Transformations of 4,9-Dimethyl-2,3,7,8-tetra-azatetracyclo-[7.3.1.0.^{4,12}0^{6,10}]trideca-1,6-diene, a Bishydrazone having Two Bridgehead Double Bonds

John M. Mellor * and Ranjith Pathirana
Department of Chemistry, The University, Southampton SO9 5NH

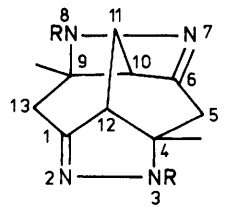
Reduction of the anti-Bredt bishydrazone 4,9-dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.^{4,12}0^{6,10}]-trideca-1,6-diene with lithium aluminium hydride–aluminium chloride or by catalytic hydrogenation gives the bishydrazine 1,6-dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.^{4,12}0^{6,10}]tridecane, but reaction with either lithium aluminium hydride or aluminium chloride gives dihydropyrazoles by ring cleavage.

The interest [1] in the preparation of alkenes having the double bond placed at a bridgehead position (anti-Bredt) has been followed by synthetic studies focussed on the preparation of dienes [2] having two double bonds with anti-Bredt character, and on the preparation of imines [3] having a carbon–nitrogen double bond placed at a bridgehead position. Following our preparation [4] of the first bishydrazone (1) having the two carbon–nitrogen double bonds at bridgehead positions we have been able to study its chemistry and we describe here both the reduction of compound (1) and its derivatives, and the cleavage reactions of (1) to give dihydropyrazoles.

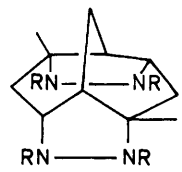
With the intention of effecting the reduction of the bishydrazone (1) to give the bishydrazine (2) we have studied the reaction of (1) with lithium aluminium hydride. Although little reaction is observed following short reaction times in diethyl ether at room temperature, more vigorous conditions lead to loss of the bishydrazone and formation of a rather unstable product, which was characterised by formation of a stable acetylated derivative. Structure (3) was assigned to the product of acetylation based on the following considerations: (i) the observation of methyl resonances at τ 8.04 and 8.10 indicated the presence of two MeC=N– groupings and a methyl resonance at τ 8.61 showed a methyl group attached to a quaternary centre. Relative to the starting material (1), an extra methyl group must have been created in the course of reaction with lithium aluminium hydride, implying a ring cleavage.

(ii) The skeleton of (3) accords with the observed spectra and might be obtained by a combination of reductive and base-catalysed processes, as shown in Scheme 1.

(iii) Analysis of the ^{1}H 400 MHz n.m.r. spectrum of the diacetyl compound (3) established the stereochemical details (see Figure; detailed assignments are given in the Experimental section). In particular, decoupling experiments establish coupling between the clearly visible signal at τ 5.60 associated with 3-H and signals at τ 6.85, 6.92, and 8.32 tentatively identified with 2- and 7-H. No coupling is observed between the signals at τ 5.60 and 7.55 implying that the latter signal is associated with 8- or 9-H. The observed couplings (*J* 12 and 4 Hz) for the signal at τ 7.55 indicates that this signal is associated with 9-H. Further assignments were made using n.O.e. Significant enhancement of the methyl signal at τ 8.61 is observed by perturbation of the resonance at τ 5.60. Similar enhancement of the signal at τ 5.60 is observed by perturbation of the methyl signal at τ 8.61. Hence, 3-H and the quaternary 1-methyl group must have a *syn* relationship. Similarly n.O.e. analysis indicates the close proximity of this methyl group to 9-H (signal at τ 7.55) and hence their *cis* relationship. Further analysis indicates the *syn* relationship of 9-H (signal at τ 7.55) and 7-H (signal at τ 6.92) and the *cis* relationship of 3-H (signal at τ 5.60) and 7-H (signal at τ 6.92).



(1) R = H
(16) R = Ac



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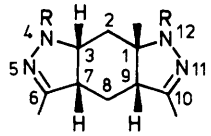

(3) R = Ac
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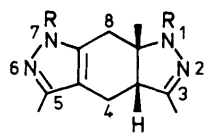

(5) R = Ac
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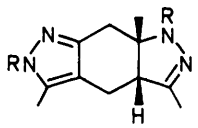

(6) R = Ac
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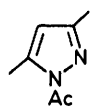

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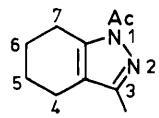

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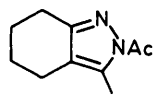

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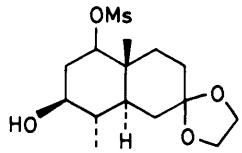

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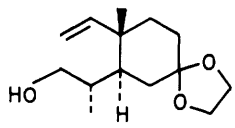

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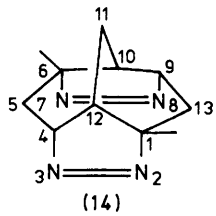


(14)

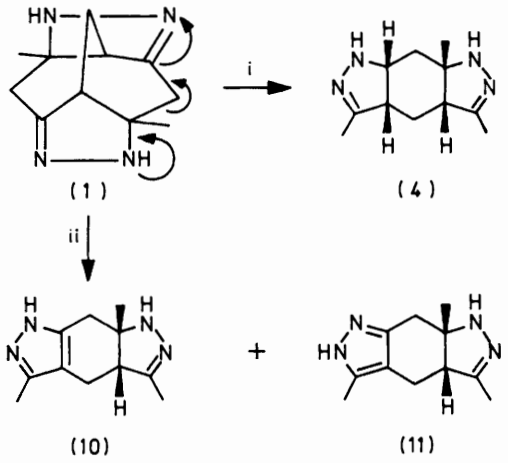
These results define the *cis-syn-cis* stereochemistry of (3). The observed coupling constants (see Experimental section) support this assignment. Crucially, both the signals at τ 5.60 (3-H) and τ 6.92 (7-H) have six lines, with observed couplings

of 12, 12 and 4 Hz for the former and 12, 12, and 6 Hz for the latter signal. With the six-membered ring adopting a boat conformation, a vicinal coupling of *ca.* 12 Hz for protons having a *cis* relationship is expected and vicinal protons having a *trans* relationship show a smaller coupling constant.

Following the study of the reaction of compound (1) with lithium aluminium hydride to give the bicyclo compound (4) and hence the diacetyl derivative (3) on acetylation, and with lithium aluminium hydride–aluminium chloride (discussed below), we have investigated the behaviour of the bishydrazone (1) with aluminium chloride in diethyl ether. After reaction, the products were characterised by acetylation. Acetylation with acetic anhydride in pyridine gives a single crystalline product but acetylation with acetic anhydride in acetic acid gives a mixture of two isomeric products. The product obtained by reaction in pyridine was established to be (5) from: (i) observation of a pyrazole moiety ($\lambda_{max.}$ 242 nm); (ii) observation of two imine resonances at 149.21 and 155.95 p.p.m.; (iii) observation of five resonances associated with methyl groups in the product (5) implying the creation of an extra methyl group on reaction of the bishydrazone (1) with aluminium chloride. Hence the similar behaviour of lithium aluminium hydride and of aluminium chloride with (1) is established; (iv) a detailed analysis distinguishing (5) from the alternative possibility (6). Distinction between structures (5) and (6) can be made by a detailed analysis of their ^{1}H n.m.r. spectra and comparison with the spectra of some model compounds. The pyrazole (7) is characterised [5] by the resonance of the 5-methyl at τ 7.48, shielded by the anisotropic effect of the carbonyl group relative to the resonance of the 3-methyl at τ 7.78. To facilitate comparisons and avoid complications of possible changes in preferred conformations a further model compound, the bicyclic pyrazole (8), was prepared by reaction of hydrazine with 2-acetylcyclohexanone and subsequent acetylation with acetic anhydride in pyridine. None of the alternative pyrazole (9) was observed. Observation of the *Me*C=N⁻ resonance at τ 7.82 defined the structure of (8), the product obtained by acetylation in pyridine. Comparison of the resonances associated with the isomers (5) and (6) indicated common values for four of the five methyl resonances. The fifth set of resonances were observed at τ 7.76 in (5) and τ 7.50 in (6). Further support for these assignments comes from the relative chemical shifts of the methylene resonances. In the bicyclic pyrazole (8) the difference between the methylene resonances at τ 7.04 and 7.63 can be attributed to a deshielding effect by the proximate acyl group. In the case of compound (5) extensive deshielding by two acetyl groups may be expected and is observed in the resonances of the non-equivalent protons at τ 5.90 and 6.71. By contrast, in (6) the analogous resonances are at τ 6.36 and 7.14; and (v) the similar mass spectral fragmentations for compounds (5) and (8) (see Scheme 2).

Hence, reaction of the bishydrazone (1) with lithium aluminium hydride gives the tricyclic compound (4) and with aluminium chloride gives the tautomeric pair (10) and (11). In the one case cleavage is initiated by base following reduction of an imine group, and in the other case the cleavage is acid catalysed. The *cis* stereochemistry in (10) and (11) is then defined by the original stereochemistry in compound (1). The reactions are shown in Scheme 1. Precedent for the ability of lithium aluminium hydride to initiate such a cleavage is known in the Grob fragmentations [6] of the bicyclic compound (12) to give the cyclohexane (13).

In contrast to the above reactions, the interaction of the



Scheme 1. *Reagents:* i, $LiAlH_4$; ii, $AlCl_3$

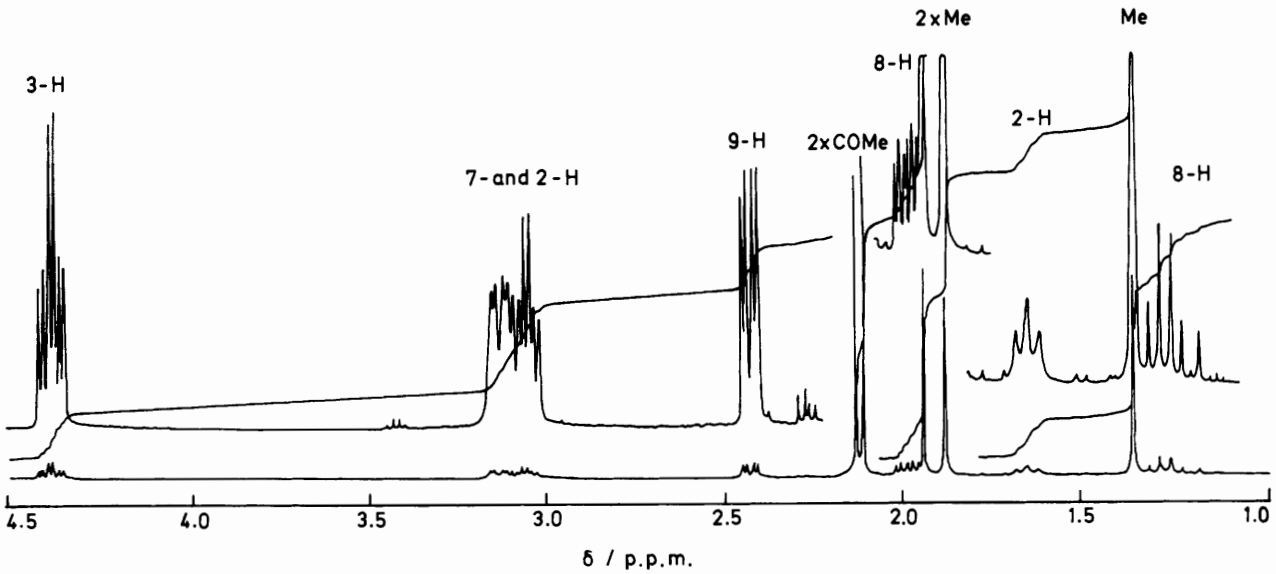
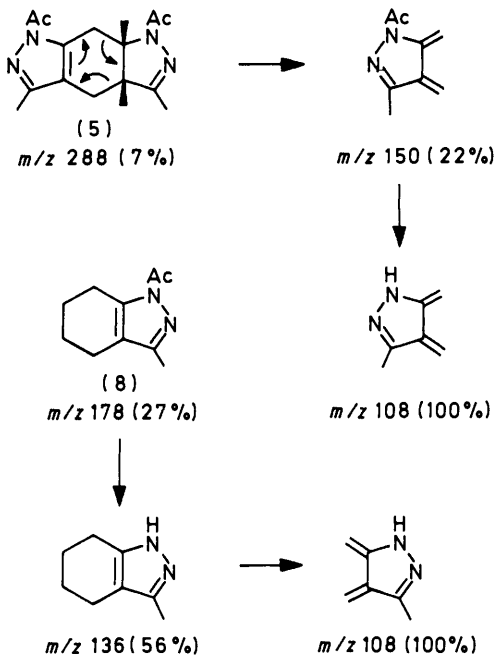


Figure. ^{1}H N.m.r. (400 MHz) spectrum of the diacetyltetra-azatricyclo[7.3.0.0^{3,7}]deca-5,10-diene (3)



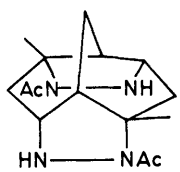
Scheme 2.

bishydrazone (1) with lithium aluminium hydride–aluminium chloride in diethyl ether gave only the bishydrazine (2) in high yield. However, the exceptional air sensitivity of (2) made isolation very difficult. Exposure of solutions of (2) to air leads to rapid and near quantitative formation of the tetracyclic compound (14). The initial observation that reaction of (1) with lithium aluminium hydride–aluminium chloride gave, after work-up, compound (14), suggested two possible pathways. Either reduction to the saturated compound (2) could be followed by an air oxidation to give the product (14), or alternatively a direct rearrangement of (1) might give (14). Such rearrangements [7] are well known. The intermediacy of (2) was clearly established by (i) acetylation of compound (2) in the absence of oxygen to give the diacetyl derivative (15), and (ii) the observation that (2) obtained by catalytic hydrogenation of (1) readily underwent oxidation to give the unsaturated compound (14).

In spite of the possible strain in the bishydrazone (1), hydrogenation does not proceed readily. Hydrogenation under pressure is required for smooth conversion of (1) into (2), or conversion of the diamide (16) into (17), the latter reaction giving some of the intermediate (18). Hydrogenation of (16) at 1 atm proceeds sluggishly to give both products (15) and (19). In contrast, compound (14) is readily hydrogenated at 1 atm to give the saturated compound (2). It may be concluded that the transformation of (1) by ring cleavage reactions to tricyclic products is evidence of the unusual structural relationship of the two hydrazone groups in (1) rather than evidence of exceptional strain. Extremes of either basicity or acidity promote the cleavage.

Experimental

M.p.s were determined in a capillary tube and are uncorrected. I.r. spectra were obtained on a Perkin-Elmer 157 spectrometer. ^1H and ^{13}C N.m.r. spectra were obtained on a Varian XL 100 spectrometer, or where stated on a Bruker 400 MHz spectrometer. U.v. spectra were obtained for solutions in ethanol on a Perkin-Elmer 402 spectrometer. Mass spectra



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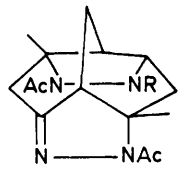

(18) R = H
(19) R = Ac

were obtained at 70 eV using a Kratos MS 30 spectrometer. Thin layer chromatography was carried out on Merck Kieselgel 60 HF 254 + 366. Flash chromatography was carried out on Macherey Nagel silica gel 60. Hydrogenations were conducted at 1 atmosphere (hydrogen uptake monitored using a gas burette), at 3 atmospheres (glass pressure bottle), or at 100 atmospheres (steel autoclave). Elemental analyses were performed at University College, London.

Method of Acetylation.—Method A. A solution of the hydrazine or hydrazone (500 mg) in pyridine (5 ml) containing acetic anhydride (1 ml) was stirred at room temperature under N_2 for 18 h. After the solvents had been removed under reduced pressure, crystalline products were obtained by addition of either diethyl ether or ethyl acetate.

Method B. A solution of the hydrazine or hydrazone (500 mg) in acetic acid (3 ml) and acetic anhydride was stirred at room temperature under N_2 for 18 h. In some cases the solution was stirred at 60 °C. When the reaction was complete (t.l.c.) the solvent was removed under reduced pressure and crystalline products obtained by addition of either diethyl ether or ethyl acetate.

4,12-*Diacetyl*-1,6,10-*trimethyl*-4,5,11,12-*tetra-azatricyclo*-[7.3.0.$0^{3,7}$]*deca*-5,10-*diene* (3).—4,9-Dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.$^{4,12}0^{6,10}$]trideca-3,8-diene (1) (500 mg) and lithium aluminium hydride (930 mg) in dry diethyl ether (100 ml) were heated under reflux under N_2 for 18 h. Water was added to the cold reaction mixture and the white gelatinous precipitate was removed by filtration and then washed with chloroform (4 × 50 ml). The combined filtrate and washings were dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure to afford a yellow oil (480 mg). Acetylation of this oil (400 mg) by Method A afforded, following removal after 20 h of solvent under reduced pressure, an oil. Crystallisation from diethyl ether gave as white crystals 4,12-*diacetyl*-1,6,10-*trimethyl*-4,5,11,12-*tetra-azatricyclo*-[7.3.0.$0^{3,7}$]*deca*-5,10-*diene* (3) (242 mg, 43%), m.p. 145—148 °C (decomp.) (Found: C, 61.6; H, 7.5; N, 19.0. $C_{15}H_{22}N_4O_2$ requires C, 62.04; H, 7.64; N, 19.30%). $\nu_{max.}$ ($CHCl_3$) 1 660 and 1 633 cm^{-1}; M^+ 290; τ($CDCl_3$) 5.57 (1 H, m, 3-H), 6.6—7.0 (2 H, m, 7- and 2-H), 7.46 (1 H, dd, *J* 12 and 4 Hz, 9-H), 7.80 (3 H, s, COMe), 7.82 (3 H, s, COMe), 7.96 (3 H, s, Me), 7.96 (1 H, m, 8-H), 8.02 (3 H, s, Me), 8.27 (1 H, m, 2-H), 8.56 (3 H, s, Me), and 8.65 (1 H, m, 8-H). The 400 MHz (^1H) spectrum of (3) is shown in the Figure; ^{13}C n.m.r. 14.08 and 14.55 (6- and 10-Me), 21.78, 23.10, and 24.23 (1-Me and 2 × CO*Me*), 22.73 (C-8), 30.60 (C-2), 45.96, 53.13, and 55.36 (C-3, -7, and -9), 62.49 (C-1), 155.23 and 156.97 (C-6 and -10), and 168.02 and 168.60 p.p.m. (2 × *CO*Me).

Similar acetylation of (4) (800 mg) by Method B afforded, after work-up and recrystallisation, the diamide (3) (48%), m.p. 146—148 °C.

1,7-*Diacetyl*-1,3a,4,7,8,8a-*hexahydro*-3,5-*dimethylbenzo*-[1,2-c : 5,4-c′]*dipyrazole* (5).—4,9-Dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.$^{4,12}0^{6,10}$]trideca-3,8-diene (1) (2.00 g) and aluminium chloride (5.2 g) were heated under reflux under

N_2 in dry diethyl ether (150 ml) for 11 h. 2M-Sodium hydroxide was added to the cold reaction mixture to afford a white gelatinous precipitate which was removed by filtration and then washed thoroughly with chloroform (3 × 100 ml). The combined filtrate and washings were dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure to afford as a brown oil a mixture of the pyrazoles (10) and (11) (1.66 g, 83%). Acetylation of the mixture (1.52 g) by Method A afforded, following removal after 15 h of the solvent under reduced pressure, an oil. Crystallisation from diethyl ether gave as off-white crystals 1,7-*diacetyl*-1,3a,4,7,8,-8a-*hexahydro*-3,5-*dimethylbenzo*[1,2-c:5,4-c']*dipyrazole* (5) (1.10 g, 52%), m.p. 147—149 °C (Found: C, 62.1; H, 6.9; N, 19.0. $C_{15}H_{20}N_4O_2$ requires C, 62.48; H, 6.99; N, 19.43%); $\nu_{max.}$ ($CHCl_3$) 1 730, 1 660, and 1 635 cm^{-1}; $\lambda_{max.}$ (EtOH) 242 nm (ε 74 890); τ 5.90 (1 H, d, *J* 18 Hz, 8-H), 6.71 (1 H, d, *J* 18 Hz, 8-H), 6.88 (1 H, t, *J* 6 Hz, 3a-H), 7.33 (2 H, m, 4-H), 7.40 (3 H, s, 7-COMe), 7.76 (3 H, s, 5-Me), 7.82 (3 H, s, 1-COMe), 8.02 (3 H, s, 3-Me), and 8.32 (3 H, s, 8a-Me); ^{13}C n.m.r. 11.87 (5-Me), 14.08 (3-Me), 19.45 (C-4), 22.94, 23.22, and 26.39 (8a-Me and 2 × CO*Me*), 31.71 (C-8), 57.11 (C-3a), 66.69 (C-8a), 117.53 (C-4a), 142.00 (C-7a), 149.21 (C-5), 155.95 (C-3), and 169.10 and 170.48 p.p.m. (2 × *C*OMe).

Acetylation of the mixture of (10) and (11) (850 mg) by Method B afforded, following removal after 10 h of solvent under reduced pressure, a brown residue. Flash chromatography gave white crystals of a mixture of (5) and (6) (72.5%), m.p. 110—113 °C. $\nu_{max.}$ 1 730, 1 660, and 1 635 cm^{-1}; M^+ 288. By subtraction of the signals of (5) from the spectrum of the mixture the following clearly observable signals were associated with isomer (6): τ 6.36 (1 H, d, *J* 16 Hz), 7.14 (1 H, d, *J* 16 Hz), 7.37 (3 H, s, COMe), 7.52 (3 H, s, MeC=N), 7.82 (3 H, s, COMe), 8.07 (3 H, s, MeC=N), and 8.33 (3 H, s, CMe); ^{13}C n.m.r. 30.99, 58.24, 66.69, 116.54, 137.57, 153.29, 155.21, 168.63, and 171.86 p.p.m.

1-*Acetyl*-3,5-*dimethyl*-1H-*pyrazole* (7).—A solution of pentane-2,4-dione (10 g) and hydrazine hydrate (5 ml) in ethanol (50 ml) was stirred at room temperature for 10 min and then under reflux for 30 min. The solution was concentrated and partitioned between brine and diethyl ether. The ethereal solution was dried ($MgSO_4$) and concentrated under reduced pressure to give a white residue. Recrystallisation (light petroleum b.p. 60—80 °C) afforded as white plates 3,5-dimethylpyrazole (8.5 g, 89%), m.p. 105—106 °C (lit., m.p. 106 °C).[8] Acetylation by Method A afforded a yellow oil, which on distillation gave as a colourless oil 1-acetyl-3,5-dimethyl-1*H*-pyrazole (7), b.p. 80—81 °C (0.1 mmHg); $\nu_{max.}$ ($CHCl_3$) 1 728 and 1 583 cm^{-1}; M^+ 138; τ ($CDCl_3$) 4.08 (1 H, s, 4-H), 7.38 (3 H, s, COMe), 7.50 (3 H, s, 5-Me), and 7.79 (3 H, s, 3-Me); ^{13}C n.m.r. 13.69 and 14.45 (3- and 5-Me), 23.36 (COMe), 111.08 (C-4), 143.85 (C-5), 151.79 (C-3), and 171.32 p.p.m. (−CO−).

1-*Acetyl*-3-*methyl*-4,5,6,7-*tetrahydro*-1H-*indazole* (8).—A solution of 2-acetylcyclohexanone (1.0 g) and hydrazine hydrate (0.4 ml) in ethanol (20 ml) was stirred at room temperature for 30 min. Concentration under reduced pressure afforded a yellow oil (1.1 g) which was acetylated by Method A at room temperature for 16 h. Concentration under reduced pressure afforded a yellow oil (1.25 g) which was purified by bulb-to-bulb distillation (100 °C/0.1 mmHg) to give initially a colourless oil which slowly solidified. Recrystallisation (diethyl ether–n-hexane) gave as white crystals 1-acetyl-3-methyl-4,5,6,7-tetrahydroindazole (8) (320 mg, 25%), m.p. 41—42 °C; M^+ 178; τ ($CDCl_3$) 7.04 (2 H, m, 7-H), 7.38 (3 H, s, COMe), 7.63 (2 H, m, 4-H), 7.82 (3 H, s, Me), and 8.26 (4 H, m, 5- and 6-H); ^{13}C n.m.r. 12.01 (Me), 20.16, 22.38, 22.54, and 24.76 (C-4, -5, -6, and -7), 120.06 (C-3a), 142.26 (C-7a), 151.10 (C-3), and 170.81 p.p.m. (CO).

1,6-*Dimethyl*-2,3,7,8-*tetra-azatetracyclo*[7.2.1.0.^{4,12}0^{6,10}]-*trideca*-2,7-*diene* (14).—Aluminium chloride (8.08 g, 0.06 mol) was added slowly to dry diethyl ether (250 ml), and with constant stirring lithium aluminium hydride (2.31 g, 0.06 mol) was slowly added. The resulting suspension was heated under reflux for 30 min and cooled to room temperature. 4,9-Dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.^{4,12}0^{6,10}]tri-deca-3,8-diene (1) (3.1 g, 0.015 mol) was added and the suspension heated under reflux under N_2 for 8 h, and then cooled to room temperature. Careful addition of aqueous sodium hydroxide (4M; 20 ml) afforded a white gelatinous precipitate, which was removed by filtration and then washed with methanol (200 ml). The combined filtrate and washings were concentrated under reduced pressure and the residue dissolved in chloroform (150 ml). After filtration air was passed through the solution for 90 min. The solution was dried ($MgSO_4$), filtered, and the solvent removed under reduced pressure to afford a pale yellow oil (2.20 g, 87%). Crystallisation from ethyl acetate afforded pale yellow crystals of 1,6-*dimethyl*-2,3,7,8-*tetra-azatetracyclo*[7.3.1.0.^{4,12}0^{6,10}]*trideca*-2,7-*diene* (14) (1.65 g, 55%), m.p. 155—160 °C (decomp.) (Found: C, 64.4; H, 7.9; N, 27.2. $C_{11}H_{16}N_4$ requires C, 64.7; H, 7.90; N, 27.4%). $\nu_{max.}$ (Nujol) 1 560w cm^{-1}; $\lambda_{max.}$ (EtOH) 335 nm (ε 408); τ ($CDCl_3$) 5.00 (2 H, m, 4- and 9-H), 7.08 (2 H, d, *J* 17 Hz, 5- and 13-H), 8.28 (2 H, dt, *J* 12, 3, and 3 Hz, 10- and 12-H), 8.4—8.5 (4 H, complex, 5-, 11-, and 13-H), and 8.64 (6 H, s, Me). ^{13}C n.m.r. 16.85 (C-11), 26.09 (C-5 and -13), 27.97 (Me), 30.99 (C-10 and -12), 86.97 (C-4 and -9), and 89.81 p.p.m. (C-1 and -6); *m/z* (chemical ionisation spectrum using CH_4) 205 (M + 1, 100%).

Alternative methods of oxidation were examined. Aerial oxidation of the dihydrazine (2) was markedly faster in chloroform than in methanol. Oxidation in the presence of palladium on charcoal showed a slight acceleration but was not a marked improvement for the preparation of (14). An efficient oxidation using hydrogen peroxide was developed. The dihydrazine (2) (950 mg) in ethanol (50 ml) was stirred at room temperature for 15 h with hydrogen peroxide (2.1 g, 30%). Excess of peroxide was destroyed by palladium on charcoal, the solvent was evaporated, and the crude product was purified by flash chromatography to afford on elution with ethyl acetate the azoalkane (14) (56%).

In the reduction of the dihydrazone (1) the effect of varying the proportions of lithium aluminium hydride and aluminium chloride upon the nature of the products was examined. Using the ratio $LiAlH_4$–$AlCl_3$ 1 : 2 gave mainly the pyrazoles (10) and (11), but the ratio $LiAlH_4$–$AlCl_3$ 3 : 1 gave mainly the dihydrazine (2) with little formation of (4).

Work-up in the absence of air under nitrogen followed by acetylation of the crude reaction products by Method B afforded the crude tetra-amide (15). Recrystallisation (ethanol–ethyl acetate) gave pure tetra-amide (15), identical with the product obtained *via* hydrogenation of (16).

Hydrogenation of the Diamide (16) *at* 1 atm *in Glacial Acetic Acid.*—A solution of the diamide (16) (2.0 g) in glacial acetic acid (50 ml) containing added PtO_2 (200 mg) was hydrogenated under hydrogen (1 atm) for 64 h. Removal of the catalyst by filtration and the solvent under reduced pressure afforded a crude residue (2.03 g). Preparative thin layer chromatography (ethanol–ethyl acetate 15 : 85) afforded the less polar (18) (45%) and the more polar (17) (12%). Recrystallisation from ethyl acetate afforded the diamide (18), m.p. 233—235 °C, $\nu_{max.}$ (Nujol) 1 655 and 1 620 cm^{-1}; M^+ 290; τ ($CDCl_3$) 6.04 (1 H, m, 6-H), 6.23 (1 H, m, NH), 6.6—8.7 (complex), 7.78

(3 H, s, COMe), 7.90 (3 H, s, COMe), and 8.22 (6 H, s, 2 × Me). Recrystallisation from ethyl acetate afforded the diamide (17), m.p. 218—220 °C (for spectral data see below).

Hydrogenation of the Diamide (16) *at* 100 atm.—A solution of the diamide (16) (4.2 g) in ethanol (400 ml) containing added Raney nickel (W2) was hydrogenated under hydrogen (100 atm) at 90 °C for 18 h. Removal of the catalyst by filtration and the solvent under reduced pressure afforded a white solid residue (5.6 g). Recrystallisation from ethyl acetate afforded the *diamide* (17) (3.8 g, 90%), m.p. 219—220 °C (Found C, 61.7; H, 8.2; N, 19.2. $C_{15}H_{24}N_4O_2$ requires C, 61.62; H, 8.27; N, 19.16%); $\nu_{max.}$ (Nujol) 3 210 and 1 620 cm^{-1}; M^+ 292; τ($CDCl_3$) 5.47 (2 H, d, *J* 6 Hz, NH), 6.4 (2 H, m, 4- and 9-H), 6.58 (2 H, d, *J* 16 Hz, 5- and 13-H), 7.62 (2 H, m, 10- and 12-H), 7.88 (6 H, s, COMe), 8.38 (2 H, t, *J* 3 Hz, 11-H), 8.5—8.7 (2 H, m, 5- and 13-H), and 8.63 (6 H, s, Me); ^{13}C n.m.r. 20.23 (C-11), 24.51 and 26.81 (Me), 33.48 (C-5 and -13), 44.25 (C-10 and -12), 54.43 (C-4 and -9), 62.03 (C-1 and -6), and 168.2 (−CO−).

The diamide (17) was further characterised by acetylation (Method B) to give the tetra-amide (15), m.p. 284—286 °C, identical with (15) obtained from reductive acetylation of (16) (see below).

Hydrogenation of the Diamide (16) *at* 1 atm *in Glacial Acetic Acid–Acetic Anhydride*.—A solution of the diamide (16) (1.0 g) in glacial acetic acid (20 ml) and acetic anhydride (20 ml) was hydrogenated under hydrogen (1 atm) for 48 h using PtO_2 (100 mg). Removal of the catalyst by filtration and the solvent under reduced pressure afforded a crude product (1.3 g). Preparative thin layer chromatography (ethanol–ethyl acetate 25 : 75) afforded the less polar compound (19) (467 mg, 40%) and the more polar (15) (450 mg, 35%). Recrystallisation from ethyl acetate–ethanol afforded the triamide (19), m.p. 230—232 °C; $\nu_{max.}$ 1 700, 1 655, and 1 620 cm^{-1}; M^+ 332; τ($CDCl_3$) 5.45 (1 H, m, 6-H), 5.90 (1 H, d, *J* 14 Hz, 5-H), 7.0—9.2 (complex), 7.76 (3 H, s, COMe), 7.88 (3 H, s, COMe), 8.05 (3 H, s, COMe), 8.23 (3 H, s, Me), and 8.38 (3 H, s, Me).

Recrystallisation from ethyl acetate–ethanol afforded the tetra-amide (15), m.p. 284—286 °C (Found C, 60.6; H, 7.5; N, 14.9. $C_{19}H_{28}N_4O_4$ requires C, 60.62; H, 7.50; N, 14.88%); $\nu_{max.}$ (Nujol) 1 700 and 1 650 cm^{-1}; M^+ 376; τ ([$^2H_5$]pyridine) 5.49 (2 H, m, 4- and 9-H), 6.08 (2 H, d, *J* 17 Hz, 5- and 13-H), 7.65 (2 H, m, 10- and 12-H), 7.71 (6 H, s, COMe), 7.81 (6 H, s, COMe), 8.35 (2 H, q, *J* 17 and 8 Hz, 5- and 13-H), 8.40 (2 H, t, *J* 3 Hz, 11-H), and 8.48 (6 H, s, Me); ^{13}C n.m.r. 19.35 (C-11), 21.79 (Me), 24.13 (Me), 28.32 (Me), 32.26 (C-5 and -13), 42.24 (C-10 and -12), 56.54 (C-4 and -9), 62.74 (C-1 and -6), and 169.11 p.p.m. (−CO−).

Hydrogenation of 4,9-*Dimethyl*-2,3,7,8-*tetra-azatetracyclo*-[7.3.1.0.^{4,12}0^{6,10}]*trideca*-1,6-*diene* (1).—4,9-Dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.^{4,12}0^{6,10}]trideca-1,6-diene (1) (600 mg) in ethanol (50 ml) was hydrogenated under hydrogen (3 atm) in the presence of PtO_2 (50 mg). After 15 h the uptake of hydrogen was complete, the catalyst was removed by filtration under nitrogen, and the solvent removed under reduced pressure to afford a brown oil (580 mg). Analysis (^1H n.m.r.) showed the absence of the starting material (1) and the presence of the dihydrazine (2) and azo compounds. Addition of ethyl acetate induced crystallisation and filtration gave as white crystals 1,6-dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.^{4,12}0^{6,10}]trideca-2,7-diene (14) (110 mg, 18%), m.p. 155—160 °C. This material was identical (t.l.c., ^1H n.m.r., and m.p.) with (14) obtained *via* reduction of (1) with lithium aluminium hydride and aluminium chloride.

Hydrogenation of 4,9-dimethyl-2,3,7,8-tetra-azatetracyclo-[7.3.1.0.^{4,12}0^{6,10}]trideca-1,6-diene (1) in ethanol at 90 °C in the presence of PtO_2 under hydrogen (100 atm) similarly afforded a brown oil. Acetylation of this oil by Method B gave the tetra-amide (15) (50%).

1,6-*Dimethyl*-2,3,7,8-*tetra-azatetracyclo*[7.3.1.0.^{4,12}0^{6,10}]-*tridecane* (2).—1,6-Dimethyl-2,3,7,8-tetra-azatetracyclo-[7.3.1.0.^{4,12}0^{6,10}]trideca-2,7-diene (14) (300 mg) in methanol was hydrogenated under hydrogen (1 atm) in the presence of PtO_2 (40 mg). When the uptake of hydrogen was complete (1 h) the catalyst was removed by filtration under nitrogen. Removal of solvent under reduced pressure afforded a white solid (310 mg) which was very air-sensitive. Recrystallisation from ethyl acetate–methanol gave 1,6-dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.^{4,12}0^{6,10}]tridecane (2) (145 mg, 47%), m.p. 120—125 °C; M^+ 208; τ($CDCl_3$) 5.63 (4 H, br, NH), 6.46 (2 H, m, 4- and 9-H), 7.4—8.6 (8 H, complex, 5-, 10-, 11-, 12- and 13-H), and 8.78 (6 H, s, Me); ^{13}C n.m.r. ($CDCl_3$) 19.78 (C-11), 28.36 (1- and 6-Me), 37.00 (C-5 and -13), 42.47 (C-10 and -12), 58.20 (C-4 and -9) and 61.34 (C-1 and -6).

In contrast to the above hydrogenation, when (1) (500 mg) was exposed to the same conditions of hydrogenation at 1 atm for 24 h there was little uptake of hydrogen. Work-up under nitrogen afforded only the starting dihydrazone (1).

1,6-Dimethyl-2,3,7,8-tetra-azatetracyclo[7.3.1.0.^{4,12}0^{6,10}]-tridecane (2) (250 mg) was further characterised by acetylation by Method B to afford a brown solid residue (390 mg). Recrystallisation from ethyl acetate afforded the tetra-amide (15) (320 mg, 69.5%), m.p. 218—283 °C, found to be identical (t.l.c., ^1H n.m.r., and m.p.) with material obtained by hydrogenation and subsequent acetylation of (14).

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