 251 (3·43), *256* (*3·41*). [g] Unstable as cation. [h] Where required, $[I^-]$ balanced in reference cell. [i] Cf. homologues (W. L. F. Armarego, *J. Chem. Soc.*, 1965, 2778).

subsequent (or parallel) formation of the prop-1-ynylpyrimidines was an indication of the additional stability conferred on the system by the triple bond in conjugation with the ring, a fact experimentally evident from the marked bathochromic shift in the ultraviolet spectra, and from the marked lowering of the pK_a values. In view of such isomerisations, two described analogues,[8] 4-hydroxy-2,6-dimethyl- and 2,4,6-trihydroxy-5-(prop-2-ynyl)pyrimidine, were made and examined for isomers; each was homogeneous and of the correct structure, probably owing primarily to the use of ethanol as solvent,[4] but also to the mild alkalinity used in preparing the first pyrimidine and the powerful electron-release by the three hydroxy-groups in the second.[7]

Dimroth Rearrangement Rates.—The four substituents (propyl, allyl, prop-2-ynyl, and prop-1-ynyl), attached in turn at the 5-position of the imine (I), are of comparable size but differ in their capacity to release or withdraw electrons. The latter fact is exemplified by the pK_a values of propylamine (10·7), allylamine (9·5), and prop-2-ynylamine (8·15); in the values (5·5, 5·1, 4·5, and 4·0) from Table 2 for the amines (V; R^1 = Pr, $CH_2{\cdot}CH{:}CH_2$, $CH_2{\cdot}C{:}CH$, or $C{:}CMe$, $R^2 = NH_2$); in those (5·6, 5·4, 4·9, and 4·1) for the corresponding 2-methylamino-derivatives; in both the basic (4·2, 4·0, 3·6, and 2·7) and acidic values (10·8, 10·7, 10·2, and 9·4) for the 2-hydroxy-analogues; and in the basic strengths of the imines themselves. Comparison with the $t_{\frac{1}{2}}$ values in Table 3 indicates that, within the group of imines (I), rate of rearrangement depends on the degree of electron withdrawal by each 5-substituent. The same relationship is equally pronounced when the substituents occupy the 1-position (Table 3).

TABLE 3

Rearrangement rates of iminopyrimidines [a]

	$t_{\frac{1}{2}}$ [b]	Analyt. λ (mμ)	pK_a
(I) R = Pr	178	345	12·2
$CH_2{\cdot}CH{:}CH_2$	157	346	12·0
$CH_2{\cdot}C{:}CH$	109	345	11·5
$C{:}CMe$	64	356	11·0
(III) R^1 = Me, R^2 = $CH_2{\cdot}CH{:}CH_2$	133	340	11·2
$CH_2{\cdot}C{:}CH$ ...	22 (44)	360	10·4
	25 (50)	*d*	
(III) R^1 = H, R^2 = Pr	55 [c]	355	11·0
$CH_2{\cdot}CH{:}CH_2$	33 [c]	355	10·5
$CH_2{\cdot}C{:}CH$ ...	5 (6·2)	*d*	10·0

[a] At pH 14 and 25°. [b] Time in minutes for disappearance of half imine; net values in parentheses (see text). [c] From ref. 1. [d] By ^1H n.m.r. spectroscopy.

In considering rearrangement of the imines (III; R^1 = H or Me, $R^2 = CH_2{\cdot}C{:}CH$), the observed $t_{\frac{1}{2}}$ values (5 and *ca.* 25 min.) for the first-order disappearance of the imines must be adjusted to allow for parallel cyclisation to the triazaindenes (IV; R = H or Me). The ^1H n.m.r. spectra revealed that the ratio of rearranged amine to triazaindene, and hence the ratio of their formation rates, was 4 : 1 when R = H but 1 : 1 when R = Me. The net $t_{\frac{1}{2}}$ values are therefore 6·2 and *ca.* 50 min., respectively. The fact that only triazaindenes were formed from the imines (III; $R^2 = CH_2{\cdot}C{:}CH$) in ethanolic media is simply confirmation that Dimroth rearrangements are very slow in non-aqueous media.[9]

EXPERIMENTAL

Analyses were done by Dr. J. E. Fildes and her staff and p.m.r. spectra by Mr. S. E. Brown at 60 Mc./sec. (33°). B.D.H. aluminium oxide was used for chromatographic separations.

3-*Allylacetylacetone*.—The diketone,[10] b. p. 110—115°/30 mm. (lit.,[10] 195—196°), and ammoniacal cupric acetate gave a *copper complex*, m. p. 218° (from benzene) (Found: C, 56·2; H, 6·6. $C_{16}H_{22}CuO_4$ requires C, 56·2; H, 6·5%).

3-(*Prop-2-ynyl*)*acetylacetone*.—Acetylacetone (25 g.) was added with stirring to ethanolic sodium ethoxide (sodium, 5·8 g.; ethanol, 120 ml.). After 10 min., prop-2-ynyl bromide (30 g.) was added and the mixture was stirred and heated under reflux for 20 hr. Light petroleum (150 ml.) was added to the cooled mixture and solid was removed. The filtrate was distilled until more solid began to precipitate and the dilution was repeated. Solid was again removed and fractional distillation of the filtrate gave propynylacetylacetone (57%), b. p. 108—112°/17 mm., characterised as the yellow-green *copper complex*, m. p. 178° (from benzene) (Found: C, 56·5; H, 5·5. $C_{16}H_{18}CuO_4$ requires C, 56·9; H, 5·4%).

[8] K. E. Schulte, J. Reisch, A. Mock, and K. H. Kauder, *Arch. Pharm.*, 1963, **296**, 235.
[9] D. D. Perrin and I. H. Pitman, *J. Chem. Soc.*, 1965, 7071.
[10] J. P. English, J. H. Clark, J. W. Clapp, D. Seeger, and R. H. Ebel, *J. Amer. Chem. Soc.*, 1946, **68**, 453.

2-Amino-4,6-dimethyl-5-propylpyrimidine.— 3-Propylacetylacetone [11] (4·0 g.) and guanidine carbonate (2·7 g.) were stirred and boiled under reflux for 1 hr. More guanidine carbonate (0·5 g.) was added and similar conditions were maintained for 5 hr. The cooled mixture was extracted with carbon tetrachloride (4 × 15 ml.). Concentration and refrigeration gave the *propylpyrimidine* (59%), m. p. 165—167° (from ethyl acetate) (Found: C, 65·2; H, 9·2; N, 25·3. $C_9H_{15}N_3$ requires C, 65·4; H, 9·15; N, 25·4%).

5-Allyl-2-amino-4,6-dimethylpyrimidine.—Prepared in a similar way, the *allylpyrimidine* (52%) had m. p. 133° (from ethyl acetate) (Found: C, 66·3; H, 8·1; N, 26·0. $C_9H_{13}N_3$ requires C, 66·2; H, 8·0; N, 25·75%). English *et al.*[10] gave m. p. 131—134° for their unanalysed product.

2-Amino-4,6-dimethyl-5-(prop-1- and -2-ynyl)pyrimidine.—3-(Prop-2-ynyl)acetylacetone and guanidine carbonate were treated as already described. One half of the crude product gave the *prop-1-ynylpyrimidine* (29%), m. p. 214° (from ethanol) (Found: C, 66·8; H, 7·1; N, 26·3. $C_9H_{11}N_3$ requires C, 67·05; H, 6·9; N, 26·1%). The other half and the residue from evaporation of the recrystallisation liquors were adsorbed on an alumina column in light petroleum. Elution with ether gave, as a middle fraction, the *prop-2-ynylpyrimidine* (15%), m. p. 153° (Found: C, 66·3; H, 7·0; N, 26·1. $C_9H_{11}N_3$ requires C, 67·05; H, 6·9; N, 26·1%). The other half and the residue from evaporation of the recrystallisation liquors were adsorbed on an alumina column in light petroleum. Elution with ether gave, as a middle fraction, the *prop-2-ynylpyrimidine* (15%), m. p. 153° (Found: C, 66·3; H, 7·0; N, 26·1. $C_9H_{11}N_3$ requires C, 67·05; H, 6·9; N, 26·1%).

5-Allenyl-2-amino-4,6-dimethylpyrimidine.—The chromatographic separation just described was repeated several times on the earlier fractions already enriched in the allene. The *allenylpyrimidine*, m. p. 142°, was obtained in small yield (Found: N, 26·4. $C_9H_{11}N_3$ requires N, 26·1%).

1,2-Dihydro-2-imino-1,4,6-trimethyl-5-propylpyrimidine.—2-Amino-4,6-dimethyl-5-propylpyrimidine (1·0 g.) and methyl iodide (10 ml.) were heated under reflux for 18 hr. The mixture was evaporated and the residue dissolved in the minimum quantity of ethanol. Addition of ethyl acetate gave the *propyliminopyrimidine hydriodide* (64%), m. p. 191° (Found: C, 39·2; H, 5·8; N, 14·0. $C_{10}H_{18}IN_3$ requires C, 39·1; H, 5·9; N, 13·7%); *picrate*, m. p. 197° (Found: C, 47·2; H, 5·15; N, 20·8. $C_{16}H_{20}N_6O_7$ requires C, 47·7; H, 4·9; N, 20·6%); *hydrochloride*, m. p. 243° (from ethanol) (Found: C, 55·2; H, 8·15; N, 19·4. $C_{10}H_{18}ClN_3$ requires C, 55·7; H, 8·4; N, 19·5%).

5-Allyl-1,2-dihydro-2-imino-1,4,6-trimethylpyrimidine.—5-Allyl-2-amino-4,6-dimethylpyrimidine (3·2 g.) was heated under reflux with methyl iodide (25 ml.) for 18 hr. Evaporation left the *allyliminopyrimidine hydriodide* (58%), m. p. 203° (from ethanol) (Found: C, 39·7; H, 5·4; N, 13·9. $C_{10}H_{16}IN_3$ requires C, 39·3; H, 5·3; N, 13·8%); *picrate*, m. p. 146° (from water) (Found: C, 47·2; H, 4·5; N, 20·5. $C_{16}H_{18}N_6O_7$ requires C, 47·3; H, 4·5; N, 20·7%); *hydrochloride*, m. p. 231° (from ethanol) (Found: C, 55·9; H, 7·5; N, 20·1. $C_{10}H_{16}ClN_3$ requires C, 56·2; H, 7·55; N, 19·7%).

1,2-Dihydro-2-imino-1,4,6-trimethyl-5-(prop-1-ynyl)pyrimidine.—2-Amino-4,6-dimethyl-5-(prop-1-ynyl)pyrimidine (1·0 g.) and methyl iodide (10 ml.) were heated overnight in a sealed tube at 100°. Evaporation left the *iminopyrimidine hydriodide* (23%), m. p. 224° (decomp.) (from ethanol) (Found: C, 39·65; H, 4·6; N, 14·0. $C_{10}H_{14}IN_3$ requires C, 39·6; H, 4·7; N, 13·9%); *hydrochloride*, m. p. 257° (Found: C, 56·8; H, 6·4; N, 19·7. $C_{10}H_{14}ClN_3$ requires C, 57·2; H, 6·7; N, 19·85%).

[11] G. T. Morgan and R. W. Thomason, *J. Chem. Soc.*, 1924, **125**, 754.

1,2-Dihydro-2-imino-1,4,6-trimethyl-5-(prop-2-ynyl)pyrimidine.—2-Amino-4,6-dimethyl-5-(prop-2-ynyl)pyrimidine (1·0 g.) and methyl iodide (10 ml.) were heated in a sealed tube at 100° for 16 hr. Removal of methyl iodide by evaporation left the *imino(prop-2-ynyl)pyrimidine hydriodide* (33%), m. p. 195—196° (from ethanol–light petroleum) (Found: C, 39·8; H, 4·6. $C_{10}H_{14}IN_3$ requires C, 39·6; H, 4·65%).

2-Hydroxy-4,6-dimethyl-5-propyl (and prop-2-ynyl)pyrimidine.—3-Propylacetylacetone [11] (23 g.) and urea (9·9 g.) were mixed in ethanol (82 ml.) and 10N-hydrochloric acid (22 ml.) was added. The mixture was left at room temperature for 21 days (cf. analogues [12]), evaporated to *ca.* 15 ml., and then diluted with water to 50 ml. Refrigeration of the neutralised solution gave the *propylpyrimidine* (46%), m. p. 181° (from water) (Found: C, 65·2; H, 8·5; N, 16·7. $C_9H_{14}N_2O$ requires C, 65·0; H, 8·5; N, 16·85%).

The *propynylpyrimidine* (65%) was prepared similarly, m. p. 231° (from water) (Found: C, 66·8; H, 6·1; N, 17·1. $C_9H_{10}N_2O$ requires C, 66·65; H, 6·2; N, 17·3%).

5-Allyl-2-hydroxy-4,6-dimethylpyrimidine.—Prepared as the analogous derivatives, the *allylpyrimidine* (64%) had m. p. 176° (from water) (Found: C, 66·1; H, 7·3; N, 17·0. $C_9H_{12}N_2O$ requires C, 65·8; H, 7·4; N, 17·1%).

2-Chloro-4,6-dimethyl-5-propyl (and prop-2-ynyl)pyrimidine.—2-Hydroxy-4,6-dimethyl-5-propylpyrimidine (6·6 g.) was refluxed for 10 hr. with phosphoryl chloride (40 ml.). After removal of the excess of volatile components, the residue was stirred in ice for 20 min. and then made alkaline. Extraction with ether, and evaporation left the *chloro(propyl)pyrimidine* (73%), m. p. 56—58° (from light petroleum) (Found: C, 58·3; H, 7·0; N, 14·95. $C_9H_{13}ClN_2$ requires C, 58·5; H, 7·1; N, 15·2%).

Prepared similarly, the *prop-2-ynylpyrimidine* (46%) had m. p. 114° (from light petroleum) (Found: C, 59·8; H, 5·1; N, 15·3. $C_9H_9ClN_2$ requires C, 59·85; H, 5·0; N, 15·5%).

5-Allyl-2-chloro-4,6-dimethylpyrimidine.—Made in the same way, the *allylchloropyrimidine* (60%) had b. p. 115°/4 mm. (Found: C, 59·0; H, 5·8; N, 15·1. $C_9H_{11}ClN_2$ requires C, 59·2; H, 6·1; N, 15·3%).

2-Hydroxy-4,6-dimethyl-5-(prop-1-ynyl)pyrimidine.—2-Chloro-4,6-dimethyl-5-(prop-2-ynyl)pyrimidine (1·5 g.) and N-sodium hydroxide (50 ml.) were heated at 100° until no chloro-compound remained (*ca.* 2 hr.). An aqueous suspension of the solid, pH adjusted to 6, gave the *hydroxy(prop-1-ynyl)pyrimidine* (55%), m. p. 257° (from water) (Found: C, 66·1; H, 6·1; N, 16·9. $C_9H_{10}N_2O$ requires C, 66·65; H, 6·2; N, 17·3%). Similar treatment of 2-hydroxy-4,6-dimethyl-5-(prop-2-ynyl)pyrimidine gave the same prop-1-ynyl isomer (62%).

2-Chloro-4,6-dimethyl-5-(prop-1-ynyl)pyrimidine.—Chlorination of the 2-hydroxypyrimidine, as of its isomer, gave the *chloro(prop-1-ynyl)pyrimidine* (50%), m. p. 127° (from light petroleum) (Found: C, 60·1; H, 4·8; N, 15·2. $C_9H_9ClN_2$ requires C, 59·85; H, 5·0; N, 15·5%).

4,6-Dimethyl-2-methylamino-5-propylpyrimidine.—2-Chloro-4,6-dimethyl-5-propylpyrimidine (2·0 g.) was heated at 100° in a sealed tube with ethanolic methylamine (30%; 15 ml.) for 1 hr. The solution was poured into 2N-hydrochloric acid (100 ml.) and the pH was adjusted to 7. Ether extraction gave the *methylaminopyrimidine* (72%), m. p. 114° (from light petroleum) (Found: C, 66·9;

[12] T. Matsukawa and B. Ohta, *J. Pharm. Soc. Japan*, 1948, **69**, 491.

H, 9·4; N, 23·3. $C_{10}H_{17}N_3$ requires C, 67·0; H, 9·6; N, 23·4%).

5-*Allyl*-4,6-*dimethyl*-2-*methylaminopyrimidine*.—The appropriate chloropyrimidine, treated as before, gave the *allylmethylaminopyrimidine* (72%), m. p. 92° (from light petroleum) (Found: C, 68·1; H, 8·4; N, 23·5. $C_{10}H_{15}N_3$ requires C, 67·8; H, 8·5; N, 23·7%).

4,6-*Dimethyl*-2-*methylamino*-5-(*prop*-2-*ynyl*)*pyrimidine*.—(*a*) The 2-chloro-4,6-dimethyl-5-(prop-2-ynyl)pyrimidine, treated with methylamine as before, gave a mixture (from light petroleum) of two isomeric methylamino-derivatives in almost equal amounts (Found: C, 68·9; H, 7·7; N, 23·6. Calc. for $C_{10}H_{13}N_3$: C, 68·5; H, 7·5; N, 24·0%). The mixture was adsorbed on an alumina column from light petroleum, and eluted with ether. 4,6-*Dimethyl*-2-*methylamino*-5-(*prop*-2-*ynyl*)*pyrimidine* (31%) was obtained from late fractions, m. p. 132° (Found: N, 23·6. $C_{10}H_{13}N_3$ requires N, 24·0%), and did not show the characteristic infrared absorption [4] of the isomeric allenylpyrimidine.

(*b*) When aqueous methylamine at pH 8·5 (acetic acid) was diluted with ethanol and used in the aminolysis, the mixture of isomers obtained was 9 : 1 in favour of the propynyl isomer (^{1}H n.m.r. spectroscopic estimation). Elution with ether, from an alumina column gave the pure propynyl compound.

5-*Allenyl*-4,6-*dimethyl*-2-*methylaminopyrimidine*.—When elution of the 1 : 1 mixture of isomers described in (*a*) was carried out *rapidly* with ether, the 5-*allenylpyrimidine*, m. p. 101°, was isolated from early fractions in small yield, identified by its infrared and ^{1}H n.m.r. spectra (Found: N, 23·6. $C_{10}H_{13}N_3$ requires N, 24·0%).

4,6-*Dimethyl*-2-*methylamino*-5-(*prop*-1-*ynyl*)*pyrimidine*.—2-Chloro-4,6-dimethyl-5-(prop-1-ynyl)pyrimidine (0·45 g.) was heated for 1 hr. at 100° with ethanolic methylamine (4·0 ml.). The *methylaminopyrimidine* (69%) had m. p. 161° (from light petroleum) (Found: C, 68·55; H, 7·65; N, 23·85. $C_{10}H_{13}N_3$ requires C, 68·5; H, 7·5; N, 24·0%).

2-*Methyl*-1,3a,7-*triazaindene*.—(*a*) Material made [3] from 1,2-dihydro-2-imino-1-(prop-2-ynyl)pyrimidine gave a *picrate*, m. p. 178° (from water) (Found: C, 43·0; H, 2·7; N, 23·5. $C_{13}H_{10}N_6O_7$ requires C, 43·10; H, 2·8; N, 23·2%).

(*b*) Condensation [6] of 2-aminopyrimidine and chloroacetone gave the *hydrochloride*, m. p. 241° (from ethanol–light petroleum) (Found: C, 49·6; H, 5·0; N, 25·0. $C_7H_8ClN_3$ requires C, 49·55; H, 4·75; N, 24·8%). This salt added to ethanolic picric acid, gave a picrate identical (mixed m. p.) with that obtained in (*a*).

1,2-*Dihydro*-2-*imino*-4,6-*dimethyl*-1-(*prop*-2-*ynyl*)*pyrimidine*.—2-Amino-4,6-dimethylpyrimidine (2·4 g.) and prop-2-ynyl bromide were rocked in a sealed tube for 16 hr. at 100°. The *iminopyrimidine hydrobromide* (78%) had m. p. 203° (from ethanol) (Found: C, 44·6; H, 5·1; N, 17·4. $C_9H_{12}BrN_3$ requires C, 44·65; H, 5·0; N, 17·4%).

2,4,6-*Trimethyl*-1,3a,7-*triazaindene*.—The hydrobromide just described (0·5 g.) in ethanol (20 ml.) was treated with ethanolic sodium ethoxide (from sodium, 1·2 g.). The mixture was heated under reflux for 1 hr. and then added to saturated aqueous potassium carbonate. Extraction with ether gave the *triazaindene* (78%), m. p. 151° (from water) (Found: C, 67·25; H, 6·9; N, 25·7. $C_9H_{11}N_3$ requires C, 67·05; H, 6·9; N, 26·1%).

4,6-*Dimethyl*-2-*prop*-2-*ynylamino*)*pyrimidine*.—The same hydrobromide (1·0 g.) was set aside in N-potassium hydroxide (10 ml.) at 25° for 24 hr. The solid obtained by evaporating the reaction mixture was extracted with boiling ether and the extract (87%) was adsorbed on an alumina column. Elution with ether gave the *propynylaminopyrimidine*, m. p. 119° (after sublimation at 70°/0·05 mm.) (Found: C, 66·9; H, 6·8; N, 26·3. $C_5H_{11}N_3$ requires C, 67·0; H, 6·9; N, 26·1%) and subsequent elution with chloroform gave the triazaindene as before in an approximately equal amount.

1-*Allyl*-1,2-*dihydro*-2-*imino*-4,6-*dimethylpyrimidine*.—2-Amino-4,6-dimethylpyrimidine (0·8 g.) was refluxed for 4 hr. with allyl iodide (6 ml.). The residue from evaporation was dissolved in ethanol (30 ml.). Dilution with ether gave the *iminopyrimidine hydriodide*, m. p. 184—186° (Found: C, 36·7; H, 4·8; N, 14·2. $C_9H_{14}IN_3$ requires C, 37·1; H, 4·85; N, 14·4%).

2-*Allylamino*-4,6-*dimethylpyrimidine*.—2-Chloro-4,6-dimethylpyrimidine [12] (2·0 g.), allylamine (10 ml.), and ethanol (20 ml.) were heated under reflux for 4 hr. Ethanolic sodium ethoxide was added (sodium, 0·5 g.) and the mixture was evaporated to dryness. Extraction with ether and removal of solvent gave the *allylaminopyrimidine* (78%), m. p. 73° (from light petroleum) (Found: C, 66·5; H, 8·0; N, 25·5. $C_9H_{13}N_3$ requires C, 66·2; H, 8·0; N, 25·75%).

Determination of $t_{\frac{1}{2}}$ *Values*.—A solution of 1,2-dihydro-2-imino-1-(prop-2-ynyl)pyrimidine hydrobromide (1 part) in deuterium oxide (5 parts) was divided into 0·5-ml. samples. Each was treated with 3N-sodium deuteroxide (0·2 ml.) and thermostatted at 25°. At intervals, a sample was acidified with 10N-deuterium chloride (*ca.* 8 drops) and the ^{1}H n.m.r. spectrum was recorded. The $t_{\frac{1}{2}}$ value was determined from the disappearance of the peak at τ 4·9, representing the methylene protons of the propynyl group, in terms of the integrated 4-H and 6-H peaks (within the range τ 0·9 to 1·4 in starting material and products). For 1,2-dihydro-2-imino-4,6-dimethyl-1-(prop-2-ynyl)pyrimidine, H-5 (τ *ca.* 2·9) was used as reference because the methyl hydrogen atoms exchanged fairly rapidly with deuterium (cf. ref. 13).

The results were confirmed, and the rearrangements of other imines were followed, by the usual [2] ultraviolet measurements (25°; pH 14) at wavelengths where the products had no absorption.

[7/293 *Received*, *March* 10*th*, 1967]

[13] T. J. Batterham, D. J. Brown, and M. N. Paddon-Row, *J. Chem. Soc.* (*B*), 1967, 171.