

Potential Non-Steroidal Estrogens and Antiestrogens, IV [1] Organic Azides in Heterocyclic Synthesis, Part 13 [2]: Synthesis of Aza- and Diazacoumestrols via Azido Derivatives

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Summary. 4-Chloro-3-aryl-coumarins and quinolones **2 a–e** undergo thermolytic ring closure by reaction with sodium azide in refluxing dimethyl formamide to yield indolo[3,2-c]coumarins and indolo[3,2-c]quinolin-6(5*H*)-ones **6 a–e**. In the case of the coumarin **2 a** the azido coumarin **5** can be isolated. The mono- and diazacoumestrol-dimethylethers **6 a–c** are converted into the coumestrol analogues **7 a–c** and their diacetyl derivatives **8 a–c**.

Keywords. Azacoumestans; Coumarin, 3-aryl, 4-hydroxy/4-chloro/4-azido; Indoles; 2(1*H*)-Quinolones, 3-aryl,4-hydroxy/4-chloro/4-azido; Ring closure; Thermolysis.

Potentielle nichtsteroidale Östrogene und Antiöstrogene, 4. Mitt. [1]: Organische Azide in der Heterocyclensynthese, Teil 13 [2]: Synthese von Aza- und Diazacumöstrolen über Azidzwischenstufen

Zusammenfassung. 4-Chlor-3-arylcumarine und -chinolone **2 a–e** reagieren thermolytisch mit Natriumazid in siedendem Dimethylformamid unter Ringschluß zu Indolo[3,2-c]cumarinen und Indolo[3,2-c]chinolin-6(5*H*)-onen **6 a–e**. Nur aus dem Cumarinderivat **2 a** kann das zwischenzeitlich gebildete Azidocoumarin **5** isoliert werden. Die so erhaltenen Mono- und Diazacumöstroldimethylether **6 a–c** werden in die entsprechenden Cumöstrole **7 a–c** und ihre Diacetylderivate **8 a–c** umgewandelt.

Introduction

The basic ring system of a number of natural products contains the coumestan ring system (6*H*-benzofuro[3,2-c]benzopyran-6-one), which is found e.g. in coumestrol, psoralidine or pterocarpin [3]. Coumestrol, which is a naturally occurring estrogen [2, 4], contains a rigid (*E*)-4,4'-dihydroxystilbene moiety, which is also present in ring systems, where one or both oxygen atoms are replaced by nitrogens. This should lead to compounds with potential biological activity either in estrogen sensitive tissue or in human breast tumor cells, where also synthetic nonsteroidal estrogen antagonists are pharmaceutically used [5]. Moreover, recently azacoumestans were found possessing an antiosteoporotic activity [6]. On the other hand, fused ring systems, which contain both the indole and the quinoline nucleus, rep-

resent another type of natural products, the carboline ring system. Diazacoumestans correspond to the alkaloids of the 3,4-benzo- γ -carboline type, which are found e.g. in ibogamine [7] or are used as pharmaceuticals [8].

Recently we reported a simple synthesis of coumestrols and azocoumestrols using a modified Heck-reaction to cyclodehydrohalogenate 3-iodo-4-aryloxy-coumarins and quinolones [1, 8] to benzofuranes, which prompted us to develop a route to the isomeric azacoumestrols and diazacoumestrols containing the indole nucleus instead of the benzofuran ring.

Results and Discussion

Some years ago we reported some syntheses of indolo[3,2-*c*]coumarins and quinolones involving a cyclization of 4-amino-[10], 4-triphenylphosphoranylideneamino-[11] or 4-azidocoumarins[11] or quinolones, resp. [10, 11] in the last step. From our results obtained in the recently developed coumestrol- and azacoumestrol syntheses we knew, that the reaction rate of the ring closure to phenyl substituents possessing methoxy groups in meta-position to the point of attack is lowered or in some cases no reaction takes place [1, 12]. So we excluded the cyclodehydrogenation reaction starting from 4-amino- or 4-triphenylphosphoranylideneamino-3-aryl derivatives [10, 11], which requires high temperatures (up to 250°C) combined with rather low yields even with unsubstituted phenyl substituents in 3-position [10, 11] and directed our attention to the ring closure of 4-azido-3-arylcoumarins and quinolones.

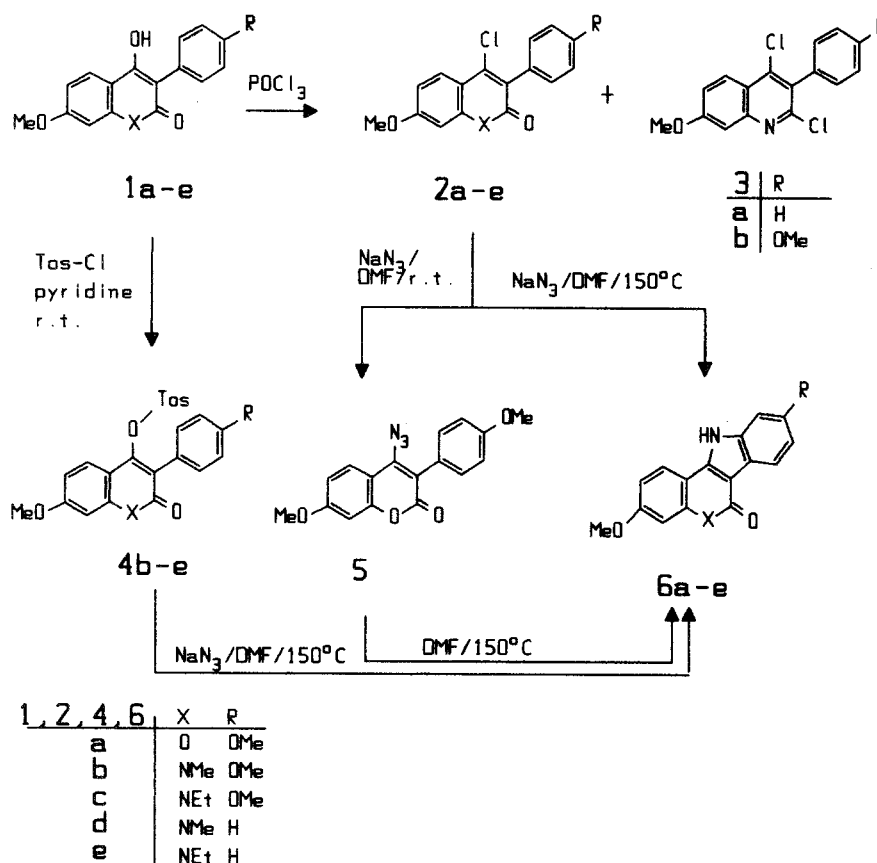
N-Unsubstituted quinolones are causing problems in the use as receptor active compounds because of their insolubility and the possibility of H-bonds, which are causing different distances as obtained with O- or N-substituted compounds. In order to avoid these problems, N-methyl- and N-ethyl-2-quinolones **1b–e** have been chosen as model compounds. Their preparation required the synthesis of N-alkyl-3-methoxyanilines, which were synthesized as described recently [1]. Condensation of these anilines with phenyl- or 4-methoxyphenyl malonates (obtained from dimethyl oxalate and 4-methoxyphenyl acetate [13]) yielded **1b–e**, 3-methoxyphenol and 4-methoxyphenylmalonate cyclizes to **1a** using the general method described in Ref. [14].

Nucleophilic exchange of the 4-hydroxy-group in the coumarin and the quinoline system for a chloro group could be achieved by the action of phosphoryl chloride. With the quinolones **1b–e**, reaction times longer than 1 h result in the formation of the dichloro quinolines **3a, b** by substitution of the oxygen function in position 2 against chlorine and acid catalyzed desalkylation of the N-1-methyl- or ethyl group, respectively. The N-methyl group in **1b, d** was shown to be more sensitive against desalkylation and yielded 30% dichloro quinoline **3** with only 50–60% yield of monochloroquinolones **2b, d**, whereas the cleavage of the ethyl group in **1c, e** led only to 10% dichloro quinolines **3** and 80% monochloro quinolones **2c, e** (Scheme 1).

The next step should lead from the chloro compounds **2** to the azides of type **5** by reaction with sodium azide, which could react in a second step by decomposition of the azido group to the desired indole. In the case of the coumarin **2a** the substitution took place at room temperature in excellent yields, but with the quinolines **2b–e** the corresponding azido quinolones could not be obtained: rising the

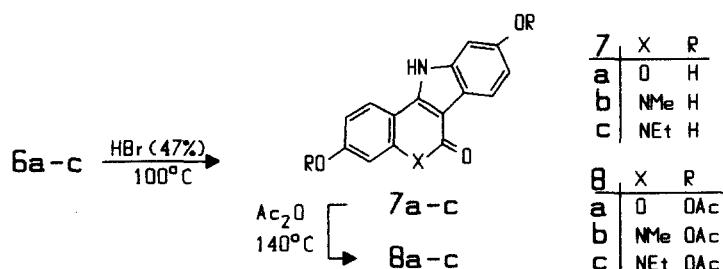
temperature till 80° did not lead to an azido compound, higher temperatures caused a slow reaction to the azide but followed by a quick decomposition and indole cyclization to yield the diazacoumestans **6b–e**. The best result in the reaction of **2b–e** to the indolo quinolones were obtained in refluxing dimethyl formamide with excess sodium azide. It is remarkable that the reaction time is dependent on the quantity of the charge; larger amounts need a reaction time of 12–24 h. The indolo coumarin **6a** was achieved in both ways: directly from the chloro coumarin **1a** in one step in 88% yield, or via the 4-azidocoumarin **5** in 92% total yield.

Another general way to obtain the desired azido quinolones of type **5** was found in the reaction of 4-tosyloxy-quinolones with sodium azide [15]. However, in the case of the 4-tosyloxy-quinolones **4b–e** this way failed too and either no reaction took place or the ring closure to **6b–e** was faster than the formation of the azido compound (Scheme 1).



Scheme 1

To transform the aza- and diazacoumestrol-dimethylethers **6a–c** into a receptor active form, the ethers were cleaved to give the free coumestrols **7a–c** in quantitative yields by reaction with hydrobromic acid. To achieve a better solubility for biological tests, the hydroxy compounds were acetylated with acetic anhydride to afford the corresponding acetoxy compounds **8a–c** (Scheme 2).



Scheme 2

Experimental Part

Melting points were obtained on a Gallenkamp Melting Point Apparatus, Mod. MFB-595 (open capillary tubes). ^1H -NMR spectra were recorded on a Varian EM 360 or on a Varian Gemini 200 instrument (TMS as internal standard, δ -values in ppm, $\text{DMSO}-d_6$ as solvent unless otherwise indicated). Microanalyses were performed on a C,H,N-Automat Carlo Erba 1106. IR spectra were recorded on a Perkin-Elmer 298 (KBr-pellets).

General Procedure for the Synthesis of 4-Chloro-7-methoxy-3-(4-methoxyphenyl)-coumarin (2a), 3-Aryl-1-alkyl-4-chloro-7-methoxy-quinolin-2(1H)-ones 2b-d and 3-Aryl-2,4-dichloro-7-methoxy-quinolines 3a,b

The appropriate 4-hydroxycoumarin or 4-hydroxyquinolones **1a-e** (10 mmol) were refluxed in phosphoryl chloride (25 ml) for 60 min (**1b-e**) or 90 min (**1a**). After cooling the mixture the excess of phosphoryl chloride was removed in vacuo and the residue was treated with 200 ml of ice/water. The precipitate was filtered to separate **3a,b** from **2b-e**. The filtrate was neutralized to pH 4–6 with 6 *N* sodium hydroxide, the precipitate collected by filtration and washed with water (data: see Tables 1 and 2).

General Procedure for the Synthesis of 1-Alkyl-3-aryl-4-(4-toluenesulfonyloxy)-2(1H)-quinolones 4b-e

A solution of the appropriate 4-hydroxyquinolone **1b-e** (7 mmol) and catalytical amounts of 4-(*N,N*-dimethyl)aminopyridine (0.01 g) in anhydrous pyridine (20 ml) was treated with 4-toluenesulfochloride (1.71 g, 9 mmol) and stirred for 12 h at room temperature. The mixture was poured into ice/water and the resulting precipitate was filtered (data: see Table 3).

4-Azido-7-methoxy-3-(4-methoxyphenyl)-coumarin (5)

Sodium azide (0.39 g, 6 mmol) was added to a suspension of **2a** (1.26 g, 4 mmol) in dimethylformamide (25 ml) and the mixture was stirred at room-temperature for 40 min. After dilution with water a precipitate was obtained, which was filtered, washed with water and dried. Yield: 94%; m.p. 142–152°C (cyclohexane, dec.). IR: 2110 s (N_3), 1610 s, 1600 s. $\text{C}_{17}\text{H}_{13}\text{ClO}_4$ (316.7): calcd. C 64.46, H 4.13; found C 64.10, H 4.25.

General Procedure for the Synthesis of [1]Benzopyrano[4,3-b]indol-6-one (6a) and Indolo[3,2-c]quinolin-6(5H)-ones (6b-e)

Method A. A mixture of the appropriate chloro compound **2a-e** (3 mmol) or the corresponding tosyloxy compound **4b-e** (3 mmol) and sodium azide (0.39 g, 6 mmol) in dimethyl formamide (20 ml)

Table 1. 3-Aryl-4-chloro-7-methoxy-coumarin (**2a**) and 1-Alkyl-3-aryl-4-chloro-7-methoxy-quinolin-2(1*H*)-ones **2b-d**

Compound	Yield (%)	M.p. (°C) Solvent	Molecular formula ^a	IR (KBr) ¹ H-NMR (<i>DMSO-d</i> ₆), δ/ppm
4-Chloro-7-methoxy-3-(4-methoxyphenyl)-coumarin (2a)	68	180–185 (toluene)	C ₁₇ H ₁₃ ClO ₄ 316.7	1720 s, 1615 m, 1595 m (CDCl ₃): 3.8 (s, OCH ₃), 3.85 (s, OCH ₃), 6.7–7.0 (m, 4 <i>Ar</i> -H), 7.2–7.45 (m, 2 <i>Ar</i> -H), 7.8 (d, H-5, <i>J</i> = 7 Hz)
4-Chloro-7-methoxy-1-methyl-3-(4-methoxyphenyl)-quinolin-2(1 <i>H</i>)-one (2b)	64	176 (toluene)	C ₁₈ H ₁₆ ClNO ₃ 329.8	1640 s, 1600 s 3.5 (s, CH ₃), 3.7 (s, OCH ₃), 3.9 (s, OCH ₃), 6.8–7.2 (m, H-6, H-8, 4 <i>Ar</i> -H), 7.8 (d, H-5, <i>J</i> = 7 Hz)
4-Chloro-1-ethyl-7-methoxy-3-(4-methoxyphenyl)-quinolin-2(1 <i>H</i>)-one (2c)	80	190 (acetic acid)	C ₁₉ H ₁₈ ClNO ₃ 343.8	1640 s, 1600 s 1.1 (t, CH ₃ , <i>J</i> = 7 Hz), 3.7 (s, OCH ₃), 3.9 (s, OCH ₃), 4.1 (q, CH ₂ , <i>J</i> = 7 Hz), 6.8–7.2 (m, H-6, H-8, 4 <i>Ar</i> -H), 7.8 (d, H-5, <i>J</i> = 7 Hz)
4-Chloro-7-methoxy-1-methyl-3-phenyl-quinolin-2(1 <i>H</i>)-one (2d)	53	151–153 (toluene)	C ₁₇ H ₁₄ ClNO ₂ 299.8	1680 s, 1620 s 3.6 (s, CH ₃), 3.9 (s, OCH ₃), 6.9–7.1 (m, H-6, H-8), 7.2–7.5 (m, 5 <i>Ar</i> -H), 7.9 (d, H-5, <i>J</i> = 7 Hz)
4-Chloro-1-ethyl-7-methoxy-3-phenyl-quinolin-2(1 <i>H</i>)-one (2e)	85	134–135 (ethanol)	C ₁₈ H ₁₆ ClNO ₂ 313.8	1650 s, 1620 s 1.3 (t, CH ₃ , <i>J</i> = 7 Hz), 3.9 (s, OCH ₃), 4.2 (q, CH ₂ , <i>J</i> = 7 Hz), 7.1–7.2 (m, H-6, H-8), 7.3–7.5 (m, 5 <i>Ar</i> -H), 7.9 (d, H-5, <i>J</i> = 7 Hz)

^a Satisfactory microanalyses obtained within ± 0.4%**Table 2.** 3-Aryl-2,4-dichloro-7-methoxyquinolines **3a, b**

Compound	Yield (%)	M.p. (°C) Solvent	Molecular formula ^a	IR (KBr) ¹ H-NMR (<i>DMSO-d</i> ₆), δ/ppm
2,4-Dichloro-7-methoxy-3-phenyl-quinolin (3a)	<i>Me</i> : 35 <i>Et</i> : 10	187–191 (ethanol)	C ₁₆ H ₁₁ Cl ₂ NO (304.2)	1620 s, 1560 m 4.0 (s, OCH ₃), 7.3–7.6 (m, 7 <i>Ar</i> -H), 8.1 (d, H-8, <i>J</i> = 7 Hz)
2,4-Dichloro-7-methoxy-3-(4-methoxyphenyl)-quinolin (3b)	<i>Me</i> : 30 <i>Et</i> : 10	214–216 (acetic acid)	C ₁₇ H ₁₃ Cl ₂ NO ₂ (334.2)	2910 m, 1610 s, 1560 m 3.8 (s, OCH ₃), 3.9 (s, OCH ₃), 7.0–7.5 (m, 6 <i>Ar</i> -H), 8.1 (d, H-8, <i>J</i> = 7 Hz)

^a Satisfactory microanalyses obtained within ± 0.4%

Table 3. 1-Alkyl-3-aryl-7-methoxy-4-(4-toluenesulfonyloxy)-2(1*H*)-quinolines **4b–e**

Compound	Yield (%)	M.p. (°C) Solvent	Molecular formula ^a	IR (KBr) ¹ H-NMR (DMSO- <i>d</i> ₆), δ/ppm
7-Methoxy-1-methyl-3-(4-methoxyphenyl)-4-(4-toluenesulfonyloxy)-2(1 <i>H</i>)-quinolone (4b)	87	183–184 (toluene)	C ₂₅ H ₂₃ NO ₆ S (465.5)	2480 s, 1630 s, 1600 s 2.3 (s, tolyl-CH ₃), 3.7 (s, N-CH ₃), 3.8 (s, <i>Ph</i> -OCH ₃), 3.9 (s, 7-OCH ₃), 6.5–7.3 (m, 10 <i>Ar</i> H), 7.8 (d, <i>J</i> = 7 Hz, H-5)
1-Ethyl-7-methoxy-3-(4-methoxyphenyl)-4-(4-toluenesulfonyloxy)-2(1 <i>H</i>)-quinolone (4c)	99	199–200 (toluene)	C ₂₆ H ₂₅ NO ₆ S (479.5)	2980 s, 1640 s, 1600 s 1.3 (t, <i>J</i> = 7 Hz, ethyl-CH ₃), 2.4 (s, tolyl-CH ₃), 3.7 (s, <i>Ph</i> -OCH ₃), 3.9 (s, 7-OCH ₃), 4.3 (q, <i>J</i> = 7 Hz, CH ₂), 6.55–6.65 (m, H-6, H-8), 6.9–7.3 (m, 8 <i>Ar</i> H), 7.8 (d, <i>J</i> = 7 Hz, H-5)
7-Methoxy-1-methyl-3-phenyl-4-(4-toluenesulfonyloxy)-2(1 <i>H</i>)-quinolone (4d)	95	202–204 (toluene)	C ₂₄ H ₂₁ NO ₅ S (435.5)	1630 s, 1600 s 2.2 (s, tolyl-CH ₃), 3.6 (s, N-CH ₃), 3.8 (s, 7-OCH ₃), 6.8–7.9 (m, 12 <i>Ar</i> H)
1-Ethyl-7-methoxy-3-phenyl-4-(4-toluenesulfonyloxy)-2(1 <i>H</i>)-quinolone (4e)	95	202–203 (toluene)	C ₂₅ H ₂₃ NO ₅ S (449.5)	1630 s, 1600 s 1.3 (t, <i>J</i> = 7 Hz, ethyl-CH ₃), 2.3 (s, tolyl-CH ₃), 3.9 (s, 7-OCH ₃), 4.3 (q, <i>J</i> = 7 Hz, CH ₂), 6.9–7.2 m, 4 <i>Ar</i> H, H-6, H-8), 7.8 (d, <i>J</i> = 7 Hz, H-5)

^a Satisfactory microanalyses obtained within ±0.4%

Table 4. Indolo[3,2-*c*]coumarin (**6a**) and Indolo[3,2-*c*]quinolin-6(5*H*)ones **6b-e**

Compound	Yield (%)	M.p. (°C) Solvent	Molecular formula ^a	IR (KBr) ¹ H-NMR (DMSO- <i>d</i> ₆), δ/ppm
3,9-Dimethoxy-11 <i>H</i> - [1]benzopyrano[4,3- <i>b</i>]- indol-6-one (6a)	A: 88 B: 98	340 (dec.) (acetic acid)	C ₁₇ H ₁₃ NO ₄ 295.3	3 300–2 800 b, 1 690 s, 1 620 m, 1 590 m 3.8 (s, 2 OCH ₃), 6.7–7.0 (m, 4 <i>Ar</i> -H), 7.7–7.9 (m, 2 <i>Ar</i> -H), 12.4 (s, NH)
3,9-Dimethoxy-5-methoxy-11 <i>H</i> -indolo[3,2- <i>c</i>]- quinolin-6(5 <i>H</i>)-one (6b)	67	315–318 (acetic acid)	C ₁₈ H ₁₆ N ₂ O ₃ 308.3	3 300–2 800 b, 1 610 m, 1 570 m 3.6 (s, CH ₃), 3.7 (s, OCH ₃), 3.8 (s, OCH ₃), 6.7–6.9 (m, 4 <i>Ar</i> -H), 7.8–8.2 (m, 2 <i>Ar</i> -H), 12.1 (s, NH)
5-Ethyl-3,9-dimethoxy-11 <i>H</i> -indolo[3,2- <i>c</i>]- quinolin-6(5 <i>H</i>)-one (6c)	78	223–225 (ethanol)	C ₁₉ H ₁₈ N ₂ O ₃ 322.4	3 200–2 800 b, 1 620 m, 1 575 m 1.3 (t, CH ₃ , <i>J</i> = 7 Hz), 3.8 (s, OCH ₃), 3.9 (s, OCH ₃), 4.3 (q, CH ₂ , <i>J</i> = 7 Hz), 6.7–7.1 (m, 4 <i>Ar</i> -H), 7.9–8.3 (m, 2 <i>Ar</i> -H), 12.1 (s, NH)
3-Methoxy-5-methyl- 11 <i>H</i> -indolo[3,2- <i>c</i>]quino- lin-6(5 <i>H</i>)-one (6d)	68	314–316 (toluene)	C ₁₇ H ₁₄ N ₂ O ₂ 278.3	3 300–2 800 b, 1 610 m, 1 560 m 3.7 (s, CH ₃), 3.9 (s, OCH ₃), 6.9–7.1 (m, H-2, H-4), 7.1–7.4 (m, H-8, H-9), 5.5–7.6 (m, H-10), 8.1–8.3 (m, H-1, H-7), 12.3 (s, NH)
5-Ethyl-3-methoxy- 11 <i>H</i> -indolo[3,2- <i>c</i>]quino- lin-6(5 <i>H</i>)-one (6e)	71	297–299 (acetic acid)	C ₁₈ H ₁₆ N ₂ O ₂ 292.3	3 200–2 800 b, 1 605 m, 1 560 m 1.3 (t, CH ₃ , <i>J</i> = 7 Hz), 3.9 (s, OCH ₃), 4.3 (q, CH ₂ , <i>J</i> = 7 Hz), 6.9– 7.5 (m, 5 <i>Ar</i> -H), 7.9–8.3 (m, 2 <i>Ar</i> -H), 12.3 (s, NH)

^a Satisfactory microanalyses obtained within ± 0.4%

Table 5. Indolo[3,2-c]coumarines and Indolo[3,2-c]quinolin-6(5H)ones (**7**, **8**)

Compound	Yield (%)	M.p. (°C) Solvent	Molecular formula ^a	IR (KBr) ¹ H-NMR (DMSO- <i>d</i> ₆), δ/ppm
3,9-Dihydroxy-11H-[1]benzopyrano[4,3-b]indol-6-one (7a)	89	> 360 (dec.) (DMF/water)	C ₁₅ H ₉ NO ₄ 267.2	3 500–2 700 b, 1 680 s, 1 630 s, 1 595 s 6.7–7.0 (m, 4 <i>Ar</i> -H), 7.7–8.0 (m, 2 <i>Ar</i> -H), 9.45 (OH, b), 10.3 (OH, b), 12.3 (s, NH)
3,9-Dihydroxy-5-methyl-11H-indolo[3,2-c]-quinolin-6(5H)-one (7b)	89	> 360 (dec.) (ethanol/water)	C ₁₆ H ₁₂ N ₂ O ₃ 280.3	3 500–2 700 b, 1 630 s, 1 570 s 3.6 (s, CH ₃), 6.7–6.9 (m, 4 <i>Ar</i> -H), 7.8–8.2 (m, 2 <i>Ar</i> -H), 9.4–9.5 (2 OH, b), 12.1 (s, NH)
5-Ethyl-3,9-dihydroxy-11H-indolo[3,2-c]-quinolin-6(5H)-one (7c)	63	355 (dec.) (ethanol/water)	C ₁₇ H ₁₄ N ₂ O ₃ 294.3	3 500–2 500 b, 1 630 s, 1 590 s 1.3 (t, CH ₃ , <i>J</i> = 7 Hz), 4.2 (q, CH ₂ , <i>J</i> = 7 Hz), 6.7–7.1 (m, 4 <i>Ar</i> -H), 7.9–8.2 (m, 2 <i>Ar</i> -H), 9.4–9.5 (2 OH, b), 12.1 (s, NH)
3,9-Diacetoxy-11H-[1]benzopyrano[4,3-b]indol-6-one (8a)	60	320 (dec.) (DMF)	C ₁₉ H ₁₃ NO ₆ 351.3	3 300–2 700 b, 1 760 s, 1 690 s
3,9-Diacetoxy-5-methyl-11H-indolo[3,2-c]-quinolin-6(5H)-one (8b)	84	318–319 (acetic acid)	C ₂₀ H ₁₆ N ₂ O ₅ 364.4	3 300–3 000 b, 1 750 s, 1 620 s 2.3 (s, 2 acetyl-CH ₃), 3.6 (s, N-CH ₃), 6.8–7.4 (m, 4 <i>Ar</i> -H), 7.9–8.3 (m, 2 <i>Ar</i> -H), 12.4 (s, NH)
3,9-Diacetoxy-5-ethyl-11H-indolo[3,2-c]-quinolin-6(5H)-one (8c)	63	282–284 (toluene)	C ₂₁ H ₁₈ N ₂ O ₅ 378.4	3 300–3 000 b, 1 750 s, 1 620 s 1.2 (t, ethyl-CH ₃ , <i>J</i> = 7 Hz), 2.3 (2 acetyl-CH ₃), 4.3 (q, N-CH ₂ , <i>J</i> = 7 Hz), 6.8–7.4 (m, 4 <i>Ar</i> -H), 8.0–8.3 (m, 2 <i>Ar</i> -H), 12.3 (s, NH)

^a Satisfactory microanalysis obtained within ±0.4%

was refluxed for 2.5 h. The solvent was removed in vacuo, water was added and the product was filtered, washed with water and dried to yield **6 a–e** (data: see Table 4).

Method B. A solution of the 4-azidocoumarin **5** (0.93 g, 10 mmol) and dimethyl formamide (40 ml) were refluxed for 12 h. The solvent was removed in vacuo and the residue was worked up as described in method A to yield **6 a** (data: see Table 4).

General Procedure for the Synthesis of 3,9-Dihydroxy-[1]benzopyrano[4,3-b]indol-6-one (7 a) and Indolo[3,2-c]quinolin-6(5 H)-ones 7 b, c

A mixture of **6 a–c** (1.0 g) and hydrobromic acid (30 ml, 47% in water) was refluxed for 12 h. Then the hydrobromic acid was removed in vacuo, the residue was treated with water and the resulting precipitate was filtered, washed with water and dried to yield **7 a–c** (data: see Table 5).

General Procedure for the Synthesis of 3,9-Diacetoxy-[1]benzopyrano[4,3-b]indol-6-one (8 a) and 3,9-Diacetoxy-indolo[3,2-c]quinolin-6(5 H)-ones 8 b, c

A solution of **7 a–c** (1.0 g) and acetic anhydride (20 ml) was heated for 90 min under reflux. The excess of acetic anhydride was removed in vacuo and after addition of water a colourless product was obtained, which was filtered, washed with water and dried (data: see Table 5).

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