Intramolecular Cycloaddition Reactions of Mono- and Di-hydroxypyrimidines

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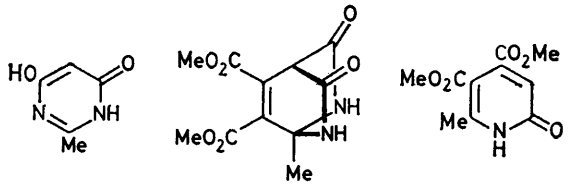
The intramolecular cycloaddition of unactivated olefins to dihydroxypyrimidines is described. The primary bridged cycloadducts may be isolated and hydrolysed, the overall process resulting in functionalisation of the olefin. The nitrile derivative (18) [4-hydroxy-2-methyl-6-oxo-5-(3-cyanopropyl)-1,6-dihydropyrimidine] also undergoes cycloaddition, although the primary adduct (19) is unstable and elimination of isocyanic acid occurs to form an annelated monohydroxypyrimidine (20). Olefins also react in an intramolecular fashion with monohydroxypyrimidines, the intermediate bicyclic adducts readily undergoing a subsequent retro-Alder reaction to yield annelated pyridines.

EXAMPLES of cycloadditions across the pyrimidine nucleus have been reported recently.[1] Certain pyrimidine betaines have also been shown to undergo cycloaddition with conventional dienophiles such as maleic anhydride.[2,3] These latter examples are significant since simple 4,6-dihydroxypyrimidines can also exist in a dipolar tautomeric form in polar solvents,[4] and similarly might be expected to participate in cycloadditions. Indeed the cycloaddition of 4,6-dihydroxy-2-methylpyrimidine (1) with dimethyl butynedioate has been reported [5] to yield the pyridone (3), formed from the intermediate (2) by a retro-Alder reaction.

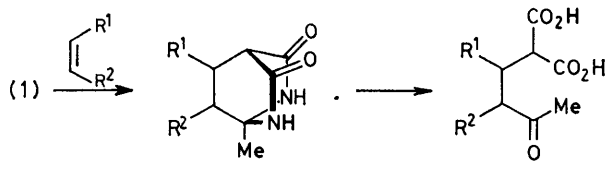
Under milder conditions some of the primary adduct (2) (12%) could be isolated along with the pyridine (3).



(1) (2) (3)

On further heating, the adduct (2) smoothly decomposed to give the pyridone (3). Chromatography over silica gel in polar solvents also effected this conversion.

It was of interest to investigate the cycloaddition of 4,6-dihydroxypyrimidines with simple olefins since the intermediates could, in principle, be transformed into saturated derivatives with the net addition of two functional groups to the starting olefin. For example, addition of cyclopentene to the pyrimidine (1) would lead to the bridged adduct (4; $R^1R^2 = -[CH_2]_3-$)



(4) (5)

SCHEME

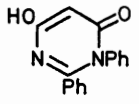
which, on hydrolysis, should give the derivatised cyclopentane (5; $R^1R^2 = -[CH_2]_3-$) (Scheme).

However, 4,6-dihydroxy-2-methylpyrimidine failed to react intermolecularly with simple olefins, or even strained olefins such as norbornadiene, under a wide variety of conditions. Attempts to secure reaction of the simple 4,6-dihydroxypyrimidines with electron-rich dienophiles such as ethyl vinyl ether, or to activate the heterocyclic system with Lewis acid catalysts, were

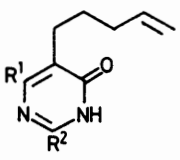
[1] H. Neunhoeffer and C. Werner, *Annalen*, 1974, 1190.
[2] K. T. Potts and M. Sorm, *J. Org. Chem.*, 1972, **37**, 1422.
[3] T. Kappe and W. Lube, *Angew. Chem. Internat. Edn.*, 1971, **10**, 925.
[4] A. R. Katritzky, F. D. Popp, and A. J. Waring, *J. Chem. Soc. (B)*, 1966, 565. See also G. M. Kheifets, N. V. Khromov-Borivsov, A. I. Koltsov, and M. V. Volkenstein, *Tetrahedron*, 1967, **23**, 1197; Y. Inoue, N. Furutachi, and K. Nakanishi, *J. Org. Chem.*, 1966, **31**, 175.
[5] P. J. Machin, A. E. A. Porter, and P. G. Sammes, *J.C.S. Perkin I*, 1973, 404.

also unsuccessful, as were reactions on the *N*-blocked pyrimidine (6) [6] which is fixed in the azabutadienone form and is expected to be reactive in cycloadditions by analogy with the similar pyrazine compounds.[5]

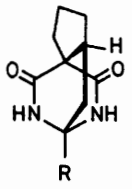
Reactivity towards cycloaddition can be described in terms of MO theory,[7] in particular through the use of frontier molecular orbital and perturbation theory approximations.[8,9] For a Diels–Alder reaction involving inverse electron demand, such as the reaction of an olefin with a pyrimidine, reactivity is mainly determined by the $HOMO_{olefin}$–$LUMO_{pyrimidine}$ interaction. Preliminary CNDO/2 calculations on the pyrimidine (1) in the tautomeric form depicted show that the symmetry, energy levels, and atomic coefficient components are all favourable for cycloaddition across the 2,5-positions with olefins. Thus it is predicted that cycloaddition is feasible in terms of electronic energy considerations provided the reaction is neither hindered by steric effects nor inhibited by thermodynamic considerations. It was therefore concluded that the intermolecular processes might be prevented by a large



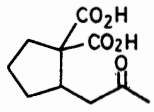
(6)



(7) R^1 = OH, R^2 = Me
(14) R^1 = OH, R^2 = Ph
(21) R^1 = Me, R^2 = Me
(25) R^1 = Ph, R^2 = Me



(8) R = Me
(15) R = Ph



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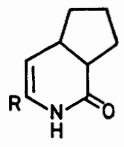
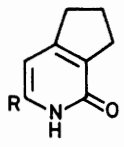


(10) R = Me
(16) R = Ph



(11) R = Me
(17) R = Ph

negative entropy barrier, and one means for overcoming this activation barrier would be for the components to react intramolecularly.

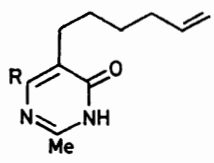
To test this suggestion the model pyrimidine (7) was prepared. Diethyl malonate was alkylated with 5-bromopent-1-ene, prepared by the action of phosphorus tribromide on pent-4-en-1-ol,[10,11] to produce diethyl 2-(pent-4-enyl)malonate.[12] Base-catalysed condensation with acetamidine [13] then yielded the new pyrimidine (7).

This pyrimidine proved stable at 80 °C under conditions in which the simple pyrimidine (1) undergoes cycloaddition with dimethyl butynedioate. On heating to 198 °C for 6 h in dimethylformamide, however, the primary cycloadduct (8) was formed (m.p. >300°), which was purified by sublimation. The ^1H n.m.r. spectrum showed no olefinic resonances, but retention of a methyl signal at higher field than in the starting material. The u.v. spectrum lacked the characteristic dihydroxypyrimidine absorptions, showing principally an end absorption, as is expected for a substantially unconjugated molecule, whilst the i.r. spectrum showed a pair of secondary *cis*-amide vibrations at 1 710 and 1 673 cm^{-1}.

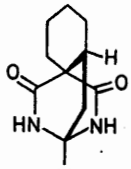
The product (8) was further characterised by acidic hydrolysis to give the substituted cyclopentane (9) in high yield. This product, m.p. 124—126°, was stable to decarboxylation up to 150 °C.

The bicyclic bis-amide adduct (8) was unstable to prolonged heating. In dimethylformamide at 200 °C a compound resulting from elimination of one mole of isocyanic acid was formed. The same product could also be formed by prolonged heating of the starting pyrimidine (7) and was identified as the dihydropyridone (10). This material was dehydrogenated to the pyridone (11) by heating in xylene over Pd–C catalyst.

The generality of this cycloaddition process was tested by application to a variety of derivatives, including the homologue (12). Thermolysis at 198 °C produced the adduct (13), although a longer reaction time (20 h) than that needed for the pentenyl derivative was necessary.



(12) R = OH
(29) R = Me



(13)

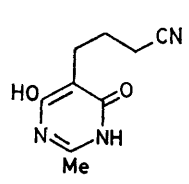
Diethyl 2-(pent-4-enyl)malonate was also condensed with benzamidine hydrochloride in the presence of an excess of base to produce the 2-phenylpyrimidine (14). Thermolysis proceeded more slowly than for the other two pyrimidines and reaction at 198 °C for 48 h was necessary to produce a moderate yield of the primary cycloadduct (15). In this case the thermolysis is so prolonged that elimination of the bridge of the intermediate adduct occurs at a similar rate. This secondary process was indicated by the isolation of the oily elimination product (16), which could be characterised by dehydrogenation to the crystalline pyridone (17). As previously, the bicyclic intermediate (15) could also be converted cleanly into the dihydropyridone (16) by heat. Rapid bridge elimination of the primary adduct (15) also occurs in the mass spectrometer, when high probe temperatures are used. Under these conditions only the molecular ion of the pyridone (17) is observed,

[6] L. B. Dashkevich and V. M. Siraya, U.S.S.R.P. 152,465 (*Chem. Abs.*, 1963, **59**, 11524h).
[7] R. B. Woodward and R. Hoffmann, *Angew. Chem. Internat. Edn.*, 1969, **8**, 781.
[8] K.-L. Mok and M. Nye, *J.C.S. Perkin I*, 1975, 1810.
[9] K. N. Houk, *Accounts Chem. Res.*, 1975, **8**, 361.
[10] F. B. LaForge, N. Green, and N. A. Gersdorff, *J. Amer. Chem. Soc.*, 1948, **40**, 3707.
[11] L. A. Brooks and H. R. Snyder, *Org. Synth.*, 1955, Coll. Vol. III, p. 698.
[12] J. I. G. Cadogan, D. H. Hey, and S. H. Ong, *J. Chem. Soc.*, 1965, 1932.
[13] A. W. Dox and L. Yoder, *J. Amer. Chem. Soc.*, 1922, **44**, 361.

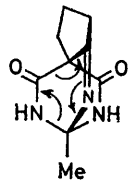
although satisfactory analytical data for the adduct (15) were obtained, as well as the expected molecular ion at lower temperatures.

The versatility of this method was also demonstrated by the incorporation of a nitrile function in place of the olefinic bond. A few examples of the incorporation of nitrile groups in the formation of heterocyclic systems by cycloaddition have been reported.[14]

Condensation of 4-bromobutyronitrile with diethyl malonate and then acetamidine afforded the pyrimidine (18). Heating this material at 198 °C for 20 h cleanly converted it into the new annelated pyrimidone (20). An unstable intermediate, probably the cycloadduct (19), was detected by t.l.c. The related monohydroxypyrimidines (21) and (25) were next prepared. Alkylation of either ethyl acetoacetate or ethyl benzoylacetate with 5-bromopent-1-ene followed by condensation with acetamidine hydrochloride in ethanolic sodium hydroxide [15] produced the new pyrimidines in good yield.



(18)



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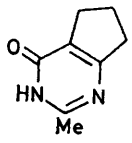
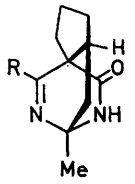
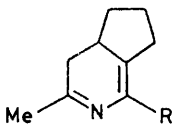


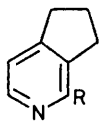
(20)



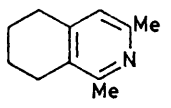
(22) R = Me
(26) R = Ph



(23) R = Me
(27) R = Ph



(24) R = Me
(28) R = Ph



(30)

Thermolysis of 2,4-dimethylpyrimidine (21) at 198 °C for 18 h led to the direct formation of the annelated pyridine (24). This can be rationalised in terms of an intramolecular cycloaddition to give the primary bridged adduct (22), followed by elimination of isocyanic acid to form the dihydropyridine (23), and subsequent aerial dehydrogenation. The bridged intermediate (22) could be observed spectroscopically only by conducting the thermolysis at 145 °C, and decomposition smoothly occurred on further heating to produce the isolated pyridine.

Thermolysis of the 4-phenylpyrimidine (25) proceeded at an even greater rate to yield the annelated pyridine (28). Preliminary studies show that the rate of cycloaddition of the pyrimidines (7), (21), and (25) can be successfully accounted for in terms of the effect of the substituents on the pyrimidine MO energy levels as calculated by the CNDO/2 method and in accord with current theory.[8,9]

Finally, the homologous pyrimidine (29) was prepared in the normal manner. Again thermolysis proceeded smoothly to give the annelated pyridine (30).

Current work with these transformations is aimed at the synthesis of naturally occurring fused pyridines and will be reported elsewhere.

EXPERIMENTAL

M.p.s were determined on a Kofler hot-stage apparatus. ^{1}H N.m.r. spectra were recorded on a Varian T-60 or HA 100 instrument for solutions in deuteriochloroform, unless otherwise stated, with tetramethylsilane as internal reference. U.v. spectra were recorded for solutions in ethanol on a Unicam SP 800 spectrophotometer and mass spectra were obtained with an A.E.I. MS-9 instrument. Solvents were purified and, where necessary, dried before use. T.l.c. was carried out on silica gel GF_{254} (1 mm layer for preparative work). Thermolysis of compounds was generally performed by sealing samples in Pyrex tubes under vacuum and heating in baths of appropriate refluxing solvents.

Reaction of 4,6-*Dihydroxy*-2-*methylpyrimidine* (1) *with Dimethyl Butynedioate.*—The pyrimidine (1.3 g) and the ester (2.8 g, 2 mol. equiv.) in dimethylformamide (20 ml) were heated at 60 ° C for 5 days under N_2. The solvent was removed *in vacuo* and the products were separated by column chromatography through SiO_2, using benzene and then benzene–acetone as eluant. First isolated was the known pyridone (3) (0.8 g, 31%), m.p. 163—165° (lit.,[5] 169—171°). Subsequently, *dimethyl* 2,6-*diaza*-3,5-*dioxobicyclo*[2.2.2]*oct*-7-*ene*-7,8-*dicarboxylate* (2) was collected (0.34 g, 12%), m.p. (EtOH) 180—182°, $\nu_{max.}$ 3 070, 2 850, 1 716, 1 680, 1 638, 1 435, 1 400, 1 290, 1 230, 1 172, 1 145, and 1 108 cm^{-1}, τ(CF_3CO_2H) 1.60br (2 H, s), 5.27 (1 H, s), 6.26 (3 H, s), 6.30 (3 H, s), and 8.26 (3 H, s) (Found: C, 49.5; H, 4.6; N, 10.4. $C_{11}H_{12}N_2O_6$ requires C, 49.3; H, 4.5; N, 10.4%).

Stirring this adduct with silica gel in methanol for 72 h, followed by preparative t.l.c., gave the pyridone (3) (60%), m.p. 165—168°. The pyridone was also formed on heating the adduct (*e.g.* during determination of the m.p.).

4-*Hydroxy*-2-*methyl*-6-*oxo*-5-(*pent*-4-*enyl*)-1,6-*dihydropyrimidine* (7).—Diethyl malonate (5.4 g) was added dropwise to a solution of sodium ethoxide [from sodium (0.77 g)] in ethanol (15 ml). 5-Bromopent-1-ene (5 g) was added and the mixture boiled under reflux with stirring for 4 h. The mixture was evaporated, saturated $CaCl_2$ solution was added, and the product was extracted into ether. Evapor-

[14] *Cf.* W. Oppolzer, *Angew. Chem. Internat. Edn.*, 1972, **11**, 1031.

[15] H. R. Snyder and H. M. Foster, *J. Amer. Chem. Soc.*, 1954, **76**, 118.

ation gave diethyl 2-(pent-4-enyl)malonate (5.3 g, 70%) as an oil, b.p. 137—142° at 10 mmHg, n_D^{20} 1.436 1. The ester (2.85 g) and acetamidine hydrochloride (1.18 g) were added to a solution of sodium ethoxide [from sodium (0.86 g)] in ethanol (50 ml). The mixture was refluxed with vigorous stirring for 6 h. After removal of the excess of ethanol, water (50 ml) was added and the liquid neutralised to pH 7 with concentrated HCl. On cooling to 0 °C a precipitate formed and this was collected to give the *dihydropyrimidine* (7) (2.01 g, 83%), which sublimed above 200°, $\nu_{max.}$ 2 600, 1 637, 1 577, 1 446, 1 340, 1 309, 1 155, 1 049, 906, 810, and 780 cm^{-1}, τ(CF_3CO_2H) 4.0—4.9 (1 H, m), 5.06—5.49 (2 H, t), 7.51 (3 H, s), and 7.30—8.92 (6 H, m), $\lambda_{max.}$ 248, 263, and 274 nm (ε 4 500, 7 100, and 5 000) (Found: C, 61.9; H, 7.3; N, 14.2. $C_{10}H_{14}N_2O_2$ requires C, 61.8; H, 7.3; N, 14.4%).

Thermolysis of the Pyrimidine (7).—(*a*) The pyrimidine (7) (0.1 g) in dimethylformamide (0.5 ml) was heated at 198 °C for 6 h. The product, isolated by trituration with ether (10 ml), was 8,11-*diaza*-9,10-*dioxo*-7-*methyltricyclo*-[5.2.2.0^{1,5}]*undecane* (8) (98 mg, 98%), which sublimed above 200°, $\nu_{max.}$ 3 170, 1 707, 1 663, 1 399, 1 320, 1 280, 1 190, 1 182, 1 118, 782, and 720 cm^{-1}, $\lambda_{max.}$ 267 nm (ε 100), τ 1.72—2.00 (2 H, s), 7.40—8.52 (9 H, m), and 8.57 (3 H, s) (Found: C, 61.6; H, 6.95; N, 14.3. $C_{10}H_{14}N_2O_2$ requires C, 61.8; H, 7.3; N, 14.4%).

The cycloadduct (8) (60 mg) was heated in sulphuric acid (1.2 ml conc. sulphuric acid and 0.55 ml H_2O) at 100 °C for 1 h. The solution was saturated with NaCl and then extracted with ether to give 2-*acetonylcyclopentane*-1,1-*dicarboxylic acid* (9) (45 mg, 67%), m.p. ($CHCl_3$–light petroleum) 123—126°, $\nu_{max.}$ 3 100—2 300, 1 687, 1 418, 1 309, 1 256, 1 240, 1 210, 1 154, 937, and 730 cm^{-1}, τ 1.44br (2 H, s), 6.72—8.90 (9 H, m), and 7.80 (3 H, s) (Found: C, 55.9; H, 6.4. $C_{10}H_{14}O_5$ requires C, 56.1; H, 6.6%).

(*b*) The pyrimidine (7) (4 g) in dimethylformamide (10 ml) was heated at 200 °C for 72 h. Work-up afforded the tricyclic adduct (8) and, from the mother liquors, 3-aza-4-methylbicyclo[4.3.0]non-4-en-2-one (10) (0.82 g, 21%), m.p. (EtOAc) 137—139°, $\nu_{max.}$ (Nujol) 3 305, 3 405, 1 660, 1 595, and 1 405 cm^{-1}, τ 1.40br (1 H, s), 5.38br (1 H, d), 7.15—7.40 (2 H, m), 8.20 (3 H, s), and 8.80—7.80 (6 H, m), *m/e* 151 (M^+, weak) and 149. The dihydropyridone (10) was obtained in 40% yield by further heating of the intermediate adduct (8) in dimethylformamide at 198 °C for 72 h. Dehydrogenation of the dihydropyridone (200 mg) was accomplished in refluxing xylene (30 ml) over 5% Pd–C (400 mg). After 48 h the mixture was filtered. Evaporation afforded 3-*aza*-4-*methylbicyclo*[4.3.0]*nona*-1(6),4-*dien*-2-*one* (11), m.p. (EtOAc) 160—161°, $\nu_{max.}$ 3 380, 1 650, 1 565, 1 458, and 1 125 cm^{-1}, τ −2.48br (1 H, s), 4.0 (1 H, s), 7.0—7.40 (4 H, m), 7.64 (3 H, s), and 7.98 (3 H, t) (Found: C, 72.0; H, 7.5; H, 9.4. $C_9H_{11}NO$ requires C, 72.45; H, 7.4; N, 9.4%).

5-(*Hex*-5-*enyl*)-4-*hydroxy*-2-*methyl*-6-*oxo*-1,6-*dihydropyrimidine* (12).—Diethyl malonate (2.1 g) and 6-bromohex-1-ene (2.25 g) were added to a solution of sodium ethoxide [from sodium (0.32 g) in ethanol (5 ml)] and the mixture was refluxed for 2 h. Addition of water and extraction with ether gave diethyl 2-(hex-5-enyl)malonate [16] (1.0 g, 30%) which was used without further purification in condensation with acetamidine hydrochloride (0.3 g) as described above. The *dihydropyrimidine* (2) (0.16 g, 18%) was precipitated from ethanol and had $\nu_{max.}$ 2 620, 1 639, 1 589, 1 452, 1 314, 1 153, 1 050, and 912 cm^{-1}, τ(CF_3CO_2H) 4.2—4.95 (11 H, m), 5.09—5.50 (2 H, t), 7.46 (3 H, s), and 7.22—9.05 (8 H, m) (Found: C, 63.3; H, 7.55; N, 13.4. $C_{11}H_{16}N_2O_2$ requires C, 63.4; H, 7.7; N, 13.45%). Heating this material (70 mg) in dimethylformamide (0.5 ml) in a sealed tube at 198 °C for 24 h afforded, by trituration with ether (10 ml), 9,12-*diaza*-10,11-*dioxo*-8-*methyltricyclo*-[6.2.2.0^{1,6}]*dodecane* (13) (30 mg, 44%), m.p. >300°, $\nu_{max.}$ 3 175, 1 710, 1 656, 1 402, 1 321, 1 291, 1 192, 1 159, 977, 760, and 723 cm^{-1}, M^+ 208 (Found: C, 63.4; H, 7.75; N, 13.4. $C_{11}H_{16}N_2O_2$ requires C, 63.4; H, 7.7; N, 13.45%).

4-*Hydroxy*-6-*oxo*-5-(*pent*-4-*enyl*)-2-*phenyl*-1,6-*dihydropyrimidine* (14).—Benzamidine hydrochloride (0.8 g) and diethyl 2-(pent-4-enyl)malonate (1.1 g) were added to a solution of sodium ethoxide [from sodium (0.23 g)] in ethanol (25 ml), and the mixture was refluxed for 6 h. Work-up in the usual manner gave pale yellow *plates* (0.48 g, 37%) m.p. (EtOAc) 280—282°, $\nu_{max.}$ 3 320—2 340, 1 610, 1 580, 1 512, 1 351, 1 290, 1 118, 918, 779, and 701 cm^{-1}, τ 2.10—2.90 (5 H, m), 4.22—4.95 (1 H, m), 5.05—5.55 (2 H, m), and 7.50—8.76 (6 H, m), $\lambda_{max.}$ 232 and 306 nm (ε 25 000 and 9 800) (Found: C, 70.2; H, 6.4; N, 11.1. $C_{15}H_{16}N_2O_2$ requires C, 70.3; H, 6.3; N, 10.9%).

Heating the pyrimidine at 198 °C for 48 h, followed by preparative t.l.c., gave 8,11-*diaza*-9,10-*dioxo*-7-*phenyltricyclo*[5.2.2.0^{1,5}]*undecane* (15) (59%), m.p. (after sublimation at 90° and 0.1 mmHg) 120—121°, $\nu_{max.}$ 3 350, 1 721, 1 659, 1 279, 1 178, 1 031, 917, 754, and 693 cm^{-1}, $\lambda_{max.}$ 224 and 269 nm (ε 4 100 and 270), τ 2.32—2.84 (5 H, m) and 6.78—8.56 (9 H, m) (Found: C, 70.1; H, 6.5; N, 10.7. $C_{15}H_{16}N_2O_2$ requires C, 70.3; H, 6.3; N, 10.9%).

On prolonged heating of either the pyrimidine (14) or the cycloadduct (15) at 198 °C in dimethylformamide a second crystalline product was isolated by preparative t.l.c. Recrystallisation (EtOAc) afforded 3-aza-4-phenylbicyclo[4.3.0]non-4-en-2-one (16), m.p. 155—156°, $\nu_{max.}$ 3 490, 3 385, 2 930, 2 860, 1 680, 1 585, 1 450, 1 375, and 901 cm^{-1}, τ 2.20br (1 H, s), 2.40—2.84 (5 H, m), 4.42 (1 H, d), 7.10—7.45 (2 H, m), 7.60—8.0 (4 H, m), and 8.10—8.20 (2 H, m), *m/e* 213 (M^+, weak) and 212.

The dihydropyridone (16) was dehydrogenated over Pd–C in xylene under the same conditions as for (10) to afford 3-aza-2-hydroxy-4-phenylbicyclo[4.3.0]nona-1,3,5-triene (17), m.p. (EtOAc) 210—211°, $\nu_{max.}$ 2 960, 1 642, 1 612, 1 596, 1 495, 1 378, 1 156, and 1 074 cm^{-1}, τ 2.4—2.6 (5 H, m), 3.48 (1 H, s), 7.00—7.40 (4 H, m), and 7.9 (2 H, m).

5-(3-*Cyanopropyl*)-4-*hydroxy*-2-*methyl*-6-*oxo*-1,6-*dihydropyrimidine* (18).—Diethyl 2-(3-cyanopropyl)malonate (2.3 g) was added slowly to a solution of sodium ethoxide [from sodium (0.7 g)] in ethanol (50 ml). Acetamidine hydrochloride (1.0 g) was added and the solution heated under reflux for 6 h. After evaporation the mixture was worked up in the normal manner to give *compound* (18) (0.58 g, 31%), m.p. >300°, $\nu_{max.}$ 3 550—2 610, 2 241, 1 630, 1 562, 1 450, 1 441, 1 418, 1 065, 981, and 652 cm^{-1}, τ(CF_3CO_2H) 7.30—8.75 (6 H, m) and 7.54 (3 H, s) (Found: C, 55.8; H, 5.9; N, 21.6. $C_9H_{11}N_3O$ requires C, 55.95; H, 5.7; N, 21.75%).

Heating the pyrimidine (50 mg) in dimethylformamide (0.5 ml) at 198 °C for 20 h gave, after sublimation, pale yellow needles of 2,4-*diaza*-5-*hydroxy*-3-*methylbicyclo*[4.3.0]-*nona*-1,3,5-*triene* (20), m.p. (benzene) 205—207°, $\nu_{max.}$ 3 070—2 500, 2 910, 2 841, 1 665, 1 596, 1 425, 1 371,

[16] J. A. Brockman, U.S.P. 2,970,161 (*Chem. Abs.*, 1961, **55**, 18599a).

1 327, 1 226, 1 140, 938, and 756 cm^{-1}, τ 6.78—7.33 (4 H, t), 7.48 (3 H, s), and 7.70—8.10 (2 H, quintet) (Found: C, 63.8; H, 6.7; N, 18.8. $C_8H_{10}N_2O$ requires C, 64.0; H, 6.7; N, 18.65%). T.l.c. of the crude reaction mixture showed the presence of a more polar product, probably the primary adduct (19). This minor component was not examined further.

Preparation and Reactions of the Monohydroxypyrimidines (21), (25), *and* (29).—(a) 2-*Methyl*-6-*oxo*-5-(*pent*-4-*enyl*)-4-*phenyl*-1,6-*dihydropyrimidine* (25). Alkylation of ethyl benzoylacetate (6.5 g) with 5-bromopent-4-ene (5 g) by treatment with sodium ethoxide in ethanol afforded *ethyl* 2-*benzoylhept*-6-*enoate* (3.9 g, 44%) as a pale yellow oil, b.p. 135—140° at 2 mmHg, $\nu_{max.}$ 3 079, 2 982, 2 920, 1 739, 1 688, 1 600, 1 582, 1 451, 1 372, 920, and 699 cm^{-1}, τ 1.84—2.37 (2 H, dd, *J* 9, 2.5 Hz), 2.39—2.83 (3 H, m), 3.95—4.92 (1 H, m), 4.92—5.36 (2 H, t), 5.68 (1 H, t, *J* 6.5 Hz), 6.07 (2 H, q, *J* 6.0 Hz), 8.01—9.05 (6 H, m), and 9.02 (3 H, t, *J* 6.0 Hz) (Found: C, 74.1; H, 7.7. $C_{16}H_{20}O_3$ requires C, 73.8; H, 7.7%).

Acetamidine hydrochloride (0.5 g) and the ester (1.24 g) were added to a solution of sodium hydroxide (0.4 g) in ethanol (10 ml) and the mixture was stirred at room temperature for 24 h. The solvent was evaporated off and the residue was treated with sodium carbonate (0.4 g) and sodium hydrogen carbonate (0.4 g). The mixture was triturated with light petroleum and then extracted with ethyl acetate (Soxhlet) to afford the *dihydropyrimidine* (25) (0.56 g, 50%), m.p. (EtOAc) 91—93°, $\nu_{max.}$ 3 140—2 550, 1 645, 1 610, 1 551, 1 507, 1 310, 1 238, 1 150, 1 094, 1 030, 920, 783, 767, and 702 cm^{-1}, $\lambda_{max.}$ 231 and 281 nm (ε 11 000 and 4 800), τ −0.72br (1 H, s), 2.51 (5 H, s), 3.78—4.81 (1 H, m), 4.80—5.26 (2 H, t), 7.50 (3 H, s), and 7.20—8.65 (6 H, m) (Found: C, 75.3; H, 7.05; N, 10.8. $C_{16}H_{18}N_2O$ requires C, 75.6; H, 7.1; N, 11.0%).

Thermolysis of this pyrimidine (45 mg) at 198 °C for 15 h followed by preparative t.l.c. afforded 3-*aza*-4-*methyl*-2-*phenylbicyclo*[4.3.0]*nona*-1,3,5-*triene* (28) (15 mg, 51%) as an oil, $\nu_{max.}$ 3 040, 2 948, 1 596, 1 560, 1 490, 1 430, 1 421, 1 376, 1 029, 859, 789, 740, and 700 cm^{-1}, $\lambda_{max.}$ 212, 239, and 282 nm (ε 8 600, 6 000, and 5 200), τ 2.23 (2 H, dd, *J* 2, 8 Hz), 2.48—2.72 (3 H, m), 2.93 (1 H, s), 6.97 (2 H, t, *J* 7.5 Hz), 7.04 (2 H, t, *J* 7.5 Hz), 7.41 (3 H, s), and 7.24—8.70 (2 H, m) (Found: C, 86.1; H, 7.3; N, 6.4. $C_{15}H_{15}N$ requires C, 86.1; H, 7.2; N, 6.7%).

(b) 2,4-*Dimethyl*-6-*oxo*-5-(*pent*-4-*enyl*)-1,6-*dihydropyrimidine* (21). This was prepared by condensation of ethyl 2-acetylhept-6-enoate with acetamidine hydrochloride in the standard way. The *pyrimidine* had m.p. (EtOAc–benzene) 111—112°, 160° (hydrate), $\nu_{max.}$ 3 060, 2 770, 1 656, 1 611, 1 321, 1 269, 1 211, 1 160, 990, 943, 912, 801, and 769 cm^{-1}, $\lambda_{max.}$ 230 and 274 nm (ε 5 360 and 5 050), τ −0.05br (1 H, s), 3.6—4.5 (1 H, m), 4.65—5.15 (2 H, t), 7.30—8.78 (6 H, m), 7.58 (3 H, s), and 7.67 (3 H, s) (Found: C, 68.55; H, 8.3; N, 14.5. $C_{11}H_{16}N_2O$ requires C, 68.7; H, 8.4; N, 14.6%).

Thermolysis of this pyrimidine at 198 °C for 18 h, extraction into 10N-H_2SO_4, basification, and extraction into ether afforded 3-*aza*-2,4-*dimethylbicyclo*[4.3.0]*nona*-1,3,5-*triene* (24) (65%) as a pale yellow oil, b.p. 150—160° at 35 mmHg, $\nu_{max.}$ 1 608, 1 580, 1 462, 1 389, 1 221, 1 149, 1 030, 939, 865, and 764 cm^{-1}, $\lambda_{max.}$ 267 nm (ε 2 700), τ 3.13 (1 H, s), 7.16br (4 H, t), 7.52 (3 H, s), 7.58 (3 H, s), and 7.98 (2 H, t). (Found: C, 81.4; H, 8.7; N, 9.3. $C_{10}H_{13}N$ requires C, 81.6; H, 8.9; N, 9.5%).

Thermolysis of either (21) or (25) at 145 °C produced (t.l.c.) an unstable intermediate which disappeared on prolonged heating.

(c) 5-(*Hex*-5-*enyl*)-2,4-*dimethyl*-6-*oxo*-1,6-*dihydropyrimidine* (29). This was prepared by condensation of ethyl 2-acetyloct-7-enoate with acetamidine hydrochloride in the standard way. The *pyrimidine* had m.p. (petroleum) 89—91°, $\nu_{max.}$ 2 926, 2 856, 1 650, 1 612, 1 440, 1 382, 1 314, 1 216, 1 160, and 914 cm^{-1}, τ 4.1—4.4 (1 H, m), 4.9—5.1 (2 H, m), 7.58 (3 H, s), 7.68 (3 H, s), and 7.40—8.64 (8 H, m), $\lambda_{max.}$ 230 and 274 nm (ε 5 240 and 5 010) (Found: C, 69.0; H, 8.8; N, 13.5. $C_{12}H_{18}N_2O$ requires C, 69.9; H, 8.8; N, 13.6%).

Thermolysis of this pyrimidine (200 mg) at 198 °C for 16 h, followed by preparative t.l.c. afforded 3-*aza*-2,4-*dimethylbicyclo*[4.4.0]*deca*-1,3,5-*triene* (30) (88 mg, 56%) as a pale yellow oil, $\nu_{max.}$ 1 608, 1 594, 1 448, 1 432, 1 395, 1 322, 910, and 854 cm^{-1}, τ 3.32 (1 H, s), 7.35 (4 H, m), 7.57 (3 H, s), and 8.08—8.34 (4 H, m) (Found: M^+, 161.1201. $C_{11}H_{15}N$ requires *M*, 161.120 4).

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