Reduction of 1-substituted anthraquinones to 1- and 4-substituted anthrones

V. A. Loskutov

Novosibirsk Institute of Organic Chemistry, Siberian Branch of the Russian Academy of Sciences, 9 prosp. Akad. Lavrent'eva, 630090 Novosibirsk, Russian Federation. Fax: 007 (783 2) 35 4752

The regioselectivity of reduction of 1-substituted anthraquinones to 1- or 4-substituted anthrones is determined by both the nature of the substituent and the type of the reducing system used.

Key words: 1-substituted anthraquinones, 1- and 4-substituted anthrones; reducing systems.

Anthrone and its derivatives are used as intermediate products in the synthesis of dyes,[1,2] drugs, cosmetics,[3] and materials suitable for recording information in the near IR region.[4] The interest in these compounds is also due to their use as starting compounds for the synthesis of monothioanthraquinone derivatives, which belong to a novel class of quinones.[5]

Two principal approaches to the synthesis of anthrones are known: cyclization of 2-benzylbenzoic acids and reduction of anthraquinones.[1,2] In our opinion, the major disadvantage of the former is that the starting products are not easily accessible. The latter is attractive because of its simplicity, but it is less regioselective than the first one (particularly, in the case of 2-substituted anthraquinones).

1-Substituted anthraquinones were reduced to 1-substituted anthrones with sodium dithionite (SDT) in alkaline medium[6] or in 50% AcOH,[7] with metals (Sn, Al, and Cu) in acid medium,[8—13] and catalytically.[14,15] Information on the synthesis of 4-substituted anthrones is rather limited.[6,9,14] The aim of the present work is to improve the procedure for the synthesis of 1- and 4-substituted anthrones by reducing 1-substituted anthraquinones (**1**) with SDT and metals.

As was shown previously,[6] reduction of 1-aminoanthraquinones **1a,b** with SDT in alkaline medium led to 1-aminoanthrones **2a,b**, while 1-hydroxyantraquinone **1c** yielded 4-hydroxyanthrone **3c**. Only 1-substituted anthrones **2a—c** (Table 1) were isolated when this procedure was reproduced. In contrast to **1a—c**, the reduction of 1-phe-

Table 1. Reduction of 1-R-anthraquinones (**1a—h**)

Initial compound	Reducing-system[a]	Products	M.p./°C		Yield	Purification of anthrones[b]
			this work	lit. data		
1a	A	**2a**	110—113	110—113[6]	47	R (PhCl)
1b	A	**2b**	116—118	111—113[6]	52	CC (SiO_2)
1c	A	**2c**	140—141	140—141[14]	42	CC (SiO_2)
1d	A	**2d**	89—91	—	16	R (PhMe)
		3d	129—131	126[18]	34	R (PhMe)
	B	**2d** + **3d** (~1 : 1)			—	
1e	A	**3e**	144—145	140—141[17]	50—55	R (EtOH—$CHCl_3$, 10:1; AcOEt)
	B	**2e**	190—193	194—195.5[8]	26	R (C_6H_6, AcOEt)
1f	A	**3f**	137—140	137[9]	53	R (C_6H_6—MeOH, 1:1)
	B	**2f** + **3f** (~1 : 1)			—	
	C	**2f**	119—122	118[9,13]	21	R (EtOH—$CHCl_3$, 10:1; AcOEt)
1g	A	**3g**	135—139	130[18]	60	R (MeOH)
	B	**2c**	140—141	—	51	
	C	**5**	101—103	—	33	CC (Al_2O_3), R (MeOH)
1h	A	**3h**	97—103	—	64	R (MeOH)
	B	**4**	228—231	—	35	CC (SiO_2), R (C_6H_6—C_6H_{14}, 1:1)

[a] A, SDT—NaOH; B, Sn—HCl; C, Al—H_2SO_4. [b] R, recrystallization; CC, column chromatography (C_6H_6).

Translated from *Izvestiya Akademii Nauk. Seriya Khimicheskaya*, No. 2, pp. 355—357, February, 1997.

1066-5285/97/4602-0341 $18.00

nyl-, 1-chloro-, 1-methoxy-, and 1-phenoxyanthraquinones **1e—h** with SDT in alkaline medium results in the corresponding 4-substituted anthrones **3e—h**, whereas the reduction of 1-methylanthraquinone **1d** yields a mixture of 1- and 4-methylanthrones **2d** and **3d** in the ratio of ~1 : 2; these anthrones were easily separated because of the better solubility of anthrone **3d** in aqueous alkali.

SDT is known to reduce 1-acetoxyanthraquinone to 4-hydroxyanthrone in 50% AcOH.[7] Our attempts to use this procedure to synthesize other 4-substituted anthrones failed: *N*-acetyl-1-methylamino- and -1-anilinoanthraquinones remained almost unchanged, while *N*-acetyl-1-aminoanthraquinone was hydrolyzed and partly converted into anthrone **2a**.

We also synthesized 1-substituted anthrones using the reduction of anthraquinones **1d—h** with metals in acidic medium. Reduction of several 1-R-anthraquinones (R — amino,[12] hydroxy,[10] phenyl,[8] methoxy,[11] and

Table 2. Analytical and spectral characteristics of the compounds obtained

Compound	Found / Calculated (%)		Molecular formula	^{1}H NMR, δ (*J*/Hz)	IR, ν/cm^{-1}	
	C	H			C=O	NH(OH)
2a				4.22 (s, 2 H, CH_2); 6.50—6.70 (m, 4 H, H(2), H(4), NH_2); 7.17—7.55 (m, 4 H, H(3), H(5)—H(7)); 8.25 (dd, 1 H, H(8), ^3J = 8.0, ^4J = 1.5)	1635	3300, 3400
2b				2.86 (d, 3 H, Me, ^3J = 10.0); 4.16 (s, 2 H, CH_2); 6.53 (m, 2 H, H(3), H(4)); 7.14—7.50 (m, 4 H, H(3), H(5)—H(7)); 8.23 (m, 1 H, H(8)); 9.50 (m, 1 H, NH)	1635	3245
2c				4.25 (s, 2 H, CH_2); 6.85 (m, 2 H, H(2), H(4)); 7.40—7.60 (m, 4 H, H(3), H(5)—H(7)); 8.24 (m, 1 H, H(8)); 12.98 (s, 1 H, OH)	1635	
2d	87.0 / 86.5	5.76 / 5.76	$C_{15}H_{12}O$	2.83 (s, 3 H, Me); 4.31 (s, 2 H, CH_2); 7.20—7.60 (m, 6 H, H(2)—H(7)); 8.23 (m, 1 H, H(8))	1650	
2e				4.40 (s, 2 H, CH_2); 7.20—7.60 (m, 11 H, H(2)—H(7), H(Ph)); 8.13 (m, 1 H, H(8))	1650	
2f				4.31 (s, 2 H, CH_2); 7.30—7.60 (m, 6 H, H(2)—H(7)); 8.23 (m, 1 H, H(8))	1660	
3d				2.39 (s, 3 H, Me); 4.07 (s, 2 H, CH_2); 7.29—7.65 (m, 5 H, H(2), H(3), H(5)—H(7)); 8.22 (m, 1 H, H(1)); 8.32 (m, 1 H, H(8))	1645	
3e				4.14 (s, 2 H, CH_2); 7.29—7.60 (m, 14 H, H(2), H(3), H(5)—H(7), H(Ph)); 8.33 (m, 1 H, H(8)); 8.41 (dd, 1 H, H(1), ^3J = 7.0, ^4J = 2.5)	1650	
3f				4.32 (s, 2 H, CH_2); 7.45 (t, 1 H, H(2), ^3J = 8.0); 7.47 (m, 1 H, H(3)); 7.52—7.75 (m, 3 H, H(5)—H(7)); 8.27 (dd, 1 H, H(1), ^3J = 8.0, ^4J = 1.5); 8.29 (m, 1 H, H(8))[a]	1655	
3g				3.92 (s, 3 H, Me); 4.16 (s, 2 H, CH_2); 7.07 (dd, 1 H, H(3), ^3J = 8.0, ^4J = 1.0); 7.30—7.60 (m, 4 H, H(2), H(5)—H(7)); 7.96 (dd, 1 H, H(1), ^3J = 8.0, ^4J = 1.0); 8.33 (m, 1 H, H(8))	1665	
3h	83.7 / 83.9	4.71 / 4.89	$C_{20}H_{14}O_2$	4.30 (s, 2 H, CH_2); 7.01—7.64 (m, 10 H, H(2), H(3), H(5)—H(7), H(Ph)); 8.16 (m, 1 H, H(1)); 8.36 (m, 1 H, H(8))	1675	
4	84.2 / 84.2	4.50 / 4.56	$C_{40}H_{26}O_4$[b]	6.47 (dd, 2 H, H(3,3′), ^3J = 6.0, ^4J = 3.0); 6.85 (m, 4 H, H(1,1′), H(2,2′)); 7.08 (m, 2 H, H(8,8′)); 7.20 (m, 2 H, H(7,7′)); 7.30 (m, 2 H, $H_{p,p'}$); 7.34 (m, 4 H, $H_{o,o'}$); 7.42 (m, 2 H, H(6,6′)); 7.48 (m, 4 H, $H_{m,m'}$); 8.62 (m, 2 H, H(5,5′)); 10.19 (s, 2 H, OH)		3440[c]
5	79.7 / 80.3	5.27 / 5.35	$C_{15}H_{12}O_2$	4.07 (s, 3 H, OMe), 6.60 (d, 1 H, H(2), ^3J = 8.0); 7.21 (t, 1 H, H(3), ^3J = 8.0); 7.44 (m, 3 H, H(4), H(6), H(7)); 7.82 (s, 1 H, H(10)); 7.86 (m, 1 H, H(5)); 8.44 (m, 1 H, H(8)); 10.21 (s, 1 H, OH)		3390[d]

[a] In CD_2Cl_2. [b] Mol. mass, found/calculated: 570.1822/570.1831. [c] In CCl_4. [d] In $CHCl_3$.

chloro[9]) under these conditions has been described previously. We (like the authors in Ref. 8) also found that the system Sn—HCl in AcOH reduced quinone **1e** to anthrone **2e** (see Table 1). 1-Methyl- and 1-chloroanthraquinones **1d,f** under the same conditions yield mixtures which, according to their ^{1}H NMR spectra, contain approximately equal amounts of 1- and 4-substituted anthrones.

The reduction of 1-methoxyanthraquinone **1g** with Sn and HCl in boiling AcOH is accompanied by hydrolysis of the methoxy group and results in 1-hydroxyanthrone **2c**, which differs from the literature data.[11] 1-Phenoxyanthraquinone **1h** is reduced with the same system to 9,9′-bi(4-phenoxy-10-hydroxyanthracene) (**4**) in high yield.

Quinone **1g** is converted into 1-methoxyanthrone under milder conditions (~30 °C) with Al and H_2SO_4 as a reducing system; according to the literature data (*cf.* Ref. 1), the resulting methoxyanthrone exists in its tautomeric form, 1-methoxy-9-anthranol (**5**) (see Table 1). Quinone **1f** is reduced with the Al—H_2SO_4 system to 1-chloroanthrone **2f**, which is in agreement with the previously reported data.[9]

Anthrones **2a—f** and **3d—h** are stable crystalline substances; they exist in their keto-form in the solid state and in chloroform solutions (*cf.* Ref. 1). Anthranols **4** and **5** are less stable (especially, on sorbents and at elevated temperature). The structure of the compounds synthesized was established on the basis of analytical and spectral data (Table 2). The IR spectra of anthrones **2a—f** and **3d—h** are characterized by an absorption band of the carbonyl group in the region of 1630—1675 cm^{-1}, and the absorption band of anthranols **4** and **5** lies in the high-frequency region (3390 and 3440 cm^{-1}). The ^{1}H NMR spectra of anthrones **2** and **3** differ in the chemical shift of the CH_2 protons and in the number of the signals for the protons deshielded by the carbonyl group. In the spectra of 1-substituted anthrones **2** there is one signal in the region of 8.2—8.3 ppm (the multiplet of the H(8) proton), while there are two signals for H(1) and H(8) protons in the spectra of 4-substituted anthrones **3**, which is in accordance with the literature data (see, for instance, Ref. 16).

The results obtained are evidence that the regioselectivity of the reduction of 1-substituted anthraquinones to 1- or 4-substituted anthrones depends on the nature of the substituent and the type of the reducing system: reduction with metals in acidic medium results in 1-substituted anthrones, and that with SDT in alkaline medium yields 4-substituted anthrones. An exception are the anthraquinone derivatives where the substituent and the adjacent carbonyl group participate in the formation of an intramolecular hydrogen bond; in this case, 1-substituted anthrones are the reduction products.

Experimental

IR spectra were recorded on an UR-20 spectrophotometer in KBr pellets, ^{1}H NMR spectra were recorded on a Bruker WP-200SY and Bruker AM-400 (for compound **4**) spectrometers in $CDCl_3$. Molecular weights and elemental composition of compound **4** were determined using the high-precision value of the molecular ion mass number obtained on a Finnigan MAT-8200 GC/MS mass spectrometer.

Reduction of anthraquinones 1a—h with sodium dithionite (SDT) in alkaline medium. General procedure. A suspension of a quinone **1** (1 mmol) in dioxane (5—7 mL) and SDT (3—6 mmol) were added with stirring (a Bunsen valve[6] was used to contact with the atmosphere) to a solution of NaOH (6—10 mmol) in water (25 mL) heated to 90—100 °C. The mixture was boiled with stirring for 30—60 min and cooled. The residue was separated, chromatographed on a SiO_2 column, and(or) recrystallized.

Reduction of anthraquinones 1a—h with a Sn—HCl system. General procedure. Conc. HCl (2—3 mL) was added dropwise to a mixture of quinone (2 mmol), tin (4—5 mg-at.), and AcOH (10 mL) heated to boiling. The boiling mixture was stirred for 1.5—2 h and poured into water after cooling. The residue was separated and recrystallized.

Reduction of anthraquinones 1f,g with an Al—H_2SO_4 system. General procedure. Powdered Al (0.2—0.3 g) was added gradually to a solution of quinone (4 mmol) in conc. H_2SO_4 (10 mL) with stirring. The mixture was stirred for 2 h and poured into an ice—water mixture. The residue was separated, chromatographed, and(or) recrystallized.

References

1. M. V. Gorelik, *Khimiya antrakhinonov i ikh proizvodnykh [The Chemistry of Anthraquinones and Their Derivatives]*, Khimiya, Moscow, 1983, 296 (in Russian).
2. O. Bayer, in *Methoden der Organischen Chemie (Houben-Weyl)*, Thieme, Stuttgart, 1979, 7/3c, 414.
3. US Pat. 4843097; *Chem. Abstrs.*, 1990, **112**, 178389.
4. Jpn. Pat. 89 238562; *Chem. Abstrs.*, 1990, **112**, 129234.
5. N.-Z. Huang, M. V. Laksshmikantam, and M. P. Cava, *J. Org. Chem.*, 1987, **52**, 169.
6. W. Bradley and R. F. Maisey, *J. Chem. Soc.*, 1954, 274.
7. K. Zahn, *Ber.*, 1934, **67**, 2063.
8. H. O. House, D. C. Koepsell, and W. J. Campbell, *J. Org. Chem.*, 1972, **37**, 1003.
9. E. Kariv and J. Blum, *Bull. Res. Counc. Israel*, 1962, **11A**, 26.
10. A. Steyermark and J. H. Gardner, *J. Am. Chem. Soc.*, 1930, **52**, 4887.
11. G. F. Attree and A. G. Perkin, *J. Chem. Soc.*, 1931, 144.
12. D. R. P. 201542; Frdl., 1911, **9**, 682.
13. E. deBarnett and M. A. Matthews, *J. Chem. Soc.*, 1923, **123**, 2549.
14. K. Zahn and H. Koch, *Ber.*, 1938, **71**, 172.
15. J. V. Braun and O. Bayer, *Ber.*, 1926, **59**, 914.
16. J. C. Meek and L. L. Koh, *J. Org. Chem.*, 1968, **33**, 2942.
17. S. C. Dickerman and D. deSouza, and Ph. Wolf, *J. Org. Chem.*, 1965, **30**, 1981.
18. E. D. Bergmann and E. Loewenthal, *Bull. Soc. Chim. France*, 1952, 66.

Received May 12, 1996;
in revised form October 16, 1996