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POLYCYCLIC HYDROXYQUINONES—VIII[1]

PREPARATION OF ACETYLHYDROXYNAPHTHAZARINS BY PHOTO-FRIES REARRANGEMENT. A CONVENIENT SYNTHESIS OF SPINOCHROME A

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Abstract—Several synthetic routes to mono- and dihydroxynaphthazarins bearing an acetyl side-chain have been explored. Methoxynaphthazarin **1** has always been the starting material. Acylation is brought about *via* a photo-Fries rearrangement of various adequately substituted acetoxynaphthalenes prepared in several steps from **1**. Further steps including oxidative demethylation, hydrolysis and ether cleavage reactions, led to the desired mono- and dihydroxysubstituted acetylnaphthazarins. A new synthesis of Spinochrome A **24**, a natural occurring pigment representative of this kind of naphthazarin derivatives, is described.

In a recent paper[2] we have shown that the photo-Fries rearrangement is a valuable method for the introduction of an acetyl side-chain into the naphthalene nucleus. The reaction allowed us to develop a convenient synthesis of acetylnaphthazarin (2 - acetyl - 5,8 - dihydroxy - 1,4 - naphthoquinone) and some fixed derivatives of its two main tautomers. These results could be exploited to synthesize compounds related to spinochromes, naturally occurring naphthoquinone pigments isolated from sea urchins and other echinoderms.[3]

Our main interest was directed to the synthesis of systems such as Spinochrome A **24** and other related naphthazarin derivatives bearing an acetyl side-chain and one or more hydroxy-groups. A simple approach to these systems, which involves the hydroxylation of an acetylnaphthazarin derivative, has been reported in a previous paper.[4] We now report on an alternative strategy which involves the acylation of mono- and dihydroxynaphthazarin methyl ethers by a photo-Fries rearrangement.

Preparation of mono- and dihydroxynaphthazarin methyl ethers. The required substrates for the photo-Fries reaction were synthesized by reductive acetylation of the di-, tri- and tetra-methyl ethers **2a**, **3a**, **3b** and **5**, which in turn could be prepared from methoxynaphthazarin **1**. This compound was obtained by acid-catalyzed methanol treatment of hydroxynaphthazarin,[5] an easy process due to the enhanced acidic properties of an OH-group attached to a quinone system. On the other hand, methylation of the chelated OH-groups required a more energic procedure. Treatment of **1** with methyl iodide, in the presence of silver oxide, led to a mixture of di- and trimethyl ethers (Scheme 1).

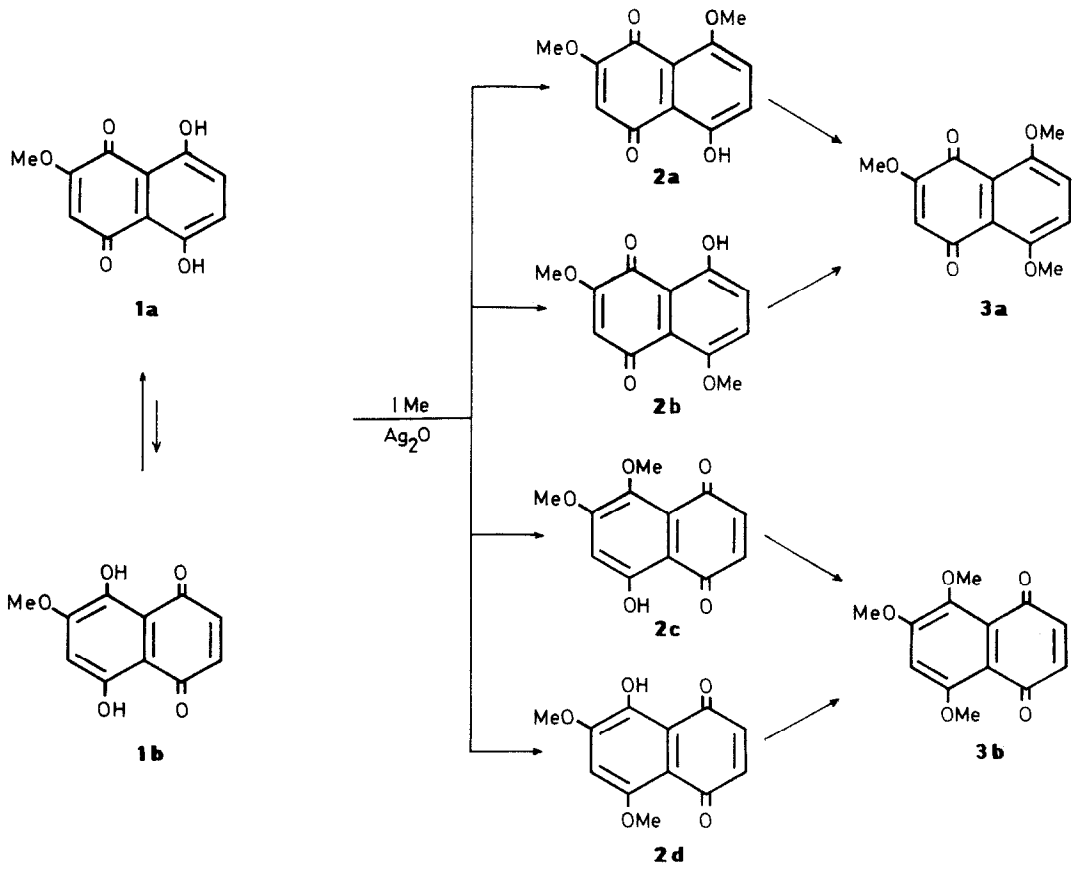
Dimethyl ether **2a** constitutes the major product in the dimethylated fraction. Silica gel chromatography of the reaction mixtures allowed the isolation of all the possible isomeric di- and trimethyl ethers, except compound **2d**. In order to increase the proportion of trimethyl ethers in the reaction a great excess of methylating agent and prolonged reaction times were necessary. It is worth noting that although **1a** is the predominant tautomer of methoxynaphthazarin, methyl ethers arising from tautomer **1b** were also formed. The structure of all these compounds follows from their ^{1}H NMR spectra. Distinction between isomers **2a** and **2b** was based on the fact[6] that the signal at δ 11.93 of the 5-OH proton in juglone (5-hydroxy-1,4-naphthoquinone) is shifted to higher field (δ 11.70) by a 3-OCH_3 and to lower field (δ 12.23) by the more distant 2-OCH_3 group. This allowed us the assignment of structure **2a** to the compound in which the *peri*-hydroxyl signal resonates at lower field (δ 12.86) and **2b** to the isomer which shows the OH-signal at higher field (δ 12.22), taking into account that in naphthazarin monomethyl ether the signal appear at δ 12.40.[7] On the other hand, the assignment of structure **2c** is based on similar arguments, the OH signal appears at δ 13.15 although in this case the absence of the isomer **2d** precludes an unambiguous conclusion.

2,5,7,8 - Tetramethoxy - 1,4 - naphthoquinone[8] **5** was prepared by methylation of 2 - hydroxy - 7 - methoxynaphthazarin **4** (Scheme 2). The latter, in turn, was synthesized by a modification of the procedure of Scheuer *et al.*[9] Oxidation of methoxynaphthazarin with lead tetraacetate followed by treatment with sulfuric acid and water yielded 2-hydroxy-7-methoxynaphthazarin **4** as the major product and a small quantity of the 2,6-isomer. The desired product was finally obtained in pure form by recrystallization, thus avoiding a tedious chromatographic separation.

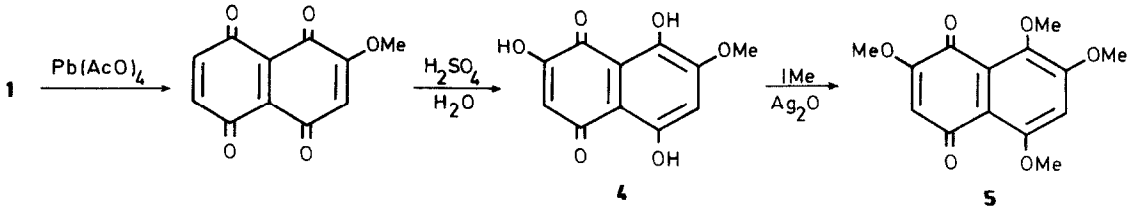
Photo-Fries rearrangement. The irradiations were carried out under experimental conditions similar to those previously described.[2]

We first irradiated the diacetoxyderivative **6**, prepared by reductive acetylation of **3a**. This trimethyl ether was obtained either following the procedure outlined above, or by a simpler and higher yielding method[4] consisting of an acid-catalyzed addition of methanol to naphthazarin dimethyl ether. Photorearrangement of **6** gave **7**, which was converted into 2-acetyl-3-hydroxynaphthazarin **9** through a direct oxidation with silver(II) oxide[10] (Scheme 3). It is interesting to point out that the primary product in this oxidative deacetoxylation is the trimethyl ether **8**, which undergoes an easy hydrolysis of the methoxy group in position-3 rapidly giving **9** as the major product.

The preparation of the free 2 - acetyl - 3 - hydroxynaphthazarin **12**, which is a naturally occurring pigment, was achieved by a different reaction sequence. Acetylation of **7** and subsequent oxidative demethylation of **10** with silver(II) oxide yielded **11b**. It is interesting to note that the expected diacetate **11a** readily undergoes an O-acetyl migration[11] and is converted into the more



Scheme 1.



Scheme 2.

stable isomer **11b**. The assignment of this structure was supported by the ^{1}H NMR spectrum which shows two aromatic protons at δ 7.48. Presumably the presence of the electron releasing OCH_3-group attached to the quinone ring play a decisive role in this isomerization.

An alternative route to **12** involves an analogous reaction sequence, but starting now from **2a**, the major product obtained by methylation of methoxynaphthazarin. Reductive acetylation of **2a** afforded triacetate **13** (Scheme 4).

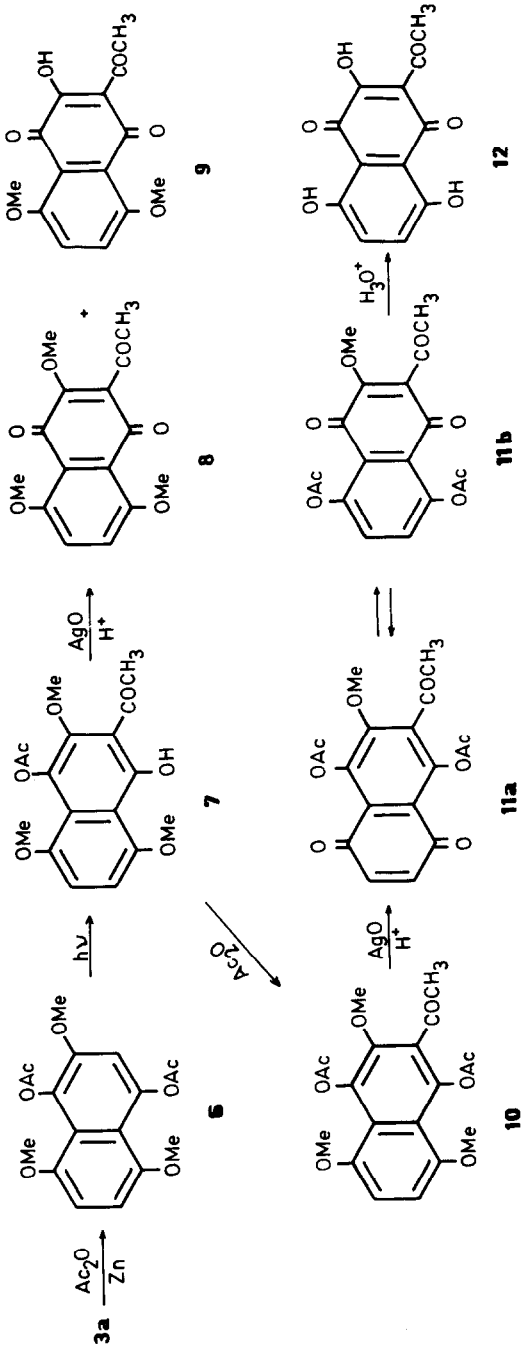
In principle, photo-Fries rearrangement of **13** could give rise to two different isomers as a result of the migration of the acetyl groups in position-4 or -5. The reaction, however, led in good yield to only one rearrangement product, **14**. Apparently this result is in contradiction with the general view that electron donors groups in *para* position facilitate the rearrangement.[12]

Oxidation of **14** with silver(II) oxide, followed by hydrolysis with 6*N* hydrochloric acid, led finally to **12**.

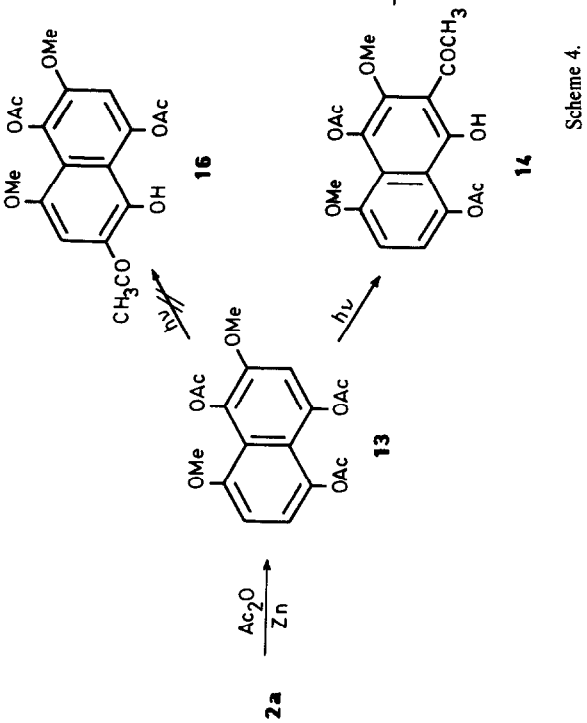
Since the expected migration of the acetyl group in position-5 did not take place, compound **16**—a very suitable precursor of Spinochrome A—could not be obtained by this route.

For another attempt to synthesize 2 - acetyl - 6 - hydroxynaphthazarin **21a**, we choose **3b** as starting material. Reductive acetylation afforded **17** (Scheme 5), in which two possible acetyl migrations could occur, one of them leading to the desired naphthazarin derivative.

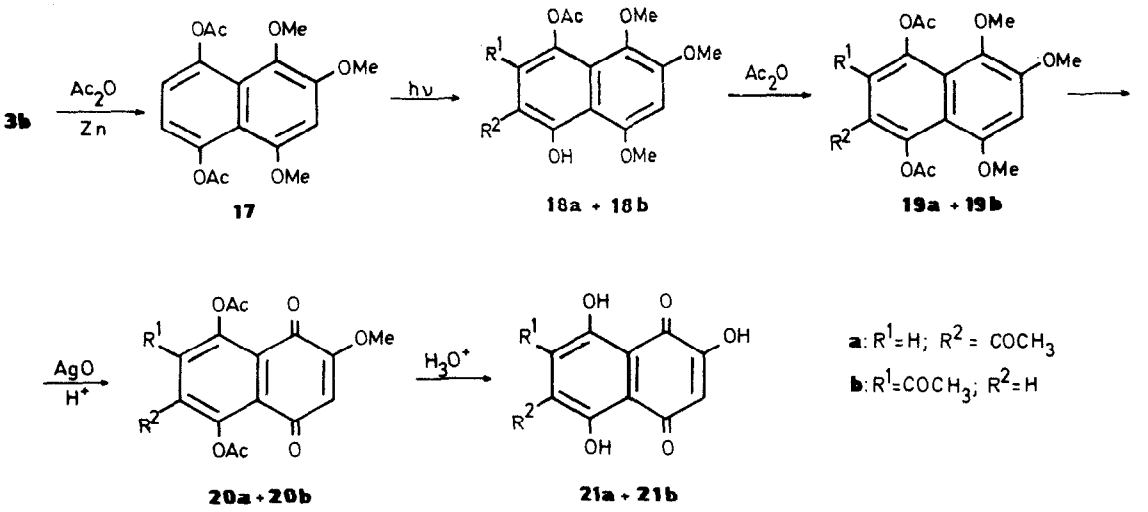
In fact, both migrations occurred in this instance as was shown by the ^{1}H NMR spectrum of the crude product isolated from the photorearrangement. Unfortunately, all our attempts to fractionate it were unsuccessful. Nevertheless, we decided to continue the projected synthetic scheme and the subsequent reac-



Scheme 3.



Scheme 4.

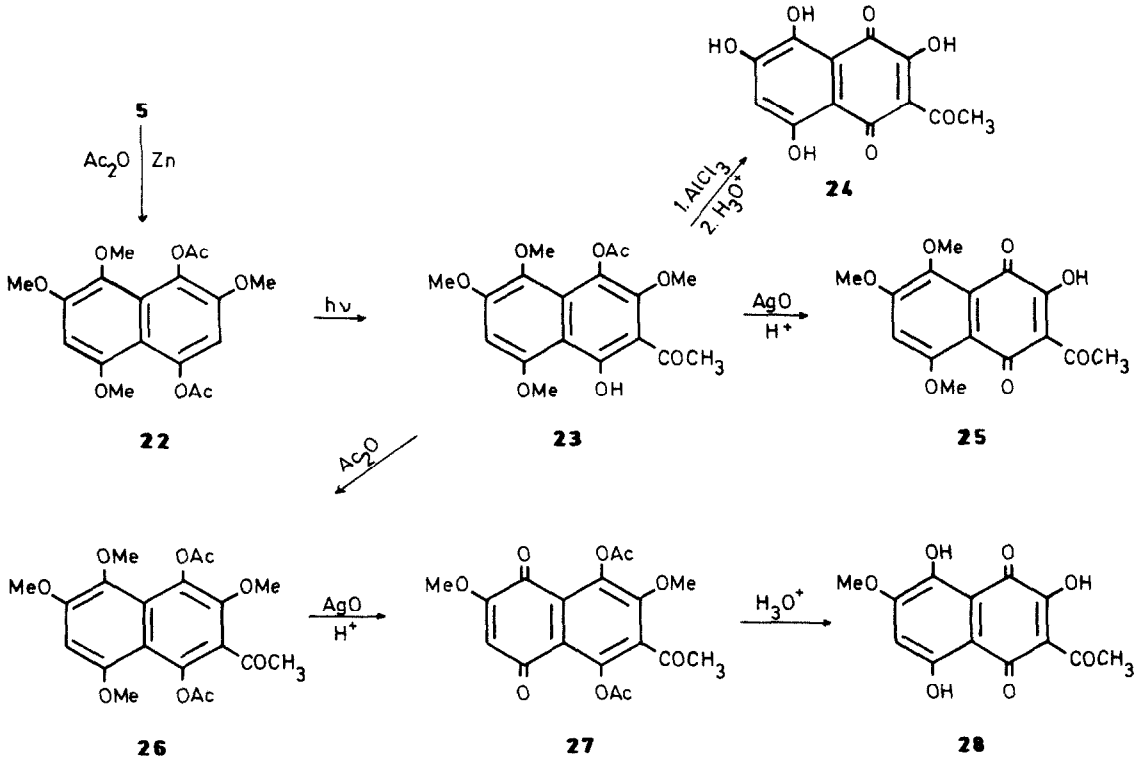


Scheme 5.

tions–acetylation, oxidative demethylation and hydrolysis were carried out. The ^1H NMR spectra of the reaction products collected in each step showed them to consist of the two corresponding isomers, approximately in 1:1 ratio, but we failed to resolve these mixtures in all the cases.

Finally, our methodology has been applied to the synthesis of Spinochrome A starting from the tetramethyl ether **5** (Scheme 6).

The reductive acetylation product **22** undergoes a photo-Fries rearrangement to give **23**. From this compound, several routes were tried in order to obtain the desired Spinochrome A (**24**). First, **23** was oxidized with silver(II) oxide and the resulting trimethyl ether **25** submitted to demethylation, but the results were rather unsatisfactory in spite of having used a variety of procedures. Next, an indirect method was followed: acetylation of **23**, subsequent oxidative demethylation of **26** and hydrolysis of **27**, afforded the Spinochrome A monomethyl ether **28**. But again the final demethylating step leading to **24** failed in this case. The severe experimental conditions required for a complete demethylation



Scheme 6.

gives rise to a loss of the acetyl group among other detrimental side reactions. In order to obviate these inconveniences, we decided to carry out the demethylating process on the naphthalene derivatives, i.e. before the quinone generation step, in the hope of avoiding the acetyl loss. In this way, we tried to demethylate **23** employing a standard procedure—treatment with aluminium chloride in nitrobenzene followed by hydrolysis—and we obtained a product which proved to be identical to an authentic sample of Spinochrome A. From this result, it was evident that during the treatment not only demethylation but also oxidation was effected. This new synthetical approach offers a marked improvement over the one previously reported,[9] which operates through an acid-catalyzed Fries bisacetylation process, with subsequent selective removal of one acetyl group.

EXPERIMENTAL

M.ps are uncorrected. ^{1}H NMR spectra were recorded with either a 60 MHz Perkin–Elmer Model R-12 or a Varian XL-100 15 FT instrument. Chemical shifts are reported in ppm downfield (δ) from TMS. Unless otherwise stated, $CDCl_3$ was used for NMR work. IR spectra were obtained by Nujol dispersion with a 257 Perkin–Elmer spectrometer. Mass spectra were determined with a Hitachi Perkin–Elmer Model RMU-6MG spectrometer. Irradiations were carried out with a mercury arc (medium pressure, 125 W) in a pyrex immersion well reactor. Solutions were N_2-purged during irradiation.

Methylation of 2 - *methoxy* - 5,8 - *dihydroxy* - 1,4 - *naphthoquinone* **1**. Partial methylation was achieved when 15 g of silver(I) oxide and 35 ml of CH_3I were added to 2 g of 2 - methoxy - 5,8 - dihydroxy - 1,4 - naphthoquinone dissolved in 500 ml of $CHCl_3$. The mixture was warmed at 30–40° with stirring for 3 days. The mixture was filtered off and the solvent removed. The solid residue was fractionated by column chromatography on silica-gel (benzene–EtOAc 4:1). Using this procedure, the yields of different products were: **2a** (45%), **2b** (8%), **2c** (4%), **3a** (20%), **3b** (12%). Increased proportion of trimethyl ethers were obtained employing 36 g of silver(I) oxide and 90 ml of CH_3I and prolonging the period of warming to 5 days. Under these conditions, the yields were: **2a** (8%), **2b** (2%), **2c** (2%), **3a** (55%), **3b** (25%).

5 - *Hydroxy* - 2,8 - *dimethoxy* - 1,4 - *naphthoquinone* **2a**. M.p. 160°. IR: 1675, 1635, 1610. NMR: 3.92, 4.00 (2s, 6H, OCH_3); 6.12 (s, 1H, C-3); 7.35 (s, 2H, C-6, C-7); 12.86 (s, 1H, OH). MS: 234 (M^+), 219, 191. (Found: C, 61.2; H, 4.5 Calc. for $C_{12}H_{10}O_5$: C, 61.5; H, 4.3%).

8 - *Hydroxy* - 2,5 - *dimethoxy* - 1,4 - *naphthoquinone* **2b**. M.p. 205°. IR: 1640, 1617, 1595. NMR: 3.90, 4.00 (2s, 6H, OCH_3); 6.16 (s, 1H, C-3); 7.40 (s, 2H, C-6, C-7); 12.22 (s, 1H, OH). MS: 234 (M^+), 219, 189, 149. (Found: C, 61.3; H, 4.6. Calc. for $C_{12}H_{10}O_5$: C, 6.15; H, 4.3%).

5 - *Hydroxy* - 7,8 - *dimethoxy* - 1,4 - *naphthoquinone* **2c**. M.p. 180°. IR: 1670, 1640, 1595. NMR: 3.90, 4.00 (2s, 6H, OCH_3); 6.76 (s, 1H, C-6); 6.90 (s, 2H, C-2, C-3); 13.15 (s, 1H, OH). MS: 234 (M^+), 219, 189, 149. (Found: C, 61.3; H, 4.6. Calc. for $C_{12}H_{10}O_5$: C, 61.5; H, 4.3%).

2,5,8 - *Trimethoxy* - 1,4 - *naphthoquinone* **3a**. M.p. 165°. Identical to compound described in Ref. [4].

5,6,8 - *Trimethoxy* - 1,4 - *naphthoquinone* **3b**. M.p. 126°. IR: 1670, 1645, 1618. NMR: 3.92, 4.05 (2s, 9H, OCH_3); 6.85 (s, 2H, C-2, C-3); 6.89 (s, 1H, C-7). MS: 248 (M^+), 233, 218. (Found: C, 62.8; H, 4.9. Calc. for $C_{13}H_{12}O_5$: C, 62.9; H, 4.9%).

2,5,8 - *Trihydroxy* - 7 - *methoxy* - 1,4 - *naphthoquinone* **4**. A soln of 1 g of **1** in 100 ml CH_2Cl_2 was shaken with 3 g $Pb(OAc)_4$. The yellow soln was vacuum evaporated and the residue was treated with 35 ml conc H_2SO_4. After standing 5 min, the mixture was poured into ice water and extracted with $CHCl_3$ to give a mixture of the starting **1**, the desired **4** and a small amount of 2,5,8 - trihydroxy - 6 - methoxy - 1,4 - naphthoquinone. The $CHCl_3$ extract was treated with $NaHCO_3$ aq followed by acidification with HCl. The acidic soln was extracted with $CHCl_3$, dried over Na_2SO_4 and the solvent was vacuum removed. The residue was crystallized from $CHCl_3$ to give 650 mg (60%) of **4**,[9] m.p. 240°. IR: 1600. NMR: 3.97 (s, 3H, OCH_3); 6.47 (s, 1H, C-3); 6.53 (s, 1H, C-6); 12.07 (s, 1H, OH in C-8); 13.13 (s, 1H, OH in C-5). MS: 236 (M^+).

2,5,7,8 - *Tetramethoxy* - 1,4 - *naphthoquinone* **5**. 20 g of silver(I) oxide and 36 ml CH_3I were added to 1 g of **4**, dissolved in 300 ml $CHCl_3$. The mixture was stirred at 30–40° for 6 days. The resulting mixture was filtered and the solvent was vacuum removed. The solid residue was purified by column chromatography on silica gel (benzene–EtOAc 1:1) to give 471 mg (40%) of **5**[6], m.p. 168–171°. IR: 1630; NMR: 3.86, 3.91, 4.00 (3s, 12H, OCH_3); 6.02 (s, 1H, C-3); 6.02 (s, 1H, C-3); 6.84 (s, 1H, C-6); MS: 278 (M^+), 263, 216.

1,4 - *Diacetoxy* - 2,5,8 - *trimethoxynaphthalene* **6**. A mixture of 2.03 g of **3a**, 2.5 g of Zn dust, 840 mg of NaOAc and 150 ml of Ac_2O, was refluxed until the colour disappeared (1 hr). The resulting soln was poured into ice–water to give a white ppt which was collected, washed with water and crystallized from benzene–hexane (1:1) to give 2.2 g (80%) of **6**, m.p. 175°. IR: 1760, 1615. NMR: 2.36, 2.38 (2s, 6H, $OCOCH_3$); 3.88, 3.92 (2s, 9H, OCH_3); 6.73, 6.74 (sist. AB; J = 9.3 Hz, 2H, C-6, C-7); 7.01 (s, 1H, C-3). MS: 334 (M^+), 292, 250, 235. (Found: C, 61.0; H, 5.7. Calc. for $C_{17}H_{18}O_7$: C, 61.1; H, 5.4%).

2 - *Acetyl* - 4 - *acetoxy* - 3,5,8 - *trimethoxy* - 1 - *naphthol* **7**. A mixture of 500 mg of **6** in 300 ml of EtOH–glycerol (1:1) was irradiated for 10 hr. The resulting soln was diluted with water and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4 and the solvent was vacuum removed. The residue was crystallized from benzene–hexane (1:1) to give 375 mg (70%) of **7**, m.p. 96–97°. IR: 3295, 1756, 1700, 1620. NMR: 2.39 (s, 3H, $OCOCH_3$); 2.64 (s, 3H, $COCH_3$); 3.90, 3.92, 4.00 (3s, 9H, OCH_3); 6.82 (s, 2H, C-6, C-7); 11.12 (s, 1H, OH). MS: 334 (M^+), 292, 277, 249. (Found: C, 61.0; H, 5.4. Calc. for $C_{17}H_{18}O_7$: C, 61.1; H, 5.4%).

2 - *Acetyl* - 3,5,8 - *trimethoxy* - 1,4 - *naphthoquinone* **8** *and* 2 - *acetyl* - 3 - *hydroxy* - 5,8 - *dimethoxy* - 1,4 - *naphthoquinone* **9**. A mixture of 334 mg of **7** (1 mmol), 496 mg of silver(II) oxide (4 mmol) and 10 ml of dioxane was stirred for 5 min. 6N HNO_3 (1 ml) was added and the mixture stirred at room temp for another 5 min. Then 40 ml of $CHCl_3$ and 10 ml of water were added and the $CHCl_3$ extract washed with water and dried over anhyd Na_2SO_4. The solvent was removed and the residue was precipitated by addition of ether to give a mixture of **8** and **9**.[4] The major product was separated by extraction with $NaHCO_3$ to give 180 mg (65%) of **9**.

The neutral extract afforded **8** (5%), m.p. 171–173°. IR: 1715, 1650, 1600. NMR: 2.50 (s, 3H, $COCH_3$); 4.00, 4.10 (2s, 9H, OCH_3); 7.40 (s, 2H, C-6, C-7). MS: 290 (M^+), 276, 248, 233. (Found: C, 62.3; H, 4.9. Calc. for $C_{15}H_{14}O_6$: C, 62.1; H, 4.9).

2 - *Acetyl* - 1,4 - *diacetoxy* - 3,5,8 - *trimethoxynaphthalene* **10**. A mixture of 700 mg of **7**, 700 mg of NaOAc and 100 ml Ac_2O was refluxed until the colour disappeared (1 hr). The resulting soln was poured into ice water to give a white ppt, which was collected, washed with water and crystallized from benzene–cyclohexane (1:1) to give 632 mg of (80%) of **10**, m.p. 76–79°. IR: 1765, 1705, 1610. NMR: 2.28, 2.38 (2s, 6H, $OCOCH_3$); 2.52 (s, 3H, $COCH_3$); 3.82, 3.84, 3.86 (3s, 9H, OCH_3); 6.72, 6.80 (sist. AB J = 8.0 Hz, 2H, C-6, C-7). MS: 376 (M^+), 334, 292, 277. (Found: C, 60.9; H, 5.7. Calc. for $C_{19}H_{20}O_8$: C, 60.6; H, 5.4).

2 - *Acetyl* - 3 - *methoxy* - 5,8 - *diacetoxy* - 1,4 - *naphthoquinone* **11b**. A mixture of 376 mg of **10** (1 mmol), 496 mg of silver(II) oxide (4 mmol) and 10 ml of dioxane was stirred for 5 min. 6N HNO_3 (1 ml) was added and stirred further at room temp for 5 min. Then 40 ml of $CHCl_3$ and 10 ml of water were added; the $CHCl_3$ extract was washed with water and dried over Na_2SO_4. The solvent was vacuum removed and the residue was crystallyzed from benzene–hexane (1:1) to give 242 mg (70%) of **11b**, m.p. 123–126°. IR: 1760, 1700, 1680, 1640, 1615. NMR: 2.42, 2.46 (2s, 6H, $OCOCH_3$); 2.50 (s, 3H, $COCH_3$); 4.09 (s, 3H, OCH_3); 7.48 (s, 2H, C-2, C-3). MS: 304 (M^+–42), 262, 247. (Found: C, 58.9; H, 4.0. Calc. for $C_{17}H_{14}O_8$: C, 59.0; H, 4.1).

2 - *Acetyl* - 3,5,8 - *trihydroxy* - 1,4 - *naphthoquinone* **12**. Hydrolysis of 100 mg **11b** with 20 ml of 6N HCl (15 min reflux) afforded 43 mg (60%) of **12**.[13] m.p. 162–163°. IR: 1620.

NMR: 2.88 (s, 3H, $COCH_3$), 7.42, 7.25 (sist. AB, J = 10.5 Hz, 2H, C-6, C-7); 12.42, 13.21 (2s, 2H, OH). MS: 248 (M^+), 220, 205.

1,4,5 - *Triacetoxy* - 2,8 - *dimethoxynaphthalene* **13**. A mixture of 468 mg of **2a**, 600 mg Zn dust, 700 mg of NaOAc and 100 ml of Ac_2O, was refluxed until the colour disappeared (1 hr). The resulting soln was poured into ice water to give a white ppt, which was collected, washed with water and crystallized from benzene to give 580 mg (80%) of **13**, m.p. 216–218°. IR: 1778, 1755, 1618. NMR: 2.36, 2.40, (2s, 9H, $OCOCH_3$); 3.94 (s, 6H, OCH_3); 6.90 (sist. AB, J = 4 Hz, 2H, C-6, C-7); 7.09 (s, 1H, C-3). MS: 362 (M^+), 320, 278, 236, 221. (Found: C, 59.9; H, 5.3. Calc. for $C_{18}H_{18}O_8$: C, 59.7; H, 5.0).

2 - *Acetyl* - 3,5 - *dimethoxy* - 4,8 - *diacetoxy* - 1 - *naphthol* **14**. A soln of 300 mg of **13** in 300 ml of EtOH–glycerol (1:1) was irradiated for 12 hr. The irradiated soln was diluted with water and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4 and the solvent was vacuum removed. The residue was crystallized from benzene-hexane (1:1) to give 210 mg (70%) of **14**, m.p. 136–138°. IR: 1755, 1615, 1605. NMR: 2.38, 2.42 (2s, 6H, $OCOCH_3$), 2.79 (s, 3H, $COCH_3$); 3.95 (s, 6H, OCH_3); 7.05 (s, 2H, C-6, C-7). $(CD_3)CO$: 2.31, 2.39 (2s, 6H, $OCOCH_3$); 2.80 (s, 3H, $COCH_3$); 7.14, 7.19 (2s, 2H, C-6, C-7). MS: 362 (M^+), 320, 278, 263. (Found: C, 59.8; H, 5.1. Calc. for $C_{18}H_{18}O_8$: C, 59.7; H, 5.0).

2 - *Acetyl* - 3 - *hydroxy* - 5 - *methoxy* - 8 - *acetoxy* - 1,4 - *naphthoquinone* **15**. A mixture of 181 mg of **14** (0.5 mmol), 248 mg of silver(II) oxide (2 mmol), and 5 ml of dioxane was stirred for 5 min. 6N HNO_3 (0.5 ml) was added and stirred at room temp for another 5 min. Then 20 ml of $CHCl_3$ and 5 ml of water were added; the $CHCl_3$ extract was washed with water and dried over Na_2SO_4. The product was separated by extraction with $NaHCO_3$ to give 94 mg (60%) of **15**, m.p. 147–150°. IR: 1765, 1700, 1680, 1640, 1585. NMR: 2.41 (s, 3H, $OCOCH_3$), 2.76 (s, 3H, $COCH_3$), 4.05 (s, 3H, OCH_3), 7.45 (s, 2H, C-6, C-7). MS: 262 ($M^+ - 42$), 234, 219, 216. The product was not further purified and after hydrolysis, by refluxing with 6N HCl, led finally to **12**, identical with an authentic sample.

1,4 - *Diacetoxy* - 5,6,8 - *trimethoxynaphthalene* **17**. A mixture of 1 g of **3b**, 1.2 g of Zn dust, 400 mg of NaOAc and 100 ml of Ac_2O, was refluxed until the colour disappeared (1 hr). The resulting soln was poured into ice water to give a white ppt, which was collected, washed with water and crystallized from benzene–hexane (1:1) to give 1.01 g (75%) of **17**, m.p. 130°. IR: 1765, 1610. NMR: 2.34 (s, 6H, $OCOCH_3$); 3.80, 3.90, 3.96 (3s, 9H, OCH_3); 6.68 (s, 1H, C-7); 6.85, 7.01 (sist. AB, J = 8 Hz, 2H, C-2, C-3); MS. 334 (M^+), 292, 250, 235. (Found: C, 60.8; H, 5.6. Calc. for $C_{17}H_{18}O_7$: C, 61.1; H, 5.4).

2 - *Acetyl* - 4 - *acetoxy* - 5,7,8 - *trimethoxy* - 1 - *naphthol* **18a** *and* 2 - *acetyl* - 4 - *acetoxy* - 5,6,8 - *trimethoxy* - 1 - *naphthol* **18b**. A soln of 500 mg of **17** in 300 ml of EtOH–glycerol (1:1) was irradiated for 10 hr. The irradiated soln was diluted with water and extracted with $CHCl_3$. After drying over Na_2SO_4, the solvent was vacuum removed and the residue crystallized from benzene–hexane (1:1) to give 375 mg (70%) of an unsolved mixture of **18a** + **18b**, m.p. 149–151°. IR: 1760, 1628, 1600; NMR: 2.36 (s, 3H, $OCOCH_3$); 2.70, (s, 3H, $COCH_3$); 3.95, 3.98, 4.04 (3s, 9H, OCH_3); 6.80, 6.92 (2s, 1H, C-6/C-7 of **18a**/**18b**); 7.24 (s, 1H, C-3); 13.91, 14.71 (2s, 1H, OH); MS: 334 (M^+), 292, 277, 249. (Found: C, 61.4; H, 5.6. Calc. for $C_{17}H_{18}O_7$: C, 61.1: H, 5.4).

2 - *Acetyl* - 1,4 - *diacetoxy* - 5,6,8 - *trimethoxynaphthalene* **19a** *and* 2 - *acetyl* - 1,4 - *diacetoxy* - 5,7,8 - *trimethoxynaphthalene* **19b**. A mixture of 375 mg of **18a** + **18b**, 375 mg of NaOAc and 50 ml of Ac_2O was refluxed until the colour disappeared (1 hr). The resulting soln was poured into ice water to give a white ppt, which was collected, washed with water and crystallized from benzene–cyclohexane to give 316 mg (80%) of **19a** + **19b**, m.p. 143–145°. IR: 1760, 1695, 1605. NMR: 2.39, 2.42 (2s, 6H, $OCOCH_3$); 2.64 (s, 3H, $COCH_3$); 3.86, 3.96, 4.02 (3s, 9H, OCH_3); 6.82, 6.90 (2s, 1H, C-6/C-7 of **19a** + **19b**); 7.44, 7.54 (2s, 1H, C-3 of 19a/19b); MS: 376 (M^+), 334, 292, 277, 249.

2 - *Methoxy* - 6 - *acetyl* - 5,8 - *diacetoxy* - 1,4 - *naphthoquinone* **20a** and 2 - *methoxy* - 7 - *acetyl* - 5,8 - *diacetoxy* - 1,4 - *naphthoquinone* **20b**. A mixture of 188 mg of **19a** + **19b** (0.5 mmol), 248 mg of silver(II) oxide (2 mmol) and 5 ml of dioxane was stirred for 5 min. 6N HNO_3 (0.5 ml) was added and stirred at room temp for 5 min more. Then were added $CHCl_3$ (20 ml) and water (5 ml) and the $CHCl_3$ extract was washed with water, dried over Na_2SO_4. The solvent was vacuum removed and the residue was analyzed by NMR: 2.46 (s, 6H, $OCOCH_3$); 2.62 (s, 3H, $COCH_3$); 3.92 (s, 3H, OCH_3); 6.16 (s, 1H, C-3); 7.76, 7.82 (2s, 1H, C-6/C-7 of **19a**/**19b**).

6-*Acetyl*-2,5,8-*trihydroxy*-1,4-*naphthoquinone* **21a** *and* 7-*acetyl* - 2,5,8 - *trihydroxy* - 1,4 - *naphthoquinone* **21b**. Hydrolysis of 100 mg of **20a** + **20b** with 20 ml of 6N HCl (15 min reflux) afforded 43 mg (60%) of **21a**[14] + **21b**. NMR: 2.73* 2.72 (2s, 3H, $COCH_3$); 6.43*, 6.42 (2s, 1H, C-3); 7.63,* 7.80 (2s, 1H, C-7/C-6); 11.27, 13.67, 12.41, 12.57 (4s, 2H, OH).

1,4 - *Diacetoxy* - 2,5,7,8 - *tetramethoxynaphthalene* **22**. A mixture of 400 mg of **5**, 520 mg of Zn dust, 160 mg of NaOAc and 40 ml of Ac_2O, was refluxed until the colour disappeared (1 hr). The resulting soln was poured into ice water to give a white ppt, which was collected, washed with water and crystallized from benzene–hexane (1:1) to give 345 mg (65%) of **22** m.p. 145°. IR: 1755, 1630, 1610. NMR: 2.37, 2.39 (2s, 6H, $OCOCH_3$); 3.82, 3.92, 3.98 (3s, 12H, OCH_3); 6.60 (s, 1H, C-3); 6.88 (s, 1H, C-6). MS: 364 (M^+), 322, 280, 265. (Found: C, 59.7; H, 5.8. Calc. for $C_{18}H_{20}O_8$: C, 59.3; H, 5.5).

2 - *Acetyl* - 4 - *acetoxy* - 3,5,6,8 - *tetramethoxy* - 1 - *naphthol* **23**. A mixture of 500 mg of **22** in 400 ml of EtOH–glycerol (1:1) was irradiated for 12 hr. The resulting soln was diluted with water and extracted with $CHCl_3$. The $CHCl_3$ extract was dried over Na_2SO_4 and the solvent was vacuum removed. The residue was precipitated by addition of ether to give 218 mg (60%) of **13**, m.p. 155°. IR: 3300, 1765, 1710, 1620, 1615. NMR: 2.40 (s, 3H, $OCOCH_3$); 2.71 (s, 3H, $COCH_3$); 3.83, 3.92, 4.03, 4.07 (4s, 12H, OCH_3); 6.71 (s, 1H, C-7); 13.96 (s, 1H, OH). MS: 364 (M^+), 322, 307. (Found: C, 59.5; H, 5.5. Calc. for $C_{18}H_{20}O_8$: C, 59.3; H, 5.5).

2 - *Acetyl* - 3,5,8 - *trihydroxy* - 1,4 - *naphthoquinone* **24**. A soln of **23** (30 mg), $AlCl_3$ (2 g) and nitrobenzene (30 ml) was stirred for 4 days at 60° and then hydrolyzed with ice water (90 ml) and conc HCl (10 ml). The suspension was warmed until a violet colour was developed, extracting then with $CHCl_3$. The extract was evaporated *in vacuo* and the residue was purified on a column of acid-treated silica gel and eluted with benzene. The product was identical with an authentic sample of Spinochrome A.

2 - *Acetyl* - 3 - *hydroxy* - 5,6,8 - *trimethoxy* - 1,4 - *naphthoquinone* **25**. A mixture of 91 mg of **23** (0.25 mmol), 124 mg of silver(II) oxide (1 mmol), and 5 ml of dioxane was stirred for 5 min. 6N HNO_3 (0.25 ml) was added and the soln stirred at room temp for another 5 min. Then $CHCl_3$ (20 ml) and water (5 ml) were added; the $CHCl_3$ extract was washed with water and dried over Na_2SO_4. The product was separated by extraction with $NaHCO_3$, to give 45 mg (60%) of **25**, m.p. 255°.[15] IR: 1695, 1655, 1600. NMR: 2.69, 2.77, (2s, 3H, $COCH_3$), 3.90, 4.00 (2s, 9H, OCH_3); 6.79, 6.84 (s, 1H, C-6). MS: 306 (M^+), 291, 278, 263, 245, 235, 207.

2 - *Acetyl* - 1,4 - *diacetoxy* - 3,5,6,8 - *tetramethoxynaphthalene* **26**. A mixture of 200 mg of **23**, 200 mg of NaOAc and 30 ml of Ac_2O was refluxed until the colour disappeared (1 hr). The resulting soln was poured into ice water to give a white ppt, which was collected, washed with water and crystallized from benzene–hexane to give 178 mg (80%) of **26**. IR: 1750, 1660, 1630. NMR: 2.30, 2.40 (2s, 6H, $OCOCH_3$); 2.53 (s, 3H, $COCH_3$); 3.82, 3.92, 4.00 (3s, 12H, OCH_3); 6.72 (s, 1H, C-7). (Found: C, 58.8; H, 5.7. Calc. for $C_{20}H_{22}O_9$: C, 59.1; H, 5.4).

6 - *Acetyl* - 5,8 - *diacetoxy* - 2,7 - *dimethoxy* - 1,4 - *naphthoquinone* **27**. A mixture of 135 mg (0.33 mol) of **26**, 164 mg (1.32 mmol) of silver(II) oxide and 4 ml of dioxane was stirred for 5 min. 6N HNO_3 (0.33 ml) was added and stirred at room temp for another 5 min. Then 15 ml of $CHCl_3$ and 5 ml of water were added and the $CHCl_3$ extract was washed with water and dried over Na_2SO_4. The solvent was vacuum removed and the residue was analyzed by NMR: 2.40, 2.51, 2.53 (3s, 9H, $OCOCH_3$, $COCH_3$); 3.90, 3.98 (2s, 6H, OCH_3); 6.10 (s, 1H, C-3).

3 - *Acetyl* - 7 - *methoxy* - 2,5,8 - *trihydroxy* - 1,4 - *naphthoquinone* **28**. Hydrolysis of 60 mg of **27** with 10 ml of 6N HCl

*Signal assigned to **21a** according to Ref. [14].

(10 min reflux) afforded 30 mg (70%) of **28**[15] m.p. 245–247°. IR: 1610. NMR: 2.86 (s, 3H, $COCH_3$); 3.96 (s, 3H, OCH_3); 6.58 (s, 1H, C-6); 14.13 (s, 1H, OH). MS: 278 (M^+).

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