XANTHENE DERIVATIVES AND *ortho-*
SUBSTITUTED PHENOLS – PRODUCTS FROM
DEHYDROGENATION OF ACYCLIC 1,5-DIKETONES

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Xanthene derivatives and ortho-substituted phenols were obtained during the dehydrogenation of 1,5-diketones and their ketol forms at a Pt/C catalyst at 280-320°C.

Keywords: 1,5-diketones, ketols, *ortho*-substituted phenols, xanthenes, xanthones, catalytic dehydrogenation.

The dehydrogenation of 1,5-diketones with six-membered rings can be regarded as a fairly simple method for the transition to aromatic compounds – derivatives of diarylmethanes or xanthenes. There is one paper on this subject in the literature [1], but the problem has not been investigated systematically.

We studied the catalytic dehydrogenation of the diketone **1** and its ketol **1a** and also the ketols **2a** and **3a** substituted in the methane fragment and the diketones **4-8** substituted at the α-CH$_2$ position on a Pt/C catalyst.

Dehydrogenation was conducted in an airtight closed flask, the outlet of which was placed in a measuring cylinder filled with water. This made it possible to judge the intensity of the release of hydrogen and its volume in various temperature ranges. The process was conducted at the temperatures at which active release of hydrogen was observed without substantial resinification of the reaction mixture.

Theoretically the dehydrogenation of 1,5-diketones can take place in two directions: A) with the formation of xanthene and its derivatives; B) with the formation of phenol derivatives of diphenylmethane (bisphenols). The experiment showed that the main products of this reaction are derivatives of xanthene and *ortho*-substituted phenols, and their ratio depends on the structure of the initial compound. Bisphenols were not obtained. The *ortho*-substituted phenols either result from retro-Michael dissociation of the initial diketones or are the products from dissociation of the bisphenols.

We traced the effect of the substituent in the methane fragment on the direction of dehydrogenation for the case of the ketones **1a-3a**. An increase in the yield of the xanthene was observed with increase in the size of the substituent. Thus, the xanthene **9** and the phenol **17** were obtained with approximately identical yields (32 and 35% respectively) from the ketol **1a**, the xanthene **10** was obtained from the ketol **2a** with a yield of 65%, and the hydrogenation of the ketol **3a** led to an almost quantitative yield of the xanthene compounds **11** and **15**. We suppose that the reason for this is the previously described effect of a bulky substituent on the transformation of a 1,5-diketone into a conformation in which the carbonyl groups are sterically close, thereby facilitating dehydrogenation by path A [2].
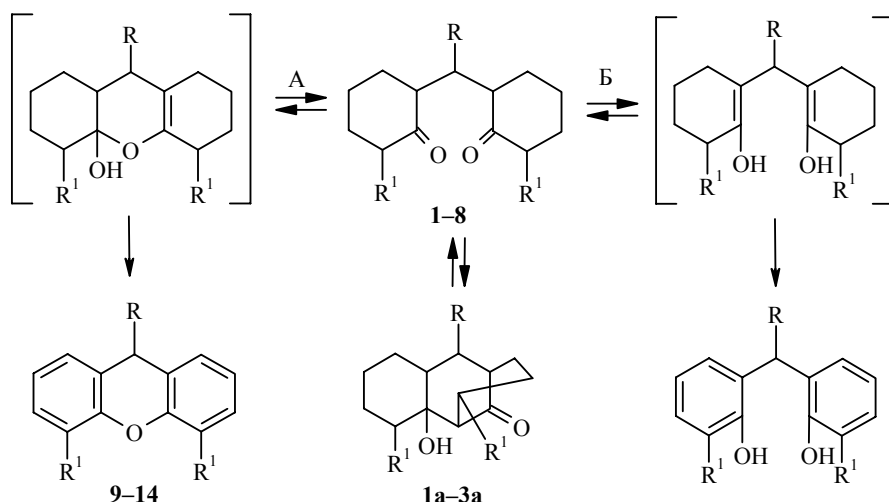

1, 1a, 4-9, 12-14 R = H; 2, 2a, 10 R = Me; 3, 3a, 11 R = Ph; 1-3, 1a-3a, 9-11 R¹ = H;
4 R¹ = cyclohexyl; 5 R¹ = cyclohexylidene, 6 R¹ = 1-chlorocyclohexyl,
7 R¹ = PhCH=; 8 R¹ = *p*-MeOC₆H₄CH=; 12 R¹ = cyclohexyl; 13 R¹ = PhCH₂;
14 R¹ = *p*-MeOC₆H₄CH₂

Dehydrogenation of the diketones **4-6** gives one and the same xanthene **12**. Under the elevated temperature conditions the chloro ketone is clearly dehydrochlorinated with the formation of an isomeric mixture of ketones **4** and **5** [3] followed by migration of the double bond (cyclohexenyl and then cyclohexylidene) to the cyclohexanone ring and dehydrogenation to compound **12**. The latter is converted by oxidation with chromic anhydride into the xanthone **22**.
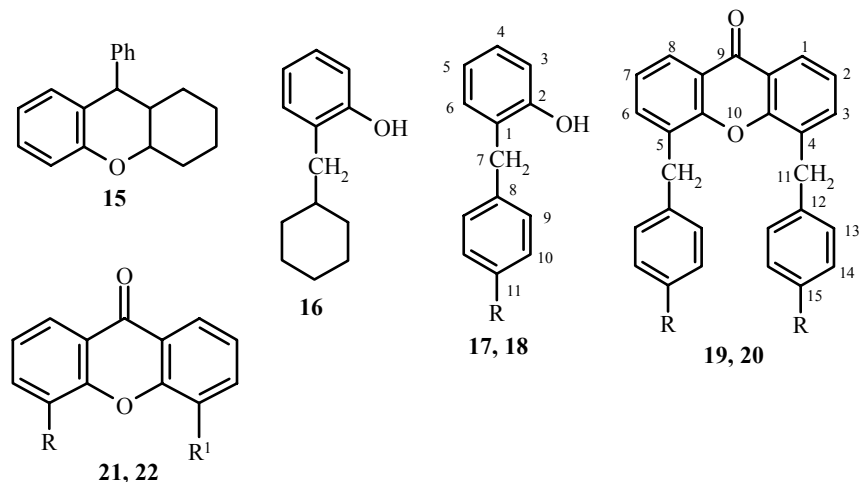
17, 19 R = H; 18, 20 R = *p*-MeO; 21 R = H, R¹ = CH₂Ph; 22 R = R¹ = cyclohexyl

During dehydrogenation of the arylidene ketones **7** and **8** appreciable amounts (up to 14%) of the xanthones **19-21** were unexpectedly obtained in addition to the xanthenes **13** and **14** and the phenols **17** and **18**. We suppose that they are formed by addition of the water released during the reaction to the intermediate fragment of the α,β-unsaturated ketone **A**, formed during dehydrogenation at positions 2 and 3 of the initial 1,5-diketone structure and stabilized by the arylidene fragment, with the subsequent probable formation of the 4-hydroxy-4H-pyran structure **B** and final dehydrogenation of the latter to the xanthone structure **C**.
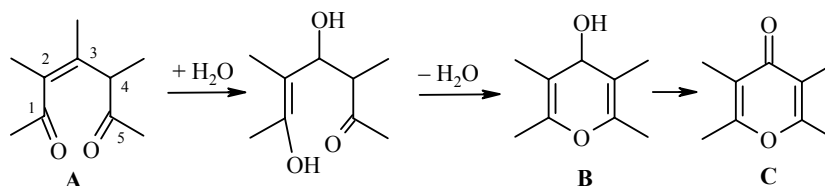
In the case of the arylidene ketones **7** and **8**, as also during dehydrogenation of the α-cycloalkyl diketones **4-6**, the *exo* double bond also migrates into the carbonyl-containing ring, but as a result of the increased stability of the arylidene C=C bond migration takes place with greater difficulty, and the addition of water to the intermediate **A** becomes competitive.

The structures of the compounds were confirmed by the data from the IR, mass, and ^{1}H and ^{13}C NMR spectra (Tables 1 and 2) and also by comparison with the spectra of the authentic substances (xanthene and xanthone) and published data [4].

The mixture of compounds **11** and **15**, which have practically identical R_f values and solubility but form crystals of different shapes, was separated by selecting the crystals according to shape. The ratio of these compounds in the reaction mixture was established from the intensity ratio of the signals for the benzyl protons H-9 (a singlet at 5.25 ppm for compound **11** and a doublet at 3.65 ppm for compound **15**). This corresponded to

TABLE 1. The Characteristics and IR Spectra of Compounds **12-16** and **18-22**

Com-pound	Empirical formula	Found, % / Calculated, %		mp, °C*	IR spectrum, ν, cm^{-1}
		C	H		
12	$C_{25}H_{30}O$	86.39 / 86.70	8.40 / 8.67	193-194	1586, 1480 (Ph); 1253, 1236, 1210 (C–O)
13	$C_{27}H_{22}O$	89.50 / 89.36	6.07 / 5.95	95-96	1601, 1578, 1486, 1456 (Ar); 1265, 1117, 1094 (C–O)
14	$C_{29}H_{26}O_3$	82.46 / 82.21	6.16 / 6.04	98-100	1610, 1584, 1510, 1456 (Ar); 1247, 1217, 1178, 1037 (C–O)
15	$C_{19}H_{20}O$	81.60 / 81.81	7.36 / 7.57	110-112	1500, 1590, 1600 (Ph); 1260, 1190, 1120 (C–O)*^{2}
16	$C_{13}H_{18}O$	82.34 / 82.10	9.25 / 9.47	61-62	3620, 3480 (OH), 1610, 1590 (Ph); 1260, 1230, 1170 (C–O)*^{2}
18	$C_{14}H_{14}O_2$	78.50 / 78.33	6.54 / 6.38	62-64	3354 (OH); 1608, 1594, 1508 (Ph); 1259, 1240, 1180, 1028 (C–O)
19	$C_{27}H_{20}O_2$	86.41 / 86.17	5.48 / 5.32	184-186	1660 (C=O); 1597, 1493 (Ph); 1215 (C–O)
20	$C_{29}H_{24}O_4$	79.98 / 79.82	5.67 / 5.50	146-148	1657 (C=O); 1597, 1512 (Ar); 1248, 1216 (Ph–O)
21	$C_{20}H_{14}O_2$	83.78 / 83.92	5.13 / 4.90	140-142	1656 (C=O); 1615, 1601 (Ph); 1224 (C–O)
22	$C_{25}H_{28}O_2$	83.17 / 83.33	8.39 / 7.95	185-186	1659 (C=O); 1609, 1490 (Ph); 1240, 1213, 1147 (C–O)

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*Solvents for recrystallization: chloroform (compound **12**), 2:1 ethanol–benzene (compound **13**), petroleum ether (compounds **14** and **16**), ethanol (compounds **15**, **20**, and **22**), 5:1 petroleum ether–benzene (compound **18**), 3:1 benzene–petroleum ether (compound **19**), and 2:1 benzene–ethanol (compound **21**).

*^{2} In carbon tetrachloride.

TABLE 2. Mass Spectra and ^{1}H and ^{13}C NMR Spectra of Compounds **12-16**, **18-22**

Com-pound	Mass spectrum, m/z (I_{rel}, %)	^{1}H NMR spectrum, δ, ppm (J, Hz)	^{13}C NMR spectrum, δ, ppm
1	2	3	4
12	346 [M$^+$] (100), 303 (6), 289(10), 263 (56), 209 (20)	1.42-1.80 (20H, m, CH$_2$); 3.17* (2H, m, H-11); 3.96 (2H, s, H-9); 6.88 (6H, m, Ar)	26.46, 27.37, 28.80 (C$_{(9)}$); 33.36, 37.10; 120.8* (s, C$_{(8a)}$); 122.6* (d), 124.6* (d), 125.9* (d, C$_{(1)}$, C$_{(2)}$, C$_{(3)}$); 135.0* (s, C$_{(4)}$); 149.4* (s, C$_{(4a)}$)
13	362 [M$^+$] (100), 284 (24), 271 (88), 239 (11), 178 (10), 165 (27), 142 (33), 91 (18)	4.01* (4H, s, H-11); 4.05 (2H, s, H-9); 6.90-7.25 (16H, m, Ar)	28.40 (t, C$_{(9)}$); 35.63* (t, C$_{(11)}$); 122.7 (d), 125.9 (d), 126.8 (d), 128.3 (d), 128.7 (d); 120.8* (s, C$_{(8a)}$); 128.5* (s, C$_{(12)}$); 140.4* (s, C$_{(4)}$); 149.9* (s, C$_{(4a)}$)
14	422 [M$^+$] (48), 315 (28), 271 (44), 221 (36), 207 (35), 195 (100), 194 (67), 182 (60), 168 (43), 115 (80), 91 (86)	3.77 (6H, s, OCH$_3$); 3.98* (4H, s, H-11); 4.05 (2H, s, H-9); Ar: 6.80* (4H, d, J = 9, H-14); 6.94* (4H, d, J = 9, H-13); 7.05 (6H, m)	28.60 (t, C$_{(9)}$); 34.90* (t, C$_{(11)}$); 55.20* (OCH$_3$); 113.8* (d, C$_{(14)}$); 122.6 (d), 126.6 (d), 128.7 (d), 129.6 (d); 120.8* (s, C$_{(8a)}$); 128.9* (s, C$_{(12)}$); 132.5* (s, C$_{(4)}$); 150.0* (s, C$_{(4a)}$); 160.0* (s, C$_{(15)}$)
15	264 [M$^+$] (64), 182 (77), 165 (33), 91 (11)	0.90-1.90 (8H, m, CH$_2$);2.25 (1H, m, H-9a); 3.65 (1H, d, J = 10, H-9); 3.85 (1H, td, J = 10; J = 1, H-4a); 6.60-7.40 (9H, Ar)	
16	190 [M$^+$] (35), 107 (100), 83 (40)	1.00-1.80 (11H, m, CH$_2$); 2.51 (2H, d, J = 7, CH$_2$-C$_6$H$_5$); 6.75-7.20 (4H, m, C$_6$H$_5$)	

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TABLE 2 (continued)

1	2	3	4
18	214 [M⁺] (100), 165 (8)	3.78 (3H, s, OCH₃); 3.93 (2H, s, H-7); Ar: 6.83 (4H, m) and 7.15 (4H, m)	35.60 (t, $C_{(7)}$); 55.30 (OCH₃); 114.2 (d, $C_{(10)}$); 115.8 (d, $C_{(3)}$); 120.9 (d), 127.6 (d), 129.5 (d), 130.7 (d), 127.3 (s) and 131.8 (s, $C_{(1)}$, $C_{(8)}$); 153.7 (s, $C_{(2)}$); 158.2 (s, $C_{(11)}$)
19	376 [M⁺] (64), 298 (100), 269 (20), 255 (10), 239 (7), 165 (28), 149 (29), 91 (24)	4.21 (4H, s, 2(H-11)); 7.14-7.31 (12H, m, Ar); 7.48* (2H, dd, J = 8; J = 1.8, H-3); 8.25* (2H, dd, J = 8; J = 1.8, H-1)	35.45* (t, $C_{(11)}$); 121.7 (s, $C_{(8a)}$); 130.0* (s, $C_{(4)}$); 139.1* (s, $C_{(12)}$); 153.8* (s, $C_{(4a)}$); 123.6 (d), 124.9 (d), 126.3 (d), 128.5 (d), 128.6 (d), 135.6 (d), 177.5 (s, $C_{(9)}$)
20	436 [M⁺] (29), 328 (63), 314 (43), 285 (35), 164, 152, 121, 91, 77 (100)	3.80 (6H, s, OCH₃); 4.18* (4H, s, H-11); 6.80* (4H, dd, J = 8, J = 1.8, H-14); 7.30* (2H, t, J = 8, H-2); 7.47* (2H, dd, J = 8, J = 1.8, H-3); 8.25* (2H, dd, J = 8, J = 1.8, H-1)	34.70* (t, $C_{(11)}$); 55.20* (OCH₃); 114.1* (d, $C_{(14)}$); 123.5 (d), 124.9 (d), 129.5 (d), 135.4 (d); 121.8* (s, $C_{(8a)}$); 130.5* (s, $C_{(4)}$); 131.3* (s, $C_{(12)}$); 153.8* (s, $C_{(4a)}$); 158.2* (s, $C_{(15)}$); 177.8 (s, $C_{(9)}$)
21	286 [M⁺] (100), 257 (9), 209 (8), 180 (13), 181 (13), 165 (8), 152 (10)	4.32 (2H, s, H-11); 7.25-7.41 (7H, m, Ar); 7.52 (2H, td, J = 8; J = 1.8); 7.72 (1H, td, J = 8, J = 1.8, H-6); 8.25 (1H, dd, J = 8, J = 1.8, H-1); 8.35 (1H, dd, J = 8, J = 1.8, H-8)	35.70 (t, $C_{(11)}$); 117.9 (d, $C_{(5)}$); 123.5 (d), 123.8 (d), 124.9 (d), 126.3 (d), 126.6 (d), 128.5 (d), 128.6 (d), 134.6 (d), 135.4 (d); 121.6 (s, $C_{(8a)}$); 121.9 (s, $C_{(9a)}$); 130.3 (s, $C_{(4)}$); 139.4 (s, $C_{(12)}$); 154.0 (s, $C_{(4a)}$); 155.9 (s, $C_{(10a)}$); 177.5 (s, $C_{(9)}$)
22	360 [M⁺] (100), 317 (23), 249 (15), 235 (15), 226 (26), 178 (5), 115 (5)	1.58 (10H, m, CH₂); 1.98 (10H, m, CH₂); 3.37 (2H, m, CH-C₆H₅); 7.34 (2H, t, J = 8, 2(H-7)); 7.60 (2H, dd, J = 8, J = 1.8, 3(H-6)); 8.20 (2H, dd, J = 8, J = 1.8. 1(H-8))	26.22, 27.20, 37.30 (t, $C_{(11)}$); 123.9 (d), 123.5 (d); 131.5* (d, $C_{(11)}$); 121.3* (s, $C_{(9a)}$); 136.6* (s, $C_{(4)}$); 153.2* (s, $C_{(4a)}$); 177.9 (s, $C_{(9)}$)

* The values of the signals for the protons at the symmetrical C atoms in the ¹H NMR spectra and the signals for the symmetrical C atoms in the ¹³C NMR spectra.

a ratio of 6:1 for compounds **11-15**. The *trans* coupling of the hydrogenated rings in the structure of compound **15** follows from the nature of the signal for the H-4a proton, shifted upfield on account of its proximity to the heteroatom – a triplet of doublets at 3.85 ppm with $J = 10$ and $J = 1$ Hz.

The IR spectra of compounds **19-22** have the carbonyl absorption characteristic of xanthones in the region of 1656-1660 cm^{-1}.

EXPERIMENTAL

The IR spectra were recorded in potassium bromide on a Perkin-Elmer Spectrum BX-II instrument. The mass spectra were recorded on a Hewlett-Packard HP 5972 MSD/HP 5890 Series II GC instrument. The ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC-250 spectrometer (250 and 62 MHz respectively in deuterochloroform) with TMS as internal standard. The Pt/C catalyst was prepared by the procedure described in [5], and the Pt content was 8%.

Catalytic Dehydrogenation of Compounds 1-8 (General Procedure). The diketone or ketol was rubbed with the catalyst in a ratio of 20:1 by weight for the ketones **1a-3a** and 10:1 for the diketones **1**, **4-8** and transferred to a flask the outlet of which was placed in a measuring cylinder filled with water and turned upside down into a crystallizer containing water. The flask was lowered into a metal bath heated to 160°C, and the temperature was raised while the released gas was collected in the measuring cylinder. Two temperature ranges for active release of gas were observed: 1) 280-300°C for compounds **1a-3a**, 240-280°C for the diketones **4-6**, 300-320°C for the diketones **7** and **8**; 2) 340-360°C for all the compounds. In the last case the process is accompanied by strong resinification of the reaction mixture, and dehydrogenation was therefore conducted in the first temperature range for all the compounds except for the diketone **1**, for which the second range was investigated. Heating was continued until the release of hydrogen had stopped (2-4 h), and usually 60-80% of the theoretical amount of gas calculated for the corresponding xanthene was collected. After cooling the reaction mixture was mixed with chloroform, the catalyst was filtered off, the filtrate was dried with magnesium sulfate, and the solvent was distilled.

1. The oily residue obtained from the ketol **1a** (8 g, 0.038 mol) was distilled under vacuum, and 5.5 g of distillate (bp 105-120°C, 1 mm Hg), which crystallized on cooling, was obtained. The distillate was mixed with 10% aqueous sodium hydroxide solution (50 ml), and the undissolved crystalline part was filtered off, washed with acidified water, to pH 7 with water, and with ethanol (2 ml). We obtained 2.1 g (32%) of the xanthene **9**; mp 99-100°C (ethanol). It was identified by its R_f value, IR spectrum, and a mixed melting test with an authentic sample of the xanthene. To the alkaline filtrate with vigorous stirring we added dropwise benzoyl chloride (7 ml, 0.05 mol) over 2 h (monitored by TLC). The oil that separated was extracted with ether (3 × 15 ml), and the extract was washed with acidified water and then with water to pH 7 and dried with magnesium sulfate. After distillation of the ether the residue was crystallized from ethanol, and 3.9 g of 2-benzylphenol benzoate was obtained; mp 28°C. It was identified by its IR, mass, and NMR spectra. This amount corresponds to 2.49 g (35%) of 2-benzylphenol (**17**).

2. From the ketol **2a** (8 g, 0.036 mol) we obtained 5.7 g of a distillate boiling at 96-101°C (1 mm Hg) that did not crystallize on cooling. During preparative separation on plates with SiO$_2$ (100:250 μ) in the 2:1 hexane–ether system we obtained 4.6 g (65%) of 9-methylxanthene (**10**); bp 96-98°C (1 mm Hg). According to data in [5], the boiling point is 95-97°C (0.3 mm Hg). The structure was confirmed by data from the IR and mass spectra.

3. From the ketol **3a** (5.5 g, 0.0176 mol) we obtained 4.4 g of a crystallization residue, representing a mixture of two substances with identical R_f values (on Silufol plates in various systems) and identical solubility but having a different crystal form – needle and cubic. From an alcohol solution of the mixture after free evaporation by selecting the crystals we isolated 9-phenylxanthene (**11**) (colorless cubes) with mp 144-145°C

(ethanol) (mp 145°C [5]) and 9-phenyl-1,2,3,4,4a,9a-hexahydroxanthene (**15**) (colorless needles). The ratio of compounds **11** and **15** was 6:1 (according to the ^{1}H NMR spectrum). Accordingly, the yield of the xanthene **11** amounted to 3.77 g (83%), and that of compound **15** to 0.63 g (14%).

4. We dehydrogenated the diketone **1** (6 g, 0.028 mol) at 340-360°C. The residue (5.8 g) partly crystallized, and 2.0 g (38%) of the xanthene **9** was filtered off. The remaining part was separated on a column of SiO$_2$ (neutral) with elution first with petroleum ether (70-100°C) and then with a 50:1 mixture of petroleum ether and ether (or ethyl acetate). We obtained a further 1.4 g (26%) of the xanthene **9** (total yield 65%) and 0.2 g (3.6%) of 2-(cyclohexylmethyl)phenol (**16**).

5. The residue obtained after dehydrogenation of the diketone **6** (1 g, 0.0027 mol) crystallized. We separated 0.3 g (38.2%) of 4,5-dicyclohexylxanthene **12**.

6. From the diketone **7** (6.2 g, 0.016 mol) we obtained 5.8 g of a residue. It was mixed with ether (10 ml), and 4,5-dibenzylxanthone (**19**) (0.5 g) was filtered off. The remaining part was separated on a column as described in expt. 4 with silica gel as sorbent. We obtained 1.5 g (26%) of 4,5-dibenzylxanthene (**13**), 1.3 g (22%) of 2-benzylphenol (**17**), 0.3 g of xanthone **19** (total yield 14%), and 0.3 g (7%) of 4-benzylxanthone (**21**).

Similarly from the diketone **8** (7.2 g, 0.016 mol) we obtained 1.6 g (24%) of 4,5-di(*p*-methoxybenzyl)xanthene (**14**), 1.4 g (20%) of 2-(*p*-methoxybenzyl)phenol (**18**), and 0.9 g (13%) of 4,5-di(*p*-methoxybenzyl)xanthone (**20**).

4,5-Dicyclohexylxanthone (22). To a suspension of the xanthene **12** (0.8 g, 0.0023 mol) in acetic acid (20 ml) we added dropwise over 10 min a solution of chromium(VI) oxide (1.8 g, 0.18 mol) in water (2 ml) with acetic acid (4 ml). The mixture was stirred at 60°C for 6 h until the initial xanthene had disappeared (TLC) and cooled. The precipitate was filtered off, and 0.6 g (72%) of compound **22** was obtained.

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