Synthesis of Tetrahydropyridazino[1,2-*a*][1,2,4] benzotriazin-6-one Derivatives. A Novel Heterocyclic System

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Synthesis of pyridazino[1,2-*a*][1,2,4]benzotriazin-6-one derivatives involving reaction of either 1,2,3,6-tetrahydropyridazine (**9**) or hexahydropyridazine **14** with 2-fluoro-5-nitrophenylisocyanate (**5**) to give, *via* intramolecular cyclization, **3a** and **16** respectively is described. Compound **3a** was converted to **18** *via* methylation and hydroxylation to give **20** followed by conversion to the acetonide derivative **18**. Both **16** and **18** were reduced to the amino derivatives **17** and **19** respectively.

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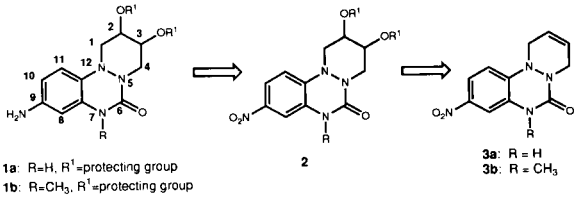
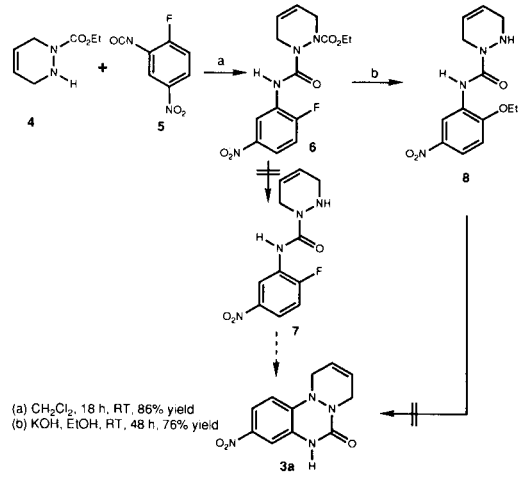
As part of our program aimed at the discovery of new pesticidal agents we decided to prepare derivatives of tetrahydropyridazino[1,2-*a*][1,2,4]benzotriazin-6-one, a novel heterocyclic system. In particular, we wished to prepare the 9-amino-2,3-*cis*-diol derivatives **1a** and **1b**. We envisioned that these intermediates could be obtained from the nitroolefin **3** *via* *cis*-hydroxylation of the double bond followed by suitable protection of the diol to give **2** (Scheme 1). Reduction of the aromatic nitro group would then provide the desired intermediates **1**.

Scheme 1



Synthesis of **3a** was first attempted *via* the reaction between 1-carbethoxy-1,2,3,6-tetrahydropyridazine **4** [1] and 2-fluoro-5-nitrophenylisocyanate (**5**) which gave a good yield of the adduct **6** (Scheme 2). We had hoped that deprotection of the *N*-carbethoxy group from **6** would give

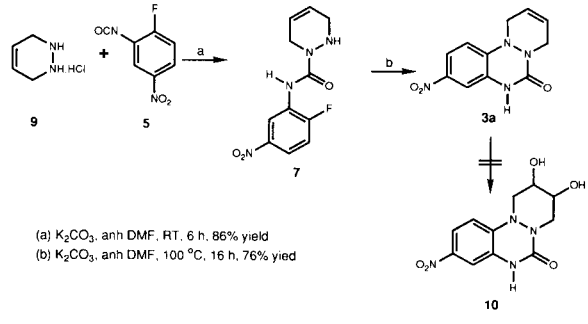
Scheme 2



7, which is set to undergo intramolecular nucleophilic displacement of fluoride to give **3a**. However, we were unable to remove the *N*-carbethoxy group from **6** without also displacing the aromatic fluorine. For example, reaction of **6** with potassium hydroxide in ethanol at room temperature gave the ethoxyphenyl derivative **8**. Attempts to prepare **3a** from **8** *via* intramolecular displacement of ethoxide was also unsuccessful.

We next examined the reaction between 1,2,3,6-tetrahydropyridazine **9** [1] and 2-fluoro-5-nitrophenylisocyanate (**5**) and obtained the adduct **7** in 86% yield (Scheme 3). Treatment of **7** with potassium carbonate in DMF at 90° resulted in smooth cyclization to the benzotriazine derivative **3a** in 76% yield. We subsequently found that **9** can be converted to **3a** in one pot without isolation of **7**. We now needed to introduce the *cis*-diol functionality to obtain **10**. However, **3a** failed to react with a catalytic amount of osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide.

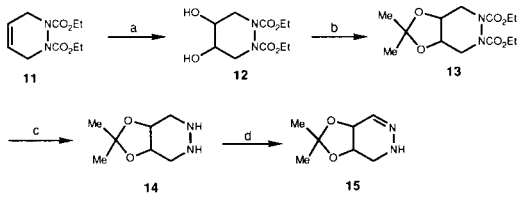
Scheme 3



We decided to introduce the diol functionality early in the synthetic sequence. Thus, treatment of **11** [1] with a catalytic amount of osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide gave the *cis*-diol derivative **12** in excellent yield (Scheme 4). This was treated with 2,2-dimethoxypropane in the presence of *p*-toluenesulfonic acid to give the acetonide derivative **13**. Saponifaction of **13** in the presence of excess alkali led to the hexahydropyridazine derivative **14**. This material is unstable and readily

oxidized to the tetrahydro derivative **15** [2] upon standing exposed to air for a few hours [3]. Thus, **14** was used immediately without further storage. Reaction of **14** with the

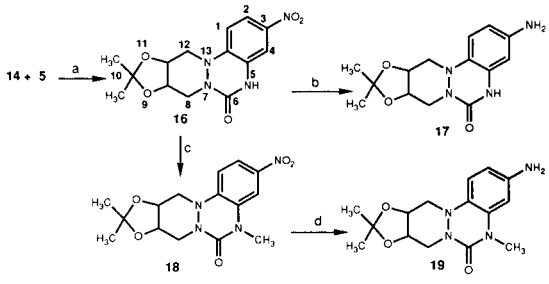
Scheme 4



(a) 4-Methylmorpholine N-oxide, OsO_4, Me_2CO, H_2O, RT, 24 h, 80% yield; (b) PTSA, 2,2-dimethoxypropane, anh toluene, 50 °C, 4 h, 83% yield; (c) KOH, EtOH, reflux, 36 h, 66% yield; (d) air.

phenylisocyanate **5** followed by treatment with potassium carbonate in DMF gave the benzotriazine derivative **16** in 35% yield after purification *via* chromatography on silica gel (Scheme 5). Finally, catalytic reduction of the nitro group with platinum oxide and hydrogen at 50 psi. gave the desired amino derivative **17** in nearly quantitative yield. We also required the *N*-methyl derivative **19**. Thus, treatment of **16** with sodium hydride in DMF followed by reaction with methyl iodide gave the *N*-methylated compound **18** in 87% yield. Catalytic reduction of the nitro group provided **19**.

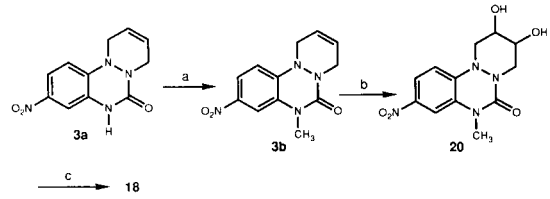
Scheme 5



(a) DMF, RT, 4 h, then 100 °C, 16 h, 35% yield; (b) PtO_2, EtOAc, H_2, 50 psi, 95% yield; (c) NaH, DMF, 0 °C; then MeI, RT, 16 h, 87% yield; (d) PtO_2, EtOAc, H_2, 50 psi, 93% yield.

We also found that reaction of **3a** with sodium hydride followed by treatment with methyl iodide gave the *N*-methyl derivative **3b** in 84% yield (Scheme 6). The site of methylation was unambiguously determined by a simple nuclear Overhauser enhancement (nOe) experiment. Thus, irradiation of the methyl protons (at δ 3.36) produced a 6.6% nOe at δ 7.78 (the C_4 proton). Interestingly, reaction of **3b** with a catalytic amount of osmium tetroxide in the presence of *N*-methylmorpholine *N*-oxide gave the diol **20** in 82% yield. Reaction of **20** with acetone and a catalytic amount of *p*-toluenesulfonic acid provided **18** which was identical in all respects to that obtained from the methylation of **16**.

Scheme 6



(a) NaH, anh DMF, 0 °C, then MeI, RT, 16 h, 84% yield; (b) 4-Methylmorpholine N-oxide, OsO_4, tert-BuOH, Me_2CO, H_2O, RT, 16 h, 82% yield; (c) PTSA, Me_2CO, RT, 48 h, 63% yield.

EXPERIMENTAL

Melting points were determined in open capillary tubes using a Thomas-Hoover apparatus and are uncorrected. The ^1H (300 MHz) and ^{13}C (75.5 MHz) nmr spectra were recorded on a General Electric QE300 spectrometer. Chemical shifts are expressed in parts per million downfield from internal tetramethylsilane. Column chromatography was performed on Merck silica gel 60 (240-400) mesh; silica gel plates were routinely used for tlc determinations. Elemental analyses were performed at FMC Corporation, Analytical Services Department.

N-(2-Fluoro-5-nitro)phenyl-*N'*-(2-carboethoxy)-3,6-tetrahydropyridazinourea (**6**).

2-Fluoro-5-nitrophenyl isocyanate (2.0 g, 10.98 mmoles) was added portionwise to a stirred solution of *N*-carbethoxy-3,6-tetrahydropyridazine **4** (1.72 g, 11.0 mmoles) in anhydrous methylene chloride (30 ml). The mixture was stirred under nitrogen for 18 hours. The solvent was removed by rotary evaporation and the residue was chromatographed on silica gel using a mixture of 2% methanol in methylene chloride as eluent. The fractions containing the product were combined and the solvent removed by rotary evaporation to give a colorless solid (3.2 g, 86%) mp 115-116°; ^1H nmr (deuteriochloroform): δ 1.2 (t, J = 6.5 Hz, 3H), 3.75 (m, 2H), 4.18 (q, J = 6.5 Hz, 2H), 4.52 (m, 2H), 5.80 (m, 2H), 7.13 (t, J = 10 Hz, 1H), 7.7 (br, 1H), 7.80 (m, 1H), 9.22 (m, 1H); ms: (Cl) m/z 339 ($M^+ + 1$, 48), 229 (20), 157 (20), 145 (21), 100 (100).

Anal. Calcd. for $C_{14}H_{15}FN_4O_5$: C, 49.7; H, 4.47; N, 16.56; F, 5.62. Found: C, 49.60; H, 4.47; N, 16.53; F, 5.88.

N-(2-Fluoro-5-nitro)phenyl-*N'*-3,6-tetrahydropyridazinourea (**7**).

Finely ground potassium carbonate (0.38 g, 5.5 mmoles) was added to a stirred suspension of 1,2,3,6-tetrahydropyridazine hydrochloride (0.51 g, 5.5 mmoles) in anhydrous *N,N*-dimethylformamide (10 ml). The mixture was stirred at room temperature under nitrogen for 5 minutes. 2-Fluoro-5-nitrophenyl isocyanate (1.0 g, 5.49 mmoles) was added in one portion and the mixture was allowed to stir for 6 hours. Water was added and the mixture was extracted with methylene chloride, dried (anhydrous magnesium sulfate) and filtered. The solvent from the filtrate was removed by rotary evaporation and the residue was chromatographed on silica gel using a mixture of 1% methanol in methylene chloride as the eluent. The fractions containing the pure product were combined and the solvent was removed by rotary evaporation to give a pale yellow solid, mp 144-145° (0.67 g, 86%); ^1H nmr (deuteriochloroform): δ 3.45 (br s, 2H), 3.72 (t, J = 6 Hz, 1H), 4.18 (br, 2H), 5.92 (m, 2H), 7.17 (t, J = 8 Hz, 1H), 7.82 (m, 1H), 8.95 (br s, 1H), 9.23 (m, 1H); ms: (EI) m/z 266 (M^+, 30), 182 (15), 83 (100), 56 (39).

Anal. Calcd. for $C_{11}H_{11}FN_4O_3$: C, 49.63; H, 4.16; N, 21.04. Found: C, 49.88; H, 4.14; N, 21.03.

1,4-Dihydro-9-nitropyridazino[1,2-*a*][1,2,4]benzotriazin-6-one (**3a**).

A mixture of **7** (1.0 g, 3.756 mmoles), finely powdered potassium carbonate (0.52 g, 3.756 mmoles) and anhydrous *N,N*-dimethylformamide was heated under nitrogen at 100° for 16 hours. The solvent was removed by rotary evaporation under reduced pressure and the residue was partitioned between water and ethyl acetate. The organic layer was dried (anhydrous magnesium sulfate) and the solvent was removed by rotary evaporation. The residue was triturated with diethyl ether to give a yellow solid. Recrystallization from ethanol gave yellow microcrystals, mp 251-253° (0.71 g, 76%); ^{1}H nmr (deuteriochloroform): δ 3.8 (m, 2H), 4.27 (m, 2H), 5.9 (m, 2H), 7.07 (d, J = 8 Hz, 1H), 7.59 (d, J = 2 Hz, 1H), 7.84 (m, 1H); ^{13}C nmr (DMSO-d_6) δ 42.6, 52.9, 108.6, 117.7, 121.5, 123.3, 124.5, 133.9, 139.5, 144.8, 154.0; ms: (EI) m/z 246 (M^+, 100), 231 (97), 185 (13), 164 (40), 118 (26), 90 (63), 54 (52).

Anal. Calcd. for $C_{11}H_{10}N_4O_3$: C, 53.66; H, 4.09; N, 22.75. Found: C, 53.60; H, 4.08; N, 22.70.

1,2-Dicarbethoxy-4,5-dihydroxyhexahydropyridazine (**12**).

To a mixture of 4-methylmorpholine *N*-oxide (5.13 g, 43.8 mmoles), Osmium tetroxide (1.5 ml, 0.12 mmole, 2.5% wt in *t*-butyl alcohol), acetone (20 ml) and water (10 ml) was added 1,2-dicarbethoxy-1,2,3,6-tetrahydropyridazine [1] (10.0 g, 43.8 mmoles). The mixture was stirred at room temperature for 24 hours and quenched with a mixture of sodium hydrosulfite (0.2 g), Florasil (2 g) and water (10 ml). The mixture was stirred for 15 minutes and filtered through a pad of Celite and the pad was washed with acetone. The *p*H of the filtrate was adjusted to 7.0 using 12*N* sulfuric acid. The acetone was removed by evaporation and the aqueous residue was acidified to *p*H 2 by adding more sulfuric acid. This mixture was extracted with ethyl acetate (3 x 30 ml). The combined organic phase was washed with brine, filtered through phase separator filter paper and the solvent was removed by rotary evaporation to give a viscous oil (9.14 g, 80%). This was converted to the acetonide **13** without further purification; ^{1}H nmr (deuteriochloroform): δ 1.12 (br s, 6H), 3.1 (br, 2H), 3.6 (br, 1H), 3.87 (br, 3H), 4.1 (br with overlapping m, 6H); ms: (EI) m/z 262 (M^+, 10), 190 (20), 85 (30), 57 (100).

Diethyl 2,2-Dimethyl-4,5,6,7-tetrahydro-1,3-dioxolo[4,5-*d*]pyridazine (**13**).

A mixture of 1,2-dicarboethoxy-4,5-dihydroxyhexahydropyridazine **12** (8.5 g, 32.4 mmoles), 2,2-dimethoxypropane (15 ml), *p*-toluenesulfonic acid (50 mg) and anhydrous toluene (10 ml) was heated to 50° for 4 hours. The mixture was concentrated by rotary evaporation and the residue was partitioned between methylene chloride (100 ml) and 5% sodium bicarbonate solution (50 ml). The organic layer was dried (anhydrous magnesium sulfate), filtered and the solvent was removed by rotary evaporation to give a colorless viscous oil which solidified upon standing. Recrystallization from tetrahydrofuran gave colorless crystals, mp 103-104° (8.17 g, 83%); ^{1}H nmr (deuteriochloroform): δ 1.15 (br t, 6H), 1.25 (s, 3H), 1.38 (s, 3H), 2.9 (br, 1H), 3.3 (br, 1H), 4.1 (br with overlapping m, 7H), 4.2 (m, 1H); ms: (EI) m/z 302 (M^+, 45), 230 (85), 171 (80), 143 (82), 99 (70), 57 (100).

Anal. Calcd. for $C_{13}H_{22}N_2O_6$: C, 51.65; H, 7.33; N, 9.27. Found: C, 51.6; H, 7.28; N, 9.21.

2,2-Dimethylhexahydro-1,3-dioxolo[4,5-*d*]pyridazine (**14**).

A mixture of 1,2-dicarboethoxy-4,5-dihydroxyhexahydropyradizine acetonide (**13**, 20.0 g, 0.0662 mole), ethanol (350 ml) and potassium hydroxide (40.0 g, 0.71 mole) was heated to reflux for 36 hours under nitrogen. The mixture was cooled to room temperature, filtered and the solvent evaporated. The residue was partitioned between ethyl acetate (400 ml) and water (300 ml). The organic layer was separated, filtered through phase separator paper and the solvent removed by rotary evaporation. The residue was purified by bulb to bulb distillation. The fraction distilling between 100-110° at 0.1 mm Hg was collected to give 7.0 g (66%) of a colorless oil. This material oxidizes readily in air to the tetrahydropyridazine derivative **15** [2] and is best used immediately. Elemental analytical data was not obtained for **14**; ^{1}H nmr (deuteriochloroform): δ 1.3 (s, 3H), 1.46 (s, 3H), 2.9 (m, 2H), 3.15 (m, 2H), 3.37 (br, 2H), 4.08 (m, 2H).

10-Dimethyl-3-nitrobenzo[*e*][1,3]dioxolo[4′,5′:4,5]-8,8a,11a,12-tetrahydropyridazino[1,2-*a*][1,2,4]triazin-6-one (**16**).

To a solution of 4,5-dihydroxyhexahydropyridazine acetonide (**14**, 0.5 g, 3.16 mmoles) in anhydrous *N,N*-dimethylformamide (10 ml) was added dropwise a solution of 2-fluoro-5-nitrophenylisocyanate (0.575 g, 3.16 mmoles) in anhydrous DMF (5 ml). The mixture was stirred at room temperature under nitrogen for 4 hours. Finely ground anhydrous potassium carbonate (0.44 g, 3.16 mmoles) was added to the reaction mixture and the mixture was heated to 100° for 16 hours. The solvent was removed by evaporation under reduced pressure and the residue was partitioned between ethyl acetate and water. The organic layer was dried (anhydrous magnesium sulfate) and the solvent was removed by rotary evaporation. The residue was chromatographed on silica gel eluting with 1% methanol in methylene chloride to give a yellow solid (0.35 g, 35%), mp >242° dec; ^{1}H nmr (deuteriochloroform): δ 1.39 (s, 3H), 1.52 (s, 3H), 3.45 (m, 2H), 3.78 (m, 1H), 4.21 (m, 1H), 4.3 (m, 1H), 4.4 (m, 1H), 7.0 (d, J = 7 Hz, 1H), 7.58 (d, J = 1.5 Hz, 1H), 7.83 (dd, J = 1.5 Hz and 7 Hz, 1H), 8.2 (br s, 1H); ^{13}C nmr (deuteriochloroform): δ 26.07, 28.1, 43.99, 56.12, 69.67, 70.94, 109.32, 109.86, 118.39, 120.93, 133.51, 138.86, 145.56, 154.75; ms: (EI) m/z 320 (M^+, 100), 206 (17), 164 (15), 85 (15), 59 (27).

Anal. Calcd. for $C_{14}H_{16}N_4O_5$: C, 52.50; H, 5.04; N, 17.49. Found: C, 52.34; H, 4.84; N, 17.38.

3-Amino-10-dimethylbenzo[*e*][1,3]dioxolo[4′,5′:4,5]-8,8a,11a,12-tetrahydropyridazino[1,2-*a*][1,2,4]triazin-6-one (**17**).

A mixture of **16** (200 mg, 0.624 mmole), platinum oxide (20 mg), and ethyl acetate (25 ml) was hydrogenated under 50 psi of hydrogen at room temperature for 20 minutes. The reaction mixture was filtered through a pad of Celite and the pad was washed with ethyl acetate. The solvent from the filtrate was removed by rotary evaporation to give a tan solid (0.17 g, 95%). An analytical sample was obtained by chromatography on a silica gel preparative tlc plate using 3% methanol in methylene chloride as eluent, mp 133-135°; ^{1}H nmr (deuteriochloroform): δ 1.39 (s, 3H), 1.52 (s, 3H), 3.15-3.33 (m, 2H), 3.6 (br, 2H), 3.68 (m, 1H), 4.12 (m, 1H), 4.24 (m, 1H), 4.56 (m, 1H), 6.0 (d, J = 1.5 Hz, 1H), 6.23 (dd, J = 1.5 Hz and 7 Hz, 1H), 6.78 (d, J = 7 Hz, 1H), 7.19 (br s, 1H); ^{13}C nmr (deuteriochloroform): δ 26.23, 28.27, 29.53, 44.53, 56.37, 69.69, 71.63, 100.65, 109.15, 109.43, 122.8, 134.17, 145.27, 156.17; ms: (EI) m/z 290 (M^+, 85), 163 (25), 66 (100).

Anal. Calcd. for $C_{14}H_{18}N_4O_3$: C, 57.92; H, 6.25; N, 19.30. Found: C, 57.67; H, 6.43; N, 19.26.

10-Dimethyl-5-methyl-3-nitrobenzo[*e*][1,3]dioxolo[4',5':4,5]-8,8a, 11a,12-tetrahydropyridazino[1,2-*a*][1,2,4]triazin-6-one (**18**).

Method A. From the Methylation of **16**.

To a solution of **16** (0.32 g, 1.0 mmole) in anhydrous *N,N*-dimethylformamide (8 ml) was added sodium hydride (60% dispersion in mineral oil, 0.04 g, 1.0 mmole) and the reaction was stirred under nitrogen for 10 minutes. The reaction mixture was cooled to 0° and methyl iodide (0.062 ml, 1.1 mmoles) was added *via* a syringe. The reaction was stirred for a further 0.5 hour at 0° and then allowed to warm to 20° and stirred for 16 hours. The reaction mixture was quenched with water (30 ml) and extracted with ethyl acetate (3 x 30 ml). The combined organic extract was washed with brine (30 ml) and then dried (anhydrous magnesium sulfate). The solvent was removed by rotary evaporation and the residue was triturated with petroleum ether. The yellow solid was collected by filtration at the pump (290 mg, 87%), mp 88-90°; ^{1}H nmr (deuteriochloroform): δ 1.40 (s, 3H), 1.54 (s, 3H), 3.37 (s, 3H), 3.44 (m, 2H), 3.83 (m, 1H), 4.04 (m, 1H), 4.30 (m, 1H), 4.39 (m, 1H), 7.04 (d, J = 7 Hz, 1H), 7.63 (d, J = 1.5 Hz, 1H), 7.9 (dd, J = 1.5 Hz, and 7 Hz, 1H); ^{13}C nmr (deuteriochloroform): δ 26.10, 28.13, 29.61, 45.19, 55.37, 69.54, 71.24, 108.09, 109.89, 118.36, 120.35, 135.89, 140.76, 145.75, 154.37; ms: (EI) m/z 334 (M^+, 100), 220 (20), 85 (35), 59 (30).

Anal. Calcd. for $C_{15}H_{18}N_4O_5$: C, 53.88; H, 5.42; N, 16.75. Found: C, 54.02; H, 5.41; N, 16.57.

Method B. From the Diol **20**.

A mixture of the diol **20** (1.0 g), *p*-toluenesolfonic acid (0.05 g), and anhydrous acetone was stirred at room temperature under nitrogen for 48 hours. The solvent was removed by evaporation and the residue was partitioned between ethyl acetate (50 ml) and 5% sodium bicarbonate solution (20 ml). The organic phase was dried (anhydrous magnesium sulfate) and the solvent was evaporated. The residue was chromatographed on silica gel eluting with 1% methanol in methylene chloride to give 0.71 g (63%) of pure product which was identical in all respects with the material obtained *via* method A.

3-Amino-10-dimethyl-5-methylbenzo[*e*][1,3]dioxolo[4',5':4,5]-8,8a, 11a,12-tetrahydropyridazino[1,2-*a*][1,2,4]triazin-6-one (**19**).

A mixture of **18** (260 mg), platinum oxide (20 mg), and ethyl acetate (30 ml) was hydrogenated under 50 psi of hydrogen at room temperature for 20 minutes. The reaction mixture was filtered through a pad of Celite and the pad washed well with ethyl acetate. The solvent from the filtrate was removed by rotary evaporation to give a tan colored oil (0.22 g, 93%). An analytical sample was obtained by preparative tlc on silica gel using a mixture of 5% methanol in methylene chloride as eluent; ^{1}H nmr (deuteriochloroform): δ 1.39 (s, 3H), 1.54 (s, 3H), 3.2-3.26 (s and m, 5H), 3.84 (m, 1H), 3.97 (m, 1H), 4.2-4.34 (m, 2H), 6.13 (d, J = 1.5 Hz, 1H), 6.26 (dd, J = 1.5 Hz and 7 Hz, 1H), 6.78 (d, J = 7 Hz, 1H); ^{13}C nmr (deuteriochloroform): δ 26.22, 28.30, 29.20, 45.56, 55.78, 69.33, 71.74, 99.99, 108.59, 109.32, 123.02, 125.49, 136.58, 145.45, 155.98; ms: (EI) m/z 304 (M^+, 100), 219 (45), 177 (50), 134 (40), 85 (75), 57 (30).

Anal. Calcd. for $C_{15}H_{20}N_4O_3$: C, 59.20; H, 6.26; N, 18.41. Found: C, 59.15; H, 6.45; N, 18.50.

1,4-Dihydro-7-methyl-9-nitropyridazino[1,2-*a*][1,2,4]benzotriazin-6-one (**3b**).

To a solution of **3a** (0.5 g, 2.033 mmoles) in anhydrous *N,N*-dimethylformamide (30 ml) was added sodium hydride (60% dispersion in mineral oil, 0.1 g, 2.5 mmoles) and the reaction was stirred under nitrogen for 10 minutes. The reaction mixture was cooled to 0° and methyl iodide (0.3 g, 2.1 mmoles) was added *via* a syringe. The reaction was stirred for a further 0.5 hour at 0° and then allowed to warm to 20° and stirred for 16 hours. The reaction mixture was quenched with water (60 ml) and extracted with ethyl acetate (3 x 30 ml). The combined organic extract was washed with brine (60 ml) and then dried (anhydrous magnesium sulfate). The solvent was removed by rotary evaporation and the residue was chromatographed on silica gel eluting with 1-2% methanol in methylene chloride. The fractions containing the product were combined. Evaporation of the solvent gave a yellow solid, mp 184-185° (0.44 g, 84%); ^{1}H nmr (deuteriochloroform): δ 3.34 (s, 3H), 3.73 (m, 2H), 4.26 (m, 2H), 5.9 (m, 2H), 7.08 (d, J = 7 Hz, 1H), 7.67 (d, J = 1.5 Hz, 1H), 7.9 (dd, J = 1.5 Hz and 7 Hz, 1H); ^{13}C nmr (deuteriochloroform): δ 29.58, 43.65, 53.29, 108.06, 118.08, 121.8, 122.7, 125.1, 136.27, 140.64, 146.1, 155.0; ms: (EI) m/z 206 (M^+, 100), 245 (86), 150 (54), 104 (86), 77 (48).

Anal. Calcd. for $C_{12}H_{12}N_4O_3$: C, 55.38; H, 4.65; N, 21.53. Found: C, 55.21; H, 4.50; N, 21.79.

2,3-Dihydroxy-7-methyl-9-nitro-1,2,3,4-tetrahydropyridazino-[1,2-*a*][1,2,4]benzotrizin-6-one (**20**).

A mixture of **3b** (0.75 g, 2.9 mmoles), 4-methylmorpholine *N*-oxide (0.37 g, 3.2 mmoles), Osmium tetroxide (2 ml, 2.5% wt in *t*-butyl alcohol and acetone (25 ml) was stirred at 20° for 16 hours. A mixture of sodium hydrosulfite (15 mg), Florisil (0.3 g) and water (1 ml) was added to the reaction and the mixture stirred for a further 15 minutes. The reaction mixture was filtered and the filter funnel was rinsed several times with acetone. The solvent from the filtrate was evaporated and the residue was diluted with water and acidified to *p*H 2 with a few drops of 12*N* sulfuric acid. This mixture was extracted with 1-butanol (3 x 20 ml). The combined organic extract was dried over anhydrous sodium sulfate, filtered and the solvent was removed by rotary evaporation to give a brown solid, mp 230-232° (0.7 g, 82%); ^{1}H nmr (DMSO-d_6): δ 3.23 (s, 3H), 3.35 (m, 3H), 3.56 (m, 2H), 3.66 (m, 1H), 3.84 (m, 1H), 4.9 (br, 2H), 7.15 (d, J = 7 Hz, 1H), 7.58 (d, J = 1.5 Hz, 1H), 7.86 (dd, J = 1.5 Hz and 7 Hz, 1H); ^{13}C nmr (DMSO-d_6): δ 29.47, 46.41, 57.72, 65.52, 66.73, 107.89, 118.63, 119.84, 134.81, 141.48, 144.06, 154.13; ms: (EI) m/z 294 (M^+, 100), 207 (65), 193 (30), 161 (25). This material was converted to the acetonide derivative **18** without further purification.

REFERENCES AND NOTES

[1] P. Baranger and J. Levisallis, *Bull. Soc. Chim. France*, 704 (1957).

[2] ^{1}H nmr for **15**: (deuteriochloroform): δ 1.35 (s, 3H), 1.46 (s, 3H), 2.7 (m, 1H), 3.3 (m, 1H), 4.22 (m, 1H), 4.31 (m, 1H), 5.78 (br, 1H), 6.93 (d, J = 2 Hz, 1H).

[3] The oxidation of 4,5-dimethylhexahydropyridazine to 4,5-dimethyl-1,4,5,6-tetrahydropyridazine with mercuric oxide has been reported; B. T. Gillis and P. E. Beck, *J. Org. Chem.*, **27**, 1947 (1962).