Trimethyl orthoacetate as a convenient reagent for selective methylation of β-OH groups of (poly)hydroxynaphthazarins

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Trimethyl orthoacetate was found to be a convenient reagent for methylation of the β-OH groups of (poly)hydroxynaphthazarins. The substrates bearing one β-OH group react with $MeC(OMe)_3$ to give the corresponding methoxy derivatives in 79—89% yields. Depending on the reaction conditions, methylation of substrates with two β-OH groups on the different and the same rings affords either the corresponding mono-*O*-methylated (43—70%) or di-*O*-methylated (71—78%) derivatives. Trimethyl orthoacetate offers a good alternative to CH_2N_2 in the preparative synthesis of *O*-methylated (poly)hydroxynaphthazarin derivatives.

Key words: polyhydroxy-1,4-naphthoquinones, naphthazarins, pigments of sea urchins, naphthopurpurin, mompain, isomompain, ethylspinazarin, antioxidants, *O*-methylation, trimethyl orthoacetate.

5,8-Dihydroxy-1,4-naphthoquinones (naphthazarins) bearing different number of the β-positioned OH-groups at the naphthalene framework are widespread in nature.[1—4] These compounds are produced by microorganisms (first of all, by Fusarium fungi[5,6]), lichens,[7,8] marine invertebrates,[1—4,9] and more seldom by higher plants.[10—12] In the kingdom Animalia, they were found usually in echinoderms (mainly in sea urchins and extremely seldom in asteroids (starfishes), holothuroids (sea cucumbers), and crinoids (sea lilies)).[9] Hydroxynaphthazarins exhibit high antiradical and antioxidant,[13—17] antimicrobial,[18] antiallergic,[19] cardioprotective,[20] and hepatoprotective[21] activities. 7-Ethyl-2,3,6-trihydroxynaphthazarin (echinochrome A), a metabolite of sea urchin *Scaphechinus mirabilis*, was used as the starting material to develop a series of domestic drugs Histochrome® for clinical use in cardiovascular medicine (treatment of acute myocardial infarction and ischemia) and ophthalmology (treatment of proliferative processes, degenerations, cataracts, and hemorrhages of different origin).[22]

Tendency of hydroxynaphthazarins to be adsorbed on different sorbents causes several technological difficulties, which are faced by the researches during their isolation from natural sources. To solve these problems, the mixtures of the starting hydroxynaphthazarins are often converted into their methoxy derivatives, whose separation into individual components is much easier. The methoxy derivatives are further cleaved to give free hydroxynaphthazarins. Methoxy derivatives are often used for identification of various natural hydroxynaphthazarins,[1—4] for studying prototropic enol-enol tautomerism of hydroxynaphthazarins by IR spectroscopy,[23,24] and in numerous syntheses of hydroxynaphthazarins and analogs of thereof, *e.g.*, hybocarpone,[25] echinamines A and B,[26,27], lomazarin and norlomazarin,[28] 2,2′-(ethane-1,1-diyl)bis(3,5,6,7,8-pentahydroxynaphthoquinone),[29] cuculoquinone,[8] spinochromes E,[30] D,[31,32] and C,[33] spinamine E,[34] and mirabiquinone A.[35]

Partially and exhaustively *O*-methylated hydroxynaphthazarins have been found in nature.[1—4] Similarly to parent polyhydroxynaphthazarins, they are produced by microorganisms,[5,6,36] lichens,[37,38] marine invertebrates (sea urchins, holothurians, starfishes, and ophiurians),[1—4] and higher plants.[1—4] Many of them possess antibacterial, antifungal, insecticidal, and phytotoxic properties.[1—6] Thus, 2,3,6-trimethoxynaphthtazarin derivative, tricrozarin B, showed *in vitro* cytotoxicity against HeLa S_3 cells and *in vivo* antitumor activity against murine sarcoma 180 cells.[39]

Several methods of *O*-methylation of the β-OH groups of (poly)hydroxynaphthazarins are known. Of them, methylation with solutions of diazomethane in either diethyl ether or MeOH is the most popular.[40] Since CH_2N_2 is toxic, explosive, and unstable in solutions upon storage, it is unsuitable for preparative syntheses and is used as a rule for analytical purposes. *O*-Methylation can also be performed with 3% solution of anhydrous HCl in MeOH;[40—42] however, this reaction is very sensitive to steric effects and mainly gives low yields of the target products. For instance, under these conditions 2-hydroxynaphthazarin was converted to 2-methoxynaphthazarin in 40—45% yields but 2-hydroxy-3-methylnaphth-

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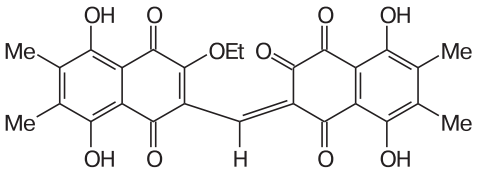
azarin was found inactive. Moreover, it was found that *O*-methylation of 3-acetyl-2,7-dihydroxynaphthazarin (spinochrome A) with HCl/MeOH is accompanied by deacetylation.[42] Such methylation systems as Me_2SO_4—calcined K_2CO_3—anhydrous acetone,[40,43] MeI—Ag_2O—$CHCl_3$,[44—46] and TsOMe—Na_2CO_3[47] are of low value for selective *O*-methylation of the polyhydroxynaphthazarin β-OH groups since they also lead to *O*-methylation of the α-OH groups.

Despite the drawbacks, diazomethane is still the most popular methylating agent for *O*-methylation of the polyhydroxynaphthazarin β-OH groups.

The aim of the present work is to evaluate the synthetic potential of orthocarboxylic acid triesters for selective *O*-methylation of the β-OH groups of hydroxynaphthazarins in a comparison with diazomethane. The reactions of orthoformates, mainly $HC(OEt)_3$, with phenols were reviewed[48—50] but no protection of the β-OH groups of polyhydroxynaphthazarins with these reagents was described.

As the substrates for *O*-methylation, we chose synthetic compounds **1**, **2**, and **5** (isomompain) and several natural pigments of sea urchins (naphthopurpurin (**3**), mompain (**4**), and ethylspinazarin (**6**)) (Scheme 1).

We showed earlier[51] that trimethyl and triethyl orthoformates can be used for selective *O*-alkylation of the β-OH groups of 2(3)-hydroxyjuglones and (poly)hydroxynaphthazarins. In the most cases, these reactions provide good yields of the target products; moreover, $HC(OEt)_3$ occurred more efficient than $HC(OMe)_3$. Certain limitation for a wide application of $HC(OEt)_3$ for selective protection of the β-OH groups of (poly)hydroxynaphthazarins is the impossibility to carry out efficiently these reactions with 3-unsubstituted substrates of the **1**—**3** type. Thus, the reaction of substrate **1** with $HC(OEt)_3$ for 1.7 h gave 2-ethoxy-6,7-dimethylnaphthazarin in 4.5% yield with the main reaction product (58% yield) of structure **7**. In the case of substrate **2**, the yield of 6,7-dichloro-2-ethoxynaphthazarin did not exceed 10%.



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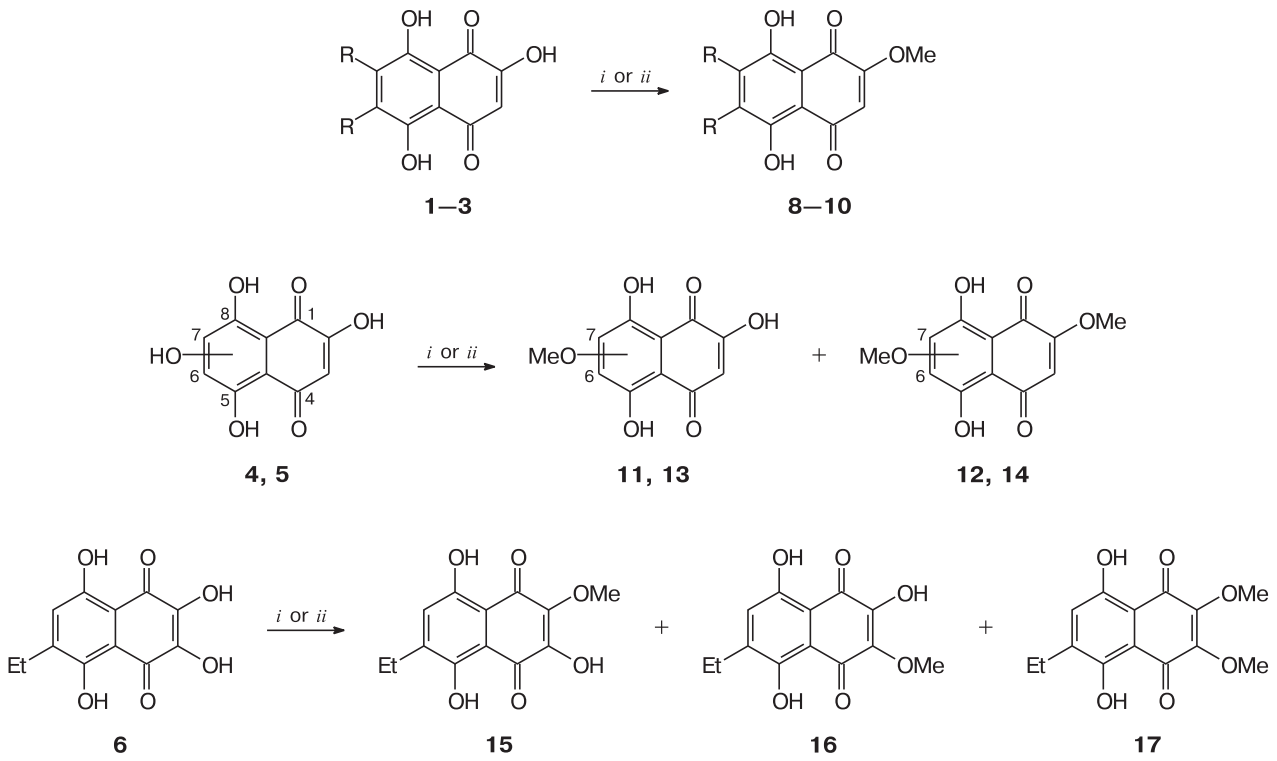
Scheme 1*



R = Me (**1**, **8**), Cl (**2**, **9**), H (**3**, **10**)
4: 7-OH; **5:** 6-OH; **11, 12:** 7-OMe; **13, 14:** 6-OMe

Reagents and conditions: *i*. $MeC(OMe)_3$, reflux; *ii*. $MeC(OMe)_3$, MeCN or dioxane, reflux.

*Here and hereafter, dominant tautomers of the discussed hydroxynaphthazarins are shown.

In the present work, we found that trimethyl orthoacetate was convenient for selective protection of the β-OH groups of (poly)hydroxynaphthazarins as the methoxy derivatives and devoid of drawbacks inherent to triethyl orthoformate. Substrates **1**—**3** readily react with the $MeC(OMe)_3$ excess under reflux (107—109 °C) to give OMe-derivatives **8**—**10** in good yields (see Scheme 1, Table 1). The nature of the substituents at the positions 6 and 7 of substrates **1**—**3** exerted only a minor effect on the reaction progress. Substrate **1** bearing electron-donating substituents (Me groups) reacted somewhat slower than the other studied substrates and compound **2** with electron-withdrawing substituents (Cl atoms) was the fastest reacting substrate.

Earlier, we obtained methoxylated compound **9** with a comparable yield (85%), when synthesizing spinochrome D by methylation of substrate **2** with a solution of CH_2N_2 in MeOH.[31] Naphthopurpurin **3**, most susceptible to the side reactions, readily reacts with $MeC(OMe)_3$ producing exclusively derivative **10**. It is of note that methylation of substrate **3** with CH_2N_2 is unselective and monitoring of the reaction progress is very difficult due to similarity in the chromatographic mobility of substrate **3** itself and its methoxy derivative **10**. Thus, the reaction of substrate **3** with a solution of CH_2N_2 in diethyl ether for 15 min results in a complex mixture, whose chromatographic separation gives monomethoxy derivative **10** (yield 24%), dimethoxy compound **18** (yield 24%), pyrazole **19** (3%), and a mixture of three pyrazoles **20**—**22** in a ratio of **20** : **21** : **22** = = 3 : 1.3 : 1 (overall yield 8%) (Scheme 2).

It is obvious that di-*O*-methylated derivative **18** is resulted from methylation of the C(8)OH group of tautomer **10A** of the initially formed monomethoxy compound **10**, pyrazole **19** is a product of 1,3-dipolar cycloaddition of CH_2N_2 at the C(2)=C(3) bond of the same tautomer **10A** *via* the reaction sequence **I** → **II** → **19**, and the mixture of pyrazoles **20**—**22** is a result of the addition of CH_2N_2 to the quinone double bond of tautomer **10B** (see Scheme 2). Form **10B** is unsymmetrical due to the presence of the 6-positioned substituent; therefore, cycloaddition of CH_2N_2 to the C(2)=C(3) bond leads to a mixture of isomeric pyrazole intermediates **III** and **IV**. These intermediates further react with CH_2N_2 to give products **20**—**22** (see Scheme 2).

Mompain **4** and isomonpain **5** bearing each two β-OH groups in the different rings react with the $MeC(OMe)_3$ excess under reflux as fast as substrates **1**—**3** producing the mixtures of mono- (**11**, **12**) and di-*O*-methylated (**13**, **14**) products with dimethoxylated derivatives being dominating products (see Scheme 1, Table 1).

Derivatives **11**—**14** were synthesized earlier in the comparable yields (35, 61, 16, and 58%, respectively) by methylation of substrates **4** and **5** with a solution of CH_2N_2 in MeOH.[23] Methylation of substrate **4** with a solution of CH_2N_2 in diethyl ether for 15 min produces compounds **11** and **12** in the yields of 20 and 50%, respectively.[40]

The reaction of ethylspinazarin **6** bearing two β-OH groups in the same ring with excess of refluxing $MeC(OMe)_3$ also proceeds readily but the result was different than that of the reactions with mompain **4** and isomompain **5**. In the case of substrates **4** and **5**, the main reaction products were di-*O*-methylated derivatives **12** and **14**, respectively. However, pigment **6** under the same conditions produced predominantly monomethoxy derivatives **15** and **16**

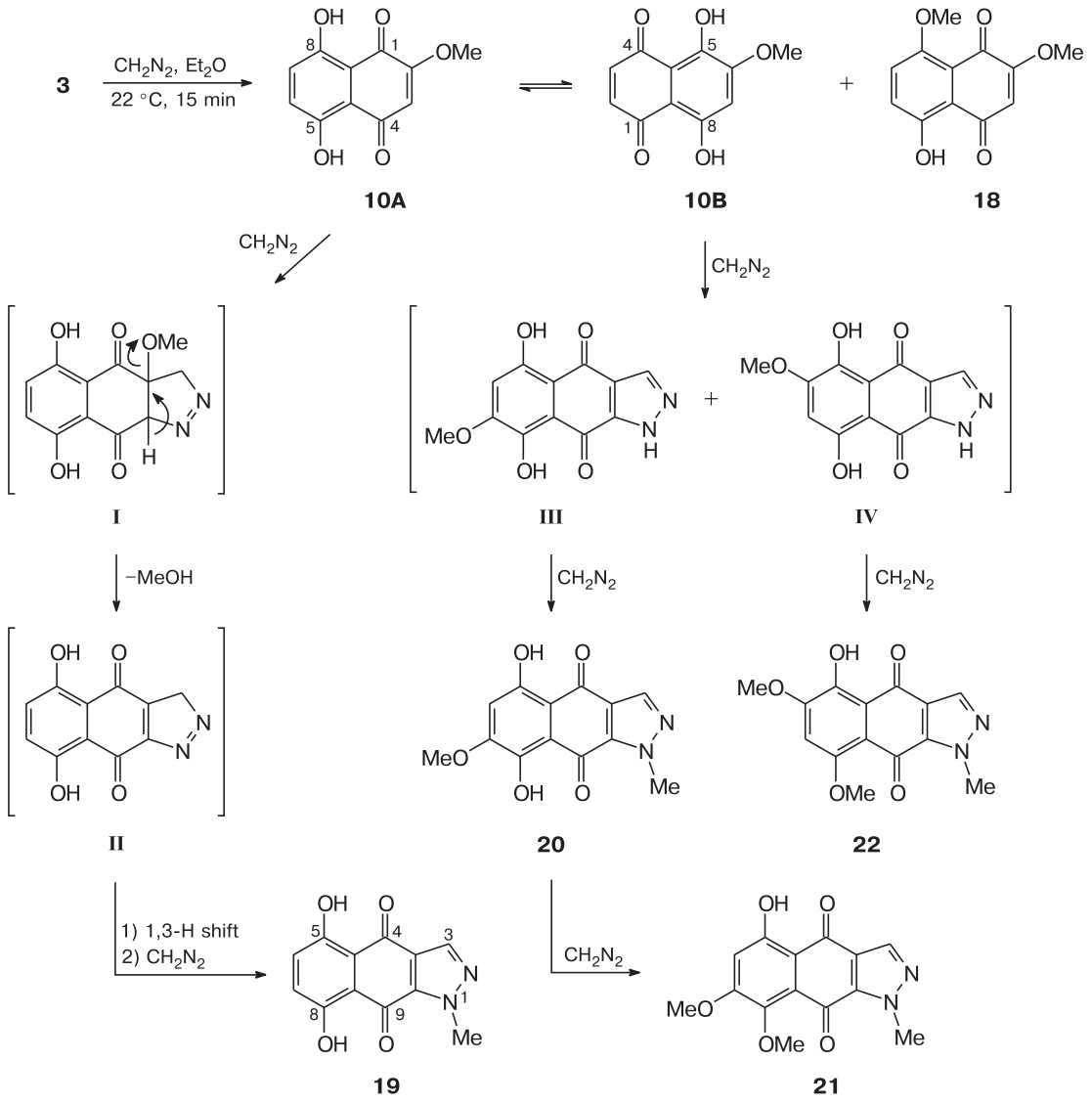
Table 1. Reactions of hydroxynaphthazarins **1**—**6** with $MeC(OMe)_3$

Substrate	Solvent	*T*/°C	τ/h	Products (yield (%))
1	$MeC(OMe)_3$	109	0.5*	**8** (81)
2	$MeC(OMe)_3$	109	0.3*	**9** (89)
3	$MeC(OMe)_3$	109	0.4*	**10** (79)
4	$MeC(OMe)_3$	109	0.5*	**11** (25), **12** (49)
4	$MeC(OMe)_3$—MeCN (1 : 2, v/v)	83	4.0**	**11** (58), **12** (20)
4	$MeC(OMe)_3$—1,4-dioxane (1 : 2, v/v)	102	1.5**	**11** (70), **12** (14)
4	$MeC(OMe)_3$	109	1.5**	**11** (7), **12** (78)
5	$MeC(OMe)_3$	109	0.5*	**13** (21), **14** (48)
5	$MeC(OMe)_3$—MeCN (1 : 2, v/v)	83	4.0**	**13** (59), **14** (17)
5	$MeC(OMe)_3$	109	1.5**	**13** (9), **14** (76)
6	$MeC(OMe)_3$	109	0.5*	**15** (34), **16** (24), **17** (19)
6	$MeC(OMe)_3$—1,4-dioxane (1 : 2, v/v)	102	1.5**	**15** (43), **16** (31), **17** (9)
6	$MeC(OMe)_3$	109	2.0**	**15** (8), **16** (5), **17** (71)

* The reaction progress was monitored by TLC (precoated Silufol UV 254 plates, hexane—acetone (2 : 1)) at 10-min intervals.

** The reaction progress was monitored by TLC at 15-min intervals.

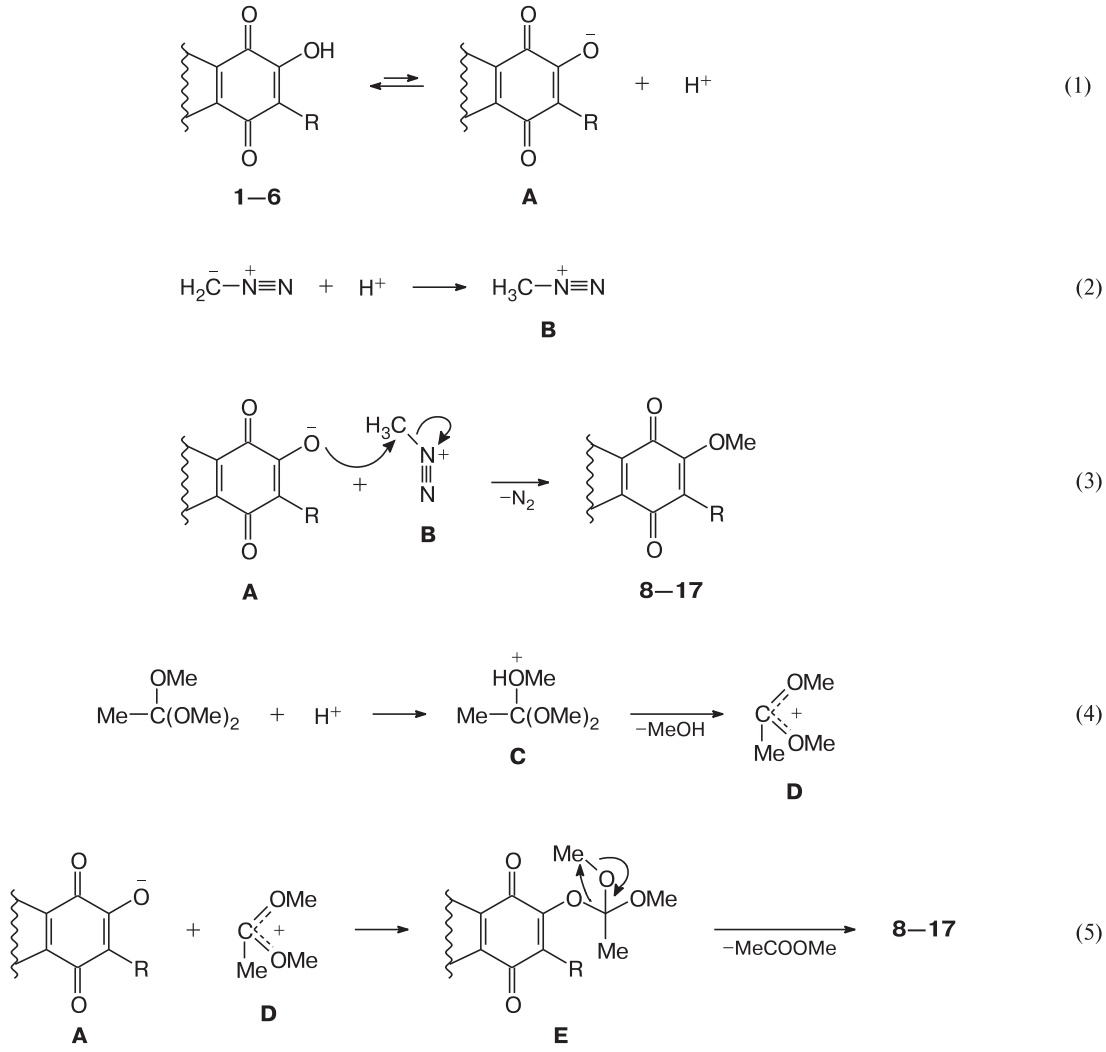
Scheme 2



(**15** : **16** = 1.4 : 1.0). Earlier, methylation of substrate **6** with CH_2N_2 was not performed, but the reaction of its analog lacking Et group with CH_2N_2 for 15 min gave a mixture of mono- (60%) and dimethoxy compounds (20%).[40] It was found that methylation of substrate **6** under conditions used by Moore *et al.*[40] produced a mixture of monomethoxy derivatives **15** (38%) and **16** (21%) and dimethoxy derivative **17** (19%). In contrast to methylation with CH_2N_2, methylation of substrates **4**—**6** with $MeC(OMe)_3$ can be controlled to some extent. The change in the refluxing time of substrates **4**—**6** with the excess of $MeC(OMe)_3$ dramatically affects the ratio of the resulting *O*-methoxylated products. The yields of the corresponding dimethoxy derivatives were 71—78% at refluxing time of 1.5—2 h. In contrast, the deceleration of the reaction by adding the solvents inert towards ortho ester (MeCN and 1,4-dioxane) results in the corresponding monomethoxy derivatives as the dominating products (see Table 1).

The rates of methylation of the β-OH groups of hydroxynaphthazarins **1**—**6** with both CH_2N_2 and $MeC(OMe)_3$ depend on the acidity of these groups, which is determined by energy of heterolytic cleavage of the O—H bond of the corresponding β-OH group. Probably, the C(2)OH groups of compounds **1**—**3** and **6** have the same acidities. In the case of compounds **4** and **5**, the acidities of the β-OH groups at positions 2 and 7 (for **4**) and 2 and 6 (for **5**) are equal due to degenerate tautomerism. *O*-Methylation of one of the β-OH groups of compound **6** retards methylation of another one not due to steric hindrance as it was suggested for spinazarin by Moore *et al.*[40] but, more probably, due to a significant decrease in the acidity of the second β-OH group. A strong electron-donating effect of the OMe

Scheme 3



group notably increases energy of heterolytic cleavage of the O—H bond of the neighboring OH group.

The *O*-methylation mechanisms of hydroxynaphthazarins **1**—**6** with diazomethane and trimethyl orthoacetate are shown in Scheme 3. The general feature of these mechanisms is the necessity of protonation of each reagent before their transformation into an active form. No external catalysis is required since substrates **1**—**6** can dissociate to anion **A** and a proton (see Scheme 3, reaction (1)). Compounds **1**—**6** show properties of organic acids similar in pK_a to AcOH and are readily titrated with $NaHCO_3$ solution. Protonation of CH_2N_2 results in diazonium cation **B** (reaction (2)), which further reacts with anion **A** to give *O*-methyl derivatives **8**—**17** (reaction (3)). Similarly, protonation of ortho ester leads to intermediate **C**, which losses the MeOH molecule to give carboxonium cation **D**, an efficient *O*-methylating agent[49] (see Scheme 3, reaction (4)). Apparently, anion **A** reacts with cation **D** to form mixed ortho ester **E** subsequently undergoing decomposition to give *O*-methylated compounds **8**—**17** and methyl acetate (reaction (5)).

Structures of the synthesized compounds **8**—**22** were established using physicochemical methods and, first of all, 1D ^1H and ^{13}C NMR spectroscopy and 2D NMR experiments.

In summary, the obtained results indicate that commercially available, stable, and safe $MeC(OMe)_3$ is a convenient reagent for *O*-methylation of the β-OH groups of different (poly)hydroxynaphthazarins. Procedures for *O*-methylation of the β-OH groups of (poly)hydroxynaphthazarins with $MeC(OMe)_3$ are simple, efficient, and enables relatively selective protection of these groups leaving the α-OH groups intact. In contrast to CH_2N_2, $MeC(OMe)_3$ can be efficiently used for large-scale preparative syntheses of *O*-methylated (poly)hydroxynaphthazarins. It is likely that its synthetic scope is not limited to hydroxylated

derivatives of a 5,8-dihydroxy-1,4-naphthoquinone (naphthazarin) series. Hydroxylated derivatives of 5-hydroxy-1,4-naphthoquinone (juglone), the parent 1,4-naphthoquinone, and numerous natural and synthetic polyphenols should react similarly. Final conclusions about synthetic potential of $MeC(OMe)_3$ can be drawn only after additional experimental studies.

Forthcoming publication will be focused on the reactions of $MeC(OMe)_3$ with natural polyhydroxynaphthazarins bearing three (spinochrom D and echinochrome A) and four (spinochrom E) β-OH groups.

Experimental

Melting points were measured on a Boetius apparatus and are given uncorrected. IR spectra were recorded with a Bruker Equinox 55 spectrometer in CCl_4 and $CDCl_3$. ^1H and ^{13}C NMR spectra were run on Bruker Avance DPX-300 (working frequencies of 300.13 (^1H) and 75.47 (^{13}C) MHz) and Bruker Avance DRX-500 (working frequencies of 500.13 (^1H) and 125.75 (^{13}C) MHz) instruments in $CDCl_3$. The chemical shifts are given in the δ scale relative to Me_4Si (an internal standard). The ^1H and ^{13}C NMR signals were assigned using various 2D ^1H—^{13}C NMR correlation experiments (HSQC, HMBC). Electron impact (EI) mass spectrometry was performed with an AMD 604 S instrument (8 kW) with energy of ionization electrons of either 15 or 70 eV using direct inlet injection. Elemental analysis was carried out with a Flash EA 1112 C,H,N elemental analyzer.

The progress of the reactions and purity of the synthesized compounds were monitored by TLC on precoated Silufol UV 254 plates (development with hexane—acetone (2 : 1)). The products were purified by either preparative TLC on Alfa Aesar plates (SiO_2, 70—230 μm) or silica gel column chromatography using hexane—acetone (2 : 1) as an eluent. Gaseous CH_2N_2 was prepared from *N*-nitroso-*N*-methylurea as earlier described[52] and used as the solutions in anhydrous Et_2O or MeOH. Commercially available $MeC(OMe)_3$ (b.p. 107—109 °C) was distilled prior to use. The starting substrates **1**[53], **2**[31], **3**[54], **4**[55], **5**,[55] and **6**[56] were synthesized by known procedures.

***O*-Methylation of hydroxynaphthazarins 1—6 with trimethyl orthoacetate (general procedures). *A*.** A solution of substrate **1—6** (0.5 mmol) in $MeC(OMe)_3$ (3 mL) was refluxed for the indicated time (Table 1) and the excess of ortho ester was removed *in vacuo*. The target products were purified by either silica gel column chromatography or preparative TLC using the hexane—acetone mixtures as the eluents. Ortho ester distilled off was regenerated and reused.

B*.** To a refluxing solution of substrate **1—6** (0.5 mmol) in MeCN or 1,4-dioxane (3 mL), a solution of $MeC(OMe)_3$ (3 mL) in the corresponding solvent (3 mL) was added by portions over 20 min and the reaction mixture was refluxed for the indicated time (Table 1). The volatiles were removed *in vacuo*. The target products were purified as described in method ***A.

5,8-Dihydroxy-2-methoxy-6,7-dimethyl-1,4-naphthoquinone (8). Yield 81%, m.p. 143—145 °C. IR (CCl_4), ν/cm^{-1}: 3600—2250 (α-OH), 3026, 2978, 2939, 2856, 1623, 1617, 1602, 1559. ^1H NMR ($CDCl_3$), δ: 2.24, 2.25 (both s, 3 H each, C(7)Me, C(6)Me); 3.93 (s, 3 H, OMe); 6.16 (s, 1 H, H(3)); 12.93, 13.27 (both s, 1 H each, C(8)OH, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 12.14 (C(7)Me); 12.50 (C(6)Me); 56.61 (OMe); 107.33 (C(4a)); 109.29 (C(3)); 109.36 (C(8a)); 137.95 (C(7)); 140.96 (C(6)); 160.41 (C(2)); 161.32 (C(5)); 163.10 (C(8)); 176.61 (C(1)); 183.30 (C(4)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 249 $[M + 1]^+$ (12), 248 $[M]^+$ (82), 231 $[M + 1 - H_2O]^+$ (4), 230 $[M - H_2O]^+$ (31), 219 (18), 205 (17), 202 (20), 174 (22), 149 (12), 135 (10), 91 (8), 77 (14), 69 (13), 53 (14), 43 (34), 32 (100). Found (%): C, 62.96; H, 4.90. $C_{13}H_{12}O_5$. Calculated (%): C, 62.90; H, 4.87.

6,7-Dichloro-5,8-dihydroxy-2-methoxy-1,4-naphthoquinone (9). Yield 89%, m.p. 227—230 °C (*cf.* Ref. 31: 227—230 °C). IR (CCl_4), ν/cm^{-1}: 3600—2200 (α-OH), 3021, 2983, 2954, 2938, 2882, 2853, 1625, 1619, 1603, 1558, 1542, 1476, 1455, 1438, 1405, 1303, 1273, 1250, 1232, 1208, 1198, 1120. ^1H NMR ($CDCl_3$), δ: 3.97 (s, 3 H, OMe); 6.28 (s, 1 H, H(3)); 12.76 (br.s, 1 H, C(8)OH); 13.26 (s, 1 H, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 57.10 (OMe); 108.52 (C(4a)); 109.70 (C(3)); 110.20 (C(8a)); 133.22 (C(7)); 135.72 (C(6)); 156.86 (C(5)); 158.18 (C(8)); 160.62 (C(2)); 177.94 (C(1)); 184.13 (C(4)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 289/291/293 $[M + 1]^+$ (12), 288/290/292 $[M]^+$ (100), 271/273/275 $[M + 1 - H_2O]^+$ (9), 270/272/274 $[M - H_2O]^+$ (72), 258/260/262 (18), 257/259/261 (11), 245/247 (15), 242/244 (16), 214 (9), 204 (13), 189 (14), 144 (7), 113 (7), 87 (15), 69 (25), 53 (19), 44 (44), 43 (18), 32 (94).

5,8-Dihydroxy-2-methoxy-1,4-naphthoquinone (10). Yield 79%, m.p. 191—193 °C (*cf.* Ref. 54: 178 °C; Ref. 57: 183—190 °C; Ref. 58: 190—195 °C). IR (CCl_4), ν/cm^{-1}: 3600—2250 (α-OH), 3023, 2973, 2938, 2855, 1621, 1603, 1573, 1456, 1410, 1388, 1348, 1312, 1295, 1271, 1224, 1208, 1190, 1179, 1076. ^1H NMR ($CDCl_3$), δ: 3.94 (s, 3 H, OMe); 6.17 (s, 1 H, H(3)); 7.21, 7.28 (both d, 1 H each, H(7), H(6), J = 9.5 Hz); 12.17, 12.64 (both s, 1 H each, C(8)OH, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 56.76 (OMe); 110.33 (C(3)); 110.72 (C(4a)); 111.58 (C(8a)); 128.31 (C(7)); 130.83 (C(6)); 157.07 (C(5)); 158.57 (C(8)); 161.02 (C(2)); 182.48 (C(1)); 188.21 (C(4)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 221 $[M + 1]^+$ (12), 220 $[M]^+$ (92), 203 $[M + 1 - H_2O]^+$ (5), 202 $[M - H_2O]^+$ (33), 191 (14), 190 (16), 189 (17), 177 (12), 174 (14), 163 (6), 149 (12), 146 (10), 121 (14), 69 (8), 65 (7), 53 (14), 51 (15), 44 (53), 43 (13), 32 (100).

2,5,8-Trihydroxy-7-methoxy-1,4-naphthoquinone (11). Yield 70%, m.p. 223—226 °C (*cf.* Ref. 23: 225—227 °C; Ref. 40: 240—241 °C). IR ($CDCl_3$), ν/cm^{-1}: 3600—2200 (α-OH), 3510 (β-OH), 3422 (β-OH), 2989, 2931, 2875, 2827, 1661, 1629, 1606, 1585. ^1H NMR ($CDCl_3$), δ: 3.97 (s, 3 H, OMe); 6.48, 6.53 (both s, 1 H each, H(3), H(6)); 7.05 (br.s, 1 H, C(2)OH); 12.08, 13.11 (both s, 1 H each, C(8)OH, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 56.70 (OMe); 104.40 (C(4a)); 109.49 (C(6)); 111.96 (C(3), C(8a)); 155.70 (C(2)); 157.41 (C(7)); 160.50 (C(8)); 167.72 (C(5)); 172.68 (C(1)); 178.99 (C(4)). MS (EI, 15 eV), *m/z* (I_{rel} (%)): 236 $[M]^+$ (100), 218 $[M - H_2O]^+$ (22), 208 $[M - CO]^+$ (13), 206 (17), 205 (11), 193 (15), 190 (14).

5,8-Dihydroxy-2,7-dimethoxy-1,4-naphthoquinone (12). Yield 78%, m.p. 268—270 °C (*cf.* Ref. 23: 270—272 °C; Ref. 40: 273—275 °C; Ref. 42: 235—236 °C; Ref. 43: 275—276 °C; Ref. 59: 260—262 °C). IR ($CDCl_3$), ν/cm^{-1}: 3500—2250 (α-OH), 2995, 2934, 2886, 2821, 1627, 1604, 1576, 1281, 1227, 1090, 1001. ^1H NMR ($CDCl_3$), δ: 3.95 (s, 6 H, 2 OMe); 6.41 (s, 2 H, H(3), H(6)); 12.72, 13.14 (both s, 1 H each, C(8)OH, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 56.68 (2 OMe); 104.13 (C(4a)); 109.30 (C(3), C(6)); 111.51 (C(8a)); 158.68 (C(2), C(7)); 167.14 (C(1), C(8)); 173.01 (C(4), C(5)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 251 $[M + 1]^+$ (10), 250 $[M]^+$ (80), 236 (5), 235 (7), 232 (18), 221

(17), 220 (8), 207 (18), 204 (11), 202 (11), 189 (15), 179 (14), 149 (22), 69 (42), 45 (12), 44 (26), 43 (100), 42 (8), 41 (25), 32 (82).

2,5,8-Trihydroxy-6-methoxy-1,4-naphthoquinone (13). Yield 59%, m.p. 226—228 °C (*cf.* Ref. 23: 224—226 °C; Ref. 40: 265—267 °C). IR ($CDCl_3$), ν/cm^{-1}: 3600—2200 (α-OH), 3512 (β-OH), 3392 (β-OH), 2991, 2942, 2866, 2832, 1628, 1602, 1582. ^{1}H NMR ($CDCl_3$), δ: 3.99 (s, 3 H, OMe); 6.41, 6.47 (both s, 1 H each, H(3), H(7)); 7.38 (br.s, 1 H, C(2)OH), 12.25, 13.30 both s, 1 H each, C(8)OH, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 56.91 (OMe); 105.43 (C(7)); 105.82 (C(8a)); 109.72 (C(4a)); 110.07 (C(3)); 157.96 (C(2)); 161.00 (C(6), C(8)); 167.72 (C(5)); 172.02 (C(1)); 182.95 (C(4)). MS (EI, 15 eV), *m/z* (I_{rel} (%)): 237 $[M + 1]^+$ (11), 236 $[M]^+$ (100), 222 (57), 218 (16), 207 (32), 194 (16).

5,8-Dihydroxy-2,6-dimethoxy-1,4-naphthoquinone (14). Yield 76%, m.p. 278—281 °C (*cf.* Ref. 23: 275—280 °C; Ref. 40: 295—296 °C). IR ($CDCl_3$), ν/cm^{-1}: 3600—2200 (α-OH), 3090, 2986, 2952, 2944, 2857, 1636, 1598, 1482, 1436, 1415, 1394, 1306, 1276, 1203, 1167, 1121, 1070. ^{1}H NMR ($CDCl_3$), δ: 3.97 (s, 6 H, C(2)OMe, C(6)OMe); 6.37 (s, 2 H, H(3), H(7)); 13.09 (s, 2 H, C(5)OH, C(8)OH). ^{13}C NMR ($CDCl_3$), δ: 56.79 (C(2)OMe, C(6)OMe); 107.44 (C(3), C(7)); 108.70 (C(4a), C(8a)); 160.73 (C(2), C(6)); 164.99 (C(5), C(8)); 175.18 (C(1), C(4)). MS (EI, 15 eV), *m/z* (I_{rel} (%)): 251 $[M + 1]^+$ (2), 250 $[M]^+$ (23), 232 (5), 221 (4), 220 (5), 208 (4), 207 (6), 206 (5), 202 (5), 179 (6), 149 (8), 121 (7), 88 (8), 69 (19), 59 (21), 46 (56), 45 (100), 44 (92), 43 (66), 42 (11), 41 (12), 32 (52).

6-Ethyl-3,5,8-trihydroxy-2-methoxy-1,4-naphthoquinone (15). Yield 43%, heavy oil. IR ($CDCl_3$), ν/cm^{-1}: 3600—2200 (α-OH), 3500 (β-OH), 3400 (β-OH), 2975, 2941, 2878, 1639, 1600, 1578, 1458, 1450, 1417, 1326, 1284, 1205, 1150, 1110, 1065. ^{1}H NMR ($CDCl_3$), δ: 1.25 (t, 3 H, Me, J = 7.6 Hz); 2.72 (dq, 2 H, CH_2, J = 7.6 Hz, J = 1.0 Hz); 4.20 (s, 3 H, OMe); 6.82 (br.s, 1 H, C(3)OH); 7.09 (t, 1 H, H(7), J = 1.0 Hz); 12.03, 12.49 (both s, 1 H each, C(5)OH, C(8)OH). ^{13}C NMR ($CDCl_3$), δ: 12.76 (Me); 22.98 (CH_2); 60.74 (C(2)OMe); 107.91 (C(8a)); 108.51 (C(4a)); 128.36 (C(7)); 140.89 (C(2)); 142.90 (C(3)); 145.82 (C(6)); 156.69 (C(5)); 158.09 (C(8)); 183.24 (C(4)); 183.85 (C(1)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 265 $[M + 1]^+$ (16), 264 $[M]^+$ (100), 263 $[M - 1]^+$ (12), 249 (19), 246 (12), 231 (12), 221 (18), 218 (20), 217 (32), 203 (18), 193 (28), 149 (15), 136 (15), 91 (14), 53 (18), 43 (22), 41 (17), 32 (17). Found (%): C, 59.16; H, 4.68. $C_{13}H_{12}O_6$. Calculated (%): C, 59.09; H, 4.58.

6-Ethyl-2,5,8-trihydroxy-3-methoxy-1,4-naphthoquinone (16). Yield 31%, heavy oil. IR ($CDCl_3$), ν/cm^{-1}: 3600—2200 (α-OH), 3491 (β-OH), 3392 (β-OH), 2973, 2945, 2859, 1651, 1602, 1583, 1455, 1422, 1393, 1324, 1278, 1198, 1154, 1107, 1035. ^{1}H NMR ($CDCl_3$), δ: 1.26 (t, 3 H, Me, J = 7.6 Hz); 2.74 (dq, 2 H, CH_2, J = 7.6 Hz, J = 1.0 Hz); 4.18 (s, 3 H, OMe); 6.97 (br.s, 1 H, C(2)OH); 7.03 (t, 1 H, H(7), J = 1.0 Hz); 11.61 (br.s, 1 H, C(8)OH); 12.99 (s, 1 H, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 12.74 (Me); 23.28 (CH_2); 60.75 (C(3)OMe); 107.40 (C(8a)); 108.94 (C(4a)); 126.06 (C(7)); 140.61 (C(3)); 143.33 (C(2)); 148.50 (C(6)); 157.30 (C(5)); 157.57 (C(8)); 182.27 (C(1)); 184.75 (C(4)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 265 $[M + 1]^+$ (13), 264 $[M]^+$ (100), 263 $[M - 1]^+$ (9), 249 (15), 246 (10), 231 (13), 221 (15), 218 (16), 217 (37), 203 (14), 193 (32). Found (%): C, 59.18; H, 4.69. $C_{13}H_{12}O_6$. Calculated (%): C, 59.09; H, 4.58.

6-Ethyl-5,8-dihydroxy-2,3-dimethoxy-1,4-naphthoquinone (17). Yield 71%, m.p. 69—71 °C (*cf.* Ref. 56: 68—70 °C). IR ($CDCl_3$), ν/cm^{-1}: 3600—2200 (α-OH), 2972, 2940, 2878, 2856, 1606, 1601, 1579, 1449, 1435, 1418, 1380, 1286, 1272, 1212, 1193, 1143, 1121, 1107, 1068, 1051. ^{1}H NMR ($CDCl_3$), δ: 1.25 (t, 3 H, Me, J = 7.6 Hz); 2.73 (dq, 2 H, CH_2, J = 7.6 Hz, J = 1.0 Hz); 4.11, 4.13 (both s, 3 H each, C(3)OMe, C(2)OMe); 7.06 (t, 1 H, H(7), J = 1.0 Hz); 12.45, 12.89 (both s, 1 H each, C(8)OH, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 12.77 (Me); 23.07 (CH_2); 61.56 (C(3)OMe); 61.61 (C(2)OMe); 108.59 (C(8a)); 109.56 (C(4a)); 127.23 (C(7)); 146.98 (C(6)); 147.68 (C(2)); 148.18 (C(3)); 157.84 (C(5)); 158.68 (C(8)); 183.38 (C(1)); 184.30 (C(4)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 279 $[M + 1]^+$ (15), 278 $[M]^+$ (100), 277 $[M - 1]^+$ (3), 264 (8), 263 (53), 261 (6), 260 (29), 249 (10), 248 (13), 245 (14), 233 (15), 217 (22), 207 (11), 149 (18), 136 (22), 77 (12), 53 (11), 32 (11).

***O*-Methylation of 2,5,8-trihydroxy-1,4-naphthoquinone (naphthopurpurin) 3 with a solution of CH_2N_2 in Et_2O.** To a solution of substrate **3** (103 mg, 0.5 mmol) in MeOH, a saturated solution of CH_2N_2 in anhydrous Et_2O (10 mL) was added and the mixture was kept at room temperature for 15 min. The volatiles were removed *in vacuo*. The residue was subjected to silica gel column chromatography. The column was first eluted with hexane—acetone (35 : 1) to obtain product **18** (28 mg, 24%). Subsequent elution with hexane—acetone (30 : 1) afforded a mixture of compounds **20—22** (12 mg, 8%) in a ratio of **20** : **21** : **22** = 3 : 1.3 : 1. Further elution with hexane—acetone (25 : 1) gave monomethoxy derivative **10** (26 mg, 24%) identical to the sample described above. Finally, elution with hexane—acetone (20 : 1) afforded compound **19** (4 mg, 3%).

5-Hydroxy-2,8-dimethoxy-1,4-naphthoquinone (18), yellow heavy oil. ^{1}H NMR ($CDCl_3$), δ: 3.89, 3.97 (both s, 3 H each, C(2)OMe, C(8)OMe); 6.06 (s, 1 H, H(3)); 7.29 (s, 2 H, H(6), H(7)); 12.74 (s, 1 H, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 56.65 (C(2)OMe); 56.93 (C(8)OMe); 107.89 (C(3)); 114.01 (C(4a)); 116.94 (C(8a)); 122.48 (C(7)); 127.53 (C(6)); 154.75 (C(8)); 156.07 (C(5)); 161.74 (C(2)); 177.54 (C(1)); 190.69 (C(4)). MS (EI, 70 eV), *m/z* (I_{rel} (%)): 235 $[M + 1]^+$ (12), 234 $[M]^+$ (74), 220 $[M + 1 - Me]^+$ (11), 219 $[M - Me]^+$ (41), 205 (11), 191 (26), 189 (16), 32 (100). Found (%): C, 61.61; H, 4.35. $C_{12}H_{10}O_5$. Calculated (%): C, 61.54; H, 4.30.

5-Hydroxy-6,8-dimethoxy-1-methylnaphtho[2,3-*d*]pyrazole-4,9-dione (22). ^{1}H NMR ($CDCl_3$), δ: 3.89, 3.96 (both s, 3 H each, C(6)OMe, C(8)OMe); 4.31 (s, 3 H, N(1)Me); 6.64, 8.00 (both s, 1 H each, H(7), H(3)); 13.17 (s, 1 H, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 39.32 (NMe); 56.55 (C(6)OMe); 61.26 (C(8)OMe); 105.22 (C(7)); 107.61 (C(4a)); 110.34 (C(8a)); 128.32 (C(3a)); 130.84 (C(9a)); 137.36 (C(3)); 162.33 (C(8)); 162.71 (C(5)); 163.32 (C(6)); 178.17 (C(9)); 179.73 (C(4)).

5-Hydroxy-7,8-dimethoxy-1-methylnaphtho[2,3-*d*]pyrazole-4,9-dione (21). ^{1}H NMR ($CDCl_3$), δ: 3.91, 3.95 (both s, 3 H each, C(7)OMe, C(8)OMe); 4.35 (s, 3 H, N(1)Me); 6.69, 7.99 (both s, 1 H each, H(6), H(3)); 13.52 (s, 1 H, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 39.45 (NMe); 56.66 (C(7)OMe); 61.18 (C(8)OMe); 106.00 (C(8a)); 106.57 (C(6)); 109.32 (C(4a)); 126.45 (C(3a)); 131.15 (C(9a)); 136.25 (C(3)); 159.11 (C(8)); 160.74 (C(7)); 163.32 (C(5)); 176.02 (C(9)); 181.92 (C(4)).

5,8-Dihydroxy-7-methoxy-1-methylnaphtho[2,3-*d*]pyrazole-4,9-dione (20). ^{1}H NMR ($CDCl_3$), δ: 3.99 (s, 3 H, C(7)OMe); 4.31 (s, 3 H, N(1)Me); 6.65, 8.05 (both s, 1 H each, H(6), H(3)); 13.08, 13.46 (both s, 1 H each, C(8)OH, C(5)OH).

5,8-Dihydroxy-1-methylnaphtho[2,3-*d*]pyrazole-4,9-dione (19). M.p. 218—220 °C. IR ($CDCl_3$), ν/cm^{-1}: 3550—2300 (α-OH), 2956, 2928, 2865, 2856, 1624, 1617, 1576, 1530, 1462, 1453, 1399, 1377, 1335, 1306, 1287, 1254, 1239, 1205, 1183, 1161,

1149, 1097, 1072, 1054. ^{1}H NMR ($CDCl_3$), δ: 4.36 (s, 3 H, N(1)Me); 7.24, 7.29 (both d, 1 H each, H(7), H(6), J = 9.4 Hz); 8.08 (s, 1 H, H(3)); 12.54, 12.94 (both s, 1 H each, C(8)OH, C(5)OH). ^{13}C NMR ($CDCl_3$), δ: 39.55 (NMe); 112.72 (C(4a)); 113.16 (C(8a)); 128.21 (C(3a)); 129.16 (C(7)); 130.87 (C(6)); 137.10 (C(3), C(9a)); 158.23 (C(5)); 159.06 (C(8)); 179.69 (C(9)); 183.66 (C(4)). MS (EI, 70 eV), m/z (I_{rel} (%)): 245 $[M + 1]^+$ (9), 244 $[M]^+$ (55), 243 $[M - 1]^+$ (38), 230 $[M + 1 - Me]^+$ (6), 229 $[M - Me]^+$ (24), 225 (9), 216 (7), 57 (100). Found (%): C, 59.12; H, 3.36; N, 11.58. $C_{12}H_8N_2O_4$. Calculated (%): C, 59.00; H, 3.30; N, 11.48.

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References

1. R. H. Thomson, *Naturally Occurring Quinones*, Butterworths, London—New York, 1957.
2. R. H. Thomson, *Naturally Occurring Quinones*, 2nd ed., Acad. Press, London—New York, 1971.
3. R. H. Thomson, *Naturally Occurring Quinones*, 3rd ed., Chapman and Hall, London—New York, 1987.
4. R. H. Thomson, *Naturally Occurring Quinones*, 4th ed., Blackie Academic and Professional, London—New York, 1997.
5. D. Parisot, M. Devys, M. Barbier, *Microbios*, 1990, **64**, 31.
6. A. G. Mezentsev, V. K. Akimenko, *Phytochem.*, 1998, **47**, 935.
7. O. E. Krivoshchekova, O. B. Maximov, L. S. Stepanenko, N. P. Mishchenko, *Phytochem.*, 1982, **21**, 193.
8. N. D. Pokhilo, S. V. Dragan, V. Ph. Anufriev, *Tetrahedron Lett.*, 2011, **52**, 3651.
9. V. A. Stonik, G. B. Elyakov, *Bioorg. Marine Chem.*, 1988, **2**, 43.
10. R. G. Cooke, J. B. Robinson, *Aust. J. Chem.*, 1970, **23**, 1695.
11. J. R. Cannon, V. Lojanapiwatha, C. L. Raston, W. Sinchai, A. H. White, *Aust. J. Chem.*, 1980, **33**, 1073.
12. T. Hanumaiah, G. S. R. Rao, C. P. Rao, K. V. J. Rao, *Tetrahedron*, 1985, **41**, 635.
13. L. V. Boguslavskaya, O. B. Maksimov, N. G. Khrapova, N. I. Kulesh, *Bull. Acad. Sci. USSR, Div. Chem. Sci.*, 1988, **37**, 201.
14. A. V. Lebedev, M. V. Ivanova, D. O. Levitsky, *Life Sci.*, 2005, **76**, 863.
15. R. Kuwahara, H. Hatate, T. Yuki, H. Murata, R. Tanaka, Y. Hama, *LWT — Food Sci. Technol.*, 2009, **42**, 1296.
16. D. Y. Zhou, B. W. Zhu, X. D. Wang, H. Tan, J. F. Yang, D. M. Li, X. P. Dong, H. T. Wu, L. M. Sun, X. L. Li, Y. Murata, *Food Chem.*, 2011, **129**, 1521.
17. N. K. Utkina, N. D. Pokhilo, *Nat. Prod. Commun.*, 2012, **7**, 901.
18. S. I. Srekhova, E. B. Shentsova, E. A. Kol´tsova, N. I. Kulesh, *Antibiotiki i Khimioterapiya* [*Antibiotics and Chemotherapy*], 1988, **33**, 831 (in Russian).
19. O. N. Pozharitskaya, A. N. Shikov, M. N. Makarova, S. A. Ivanova, V. M. Kosman, V. G. Makarov, V. Bazgier, K. Berka, M. Otyepka, J. Ulrichova, *Planta Medica*, 2013, **79**, 1698.
20. V. Ph. Anufriev, V. L. Novikov, O. B. Maximov, G. B. Elyakov, D. O. Levitsky, A. V. Lebedev, S. M. Sadretdinov, A. V. Shvilkin, N. I. Afonskaya, M. Y. Ruda, N. M. Cherpachenko, *Bioorg. Med. Chem. Lett.*, 1998, **8**, 587.
21. A. A. Artyukov, A. M. Popov, A. V. Tsybulsky, O. N. Krivoshapko, N. V. Polyakova, *Biochemistry (Moscow)*, *Ser. B, Biomed. Chem.*, 2013, **7**, 239.
22. N. P. Mishchenko, S. A. Fedoreev, V. L. Bagirova, *Pharm. Chem. J.*, 2003, **37**, 48.
23. V. P. Glazunov, A. Ya. Tchizhova, O. P. Shestak, G. I. Sopelnyak, V. Ph. Anufriev, *Russ. Chem. Bull.*, 2001, **50**, 95.
24. V. P. Glazunov, A. Ya. Yakubovskaya, N. D. Pokhilo, N. V. Bochinskaya, V. Ph. Anufriev, *Russ. Chem. Bull.*, 2003, **52**, 198.
25. K. C. Nicolaou, D. L. F. Gray, *J. Am. Chem. Soc.*, 2004, **126**, 607.
26. N. D. Pokhilo, M. I. Shuvalova, M. V. Lebedko, G. I. Sopelnyak, A. Ya. Yakubovskaya, N. P. Mishchenko, S. A. Fedoreev, V. Ph. Anufriev, *J. Nat. Prod.*, 2006, **69**, 1125.
27. N. D. Pokhilo, A. Ya. Yakubovskaya, V. A. Denisenko, V. Ph. Anufriev, *Tetrahedron Lett.*, 2006, **47**, 1385.
28. D. N. Pelageev, M. N. Panchenko, N. D. Pokhilo, V. A. Denisenko, V. Ph. Anufriev, *Chem. Nat. Compd.*, 2008, **44**, 719.
29. D. N. Pelageev, M. N. Panchenko, N. D. Pokhilo, V. Ph. Anufriev, *Russ. Chem. Bull.*, 2010, **59**, 1472.
30. O. P. Shestak, V. Ph. Anufriev, V. L. Novikov, *Nat. Prod. Commun.*, 2014, **9**, 953.
31. N. N. Balaneva, O. P. Shestak, V. Ph. Anufriev, V. L. Novikov, *Chem. Nat. Compd.*, 2016, **52**, 213.
32. O. P. Shestak, N. N. Balaneva, V. L. Novikov, *Nat. Prod. Commun.*, 2016, **11**, 1307.
33. N. D. Pokhilo, V. Ph. Anufriev, *Chem. Nat. Compd.*, 2016, **52**, 939.
34. G. I. Melman, K. L. Borisova, N. D. Pokhilo, V. V. Makhankov, V. Ph. Anufriev, *Tetrahedron Lett.*, 2016, **57**, 736.
35. D. N. Pelageev, V. Ph. Anufriev, *Synthesis*, 2016, **48**, 761.
36. P. Kittakoop, J. Punya, P. Kongsaeree, Y. Lertwerawat, A. Jintasirikul, M. Tanticharoen, Y. Thebtaranonth, *Phytochem.*, 1999, **52**, 453.
37. Y. Yamamoto, H. Matsubara, Y. Kinoshita, K. Kinoshita, K. Koyama, K. Takahashi, V. Ahmadjiam, T. Kurokawa, I. Yoshimura, *Phytochem.*, 1996, **43**, 1239.
38. M. A. Ernst-Russel, J. A. Elix, C. L. L. Chai, M. J. Rive, J. H. Wardlaw, *Aust. J. Chem.*, 2000, **53**, 303.
39. K. Masuda, S. Funayama, K. Komiyama, I. Umezawa, K. Ito, *J. Nat. Prod.*, 1987, **50**, 958.
40. R. E. Moore, H. Singh, C. W. J. Chang, P. J. Scheuer, *Tetrahedron*, 1967, **23**, 3271.
41. H. A. Anderson, J. Smith, R. H. Thomson, *J. Chem. Soc.*, 1965, 2141.
42. C. W. J. Chang, R. E. Moore, P. J. Scheuer, *J. Am. Chem. Soc.*, 1964, **86**, 2959.
43. N. N. Gerber, B. Wieclawek, *J. Org. Chem.*, 1966, **31**, 1496.
44. R. Huot, P. Brassard, *Can. J. Chem.*, 1974, **54**, 838.
45. F. Farina, R. Martinez-Utrilla, C. Paredes, *Tetrahedron*, 1982, **38**, 1531.
46. M. C. Carreno, J. L. G. Ruano, A. Urbano, *Tetrahedron*, 1994, **50**, 5013.
47. D. B. Bruce, R. H. Thomson, *J. Chem. Soc.*, 1955, 1089.
48. R. H. DeWolfe, in *Carboxylic Ortho Acid Derivatives: Preparation and Synthetic Applications*, Acad. Press, New York—London, 1970, p. 146.
49. V. V. Mezheritskii, E. P. Olekhnovich, G. N. Dorofeenko, *Russ. Chem. Rev.*, 1973, **42**, 392.

50. V. V. Mezheritskii, E. P. Olekhnovich, S. M. Luk´yanov, G. N. Dorofeenko, in *Ortoefiry v organicheskom sinteze* [*Application of Ortho esters in Organic Synthesis*], Rostov State Univ., Rostov-on-Don, 1976, p. 43 (in Russian).
51. V. Ph. Anufriev, V. L. Novikov, G. V. Malinovskaya, V. P. Glazunov, *Synth. Commun.*, 1997, **27**, 119.
52. W. Bachmann, W. Struve, in *Organic Reactions*, Ed. R. Adams, J. Wiley and Sons, New York, 1942.
53. V. Ph. Anufriev, A. Ya. Tchizhova, V. A. Denisenko, V. L. Novikov, *Russ. J. Org. Chem.*, 1993, **29**, 2008.
54. N. Donaldson, *The Chemistry and Technology of Naphthalene Compounds*, Arnold, London, 1960.
55. G. V. Malinovskaya, A. Ya. Tchizhova, V. Ph. Anufriev, *Russ. Chem. Bull.*, 1999, **48**, 1010.
56. A. Ya. Yakubovskaya, N. D. Pokhilo, N. P. Mishchenko, V. Ph. Anufriev, *Russ. Chem. Bull.*, 2007, **56**, 819.
57. D. V. Berdyshev, V. P. Glazunov, A. Ya. Yakubovskaya, T. Yu. Kochergina, V. Ph. Anufriev, *J. Appl. Spectroscopy*, 2006, **73**, 798.
58. A. Arnone, L. Merlini, G. Nasini, O. V. de Pava, *Synth. Commun.*, 2007, **37**, 2569.
59. S. Natori, Y. Inouye, H. Nishikawa, *Chem. Pharm. Bull.,* 1967, **15**, 380.

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