Chem. Ber. 116, 970–979 (1983)

Synthesis and Reactivity of 2-Aroylbenzoic Acids, III[1]

2-(4-Hydroxy-3,5-dimethylbenzoyl)benzoic Acid[2]

Jan K. Rumiński

Institute of Chemistry, Nicolas Copernicus University,
ul. Gagarina 7, 87-100 Toruń, Poland

Received June 28, 1982

Friedel-Crafts 2-carboxybenzoylation of 2,6-xylenol with phthalic anhydride resulted in the formation of a new *p*-acylphenol type compound: 2-(4-hydroxy-3,5-dimethylbenzoyl)benzoic acid (**1**) (74% yield). Similar reactions of 2,6-xylenol with tetrabromo- and tetrachlorophthalic anhydride gave the benzoic acid derivatives **13** and **14**, respectively. Another practical and efficient (93%) method for preparation of compound **1** was semi-Stieglitz rearrangement of the known 3,3-bis(4-hydroxy-3,5-dimethylphenyl)phthalide (**9**). Reactions of the acid **1** have been investigated, leading to its derivatives **2** – **12**.

Synthese und Reaktivität von 2-Aroylbenzoesäuren, III[1]

2-(4-Hydroxy-3,5-dimethylbenzoyl)benzoesäure[2]

Durch Friedel-Crafts 2-Carboxybenzoylierung von 2,6-Xylenol mit Phthalsäureanhydrid wurde eine neue Verbindung vom *p*-Acylphenol-Typ erhalten: 2-(4-Hydroxy-3,5-dimethylbenzoyl)benzoesäure (**1**) (Ausbeute 74%). In einer analogen Reaktion von 2,6-Xylenol mit Tetrabrom- und Tetrachlorphthalsäureanhydrid wurden die Benzoesäure-Derivate **13** bzw. **14** dargestellt. **1** wurde auch mit 93% Ausbeute durch Semi-Stieglitz-Umlagerung von 3,3-Bis(4-hydroxy-3,5-dimethylphenyl)phthalid (**9**) gewonnen. Verschiedene Reaktionen der Säure **1** führten zu den Derivaten **2** – **12**.

Several reports stated the preparation of symmetrically substituted 3,3-diarylphthalides[3–6] and fluorans[6–8], starting from xylenols and phthalic anhydride in the presence of Lewis acids or conc. H_2SO_4. Three *o*-acylphenol type 2-aroylbenzoic acids from xylenols have also been synthesized until now[8–11]. However, no data are available on *p*-acylphenol type 2-aroylbenzoic acids – derivatives of xylenols, being important intermediates in the synthesis of 3,3-diarylphthalides.

In connection with another study on the semi-Stieglitz rearrangement of some unsymmetrically substituted 3,3-bis(4-hydroxyphenyl)phthalide (phenolphthalein) derivatives, a synthesis of 2-(4-hydroxy-3,5-dimethylbenzoyl)benzoic acid (**1**) was required. This paper deals with efficient Friedel-Crafts 2-carboxybenzoylations of 2,6-xylenol with phthalic anhydride and investigations on the reactivity of the acid **1** thus obtained. Two similar acids, 2,3,4,5-tetrabromo-6-(4-hydroxy-3,5-dimethylbenzoyl)-benzoic acid (**13**) and 2,3,4,5-tetrachloro-6-(4-hydroxy-3,5-dimethylbenzoyl)benzoic acid (**14**) have also been obtained.

0009 – 2940/83/0303 – 0970 $ 02.50/0

Results and Discussion

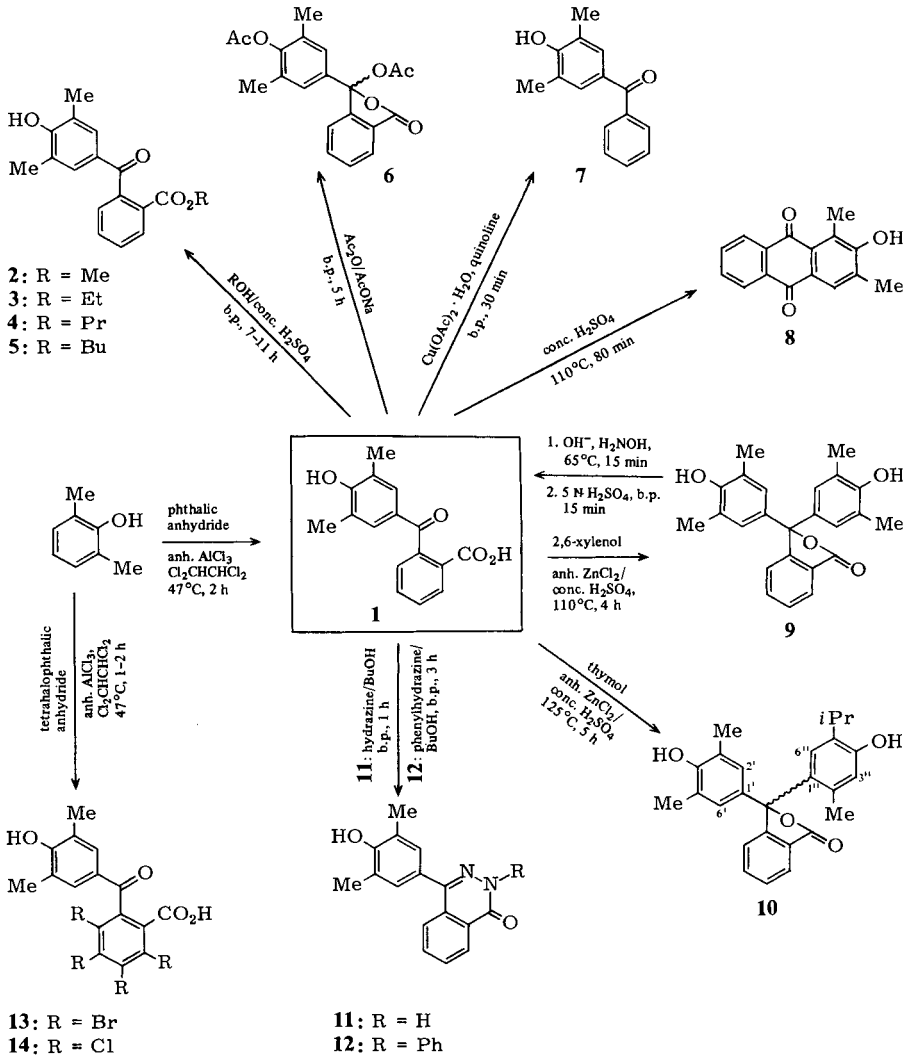
2-Carboxybenzoylation of 2,6-xylenol leading to a *p*-acylphenol derivative cannot be complicated by the formation of any isomer. Problems may arise by migration of methyl groups or through secondary reactions at elevated temperatures. It is known[12-21], that methyl group does not migrate during selective Friedel-Crafts transalkylations and transhalogenations of polyalkyl- and haloalkylphenols, carried out at room or slightly elevated temperatures with $AlCl_3$ or $AlCl_3$-$MeNO_2$ as catalysts and in the presence of benzene, toluene, or *m*-xylene. Similar conclusions may be drawn from the results of Fries rearrangements of xylenyl propionates promoted by $AlCl_3$-$MeNO_2$ catalyst[22,23]. On the contrary, high temperatures (above 130°C), the absence of solvent, excess of anhydrous $AlCl_3$, and extended reaction times favour isomerizations of both starting substances[10] and primarily formed products[24,25]. Temperatures above 165°C (e. g. 180–200°C) under similar conditions facilitate migrations of both acyl and methyl groups; thus rearrangements of 4-acylxylenols into 2-acyl-4,5-xylenols and 2-acyl-4,6-xylenols have been observed[22,23,26]. Attempting *C*-acylation with phthalic anhydride, one should take into account specific side-reactions involving formation of secondary by-products such as 3,3-diarylphthalides and intramolecular cyclodehydratation to anthraquinones[10,27]. Several experiments performed indicated that conditions for the effective 2-carboxybenzoylation of 2,6-xylenol into the acid **1** are as follows: solvent 1,1,2,2-tetrachloroethane, molar ratio of reagents 1:1:3, addition of anh. $AlCl_3$ in one portion, temp. ca. 46°C, reaction time 2 hours, and intensive stirring. The best yield obtained (74%) is in accordance with that of 80%, given by *Martin*[28] as the maximum yield of various 2,6-disubstituted *p*-acylphenols, obtained in Fries rearrangements of appropriate phenyl esters.

Another practical and efficient (93%) method for the preparation of the acid **1** was the semi-Stieglitz rearrangement of the known indicator[5,29] 3,3-bis(4-hydroxy-3,5-dimethylphenyl)phthalide (**9**). This process consists of oximation of **9** in aqueous alcalic medium and acidic hydrolysis of the resulting intermediate 4''-hydroxy-3'',5''-dimethylanil of the acid **1**. Purification of **1** was effected through the propyl ester **4**.

Reactivity of the Acid 1 (Scheme)

Standard esterification of compound **1** with an excess of boiling alcohols gave the esters **2**–**5**. The ^1H NMR spectra showed signals of ester alkyl chains and a single, six-protonic methyl signals in each case, thus proving the presence of two equivalent aromatic methyl groups. Melting points of all esters prepared were observed to shift down regularly with expanding their saturated ester function. Similar observations were previously made by *Hahn* and *Reid*[30] with a series of alkyl esters of 2-(4-halobenzoyl)benzoic acids. Also νC=O values for ester functions were found to change regularly in **2**–**5** (1731, 1726, 1724, and 1720 cm^{-1}).

The mass spectrum of methyl ester **2** showed the molecular ion peak $M^{+\bullet}$ at *m/e* = 284. The base peak was found at *m/e* = 149 according to the principal mode of fragmentation, producing 4-HO-3,5-$Me_2C_6H_2CO^{+\bullet}$ acylium ion. This is consistent with a fragmentation pattern found by *Böhmer* and co-workers[31] in the case of similar benzophenone derivatives, possessing *para*-conjugation between phenolic hydroxyl and



carbonyl groups through a phenyl nucleus. Another peak at m/e = 163 of acylium ion $MeOCOC_6H_4CO^{+\bullet}$ was less important (18%). The mass spectrum showed no indications of rearrangement processes[31], characteristic of benzophenone derivatives with methyl and hydroxyl groups located in *ortho*-position with respect to the central carbonyl group. Thus, the extremely low ketone carbonyl stretching frequencies of the acid **1** (νC=O 1625 cm^{-1}) as well as of the corresponding benzophenone **7** (νC=O 1626 cm^{-1}), usually attributed to intramolecular hydrogen bonded aromatic *o*-hydroxyketone systems[32], must be due to conjugation in *p*-acylphenol and not in *o*-acylphenol structures. Here it seems that participation of the phenolic oxygen electron pairs

in intermolecular hydrogen bonds is considerably hindered by both *o*-methyl groups. Thus, these electrons can be involved effectively in conjugation from hydroxyl to carbonyl through a phenyl nucleus. A specific spatial arrangement, involving coplanar 4-HO-3,5-$Me_2C_6H_2CO$-fragments in a crystalline, dimeric associated acid **1** and in polymeric associated benzophenone **7** molecules is postulated.

Due to the characteristic dually reactive nature of all 2-aroylbenzoic acids, esterification of the acid **1** with a boiling acetic anhydride/anhydrous sodium acetate mixture gave a pseudoester type derivative: 3-acetoxy-3-(4-acetoxy-3,5-dimethylphenyl)phthalide (**6**). This was proved by the ^{1}H NMR spectrum, which presented two non-equivalent triprotonic singlets, located at δ = 2.29 (phenolic acetate) and 2.12 (γ-lactol acetate). Thus, compound **6** is a derivative of an unknown γ-hydroxylactone: 3-hydroxy-3-(4-hydroxy-3,5-dimethylphenyl)phthalide, being a "tautomeric" ring form of γ-ketocarboxylic acid **1**.

Decarboxylation of the acid **1** in boiling quinoline, catalyzed with cupric acetate monohydrate, gave 4-hydroxy-3,5-dimethylbenzophenone (**7**) with 98% yield. Previously this ketone was obtained by *Auwers* and *Markovits*[33] as a result of demethylation of 4-methoxy-3,5-dimethylbenzophenone effected with an excess of $AlCl_3$ and has also been obtained[34] by Fries rearrangement of 2,6-xylenyl benzoate.

Intramolecular cyclodehydratation of the acid **1** carried out in conc. H_2SO_4 at 110°C resulted in the isolation of 2-hydroxy-1,3-dimethylanthraquinone (**8**) with 77% yield. The IR spectrum of **8** presented two different quinone carbonyl bands; one at $\nu C=O$ 1669 cm^{-1} is probably due to C=O stretching vibrations at C-9 and that at 1652 cm^{-1} to C=O vibrations at C-10. The ^{1}H NMR spectrum of **8** showed methyl signals at δ = 2.35, attributed to the Me group at C-3, and at δ = 2.58, which was associated with the more deshielded (by neighbouring quinone C=O) Me group, located at C-1.

3-Arylphthalidylation of 2,6-xylenol with the acid **1**, carried out at 110°C for 4 h and catalyzed by anh. $ZnCl_2$ and a drop of conc. H_2SO_4, gave the known[5,29] indicator dye 3,3-bis(4-hydroxy-3,5-dimethylphenyl)phthalide (**9**) (yield 55%).

3-Arylphthalidylation of 2-isopropyl-5-methylphenol (thymol) with the acid **1**, effected at 125°C for 5 h in the presence of anh. $ZnCl_2$ and a drop of conc. H_2SO_4, gave the unknown, easily crystallizable phthalide **10** (58% yield). Its IR spectrum showed a γ-lactone carbonyl band with two (and not one as was previously observed[35]) maxima located at 1740 and 1723 cm^{-1}. The ^{1}H NMR spectrum of **10** presented two monoprotonic singlets at δ = 6.74 and 6.98, which were attributed to two aromatic protons in the *p*-substituted thymol molecule[35]. Addition of D_2O to a [D_6]acetone solution of compound **10** caused a downfield shift (Δ = 0.06 ppm) of the former singlet (to δ = 6.80) while no shift of the latter signal occurred. Thus, it was concluded that the signal at δ = 6.74 must be due to the thymolic aromatic proton at C-3′′ and that at δ = 6.98 to 6′′-H. This deuterium oxide-induced shift can be attributed to development of intensive intermolecular hydrogen-type bonds involving electron pairs of the thymolic OH group. The phenomenon can be exploited to facilitate interpretation of other ^{1}H NMR spectra.

Friedel-Crafts *C*-acylation of 2,6-xylenol with tetrabromo- and tetrachlorophthalic anhydrides gave 2,3,4,5-tetrabromo-6-(4-hydroxy-3,5-dimethylbenzoyl)benzoic acid

(13) and 2,3,4,5-tetrachloro-6-(4-hydroxy-3,5-dimethylbenzoyl)benzoic acid (14) with 67 and 66% yield, respectively. The ^{1}H NMR spectra of both acids showed two signals only. Tetrachloroacid 14 can be used in organic analysis as an useful, easily crystallizable derivative of 2,6-xylenol.

The author is indebted to Prof. Dr. *L. Borowiecki* for a helpful discussion of this paper.

Experimental Part*)

Melting points: Boetius type microhot-stage apparatus (German Democratic Republic), corrected. – Thin layer chromatograms (TLC): mobile phase A toluene/methanol (5:1) or B toluene/methanol/acetic acid (45:8:4). – IR: Specord 71 IR (Zeiss, Jena) spectrophotometer, in nujol (N) and hexachlorobutadiene (HCB) mulls. For other details see Part II of this series[1].

2-(4-Hydroxy-3,5-dimethylbenzoyl)benzoic acid (1)

a) Finely powdered anh. $AlCl_3$ (40.0 g, 0.30 mol) was added within 5 min to a mixture of phthalic anhydride (14.8 g, 0.10 mol), 2,6-xylenol (12.2 g, 0.10 mol), and 1,1,2,2-tetrachloroethane (100 ml). Stirring for 2 h at 45–47 °C, followed by cooling and addition of crushed ice (150 g) resulted in decomposition of the reaction complex. After 15 min the mixture was subjected to steam distillation to separate the solvent. When still hot, nonvolatile components were filtered off. The resulting solid mass was extracted several times with boiling dil. Na_2CO_3. The combined alkaline extracts were cooled and acidified with dil. HCl. A crude mass of 1 deposited, yield 19.93 g (74%). Crystallization from a small volume of acetic acid and then from dil. acetic acid gave a TLC-pure, colourless sample, m. p. 231.0–231.4 °C.

b) A solution of the phthalide 9 (9.36 g, 25 mmol) in 2.5 N NaOH (60 ml) was stirred at 65 °C for 15 min. Then a solution of hydroxylamine sulfate (3.37 g, 20.5 mmol) in water (15 ml) was added and heating continued for 15 min. The reaction mixture was then acidified with dil. H_2SO_4 until it was slightly acidic. A yellow, colloidal mass (anil of the acid 1) was filtered off. The solid obtained was refluxed with 5 N H_2SO_4 (100 ml) for 15 min. A brown crystalline mass deposited. This was treated with hot dil. NaOH. Filtration of the resulting solution followed by acidification with dil. HCl (1:1) gave a crude sample of 1, 6.31 g (93%). Esterification of the sample with propyl alcohol and purification of the propyl ester 4 by pseudosublimation at ca. 180 °C/ca. 1 Torr gave TLC-pure fractions of the ester 4. These were hydrolyzed with hot dil. NaOH. Acidification of the alkaline solution with dil. HCl yielded TLC-pure 1, m. p. 231.8–232.0 °C (from dil. acetic acid). IR and ^{1}H NMR spectra were identical with those obtained in a). TLC: R_F (B) = 0.30 (conc. H_2SO_4 → yellow). – UV/VIS (Ethanol): λ_{max} (lg ε) = 296 (4.17), λ_{min} 255 nm (3.71). – IR (N, HCB): 3440 sb (OH), 2910 mb, 2780 mb, 2590 mb, 2490 mb (CO_2H), 1704 s (CO_2H), 1624 s (C=O), 1584 sb, 1340 s, 1272 s, 1227 s, 1202 s, 1137 s, 946 mb (CO_2H), 859 m, 775 m, 750 m, 731 m, 622 m cm^{-1}. – ^{1}H NMR ([D_6]Acetone/TMS int.): δ = 2.22 (s; 6H, CH_3), 7.26–7.41 (m; 3H, 3-, 2'-, 6'-H), 7.55–7.71 (m; 2H, 4-, 5-H), 7.94–8.11 (m; 1H, 6-H).

$C_{16}H_{14}O_4$ (270.3) Calc. C 71.10 H 5.22 Found C 71.26 H 4.95

Methyl 2-(4-hydroxy-3,5-dimethylbenzoyl)benzoate (2): A mixture of 1 (2.0 g, 7.4 mmol), methanol (40 ml, ca. 1 mol), and conc. H_2SO_4 (1.5 ml) was heated under reflux for 7 h. After partial evaporation of methanol (ca. 20 ml) and addition of ether (50 ml) the solution was washed several times with 5% $NaHCO_3$ aq. for separation of unreacted 1. Washing with water, drying over $MgSO_4$, and evaporation of the solvent afforded the crude ester 2 (1.95 g, 93%). Pseudosublimation at ca. 165–170 °C/ca. 1 Torr gave TLC-pure, colourless crystals, m. p. 161.7 to

*) Thanks are due to Ms. *Z. Markwitan* for experimental assistance.

162.7 °C (from methanol). TLC: R_F (A) = 0.42 (conc. H_2SO_4 → yellow). – UV (Ethanol): λ_{max} (lg ε) = 299 (4.17), λ_{min} 258 nm (3.73). – IR (N, HCB): 3360 sb (OH), 2940 w, 2910 w (CH_3), 1731 s (CO_2CH_3), 1652 s (C=O), 1587 sb, 1330 s, 1278 s, 1191 mb, 1131 m, 1081 m, 706 m cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 2.22 (s; 6H, CH_3), 3.59 (s; 3H, OCH_3), 7.31 – 7.42 (m; 3H, 3-, 2'-, 6'-H), 7.53 – 7.70 (m; 2H, 4-, 5-H), 7.87 – 8.03 (m; 1H, 6-H). – MS (70 eV): *m/e* = 285 (7.6%, M + 1), 284 (29, M^+), 253 (6.7, M – CH_3O; 4-HO-3,5-$(CH_3)_2C_6H_2COC_6H_4CO^+$), 195 (4.6), 163 (18, M – 121; $CH_3OCOC_6H_4CO^+$), 150 (12), 149 (100, M – 135; 4-HO-3,5-$(CH_3)_2C_6H_2CO^+$), 121 (5.6, M – 163; 4-HO-3,5-$(CH_3)_2C_6H_2^+$), 92 (5.6).

$C_{17}H_{16}O_4$ (284.3) Calcd. C 71.81 H 5.67 Found C 71.38 H 5.58

Ethyl 2-(4-hydroxy-3,5-dimethylbenzoyl)benzoate (**3**): A mixture of TLC-pure **1** (0.6687 g, 2.47 mmol), anh. (99.8%) ethanol (20 ml, ca. 390 mmol), and conc. H_2SO_4 (0.7 ml) was heated under reflux for 6 h. After similar work-up as above TLC-pure colourless crystals of **3** were obtained, yield 0.725 g (98%), m. p. 144.0 – 144.8 °C (from ethanol). TLC: R_F (A) = 0.42 (conc. H_2SO_4 → yellow). – UV (Ethanol): λ_{max} (lg ε) = 299 (4.19), λ_{min} 259 nm (3.75). – IR (N, HCB): 3385 sb (OH), 2965 w, 2905 w (CH_3, C_2H_5), 1726 s ($CO_2C_2H_5$), 1648 s (C=O), 1582 sb, 1323 s, 1287 s, 1189 s, 1132 s, 771 m, 761 m, 709 m cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 1.03 (t, *J* = 7 Hz; 3H, OCH_2CH_3), 2.23 (s; 6H, CH_3), 4.04 (q, *J* = 7 Hz; 2H, OCH_2), 7.29 – 7.44 (m; 3H, 3-, 2'-, 6'-H), 7.54 – 7.71 (m; 2H, 4-, 5-H), 7.89 – 8.05 (m; 1H, 6-H).

$C_{18}H_{18}O_4$ (298.3) Calcd. C 72.47 H 6.08 Found C 72.88 H 6.29

Propyl 2-(4-hydroxy-3,5-dimethylbenzoyl)benzoate (**4**): A mixture of **1** (2.0 g, 7.4 mmol), propyl alcohol (40 ml, 535 mmol), and conc. H_2SO_4 (1.5 ml) was heated under reflux for 7 h. After similar workup as for **2** crude **4** (2.01 g, 87%) was obtained. Pseudosublimation at ca. 140 °C/ca. 1 Torr gave TLC-pure, colourless mass, m. p. 128.5 – 130.5 °C (from aq. methanol). TLC: R_F (A) = 0.42 (conc. H_2SO_4 → yellow). – UV (Ethanol): λ_{max} (lg ε) = 300 (4.01), λ_{min} 259 nm (3.53). – IR (N, HCB): 3225 mb (OH), 2950 m, 2915 m (CH_3, C_3H_7), 1724 s ($CO_2C_3H_7$), 1648 s (C=O), 1575 sb, 1322 s, 1287 s, 1205 s, 1138 s, 1126 s, 778 m, 760 m, 713 m cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 0.78 (t, *J* = 7 Hz; 3H, CH_3 of Pr), 1.41 (m; 2H, $CO_2CH_2CH_2$), 2.23 (s; 6H, CH_3), 3.95 (t, *J* = 7 Hz; 2H, OCH_2), 7.28 – 7.43 (m; 3H, 3-, 2'-, 6'-H), 7.52 – 7.70 (m; 2H, 4-, 5-H), 7.93 – 8.05 (m; 1H, 6-H).

$C_{19}H_{20}O_4$ (312.4) Calcd. C 73.06 H 6.45 Found C 73.27 H 6.38

Butyl 2-(4-hydroxy-3,5-dimethylbenzoyl)benzoate (**5**): A mixture of **1** (2.0 g, 7.4 mmol), butyl alcohol (35 ml, 381 mmol), and conc. H_2SO_4 (1.5 ml) was heated under reflux for 11 h. After similar work-up as for **2** crude **5** (2.40 g, 99%) was obtained. Several crystallizations from methanol, benzene, and aq. methanol afforded TLC-pure colourless crystals, m. p. 123.5 to 124.4 °C. TLC: R_F (A) = 0.47 (conc. H_2SO_4 → yellow). – UV (Ethanol): λ_{max} (lg ε) = 298.5 (4.14), λ_{min} 258 nm (3.68). – IR (N, HCB): 3220 mb (OH), 2935 m, 2900 m, 2850 w (CH_3, C_4H_9), 1720 s ($CO_2C_4H_9$), 1649 s (C=O), 1582 sb, 1325 s, 1279 sb, 1210 s, 1133 s, 1083 s, 772 m, 753 m, 705 m cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 0.66 – 0.89 (m; 3H, CH_3 in Bu), 1.03 – 1.51 (m; 4H, $OCH_2CH_2CH_2$), 2.24 (s; 6H, CH_3), 4.01 (t, *J* = 6 Hz; 2H, OCH_2), 7.29 – 7.43 (m; 3H, 3-, 2'-, 6'-H), 7.56 – 7.71 (m; 2H, 4-, 5-H), 7.93 – 8.08 (m; 1H, 6-H).

$C_{20}H_{22}O_4$ (326.4) Calcd. C 73.59 H 6.79 Found C 73.95 H 6.71

3-Acetoxy-3-(4-acetoxy-3,5-dimethylphenyl)phthalide (**6**): A mixture of **1** (1.1615 g, 4.297 mmol), Ac_2O (70 ml, ca. 742 mmol), and anh. AcONa (7 g, ca. 85 mmol) was heated under reflux for 5 h. When cooled, the reaction mixture was poured onto vigorously stirred water (200 ml). A crystalline mass of ester **6** deposited (1.45 g, 95%). After several crystallizations from aq. methanol, aq. ethanol, and aq. acetic acid TLC-pure colourless crystals were obtained, m.p.

132.5 – 135.0 °C. TLC: R_F (A) = 0.56 (conc. H_2SO_4 → yellow). – UV (Ethanol): λ_{max} (lg ε) = 277 (3.15), λ_{min} 261 nm (3.02). – IR (N, HCB): 1786 s (COC=O), 1766 s ($OCOCH_3$), 1215 s (C – O), 1247 s, 1025 m, 971 m, 943 m, 764 m, 730 w, 725 w cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 2.12 (s; 9H, 3-$OCOCH_3$ and CH_3), 2.29 (s; 3H, 4'-$OCOCH_3$), 8.57 – 8.97 (m; 4H, 4-, 5-, 6-, 7-H).

$C_{20}H_{18}O_6$ (354.4) Calcd. C 67.79 H 5.12 Found C 67.55 H 5.30

4-Hydroxy-3,5-dimethylbenzophenone (**7**): Decarboxylation of **1** was carried out following a general procedure by *Hubacher*[36]. A solution of **1** (2.7 g, 10 mmol) in freshly distilled quinoline (5 ml) was heated to the boiling point. Then $Cu(OAc)_2 \cdot H_2O$ (100 mg) was added and heating under reflux was continued for 0.5 h. After cooling, the reaction mixture was treated with ether (110 ml) and filtered. Extraction of the filtrate with 3 N HCl resulted in the separation of quinoline. The remaining solution was washed with water and dried over $MgSO_4$. Evaporation of the solvent gave crude **7** (2.21 g, 98%). Pseudosublimation of this mass at ca. 160 °C/ca. 1 Torr resulted in the separation of colourless, yellow, and rose-coloured, TLC-impure fractions. These were combined and carefully pulverized. Another vacuum (ca. 1 Torr) sublimation at 105 – 115 °C gave TLC-pure fractions of **7**. Successive crystallizations from benzene, aq. methanol, and ether afforded colourless **7**, m.p. 143.3 – 144.5 °C (lit.[33] 141 – 142 °C, lit.[34] 142.0 – 142.5 °C). TLC: R_F (A) = 0.46 (conc. H_2SO_4 → yellow). – UV (Ethanol): λ_{max} (lg ε) = 240 (4.07), 304 (4.08), λ_{min} 228 (3.96), 267 nm (3.65). – IR (N, HCB): 3265 mb (OH), 1626 s (C=O), 1569 s, 1322 s, 1221 s, 1188 sb, 1124 s, 1016 m, 966 m, 933 m, 890 w, 778 w, 737 m, 715 s, 687 m cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 2.30 (s; 6H, CH_3), 7.43 – 7.80 (m; 7H, aromat. H), 8.18 (s; 1H, OH).

$C_{15}H_{14}O_2$ (226.3) Calcd. C 79.62 H 6.24 Found C 79.50 H 6.72

2-Hydroxy-1,3-dimethylanthraquinone (**8**): A mixture of **1** (0.50 g, 1.9 mmol) and conc. H_2SO_4 (20 ml) was heated at 110 °C for 1 h 20 min. After cooling the reaction mixture was poured onto water (100 ml). An amorphous solid was coagulated by heating to the boiling point. After filtration the solid was dissolved in dil. NaOH, the solution was filtered and acidified with dil. HCl. The resulting precipitate was coagulated and filtered off, yield 0.36 g (77%). Sublimation at ca. 200 °C/ca. 1 Torr, followed by crystallization from acetone afforded long, yellow, TLC-pure crystals, m.p. 234.3 – 235.8 °C. TLC: R_F (A) = 0.47 (conc. H_2SO_4 → reddish-brown). – UV/VIS (Ethanol): λ_{max} (lg ε) = 242 (4.36), 276 (4.53), 375 (3.61), 515 (2.51), λ_{min} 222 (4.26), 254 (4.38), 338 (3.57), 469 nm (2.47). – IR (N, HCB): 3350 mb (OH), 1669 m (C=O), 1652 m (C=O), 1588 m, 1556 m, 1345 s, 1293 m, 1256 m, 1223 mb, 1175 mb, 969 m, 759 w, 710 s cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 2.35 (s; 3H, 3-CH_3), 2.58 (s; 3H, 1-CH_3), 7.65 – 8.10 (m; 5H, aromat. H).

$C_{16}H_{12}O_3$ (252.3) Calcd. C 76.18 H 4.76 Found C 76.08 H 5.05

3,3-Bis(4-hydroxy-3,5-dimethylphenyl)phthalide (**9**): A small amount of anh. $ZnCl_2$ and one drop of conc. H_2SO_4 were added to a clear melt, prepared by careful heating of a mixture of **1** (1.0592 g, 3.92 mmol) and 2,6-xylenol (1.0 g, 8.2 mmol). The dark-red mass was heated at 110 °C for 4 h. The resulting melt, when dissolved in boiling methanol, was subjected to steam-distillation until the odour of 2,6-xylenol had disappeared. The nonvolatile mixture was then cooled and filtered. This gave TLC-pure phthalide **9** (0.805 g, 55%). Successive crystallizations from benzene, aq. ethanol, and aq. methanol afforded a colourless sample, m.p. 247.5 – 249.0 °C (lit.[5] 256 °C, aq. ethanol). TLC: R_F (A) = 0.47 (conc. H_2SO_4 → reddish-brown). – UV (Ethanol): λ_{max} (lg ε) = 205 (4.95), 276 (3.66), λ_{min} 263 nm (3.89). – IR (N, HCB): 3570 w (OH), 3365 mb (OH), 2920 w, 2860 w (CH_3), 1738 s (C=O), 1493 m, 1313 m, 1208 m, 1198 m, 1179 m, 1128 m, 956 m, 927 m, 883 w, 879 w, 802 w, 772 w, 737 w, 713 m, 706 m cm^{-1}. – ^1H NMR

([D_6]Acetone/ TMS int.): δ = 2.19 (s; 12H, CH_3), 6.93 (s; 4H, 2'-, 6'-, 2''-, 6''-H), 7.51 (s; 2H, OH), 7.56 – 7.93 (m; 4H, 4-, 5-, 6-, 7-H).

$C_{24}H_{22}O_4$ (374.4) Calcd. C 76.98 H 5.92 Found C 76.95 H 6.37

3-(4-Hydroxy-3,5-dimethylphenyl)-3-(4-hydroxy-5-isopropyl-2-methylphenyl)phthalide (**10**): A mixture of **1** (2.027 g, 7.50 mmol) and thymol (2-isopropyl-5-methylphenol; 2.0 g, 3.31 mmol) was heated until a clear melt developed. Then a small portion of anh. $ZnCl_2$ and one drop of conc. H_2SO_4 were added. The dark-red mixture was heated at ca. 125 °C for 5 h. The clear melt was dissolved in boiling methanol and subjected to steam-distillation until no thymolic odour remained. The nonvolatile mixture was filtered off and washed with water. This gave crude **10** (1.7479 g, 58%). The solid was dissolved in dil. NaOH and the solution was filtered. Precipitation with dil. HCl gave an amorphous mass that, when crystallized from acetic acid, yielded colourless TLC-pure **10**, m.p. 255.5 – 257.2 °C. TLC: R_F (A) = 0.39 (conc. H_2SO_4 → reddish-brown). – UV (Ethanol): λ_{max} (lg ε) = 205 (4.97), 279 (3.68), λ_{min} 264 nm (3.58). – IR (N, HCB): 3560 w (OH), 3410 m, 3305 m (OH), 2955 m, 2865 w (CH_3 and iPr), 1740 s (C=O), 1723 s (C=O), 1592 m, 1292 m, 1255 m, 1196 m, 1156 m, 1130 m, 1098 m, 1047 w, 957 w, 937 w, 894 w, 872 w, 808 w, 772 w, 748 w, 730 w, 714 w; 702 w cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 0.97 (d; J = 7 Hz; 3H, CH_3 of iPr), 1.11 (d, J = 7 Hz; 3H, CH_3 of iPr), 2.02 (s; 3H, 2''-CH_3), 2.17 (s; 6H, 3'-, 5'-CH_3), 3.16 (sept., J = 7 Hz; 1H, CH of iPr), 6.74 (s; 1H, 3''-H), 6.84 (s; 2H, 2'-, 6'-H), 6.98 (s; 1H, 6''-H), 7.43 (s; 1H, 4'-OH), 7.47 – 7.95 (m; 4H, 4-, 5-, 6-, 7-H), 8.49 (s; 1H, 4''-OH).

$C_{26}H_{26}O_4$ (402.5) Calcd. C 77.59 H 6.51 Found C 77.80 H 6.93

4-(4-Hydroxy-3,5-dimethylphenyl)-1(2H)-phthalazinone (**11**): A mixture of **1** (1.0 g, 3.7 mmol), hydrazine hydrate (0.27 ml, 5.6 mmol), and 1-butanol (20 ml) was heated under reflux for 1 h. The solvent was evaporated, which gave crude **11** (0.93 g, 94%). Crystallization from ethanol afforded TLC-pure, colourless crystals, m.p. 281.0 – 281.6 °C. TLC: R_F (A) = 0.31 (conc. H_2SO_4 → yellow). – UV (Ethanol): λ_{max} (lg ε) = 209 (4.70), 305 (3.97), λ_{min} 281 nm (3.88). – IR (N, HCB): 3386 mb (OH), 3171 mb (OH and NH), 3036 w, 2951 w, 2913 w (CH_3), 1661 s (C=O), 1607 m (C=N), 1582 w, 1499 m, 1481 s, 1468 m, 1376 w, 1346 m, 1239 m, 1197 m, 1176 s, 1156 w, 1022 w, 943 w, 867 w, 797 w, 789 w, 773 w, 751 w, 734 w, 684 w cm^{-1}. – ^1H NMR ([D_6]DMSO/HMDS ext.): δ = 2.44 (s; 6H, CH_3), 7.30 (s; 2H, 2'-, 6'-H), 7.63 – 8.15 (m; 3H, 5-, 6-, 7-H), 8.37 – 8.60 (m; 1H, 8-H), 8.80 (s; 1H, OH), 12.93 (s; 1H, NH).

$C_{16}H_{14}N_2O_2$ (266.3) Calcd. C 72.16 H 5.30 N 10.52 Found C 72.60 H 5.59 N 10.47

4-(4-Hydroxy-3,5-dimethylphenyl)-2-phenyl-1(2H)-phthalazinone (**12**): A mixture of **1** (0.70 g, 2.6 mmol), phenylhydrazine (99%, 0.32 ml, 3.213 mmol), and 1-butanol (20 ml) was heated under reflux for 3 h. Evaporation of the solvent left crude **12** (0.815 g, 92%). Washing with hot 1-butanol followed by crystallization from 1-butanol gave TLC-pure, colourless **12**, m.p. 282.2 – 282.6 °C. TLC: R_F (A) = 0.32 (conc. H_2SO_4 → yellow). – UV (Ethanol): λ_{max} (lg ε) = 208 (4.68), 312.5 (4.02), λ_{min} 281 nm (3.84). – IR (N, HCB): 3327 mb (OH), 2932 w (CH_3), 1646 s (C=O), 1608 m (C=N), 1595 m, 1580 m, 1493 s, 1480 m, 1456 w, 1337 s, 1308 s, 1259 m, 1209 s, 1167 s, 1136 m, 1027 m, 981 w, 947 w, 871 m, 779 m, 774 m, 756 m, 737 w, 727 m, 692 s, 662 w cm^{-1}. – ^1H NMR ([D_6]DMSO/HMDS ext.): δ = 2.47 (s; 6H, CH_3), 7.39 (s; 2H, 2'-, 6'-H), 7.53 – 8.20 (m; 9H, aromat. H and OH), 8.47 – 8.78 (m; 1H, 8-H).

$C_{22}H_{18}N_2O_2$ (342.4) Calcd. C 77.17 H 5.30 N 8.18 Found C 77.31 H 5.45 N 7.88

2,3,4,5-Tetrabromo-6-(4-hydroxy-3,5-dimethylbenzoyl)benzoic acid (**13**): 2,6-Xylenol (3.054 g, 25 mmol) was added to a mixture of tetrabromophthalic anhydride (11.59 g, 25 mmol), anh. $AlCl_3$ (10.0 g, 75 mmol), and 1,1,2,2-tetrachloroethane (50 ml). The mixture was heated at

45 – 47 °C for 2 h with intensive stirring. When cooled, the reaction complex was decomposed by addition of ice (100 g). After 0.5 h the solvent was removed by steam-distillation. The residue was filtered, and the resulting solid was extracted several times with Na_2CO_3 aq. The extracts were filtered and acidified with dil. HCl. This caused precipitation of **13** (9.76 g, 67%). Successive crystallizations from a small volume of acetic acid and then from aq. acetic acid afforded TLC-pure crystals of **13**, m.p. 252.5 °C (dec.). TLC: R_F (B) = 0.20 (conc. H_2SO_4 → brownish-orange). – IR (N, HCB): 3460 sb (OH), 3100 mb (CO_2H), 1725 s (CO_2H), 1662 m (C=O), 1638 m (C=O), 1587 sb, 1319 s, 1279 s, 1192 s, 1184 s, 1155 m, 1100 m, 1025 w, 981 w, 943 w, 897 w, 860 w, 794 w, 743 w, 720 w, 692 m cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 2.24 (s; 6H, CH_3), 7.43 (s; 2H, 2'-, 6'-H).

$C_{16}H_{10}Br_4O_4$ (585.9) Calcd. C 32.80 H 1.72 Br 54.67 Found C 32.78 H 2.07 Br 55.10

2,3,4,5-Tetrachloro-6-(4-hydroxy-3,5-dimethylbenzoyl)benzoic acid (**14**): A mixture of tetrachlorophthalic anhydride (28.59 g, 0.10 mol), 2,6-xylenol (12.2 g, 0.10 mol), anh. $AlCl_3$ (40.0 g, 0.30 mol), and 1,1,2,2-tetrachloroethane (100 ml) was heated at 45 – 47 °C for 1 h. After work-up as described for **13** crude **14** (26.36 g, 66%) was obtained. Several crystallizations from acetic acid and aq. acetic acid afforded TLC-pure, colourless crystals, m.p. 225.3 – 225.8 °C. A thermal transformation of an original crystalline sample into colourless, long, rhomboidal crystals has been observed in the range of 180 – 210 °C. TLC: R_F (B) = 0.20 (conc. H_2SO_4 → brownish-orange). – UV (Ethanol): λ_{max} (lg ε) = 209 (4.74), 308 (4.21), λ_{min} 267 nm (3.72). – IR (N, HCB): 3465 sb (OH), 3080 sb (CO_2H), 1728 s (CO_2H), 1660 m (C=O), 1641 s (C=O), 1588 sb, 1421 m, 1321 s, 1283 s, 1221 s, 1184 sb, 1121 s, 1029 w, 988 w, 945 w, 898 w, 803 wb, 742 w, 718 w, 663 m cm^{-1}. – ^1H NMR ([D_6]Acetone/TMS int.): δ = 2.24 (s; 6H, CH_3), 7.43 (s; 2H, 2'-, 6-H).

$C_{16}H_{10}Cl_4O_4$ (408.1) Calcd. C 47.09 H 2.47 Cl 34.75 Found C 46.77 H 2.69 Cl 35.19

1) Part. II: *J. K. Rumiński* and *K. D. Przewoska,* Chem. Ber. **115**, 3436 (1982).
2) *N. Copernicus University* (*J. K. Rumiński,* inventor), Polish Patent Report P-207800 (June 20, 1978); Biul. Urzedu Patentowego **2** (**160**), 43 (1980).
3) *W. Csanyi,* Z. Elektrochem. Angew. Phys. Chem. **27**, 65 (1921).
4) *A. Thiel* and *L. Jungfer,* Z. Anorg. Allg. Chem. **178**, 49 (1929).
5) *E. Ziegler* and *G. Zigeuner,* Monatsh. Chem. **79**, 370 (1948).
6) *M. Dominikiewicz,* Rocz. Chem. **11**, 113 (1931).
7) *F. Ullman* and *W. Schmidt,* Ber. Dtsch. Chem. Ges. **52**, 2098 (1919).
8) *W. H. Bentley, H. D. Gardner jr.,* and *C. Weizmann,* J. Chem. Soc. **91 – 2**, 1637 (1907).
9) *I. G. Farbenindustrie AG* (*S. Grassner* and *B. Bienert,* inventors), D.R.P. 517478 (Feb. 12, 1929) [Chem. Abstr. **25**, 2154 (1931)].
10) *G. Baddeley, G. Holt,* and *S. M. Makar,* J. Chem. Soc. **1952**, 2415.
11) *A. Fairbourne* and *J. M. Gauntlett,* J. Chem. Soc. **123**, 1137 (1923).
12) *W. Tashiro, H. Watanabe,* and *O. Tsuge,* Org. Prep. Proced. Int. **6**, 107 (1974).
13) *W. Tashiro, H. Watanabe,* and *O. Tsuge,* Org. Prep. Proced. Int. **6**, 117 (1974).
14) *W. Tashiro, H. Watanabe,* and *O. Tsuge,* Org. Prep. Proced. Int. 7, 43 (1975).
15) *W. Tashiro, G. Fukata,* and *K. Oe,* Org. Prep. Proced. Int. 7, 183 (1975).
16) *W. Tashiro. H. Watanabe, K. Oe,* and *O. Tsuge,* Org. Prep. Proced. Int. 7, 255 (1975).
17) *W. Tashiro* and *G. Fukata,* Org. Prep. Proced. Int. **8**, 51 (1976).
18) *W. Tashiro, G. Fukata, T. Yamato, H. Watanabe, K. Oe,* and *O. Tsuge,* Org. Prep. Proced. Int. **8**, 249 (1976).
19) *W. Tashiro, G. Fukata,* and *T. Yamato,* Org. Prep. Proced. Int. **8**, 263 (1976).
20) *W. Tashiro* and *G. Fukata,* J. Org. Chem. **42**, 1208 (1977).
21) *W. Tashiro* and *T. Yamato,* Org. Prep. Proced. Int. **10**, 143 (1978).
22) *R. Martin,* Bull. Soc. Chim. Fr. **1974**, 1519.
23) *R. Martin* and *G. Cotton,* Bull. Soc. Chim. Fr. **1973**, 1438.

[24] *G. Baddeley,* J. Chem. Soc. **1943**, 527.
[25] *K. Auwers, H. Bundesmann,* and *F. Wieners,* Liebigs Ann. Chem. **447**, 162 (1926).
[26] *R. Martin,* Bull. Soc. Chim. Fr. **1968**, 1503.
[27] *H. Waldman* and *P. Sellner,* J. Prakt. Chem. **150**, 145 (1938).
[28] *R. Martin,* Bull. Soc. Chim. Fr. **1974**, 983.
[29] *S. Glöckner,* Monatsh. Chem. **80**, 489 (1949).
[30] *H. C. Hahn* and *E. E. Reid,* J. Am. Chem. Soc. **46**, 1645 (1924).
[31] *V. Böhmer, I. Lüderwald,* and *R. Martin,* Z. Anal. Chem. **297**, 354 (1979).
[32] *A. D. Cross,* An Introduction to Practical Infrared Spectroscopy, 2nd. ed., p. 68, Butterworths, London 1964.
[33] *K. Auwers* and *T. Markovits,* Ber. Dtsch. Chem. Ges. **41**, 2339 (1908).
[34] *K. Auwers* and *E. Janssen,* Liebigs Ann. Chem. **483**, 44 (1930).
[35] *J. K. Rumiński,* Ph. D. Thesis, p. p. 62–66, Univ. Toruń 1973.
[36] *M. H. Hubacher,* Anal. Chem. **21**, 945 (1949).

[203/82]