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We have prepared the pyrrolopyridazines **7a-f** starting from the diazo compounds **4**. The synthesis involves a tandem condensation-aza-Wittig reaction or a combination of Wittig and aza-Wittig reactions as key steps. Reaction of pyridazine **7d** with diazomethane results in *C*-methylation to yield **7g**. Sodium borohydride reduces **7d** to either the dihydropyridazine **12** or the hydroxylactam **13b** depending of the reaction conditions.

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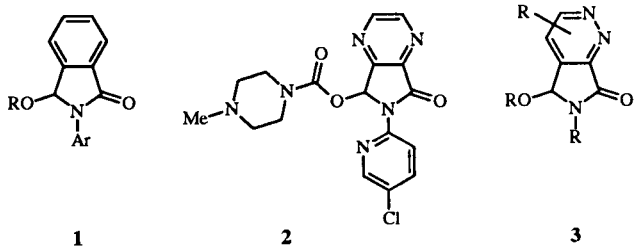
Isoindolones like **1** are potent drugs used as antiarrhythmics and tranquillizers [1]. Similar in structure are the so-called cyclopyrrolones with Zopiclone **2** as a prototype which displays a pharmacological profile familiar with the benzodiazepines [2]. In this context we sought to synthesize some pyrrolo[3,4-*c*]pyridazines **3** (Figure 1), a type of compound rarely mentioned in literature [3].

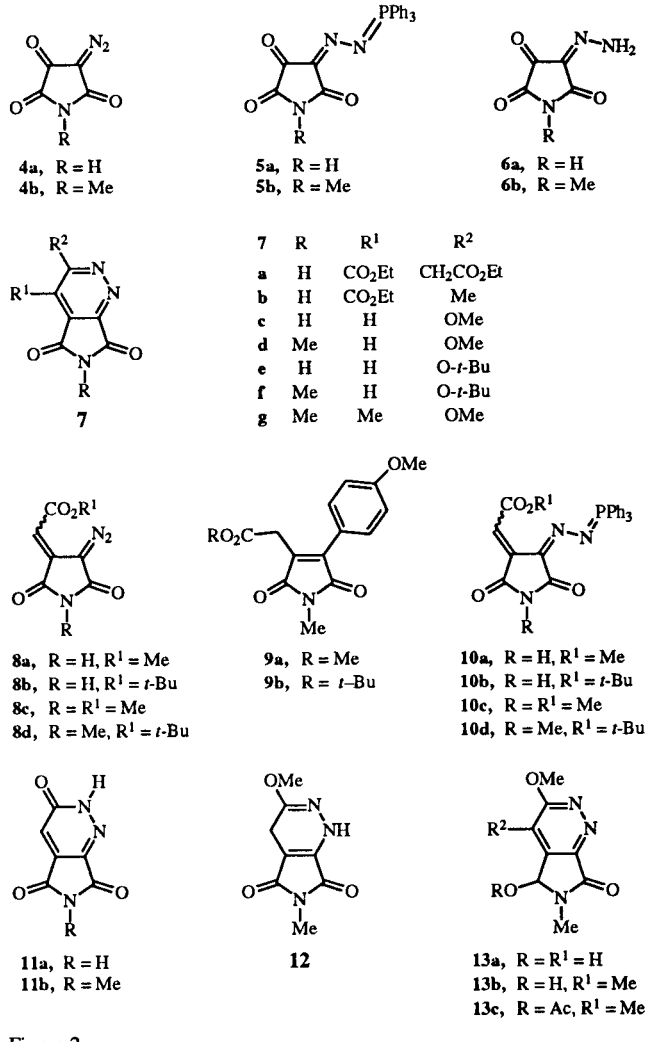


1 **2** **3**

Figure 1

By reaction of the known diazo succinimides **4** [4] with triphenylphosphine we obtained the phosphazines **5** which easily hydrolyzed to the hydrazones **6**. Surprisingly these failed to cyclize with β-ketoesters to the corresponding pyridazinones. On the other hand, the phosphazine **5b** reacted easily with diethyl acetonedicarboxylate or ethyl acetoacetate to yield the pyrrolo[3,4-*c*]pyridazines **7a** or **7b** respectively. The synthesis can be carried out as one-pot reaction by heating equimolar amounts of **4b**, triphenylphosphine and the keto esters in dimethylformamide. In this procedure the phosphazine **5b** apparently acts as an aza-Wittig reagent [5]. It must be left open whether the aza-Wittig reaction occurs first and the cyclization is then completed by aldol type condensation or, more likely, the reaction is running inversely (Figure 2).

The high reactivity of the ketocarbonyl group of compounds **4** is demonstrated by their reaction with alkoxycarbonylmethylene-triphenylphosphoranes. Within a few minutes at room temperature the diazoketones **4** yielded the diazo compounds **8**. Considering the fact that Wittig reactions with diazoketones are rarely mentioned in the literature [6], the olefination could well have taken place at either of the imide carbonyl groups [7]. But such isomeric structures can be ruled out by the following reactions of compounds **8c/d**. When heated in anisole with catalytic amounts of rhodium acetate, we isolated the arylated maleimides **9a/b** identified by their high frequency carbonyl absorptions at 1770 cm^{-1} in the ir spectra and signals for methylene groups in the ^1H nmr spectra. In daylight, solutions of these compounds are strongly fluorescent.



4a, R = H
4b, R = Me

5a, R = H
5b, R = Me

6a, R = H
6b, R = Me

7

7	R	R^1	R^2
a	H	CO_2Et	CH_2CO_2Et
b	H	CO_2Et	Me
c	H	H	OMe
d	Me	H	OMe
e	H	H	O-*t*-Bu
f	Me	H	O-*t*-Bu
g	Me	Me	OMe

8a, R = H, R^1 = Me
8b, R = H, R^1 = *t*-Bu
8c, R = R^1 = Me
8d, R = Me, R^1 = *t*-Bu

9a, R = Me
9b, R = *t*-Bu

10a, R = H, R^1 = Me
10b, R = H, R^1 = *t*-Bu
10c, R = R^1 = Me
10d, R = Me, R^1 = *t*-Bu

11a, R = H
11b, R = Me

12

13a, R = R^1 = H
13b, R = H, R^1 = Me
13c, R = Ac, R^1 = Me

Figure 2

When heated with triphylphosphine, compounds **8** gave first the phosphazines **10** and then, beside of triphenylphosphine oxide, new compounds corresponding the pyrrolopyridazines **7c-7f** in all respects. The cyclizations of compounds **10** can be regarded as intramolecular aza-Wittig reactions between the phosphazine and the ester-carbonyl groups.

The pyridazine **7d** reacted with diazomethane by *C*-methylation to yield **7g**. This compound was also obtained by both *C*- and *N*-methylation from **7c** and diazomethane. *C*-methylations of pyridazines are well documented [8]. Acid-catalyzed hydrolyses of the *tert*-butyl ethers **7e** and **7f** furnished the pyridazinones **11a/b**. The new compounds show only one set of signals in their ^{1}H nmr spectra and a uv absorption characteristic different from the ethers **7e/f**. Therefore in solution the pyridazinones appear to be predominant with no indication of a lactam-lactim-tautomerism.

The pyrrolopyridazine **7d** is attacked by sodium borohydride in two ways depending on reaction conditions. If the reduction of **7d** was carried out in dimethoxyethane at low temperature the dihydropyridazine **12** was obtained. The ir spectrum still shows the imide carbonyl bands. Reduction of the imides **7d** or **7g** in methanol yielded the hydroxylactams **13a/b** as shown by their ^{1}H nmr spectra. NOe experiments with **13b** show the neighbourhood of the hydroxyl and the pyridazine methyl groups. On treatment with acetic anhydride **13b** was easily converted to the *O,N*-acylal **13c**.

EXPERIMENTAL

All melting points were determined with a Dr. Tottoli melting point apparatus (Fa. Büchi) and are uncorrected. Infrared spectra were measured as potassium bromide plates using IR Spectrometer FT-IR 1600 Series (Fa. Perkin Elmer). Ultraviolet spectra were determined in methanolic solutions on Uvicon 810 Anacomp 220 (Fa. Kontron Analytik). The ^{1}H nmr spectra were recorded using tetramethylsilane as internal standard on spectrometer A 60 A, EM 360 A (Fa. Varian) and JEOL GSX 400 (Fa. Jeol). Microanalyses were performed by an Analysator CHNO-Rapid (Fa. Heraeus).

4-(Triphenylphosphoranediylhydrazono)pyrrolidine-2,3,5-trione (**5a**).

Compound **4a** (0.70 g, 5 mmoles) and triphenylphosphine (1.30 g, 5 mmoles) were dissolved in 50 ml of dioxane. After standing overnight at room temperature the reddish precipitate was filtered off and dried, 1.80 g (90%), dec 159°; uv: λ max 208, 370 nm; ir: 3178, 1764, 1731, 1686 cm^{-1}.

Anal. Calcd. for $C_{22}H_{16}N_3O_3P$: C, 65.84; H, 4.02; N, 10.47. Found: C, 65.42; H, 4.06; N, 10.20.

1-Methyl-4-(triphenylphosphoranediylhydrazono)pyrrolidine-2,3,5-trione (**5b**).

Compound **5b** was prepared, by a similar procedure as for **5a**, from **4b** (0.77 g, 5 mmoles) and triphenylphosphine (1.30 g, 5 mmoles), reddish powder, 1.7 g (82%), mp 167° dec; uv: λ max 215, 372 nm; ir: 1776, 1737, 1693 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 8.00-7.60 (m, 15H), 3.53 (s, 3H).

Anal. Calcd. for $C_{23}H_{18}N_3O_3P$: C, 66.51; H, 4.37; N, 10.12. Found: C, 66.32; H, 4.48; N, 10.01.

4-Hydrazonopyrrolidine-2,3,5-trione (**6a**).

Compound **5a** (0.80 g, 2 mmoles) and strong-acid cation exchanger (1 g, Fa. Merck) were stirred in 50 ml of diisopropyl ether/ethanol for 1 hour. After filtration, the solution was concentrated and cooled. The precipitate was collected and recrystallized from diisopropyl ether/ethanol to give a yellow powder, 0.16 g (57%), mp 150° dec; uv: λ max 207, 235, 309 nm; ir: 3382, 3167, 1787, 1714, 1700 cm^{-1}.

Anal. Calcd. for $C_4H_3N_3O_3$: C, 34.05; H, 2.14; N, 29.78. Found: C, 34.10; H, 2.24; N, 30.02.

4-Hydrazono-1-methylpyrrolidine-2,3,5-trione (**6b**).

Compound **6b** was prepared, by a similar procedure as for **6a**, from **5b** (0.83 g, 2 mmoles) and strong-acid cation exchanger (1 g, Fa. Merck), yellow powder, 0.19 g (61%), mp 130° dec (diisopropyl ether/ethanol); uv: λ max 211, 236, 314 nm; ir: 3390, 3156, 1775, 1694 cm^{-1}.

Anal. Calcd. for $C_5H_5N_3O_3$: C, 38.72; H, 3.25; N, 27.09. Found: C, 38.81; H, 3.28; N, 27.12.

Ethyl 3-Ethoxycarbonylmethyl-6,7-dihydro-5,7-dioxo-6-methyl-5*H*-pyrrolo[3,4-*c*]pyridazine-4-carboxylate (**7a**).

Compound **4b** (0.30 g, 2 mmoles), diethyl acetonedicarboxylate (0.60 g, 3 mmoles) and triphenylphosphine (0.52 g, 2 mmoles) were heated in 20 ml of DMF at 60°. After 1 hour the red solution was diluted with water and twice extracted with ethyl acetate. The organic layer was separated, dried and the solvent was evaporated. The residue was recrystallized from diisopropyl ether/ethanol to yield yellow crystals, 0.30 g (47%), mp 101°; uv: λ max 211 nm; ir: 2988, 1792, 1739 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 4.57 (q, 2H), 4.53 (s, 2H), 4.23 (q, 2H), 3.33 (s, 3H), 1.50 (t, 3H), 1.27 (t, 3H).

Anal. Calcd. for $C_{14}H_{15}N_3O_6$: C, 52.34; H, 4.71; N, 13.08. Found: C, 52.41; H, 4.73; N, 13.12.

Ethyl 6,7-Dihydro-3,6-dimethyl-5,7-dioxo-5*H*-pyrrolo[3,4-*c*]-pyridazine-4-carboxylate (**7b**).

The compound was obtained analogously to **7a** from **4b** (0.30 g, 2 mmoles) and ethyl acetoacetate (0.39 g, 3 mmoles) to give yellow crystals, 0.21 g (42%), mp 104° (diisopropyl ether/ethanol); uv: λ max 211, 270 nm; ir: 2994, 1788, 1724 cm^{-1}; ^{1}H nmr (deuteriochloroform): δ 4.60 (q, 2H), 3.30 (s, 3H), 2.95 (s, 3H), 1.43 (t, 3H).

Anal. Calcd. for $C_{11}H_{11}N_3O_6$: C, 53.01; H, 4.45; N, 16.86. Found: C, 53.05; H, 4.48; N, 16.81.

3-Methoxy-5*H*-pyrrolo[3,4-*c*]pyridazine-5,7(6*H*)-dione (**7c**).

Compound **8a** (0.59 g, 3 mmoles) and triphenylphosphine (0.92 g, 3.5 mmoles) were refluxed in 20 ml of toluene. After five hours the solution was concentrated and cooled. The precipitate was collected and recrystallized from ethyl acetate to give pale yellow crystals, 0.32 g (59%), dec 214°; uv: λ max 209, 236, 270 nm; ir: 3210, 1780, 1728 cm^{-1}; ^{1}H nmr (DMSO-d_6): δ 12.00 (broad, 1H), 7.73 (s, 1H), 4.23 (s, 3H).

Anal. Calcd. for $C_7H_5N_3O_3$: C, 46.94; H, 2.81; N, 23.46. Found: C, 46.87; H, 2.90; N, 23.56.

3-Methoxy-6-methyl-5*H*-pyrrolo[3,4-*c*]pyridazine-5,7(6*H*)-dione (**7d**).

This compound was prepared analogously to **7c** from **8c** (0.63 g, 3 mmoles) and triphenylphosphine (0.92 g, 3.5 mmoles), colourless needles, 0.40 g (69%), mp 159° (diisopropyl ether/ethanol); uv: λ max 227, 241, 270 nm; ir: 1786, 1717, 1636 cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.43 (s, 1H), 4.33 (s, 3H), 3.33 (s, 3H).

Anal. Calcd. for $C_8H_7N_3O_3$: C, 49.74; H, 3.65; N, 21.75. Found: C, 49.91; H, 3.66; N, 21.82.

tert-Butoxy-5*H*-pyrrolo[3,4-*c*]pyridazine-5,7(6*H*)-dione (**7e**).

Compound **8b** (0.48 g, 2 mmoles) and triphenylphosphine (0.60 g, 2.3 mmoles) were refluxed in 20 ml of toluene. After 5 hours the solution was evaporated to dryness. The residue was purified on a silica gel column, using ether/petroleum ether as eluent to yield **7e** as a pale yellow powder, 0.18 g (27%), mp 175° dec (diisopropyl ether/ethanol); uv: λ max 211, 238, 272 nm; ir: 3227, 1790, 1733, 1625 cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.30 (s, 1H), 1.70 (s, 9H).

Anal. Calcd. for $C_{10}H_{11}N_3O_3$: C, 54.30; H, 5.01; N, 18.99. Found: C, 54.22; H, 5.20; N, 18.92.

tert-Butoxy-6-methyl-5*H*-pyrrolo[3,4-*c*]pyridazine-5,7(6*H*)-dione (**7f**).

The compound was prepared analogously to **7e** from **8d** (0.50 g, 2 mmoles) and triphenylphosphine (0.60 g, 2.3 mmoles), colourless crystals, 0.20 g (43%), mp 130° (diisopropyl ether/ethanol); uv: λ max 209, 243, 280 nm; ir: 3087, 2987, 1787, 1720, 1628 cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.40 (s, 1H), 3.40 (s, 3H), 1.80 (s, 9H).

Anal. Calcd. for $C_{11}H_{13}N_3O_3$: C, 56.16; H, 5.57; N, 17.86. Found: C, 56.21; H, 5.59; N, 17.81.

3-Methoxy-4,6-dimethyl-5*H*-pyrrolo[3,4-*c*]pyridazine-5,7(6*H*)-dione (**7g**).

An excess of an ethereal solution of diazomethane was added to a solution of **7d** (0.38 g, 2 mmoles) in dioxane. After 30 minutes the volatile material was removed and the residue recrystallized from diisopropyl ether/ethanol to afford colourless crystals, 0.25 g (60%), mp 164°; uv: λ max 212, 241, 273 nm; ir: 3009, 2964, 1782, 1714, 1638 cm^{-1}; ^1H nmr (deuteriochloroform): δ 4.28 (s, 3H), 3.24 (s, 3H), 2.60 (s, 3H).

Anal. Calcd. for $C_9H_9N_3O_3$: C, 52.22; H, 4.38; N, 20.28. Found: C, 52.13; H, 4.35; N, 20.20.

Methyl (4-Diazo-2,5-dioxo-3-pyrrolidinylidene) acetate (**8a**).

Compound **4a** (0.42 g, 3 mmoles) and methoxycarbonylmethylenetriphenylphosphorane (1.0 g, 3 mmoles) were dissolved in 30 ml of dichloromethane. After 15 minutes the solvent was evaporated and the residue purified on a silica gel column, using ether/petroleum ether as eluent, pale yellow crystals, 0.35 g (60%), mp 160° (diisopropyl ether/ethanol); uv: λ max 207, 280, 341 nm; ir: 3182, 3066, 2152, 1760, 1722, 1698, 1632 cm^{-1}; ^1H nmr (deuteriochloroform): δ 11.50 (broad, 1H), 6.43 (s, 1H), 3.83 (s, 3H).

Anal. Calcd. for $C_7H_5N_3O_4$: C, 43.09; H, 2.58; N, 21.53. Found: C, 43.00; H, 2.64; N, 21.67.

tert-Butyl (4-Diazo-2,5-dioxo-3-pyrrolidinylidene)acetate (**8b**).

Compound **8b** was prepared analogously to **8a** from **4a** (0.42 g, 3 mmoles) and (1.13 g, 3 mmoles) *tert*-butoxycarbonylmethylenetriphenylphosphorane, yellow crystals, 0.35 g (49%), mp 98° (diisopropyl ether/ethanol); uv: λ max 209, 281, 340 nm; ir: 3189, 2114, 1771, 1709, 1687, 1638 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.90 (broad, 1H), 6.50 (s, 1H), 1.50 (s, 9H).

Anal. Calcd. for $C_{10}H_{11}N_3O_4$: C, 50.63; H, 4.67; N, 17.71. Found: C, 50.78; H, 4.67; N, 17.54.

Methyl (4-Diazo-2,5-dioxo-1-methyl-3-pyrrolidinylidene)-acetate (**8c**).

Compound **8c** was prepared analogously to **8a** from **4b** (0.46 g, 3 mmoles) and methoxycarbonylmethylenetriphenylphosphorane (1.0 g, 3 mmoles), pale yellow crystals, 0.47 g (75%), mp 157° (diisopropyl ether/ethanol); uv: λ max 214, 250, 260, 280, 343 nm; ir: 2142, 1764, 1715, 1698, 1636 cm^{-1}; ^1H nmr (deuteriochloroform): δ 6.60 (s, 1H), 3.87 (s, 3H), 3.20 (s, 3H).

Anal. Calcd. for $C_8H_7N_3O_4$: C, 45.94; H, 3.37; N, 20.09. Found: C, 46.02; H, 3.54; N, 20.12.

tert-Butyl (4-Diazo-2,5-dioxo-1-methyl-3-pyrrolidinylidene)-acetate (**8d**).

Compound **8d** was prepared analogously to **8a** from **4b** (0.46 g, 3 mmoles) and *tert*-butoxycarbonylmethylenetriphenylphosphorane (1.13 g, 3 mmoles), yellow crystals, 0.60 g (80%), mp 97° (diisopropyl ether/ethanol); uv: λ max 216, 248, 260, 280, 343 nm; ir: 2976, 2120, 1762, 1712, 1698, 1643 cm^{-1}; ^1H nmr (deuteriochloroform): δ 6.57 (s, 1H), 3.17 (s, 3H), 1.53 (s, 9H).

Anal. Calcd. for $C_{11}H_{13}N_3O_4$: C, 52.59; H, 5.22; N, 16.72. Found: C, 52.68; H, 5.24; N, 16.53.

Methyl [2,5-Dioxo-4-(4-methoxyphenyl)-1-methyl-3-pyrrolidinyl]-acetate (**9a**).

Compound **8c** (0.42 g, 2 mmoles) was heated at 65° in 20 ml of anisole with catalytic amounts of rhodium(II) acetate. After ten minutes the solvent was removed under reduced pressure and the residue was purified on a silica gel column, using petroleum ether as eluent, pale yellow crystals, 0.20 g (35%), mp 136° (diisopropyl ether); uv: λ max 229, 278, 360 nm; ir: 2956, 1769, 1736, 1702, 1606 cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.55 and 6.99 (2 sym. m, 2H), 3.85 (s, 3H), 3.74 (s, 3H), 3.62 (s, 2H), 3.09 (s, 3H).

Anal. Calcd. for $C_{15}H_{15}NO_5$: C, 62.28; H, 5.23; N, 4.84. Found: C, 62.14; H, 5.38; N, 4.67.

tert-Butyl [2,5-Dioxo-4-(4-methoxyphenyl)-1-methyl-3-pyrrolidinyl]acetate (**9b**).

The compound was prepared in the same manner as for **9a**, from **8d** (0.50 g, 2 mmoles), pale yellow crystals, 0.20 g (30%), mp 113° (diisopropyl ether); uv: λ max 230, 281, 360 nm; ir: 2980, 1770, 1720, 1706, 1607 cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.65 and 7.05 (2 sym. m, 2H), 3.87 (s, 3H), 3.53 (s, 2H), 3.05 (s, 3H), 1.43 (s, 9H).

Anal. Calcd. for $C_{18}H_{21}NO_5$: C, 65.24; H, 6.39; N, 4.23. Found: C, 65.14; H, 6.48; N, 4.27.

Methyl (2,5-Dioxo-3-pyrrolidinylidene-4-triphenylphosphoranediylhydrazono)acetate (**10a**).

Compound **8a** (0.39 g, 2 mmoles) and triphenylphosphine (0.52 g, 2 mmoles) were dissolved in 30 ml of toluene. After two days at room temperature the solution was cooled. The precipitate was collected and dried, yellow powder, 0.28 g (30%),

dec 133°; uv: λ max 348 nm; ir: 3238, 3061, 1764, 1727, 1635 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.32 (s, 1H), 7.70 (s, 1H), 7.50 (m, 15H), 3.87 (s, 3H).

Anal. Calcd. for $C_{25}H_{20}N_3O_4P$: C, 65.64; H, 4.41; N, 9.19. Found: C, 65.48; H, 4.41; N, 9.39.

tert-Butyl (2,5-Dioxo-3-pyrrolidinylidene-4-triphenylphosphoranediylhydrazono)acetate (**10b**).

Compound **10b** was prepared, in the same manner as for **10a**, from **8b** (0.48 g, 2 mmoles) and triphenylphosphine (0.52 g, 2 mmoles), yellow powder, 0.70 g (70%), mp 155° dec; uv: λ max 348 nm; ir: 3327, 1760, 1731, 1798, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.26 (s, 1H), 7.66 (s, 1H), 7.50 (m, 15H), 1.58 (s, 9H).

Anal. Calcd. for $C_{28}H_{26}N_3O_4P$: C, 67.33; H, 5.25; N, 8.41. Found: C, 67.68; H, 5.38; N, 8.22.

tert-Butyl (2,5-Dioxo-1-methyl-3-pyrrolidinylidene-4-triphenylphosphoranediylhydrazono)acetate (**10d**).

The compound was prepared in the same manner as for **10a**, from **8d** (0.50 g, 2 mmoles) and triphenylphosphine (0.52 g, 2 mmoles), yellow powder, 0.62 g (60%), mp 153° dec; uv: λ max 346 nm; ir: 3450, 3055, 2975, 1763, 1709, 1635 cm^{-1}; ^1H nmr (deuteriochloroform): δ 8.26 (s, 1H), 7.50 (m, 15H), 3.08 (s, 3H), 1.60 (s, 9H).

Anal. Calcd. for $C_{29}H_{28}N_3O_4P$: C, 67.83; H, 5.50; N, 8.18. Found: C, 67.69; H, 5.42; N, 8.27.

2*H*-Pyrrolo[3,4-*c*]pyridazine-3,5,7(6*H*)-trione (**11a**).

Compound **7e** (0.22 g, 1 mmole) was stirred in 5 ml of trifluoroacetic acid. After 15 minutes the volatile products were removed *in vacuo* and the residue was washed with small portions of acetone to give a colourless powder, 0.10 g (60%), mp > 330° dec; uv: λ max 212, 245, 278 nm; ir: 3264, 3151, 3072, 1780, 1755, 1664 cm^{-1}; ^1H nmr (DMSO-d_6): δ 13.71 (s, broad, 1H), 12.17 (s, broad, 1H), 7.26 (s, 1H).

Anal. Calcd. for $C_6H_3N_3O_3$: C, 43.65; H, 1.83; N, 25.45. Found: C, 43.70; H, 1.93; N, 25.32.

6-Methyl-2*H*-pyrrolo[3,4-*c*]pyridazine-3,5,7(6*H*)-trione (**11b**).

The compound was prepared in the same manner as **11a** from **7d** (0.38 g, 2 mmoles). The residue was twice recrystallized from diisopropyl ether/ethanol to give fine colourless needles, 0.23 g (64%), mp 230° dec; uv: λ max 209, 250, 285 nm; ir: 3152, 3036, 2890, 1784, 1722, 1684 cm^{-1}; ^1H nmr (deuteriochloroform): δ 14.00 (s, broad, 1H), 7.37 (s, 1H), 3.30 (s, 3H).

Anal. Calcd. for $C_7H_5N_3O_3$: C, 46.94; H, 2.81; N, 23.46. Found: C, 47.02; H, 3.01; N, 23.35.

1,4-Dihydro-3-methoxy-6-methyl-5*H*-pyrrolo[3,4-*c*]pyridazine-5,7(6*H*)-dione (**12**).

To a stirred and cooled (-20°) solution of **7d** (0.19 g, 1 mmole) in dimethoxyethane was added sodium borohydride (0.04 g, 1 mmole). After five minutes the solution was acidified with strong-acid cation exchanger (1 g, Fa. Merck) and filtered. The filtrate was evaporated and the residue recrystallized from methanol to give yellow crystals, 0.10 g (51%), mp 180° dec; uv: λ max 224, 425 nm; ir: 3284, 1770, 1723, 1664, 1630 cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.65 (s, 1H), 3.78 (s, 3H), 3.22 (s, 2H), 2.97 (s, 3H).

Anal. Calcd. for $C_8H_9N_3O_3$: C, 49.23; H, 4.65; N, 21.52. Found: C, 49.19; H, 4.69; N, 21.50.

5,6-Dihydro-5-hydroxy-3-methoxy-6-methyl-7*H*-pyrrolo[3,4-*c*]-pyridazin-7-one (**13a**).

Sodium borohydride (0.08 g, 2 mmoles) was added to a cooled solution of 0.19 g (1 mmole) of **7d** in methanol at -10°. After one minute the solution was acidified with strong-acid cation exchanger (1 g, Fa. Merck) and filtered. The filtrate was evaporated *in vacuo* and the residue recrystallized from acetonitrile to give colourless crystals, 0.04 g (20%), mp 165° dec; uv: λ max 207, 230, 279 nm; ir: 3160, 1733, 1703, 1634 cm^{-1}; ^1H nmr (DMSO-d_6): δ 7.43 (s, 1H), 6.95 (d, 1H, J = 9 Hz, after deuterium oxide-exchange s), 5.79 (d, 1H, J = 9 Hz, after deuterium oxide-exchange s), 4.13 (s, 3H), 2.99 (s, 3H).

Anal. Calcd. for $C_8H_9N_3O_3$: C, 49.23; H, 4.65; N, 21.52. Found: C, 49.10; H, 4.78; N, 21.67.

5,6-Dihydro-4,6-dimethyl-5-hydroxy-3-methoxy-7*H*-pyrrolo-[3,4-*c*]pyridazin-7-one (**13b**).

Sodium borohydride (0.08 g, 2 mmoles) was added to an ice-cold solution of **7g** (0.20 g, 1 mmole) in 30 ml of methanol. After ten minutes the solution was acidified with strong-acid cation exchanger (1 g, Fa. Merck) and filtered. The volatile products were removed *in vacuo* and the residue recrystallized from acetonitrile to give colourless crystals, 0.12 g (57%), mp 210° dec; uv: λ max 207, 239, 270 nm; ir: 3102, 2920, 1718, 1630 cm^{-1}; ^1H nmr (DMSO-d_6): δ 6.86 (d, 1H, J = 7 Hz), 5.85 (d, 1H, J = 7 Hz), 4.15 (s, 3H), 3.00 (s, 3H), 2.28 (s, 3H). After irridiation at δ 2.26 intensity enhancement was observed at 6.86 and 5.85.

Anal. Calcd. for $C_9H_{11}N_3O_3$: C, 51.67; H, 5.30; N, 20.08. Found: C, 51.56; H, 5.58; N, 19.97.

5-Acetoxy-5,6-dihydro-4,6-dimethyl-3-methoxy-7*H*-pyrrolo[3,4-*c*]pyridazin-7-one (**13c**).

Compound **13b** (0.20 g, 1 mmole), 0.5 ml of acetic anhydride and 0.5 ml of triethylamine were dissolved in 25 ml of dichloromethane. After standing for two hours the volatile was removed *in vacuo* and the residue recrystallized from diisopropyl ether/ethanol to yield colourless crystals, 0.15 g (60%), mp 136°; uv: λ max 209, 243, 275 nm; ir: 2952, 1757, 1725, 1635 cm^{-1}; ^1H nmr (deuteriochloroform): δ 7.10 (s, 1H), 4.25 (s, 3H), 3.10 (s, 3H), 2.21 (s, 6H).

Anal. Calcd. for $C_{11}H_{13}N_3O_4$: C, 52.58; H, 5.21; N, 16.72. Found: C, 52.60; H, 5.30; N, 16.54.

REFERENCES AND NOTES

[1] H. Spreitzer and S. Mustafa, *Pharm. Unserer Zeit*, **20**, 83 (1991).

[2] Römpp Chemie Lexikon, J. Falbe and M. Regitz, eds, Georg Thieme Verlag, Stuttgart, New York, 1992, p 5163.

[3] F. Angelico and F. Monforte, *Gazz. Chim. Ital.*, **53**, 795 (1923); G. Dattolo, G. Cirrincione, A. M. Almerico and E. Aiello, *Heterocycles*, **20**, 255 (1983); G. Dattolo, G. Cirrincione, A. M. Almerico, G. Presti and E. Aiello, *Heterocycles*, **22**, 2269 (1984).

[4] H. Poschenrieder and H.-D. Stachel, *Arch. Pharm. (Weinheim)*, **322**, 301 (1989).

[5] P. Molina and M. Vilaplana, *Synthesis*, 1197 (1994).

[6] L. Capuano, S. Drescher and V. Huch, *Liebigs Ann. Chem.*, 331 (1991).

[7] W. Flitsch and S. R. Schindler, *Synthesis*, 685 (1975).

[8] M. Franck-Neumann and G. Leclerc, *Tetrahedron Letters*, 1063 (1969).