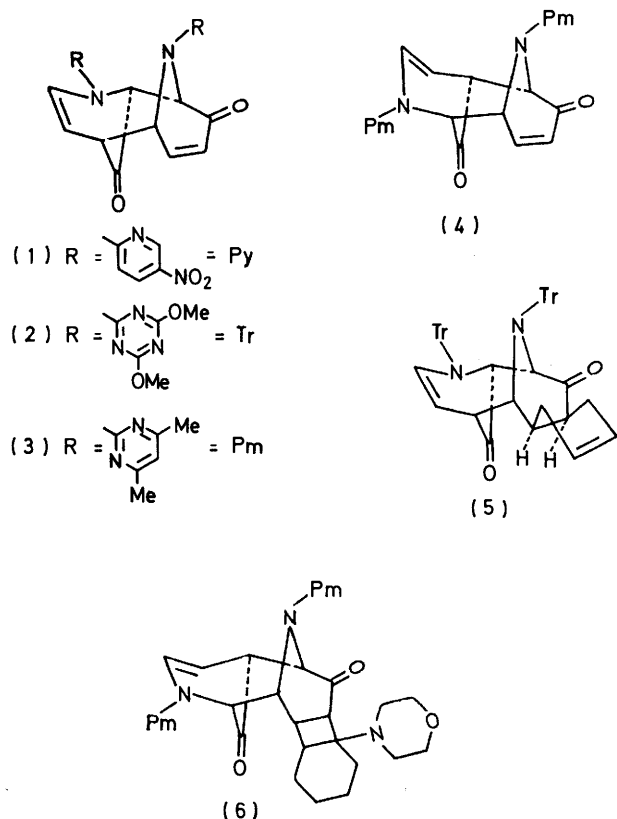


1,3-Dipolar Character of Six-membered Aromatic Rings. Part 48.^{1,2} Novel Conversions of Pyridines to Isoquinolines

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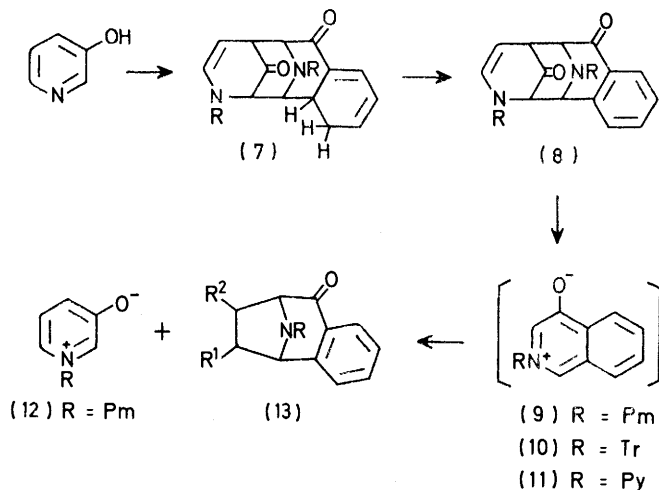
1-Heteroaryl-3-oxidopyridinium dimers with dienamines give cycloadducts which are dehydrogenated to 'mixed dimers' of the corresponding 2-heteroaryl-4-oxidoisoquinolinium with the starting 1-heteroaryl-3-oxidopyridinium. The 'mixed dimer' (21) is also effectively prepared by a two-step sequence of a novel intramolecular oxidation-reduction, followed by oxidation of the resulting alcohol. The 'mixed dimers' undergo reversible thermal dissociation and in one case the corresponding monomers could be trapped as various cycloadducts.

1-(5-NITRO-2-PYRIDYL)-, 1-(4,6-dimethoxy-1,3,5-triazin-2-yl)-,³ and 1-(4,6-dimethylpyrimidin-2-yl)-3-oxidopyridinium⁴ betaines spontaneously yield dimers (1)–(3) which act as a source of the corresponding nascent 3-oxidopyridiniums by thermally allowed retrocycloaddition.⁵ The dimers (1) and (2) exist as single regioisomers but the pyrimidinyl dimer (3) equilibrates on standing in chloroform to a mixture of (3) and its regioisomer (4) in 1:4 ratio. Some other reactions of the dimers have been reported, of (2) with buta-1,3-diene to give (5) in 60% yield,⁶ and of (3) with 1-morpholinocyclohexene to give (6) in 50% yield.⁷



The present work concerns transformations of dimers (1), (2), and (3) \rightleftharpoons (4) to tetracyclic systems (7) [e.g. (14)–(16)] and (8) [e.g. (21)] and in certain cases subsequently *via* the isoquinolinium derivatives (9)–(11) to 1,3-ethanoisoquinolines (13) [e.g. (38), (44), (45), and (47)], examples of which ring system were previously

prepared directly from 2-(2,4-dinitrophenyl)-4-oxidoisoquinolinium.⁸ The present work thus constitutes the first route to isoquinolines from pyridines (Scheme 1).



SCHEME 1

Reactions with Dienamines.—High-yield annelation reactions of 1-dialkylaminobuta-1,3-dienes have previously been reported with electron-deficient alkenes,⁹ naphthoquinone,¹⁰ and nitroso-compounds.¹¹ In the present investigation the three dimers (1), (2), and (3) \rightleftharpoons (4) each reacted at 20 °C with 1-dimethylaminobuta-1,3-diene [and also with 1-diethylaminobuta-1,3-diene in the case of (3) \rightleftharpoons (4)] regio- and stereospecifically to give the tetracycles (14) (24%), (15) (67%), and (16) (95–98%), respectively.

The initially formed Diels–Alder adducts normally spontaneously eliminated dimethylamine (or diethylamine) during work-up; however, the initial adduct (18) (5%) could be isolated from the triazinyl dimer under special conditions; it readily lost dimethylamine on heating in solution to yield (15). The structural assignment of adduct (18) was made on the basis of i.r. and ¹H n.m.r., particularly the saturated carbonyl $\nu(\text{C}=\text{O})$ 1770 cm⁻¹ in the i.r. and in the ¹H n.m.r. the 4-H doublet at δ 7.42, and the 5-H double doublet at δ 4.90 ($J_{4,5}$ 8 Hz) which collapsed to a doublet on irradiation of 4-H ($J_{5,6}$ 6 Hz). The 6-H resonance was found at *ca.* δ 3.1 by irradiation of 5-H. The low-field resonance at δ 6.16 for 12-H present in (15) was replaced by a high-field resonance δ 3.0–3.2 in (18).

The tetracycles (14)—(16) show characteristic absorptions in the i.r. at 1740—1720 and 1680—1675 (C=C—C=O), 1640 (C=C—N), and 1618—1615 cm⁻¹ (C=C—C=C). The n.m.r. spectra (Table 1) established the structures of the tetracycles. The regiochemistry

butadienyl grouping is evident in the n.m.r. spectra of compounds (14)—(16). The geminal protons 9A and 9B in each of the three compounds exhibit a double doublet and a doublet respectively. Irradiation of the vicinal 10-H in all cases collapses the 9A multiplet to a

TABLE 1

¹H N.m.r. spectra of cyclohexadienyl dimers ^{a,*}

| Chemical shifts (δ) | (14) ^b | (15) ^b | (16) ^b | (16) ^c | (17) ^b | (18) ^b | (20) ^b |
|-----------------------------------|-------------------|--------------------------------------|--|-------------------|------------------------|----------------------|-----------------------|
| 1 | 6.21 ^d | 6.16 ^e | 6.40 ^f | 6.28 ^g | 6.40 ^g | 5.3—5.5 ^h | 6.78 ^{g,i} |
| 2 | 5.20 ^j | 5.16 ^k | 5.29 ^g | 5.08 ^g | 5.31 ^g | 4.70 ^l | 5.52 ^g |
| 4 | 6.43 ^m | 7.38 ^m | 7.37 ^m | 7.28 ^m | 7.65 ⁿ | 7.42 ^m | ca. 7.30 ^o |
| 5 | 5.13 ^k | 5.03 ^k | 4.78 ^k | 4.78 ^k | | 4.90 ^k | 4.69 ^k |
| 6 | 3.11 ^p | 2.96 ^q | 2.90 ^q | 2.92 ^q | 3.16 ^q | 3.0—3.2 ^h | 2.88 ^q |
| 7 | 5.20 ^g | 5.30 ^g | 5.47 ^g | 5.42 ^g | 5.80 ^g | 5.3—5.5 ^h | 5.67 ^k |
| 8 | 2.48 ⁿ | 2.42 ^{n,r} | s | | s | 2.1 ^h | s |
| 9A | 2.94 ^k | 2.78 ^k | 2.80 ^{t,k} | | 2.82 ^k | 3.0—3.2 ^h | s |
| 9B | 2.50 ^m | 2.26 ^m | s | | s | 2.1 ^h | s |
| 10 | s | 6.93 ^t | 6.90 ^t | 6.78 ^t | 6.93 ^t | 5.3—5.5 ^h | 3.41 ^{l,u,v} |
| 11 | 6.21 ^d | 6.16 ^e | 6.10 ^w | 6.08 ^w | 6.10 ^w | 5.3—5.5 ^h | 6.22 ^k |
| 12 | 6.21 ^d | 6.16 ^e | 6.10 ^w | 6.08 ^w | 6.10 ^w | 3.0—3.2 ^h | 6.84 ^{m,r} |
| 16 | | | | | | | 3.77 ^m |
| 17 | | | | | | | 3.13 ^k |
| 3',3'' | 7.00 ^m | | | | | | |
| | 6.78 ^m | | | | | | |
| 4',4'' | 8.37 ^k | | | | | | |
| | 8.07 ^k | | | | | | |
| 5',5'' | | | 6.47 ⁿ | 6.52 ⁿ | 6.53 ⁿ | | 6.50 ⁿ |
| | | | 6.17 ⁿ | 6.18 ⁿ | 6.26 ⁿ | | 6.26 ⁿ |
| 6',6'' | 9.19 ^m | | | | | | |
| | 8.75 ^m | | | | | | |
| CH ₃ | | | 2.4, ^{n,w} 1.6 ^{n,u} | | 2.60—2.30 ^h | | 2.32 ⁿ |
| | | | 2.1, ^{n,u} 2.3 ⁿ | | 1.7 ⁱ | | 2.25 ⁿ |
| | | | | | | | 1.60 ⁿ |
| CH ₃ O | | 4.02 ⁿ | | | | 3.80 ^m | |
| | | 3.86, ⁿ 3.48 ⁿ | | | | 3.75 ^m | |
| | | | | | | 3.48 ^m | |
| C ₆ H ₅ | | | | | | | 7.4—7.25 ^h |
| | | | | | | | 7.1—7.0 ^h |
| (CH ₃) ₂ N | | | | | | 2.10 ⁿ | |
| Coupling constants (Hz) | (14) | (15) | (16) | (16) | (17) | (18) | (20) |
| 1,2 | x | 2 | 4 | 4 | 4 | | 4 |
| 1,7 | x | 2 | 3 | 3 | 3 | | 3 |
| 2,6 | 2 | 2 | 3 | 3 | 3 | | 2.5 |
| 4,5 | 8 | 8 | 8 | 8 | | 8 | 8 |
| 5,6 | 6 | 6 | 6 | 6 | | 6 | 6 |
| 6,7 | x | 2 | 4 | 4 | 4 | | 4 |
| 7,8 | 0 | 0 | | | | | |
| 9A,9B | 9 | 9 | | | | | |
| 9A,10 | 3 | 3 | 3 | 3 | x | | |
| 9B,10 | 0 | 0 | | | | | |
| 10,11 | x | 4 | 4 | 4 | x | | 6 |
| 10,12 | x | 3 | 3 | 3 | x | | 1.5 |
| 11,12 | | | 2 | 2 | x | | 8 |
| 16,17 | | | | | | | 8 |
| 3',4' | 9 | | | | | | |
| 4',6' | 2 | | | | | | |

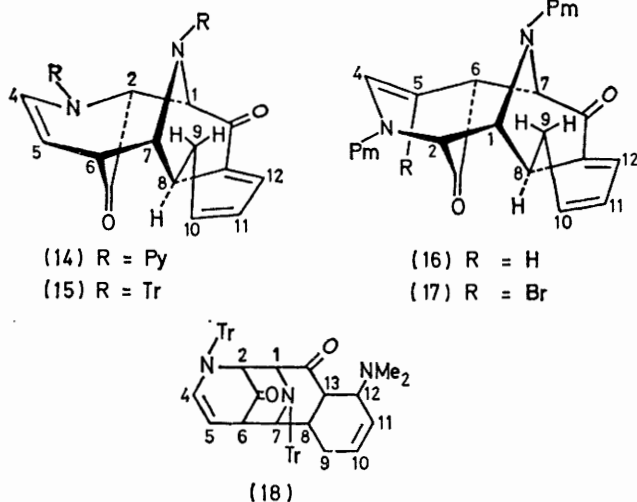
* See formulae for numbering which is non-systematic. ^a Me₄Si as internal standard. ^b In CDCl₃. ^c In (CD₃)₂SO—CDCl₃ (1:2). ^d As a three-line signal. ^e As a four-line signal. ^f Superimposed on 5'-H of pyrimidinyl group. ^g Triplet. ^h Complex. ⁱ Partially masked. ^j Protons 2- and 7-H are superimposed. ^k Double doublet. ^l Pseudo-singlet. ^m Doublet. ⁿ Singlet. ^o Masked by aromatics; assignment based on decoupling of 5-H by irradiation at this point. ^p Double triplet. ^q Quintet; more accurately, an ill resolved double triplet. ^r Slightly broadened. ^s Masked. ^t Pseudo-quartet. ^u Broad. ^v Possesses fine splitting. ^w As a two-line signal. ^x Not possible to determine since spin-spin decoupling experiments were not carried out.

of (14)—(16) was assumed in view of known^{3,4} regiochemistry of parent dimers (1), (2), and (3) \rightleftharpoons (4). The *exo*-stereochemistry was established^{3,4} by the coupling (2—3 Hz) between 2- and 6-H: molecular models demonstrate that only in the *exo*-structure does the four-bond system connecting 2- and 6-H assume a planar arrangement^{3,4} necessary for W-type coupling. A distinct ABX pattern due to the three protons of the

doublet. The *exo*-configuration of the molecules at the site of annelation, C-8, is established by the lack of coupling between 7-H [in (14) and (15)]/1-H [in (16)] and 8-H. Only in the *exo*-configuration does the dihedral angle between 7-H (1-H) and 8-H (90—120 °C) correspond¹² to a coupling constant of ca. 0 Hz. Spin-spin decoupling experiments further support the above assignments. In (16), irradiation of the 1-H triplet

causes the triplets of 2- and 7-H to collapse to doublets ($J_{2,6}$ 3 and $J_{6,7}$ 4 Hz).

The mass spectra of (14)–(16) exhibited the expected molecular ions which readily fragment by retrocycloaddition to a 3-oxidopyridinium fragment and a 4-oxidodihydroisoquinolinium fragment [cf. mass spectrum of dimer (3) \rightleftharpoons (4)].¹³ The molecular ions also readily lose the bridging heterocyclic amine on electron impact.



Dienamine (HOMO) to electron-deficient alkene (LUMO) interaction as the principal orbital interaction is suggested both by simple frontier orbital considerations and CNDO/2 energies (8.5 eV compared with 13.4 eV for the opposite mode¹⁴). The orbital coefficients then predict the observed regiostructure. No evidence was found for any regioisomer of (16). As the initial dimer was a mixture of 80% of (4) and 20% of (3) a small quantity of (19) could have been expected: however a rapid attack on (4) could displace the equilibrium away from (3).

Reactions of the Dimer–Cyclohexadienyl Annulation Products.—Tetracycle (16) underwent Diels–Alder cycloaddition at the cyclohexadienyl moiety with *N*-phenylmaleimide to give the cycloadduct (20) (67%). Steric congestion should preclude *exo*-attack on the butadienyl group. The n.m.r. spectra indicates that (20) is formed, but does not define the stereochemistry at C-16 and -17. The n.m.r. spectrum (Table 1) of the Diels–Alder adduct (20) resembles that of the diene (16) except that the ABX pattern for the butadienyl group of (16) is absent. The *exo*-stereochemistry at C-8 is retained in (20) since irradiation of the resonances of 2- and 7-H collapses the triplet of 1-H to a singlet at δ 6.78. The vinylic protons 11-H (a double doublet) and 12-H (a broadened doublet) resonate at δ 6.22 and 6.84, respectively. The mass spectrum of (20) exhibited a molecular ion at m/e 628 (1%) and intense fragment ions at m/e 252 (48%) and 202 (100) due to retrocycloaddition fragmentation, together with a peak for *N*-phenylmaleimide (92%).

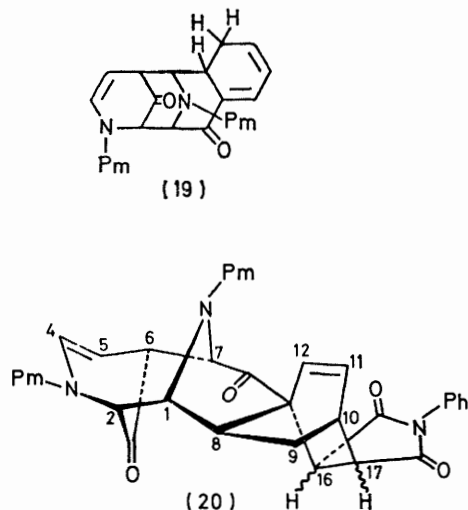
Tetracycle (16) with 1 mol. equiv. of bromine or *N*-bromosuccinimide gave the 5-bromo-derivative (17).

Structure (17) follows from the ¹H n.m.r. spectrum (see Table 1) and particularly from the singlet for 4-H at δ 7.65. The mass spectrum exhibited molecular ion peaks at m/e 534 (1%) and 532 (1), intense peaks at m/e 282 (20%) and 280 (20) for the pyridinium fragment, and a base peak at m/e 252 for the isoquinolinium fragment. With 2 mol. equiv. of bromine, tetracycle (16) yielded a complex mixture of polybromo-derivatives of (16).

Aromatisation of Cyclohexadienyl Adducts.—Dehydrogenation of the cyclohexadienyl tetracycle (16), with 10% Pd–C by refluxing in cyclohexane for 7 days, gave the benzenoid tetracycle (21) (29%). Many attempts to improve the yield of compound (21) by varying the activity of the Pd–C (e.g. by using the 'formalin procedure'¹⁵), the purity of the cyclohexane, and the reaction time (up to 6 weeks), all failed. Decalin as solvent at 140 °C caused decomposition. Attempted dehydrogenation of (16) with trityl fluoroborate¹⁶ gave starting material or complete decomposition as did chloranil¹⁷ and 2,3-dichloro-5,6-dicyano-1,4-benzoquinone.¹⁸

Active manganese dioxide¹⁹ without prior thermal activation degraded tetracycle (15) to 2-amino-4,6-dimethoxy-1,3,5-triazine (55%), however activated manganese dioxide (80 °C for 4 days) led to dehydrogenation of the cyclohexadienyl moiety of (15) to give (23) in 40% yield.

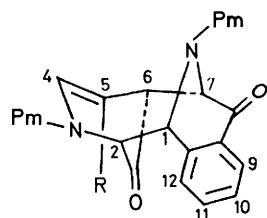
Treatment of the cyclohexadienyl tetracycles (15) and (16) with 1% ethanolic potassium hydroxide at reflux for 15 min gave smooth internal dehydrogenation–hydrogenation to form the benzenoid alcohols (25)



(24%) and (27) (96%); the latter was isolated in high purity. Reaction of tetracycle (15) with methanolic potassium hydroxide, led similarly to the alcohol (26) (20%). The benzenoid alcohols (25)–(27) exhibit ν (O–H) at 3 400, 3 440, and 3 460 cm^{-1} , respectively, but no ν (C=O) saturated absorptions.

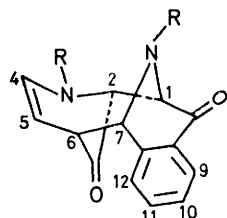
The configuration (27) was established from the ¹H n.m.r. evidence (Table 2), indicating a highly stereospecific reaction. The configuration of C-14 was estab-

lished by spin-spin decoupling: irradiation of the 14-H resonance at δ 3.83 collapsed the septet of the enamine proton 5-H at δ 4.80 to a double doublet ($J_{4,5}$ 8, $J_{5,6}$ 6 Hz). This coupling between 5- and 14-H is the result of W-type coupling only possible in the C-14 configuration ascribed to (27). Further evidence was obtained



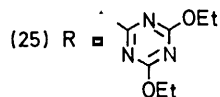
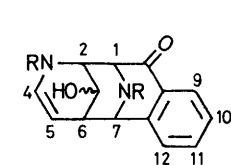
(21) R = H

(22) R = C(CN) = C(CN)₂

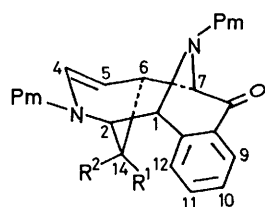


(23) R = Tr

(24) R = Pm



(26) R = Tr



(27) R² = HO, R¹ = H

(28) R² = H, R¹ = HO

(29) R² = MeSCH₂O, R¹ = H

(30) R² = MeCO₂, R¹ = H

by irradiation at the resonances of the 6- and 4-H at δ 2.68 and 7.60 respectively which caused the 5-H septet to collapse to double doublets ($J_{5,14}$ 2, $J_{4,5}$ 8 Hz) in both cases. The addition of D₂O resulted in the removal of the coupling between O-H and 14-H thus collapsing the 14-H broad pseudo-singlet to a pseudo-quartet.

The ¹H n.m.r. spectra of (25) and (26) were assigned by comparison with (27) (Table 2). The aromatic protons 10-, 11-, and 12-H resonate with 4-H at δ 7.6–7.3 in (25) (CDCl₃) and at δ 7.9 in (26) [(CD₃)₂SO]. Proton 9-H resonates at δ 7.94 in (25) and at δ 8.02 in (26), each as a double doublet whose secondary splitting is very fine ($J_{9,10}$ 7, $J_{9,11}$ 1.5 Hz). Long range coupling did not define the configuration at C-14 in (25) and (26) because of the superposition of peaks.

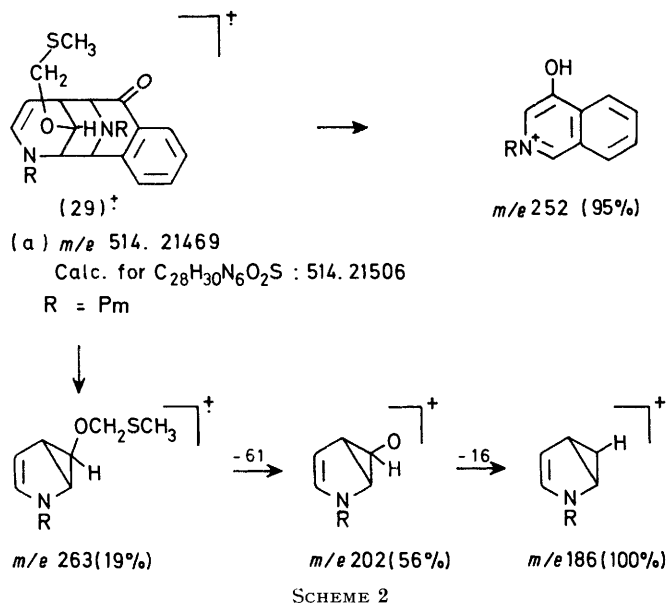
The mass spectra of (25) and (27) both show characteristic peaks due to parent molecular ions together with intense peaks due to the 4-oxidoisoquinolinium betaine ion.

The aromatisation of the cyclohexadiene portion could involve an intermediate hexa-1,3-dienyl anion losing a hydride ion to reduce to the alcohol a bridging carbonyl group. There appears to be no literature precedent for such an aromatisation procedure. There is evidence to suggest that this reaction proceeds by an intramolecular mechanism. The reduction of the diketone (21) to the S-alcohol (28) with ethanolic potassium hydroxide, follows the expected stereochemical course of attack from the less hindered side. Using identical

reaction conditions, the conversion of the diketone (16) to the R-alcohol (27) proceeds without the formation of any of the S-alcohol (28). Thus the postulated intramolecular reduction must proceed at a much faster rate than the expected intermolecular process of the type (21) → (28). The configuration of C-14 of (28) was readily elucidated since the 5-H appears as a double doublet in the ¹H n.m.r. spectrum, and therefore does not couple to 14-H.

The reaction of the alcohol (27) with MnO₂, pyridinium chlorochromate, or CrO₃ yielded a ketone of unknown structure for which i.r. absorption at 1 685 cm⁻¹ indicates the presence of an $\alpha\beta$ -unsaturated carbonyl group, but for which the enamine absorption present in (27) is absent. The mass spectrum shows a molecular ion at *m/e* 470 (16%) and the isoquinolinium fragment at 252 (100%) as the base peak. A second unknown product was isolated from the MnO₂ reaction.

Oxidation of the benzenoid alcohol (27) with dimethyl sulphoxide-acetic anhydride²⁰ gave a mixture of three compounds (29) (12%), (30) (12%), and (21) (36%) from which the last component could not be satisfactorily separated in this experiment. The methylthiomethyl ether (29) was separated by multiple development thick-layer chromatography: the ¹H n.m.r. spectrum (Table 2) is similar to that of the precursor (27), but with an additional singlet at δ 4.46 (OCH₂S). The acetate (30) was separated by fractional crystallisation from ethanol: it possessed a ¹H n.m.r. spectrum similar to that of (27); the i.r. displays an additional ester ν (C=O) at



1 735 cm⁻¹. The strong ν (O-H) in the i.r. spectrum of (27) was absent in (29) and (30). The mass spectra of (29) and (30) exhibited molecular ions at *m/e* 514.2 and 496.2, respectively, the isoquinolinium ion, and a number of other characteristic ions (Scheme 2).

Oxidation of the benzenoid alcohol (27) with dimethyl sulphoxide-dicyclohexylcarbodi-imide²¹ gave the pure

ketone (21) (56%) without side-products. The i.r. of (21) is similar to that of the cyclohexadienyl compound (16) with carbonyl absorptions at 1 730 and 1 680 cm^{-1} , and an enamine absorption at 1 630 cm^{-1} . The butadienyl absorption observed in (16) at 1 618 cm^{-1} is absent. The ^1H n.m.r. spectrum (Table 2, Figure) fully established the structure. For instance, irradiation of the bridgehead double triplet 6-H at δ 3.22 collapsed the 7-H triplet at δ 6.60 to a doublet ($J_{1,7}$ 2 Hz). Protons 1- and 7-H are appreciably deshielded by aromatisation

of the vinylic 5-H proton (δ 5.20). Further irradiation of 5-H identified the 6-H signal (δ 3.24) which is coupled to the vicinal proton, 7-H, and to the bridgehead proton, 2-H, by *W*-type long-range coupling ($J_{2,6}$ 2 Hz). The mass spectrum of (23) shows a molecular ion at m/e 518.16 (14.6%) (Scheme 3).

Hydrolysis of the triazinyl keto-alcohol (26) in hydrochloric acid gave cyanuric acid (68%) but no 4-hydroxyisoquinoline. Then benzenoid alcohol (27) did not react with molten *N*-phenylmaleimide nor with acrylonitrile.

TABLE 2
 ^1H N.m.r. spectra ^a of aromatic dimers *

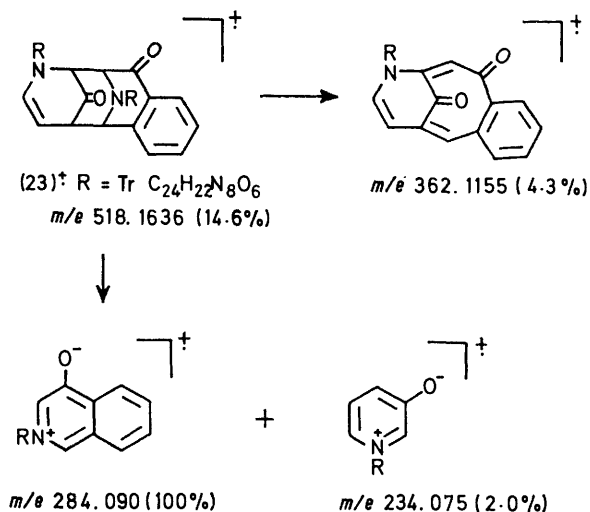
| Chemical shifts (δ) ^a | (21) ^b | (22) ^b | (23) ^b | (24) ^b | (25) ^b | (26) ^c | (27) ^b | (28) ^b | (29) ^b | (30) ^b |
|---|----------------------|----------------------|------------------------|----------------------|----------------------|-----------------------|-----------------------|----------------------|----------------------|----------------------|
| 1 | 6.70 ^d | 6.55 ^d | 6.45 ^{e,f} | 7.16 ^d | 6.04 ^{g,h} | 6.14 ^{g,h} | 6.23 ^{e,f} | 6.19 ^g | 6.25 ^{e,f} | 6.20 ^h |
| 2 | 5.34 ^d | 5.58 ^d | 5.20 ^{i,j} | 5.21 ^d | 5.1 ^{g,h} | 5.0—5.15 ⁱ | 5.23 ^k | 5.24 ^k | 5.44 ^{f-h} | 5.32 ^k |
| 4 | 7.43 ^{l,m} | 8.98 ⁿ | 7.47 ^{l,m} | 7.39 ^{l,m} | 7.3—7.6 ⁱ | 7.2—7.9 ⁱ | ca. 7.60 ^o | \bar{p} | \bar{p} | \bar{p} |
| 5 | 4.90 ^g | | 5.20 ^{i,j} | 4.85 ^g | 5.1 ^{g,h} | 5.0—5.15 ⁱ | 4.80 ^r | 4.97 ^g | 4.90 ^r | 4.80 ^r |
| 6 | 3.22 ^s | 4.40 ^d | 3.24 ^t | 3.30 ^s | 2.78 ^{g,h} | 2.79 ^{g,h} | 2.68 ^u | 2.81 ^u | 2.76 ^t | 2.86 ^t |
| 7 | 6.60 ^d | 7.14 ^d | 6.45 ^{e,f} | 6.14 ^d | 6.04 ^{g,h} | 6.14 ^{g,h} | 6.23 ^{e,f} | 6.02 ^{e,f} | 6.25 ^{e,f} | 6.20 ^h |
| 8 | | | 7.3—7.7 ^{l,m} | 7.3—7.6 | 5.96 ^{g,h} | 5.92 ^{g,h} | | | | |
| 9 | 8.05 ^g | 7.3—8.1 ^v | 8.02 ^g | 8.05 ^g | 7.94 ^g | 8.02 ^g | 8.05 ^g | 7.98 ^g | 8.10 ^g | 8.04 ^g |
| 10 | 7.2—7.6 ⁱ | 7.3—8.1 ^v | 7.3—7.7 ⁱ | 7.3—7.6 ⁱ | 7.3—7.6 ⁱ | 7.2—7.9 ⁱ | 7.2—7.6 ⁱ | 7.2—7.5 ⁱ | 7.2—7.6 ⁱ | 7.2—7.6 ⁱ |
| 11 | 7.2—7.6 ⁱ | 7.3—8.1 ^v | 7.3—7.7 ⁱ | 7.3—7.6 ⁱ | 7.3—7.6 ⁱ | 7.2—7.9 ⁱ | 7.2—7.6 ⁱ | 7.2—7.5 ⁱ | 7.2—7.6 ⁱ | 7.2—7.6 ⁱ |
| 12 | 7.2—7.6 ⁱ | 7.3—8.1 ^v | 7.3—7.7 | 7.3—7.6 ⁱ | 7.3—7.6 ⁱ | 7.2—7.9 ⁱ | 7.2—7.6 ⁱ | 7.2—7.5 ⁱ | 7.2—7.6 ⁱ | 7.2—7.6 ⁱ |
| 14 | | | | | 5.1 ^{g,h} | 5.0—5.15 ⁱ | 3.83 ^{g,h} | 4.32 ^{g,h} | 4.02 ^{f-h} | 4.96 ^{f-h} |
| 5',5'' | 6.13 ⁿ | 6.36 ⁿ | | 6.18 ⁿ | | | 6.48 ⁿ | 6.45 ⁿ | 6.45 ⁿ | 6.42 ⁿ |
| | 6.60 ⁿ | 6.90 ⁿ | | 6.52 ⁿ | | | 6.09 ⁿ | 6.05 ⁿ | 6.10 ⁿ | 6.06 ⁿ |
| CH ₃ | 1.7 ^{g,n} | 1.7—2.4 ⁱ | 4.12 ⁿ | 1.7—2.4 ⁱ | | | 1.7—2.3 ⁱ | 2.35 ⁿ | 2.3—1.7 ⁱ | 2.3 ^{g,n} |
| | 2.3 ^g | | 3.94 ⁿ | | | | | 2.19 ⁿ | 1.2 ⁿ | 2.2 ^{g,n} |
| | | | 3.76 ⁿ | | | | | 1.71 ⁿ | | 1.8 ^{g,n} |
| | | | 3.56 ⁿ | | | | | 1.67 ⁿ | | 1.7 ^{g,n} |
| —CH ₂ — | | | | | | | | | 4.46 ⁿ | |
| Coupling constants (Hz) | (21) | (22) | (23) | (24) | (25) | (26) | (27) | (28) | (29) | (30) |
| 1,2 | 3 | 2.5 | ca. 2 | 3 | | | 4 | <i>x</i> | <i>x</i> | <i>x</i> |
| 1,7 | 2 | 2 | <i>w</i> | 2 | | | ca. 2 ^w | <i>x</i> | <i>x</i> | <i>x</i> |
| 2,6 | <i>z</i> | 2 | 2 | 2 | | | 4 | <i>x</i> | <i>x</i> | <i>x</i> |
| 2,14 | | | | | | | ca. 2 | <i>x</i> | <i>x</i> | <i>x</i> |
| 4,5 | 8 | | 8 | 8 | | | 8 | 8 | 8 | 8 |
| 5,6 | 6 | | 6 | 6 | | | 6 | 6 | 6 | 6 |
| 5,14 | | | | | | | 2 | 0 | 2 | 2 |
| 6,7 | 3 | 2.5 | ca. 2 | 2.5 | | | ca. 2 ^w | <i>x</i> | <i>x</i> | <i>x</i> |
| 6,14 | | | | | | | ca. 3 | <i>x</i> | <i>x</i> | <i>x</i> |
| 5,10 | 3 | | 7 | 8 | 7 | 7 | 8 | 8 | 8 | 8 |
| 9,11 | 1.5 | | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 | 1.5 |

* See formulae for numbering which is non-systematic. ^a Me₄Si as internal standard. ^b In CDCl₃. ^c In (CD₃)₂SO. ^d Triplet. ^e As a two-line signal. ^f Possesses fine splitting. ^g Broad. ^h Pseudo-singlet. ⁱ Complex. ^j An expansion (\times 4) reveals that the double doublet due to 6-H is superimposed on the finely split pseudo-singlet due to 2-H. ^k Pseudo-quartet. ^l Doublet. ^m As determined by collapse to a well defined singlet when 5-H was irradiated. ⁿ Singlet. ^o Masked by aromatics; assignment based on decoupling of 5-H by irradiation at this point. ^p Masked. ^q Double doublet. ^r Septet. ^s Double triplet. ^t Pseudo-quintet. ^u Pseudo-sextet. ^v First-order multiplet. ^w Protons 1- and 7-H are superimposed. ^x Not possible to determine as spin-spin decoupling experiments were not carried out.

of the cyclohexadienyl ring (7-H deshielded by 1.13 p.p.m.). The mass spectrum of (21) gave a significant molecular ion at m/e 452 (28%) and fragment peaks at m/e 329 (10%, *M* - NH₂R), 251 (100, isoquinolinium), and 201 (10, pyridinium) [*cf.* spectrum of (23) in Scheme 3].

The dehydrogenation of the cyclohexadienyl compound (15) with very active manganese dioxide provides a moderate yield of compound (23) (44%). The i.r. shows absorptions at 1 740, 1 690, and 1 640 cm^{-1} . The ^1H n.m.r. spectrum (Table 2) established the structure. Irradiation of the low field signal for 4-H identi-

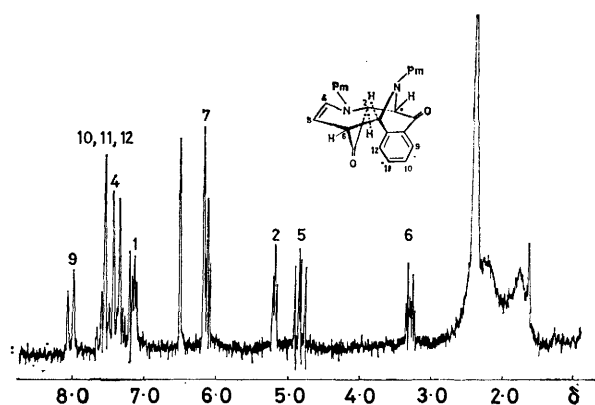
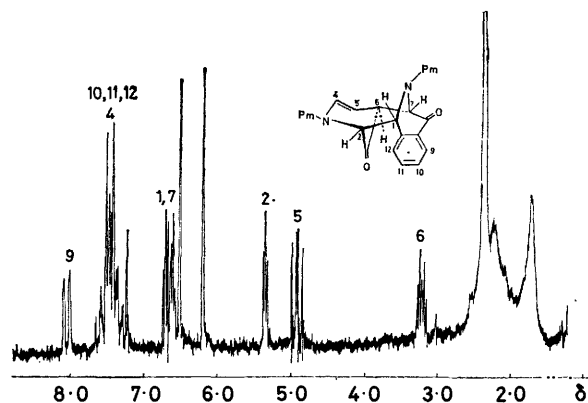
Regiosomerisation of Mixed Dimer.—The tetracyclic diketone (21) is effectively a cycloadduct of 1-(4,6-dimethylpyrimidin-2-yl)-4-oxidoisoquinolinium (9) and the 3-oxidopyridinium betaine (12). Similarly (23) is also a mixed dimer. The tetracyclic diketone (21) is partially converted into the regioisomer (24), in 1,2-dichloroethane after two days under reflux. No other compound was produced. The i.r. spectrum of (24) closely resembles that of (21) but small intensity variations occur for some absorptions. The ^1H n.m.r. spectrum (Table 2, Figure) established the *exo*-stereochemistry of (24) at the C-2,C-6 ring junction in view of



SCHEME 3

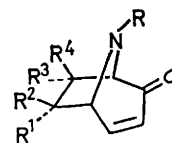
the W-type coupling between 2- and 6-H ($J_{2,6}$ 2 Hz). The opposite regiochemistry of the molecule relative to (21) was indicated by the upfield shift of the bridging proton 1-H by 0.56 p.p.m. and by the downfield shift of 7-H by 0.56 p.p.m.

Electrophilic attack on the diketone (21) with tetracyanoethylene gave the 5-substituted derivative (22) by

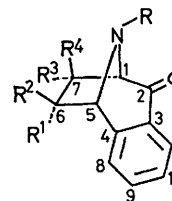


100 MHz ¹H N.m.r. spectra (CDCl₃) of: (a) 3,13-bis-(4,6-dimethylpyrimidin-2-yl)-(8a,12a-benzo)-3,13-diazatricyclo-[5.3.1.1^{3,6}]dodec-4-ene-8,14-dione (21); (b) 3,13-bis-(4,6-dimethylpyrimidin-2-yl)-(7a,11a-benzo)-3,13-diazatricyclo-[5.3.1.1^{3,6}]dodec-4-ene-12,14-dione (24)

dehydrocyanation of the initial product. The i.r. spectrum shows a nitrile absorption at 2200 cm⁻¹ and the absence of the enamine absorption. The ¹H n.m.r. spectrum of (22) (Table 2) established the postulated structure. The enamine proton 4-H resonates as a singlet while the bridgehead proton 6-H resonates as a triplet thus establishing the absence of a proton at 5-H. Both 4- and 6-H are deshielded by the tricyanoethylene group, by 1.5 and 1.18 p.p.m. respectively. The visible spectrum shows an intense absorption at 460 nm (ϵ_{\max} .



- (31) R¹ = Ph, R² = R³ = R⁴ = H, R = Pm
 (32) R¹ = R³ = H, R²-R⁴ = CON(Ph)CO, R = Pm
 (33) R¹-R³ = CON(Ph)CO, R² = R⁴ = H, R = Pm
 (34) R¹ = R³ = R⁴ = H, R² = CN, R = Pm
 (35) R¹, R² = CN, Cl, R³ = R⁴ = H, R = Pm
 (36) R¹ = R³ = H, R², R⁴ = CO₂CO, R = Pm
 (37) R¹, R³ = CO₂CO, R² = R⁴ = H, R = Py



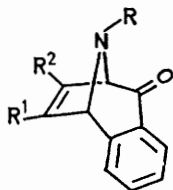
- (38) R¹ = R³ = H, R²-R⁴ = CON(Ph)CO, R = Pm
 (39) R¹-R³ = CON(Ph)CO, R² = R⁴ = H, R = 2,4-dinitrophenyl
 (40) R¹ = Ph, R² = R³ = R⁴ = H, R = 2,4-dinitrophenyl
 (41) R¹ = R² = R⁴ = H, R³ = Ph, R = 2,4-dinitrophenyl
 (42) R¹ = Ph, R² = R³ = R⁴ = H, R = Py
 (43) R¹ = R² = R⁴ = H, R³ = Ph, R = Py
 (44) R² = CN, R¹ = R³ = R⁴ = H, R = Pm
 (45) R⁴ = CN, R¹ = R² = R³ = H, R = Pm
 (46) R¹ = CN, R² = R³ = R⁴ = H, R = 2,4-dinitrophenyl
 (47) R¹, R² = CN, Cl, R³ = R⁴ = H, R = Pm

22500) due to strong conjugation of the enamine group with the tricyanoethylene group.

Cycloaddition Reactions of the Mixed Dimer (21).— Attempted cycloadditions with diethyl diazodicarboxylate, diethyl maleate, cyclopentadiene, diphenylcyclopropenone, norbornene, and diphenylacetylene failed. However, cycloaddition products were isolated from reactions of the diketone (21) with the acrylonitrile, α -chloroacrylonitrile, *N*-phenylmaleimide, and maleic anhydride, all dipolarophiles which involve betaine (HOMO)-dipolarophile (LUMO) FMO control. Styrene also reacted with the mixed dimer but from this reaction only the 3-oxidopyridinium adduct (31) was isolated.

Reaction with *N*-phenylmaleimide gave a single iso-

quinolinium adduct (38) together with mixed *exo*- and *endo*-pyridinium adducts (32),(33) which were identical with an authentic sample prepared from 1-(4,6-dimethyl-



(48) $R^1 = \text{Ph}$, $R^2 = \text{H}$, $R = 2,4\text{-dinitrophenyl}$

(49) $R^1 = \text{H}$, $R^2 = \text{Ph}$, $R = 2,4\text{-dinitrophenyl}$

pyrimidin-2-yl)-3-oxidopyridinium. In the isoquinoline series the only *N*-phenylmaleimide adduct previously prepared⁸ is the dinitrophenyl derivative (39). In the mass spectrum (38) exhibited a molecular ion at m/e 424 (21%) and typically, a base peak due to 2-(4,6-dimethylpyrimidin-2-yl)-4-oxidoisoquinolinium at m/e 251.

Reaction of the diketone (21) with acrylonitrile gave a

Pyridinium betaines produce regioselectively the 6-substituted azabicyclo-octenones.^{3,5,23,24} Since no stereoselectivity was expected for acrylonitrile there could be up to six products. In the event, the 6-*exo*-pyridine derivative (34) was isolated pure (71%) and the two regioisomeric *exo*-isoquinoline adducts (44) and (45) were characterised as a *ca.* 1:1 mixture (15%). The reaction of acrylonitrile with 2-(2,4-dinitrophenyl)-4-oxidoisoquinolinium is complex: only (46) was isolated.⁸

2-Chloroacrylonitrile with 3-oxidopyridinium betaines gives a mixture of 6-substituted cycloadducts.²⁵ The mixed dimer (21) gave the known pyridine derivative (35) (56%)²⁶ and the mixed *endo* and *exo* isoquinoline derivatives (47) (48%) (ratio 1:2, according to ¹H n.m.r.).

Maleic anhydride reacted readily with the mixed dimer: the pyridine derivative (36) (50%) was isolated, identical with an authentic sample prepared from 1-(4,6-dimethylpyrimidin-2-yl)-3-oxidopyridinium. The isoquinoline adduct was detected but was not readily

TABLE 3
¹H N.m.r. spectra of cycloadducts ^{a,b,*}

| Chemical shifts (δ) | (32) + (33) | (36) | (38) | (44) + (45) | (47) |
|-------------------------------|--|--|--|--|--|
| 1 | 5.6—5.8 ^c | 4.95 ^d | <i>e</i> | 5.40 ^f 5.58 ^g | 5.36 ^f 5.50 ^f |
| 3 | 5.6—5.8 ^c | 5.92 ^f | | | |
| 4 | <i>h</i> | 7.56 ^f | | | |
| 5 | 5.6—5.8 ^c | 5.36 ^d | <i>e</i> | 5.87 ^d 6.04 ⁱ | 6.06 ⁱ 6.15 ⁱ |
| 6- <i>exo</i> | 4.08 ^c | | | 2.0—3.2 ^e | |
| 6- <i>endo</i> | 3.34 ^d 3.50 ^d | 3.78 ^d 3.98 ^d | 3.46 ⁱ 3.48 ⁱ | 2.0—3.2 ^e 2.0—3.2 ^e | |
| 7- <i>exo</i> | 4.08 ^c | | | 2.0—3.2 ^e | 3.60 ^f 3.28 ^f |
| 7- <i>endo</i> | 3.34 ^d 3.50 ^d | 3.78 ^d 3.98 ^d | 3.46 ⁱ 3.48 ⁱ | 2.0—3.2 ^e | |
| 8 | | | 7.1—7.5 ^c | 7.25—7.5 ^c | 7.2—7.5 ^c |
| 9 | | | 7.1—7.5 ^c | 7.25—7.5 ^c | 7.2—7.5 ^c |
| 10 | | | 7.1—7.5 ^c | 7.25—7.5 ^c | 7.2—7.5 ^c |
| 11 | | | 7.98 ^f | 7.92 ^f | 7.98 ^f |
| 5' | 6.36 ⁱ 6.38 ⁱ | 6.64 ⁱ | <i>e</i> | 6.30 ⁱ | 6.34 ⁱ |
| CH ₃ | 2.25 ^{i,j} | 2.20 ⁱ | 2.20 ⁱ | 2.20 ^{i,j} | 2.2 ^{i,j} |
| C ₆ H ₅ | 7.1—7.5 ^c | | 7.1—7.5 ^c | | |
| Coupling constants (Hz) | (32) + (33) | (36) | (38) | (44) + (45) | (47) |
| 1,3 | 1 | 1 | | | |
| 1,7 | | | 8 | 8 | 8 |
| 3,4 | 10 | 10 | | | |
| 4,5 | 5 | 5 | | | |
| 5,6- <i>exo</i> | | | | 6 | |
| 6,7 | 8 | 8 | | | |
| 7- <i>exo</i> ,7- <i>endo</i> | | | 14 | 14 | 14 |
| 9,11 | | | 1.5 | 1.5 | 1.5 |
| 10,11 | | | 8 | 8 | 8 |

* See formulae for numbering which is non-systematic. ^a Me₄Si as internal standard. ^b In CDCl₃. ^c Complex. ^d Doublet. ^e 6.32, 6.14, ⁱ or 5.98. ^f Double doublet. ^g Protons 2- and 7-H are superimposed. ^h Masked. ⁱ Singlet. ^j Broad.

complex mixture. A notable contrast between 4-oxidoisoquinolinium betaines and 3-oxidopyridinium betaines is that the former show little regioselectivity: betaine (10) with styrene gives⁸ regioisomers (40) (26%) and (41) (40%) and with phenylacetylene (48) (26%) and (49) (25%). Betaine (11) with styrene gives regioisomeric adducts (42) (24%) and (43) (38%).²²

separated by chromatography. A single 3-oxidopyridinium maleic anhydride adduct (37)⁵ has been reported previously.

The mixed dimer with styrene gave after chromatography the pyridine derivative (31) (18%).⁵

N.m.r. Spectra of Cycloadducts.—The n.m.r. spectra of pyridinium and isoquinolinium cycloadducts are in Table

3. The pyridinium adducts [(32), (33) and (36)] exhibit characteristic ²⁷ resonances and multiplicities for the vinylic protons, 3- and 4-H. These are absent in the spectra of the isoquinolinium adducts [(38), (44), (45), and (47)]. In both series of adducts, lack of coupling between 5- and 6-H is indicative ²⁷ of *exo*-substituent stereochemistry at 6-C, while coupling between 5- and 6-H (*J* 6 Hz) signifies the *exo*-hydrogen at C-6.

Conclusions.—The present work provides a route from 3-hydroxypyridine to derivatives of 4-hydroxyisoquinoline and represents the first synthesis of isoquinolines by annelation of a benzenoid ring to an existing pyridine system.

EXPERIMENTAL

M.p.s were determined with a Reichert apparatus. Spectra were recorded with a Perkin-Elmer 257 grating i.r. spectrophotometer, a Perkin-Elmer SP 800 u.v. spectrophotometer, Perkin-Elmer RMU-6E and AEI MS-9 mass spectrometers, and a Varian HA-100 n.m.r. spectrometer. High resolution mass spectra were recorded on an AEI MS-9 spectrometer coupled to an IBM 1130 computer. Compounds were purified until they were observed as single spots when subjected to multiple development t.l.c. (Kieselgel GF 254). Preparative thick-layer chromatography (prep. t.l.c.) was carried out on Kieselgel PF 254. Column chromatography was carried out on alumina (Brockmann grade I; B.D.H.) and silica gel (60–120 mesh; B.D.H.). Unless otherwise stated, solvents were removed under reduced pressure below 50 °C. Toluene was sodium-dried; other solvents were standard reagents. Light petroleum refers to the fraction with b.p. 40–60 °C. Compounds crystallised from cyclohexane were heated at 80 °C for 6 h to remove adsorbed solvent.

3,13-Bis-(5-nitro-2-pyridyl)-7a,8-dihydro-(7a,11a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-ene-12,14-dione (14).^{*}—A suspension of the pyridyl dimer (1)⁴ (1.50 g, 3.45 mmol) in a solution of 1-dimethylaminobuta-1,3-diene ²⁸ (*ca.* 0.30 g, 3.1 mmol) and tetrahydrofuran (100 ml) was stirred overnight at room temperature. The resulting solution was concentrated (10 ml) *in vacuo* and chromatographed (column) (150 g SiO₂; CHCl₃–MeOH, 95 : 5) producing the *title compound* (14) (400 mg, 24%), as canary-yellow needles, m.p. 253–254 °C (decomp.) (MeCN) (Found: C, 59.0; H, 4.0; N, 16.8. C₂₄H₁₈N₆O₆ requires C, 59.3; H, 3.7; N, 17.3%); ν_{\max} (CHBr₃ film) 1 732 (sat. ketone C=O), 1 675 ($\alpha\beta$ -unsat. ketone C=O), 1 640 (enamine), 1 615 (C=C), 1 600, 1 590, and 1 580 cm⁻¹; λ_{\max} (EtOH) 215sh (ϵ 1 350), 228 (14 500), 247sh (11 000), and 366 nm (22 000); *m/e* (inlet 180 °C) 486 (10%).

3,13-Bis-(4,6-dimethoxy-1,3,5-triazin-2-yl)-7a,8-dihydro-(7a,11a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-ene-12,14-dione (15) and its Precursor (18).—A suspension of the triazinyl dimer (2)³ (10.0 g, 20.5 mmol) in a solution of 1-dimethylaminobuta-1,3-diene ²⁸ (2.5 g, 0.26 mmol) and benzene (500 ml) was stirred at room temperature overnight. The precipitate of *compound* (18) (0.5 g, 5%) was filtered off, m.p. 190 °C (decomp.) (Found: N, 21.6. C₂₆H₃₁N₉O₆ requires N, 22.3%); ν_{\max} (CHBr₃ film) 1 770 (sat. ketone C=O), 1 630 (enamine), 1 615 (C=C), 1 580, and 1 540 cm⁻¹;

* Systematic name: 13,15-bis-(5-nitro-2-pyridyl)-13,15-diazatetracyclo[7.5.1.1^{10,14}.0^{3,8}]hexadeca-3,5,11-triene-2,16-dione. Other compounds should be named similarly, *i.e.* (15)–(17).

λ_{\max} (CHCl₃) 252sh (15 000) and 270 nm (17 000); the filtrate was concentrated (20 ml) *in vacuo* and chromatographed (column) (300 g SiO₂; light petroleum–EtOAc, 1 : 1 then EtOAc) by gradient elution to yield the *title compound* (15) (7.5 g, 67%) as microcrystals, m.p. 204–206 °C (cyclohexane) (Found: C, 55.1; H, 4.8; N, 20.9. C₂₄H₂₄N₈O₆ requires C, 55.4; H, 4.7; N, 21.5%); ν_{\max} (CHBr₃ film) 1 740 (sat. ketone C=O), 1 680 ($\alpha\beta$ -unsat. ketone C=O), 1 640 (enamine), 1 615 (C=C), and 1 580–1 540 cm⁻¹; λ_{\max} (EtOH) 215sh (ϵ 10 000), 232 (13 000), and 269 nm (13 000); *m/e* 520.180 62.

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-12a,12-dihydro-(8a,12a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-ene-8,14-dione (16).—A suspension of the pyrimidinyl dimer (3) \rightleftharpoons (4)⁴ (39 g, 97 mmol) in a solution of 1-dimethylaminobuta-1,3-diene ²⁸ (18.7 g, 193 mmol) and toluene (750 ml) was stirred at room temperature overnight. The solution was concentrated *in vacuo* (50 ml) and chromatographed (column) (1 000 g SiO₂; EtOAc) to give *compound* (16) (42 g, 95%) as yellow plates, m.p. 225–226 °C (EtOH) (Found: C, 68.3; H, 5.8; N, 18.4. C₂₆H₂₆N₆O₂ requires C, 68.7; H, 5.8; N, 18.5%); ν_{\max} (CHBr₃ film) 1 730 and 1 720 (sat. ketone C=O), 1 675 ($\alpha\beta$ -unsat. ketone C=O), 1 640 (enamine), 1 618 (C=C), 1 580, 1 560, and 1 545 cm⁻¹; λ_{\max} (EtOH) 213sh (ϵ 12 400), 250sh (22 500), 270 (27 500), and 295sh (11 250) nm; *m/e* 454.210 7.

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-8,14-dioxo-8a,11-,12,12a-tetrahydro-(8a,12a-benzo)-N-phenyl-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-ene-8a,11-dicarboximide (20).—A solution of (16) (0.50 g, 1.1 mmol) and *N*-phenylmaleimide ²⁹ (0.38 g, 2.2 mmol) in 1,2-dichloroethane (25 ml) was heated under reflux for 4 days. The resulting precipitate was filtered off to give the *title compound* (20) (140 mg, 21%) as pale yellow plates, m.p. 289–290 °C (MeCN) (Found: C, 68.9; H, 5.3; N, 15.3. C₃₆H₃₃N₇O₄ requires C, 68.9; H, 5.3; N, 15.6%); ν_{\max} (CHBr₃ film) 1 770w, 1 715br, 1 640 (enamine), 1 580, and 1 560 cm⁻¹; λ_{\max} (CHCl₃) 252sh (ϵ 15 000) and 272 nm (22 000); *m/e* (inlet 190 °C) 628 (1%), 252 (48), and 202 (100%); a second crop was obtained as an off-white solid (120 mg, 17%) when the filtrate was refluxed for a further 7 days. The remaining solution was subjected to chromatography (column) (60 g Al₂O₃; light petroleum–EtOAc, 1 : 1) to yield a further 200 mg (29%) of the adduct.

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-5-bromo-12a,12-dihydro-(8a,12a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-ene-8,14-dione (17).—A solution of (16) (0.50 g, 1.1 mmol) and *N*-bromosuccinimide (0.20 g, 1.1 mmol) in carbon tetrachloride (25 ml) was refluxed for 4 h. On cooling, the precipitated succinimide was filtered off and the filtrate was evaporated to dryness *in vacuo*. The bright yellow crystalline residue was chromatographed (50 g SiO₂; light petroleum–EtOAc, 2 : 1) to yield *compound* (17) (0.56 g, 95%), as yellow microcrystals, m.p. 197–198 °C (cyclohexane) (Found: C, 58.6; H, 5.0; Br, 14.6; N, 15.4. C₂₆H₂₅BrN₆O₂ requires C, 58.5; H, 4.7; Br, 15.0; N, 15.8%); ν_{\max} (CHBr₃ film) 1 735 (sat. ketone C=O), 1 680 ($\alpha\beta$ -unsat. ketone C=O), 1 635 (enamine), and 1 618 cm⁻¹ (C=C); λ_{\max} (EtOH) 211sh (ϵ 18 000), 245 (38 000), 279 (44 000), and 300sh nm (19 000); *m/e* (inlet 160 °C) 534 (1%), 532 (1), 282 (20), and 280 (20%).

(b) A deep-orange solution of (16) (0.50 g, 1.1 mmol) in 1,2-dichloroethane (20 ml) was treated with bromine (0.18 g, 1.1 mmol) in dichloromethane (5 ml), dropwise, during 20 min at room temperature. The resulting yellow solution

was stirred for a further 4 h, then evaporated to dryness *in vacuo*. The residue (0.6 g) was chromatographed by preparative t.l.c. (light petroleum–EtOAc, 2 : 1) to produce compound (17) (130 mg, 22%) as a yellow microcrystalline solid having spectral (n.m.r., i.r.) data as above.

3,13-Bis-(4,6-dimethoxy-s-triazin-2-yl)-(7a,11a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-ene-12,14-dione (23).—A mixture of (15) (0.50 g, 0.96 mmol), activated manganese dioxide¹⁹ (8.0 g) (activated at 80 °C for 4 days), and EtOAc (250 ml) was stirred under reflux for 3 days. The hot mixture was filtered and the manganese dioxide was subjected to continuous extraction (3 days) with EtOAc (250 ml). The combined extracts were evaporated *in vacuo* to produce a pale brown solid of (23) (0.22 g, 44%). Preparative t.l.c. (light petroleum–EtOAc, 2 : 3) produced the title compound (23) (60 mg, 12%) as needles, m.p. 234–235 °C (EtOH); ν_{\max} . (CHBr₃ film) 1 740 (sat. ketone C=O), 1 690 ($\alpha\beta$ -unsat. ketone C=O), 1 640 (enamine), and 1 590–1 530 cm⁻¹; λ_{\max} . (EtOH) 213 (ϵ 6 850), 250 (6 400), and 265sh nm (4 350) (Found: *m/e*, 518.163 6. C₂₄H₂₂N₈O₆ requires *M*, 518.490 0; calc. % *M* + 1/*M* = 29.3%, obs. % *M* + 1/*M* = 28.6%; calc. % *M* + 2/*M* = 4.4%, obs. % *M* + 2/*M* = 4.1%).

2-Amino-4,6-dimethoxy-1,3,5-triazine.—Following the same procedure as above with (15) (3.0 g, 5.8 mmol), activated manganese dioxide (33.0 g) (dried at room temperature without thermal activation), and EtOAc (500 ml) produced the title compound (0.50 g, 55%) as plates, m.p. 218–219 °C (EtOH) (lit.³⁰ 219 °C) (Found: C, 38.5; H, 5.2; N, 35.7. C₅H₈N₄O₂ requires C, 38.5; H, 5.2; N, 35.9%); ν_{\max} . (CHBr₃ film) 3 320 and 3 160 (NH₂), 1 640, and 1 560 cm⁻¹; *m/e* (inlet 300 °C) 156 (100%).

3,13-Bis-(4,6-dimethoxy-1,3,5-triazin-2-yl)-(7a,11a-benzo)-14-hydroxy-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-en-12-one (26).—A solution of methanolic 1% KOH (10 ml) and (15)³ (1.0 g, 1.9 mmol) was heated under reflux for 3 h. The reaction was monitored by t.l.c. (MeOH–CHCl₃, 1 : 9). The solution was evaporated to dryness *in vacuo* to produce a solid residue which was dissolved in water (15 ml) and neutralised with glacial HOAc (*ca.* 20 drops). The resulting yellow precipitate was filtered off and dried under suction (0.67 g). Preparative t.l.c. yielded the title compound (26) (200 mg, 20%) as prisms, m.p. 294–295 °C (EtOH) (Found: N, 21.0. C₂₄H₂₄N₈O₆ requires N, 21.5%); ν_{\max} . (CHBr₃ film) 3 440 (O–H), 1 686 ($\alpha\beta$ -unsat. ketone C=O), 1 660, 1 610, 1 580, and 1 540 cm⁻¹.

3,13-Bis-(4,6-diethoxy-1,3,5-triazin-2-yl)-(7a,11a-benzo)-14-hydroxy-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-en-12-one (25).—A solution of (15)³ (1.0 g, 1.9 mmol) in absolute EtOH (20 ml) was refluxed for 5 min. Ethanolic 1% KOH solution was added (10 ml) and the resulting solution was refluxed for 15 min. After work-up (as above), a pale peach solid was obtained which after t.l.c. (CHCl₃, 4 developments) yielded the title compound (0.30 g, 24%) as yellow microcrystals, m.p. 205 °C; ν_{\max} . (CHBr₃ film) 3 400 (OH), 1 685 ($\alpha\beta$ -unsat. ketone C=O), 1 575, and 1 545 cm⁻¹; λ_{\max} . (EtOH) 220sh (ϵ 20 000), 235 (20 000), and 265sh nm (19 000); *m/e* (inlet 220 °C) 576.244 3 (3.4%) (calc. for C₂₈H₃₂N₈O₆: 576.582), and 313 (97, C₁₆H₁₇N₄O₃).

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-(8a,12a-benzo)-14R-hydroxy-3,13-diazatricyclo[5.3.1.1^{2,6}]dodec-4-en-8-one (27).—(a) A suspension of (16) (5.0 g, 10.1 mmol) in absolute EtOH (150 ml) was heated under reflux for 5 min. Then ethanolic 1% KOH was added in two portions (50 ml) and the resulting solution was refluxed for 15 min.

The reaction was monitored by t.l.c. (light petroleum–EtOAc, 3 : 1). The solution was concentrated *in vacuo* (5 ml), poured into ice-water (200 ml), and neutralised with glacial HOAc (*ca.* 4 ml). The resulting precipitate yielded the title compound (27) (4.7 g, 96%), as lemon-yellow plates, m.p. 241–242 °C (EtOH) (Found: C, 68.3; H, 5.9; N, 18.4. C₂₆H₂₆N₆O₂ requires C, 68.7; H, 5.8; N, 18.5%); ν_{\max} . (CHBr₃ film) 3 460 (OH), 1 730w, 1 675 ($\alpha\beta$ -unsat. ketone C=O), 1 635 (enamine), 1 570, and 1 450 cm⁻¹; λ_{\max} . (EtOH) 212 (ϵ 18 000), 254 (35 000), 264sh (27 000), and 303 nm (4 300); *m/e* (inlet 140 °C) 454 (18%), and 252 (100, C₁₅H₁₄N₃O).

(b) A suspension of (16) (0.485 g, 1.07 mmol) in absolute EtOH (15 ml) and benzaldehyde (0.11 g, 1.04 mmol) were heated under reflux for 5 min. This was then treated as above with ethanolic 4% KOH (5 ml), ice-water (80 ml), and glacial HOAc (only 2 drops) to produce the crystalline title compound (27) (0.49 g, 100%), m.p. 241–242 °C.

Oxidation of (27) with Chromate.—(a) A solution of the alcohol (27) (0.454 g, 1.00 mmol) in CH₂Cl₂ (*ca.* 1 ml) was added in one portion at room temperature to a well-stirred solution of pyridinium chlorochromate³¹ (0.324 g, 1.50 mmol) in dichloromethane (*ca.* 2 ml; P₄O₁₀ dried). The reaction was monitored by t.l.c. (light petroleum–EtOAc, 2 : 1). After 2 h, the tarry deposit produced was filtered off and washed with CH₂Cl₂ (2 ml). The combined extracts were treated with Et₂O (10 ml) to induce precipitation of chromium residues (0.4 g). The yellow filtrate was evaporated to dryness *in vacuo* to produce a ketone (100 mg, 21%), recrystallised as needles, m.p. 210–211 °C (EtOH) (Found: C, 66.3; H, 5.6; N, 17.7. C₂₆H₂₆N₆O₃ requires C, 66.4; H, 5.6; N, 17.9%); ν_{\max} . (CHBr₃ film) 1 685 ($\alpha\beta$ -unsat. ketone C=O), and 1 600–1 540 cm⁻¹; λ_{\max} . (EtOH) 215 (ϵ 18 000), 241 (41 000), and 280sh nm (12 000); *m/e* 470.205 94, and 252 (100%, C₁₅H₁₄N₃O); δ (CDCl₃) 8.04 (1 H, dd, *J* 7, 1.5 Hz), 7.6–7.3 (3 H, complex), 7.45 (1 H), 6.57 (2 H, d, *J* 2.2 Hz), 6.36 (1 H, s, 5'-H), 6.16 (1 H, s), 6.12 (1 H, s, 5''-H), 4.55 (1 H, t, *J* 4, 4 Hz), 4.20 (1 H, t, *J* 4, 2 Hz), 4.10 (1 H, s), 2.4 (1 H), 2.3 (3 H, s, Me), and 2.1 (3 H, s, Me).

(b) Chromium trioxide (0.665 g, 9.20 mmol) was added at room temperature to a well stirred mixture of pyridine (1.06 g, 13 mmol) and CH₂Cl₂ (15 ml; P₄O₁₀ dried). The alcohol (27) (0.500 g, 1.10 mmol) in CH₂Cl₂ (1 ml; P₄O₁₀ dried) was added to this mixture in one portion. A dark brown deposit soon formed and the mixture was stirred for a further 15 min. The deposit was filtered off, washed with CH₂Cl₂ (5 ml), and the combined extracts were washed successively with 5% solutions of aqueous NaOH (3 × 10 ml), HCl (10 ml), aqueous NaHCO₃ (10 ml), and finally with saturated NaCl (10 ml), and dried (MgSO₄). The solvent was removed *in vacuo* to leave a yellow solid (100 mg). Preparative t.l.c. (light petroleum–EtOAc, 2 : 1, 3 developments) yielded the same ketone as a pale yellow crystalline solid (54 mg, 10%), m.p. 210–211 °C.

Oxidation of (27) with Manganese Dioxide.—A mixture of the alcohol (27) (0.40 g, 0.88 mmol), very active manganese dioxide¹⁹ (2.0 g) (activated at 80 °C for 4 days), and CHCl₃ (100 ml) was stirred and refluxed for 21 h. The hot mixture was filtered under suction, and the manganese dioxide was extracted with boiling CHCl₃ (6 × 50 ml). The combined filtrates were evaporated to dryness *in vacuo* and the residue chromatographed on silica (preparative t.l.c. light petroleum–EtOAc, 2 : 1). The foremost band yielded a further ketone (17 mg) as plates, m.p. 294 °C (benzene) (Found: C, 66.9; H, 5.4; N, 17.9. C₂₆H₂₅N₆O₃ requires C, 66.5; H,

5.4; N, 17.9%); ν_{\max} (CHBr₃ film) 1 782 (sat. ketone C=O), 1 678 ($\alpha\beta$ -unsat. ketone C=O), 1 595, 1 580, and 1 565 cm⁻¹; λ_{\max} (CHCl₃) 250 (ϵ 7 500) and 280sh (2 500) nm; m/e , no M^{+} ; δ (CDCl₃) 8.02 (1 H, dd, J 7, 1.5 Hz), 7.45 (1 H), 7.6—7.2 (3 H, complex), 6.70 (1 H, dd, J 4, 2 Hz), 6.60 (1 H, s), 6.40 (1 H, s), 6.22 (1 H, s), 6.12 (1 H, s), 4.86 (1 H, dd, J 6, 5 Hz), 4.48 (1 H, t, J 5, 4 Hz), 2.92 (1 H, dd, J 6, 3 Hz), 2.3 (3 H, s, Me), and 2.1 (3 H, s, Me).

The next band produced starting material (27) (20 mg, 5%). The lowest band produced a ketone (33 mg, 16%), identical (n.m.r., i.r.) with that prepared by the chromate reaction above.

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-(8a,12a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]-14S-hydroxydodec-4-en-8-one (28).—Ethanol potassium hydroxide (4%, 10 ml) was added to a solution of the diketone (21) (1.0 g, 2.2 mmol) in EtOH (20 ml) and the mixture heated under reflux for 90 min. The reaction product was evaporated to dryness *in vacuo* and the residual gum treated with water (100 ml). Glacial acetic acid was added until the mixture was neutral to litmus. The resulting precipitate was collected, dried, and purified by preparative t.l.c. on silica gel (MeCOEt-light petroleum). The *title compound* (28) was isolated as yellow plates (50 mg, 10%), m.p. 285—286 °C (EtOH) (Found: C, 68.6; H, 5.9; N, 18.1. C₂₆H₂₆N₆O₂ requires C, 68.7; H, 5.8; N, 18.5%); ν_{\max} (CHBr₃) 3 400 (O-H), 1 680 ($\alpha\beta$ -unsat. ketone, C=O), 1 625 (N=C=C), 1 570, 1 470, and 1 425 cm⁻¹; λ_{\max} (EtOH) 215 (ϵ 13 000), 256 (29 000), 265 (23 000), and 304 nm (7 600).

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-14-methylthio-methoxy-(8a,12a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]-dodec-4-en-8-one (29) and *its Acetate* (30).—The alcohol (27) (4.50 g, 10 mmol), Me₂SO (30 ml), and Ac₂O (20 ml, ca. 200 mmol) were stirred for 24 h at room temperature. The reaction was monitored by t.l.c. (light petroleum-EtOAc, 4:1). The mixture was diluted with EtOH (150 ml) and water (20 ml), cooled and basified with ammonia (d 0.88), and finally diluted with water (200 ml). The precipitate formed was filtered off, dried under suction (3.0 g), and 0.5 g chromatographed on silica (preparative t.l.c., light petroleum-EtOAc, 4:1, 4 developments). The two-component mixture was narrowly resolved. The foremost band yielded the *ether* (29) (100 mg, 12%) as pale yellow needles, m.p. 193—194 °C (EtOH) (Found: C, 65.5; H, 5.8; N, 16.7. C₂₈H₃₀N₆O₂S requires C, 65.4; H, 5.9; N, 16.3%); ν_{\max} (CHBr₃ film) 1 685 ($\alpha\beta$ -unsat. ketone C=O), 1 640 (enamine), and 1 600—1 560 cm⁻¹; λ_{\max} (EtOH) 212 (ϵ 18 000), 254 (25 500), 265sh (20 000), and 305sh nm (5 500); m/e 514.214 69; the second band yielded a pale yellow solid (350 mg). This was a mixture of the ester (30) and the ketone (21) (1:3, according to n.m.r.). Recrystallisation produced the *acetate* (30) (100 mg, 12%), as pale yellow prisms, m.p. 269—270 °C (EtOH) (Found: C, 67.5; H, 5.7; N, 17.0. C₂₈H₂₈N₆O₃ requires C, 67.7; H, 5.7; N, 16.9%); ν_{\max} (CHBr₃ film) 1 735 (ester C=O), 1 685 ($\alpha\beta$ -unsat. ketone C=O), 1 640 (enamine), and 1 600—1 550 cm⁻¹; λ_{\max} (EtOH) 210 (ϵ 18 000), 255 (19 000), 270sh (14 000), and 300sh nm (4 400); m/e 496.223 36.

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-(8a,12a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]-dodec-4-ene-8,14-dione (21).—(a) Trifluoroacetic acid (2.52 g, 30 mmol) was added to cold pyridine (3.2 ml, 40 mmol) dropwise. The solid pyridinium trifluoroacetate in dimethyl sulphoxide (35 ml) was added to a stirred solution of the alcohol (27) (20.0 g, 35 mmol) in dimethyl sulphoxide (25 ml) and toluene (60 ml). Dicyclo-

hexylcarbodi-imide was added (30 g, 150 mmol) and the mixture was stirred for 24 h at 18 °C. The reaction was monitored by t.l.c. (light petroleum-EtOAc, 2:1). The resulting solution was poured into Et₂O (1 l). A solution of oxalic acid (18.0 g, 180 mmol) in MeOH (25 ml) was added in one portion. The mixture was stirred frequently until the mild effervescence subsided (60 min). Some precipitation of dicyclohexylurea occurred at this stage. Water was added (1 l) and the mixture was stirred vigorously to induce further precipitation of the urea. The ethereal layer was carefully decanted, extracted with aqueous 5% NaHCO₃ (2 × 400 ml) (until effervescence ceased), and then with water (3 × 400 ml), and finally dried (MgSO₄). The solution was concentrated to small volume (50 ml) *in vacuo* and on standing (3 h) yielded the *title compound* (21) (5.4 g, 27%), as pale yellow cubes, m.p. 203—204 °C (EtOH) (Found: C, 69.1; H, 5.5; N, 18.6. C₂₆H₂₄N₆O₂ requires C, 69.0; H, 5.4; N, 18.6%); ν_{\max} (CHBr₃ film) 1 730 (sat. ketone C=O), 1 680 ($\alpha\beta$ -unsat. ketone C=O), 1 632 (enamine), and 1 600—1 560 cm⁻¹; λ_{\max} (EtOH) 212 (ϵ 19 000), 240sh (20 000), 258 (37 000), 265sh (28 000), and 290 nm (9 800); m/e (inlet 130 °C) 452 (28%), 329 (10), 251 (100), and 201 (10). The filtrate was chromatographed (column) (300 g SiO₂; light petroleum-EtOAc, 2:1) to yield a further 5.8 g (29%) of compound (21).

(b) Compound (16) (0.45 g, 1.0 mmol), 10% Pd-C (0.20 g), and cyclohexane (200 ml) were heated under reflux for one week. The filtrate was allowed to stand at room temperature for two weeks to precipitate the *title compound* (21) (130 mg, 29%), identical (n.m.r., i.r., t.l.c.) with that prepared above.

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-(7a,11a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]-dodec-4-ene-12,14-dione (24).—A solution of (21) (0.50 g, 1.10 mmol) in 1,2-dichloroethane (30 ml) was heated under reflux for 48 h. The reaction was monitored by t.l.c. Preparative t.l.c. (light petroleum-EtOAc, 2:1) produced *compound* (24) (50 mg, 10%), as diamond prisms, m.p. 233—234 °C (EtOH) (Found: C, 68.9; H, 5.4; N, 18.3. C₂₆H₂₄N₆O₂ requires C, 69.0; H, 5.4; N, 18.6%); ν_{\max} (CHBr₃ film) 1 730 (sat. ketone C=O), 1 680 ($\alpha\beta$ -unsat. ketone C=O), 1 632 (enamine), and 1 600—1 560 cm⁻¹; λ_{\max} (EtOH) 211 (ϵ 18 000), 240sh (23 000), 253 (30 000), 260sh (22 500), and 300sh nm (7 000); m/e 452.193 2 (16.0%).

3,13-Bis-(4,6-dimethylpyrimidin-2-yl)-5-tricyanovinyl-(8a,12a-benzo)-3,13-diazatricyclo[5.3.1.1^{2,6}]-dodec-4-ene-8,14-dione (22).—Compound (21) (200 mg, 0.440 mmol), tetracyanoethylene (200 mg, 1.56 mmol), and hydroquinone (ca. 50 mg) in 1,2-dichloroethane (10 ml) were heated under reflux for 30 min. The reaction was monitored by t.l.c. The copious precipitate was removed and the orange filtrate chromatographed (preparative t.l.c., light petroleum-EtOAc, 2:1) to yield an orange solid (9) (40 mg); ν_{\max} (CHBr₃ film) 3 380, 2 200, 1 685, 1 595, 1 580, and 1 560—1 540 cm⁻¹; recrystallisation yielded the *title compound* (22) (10 mg, 4%) as orange needles, m.p. 295 °C (decomp.) (EtOAc) (Found: C, 67.2; H, 4.5; N, 22.5. C₃₁H₂₃N₉O₂ requires C, 67.3; H, 4.2; N, 22.8%); ν_{\max} (CHBr₃ film) 2 200 (C≡N), 1 745 (sat. ketone C=O), 1 695 ($\alpha\beta$ -unsat. ketone C=O), 1 595, 1 580, 1 560, and 1 540 cm⁻¹; λ_{\max} (EtOH) 213 (ϵ 16 000), 247 (15 000), 290sh (6 300), and 460 nm (22 500); m/e (inlet 140 °C) 553 (12%).

Mixed Cycloaddition Reactions with the Dimer (21).—(i) *With N-phenylmaleimide*. The dimer (0.30 g, 0.66 mmol)

and *N*-phenylmaleimide (0.20 g, 1.2 mmol) in 1,2-dichloroethane (30 ml) were heated under reflux overnight. The solution was concentrated *in vacuo* and chromatographed on silica (preparative t.l.c., light petroleum-EtOAc, 2:1). The second band yielded 2-(4,6-dimethylpyrimidin-2-yl)-1,3-ethano-4-oxo-1,2,3,4-tetrahydro-*N*-phenylisoquinoline-9,10-exo-dicarboximide (38) (50 mg, 20%), as prisms, m.p. 267—268 °C (EtOH-MeCN) (Found: C, 70.3; H, 4.7; N, 13.1. $C_{25}H_{20}N_4O_3$ requires C, 70.7; H, 4.8; N, 13.2%); ν_{\max} (CHBr₃ film) 1 780, 1 730—1 690, and 1 600 cm^{-1} ; λ_{\max} (EtOH) 215 (ϵ 12 000) and 240 (11 000) nm; *m/e* (inlet 70 °C) 424 (21%) and 251. The lowest band yielded 8-(4,6-dimethylpyrimidin-2-yl)-2-oxo-*N*-phenyl-8-azabicyclo[3.2.1]oct-3-ene-6,7-exo- and -endo-dicarboximide (32) and (33) (80 mg, 36%), as yellow needles, m.p. 216 °C (EtOH) (Found: C, 67.7; H, 4.8; N, 14.4. $C_{21}H_{18}N_4O_3$ requires C, 67.4; H, 4.9; N, 15.0%); ν_{\max} (CHBr₃ film) 1 780, 1 725, 1 705, and 1 685 cm^{-1} ; λ_{\max} (CHCl₃) 242 (ϵ 21 000) and 280 nm (5 000); *m/e* (inlet 350 °C) 374 (70%).

(ii) *With acrylonitrile*. The dimer (21) (1.2 g, 2.7 mmol), acrylonitrile (20 ml), and hydroquinone (25 mg) in 1,2-dichloroethane (40 ml) were heated under reflux for 24 h. The solution was concentrated *in vacuo* and chromatographed on silica (preparative t.l.c., light petroleum-EtOAc, 3:1). A solid (500 mg) was isolated and further chromatographed by preparative t.l.c. (light petroleum-EtOAc, 8:1, 12 developments). 2-(4,6-Dimethylpyrimidin-2-yl)-1,3-ethano-4-oxo-tetrahydroisoquinoline-9-exo- and -10-exo-carbonitrile (44) and (45) (50 mg, 15%) were isolated as plates, m.p. 203 °C (decomp.) (EtOH) (Found: C, 71.1; H, 5.2; N, 18.2. $C_{18}H_{16}N_4O$ requires C, 71.0; H, 5.3; N, 18.4%); ν_{\max} (CHBr₃ film) 2 220 (C≡N), 1 690 ($\alpha\beta$ -unsat. ketone C=O), 1 595, and 1 585 cm^{-1} ; λ_{\max} (EtOH) 215 (ϵ 3 000) and 235 (4 000) nm; *m/e* (inlet 300 °C) 304 (77%). The least polar substance was 8-(4,6-dimethylpyrimidin-2-yl)-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-exo-carbonitrile (34) (200 mg, 71%), identical (n.m.r., i.r.) with that previously prepared.²⁶

(iii) *With α -chloroacrylonitrile*. The dimer (21) (1.0 g, 2.2 mmol), α -chloroacrylonitrile (10 ml), and hydroquinone (25 mg) in 1,2-dichloroethane (30 ml) were heated under reflux for 48 h. The resulting solution was filtered, concentrated *in vacuo*, and chromatographed on silica (preparative t.l.c., light petroleum-EtOAc, 9:1, 10 developments). 6-Chloro-8-(4,6-dimethylpyrimidin-2-yl)-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-carbonitrile (35) (360 mg, 56%) was separated as pale yellow microcrystals having identical spectral (n.m.r., i.r.) properties with that previously prepared.²⁶ 9-Chloro-2-(4,6-dimethylpyrimidin-2-yl)-1,3-ethano-4-oxo-1,2,3,4-tetrahydroisoquinoline-9-carbonitrile (47) (360 mg, 48%) was isolated and crystallised as colourless microcrystals, m.p. 189—191 °C (EtOH) (Found: C, 63.6; H, 4.6; Cl, 10.5; N, 16.4. $C_{18}H_{15}ClN_4O$ requires C, 63.8; H, 4.5; Cl, 10.5; N, 16.5%); ν_{\max} (CHBr₃ film) 2 230 (C≡N), 1 700 ($\alpha\beta$ -unsat. ketone C=O), 1 595, 1 585, and 1 555 cm^{-1} ; λ_{\max} (EtOH) 216 (ϵ 10 000), 247 (24 000), and 287 nm (5 100); *m/e* (inlet 300 °C) 340 (20%) and 338 (56).

(iv) *With maleic anhydride*. The dimer (21) (0.30 g, 0.66 mmol) and maleic anhydride (0.13 g, 1.3 mmol) in 1,2-dichloroethane (10 ml) were heated under reflux for 24 h. The solution, after standing overnight at room temperature yielded 8-(4,6-dimethylpyrimidin-2-yl)-2-oxo-azabicyclo[3.2.1]oct-3-ene-6-exo,7-exo-dicarboxylic anhydride (36) (100 mg, 50%), as cubes, m.p. 263—264 °C (decomp.)

(1,2-dichloroethane) (Found: C, 59.6; H, 4.6; N, 13.6. $C_{15}H_{13}N_3O_4$ requires C, 60.2; H, 4.4; N, 14.0%); ν_{\max} (CHBr₃ film) 1 860, 1 790, 1 780, 1 705, 1 685 ($\alpha\beta$ -unsat. ketone C=O), 1 585, and 1 570 cm^{-1} ; λ_{\max} (CHCl₃) 246 (4 600) and 280 nm (1 300); *m/e* (inlet 320 °C) 299 (100%).

(v) *With styrene*. The dimer (21) (0.40 g, 0.89 mmol) and styrene (3 g, 19 mmol) in 1,2-dichloroethane (50 ml) were heated under reflux for 4 days. The solution was concentrated *in vacuo*, and the residue chromatographed (50 g SiO₂; EtOAc). 8-(4,6-Dimethylpyrimidin-2-yl)-6-endo-phenyl-8-azabicyclo[3.2.1]oct-3-en-2-one (31) (50 mg, 18%) was isolated as yellow microcrystals with spectral (n.m.r., i.r.) properties identical with those previously prepared.⁵

8-(4,6-Dimethylpyrimidin-2-yl)-2-oxo-8-azabicyclo[3.2.1]oct-3-ene-6-exo,7-exo-dicarboxylic Anhydride (36).—The pyrimidinyl dimer (3) \rightleftharpoons (4) (0.30 g, 0.75 mmol) and maleic anhydride (0.15 g, 1.5 mmol) in 1,2-dichloroethane (10 ml) were heated under reflux for 3 h. The solution, after standing overnight at room temperature gave the title compound (36) (210 mg, 47%), as cubes, m.p. 265—266 °C (decomp.) (1,2-dichloroethane) (Found: C, 59.9; H, 4.5; N, 14.0. $C_{15}H_{13}N_3O_4$ requires C, 60.2; H, 4.4; N, 14.0%), identical (n.m.r., i.r.) with that prepared above.

8-(4,6-Dimethylpyrimidin-2-yl)-2-oxo-*N*-phenyl-8-azabicyclo[3.2.1]oct-3-ene-6,7-exo-dicarboximide (32).—The pyrimidinyl dimer (0.50 g, 1.2 mmol) and *N*-phenylmaleimide (0.43 g, 2.5 mmol) in 1,2-dichloroethane (15 ml) were heated under reflux for 1 week. The solution, after standing overnight at room temperature produced the *exo*-adduct (32) (0.46 g, 50%), as yellow needles, m.p. 238—239 °C (MeCN) (Found: C, 67.4; H, 5.0; N, 15.0. $C_{21}H_{18}N_4O_3$ requires C, 67.4; H, 4.9; N, 15.0%); identical to that [*exo*-component (32) of the mixture (32) and (33), ¹H n.m.r.] prepared above.

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