A novel heterocyclization of 1-acetylenyl-9,10-anthraquinones

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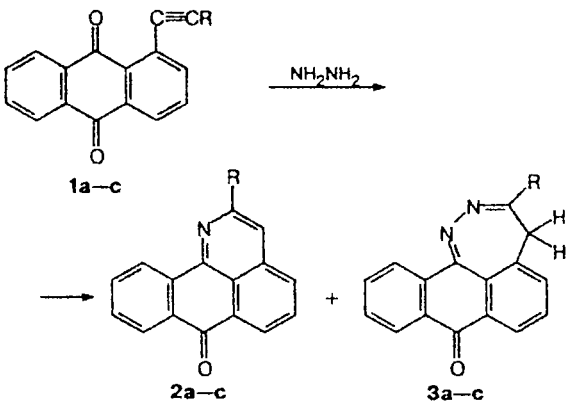
1-Acetylenyl-9,10-anthraquinones react with an excess of NH_2NH_2 at 80—115 °C to give a mixture of substituted 7*H*-dibenzo[*de*,*h*]quinolin-7-ones and anthra[9,1-*cd*]-1,2-diazepin-8-ones. The latter compounds undergo reductive contraction of the seven-membered ring to give the corresponding 7*H*-dibenzo[*de*,*h*]quinolin-7-ones. Bulky substituents in position 2 of the initial acetylenylanthraquinones prevent the formation of the seven-membered heterocycle. A scheme of the cyclocondensation was proposed.

Key words: 1-acetylenyl-9,10-anthraquinones, hydrazine, cyclocondensation, 7*H*-dibenzo[*de*,*h*]quinolin-7-ones, 4*H*-anthra[9,1-*cd*]-1,2-diazepin-8-ones, contraction of the seven-membered heterocycle.

Alkyl 1-acetylenyl-9,10-anthraquinone-2-carboxylates condense with NH_2NH_2 to give a mixture of substituted 7*H*-dibenzo[*de*,*h*]quinolin-7-one (pyridinoanthrone) and 3,4-dihydro-3-aminonaphtho[2,3-*f*]isoquinolin-4,7,12-trione (*N*-aminolactam).[1] A feature of the cyclocondensation to pyridinoanthrones is the insertion of only one of two nitrogen atoms of the reagent into the molecule of the final product.

To study further this unusual heterocyclization, we introduced into the reaction with NH_2NH_2 1-acetylenyl-9,10-anthraquinones (**1a—c**) that do not contain the alkoxycarbonyl group in position 2, thus excluding competitive processes of lactam formation (previous report[2]). Pyridine was used instead of ethanol as a solvent. In the absence of a vicinal electron-withdrawing group, which makes the triple bond more electrophilic, **1a—c** react with NH_2NH_2 in boiling ethanol much more slowly than esters. In pyridine, the reaction was completed at 90—115 °C over 40—90 min. In all cases, two main products were obtained (independently of the solvent) that could be easily separated by chromatographing on silica gel (Scheme 1).

Scheme 1



R = Bu (**a**), Ph (**b**), CH_2OPh (**c**)

The products of the first type are the expected 7*H*-dibenzo[*de*,*h*]quinolin-7-ones (**2a—c**) (yields 17—38%, Table 1). This structure completely corresponds to analytical and spectral data. When chromatographed, compounds **2a—c** behave (R_f, luminescence) like alkyl pyridinoanthronecarboxylates described earlier.[1]

The products of the other type are 4*H*-anthra[9,1-*cd*]-1,2-diazepin-8-ones (**3a—c**) (yields 31—70%, Table 2). The ^1H NMR spectra of compounds **3a—c** exhibit both signals for the protons of the substituents and the aromatic ring and two doublets of the protons of the methylene group of the diazepine ring at δ 2.94—3.64 and 3.64—4.43.

That the reaction of 1-acetylenylanthraquinones **1a—c** with NH_2NH_2 results in the formation of the diazepine ring was surprising because a similar reaction of 2-methoxycarbonyl derivatives of these acetylenes yields only the six-membered pyridine ring. Comparing the results of cyclization of acetylenes **1** in different solvents, we note that prolonging the reaction time changes, as a rule, the ratio between products **2** and **3** in favor of pyridinoanthrones **2**. It was supposed that diazepines **3** can be transformed into pyridines **2** with loss of an N atom under the reaction conditions, which

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Table 1. 7*H*-Dibenzo[*de*,*h*]quinolin-7-ones

Compound	Yield (%)	M.p./°C (benzene—hexane)	Found / Calculated (%) C	H	N	Molecular formula	^{1}H NMR, δ (*J*/Hz)
2a	20.0	97—98	83.46 83.59	6.05 5.96	4.52 4.87	$C_{20}H_{17}NO$	1.00 (t, 3 H, CH_3, J = 7.0); 1.20—2.10 (m, 4 H, β- and γ-CH_2); 3.06 (t, 2 H, α-CH_2, J = 7.0); 7.35 (s, 1 H, H(3)); 7.60—8.65 (m, 6 H, H(4)); 8.97 (d, 1 H, H(11), J = 7.2)
2b	16.7	207—208	85.84 85.97	4.08 4.26	4.68 4.56	$C_{22}H_{13}NO$	—
2c	28.0	173—174	82.05 81.88	4.61 4.48	4.19 4.15	$C_{22}H_{15}NO_2$	—
5	75.0	75—76 (hexane)	77.10 77.09	7.17 6.99	3.61 3.60	$C_{25}H_{27}NO_3$	1.00 (t, 3 H, $CH_3(CH_2)_3$, J = 7.0); 1.25 (t, 6 H, CH_3CH_2O, J = 7.0); 1.30—2.10 (m, 4 H, $CH_3CH_2CH_2CH_2$); 3.08 (t, 2 H, $CH_2C_3H_7$, J = 7.0); 3.64 (q, 4 H, OCH_2, J = 7.0); 6.08 (s, 1 H, CH); 7.50—8.65 (m, 5 H, H(5,6,8—10)); 8.00 (s, 1 H, H(3)); 8.98 (d, 1 H, H(11))
6	83.3*	128—129	79.98 79.96	5.43 5.56	4.44 4.33	$C_{21}H_{17}NO_2$	1.1 (t, 3 H, CH_3, J = 7.0); 1.20—2.10 (m, 4 H, β- and γ-CH_2); 3.10 (t, 2 H, α-CH_2, J = 7.0); 7.45—7.90 (m, 2 H, H(9,10)); 8.15—8.45 (m, 2 H, H(5(6),8)); 8.50—8.80 (m, 2 H, H(3,6(5))); 8.93 (d, 1 H, H(11), J = 7.3); 10.45 (s, 1 H, CHO)

* Obtained by hydrolysis of compound **5**.

Table 2. 4*H*-Anthra[9,1-*cd*]-1,2-diazepin-8-ones

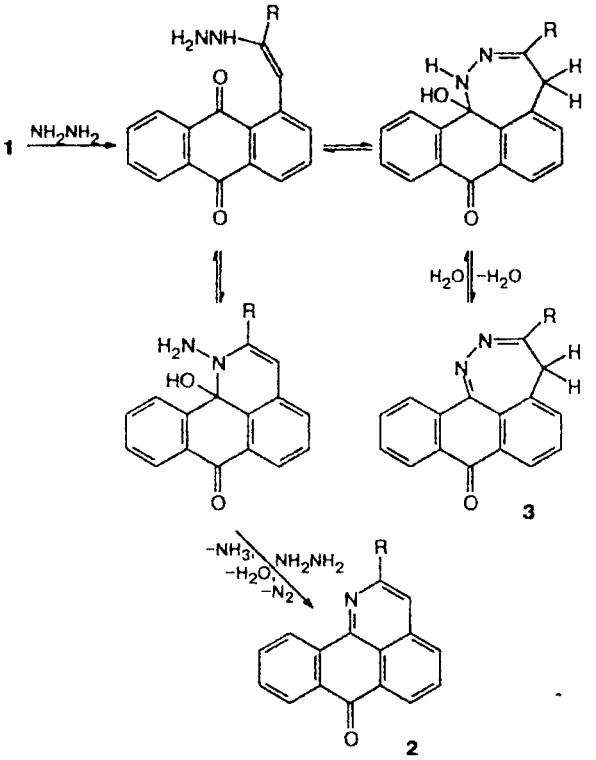
Compound	Yield (%)	M.p./°C (benzene—hexane)	Found / Calculated (%) C	H	N	Molecular formula	^{1}H NMR, δ (*J*/Hz)
3a	57.1	116—117 (decomp.)	79.47 79.44	6.08 6.00	9.05 9.26	$C_{20}H_{18}N_2O$	0.88 (t, 3 H, CH_3, J = 7.2); 1.32 (sextet, 2 H, γ-CH_2, J = 7.2); 1.67 (quintet, 2 H, β-CH_2, J = 7.2); 2.55 (t, 2 H, α-CH_2, J = 7.2); 2.94 (d, 1 H, C(4)H, J = 12.2); 3.64 (d, 1 H, C(4)H, J = 12.2); 7.40—7.75 (m, 4 H, H(5,6,10,11)); 8.15—8.40 (m, 3 H, H(7,9,12))
3b	48.0	238—239	81.79 81.97	4.43 4.38	8.61 8.69	$C_{22}H_{14}N_2O$	3.13 (d, 1 H, C(4)H, J = 13.5); 4.43 (d, 1 H, C(4)H, J = 13.5); 7.30—8.55 (m, 12 H, H arom.)
3c	63.5	183—184 (benzene)	78.35 78.39	4.69 4.58	7.93 7.95	$C_{23}H_{16}N_2O_2$	2.92 (d, 1 H, C(4)H, J = 12.4); 4.03 (d, 1 H, C(4)H, J = 12.4); 4.83 (s, 2 H, CH_2O); 6.75—7.10 (m, 3 H, Ph); 7.25—7.85 (m, 6 H, H(5,6,10,11), Ph); 8.10—8.45 (m, 3 H, H(7,9,12))

was confirmed later by direct experiments. Thus, diazepinoanthrone **3b** (yield 55%) is dominant in the products of the reaction of **1b** with NH_2NH_2 in ethanol after 13 h, the yield of **2b** amounting to 19% and of unreacted **1b** remaining, 7%. Additional heating for 16 h makes pyridinoanthrone **2b** virtually the sole reaction product, its yield reaching 63%. The preliminarily obtained individual diazepinoanthrone **3b**, when heated in pyridine in the presence of NH_2NH_2, is completely recyclized into **2b** over 9.5 h (yield 78%). This reaction does not occur in the absence of NH_2NH_2 as well as in the presence of other bases (KOH or NEt_3).

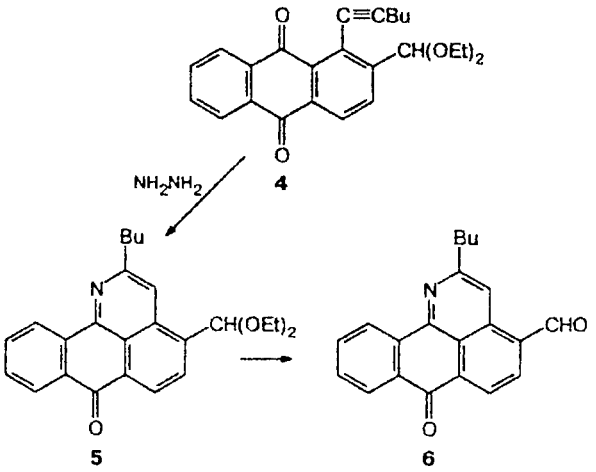
Based on the data obtained, one can assume that cyclocondensation occurs *via* Scheme 2 (the product of addition of hydrazine at the C≡C bond is represented by one of the tautomeric forms). According to this, the contraction of the seven-membered ring involves its hydration, opening, and recyclization into a six-membered ring with consequent reduction by an excess of NH_2NH_2. The opening of the seven-membered ring is the reverse of its closure, while the stage of reduction is, in contrast to the others, irreversible.

Scheme 2 allows one to explain why no substituted diazepinoanthrone is observed among the products of

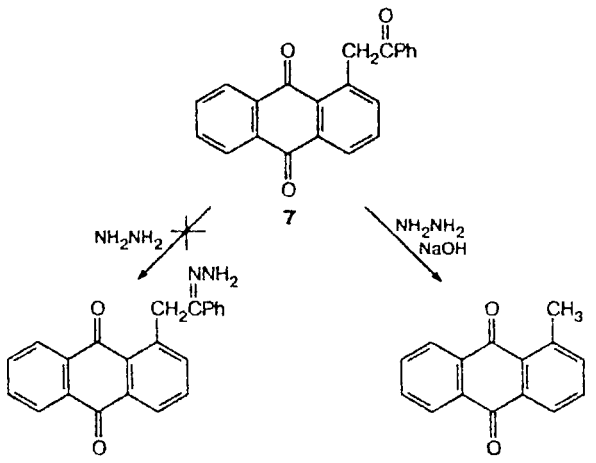
Scheme 2



Scheme 3



Scheme 4



the reaction of alkyl 1-acetylenyl-9,10-anthraquinone-2-carboxylates with NH_2NH_2. Indeed, the bulky group in position 2 of the initial anthraquinone creates additional steric hindrances, which prevent formation of the seven-membered ring or, if formed, destabilize it, thus accelerating its transformation into the six-membered ring.

In accordance with this, 2-diethoxymethyl-1-hexyn-1-yl-9,10-anthraquinone (**4**) containing in position 2 a bulky group (which, however, unlike alkoxycarbonyl, does not react with NH_2NH_2) react with hydrazine (ethanol, 78 °C, 13 h) to give only 7*H*-2-butyl-4-diethoxymethyldibenzo[*de*,*h*]quinolin-7-one (**5**) in 75% yield. Compound **5** is easily hydrolyzed in an acidified aqueous dioxane (20 °C, 7 min) to give aldehyde **6** (Scheme 3).

Since the first stage of the cyclocondensation of 1-acetylenylanthraquinones is the addition of NH_2NH_2 at the triple bond with the formation of hydrazone tautomer, we hoped to perform a similar reaction with the corresponding ketones. However, our attempt to condense phenacylanthraquinone **7** failed because, unfortunately, ketone **7** does not react with NH_2NH_2 in boiling ethanol (Scheme 4). Addition of NaOH, which usually catalyzes this reaction,[3] leads to the decomposition of ketone **7** to 1-methylanthraquinone, and compounds **2b** and **3b** are formed only in minor amounts.

The initial acetylenylanthraquinones **1b,c** were synthesized in 78—81% yields by cross-linking of 1-iodoanthraquinone with phenylacetylene and phenyl propargyl ether in the effective catalytic $Pd(PPh_3)_2Cl_2$—CuI—Na_2CO_3—aqueous pyridine system, which was proposed earlier.[4] Compound **1a** was obtained by condensation of copper butylacetylide with the same iodide, and compound **4** was obtained similarly from 2-diethoxymethyl-1-iodo-9,10-anthraquinone (pyridine, 50—60 °C, 40—60 min; 69 and 90% yields, respectively).

Experimental

^1H NMR spectra were recorded on Bruker-250 and Jeol FX-90 spectrometers in $CDCl_3$ at 25 °C. IR spectra were recorded on a UR-20 spectrophotometer in $CHCl_3$.

1-(3-Phenoxyprop-1-ynyl)anthraquinone (1c). A mixture of 1-iodoanthraquinone (2.80 g, 8.0 mmol), 3-phenoxyprop-

1-yne (2.00 g, 15.0 mmol), $Pd(PPh_3)_2Cl_2$ (30 mg), and CuI (15 mg) in 50 mL of pyridine was heated in an argon atmosphere to 60 °C. A hot (70 °C) solution of $NaHCO_3$ (5.00 g) in 25 mL of water was added, and the reaction mixture was refluxed with stirring for 30 min (monitored by TLC: Silufol, $CHCl_3$), cooled, diluted with 300 mL of $CHCl_3$, and washed with 18% HCl and water. Elution with CHC_3 on anhydrous Al_2O_3 followed by recrystallization from benzene gave compound **1c** (2.30 g, 81.3%), m.p. 140—141 °C. Found (%): C, 81.65; H, 4.29. $C_{23}H_{14}O_3$. Calculated (%): C, 81.64; H, 4.17. ^1H NMR, δ: 4.98 (s, 2 H, OCH_2); 6.90—8.40 (m, 12 H, H arom.). IR, ν/cm^{-1}: 2240 (C≡C), 1680 (CO).

Compound **1b** was obtained similarly (Na_2CO_3 as a base, 75 °C, 20 min), yield 77.9%, m.p. 159—160 °C (benzene).[5]

1-Iodo-2-diethoxymethylanthraquinone. 1-Iodo-2-formylanthraquinone[6] (0.50 g, 1.4 mmol) was diluted with heating in 55 mL of dry $CHCl_3$. Anhydrous ethanol (55 mL), ethyl orthoformate (75 mL), and conc. HCl (0.5 mL) were added and the reaction mixture was refluxed for 15 min (monitored by TLC: Silufol, $CHCl_3$), diluted with 200 mL of $CHCl_3$, and washed with an aqueous $NaHCO_3$ solution and water. The yield of 1-iodo-2-diethoxymethylanthraquinone was 0.54 g (90.0%), m.p. 118—119 °C (from a benzene—hexane mixture). Found (%): C, 52.24; H, 4.02; I, 29.30. $C_{19}H_{17}IO_4$. Calculated (%): C, 52.31; H, 3.93; I, 29.09. ^1H NMR, δ: 1.26 (t, 6 H, CH_3); 3.68 (m, 4 H, CH_2); 5.85 (s, 1 H, CH); 7.70—7.90 (m, 2 H, H(6,7)); 7.98 (d, 1 H, H(3(4))); 8.15—8.35 (m, 2 H, H(5,8)); 8.38 (d, 1 H, H(4(3))). IR, ν/cm^{-1}: 1680 (CO), 1180, 1120, 1050 (C—O—C—O—C).

1-(Hexyn-1-yl)-2-diethoxymethylanthraquinone (4). A mixture of 1-iodo-2-diethoxymethylanthraquinone (0.85 g, 1.9 mmol) and copper butylacetylide (0.50 g, 3.4 mmol) in 80 mL of pyridine was stirred in an argon atmosphere at 50—55 °C for 1 h (monitored by TLC: Silufol; benzene—hexane, 8 : 1), diluted with 300 mL of $CHCl_3$, neutralized with 400 mL of dilute HCl (1 : 2), and washed with water. Elution with benzene on silica gel gave compound **4** (0.64 g, 84.2%), m.p. 40—42 °C (from a benzene—hexane mixture). Found (%): C, 76.08; H, 6.61. $C_{25}H_{26}O_4$. Calculated (%): C, 76.90; H, 6.71. ^1H NMR, δ: 1.00 (t, 3 H, $\underline{CH}_3(CH_2)_3$); 1.25 (t, 6 H, $\underline{CH}_3CH_2O$); 1.45—1.85 (m, 4 H, β- and γ-CH_2); 2.65 (t, 2 H, α-CH_2); 3.70 (m, 4 H, CH_2O); 6.00 (s, 1 H, CH); 7.65—7.85 (m, 2 H, H(6,7)); 8.05, 8.30 (both d, 2 H, H(3,4)); 8.15—8.40 (m, 2 H, H(5,8)). IR, ν/cm^{-1}: 2220 (C≡C), 1060, 1105, 1130, 1160 (C—O—C—O —C).

Compound **1a** was obtained in the same way (60 °C, 40 min), yield 69.4%, m.p. 92—93 °C (from heptane).[7]

Cyclocondensation of 1-phenylethynylanthraquinone (1b) with NH_2NH_2. A solution of **1b** (1.20 g, 3.8 mmol) and NH_2NH_2 (2.0 g, 62.5 mmol, 2.0 mL) in 10 mL of pyridine was refluxed with stirring for 40 min (monitored by TLC: Silufol, $CHCl_3$), diluted with 400 mL of $CHCl_3$, and washed with 10% HCl and water. Elution with benzene and its mixture with ether (15 : 1) on silica gel gave compound **2b** (0.20 g) (see Table 1) and compound **3b** (0.60 g) (see Table 2).

Compounds **2a** and **3a** were obtained similarly from **1a** (45 min), compounds **2c** and **3c** from **1c** (90 °C, 1.5 h), and compound **5** from **4** (ethanol, 78 °C, 13 h). The yields and the constants are given in Tables 1 and 2.

Contraction of the diazepine ring of 4*H*-3-phenylanthra[9,1-*c*,*d*]-1,2-diazepin-8-one (3b). A solution of **3b** (0.20 g, 0.6 mmol) and NH_2NH_2 (0.30 g, 9.3 mmol, 0.3 mL) in 3 mL of pyridine was refluxed for 9 h. The yield of **2b** was 0.15 g (77.7%).

7*H*-2-Butyl-4-formyldibenzo[*de*,*h*]quinolin-7-one (6). A solution of compound **5** (0.34 g, 0.9 mmol) in 35 mL of dioxane and 10 mL of 15% HCl was stirred at 20 °C for 7 min, diluted with 200 mL of $CHCl_3$, and washed with water. The solvent was removed, and the residue was recrystallized from a mixture of benzene and hexane (1 : 5) to give compound **6** (0.23 g) (see Table 1).

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