Synthesis and Reactions of 11*H*-Benzo[*b*]pyrano[3,2-*f*]indolizines and Pyrrolo[3,2,1-*ij*]pyrano[3,2-*c*]quinolines [1]

Thomas Kappe, Peter Roschger, Birgit Schuiki and Wolfgang Stadlbauer*

Department of Chemistry, Organic Synthesis Group, Karl-Franzens University of Graz
Heinrichstrasse 28, A-8010 Graz, Austria/Europe

Received December 20, 2002

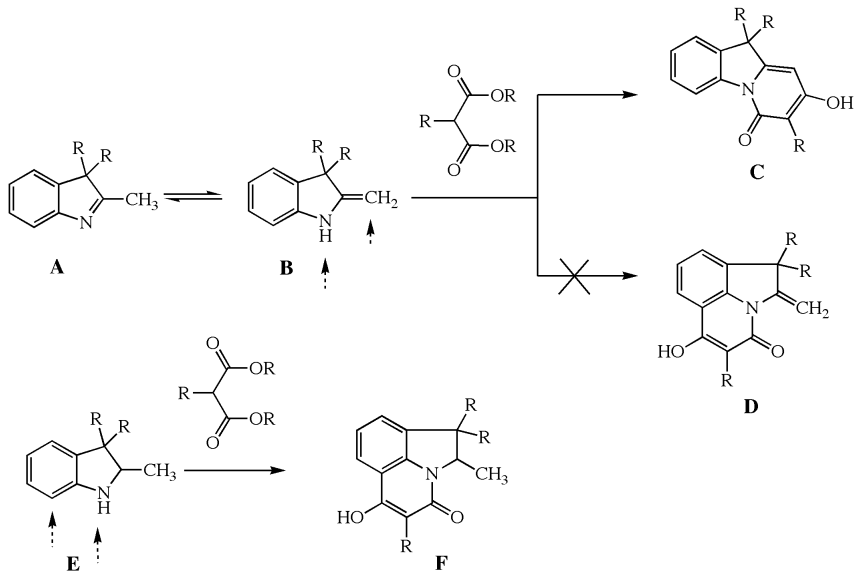
2-Methyl-3*H*-indoles **1** cyclize with two equivalents of ethyl malonate **2** to form 4-hydroxy-11*H*-benzo[*b*]pyrano[3,2-*f*]indolizin-2,5-diones **3**, whereas 2-methyl-2,3-dihydro-1*H*-indoles **9** give under similar conditions regioisomer 8-hydroxy-5-methyl-4,5-dihydro-pyrrolo[3,2,1-*ij*]pyrano[3,2-*c*]quinolin-7,10-diones **10**. The pyrone rings of **3** and **9** can be cleaved either by alkaline hydrolysis to give 7-acetyl-8-hydroxy-10*H*-pyrido[1,2-*a*]indol-6-ones **4** or 5-acetyl-6-hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo-[3,2,1-*ij*]quinolin-4-ones **11**, respectively. Chlorination of **3** and **9** with sulfurylchloride gives under subsequent ring opening 7-dichloroacetyl-8-hydroxy-10*H*-pyrido[1,2-*a*]indol-6-ones **5** or 5-dichloracetyl-6-hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-ones **12**. The dichloroacetyl group of **5** can be reduced with zinc to 7-acetyl-8-hydroxy-10*H*-pyrido[1,2-*a*]indol-6-ones **7**. Treatment of the acetyl compounds **4**, **7** and **11** with 90% sulfuric acid cleaves the acetyl group and yields 8-hydroxy-10*H*-pyrido[1,2-*a*]-indol-6-ones **6** and **8**, and 6-hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-ones **13**. Reaction of dichloroacetyl compounds **12** with sodium azide yields 6-hydroxy-2-methyl-5-(1*H*-tetrazol-5-ylcarbonyl)-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-ones **14** *via* intermediate geminal diazides.

J. Heterocyclic Chem., **40**, 297 (2003).

Pyrido[1,2-*a*]indolones **C** are of interest because they contain two biologically active structure elements, an 4-hydroxypyridone together with the indole system. Recently we could show [2] that 2,3,3-trimethyl-3*H*-indoles react with 2-substituted dialkyl or bis(2,4,6-trichlorophenyl) malonates by cyclocondensation to 8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-ones. This means that the fixed imino moiety of the 3*H*-indole **A** isomerizes to the 1,3-dinucleophilic enamine structure **B** having an exocyclic double bond which gives by cyclocondensation with malonates fused hydroxy-2-pyridones of type **C**, similar to other syntheses of such pyridones [3]. The other possible enamine reaction by attack of the aromatic ring giving structure **D** is rather unlikely and could not be observed. If 1,2-dihydro-3*H*-indoles **E** are used as 1,3-dinucleophilic partner, it could be shown in this work that **E** behaves like a N-substituted aniline [3] and only the regioisomer hydroxy-2-pyridones **F** are formed.

Cyclocondensation of such 1,3-dinucleophiles with unsubstituted malonates are known to react not in a 1:1 ratio, but a second equivalent malonate reacts with the primary cyclocondensation product to give pyrono fused hydroxy-2-pyridones, quinolones or related heterocycles [4-6]. These pyrones are valuable intermediates and offer a high flexibility for further substitution patterns, which are of interest in our projects for new syntheses of fused

Scheme 1



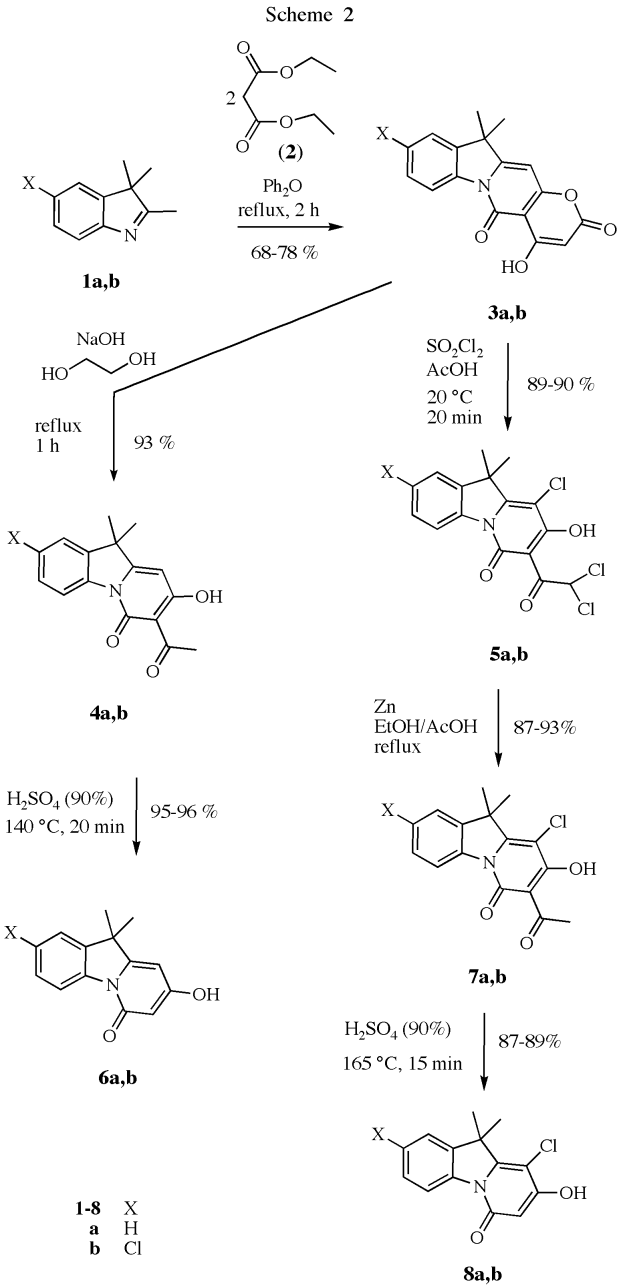
heterocycles containing the biologically active 4-hydroxy-2-pyridone moiety.

The reaction of 2,3,3-trimethyl-3*H*-indoles **1a**,**b** with two equivalents of diethyl malonate (**2**) in refluxing diphenylether afforded in 68-78% yield the 11*H*-benzo[*b*]pyrano[3,2-*f*]indolizinediones **3a**,**b**. During the cyclocondensation the liberated ethanol had to be removed by distillation, because otherwise lower yields were obtained. The stop of ethanol liberation is also a good hint for the reaction time. The cleavage of the pyrano ring in the literature follows two methods: either alkaline hydrolysis of the cyclic ester to a β-keto acid, which decarboxylates upon acidification to the acetyl group [5,6], or chlorination of the cyclic malonyl system with sulfuryl chloride, which gives in the first step an instable 3,3-dichloro pyrane-2,4-dione, and reacts then *via* a β-keto acid to a dichloroacetyl group [7]. The alkaline ring opening reaction was performed by an improved method we have developed for quinolones [5] using sodium hydroxide in glycole/water as solvent. This offers two advantages: the boiling point of the mixture is raised to about 140 °C, and the sodium salts of **3** are well soluble, in contrast to solely water as solvent. The reaction was finished after one hour and the products were obtained in high yield and high purity. When only water was used as solvent, **4a** was obtained in good yield after several hours, whereas the reaction to **4b** was not finished after 24 hours with a yield of less than 50%.

Removal of the acetyl group of **4a**,**b** to give 7-unsubstituted 8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-ones **6a**,**b** was performed *via* an *ipso* substitution with 90% sulfuric acid using an adapted procedure developed for corresponding quinolones [5].

Recently we could show that chlorination of pyronoquinolones and pyronopyridones with sulfuryl chloride gives in an electrophilic substitution as unstable intermediates 3,3-dichloropyrane-2,4-diones which are hydrolyzed during the aqueous work-up due to the rather strong acidic conditions to unstable β-keto acids and decarboxylate then readily to the 3-dichloroacetyl-4-hydroxyquinolones or pyridones [7,8]. Using this reaction sequence, 11*H*-benzo[*b*]pyrano[3,2-*f*]indolizindiones **3a**,**b** gave in excellent yields 9-chloro-7-dichloroacetyl-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-ones **5a**,**b**. In both cases it was found that also the unsubstituted pyridone moiety at position 12 of the pyrone **3a**,**b** was chlorinated too and thus gave 9-chlorosubstituted pyrido[1,2-*a*]indol-6-ones **5**. Reaction of dichloroacetylpyrido[1,2-*a*]indol-6-ones **5a**,**b** with zinc in a mixture of ethanol and glacial acetic acid afforded a selective reduction to the 7-acetyl-9-chloro-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-ones **7a**,**b**. The chloro substituent in position 9 remained unchanged, and also the 2-chloro substituent in the benzo part of **7b**. Deacetylation was again achieved by heating of **7a**,**b** with 90% sulfuric acid and yielded in excellent yields the 7-unsubstituted 9-chloro-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-ones **8a**,**b**. However, the reaction temperature had to be raised from 140 to 165 °C to obtain a similar reaction speed as obtained for the synthesis of **6**, probably caused by the deactivating effect of the chloro substituent in position 9.

Scheme 2



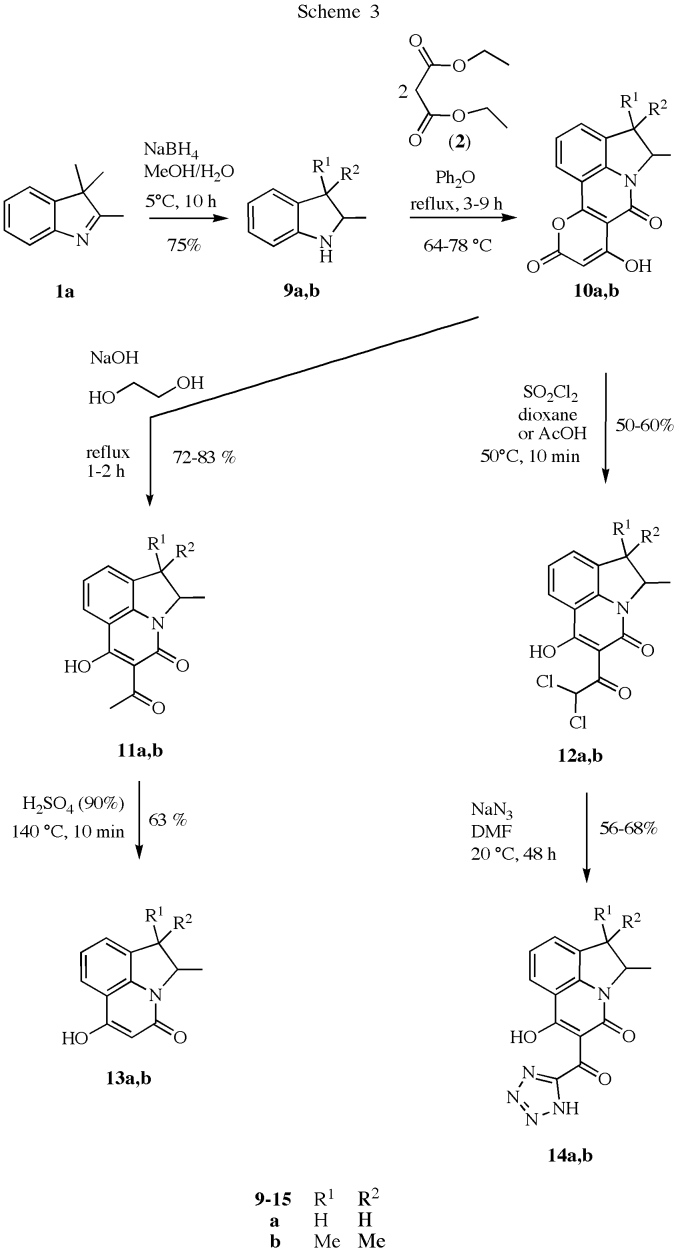
In the second part of this work the reaction of 2,3-dihydro-1*H*-indoles **9a**,**b** with diethyl malonate (**2**) was investigated. 2-Methyl-2,3-dihydro-1*H*-indole **9a** is commercially available, 2,3,3-trimethyl-2,3-dihydro-1*H*-indole **9b** was obtained

by reduction of the C=N double bond of 2,3,3-trimethyl-3*H*-indole (**1a**) with sodium borohydride without affection of the aromatic ring. The reaction of 2,3-dihydro-1*H*-indoles **9a**,**b** with diethyl malonate (**2**) gave again pyrono compounds, however in this case the attack of the first equivalent of diethyl malonate (**2**) was directed to the aromatic ring due to the enamine character of **9**. As primary cyclization product resulted - as outlined in Scheme 1 - the pyrrolo[3,2,1-*ij*]-quinoline structure of type **F**. Cyclocondensation of the second equivalent of diethyl malonate (**2**) formed in good yields 8-hydroxy-5-methyl-4,5-dihydropyrrolo[3,2,1-*ij*]pyrano-[3,2-*c*]quinoline-7,10-diones **10a,b**.

Alkaline ring opening of **10** was performed in a similar manner as described for the sequence **3** → **4** with sodium hydroxide in glycole/water as solvent and resulted in the isolation of 5-acetyl-6-hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-ones **11a**,**b**. The cleavage of the 5-acetyl group could be achieved similar to the sequence **4** → **6** by *ipso*-substitution with 90% sulfuric acid and gave in good yields the 5-unsubstituted 6-hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-ones **13a**,**b**.

The ring cleavage of the pyrone ring of pyrrolo[3,2,1-*ij*]-pyrano[3,2-*c*]quinolin-7,10-diones **10a,b** with sulfuryl chloride was performed as described in the sequence **3** → **5**, either in glacial acetic acid or in dioxane as solvent and gave in medium yields 5-dichloracetyl-6-hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-ones **12a**,**b**. Dichloroacetyl compounds of type **12** are versatile intermediates for further functionalization of position 5 of the heterocyclic ring. As an example, the reaction of **12a**,**b** with sodium azide is described. In the first step the chloro atoms were nucleophilic exchanged against the azido group to produce a geminal diazide as unstable intermediate [9,10]. In a subsequent reaction step, nitrogen was evolved and a tetrazole ring formed by reaction of the nitrene moiety with the azide moiety, which gave 6-hydroxy-2-methyl-5-(1*H*-tetrazol-5-ylcarbonyl)-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-ones **14a**,**b**. This class of tetrazol-5-ylcarbonyl heterocyclic compound is if interest because of safener properties in herbicide screening programs [10,11].

Scheme 3



9-15	R^1	R^2
a	H	H
b	Me	Me

EXPERIMENTAL

Melting points were determined on a Gallenkamp Melting Point Apparatus, Model MFB-595 in open capillary tubes. Infrared spectra were taken as potassium bromide pellets on a Perkin-Elmer 298 or a Galaxy Series FTIR 7000 spectrophotometer. The ^{1}H nmr spectra were recorded on a Bruker AMX instrument (360 MHz) or a Bruker Avance DRX (500 MHz); ^{13}C nmr spectra were recorded on a Bruker AM 360 instrument (90 MHz). Chemical shifts are reported in ppm from internal tetramethylsilane standard and are given in δ-units. Microanalyses were performed on a Fisons elemental analyzer, Mod. EA1108 and are within ±0.4 of the theoretical percentages. All reactions were monitored by thin layer chromatography, carried out on 0.2 mm silica gel 60 F-254 (Merck) plates using uv light (254 and 366 nm) for detection. Common reagent-grade chemicals are either commercially available and were used without further purification or prepared by standard literature procedures.

2,3,3-Trimethyl-3*H*-indole (**1a**) and 5-chloro-2,3,3-trimethyl-3*H*-indole (**1b**) were prepared according to the procedure described in ref. [2]. 2-Methyl-2,3-dihydro-1*H*-indole (**9a**) is commercially available (e.g. Aldrich M3,840-0).

4-Hydroxy-11,11-dimethyl-11*H*-benzo[*b*]pyrano[3,2-*f*]-indolizine-2,5-dione (**3a**).

A solution of 2,3,3-trimethyl-3*H*-indole (**1a**) (15.9 g, 0.1 mol), diethyl malonate (**2**) (32.1 g, 0.2 mol) in diphenylether (50 g) was heated for about 1.5 hours to 200-250 °C. During this time

ethanol (about 22 mL) was liberated. When the liberation of ethanol had stopped, the reaction mixture was cooled to about 50 °C and to the crystal mush methanol (50 mL) was added. After several hours the solid was collected by suction filtration and washed with methanol until the filtrate was only pale yellowish. Then the precipitate was washed with diethyl ether and dried. The yield was 20.1 g (68%), yellow prisms, mp 243-248 °C (glacial acetic acid); ir: 3070 w, 1730 s, 1660 s, 1620 m, 1560 s cm^{-1}; ^1H nmr (CF_3COOH): δ = 1.50 (s, 6 H, 2 CH_3), 5.75 (s, 1 H, 3-H), 6.75 (s, 1 H, 12-H), 7.20-7.50 (m, 2 H, ArH), 8.30 (dd, J = 2 and 8 Hz, 1 H, 7-H).

Anal. Calcd. for $C_{17}H_{13}NO_4$: C; 69.15; H, 4.44; N, 4.74. Found: C, 69.51; H 4.52; N, 4.72.

9-Chloro-4-hydroxy-11,11-dimethyl-11*H*-benzo[*b*]pyrano[3,2-*f*]-indolizin-2,5-dione (**3b**).

5-Chloro-2,3,3-trimethyl-3*H*-indole (**1b**) (19.3 g, 0.1 mol) and diethyl malonate (**2**) (32.1 g, 0.2 mol) were reacted for 2 hours as described for **1a**. The still hot reaction mixture was then poured quickly under vigorous stirring into methanol (500 mL) (attention: danger of local superheating). Further work up was performed as described for **1a**. The yield was 25.8 g (78%), yellow prisms, mp 304 °C (dec.) (glacial acetic acid); ir: 3090 w, 2970 w, 1670 s, 1630 m, 1560 m cm^{-1}; ^1H nmr (CF_3COOH): δ = 1.50 (s, 6 H, 2 CH_3), 5.70 (s, 1 H, 3-H), 6.70 (s, 1 H, 12-H), 7.10-7.40 (m, 2 H, ArH), 8.25 (d, J = 8 Hz, 1 H, 7-H).

Anal. Calcd. for $C_{17}H_{12}ClNO_4$: C, 61.92; H, 3.67; N, 4.25. Found: C, 61.97; H, 3.67; N, 4.13.

7-Acetyl-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-one (**4a**).

To a suspension of benzo[*b*]pyrano[3,2-*f*]indolizinedione **3a** (14.77 g, 50 mmol) in 1,2-ethanediole (100 mL), a solution of sodium hydroxide (10.0 g, 250 mmol) in water (10 mL) was added and the mixture heated under reflux for 1 hour. During the first 10 minutes a strong foaming of the mixture was observed (evolution of carbon dioxide). In this period the reaction flask was shaken several times to dissolve the starting material. At the end of the reaction time, sodium carbonate precipitated and the solution began to bump which made a careful control of heating necessary. After cooling, the mixture was poured onto ice/water (300 mL) and acidified with conc. hydrochloric acid to pH = 1. Attention: the evolution of carbon dioxide from the formed sodium carbonate caused strong foaming of the solution. The precipitate was allowed to stand several hours and then collected by suction filtration and washed with water until neutral. The yield was 12.5 g (93%), light yellowish prisms, mp 161-163 °C (methanol); ir: 2960 w, 2920 w, 2860 w, 1665 s, 1635 m, 1600 m, 1550 m cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.50 (s, 6 H, 2 CH_3), 2.65 (s, 3 H, acetyl-CH_3), 6.40 (s, 1 H, 9-H), 7.10-7.60 (m, 3 H, ArH), 8.35 (dd, J = 2 and 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{16}H_{15}NO_3$: C, 71.36; H, 5.61; N, 5.20. Found: C, 71.75; H, 5.55; N, 5.04.

7-Acetyl-2-chloro-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]-indol-6-one (**4b**).

Benzo[*b*]pyrano[3,2-*f*]indolizinedione **3b** (16.49 g, 50 mmol) was reacted and worked up as described for **4a**. The yield was 14.1 g (93%); light yellowish prisms, mp 188-190.5 °C /ethanol/water); ir: 2970 w, 1655 s, 1630 s, 1590 s, 1540 m cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.50 (s, 6 H, 2 CH_3), 2.60 (s, 3 H, acetyl-CH_3), 6.40 (s, 1 H, 9-H), 7.3 (dd, J = 2 and 8 Hz, 1 H, 3-H), 7.65 (d, J = 2 Hz, 1 H, 1-H), 8.3 (d, J = 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{16}H_{14}ClNO_3$: C, 63.27; H, 4.65; N, 4.61. Found: C, 62.93; H, 4.92; N, 4.37.

9-Chloro-7-dichloroacetyl-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-one (**5a**).

To a suspension of benzo[*b*]pyrano[3,2-*f*]indolizinedione **3a** (14.77 g, 50 mmol) in glacial acetic acid (300 mL) sulfurylchloride (35 mL, 0.43 mol) was added and stirred for 20 min at 20 °C. Then the mixture was poured onto ice/water (300 mL), and after 12 hours the precipitate was collected by suction filtration. The yield was 16.6 g (89%), yellow prisms, mp 155-156 °C (ethanol); ir: 3040 w, 2970 w, 1650 s, 1610 s, 1575 m, 1530 m cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.80 (s, 6 H, 2 CH_3), 7.20-7.60 (m, 3 H, ArH), 7.95 (s, 1 H, dichloroacetyl-H), 8.60 (dd, J = 2 and 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{16}H_{12}Cl_3NO_3$: C, 51.57; H, 3.25; N, 3.76. Found: C, 51.24; H, 3.23; N, 3.76.

2,9-Dichloro-7-dichloroacetyl-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-one (**5b**).

Benzo[*b*]pyrano[3,2-*f*]indolizinedione **3b** (16.49 g, 50 mmol) was reacted and worked up as described for **5a**. The yield was 18.3 g (90%), yellow prisms, mp 174-176 °C (ethanol); ir: 3020 w, 2970 w, 1650 s, 1615 s, 1580 m, 1525 m cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.85 (s, 6 H, 2 CH_3), 7.20-7.55 (m, 2 H, ArH), 7.95 (s, 1 H, dichloroacetyl-H), 8.60 (J = 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{16}H_{11}Cl_4NO_3$: C, 47.21; H, 2.72; N, 3.44. Found: C, 47.53; H, 2.78; N, 3.36.

8-Hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-one (**6a**).

A solution of acetyl-pyrido[1,2-*a*]indolone **4a** (10.77 g, 40 mmol) in 90% sulfuric acid (20 mL) was heated for 20 min to 140 °C. After cooling to 20 °C the mixture was poured onto ice/water (300 mL), the formed precipitate allowed to stand overnight and then collected by suction filtration and washed with water until neutral. The yield was 8.7 g (96%), colorless prisms, mp 261-264 °C (glacial acetic acid); ir: 3200-2300 b, 1640 m, 1605 s, 1555 s cm^{-1}; ^1H nmr (CF_3COOH): δ = 1.65 (s, 6 H, 2 CH_3), 6.85 (d, J = 2 Hz, 1 H, H-9), 7.05 (d, J = 2 Hz, 1 H, 7-H), 7.40-7.70 (m, 3 H, ArH), 8.30 (dd, J = 2 and 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.77; N, 6.16. Found: C, 73.97; H, 5.58; N, 6.09.

2-Chloro-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-one (**6b**).

Acetylpyrido[1,2-*a*]indolone **4b** (12.15 g, 40 mmol) was reacted and worked up as described for **6a**. The yield was 9.9 g (95%), colorless prisms, mp 301 °C (dec) (glacial acetic acid); ir: 3150-2300 b, 1640 m, 1605 m, 1550 s cm^{-1}; ^1H nmr (CF_3COOH): δ = 1.65 (s, 6 H, 2 CH_3), 6.75 (d, J = 2 Hz, 1 H, 9-H), 6.95 (d, J = 2 Hz, 1 H, 7-H), 7.30-7.55 (m, 2 H, ArH), 8.2 (d, J = 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62; N, 5.35. Found: C, 63.94; H, 4.56; N, 5.22.

7-Acetyl-9-chloro-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-one (**7a**).

Dichloroacetylpyrido[1,2-*a*]indolone **5a** (8.19 g, 22 mmol) was dissolved in a boiling mixture of ethanol (300 mL) and glacial acetic acid (50 mL). Then zinc powder (18 g) was added quickly,

and then the reaction mixture was filtered immediately to remove unreacted zinc powder. The filtrate was concentrated under reduced pressure to about 40 mL and then diluted with ice/water (400 mL). The precipitate was kept at 4 °C for 24 hours and then collected by suction filtration. The yield was 5.80 g (87%), colorless prisms, mp 147-148.5 °C (glacial acetic acid); ir: 3000 w, 2930 w, 1665 s, 1650 w, 1610 w, 1590 m, 1545 m cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.75 (s, 6 H, 2 CH_3), 2.70 (s, 3 H, acetyl-CH_3), 7.10-7.40 (m, 3 H, ArH), 8.60 (dd, J = 2 and 8 Hz, 4-H).

Anal. Calcd. for $C_{16}H_{14}ClNO_3$: C, 63.27; H, 4.65; N, 4.61. Found: C, 63.65; H, 4.62; N, 4.60.

7-Acetyl-2,9-dichloro-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-one (**7b**).

Dichloroacetylpyrido[1,2-*a*]indolone **5b** (8.95 g, 22 mmol) was reacted and worked up as described for **7a**. The yield was 6.95 g (93%), colorless prisms, mp 236-238 °C (glacial acetic acid); ir: 3000 w, 1665 s, 1615 m, 1595 m, 1585 m, 1545 m cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.75 (s, 6 H, 2 CH_3), 2.75 (s, 3 H, acetyl-CH_3), 7.10-7.40 (m, 2 H, ArH), 8.50 (J = 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{16}H_{13}Cl_2NO_3$: C; 56.83; H; 3.87; N; 4.14. Found: C; 56.70; H; 3.87; N; 4.05.

9-Chloro-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]indol-6-one (**8a**).

Acetylpyrido[1,2-*a*]indolone **7a** (3.04 g, 10 mmol) and 90 % sulfuric acid (15 mL) was reacted for 15 min at 155-165 °C and worked up as described for **6a**. The yield was 2.28 g (87%), colorless prisms, mp 287-289 °C (glacial acetic acid); ir: 3200-2300 b, 1650 m, 1610 m, 1540 s, cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.70 (s, 6 H, 2 CH_3), 5.80 (s, 1 H, 7-H), 7.05-7.55 (m, 3 H, ArH), 8.35 (dd, 2 and 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{14}H_{12}ClNO_2$: C, 64.25; H, 4.62; N, 5.35. Found: C, 64.08; H, 4.72; N, 5.13.

2,9-Dichloro-8-hydroxy-10,10-dimethyl-10*H*-pyrido[1,2-*a*]-indol-6-one (**8b**).

Acetylpyrido[1,2-*a*]indolone **7b** (3.38 g, 10 mmol) was reacted for 15 min at 155-165 °C and worked up as described for **6a**. The yield was 2.65 g (89%), colorless prisms, mp 281.5-283.5 °C (glacial acetic acid); ir: 3300-2400 b, 1635 m, 1610 m, 1560 s cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.70 (s, 6 H, 2 CH_3), 5.85 (s, 1 H, 7-H), 7.40 (dd, J = 2 and 8 Hz, 1 H, 3-H), 7.70 (d, J = 8 Hz, 1 H, 1-H), 8.50 (d, J = 8 Hz, 1 H, 4-H).

Anal. Calcd. for $C_{14}H_{11}Cl_2NO_2$: C, 56.78; H, 3.74; N, 4.73. Found: C, 56.99; H, 3.67; N, 4.53.

2,3,3-Trimethyl-2,3-dihydro-1*H*-indole (**9b**).

This compound was prepared using an adapted literature procedure [12]. To a solution of 2,3,3-trimethyl-3*H*-indole (**1a**) in 80% aqueous methanol (150 mL) at 0 °C sodium borohydride (5.3 g, 0.14 mol) was added in portions keeping the temperature between 0-10 °C. The reaction mixture was then stirred at 5 °C for 10 hours followed by 3 hours at reflux. After cooling, the solvent was removed under reduced pressure and the yellow residual solution diluted with water (50 mL) and made alkaline with 2 *N* sodium hydroxide solution. The product was extracted with diethylether (2x 100 mL) and the extract dried with sodium sulfate, filtered and the ether removed under reduced pressure. Vacuum distillation of the yellow residue gave a bright yellow oil (31.45 g, 75%), bp 118 °C/19 Torr (lit. bp 234-235 °C/753 Torr [13]); ^1H nmr ($CDCl_3$): δ = 1.10 (s, 3 H, 3-CH_3), 1.24 (d, J = 7 Hz, 3 H, 2-CH_3), 1.35 (s, 3 H, 3-CH_3), 3.55 (q, 1 H, 2-H), 3.65 (s, b, 1 H, NH), 6.62-7.13 (m, 4 H, ArH).

8-Hydroxy-5-methyl-4,5-dihydro-pyrrolo[3,2,1-*ij*]pyrano[3,2-*c*]-quinoline-7,10-dione (**10a**).

Methylindoline **1a** (47.4 g, 0.36 mol) and diethyl malonate (**2**) (114.34 g, 0.71 mol) were reacted for about 9 hours and work up was as described for **3a**. The yield was 61.5 g (64%) yellow prisms, mp 210 °C (1-butanol); ir: 1760 m, 1735 s, 1675 s, 1620 m, 1610 m, 1560 m cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.65 (d, J = 7 Hz, 3 H, CH_3), 3.10 (dd, J = 1.5 and 7 Hz, 1 H, 4-H), 3.75 (dd, J = 1.5 and 7 Hz, 1 H, 4-H), 5.15-5.24 (m, 1 H, H-5), 5.65 (s, 1 H, 9-H), 7.30-7.60 (m, 2 H, ArH), 7.95 (dd, J = 1.5 and 7 Hz, 1 H, 1-H), 13.2 (s, 1 H, OH).

Anal. Calcd. for $C_{15}H_{11}NO_4$: C, 66.91; H, 4.12; N, 5.20. Found: C, 67.08; H, 3.95; N, 5.14.

8-Hydroxy-4,4,5-trimethyl-4,5-dihydropyrrolo[3,2,1-*ij*]pyrano-[3,2-*c*]quinoline-7,10-dione (**10b**).

Trimethylindoline **9b** (13.2 g, 0.082 mol) and diethyl malonate (**2**) (40.0 g, 0.25 mol) were reacted for 2.5 hours and work up was as described for **3a**. The yield was 18.9 g (78%), yellow needles, mp 203 °C (1-butanol); ir: 2940 w, 1740 s, 1660 s, 1550 s cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.30 (s, 3 H, 4-CH_3), 1.50 (d, J= 7 Hz, 3 H, 5-CH_3), 1.55 (s, 3 H, 4-CH_3), 4.70 (q, J = 7 Hz, 1 H, 5-H), 5.65 (s, 1 H, 9-H), 7.30-7.60 (m, 2 H, ArH), 7.95 (dd, J = 1.5 and 7 Hz, 1 H, 1-H), 13.25 (s, 1 H, OH).

Anal. Calcd. for $C_{17}H_{15}NO_4$: C, 68.68; H, 5.09; N, 4.71. Found: C, 68.59; H, 5.01; N, 4.60.

5-Acetyl-6-hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]-quinolin-4-one (**11a**).

Pyrrolo[3,2,1-*ij*]pyrano[3,2-*c*]quinolinedione **10a** (13.45 g, 0.05 mol) was reacted and work up was as described for **4a**. The yield was 10.05 g (83%), colorless prisms, mp 163 °C (glacial acetic acid); ir: 2910 w, 1740 w, 1650 s, 1610 s, 1550 m cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.46 (d, J = 7 Hz, 3 H, Ch_3), 2.70 (s, 3 H, acetyl-CH_3), 2.92 (dd, J = 1.5 and 7 Hz, 1 H, H-1), 3.57 (dd, J = 1.5 and 7 Hz, 1 H, H-1), 4.75-4.95 (m, 1 H, H-2), 7.20 (m, 1 H, H-8), 7.58 (dd, J = 1.5 and 7 Hz, 1 H, H-8), 7.68 (dd, J = 1.5 and 7 Hz, 1 H, H-7).

Anal. Calcd. for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.21; H, 5.27; N, 5.63.

5-Acetyl-6-hydroxy-1,1,2-trimethyl-1,2-dihydro-4*H*-pyrrolo-[3,2,1-*ij*]quinolin-4-one (**11b**).

Pyrrolo[3,2,1-*ij*]pyrano[3,2-*c*]quinolinedione **10b** (8.92 g, 0.03 mol) in 1,2-dihydroxyethane (70 mL) was reacted and worked up as described for **4a**. The yield was 5.86 g (72%), beige prisms, mp 144 °C (glacial acetic acid); ir: 2960 w, 1700 sh, 1650 s, 1615 s, 1550 b, w cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.30 (s, 3 H, 1-CH_3), 1.40 (s, 3 H, 1-CH_3), 1.44 (d, J = 7 Hz, 3 H, 2-CH_3), 2.82 (s, 3 H, acetyl-CH_3), 4.54 (q, 1 H, H-2), 7.10-7.43 (m, 2 H, ArH), 7.8 (dd, J = 1.5 and 7 Hz, 1 H, H-7).

Anal. Calcd. for $C_{16}H_{17}NO_3$: C, 70.83; H, 6.32; N, 5.16. Found: C, 70.79; H, 6.43; N, 5.10.

5-Dichloracetyl-6-hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo-[3,2,1-*ij*]quinolin-4-one (**12a**).

To a suspension of pyrrolo[3,2,1-*ij*]pyrano[3,2-*c*]quinolindione **10a** (5.39 g, 0.02 mol) in glacial acetic acid (50 mL)

sulfurylchloride (10 mL, 0.12 mol) was added in portions to keep the temperature below 50 °C. After 10 minutes at this temperature, the mixture was heated to reflux for 5 minutes, cooled to room temperature and poured onto ice/water (500 mL). The resulting yellow oil was stirred with water for 6 hours, the formed precipitate was collected by suction filtration and washed with water until neutral. The yield was 3.09 g (50%), yellow prisms, mp 178 °C (glacial acetic acid); ir: 3020 w, 1645 s, 1630 sh, 1615 s, 1550 m cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.60 (d, J = 7 Hz, 3 H, CH_3); 3.0 (dd, J = 1.5 and 7 Hz, 1 H, 1-H), 3.60 (dd, J = 1.5 and 7 Hz, 1 H, 1-H), 4.90-5.10 (m, 1 H, 2-H), 7.10-7.55 (m, 2 H, ArH), 7.85 (dd, J = 1.5 and 7 Hz, 1 H, 7-H), 8.05 (s, 1 H, $CHCl_2$), 15.4 (s, 1 H, OH).

Anal. Calcd. for $C_{14}H_{11}Cl_2NO_3$: C, 53.87; H, 3.55; Cl, 22.72; N, 4.49. Found: C, 54.01; H, 3.39; Cl, 22.98; N, 4.41.

5-Dichloracetyl-6-hydroxy-1,1,2-trimethyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one (**12b**).

Pyrrolo[3,2,1-*ij*]pyrano[3,2-*c*]quinolindione **10b** (4.46 g, 15 mmol) in dioxane (35 mL) was reacted with sulfurylchloride (3.2 mL, 40 mmol) and work up was as described for **12a**. The yield was 3.05 g (60%), yellow prisms, mp 112 °C (glacial acetic acid); ir: 3030 w, 2960 w sh, 1640 s, b, 1610 s, 1550 s, b cm^{-1}; ^1H nmr ($CDCl_3$): δ = 1.35 (s, 3 H, 1-CH_3), 1.40 (s, 3 H, 1-CH_3), 1.45 (d, J = 7 Hz, 3 H, 2-CH_3), 4.58 (q, 1 H, 1-H), 7.15-7.50 (m, 2 H, ArH), 7.85 (dd, J = 1.5 and 7 Hz, 1 H, H-7), 8.05 (s, 1 H, $CHCl_2$).

Anal. Calcd. for $C_{16}H_{15}Cl_2NO_3$: C, 56.49; H, 4.44; N, 4.12. Found: C, 56.40; H, 4.20; N, 3.98.

6-Hydroxy-2-methyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one (**13a**).

Acetylpyrrolo[3,2,1-*ij*]quinolinone **11a** (7.29 g, 0.03 mol) and 90% sulfuric acid (25 mL) were reacted for 10 minutes and work up was as described for **6a**. The yield was 3.82 g (63%), colorless prisms, mp 307 °C (dimethylformamide); ir: 2930 w, 2600-2400 b, 1640 s, 1620 m, 1585 s cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.45 (d, J = 7 Hz, 3 H, CH_3), 2.94 (dd, J = 1.5 and 7 Hz, 1 H, 1-H), 3.6 (dd, J = 1.5 and 7 Hz, 1 H, 1-H), 4.75-4.92 (m, 1 H, 2-H), 5.77 (s, 1 H, 5-H), 7.10-7.57 (m, 3 H, ArH).

Anal. Calcd. for $C_{12}H_{11}NO_2$: C, 71.63; H, 5.51; N, 6.96. Found: C, 71.45; H, 5.32; N, 6.73.

6-Hydroxy-1,1,2-trimethyl-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]-quinolin-4-one (**13b**).

Acetyl-pyrrolo[3,2,1-*ij*]quinolinone **11b** (5.21 g, 0.0192 mol) and 90% sulfuric acid (25 mL) were reacted for 10 minutes at 135 °C and work up was as described for **6a**. The yield was 2.2 g (63%), colorless prisms, mp 264 °C (dimethylformamide); ir: 2960 w, 1645 m, 1620 m, 1590 s, b, 1500 s, b cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.28 (s, 3 H, 1-CH_3), 1.34 (d, J = 7 Hz, 3 H, 2-CH_3), 1.36 (s, 3 H, 1-CH_3), 4.38 (q, J = 7 Hz, 1 H, 1-H), 5.78 (s, 1 H, 5-H), 7.15 (m, 1 H, 8-H), 7.20 (dd, J = 1.5 and 7 Hz, 1 H, 9-H), 7.28 (dd, J = 1.5 and 7 Hz, 1 H, 7-H).

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.60; H, 6.50; N, 5.90.

6-Hydroxy-2-methyl-5-(1*H*-tetrazol-5-ylcarbonyl)-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one (**14a**).

A mixture of dichloroacetylpyrrolo[3,2,1-*ij*]quinolinone **12a** (3.15 g, 0.01 mol) and sodium azide (2.6 g, 0.04 mol) in dimethylformamide (50 mL) was stirred at 20 °C for 48 h and then poured onto ice/water (500 mL). This mixture was acidified with 2 *M* hydrochloric acid in small portions (attention: HN_3 is set free), the resulting precipitate was collected by suction filtered and washed with water. The yield was 2.02 g (68%) colorless prisms, mp 211 °C (glacial acetic acid); ir: 2970 w, 1660 sh, 1650 s, 1625 sh, 1615 s, 1590 cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.41 (d, J = 7 Hz, 3 H, CH_3), 2.95 (dd, J = 1.5 and 7 Hz, 1 H, 1-H), 3.42 (s, b, 1 H, tetrazolyl-H), 3.62 (m, 1 H, 1-H), 4.80-4.86 (m, 1 H, 2-H), 7.25 (m, 1 H, 8-H), 7.57 (dd, J = 1.5 and 7 Hz, 1 H, 9-H), 7.79 (dd, J = 1.5 and 7 Hz, 1 H, 7-H).

Anal. Calcd. for $C_{14}H_{11}N_5O_3$: C, 56.57; H, 3.73; N, 23.56. Found C, 56.33; H, 3.66; N, 23.54.

6-Hydroxy-1,1,2-trimethyl-5-(1*H*-tetrazol-5-ylcarbonyl)-1,2-dihydro-4*H*-pyrrolo[3,2,1-*ij*]quinolin-4-one (**14b**).

Dichloroacetylpyrrolo[3,2,1-*ij*]quinolinone **12b** (3.4 g, 0.01 mol) was reacted and work up was as described for **14a**. The yield was 1.82 g (56%), colorless prisms, mp 201 °C (glacial acetic acid); ir: 2960 w, 1645 sh, 1600 s, b, 1549 m, b cm^{-1}; ^1H nmr (DMSO-d_6): δ = 1.39 (s, 3 H, 1-CH_3), 1.50 (s, 3 H, 1-CH), 1.52 (d, J = 7 Hz, 3 H, 2-CH_3), 4.70 (q, J = 7 Hz, 1 H, 2-H), 7.35 (m, 1 H, 8-H), 7.55 (dd, J = 1.5 and 7 Hz, 1 H, 9-H), 8.0 (dd, J = 1.5 and 7 Hz, 1 H, 7-H).

Anal. Calcd. for $C_{16}H_{15}N_5O_3$: C, 59.07; H, 4.65; N, 21.53. Found: C, 59.04; H, 4.52; N, 21.50.

REFERENCES AND NOTES

[1] Organic Azides in Heterocyclic Synthesis, Part 32; Part 31: A. E. Täubl, K. Langhans, T. Kappe and W. Stadlbauer, *J. Heterocyclic Chem.*, **39**, 1259 (2002).

[2] T. Kappe, F. Frühwirth, P. Roschger, B. Jocham, J. Kremsner and W. Stadlbauer, *J. Heterocyclic Chem.*, **39**, 391 (2002).

[3] W. Stadlbauer, E.-S. Badawey, G. Hojas, P. Roschger and T. Kappe, *Molecules*, **6**, 345 (2001).

[4] R. E. Bowman, A. Campbell and E. M. Tanner, *J. Chem. Soc.*, 444 (1959).

[5] P. Roschger and W. Stadlbauer, *Liebigs Ann. Chem.*, 821 (1990); W. Fiala, P. Roschger and W. Stadlbauer, *J. Heterocyclic Chem.*, **29**, 225 (1992).

[6] T. Kappe, *Il Farmaco*, **54**, 309 (1999).

[7] C. O. Kappe and T. Kappe, *J. Heterocyclic Chem.*, **26**, 1555 (1989).

[8] T. Kappe, R. Aigner, P. Hohengassner and W. Stadlbauer, *J. Prakt. Chem.*, **336**, 596 (1994).

[9] K. Faber and T. Kappe, *J. Heterocyclic Chem.*, **21**, 1881 (1984); T. Kappe and C. O. Kappe in "Progress in Heterocyclic Chemistry" (H. Suschitzky and G. W. Gribble, eds), vol. **8**, Pergamon, Oxford, UK, 1996, pp 1-13.

[10] T. Krivitchenko, Dissertation, University of Graz, 1999.

[11] J. J. Kulagowski, R. Baker, N. Curtis, P. D. Leeson, I. M. Mawer, A. M. Mosley, M. P. Ridgilli, M. Rowley, I. Stansfield, A. C. Foster, S. Grimwood, R. G. Hill, J. A. Kemp, G. R. Marshall, K. L. Saywell and M. D. Tricklebank, *J. Med. Chem.*, **37**, 1402 (1994).

[12] N. P. Buu-Hoi, P. Jaquinon and T. B. Loc, *J. Chem. Soc.*, 738 (1958); S. Sakai, M. Wakabayashi and M. Nishina, *Yakugaku Zasshi*, **89**, 1061 (1969); *Chem. Abstr.*, **72**, 3308d (1970).

[13] A. Ferratini, *Gazz. Chim. Ital.*, **23 II**, 112 (1893).