Diazaindenes (Azaindoles.) Part V.[1] Synthesis, Spectra, and Tautomerism of 1,5-Diazainden-4(5*H*)-one, 1,4- and 1,6-Diazainden-2(3*H*)-one, and some 3-Substituted Derivatives

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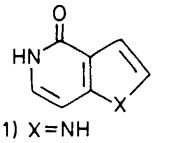
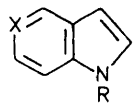
1,5-Diazaindene 5-oxide has been prepared and rearranged, giving 1-acetyl-1,5-diazainden-4(5*H*)-one (1). Compound (1) has also been obtained from either (a) *cis*-3-(pyrrol-2-yl)acrylic acid or (b) 1,5-oxazainden-4(5*H*)-one. 1,4- and 1,6-Diazainden-2(3*H*)-one and some 3-substituted derivatives have been synthesised from the corresponding chloronitropyridines. Spectra show that the location of the nitrogen atom in the pyridine ring and the type of 3-substituent markedly influence the position of tautomeric equilibrium.

DIAZAINDENONES containing the carbonyl group as part of a lactam system [*e.g.* (1)] would be useful intermediates in the synthesis of the parent diazaindenes or substituted derivatives, but relatively few such lactams have been reported,[2-4] though mention has been made of attempts to obtain some of them.[5,6] We report syntheses and some properties of three members of this series of compounds.

An efficient route to 1,5-diazainden-4(5*H*)-one (1) is particularly interesting since compound (1) is a potential intermediate in the synthesis of analogues of important purines and the pyrrolopyrimidine nucleoside antibiotics.[7] A recent synthesis of 1-substituted derivatives [*e.g.* (2)] could not be modified to yield (1).[8] A potential approach to (1) involves the *N*-oxidation of 1,5-diazaindene (5) and rearrangement of the *N*-oxide (6) in the presence of acetic anhydride. Our initial attempt to obtain (6) by treatment of 1-acetyl-1,5-diazaindene (7) with



(1) X=NH
(2) X=NMe
(3) X=NAc
(4) X=O



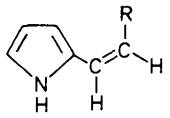
(5) R=H, X=N
(6) R=H, X=$\overset{+}{N}-\bar{O}$
(7) R=Ac, X=N

hydrogen peroxide in acetic acid caused ring opening of the pyrrole system.[1]

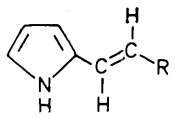
[1] Part IV, B. A. J. Clark and J. Parrick, *Tetrahedron*, 1974, **30**, 475.
[2] R. E. Willette, *Adv. Heterocyclic Chem.*, 1968, **9**, 27.
[3] L. N. Yakhontov, *Russ. Chem. Rev.*, 1968, **37**, 551.
[4] B. Frydman, S. J. Reil, J. Boned, and H. Rapoport, *J. Org. Chem.*, 1968, **33**, 3762.
[5] R. E. Willette, *J. Chem. Soc.*, 1965, 5874.
[6] S. Okuda and M. M. Robison, *J. Org. Chem.*, 1959, **24**, 1008.
[7] R. J. Suhadolnik, 'Nucleoside Antibiotics,' Wiley-Interscience, New York, 1970, p. 298.
[8] E. Bisagni, J.-D. Bourzat, and J. André-Louisfert, *Tetrahedron*, 1970, **26**, 2087.

Treatment of the acetyldiazaindene (7) with *m*-chloroperoxybenzoic acid in dichloromethane yielded the 5-oxide (6), isolated as its hydrochloride. This gave a low yield of a 1-acetyl lactam on treatment with acetic anhydride. Only one product was isolated and this was thought to be (3), since formation of the isomeric 1-acetyl-1,5-diazainden-6(7*H*)-one would involve a higher energy transition state. The structure was not confirmed at this stage because the two pyridone ring protons had the same n.m.r. chemical shift. Although addition of sodium acetate to the rearrangement reaction mixture was expected to improve the yield of lactam, this route to (1) was not satisfactory since, in our hands, the preparation of 1,5-diazaindene proved to be troublesome and did not give the yields expected.[9]

The application of the recently described [10] pyrolytic ring closure of β-arylacryloyl azides in the presence of base to give lactams was then investigated. The direct approach from 3-(pyrrol-2-yl)acryloyl azides [(8) and (11)] was studied, since the corresponding acids [(9) and (12)] can be obtained from the readily available pyrrole-2-carbaldehyde and the cyclisation step does not involve acidic conditions. The Wittig reaction of pyrrole-2-carbaldehyde with ethoxycarbonylmethylene-(triphenyl)phosphorane gave the *cis*- (10) and the *trans*-ester (13) (15—20 and 50—55%, respectively), which were easily separated. The *trans*-acid (12) (90%) was obtained by hydrolysis of the *trans*-ester for 1 h; the *cis*-ester yielded the corresponding acid (65%) only after 12 h under the same conditions.[11] The more plentiful *trans*-acid was first converted into its azide (11), which



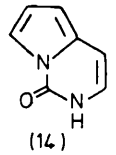
(8) R=CON_3
(9) R=CO_2H
(10) R=CO_2Et



(11) R=CON_3
(12) R=CO_2H
(13) R=CO_2Et

was stable enough for characterisation but not sufficiently soluble in suitable solvents; the pyrolysis reaction yielded an intractable black solid.

The *cis*-acid (9) yielded the azide (8) which was much less stable than the *trans*-isomer. Analytical data were not obtained but the i.r. spectrum confirmed the presence of the azide group ($\nu_{max.}$ 2150 cm^{-1}). The *cis*-azide was very soluble in dichloromethane and addition of such a solution to hot diphenyl ether–tri-n-butylamine gave 1,5-diazainden-4(5*H*)-one (1), $\nu_{max.}$ 1648 (amide CO) and 3150 and 3250 cm^{-1} (2 × NH). The n.m.r. spectrum showed the presence of six protons [two (δ 10·83 and 11·47) exchangeable], ruling out the alternative structure (14). Other cyclisations of this type are known.[10] Acetylation of (1) gave the 1-acetyl lactam (3), identical with that obtained earlier by rearrangement of the *N*-oxide.



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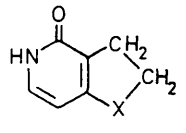
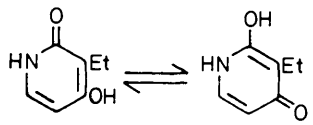


(15) X=O (16) X=N·CH_2Ph



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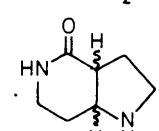


(18)

The main disadvantage of the synthesis was the small proportion of *cis*-isomer obtained in the Wittig reaction. Photochemical isomerisation of the *trans*-ester has been reported [11] and a similar conversion of *trans*-acid into *cis*-acid was obtained (*ca.* 40%), but the relatively unstable *cis*-acid was not readily separated from the mixture. Neither isomerisation process was suitable for the scale of work required. No increase in the ratio of (10) to (13) was obtained when lithium iodide was added to the Wittig reaction mixture.[12]

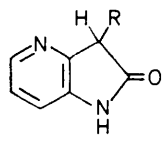
A modification of the route to (1) employing the azide pyrolysis technique as a first stage was successful. 1,5-Oxazainden-4(5*H*)-one (4) was readily obtained from commercial 3-(2-furyl)acrylic acid (shown by n.m.r. spectroscopy to be greater than 95% *trans*-isomer). Attempted hydrogenation of (4) at atmospheric pressure and 70° over Raney nickel (W2) was unsuccessful, in contrast to the reported reduction of 2-acetylbenzofuran to the 2,3-dihydro-derivative.[13] When platinum oxide and hydrogen were used at 65° and 3 atm. pressure, the product had an n.m.r. spectrum which indicated the presence of starting material (4), the required dihydro-derivative (15), and a third component, in the ratio 10 : 28 : 62, respectively. The third component was isolated; its i.r. spectrum showed the presence of NH, CO(amide), and OH groups. The n.m.r. spectrum showed two singlets at low field (each 1H and exchangeable with D_2O) and the presence of an ethyl group and two vicinal aromatic protons. Thus, the compound must have been formed by hydrogenolysis and was assigned the structure (17); it may exist in either or both of the tautomeric forms. Under similar hydrogenation conditions, but in the presence of palladised charcoal as catalyst, the dihydro-derivative (15) was obtained in high yield.

Treatment of (15) with benzylamine gave the diazaindene derivative (16). No reaction occurred at room temperature or 65° when (16) was treated with hydrogen and palladised charcoal at 3 atm. pressure in the presence of a trace of acid. When palladium black was used at room temperature and 3 atm. pressure, 3 mol. equiv. of hydrogen were absorbed and the product had i.r., n.m.r.,

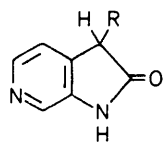
[9] R. R. Lorenz, B. F. Tullar, C. F. Koelsch, and S. Archer, *J. Org. Chem.*, 1965, **30**, 2531.
[10] F. Eloy and A. Deryckere, *Helv. Chim. Acta*, 1969, **52**, 1755.
[11] W. Flitsch and U. Neumann, *Chem. Ber.*, 1971, **104**, 2170.
[12] L. D. Bergelison, V. A. Vaver, L. T. Barsukov, and M. M. Shemyakin, *Doklady Akad. Nauk S.S.S.R.*, 1962, **143**, 111.
[13] R. L. Shriner and J. Anderson, *J. Amer. Chem. Soc.*, 1939, **61**, 2705.

and mass spectra consistent with a mixture of the *cis*- and the *trans*-octahydrodiazaindene derivatives (18). Dehydrogenation of (18) over palladium–charcoal occurred smoothly to give 1,5-diazainden-4(5*H*)-one (1) in an overall yield of 18% from furylacrylic acid.

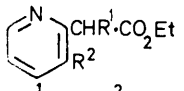
1,4- and 1,6-Diazaindene are not readily available. Syntheses of 1,4- (19) and 1,6-diazainden-2(3*H*)-one (22) appeared to provide a potential route to these compounds, since reduction of the lactam followed by oxidation would give the diazaindene. The synthesis of the 3-esters (20) and (23) was attractive, since the ester group could then be removed or modified as required. The proposed routes involved nucleophilic displacement of chlorine from the appropriate chloronitropyridine by diethyl malonate anion, followed by reduction of the nitro-group and cyclisation. When this work was started, the only aza-oxindole reported, *i.e.* 1,7-diazainden-2(3*H*)-one, had been obtained by cyclisation of 2-amino-3-pyridylacetic acid.[2] However, Willette's attempts to obtain (19) and (22) failed because the nitropyridylcyanoacetates (25) and (28) could not be hydrogenated under a variety of conditions.[5] Also, catalytic hydrogenation of (32) gave the zwitterion (33), which did not cyclise.[14]



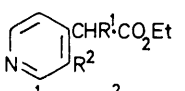
(19) R=H
(20) R=CO_2Et
(21) R=CN



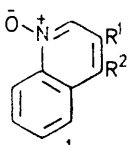
(22) R=H
(23) R=CO_2Et
(24) R=CN



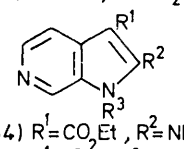
(25) R^1=CN, R^2=NO_2
(26) R^1=CO_2Et, R^2=NO_2
(27) R^1=CO_2Et, R^2=NH_2



(28) R^1=CN, R^2=NO_2
(29) R^1=CO_2Et, R^2=NO_2
(30) R^1=CO_2Et, R^2=NH_2
(31) R^1=CN, R^2=NH_2



(32) R^1=$CH(CO_2Et)_2$, R^2=NO_2
(33) R^1=$\bar{C}(CO_2Et)_2$, R^2=$\overset{+}{N}H_3$



(34) R^1=CO_2Et, R^2=NH_2, R^3=OH
(35) R^1=R^3=H, R^2=OH
(36) R^1=CN, R^2=OH, R^3=H

4-Bis(ethoxycarbonyl)methyl-3-nitropyridine (29) was obtained as a viscous oil and was readily reduced with hydrogen over palladised charcoal to the corresponding amino-diester (30); the i.r. spectrum showed twin bands attributable to NH_2 (3250 and 3450 cm^{-1}) and no evidence of zwitterion formation. This compound cyclised readily at room temperature to give ethyl 2,3-dihydro-2-oxo-1,6-diazaindene-3-carboxylate (23). Alkaline hydrolysis of (23) gave a mixture which was difficult to purify, but acidic hydrolysis and basification yielded a yellow solid (22), identified on the basis of elemental analysis and i.r. and n.m.r. spectra. N.m.r. data indicated the presence of carbonyl and hydroxy-forms, and the tautomerism of this and related compounds is discussed later. A similar synthesis from 2-chloro-3-nitropyridine gave compounds (26) and (27), the lactam (20), and then the diazaindenone (19) on acidic hydrolysis.

At about this stage in our work, a report by Finch *et al.*[15] of the preparation of 1,4-diazainden-2(3*H*)-one (19) by a similar route from ethyl 3-nitro-2-pyridylcyanoacetate (25) became available to us and, since neither they nor we had found difficulty in reducing the nitropyridylacetic esters, it was of interest to reinvestigate the reduction of ethyl 3-nitro-4-pyridylcyanoacetate (28).

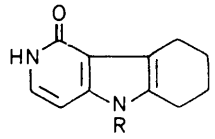
Catalytic hydrogenation of (28) gave two products. One was the amino-ester (31); on refluxing in xylene this yielded 2,3-dihydro-2-oxo-1,6-diazaindene-3-carbonitrile (24), and acidic hydrolysis gave (22). The second product was assigned structure (34) on the basis of elemental analysis and mass spectroscopic data ($C_{10}H_{11}N_2O_3$), the i.r. spectrum (overlapping absorptions of OH, NH_2, and CH), and the n.m.r. spectrum, which showed five ethyl protons and signals for six protons in the aromatic region. Of the latter, two singlets (2H and 1H, both exchangeable) were assigned to amino- and hydroxy-groups, respectively, and the remaining signals were as expected for the 4-, 5-, and 7-protons of the 1,6-diazaindene nucleus. Compound (34) was probably formed by partial reduction of the nitro-group to the hydroxylamine, followed by relatively rapid nucleophilic intramolecular attack on the cyano- or partially reduced cyano-group.[16]

The i.r. spectrum (KBr) of the 1,5-diazaindenone (1) shows peaks due to carbonyl (1648) and two NH groups (3150 and 3250 cm^{-1}); no evidence for an OH group was found. The n.m.r. spectrum [$(CD_3)_2SO$] is not first-order and shows two multiplets (each 2H) centred at δ 6·47 and 7·03, and two NH signals at δ 10·83 and 11·47. The spectrum of the 1-methyl derivative (2) shows similar multiplets at δ 6·48 and 7·05, and a singlet at 10·93, and 5,6,7,8-tetrahydro-γ-carbolin-4-one (37) shows one-proton doublets at 6·83 and 7·50 and singlets at 11·53 and 12·05 [this last peak is not present in the spectrum of the 1-acetyl derivative (38)].[17] Comparison of these spectra led to the following assignments for the spectrum of (1): δ 6·47 (H-3 and -7), 7·03 (H-2 and -6), 10·83 (H-5), and 11·47 (H-1).

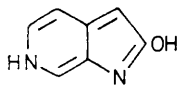
The corresponding spectra of the azaoxindoles (19) and (22) and their derivatives showed significant differences. The i.r. spectrum (KBr) of (19) showed a strong carbonyl peak at 1695, with shoulders at 1710 and 1760 cm^{-1}. Multiple peaks due to the carbonyl group in the

[14] H. J. Richter and N. E. Rustad, *J. Org. Chem.*, 1964, **29**, 3381.
[15] N. Finch, M. M. Robison, and M. I. Valerio, *J. Org. Chem.*, 1972, **37**, 51.
[16] R. J. Sundberg, 'The Chemistry of Indoles,' Academic Press, 1970, p. 180.
[17] B. A. J. Clark and J. Parrick, unpublished result.

spectrum of oxindoles have been reported and discussed.[18] However, the spectrum of the 1,6-isomer (22) showed a weak carbonyl peak at 1660 and a broad peak (3400—2200) with $\nu_{max.}$ 2750 cm^{-1} assigned to OH. It seems likely that the 1,6-isomer exists under these conditions



(37) R=H
(38) R=Ac



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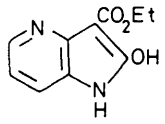

(40)

largely in the enol form (35), though the form (39) has not been excluded. The spectrum of the ester of the 1,4-diazaindene system (20) shows a weak carbonyl band at 1700 cm^{-1} (shoulder at 1720) and a broad absorption at 2600—3400 cm^{-1}, showing the importance of the form (40). The isomeric ester (23) shows a strong absorption at 1690 cm^{-1} and little evidence of an OH group. In contrast, the spectrum of the 3-cyano-derivative (36) of the 1,6-diazaindene system has a strong broad peak (2400—3700) with $\nu_{max.}$ 3200 cm^{-1} and a weak peak at 1640 cm^{-1}. This difference in preferred tautomeric form with the nature of the substituent is in line with the findings of Finch *et al.* for the 1,4-diazainden-2(3*H*)-one series.[15]

The existence of the enol forms (36) and (40) in [$^2H_6$]dimethyl sulphoxide is shown by their n.m.r. spectra, which each exhibit two low-field peaks, at δ 10·6 and 13·6, and 10·3 and 12·6, respectively. [These values differ markedly from those (δ 5·4 and 4·55) of the methine protons in (29) and (26), respectively.] Again, these results for 3-substituted azaoxindoles contrast markedly with the n.m.r. spectra of the parent azaoxindoles (19) and (22). Finch *et al.* reported [15] a two-proton singlet at δ 3·62 in the spectrum of (19). We confirmed this and noted that both this peak (due to CH_2) and the one at 10·4 (NH) disappear on addition of D_2O. The spectrum of oxindole under similar conditions shows only the disappearance of the peak due to NH, indicating the much greater acidity of the CH_2 group in the azaoxindole. The spectrum of the 1,6-isomer is more complex and shows the presence of both keto (22) and enol (35) forms in the ratio *ca.* 3 : 2, and has peaks at δ 3·6 (CH_2), 5·0 (3-H), and 9·9, 10·6, and 11·4 (2 × NH and OH) (all of which were exchangeable with D_2O), together with groups of peaks centred at 6·6 (d), 7·3 (m), and 8·2 (t) assigned to enol 4-, 5-, and 7-H, respectively.

EXPERIMENTAL

I.r. spectra were measured (for KBr discs) with a Unicam SP 200 spectrometer, and n.m.r. spectra with a Varian T 60 instrument (tetramethylsilane as internal standard). Mass spectra were recorded by the P.C.M.U. or at the School of Pharmacy, University of London.

1,5-Diazaindene 5-Oxide (1H-*Pyrrolo*[3,2-c]*pyridine* 5-*Oxide*) (6).—*m*-Chloroperoxybenzoic acid (4·7 g) in dichloromethane (45 ml) was added to 1-acetyl-1,5-diazaindene [1] (1·5 g) in dichloromethane (25 ml), and the mixture was kept at room temperature for 10 days. The solid was filtered off and the filtrate evaporated to dryness. The residue was dissolved in aqueous potassium carbonate and then acidified to pH 2 with dilute hydrochloric acid. The precipitated organic acids were filtered off, the filtrate was evaporated to dryness, and the residue was extracted with hot ethanol. Evaporation of the ethanolic solution yielded *1,5-diazaindene 5-oxide hydrochloride* (1·4 g, 86%), m.p. 205—206° (from ethanol–ethyl acetate) (Found: C, 49·4; H, 4·25; N, 16·3; Cl, 20·4. $C_7H_7ClN_2O$ requires C, 49·3; H, 4·1; N, 16·4; Cl, 20·8%), $\nu_{max.}$ 3250 cm^{-1} (NH); δ [$(CD_3)_2$SO] 14·07 (1H, s, exchanged in D_2O, OH), 11·90 (1H, s, exchanged in D_2O, NH), 9·43 (1H, s, 4-H), 8·52 (1H, d, 6-H, *J* 7·0 Hz), 7·97 (1H, d, 7-H, *J* 7·0 Hz), 7·93 (1H, d, 2-H, *J* 3·0 Hz), and 6·93 (1H, d, 3-H, *J* 3·0 Hz). An aqueous solution of the hydrochloride was basified with saturated aqueous potassium carbonate to give a precipitate of *1,5-diazaindene 5-oxide*, m.p. 198—199° (from ethanol–ethyl acetate) (Found: M^+, 134·0479. $C_7H_6N_2O$ requires *M*, 134·0480), $\nu_{max.}$ 3320 cm^{-1} (NH); δ [$(CD_3)_2$SO] 12·70br (1H, exchanged in D_2O, NH), 8·57 (1H, s, 4-H), 7·89 (1H, d, 6-H, *J* 7·0 Hz), 7·50 (1H, d, 2-H, *J* 3·4 Hz), 7·40 (1H, d, 7-H. *J* 7·0 Hz), and 6·52 (1H, d, 3-H, *J* 3·4 Hz).

1-Acetyl-1,5-diazainden-4(5H)-one {*1-Acetylpyrrolo*[3,2-c]*pyridine-4(5H)-one*} (3).—1,5-Diazaindene 5-oxide hydrochloride (0·15 g) was refluxed in acetic anhydride (10 ml) for 3 h. The mixture was cooled, the solid was filtered off, and the filtrate was evaporated to dryness under reduced pressure. Water was added to the residue and the insoluble material was filtered off, crystallised from aqueous ethanol (charcoal), and recrystallised from ethanol–ethyl acetate to give *1-acetyl-1,5-diazainden-4(5H)-one* (16 mg, 10%), m.p. 359—360° (Found: C, 61·1; H, 4·6; N, 16·1. $C_9H_8N_2O_2$ requires C, 61·4; H, 4·5; N, 15·9%), $\nu_{max.}$ 3150 (NH), 1720 (CO), and 1642 (CO) cm^{-1}; δ [$(CD_3)_2$SO] 12·08 (1H, s, exchanged in D_2O, NH), 8·18 (1H, d, 2-H, *J* 3·7 Hz), 7·65 (2H, s, 6- and 7-H), 7·18 (1H, d, 3-H, *J* 3·7 Hz), and 2·83 (3H, s, Me).

trans-3-(*Pyrrol-2-yl*)*acryloyl Azide* (11).—Ethyl chloroformate (2·7 g) in acetone (20 ml) was added to a stirred solution of *trans*-3-(pyrrol-2-yl)acrylic acid [11] (2·6 g) and triethylamine (2·25 g) in acetone (10 ml) maintained at 0°. The stirring was continued for 0·5 h and sodium azide (1·8 g) in water (7·0 ml) was then added with the temperature kept below 10°. After a further 1 h the mixture was poured onto crushed ice. The precipitated *azide* was crystallised from dichloromethane; it decomposed on heating and had an indefinite m.p. (Found: C, 51·8; H, 4·0; N, 34·6. $C_7H_6N_4O$ requires C, 51·8; H, 3·7; N, 34·6%), $\nu_{max.}$ 3360 (NH), 2180 and 2140 (N_3), and 1659 (CO) cm^{-1}; δ [$(CD_3)_2$SO] 11·7 (1H, s, exchanged in D_2O, NH) 7·58 (1H, d, CH, *J* 16 Hz), 7·13 (1H, m, 5-H), 6·70 (1H, m, 4-H), 6·25 (1H, m, 3-H), and 6·23 (1H, d, CH, *J* 16 Hz).

1,5-Diazainden-4(5H)-one {*Pyrrolo*[3,2-c]*pyridin-4(5H)-one*} (1).—Ethyl chloroformate (1·35 g) in acetone (10 ml) was added to *cis*-3-(pyrrol-2-yl)acrylic acid [11] (1·1 g) and

[18] A. H. Beckett, R. W. Daisley, and J. Walker, *Tetrahedron*, 1968, **24**, 6093.

triethylamine (1·12 g) in acetone maintained below 5°. The mixture was stirred for 0·75 h and sodium azide (0·9 g) in water (3·5 ml) was added at the same temperature. The mixture was stirred, allowed to warm to room temperature during 1·5 h, and then poured onto ice. The precipitate was dissolved in dichloromethane, dried ($MgSO_4$,H_2O), and added during 0·33 h to diphenyl ether (40 ml) and tri-n-butylamine (4 ml) at 220°. The temperature was maintained at 220—225° for a further 10 min. The mixture was then cooled and the solid was filtered off, washed with ether, and recrystallised from ethanol (charcoal) to give 1,5-*diazainden*-4(5H)-*one* (0·36 g, 34%), m.p. 346·5—348° (Found: C, 62·5; H, 4·6; N, 20·7. $C_7H_6N_2O$ requires C, 62·7; H, 4·5; N, 20·9%), $\nu_{max.}$ 3250 (NH), 3150 (NH), and 1648 (CO) cm^{-1}; δ [$(CD_3)_2SO$] 11·47 and 10·83 (each 1H, s, exchanged in D_2O, NH), 7·03 (2H, m, 2- and 6-H), 6·47 (2H, m, 3- and 7-H).

Photoisomerisation of trans-3-(*Pyrrol-2-yl*)*acrylic Acid*.—The acid (2·0 g) in sodium carbonate solution (2·0 g in 400 ml of water) was irradiated with u.v. light (medium-pressure mercury arc) for 10 h under nitrogen. The solution was concentrated to 50 ml and acidified with hydrochloric acid to give a 4 : 6 mixture (n.m.r.) of *cis*- and *trans*-acids (1·65 g, 82%).

2,3-*Dihydro*-1,5-*oxazainden*-4(5H)-*one* {2,3-*Dihydrofuro*-[3,2-c]*pyridin*-4(5H)-*one*} (15).—1,5-Oxazainden-4(5*H*)-one [19] (5·5 g) in ethanol (170 ml) was shaken in the presence of hydrogen and palladised charcoal (0·6 g; 10%) at 70° and 3 atm initial pressure for 10 h. More catalyst (0·5 g) was added and shaking was continued for 5 h. Removal of the catalyst and solvent left gum which solidified on trituration with ether and was crystallised from ethanol to give 2,3-*dihydro*-1,5-*oxazainden*-4(5H)-*one* (4·6 g, 82%), m.p. 241—242° (subl.) (Found: C, 61·3; H, 5·2; N, 10·4. $C_7H_7NO_2$ requires C, 61·3; H, 5·1; N, 10·2%), $\nu_{max.}$ 3138 (NH) and 1665 (CO) cm^{-1}; δ [$(CD_3)_2SO$] 11·17 (1H, s, exchanged in D_2O, NH), 7·24 (1H, d, 6-H, *J* 7·0 Hz, 5·97 (1H, d, 7-H, *J* 7·0 Hz), 4·58 (2H, t, 2-H, *J* 9·1 Hz), and 2·90 (2H, t, 3-H, *J* 9·1 Hz).

3-*Ethyl*-4-*hydroxy*-2-*pyridone* (17).—1,5-Oxazainden-4(5*H*)-one (2·0 g) in ethanol (50 ml) was shaken with platinum oxide (0·1 g) and hydrogen at 65° and 3 atm pressure for 24 h. The catalyst and solvent were removed and the residue was dissolved in sodium hydroxide solution (3N), which was then extracted with chloroform. The aqueous solution was acidified to pH 3 with hydrochloric acid and the precipitate collected, washed with water, and dried. Crystallisation from ethanol afforded 3-*ethyl*-4-*hydroxy*-2-*pyridone* (0·8 g, 40%), m.p. 303—304° (subl.) (Found: C, 60·4; H, 6·6; N, 10·1. $C_7H_9NO_2$ requires C, 60·4; H, 6·5; N, 10·1%), $\nu_{max.}$ 3260 (NH), 2698, (OH), and 1647 (CO) cm^{-1}; δ [$(CD_3)_2SO$] 10·17 (2H, s, exchanged in D_2O, NH and OH), 7·12 (1H, d, 6-H, *J* 6·8 Hz), 5·98 (1H, d, 5-H, *J* 6·8 Hz), 2·42 (2H, q, CH_2, *J* 6·5 Hz), and 1·00 (3H, t, Me, *J* 6·5 Hz).

1-*Benzyl*-2,3-*dihydro*-1,5-*diazainden*-4(5H)-*one* {1-Benzyl-2,3-*dihydropyrrolo*[3,2-c]*pyridin*-4(5H)-*one*} (16).—2,3-Dihydro-1,5-oxazainden-4(5*H*)-*one* (3·8 g) and benzylamine (8·9 g) were refluxed under nitrogen for 8 h. The solution was cooled, and the precipitate (2·44 g) filtered off. Distillation of the benzylamine from the filtrate and addition of water to the residue produced more 1-*benzyl*-2,3-*dihydro*-1,5-*diazainden*-4(5H)-*one* (56%), m.p. 205—206° (from ethanol) (Found: C, 74·3; H, 16·1; N, 12·3. $C_{14}H_{14}N_2O$ requires C, 74·3; H, 6·2; N, 12·4%), $\nu_{max.}$ 3120 (NH) and 1640 (CO) cm^{-1}; δ ($CDCl_3$) 10·0 (1H, s, exchanged in D_2O, NH), 7·32 (6H, m, Ph and 6-H), 5·82 (1H, d, 7-H, *J* 7·2 Hz), 4·32 (2H, s, PhCH_2), 3·45 (2H, m, 2-H), and 3·03 (2H, m, 3-H).

Perhydro-1,5-*diazainden*-4-*one* (*Perhydropyrrolo*[3,2-c]-*pyridin*-4-*one*) (18).—The aforementioned benzyl derivative (0·97 g), in ethanol (35 ml) and conc. hydrochloric acid (2 drops), was shaken with palladium black at 65° and 3 atm pressure for 4·5 h. Removal of the catalyst and solvent gave *perhydro*-1,5-*diazainden*-4-*one* (0·55 g, 91%) as an oil which slowly solidified (Found: M^+, 140·0953. $C_7H_{15}N_2O$ requires *M*, 140·0950), $\nu_{max.}$ 3520 (NH), 3311 (NH), and 1667 (CO) cm^{-1}; δ ($CDCl_3$) 7·77 (1H, s, exchanged in D_2O, NH), 3·87 (2H, m), 3·07 (4H, m), and 2·00 (4H, m).

Dehydrogenation of Perhydro-1,5-*diazainden*-4-*one*.—The perhydro-compound (0·5 g), palladium–charcoal (0·3 g; 10%), and Dowtherm A (12·5 ml) were mixed and refluxed under nitrogen for 1·5 h. The catalyst was filtered from the hot mixture and, after cooling, the filtrate deposited a solid. Addition of ether to the filtrate yielded more solid which was collected and washed with benzene. Crystallisation from benzene gave 1,5-diazainden-4(5*H*)-one (0·33 g, 69%), identical with that prepared earlier.

Ethyl 2,3-*Dihydro*-2-*oxo*-1,6-*diazaindene*-3-*carboxylate* (*Ethyl* 2,3-*Dihydro*-2-*oxopyrrolo*[2,3-c]*pyridine*-3-*carboxylate*) (23).—4-Bis(ethoxycarbonyl)methyl-3-nitropyridine [20] (20 g) in methanol (150 ml) was hydrogenated over palladised charcoal (2 g; 10%) at atmospheric pressure and ambient temperature. Removal of the catalyst and solvent left a viscous yellow oil (13·5 g, 91%), thought to be 3-amino-4-bis(ethoxycarbonyl)methylpyridine, $\nu_{max.}$ (liquid) 3450 and 3250 (NH_2) and 1725 (CO) cm^{-1}. The compound was not characterised further, since a methanolic solution (15 ml) slowly deposited green crystals (2·9 g) at room temperature during 2 days. After removal of the solid, the filtrate was refluxed for 0·25 h and, after cooling, gave more *ethyl* 2,3-*dihydro*-2-*oxo*-1,6-*diazaindene*-3-*carboxylate* (3·2 g, total yield 42%). Recrystallisation from dimethyl sulphoxide gave cream micro-crystals, m.p. >340° (Found: C, 58·0; H, 4·6; N, 13·6. $C_{10}H_{10}N_2O_3$ requires C, 58·3; H, 4·9; N, 13·6%), $\nu_{max.}$ 3100 (NH) and 1690 (CO) cm^{-1}; δ ($CF_3{\cdot}CO_2H$) 1·55 (3H, t, Me, *J* 7·0 Hz), 4·65 (2H, q, CH_2, *J* 7·0 Hz), 8·25 (2H, d, 4- and 7-H, *J* 5·0 Hz), and 8·7 (1H, d, 5-H, *J* 5·0 Hz).

Ethyl 2-*Amino*-1-*hydroxy*-1,6-*diazaindene*-3-*carboxylate* (*Ethyl* 2-*Amino*-1-*hydroxypyrrolo*[2,3-c]*pyridine*-3-*carboxylate*) (34) *and* 2-*Hydroxy*-1,6-*diazaindene*-3-*carbonitrile* (2-*Hydroxypyrrolo*[2,3-c]*pyridine*-3-*carbonitrile*) (36).—A solution of 3-nitro-4-pyridylcyanoacetate [5] (6·0 g) in methanol (350 ml) was hydrogenated over palladised charcoal (0·5 g; 10%) at an initial pressure of 3 atm. and ambient temperature. Removal of the catalyst and solvent left a solid which was extracted with warm ethyl acetate. On evaporation the extract yielded the *ester* (34) (3·1 g, 56%), obtained as cream needles, after crystallisation from ethanol–ether; m.p. 234—235° (decomp.) (Found: C, 54·6; H, 4·9; N, 18·7. $C_{10}H_{11}N_3O_3$ requires C, 54·3; H, 5·0; N, 19·0%), M^+ 221·0804, $\nu_{max.}$ 1690 cm^{-1} (CO); δ [$(CD_3)_2SO$] 1·3 (3H, t, Me, *J* 7 Hz), 4·1 (2H, q, CH_2, *J* 7 Hz), 7·2 (2H, s, exchangeable, NH_2), 7·5 [2H, d, overlying a broad peak, 4-H and OH (exchangeable) respectively, *J* 5 Hz], 8·1 (1H, d, 5-H, *J* 5 Hz), and 8·4 (1H, s, 7-H).

The residue left after extraction with ethyl acetate was refluxed in xylene for 24 h; on cooling the solution tan

[19] F. Eloy and A. Deryckere, *Helv. Chim. Acta*, 1970, **53**, 645.
[20] O. Brenner, *Annalen*, 1937, **529**, 288.

crystals (1·8 g, 40%) were obtained. Recrystallisation from ethanol (charcoal) gave the cream-coloured *nitrile*, m.p. >340° (Found: C, 60·5; H, 3·0; N, 26·6. $C_8H_5N_3O$ requires C, 60·4; H, 3·1; N, 26·4%), $\nu_{max.}$ 3200 (partially due to OH), 2230 (CN), and 1640 (CO) cm^{-1}; δ [$(CD_3)_2SO$] 7·05 (1H, d, 4-H, *J* 6 Hz), 7·8 (2H, d, 5- and 7-H, *J* 7 Hz), 10·6 (1H, s, exchangeable, OH), and 13·6br (1H, exchangeable, NH).

1,6-*Diazainden*-2(3H)-*one* {*Pyrrolo*[2,3-c]*pyridin*-2(3H)-*one*} (22).—(a) A mixture of the ester (23) (1·85 g) and conc. hydrochloric acid (200 ml) was refluxed for 29 h and evaporated to dryness. The residue was dissolved in a small quantity of water, basified with solid sodium hydrogen carbonate, and extracted with chloroform. The extract yielded a yellow solid (1·0 g, 83%). This was dissolved in benzene and chromatographed on basic alumina to give a product which was sublimed under reduced pressure to give the yellow *diazaindenone*, m.p. 227—228° (decomp.) (Found: C, 62·3; H, 5·1; N, 20·7%; M^+, 134·0482. $C_7H_6N_2O$ requires C, 62·7; H, 4·5; N, 20·9%; *M*, 134·0480), $\nu_{max.}$ 3200 (NH), broad peak with a max. at 2750 (bonded OH), and 1660 (CO) cm^{-1}; δ [$(CD_3)_2SO$] 3·6 (1·2H, s, CH_2 of carbonyl tautomer), 5·0 (0·4H, s, H of enol tautomer, exchanged in D_2O), 6·6 (d), 7·7 (m), and 8·2 (t) (total area of 3H, 4-, 5-, and 7-H), and 9·9 (s, NH), 10·6 (s, NH), and 11·4 (s, OH) (total area 1·4H, all exchanged in D_2O).

(*b*) A similar procedure with 2,3-dihydro-2-oxo-1,6-diazaindene-3-carbonitrile (1·25 g) and conc. hydrochloric acid (30 ml) afforded the azaoxindole (0·071 g, 30%) from the chloroform extract.

2-*Bis*(*ethoxycarbonyl*)*methyl*-3-*nitropyridine* (26).—Diethyl malonate (25·6 g, 0·16 mol) was added to a stirred solution of potassium t-butoxide (18 g, 0·16 mol) in dry t-butyl alcohol (200 ml). A hot solution of 2-chloro-3-nitropyridine (12·7 g, 0·08 mol) in t-butyl alcohol (150 ml) was then added and the mixture was refluxed for 17 h. The alcohol was distilled off and hydrochloric acid was added to the residue. Extraction with ether yielded a dark liquid after evaporation, and diethyl malonate and 2-chloro-3-nitropyridine (0·7 g) were removed by distillation under reduced pressure (0·3 mmHg). The residue was cooled and crystallised from petroleum (b.p. 40—60°) to give 2-*bis*(*ethoxycarbonyl*)-*methyl*-3-*nitropyridine* (16·6 g, 70%), m.p. 63—64° (Found: C, 51·4; H, 5·0; N, 10·2. $C_{12}H_{14}N_2O_6$ requires C, 51·1; H, 5·0; N, 9·9%), M^+ 282, $\nu_{max.}$ 1740 (CO) and 1720 (CO) cm^{-1}; δ ($CDCl_3$) 1·3 (6H, t, 2 × Me, *J* 6 Hz), 4·3 (4H, q, 2 × CH_2, *J* 6 Hz), 4·55 (1H, s, CH), 7·5 (1H, q, 5-H, $J_{5,6}$ 4, $J_{4,5}$ 8·5 Hz), 8·5 (1H, d, 4-H, *J* 8·5 Hz), and 8·8 (1H, d, 6-H, *J* 4 Hz).

Ethyl 2-*Hydroxy*-1,4-*diazaindene*-3-*carboxylate* (*Ethyl* 2-*Hydroxypyrrolo*[3,2-b]*pyridine*-3-*carboxylate*) (40).—2-Bis(ethoxycarbonyl)methyl-3-nitropyridine (9·4 g) in methanol (200 ml) was hydrogenated over palladised charcoal (1·0 g; 10%) at an initial pressure of 2 atm and room temperature. The catalyst was filtered off and the filtrate was evaporated to half its bulk and refluxed on a water-bath for 0·5 h. The cold solution was set aside overnight and a green precipitate (4·7 g, 88%) was obtained; recrystallisation from methanol gave the pale green *diazaindene ester*, m.p. 282° (decomp.) (Found: C, 57·6; H, 5·1; N, 13·3. $C_{10}H_{10}N_2O_3$ requires C, 58·2; H, 4·8; N, 13·6%), M^+ 206; $\nu_{max.}$ 3400—2600 (partially due to OH and NH) and 1700 (CO) cm^{-1}; δ [$(CD_3)_2SO$] 1·2 (3H, t, Me, *J* 6 Hz), 4·2 (2H, q CH_2, *J* 6 Hz), 6·8 (1H, d, 7-H, *J* 6 Hz), 7·5 (1H, d, 5-H, *J* 6 Hz), 10·3 (1H, s, exchangeable NH), and 12·6br (1H, exchangeable OH).

1,4-*Diazainden*-2(3H)-*one* {*Pyrrolo*[3,2-b]*pyridin*-2(3H)-*one*} (19).—The diazaindene ester (40) (1·0 g) in conc. hydrochloric acid (60 ml) was refluxed for 24 h and then evaporated to dryness. The residue was dissolved in a small quantity of water and made basic (pH 7—8) with solid sodium hydrogen carbonate. The solution was extracted with chloroform and the extract afforded 1,4-diazainden-2(3*H*)-one (0·45 g, 78%) on evaporation. Crystallisation from toluene gave pale yellow prisms, m.p. 206—207° (decomp.) (lit.,[15] 205—207°).

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