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

2-(4-Hydroxy-3-isopropylbenzoyl)benzoic Acid

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Synthese und Reaktionsfähigkeit von 2-Aroylbenzoesäuren, II[1)]

2-(4-Hydroxy-3-isopropylbenzoyl)benzoesäure

Die Friedel-Crafts-Acylierung von 2-Isopropylphenol mit Phthalsäureanhydrid liefert nur die 2-(4-Hydroxy-3-isopropylbenzoyl)benzoesäure (**1**) vom *p*-Acylphenol-Typ. Die Reaktionsfähigkeit der Säure **1** wurde untersucht, und ihre Derivate **2** – **10** werden beschrieben.

In connection with a further study on semi-*Stieglitz* rearrangement of unsymmetrically substituted derivatives of 3,3-bis(4-hydroxyphenyl)phthalide, we found it necessary to prepare 2-(4-hydroxy-3-isopropylbenzoyl)benzoic acid (**1**) as a starting material as well as a reference sample. No data are available in the literature either for this acid **1** or any of its derivatives.

The present paper describes the 2-carboxybenzoylation of 2-isopropylphenol with phthalic anhydride by Friedel-Crafts method, which led selectively to the *p*-acylphenol-type compound 2-(4-hydroxy-3-isopropylbenzoyl)benzoic acid (**1**). The reactivity of this acid **1** has also been investigated and derivatives thus obtained (**2** – **10**) were characterized by TLC, UV/VIS, IR, ^{1}H NMR and MS.

Aromatic hydrocarbons and ketones as well as phenolic derivatives, all substituted with alkyl groups such as isopropyl and especially *tert*-butyl, are known to undergo dealkylation, transalkylation, and isomerization promoted by acid catalysts[2-14)]. These phenomena were usually observed in the case of Friedel-Crafts reactions, particularly at elevated temperatures[2,3)]. Actually we have succeeded in effective Friedel-Crafts 2-carboxybenzoylation of 2-isopropylphenol with phthalic anhydride at 50 °C with no dealkylation. This reaction was carried out in 1,2-dichloroethane with 3 molar equivalents of anhydrous $AlCl_3$ and after 3 h resulted in the formation of compound **1** with 52 % yield. The isomeric *o*-acylphenol 2-(2-hydroxy-3-isopropylbenzoyl)benzoic acid was not observed, but traces of secondary formed 3,3-bis(4-hydroxy-3-isopropylphenyl)phthalide (**6**) were detected (TLC). Application of other solvents lowered the yield – in 1,1,2,2-tetrachloroethane and in nitromethane solutions compound **1** was obtained with 39 % and 19 % yield, respectively.

Another, almost quantitative route to the acid **1** was found to be semi-*Stieglitz* rearrangement of the phthalide **6**. Unfortunately, a synthesis gives compound **6** with not better than 30 % yield and phthalide **6** is not easy obtainable in a pure form.

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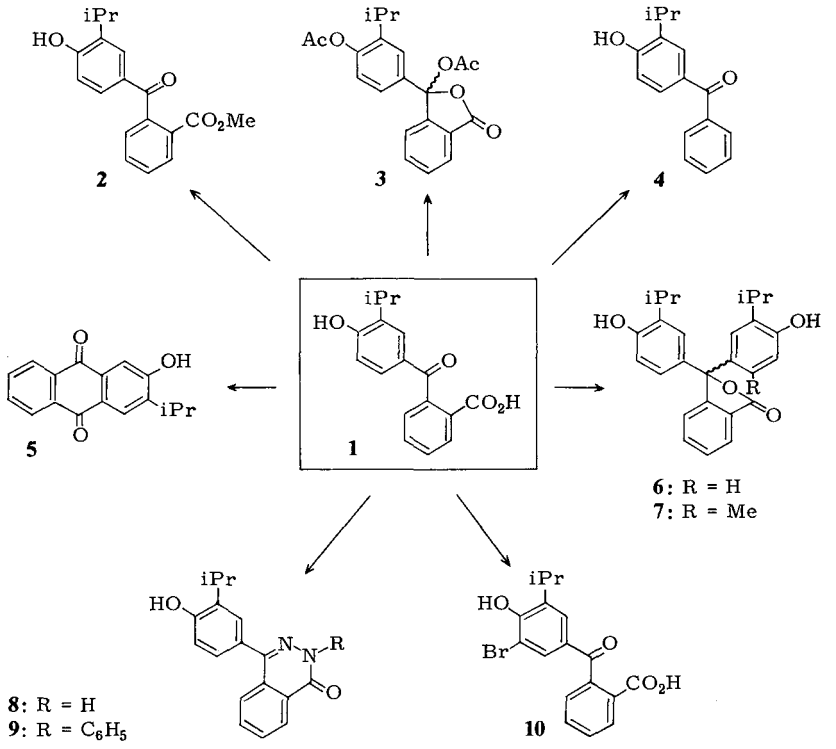
Reactivity of the acid **1** (Scheme). On treatment with boiling methanol in the presence of conc. H_2SO_4 compound **1** gave the methyl ester **2**. This was shown by the ^1H NMR spectrum (three-protonic singlet at $\delta = 3.55$). The mass spectrum of compound **2** (the parent acid **1** could not be analyzed directly because of its low volatility) presented an intense (48.83%) peak of molecular ion M^+ at *m/e* = 298 thus proving the molecular structure formula $C_{18}H_{18}O_4$. The base peak (100%) was observed at *m/e* 163 (M − 135) due to two principal modes of fragmentation involving splitting of two different $Ar^1 - CO - Ar^2$ single bonds. Accidentally both acylium ions: 4'-HO-3'-iPr$C_6H_3CO^{+\cdot}$ and $MeOCOC_6H_4CO^{+\cdot}$ have the same *m/e* values (163). In the mass spectrum there were no indications of rearrangement processes, which require hydroxyl or methy substituents in the *ortho* positions in one of the phenyl nuclei of benzophenone[15,16]. Thus the absence of hydroxyl or isopropyl substituents in the *ortho* (2') position of ester **2** was obvious.



A specific, dually reactive[17] nature of the acid **1** was clearly demonstrated by esterification with acetic anhydride/anhydrous sodium acetate mixture. ^1H NMR spectrum of the resulting derivative **3** showed two different acetyl singlets: one at $\delta = 2.11$ derived from a lactol acetate and the other at $\delta = 2.27$ from a phenolic acetate. Thus the synthesized compound **3** was a diacetate – a derivative of a hypothetical γ-hydroxylactone being a "tautomeric" ring form of γ-keto acid **1**. On standing for several weeks or after several crystallizations from ethanol/water, compound **3** underwent undetermined transformation to another compound (TLC) with a low R_F value (ca. 0.3). This may be probably due to isomerization involving benzofuran ring-opening transformation, which leads to 2-(4-acetoxy-3-isopropylbenzoyl)benzoic acetic anhydride. Ther-

mal isomerization of 3-acetoxy-3-phenylphthalide to a mixed anhydride has also been reported by *Schmid* and co-workers[18].

Decarboxylation of the acid **1** gave 4-hydroxy-3-isopropylbenzophenone (**4**). The IR spectrum of compound **4** in 1,2-dichloroethane presents in the aromatic overtone region (1650–2000 cm^{-1}) a complex variety of maxima (Experimental). Their position is in fairly good agreement with data published by *Young* and co-workers[19] for the appropriate combination of mono- and 1,2,4-trisubstituted benzene derivatives. The indicated pattern gives no evidence for a combination of mono- and 1,2,3-trisubstituted modes of aromatic C–H vibrations. This indicates the absence of isomeric 2-hydroxy-3-isopropylbenzophenone.

Intramolecular cyclodehydration of the acid **1** was effected by heating with conc. H_2SO_4 at 110 °C for 50 minutes to give the anthraquinone **5** with 80% yield.

Reaction of the acid **1** with 2-isopropylphenol or 2-isopropyl-5-methylphenol in either ether/conc. H_2SO_4 or conc. H_2SO_4 gave after 15 minutes at 0 °C or at 20 °C 3,3-diarylphthalides: **6** and **7** with 49% and 39% yield, respectively. Both compounds **6** and **7** were the only detected (TLC) phthalides in crude reaction mixtures. This method of 3-arylphthalidylation of many other phenols with 2-aroylbenzoic acids may be used in some cases instead of classical reactions involving anhydrous $ZnCl_2$ and temperatures above 105 °C, which sometimes lead to the formation of many products[20].

The acid **1** has also been treated with hydrazine and with phenylhydrazine in boiling butanol to give 4-(4-hydroxy-3-isopropylphenyl)-1(2*H*)-phthalazinone (**8**) and 4-(4-hydroxy-3-isopropylphenyl)-2-phenyl-1(2*H*)-phthalazinone (**9**), respectively, in quantitative yields. Simple preparation, purification, and a sharp melting point proved the phthalazinone **8** to be useful crystalline derivative of compound **1**.

Bromination of the acid **1** with a molar equivalent of bromine yielded the monobromo acid **10** in quantitative yield. Thus there are no doubts that the acid **1** molecule possesses only one preferential position, susceptible to electrophilic substitution. Compound **10** may also be used for identification purposes.

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Experimental Part

Melting points were determined on a Boëtius apparatus and are stated as corrected. – TLC: Standard aluminium sheets (Merck No. 5553) of 1 × 6 cm size, pre-coated with silica gel 60 of 0.2 mm thickness; chamber 1.7 cm in diameter and 8.8 cm high; volume of mobile phases 1 ml, developing distance 5 cm. Solvent systems: A toluene/dioxane /acetic acid = 11:3:1, B benzene/isopropyl alcohol = 8:1, C benzene/methanol = 5:1, D benzene/methanol = 10:1. Spots were visualized by spraying with conc. H_2SO_4. R_B values were calculated with respect to phenolphthalein (R_F = 1). – PLC: Glass plates 20 × 20 cm, covered with either silica gel 60 $PF_{254+366}$ (Merck No. 7748) or silica gel H acc. to Stahl (Merck No. 7736); layers were 1 mm thick. Identification of bands was achieved by irradiation with Emita VP-60 ultraviolet lamp (λ_{max} 366 nm). – UV/VIS: Specord UV/VIS spectrophotometer (Zeiss, Jena) in ethanol, water, and 0.01 N KOH; conc. of samples = 5 × 10^{-5} mol/l. – IR: Specord 71 IR (Zeiss, Jena) spectrophotometer in nujol (650–2800 cm^{-1}) and hexachlorobutadiene (1300–3800 cm^{-1}) mulls; correction was made with respect to λ_{max} 1027, 1603, and 2851 cm^{-1} of polystyrene. – ^{1}H-NMR: Tesla model BS 487 S (80 MHz) spectrometer; solutions in [D_6]acetone with tetramethylsilane (TMS) as internal standard (δ = 0.00 ppm) or in [D_6]DMSO with hexamethyldisiloxane (HMDS) as external standard (δ = 0.00 ppm). – MS: MX-1320 mass spectrometer (USSR), operating under

6.85 (d, J = 8.5 Hz; 5'-H), 7.23 – 7.44 (m; 2H, 2',6'-H), 7.49 – 7.71 (m; 3H, 3,4,5-H), 7.89 – 8.01 (m; 1H, 6-H), 9.36 (s; 1H, 4'-OH). – MS (70 eV): m/e = 299 (6.87%; M^+ + 1), 298 (48.83; M^+), 267 (2.78; M – CH_3O), 253 (8.85), 251 (42.97; M – CH_3O_2), 225 (6.07), 165 (7.6), 164 (12.09), 163 (100; 4'-HO-3'-$iPrC_6H_3CO^{+\cdot}$ and $CH_3OCOC_6H_4CO^{+\cdot}$), 152 (6.38), 147 (5.43), 135 (5.22; 4'-HO-3'-$iPrC_6H_3^{+\cdot}$ and $CH_3OCOC_6H_4^{+\cdot}$), 120 (9.98; 4'-$HOC_6H_3CO^{2+\cdot}$), 115 (6.61), 107 (6.99; $iPrC_5H_4^{+\cdot}$), 105 (6.59), 104 (9.08), 92 (12.99; 4'-$HOC_6H_3^{2+\cdot}$), 91 (23.64; $C_7H_7^{+\cdot}$), 79 (7.20), 77 (27.68; $C_6H_5^{+\cdot}$), 76 (6.30), 65 (7.46), 43 (4.99; $C_3H_7^{+\cdot}$), 40 (12.86), 27 (6.05), 15 (10.70; CH_3^+).

$C_{18}H_{18}O_4$ (298.3) Calcd. C 72.47 H 6.08 Found C 72.58 H 6.52

3-Acetoxy-3-(4-acetoxy-3-isopropylphenyl)phthalide (**3**): A mixture of **1** (2.0 g, 7.0345 mmol), Ac_2O (50 ml, ca. 0.53 mol), and freshly fused, anhydrous AcONa (5.0 g) was heated under reflux for 8 h. Cooling, followed by pouring of the reaction mixture onto ice-water (300 g) gave a brownish mass of diacetate **3** (2.12 g, 82%). Purification by PLC (silica gel 60 $PF_{254+366}$, mobile phase benzene), elution of the nonfluorescent (UV 366 nm) band with ether and evaporation of the solvent deposited TLC-pure **3**. Crystallization from ether, followed by drying under vacuum (ca. 1 torr) at 50 °C gave colourless sample of **3**, m. p. 100.3 – 101.9 °C. – TLC: R_F(B) 0.69 (conc. H_2SO_4 → yellow), R_B 1.44. – UV (EtOH): λ_{max} (lg ε) = 274 (3.31), λ_{min} = 262 nm (3.26). – IR (N, HCB): 2964 w, 2866 w (iPr), 1768 s (γ-lactone), 1762 s (acetate), 1597 w, 1481 w, 1462 w, 1410 w, 1362 w, 1331 w, 1261 m, 1202 s, 1191 s, 1175 s, 1087 m, 1074 m, 1032 w, 995 m, 954 m, 905 w, 896 w, 887 w, 790 w, 761 m, 725 m, 683 cm^{-1} w. – ^1H NMR ([D_6]acetone/TMS int.): δ = 1.14 (d, J = 7 Hz; 3H, $(CH_3)CHCH_3$), 1.17 (d, J = 7 Hz; 3H, $(CH_3)CHCH_3$), 2.11 (s; 3H, 3-$OCOCH_3$), 2.27 (s; 3H, 4'-$OCOCH_3$), 3.07 (sept, J = 6.5 Hz; 1H, $CH(CH_3)_2$), 7.08 (d, J = 8.5 Hz; 1H, 5'-H), 7.37 – 7.79 (m; 5H, 4,5,6,2',6'-H), 7.80 – 7.97 (m; 1H, 7-H).

$C_{21}H_{20}O_6$ (368.4) Calcd. C 68.47 H 5.47 Found C 68.80 H 5.25

4-Hydroxy-3-isopropylbenzophenone (**4**): Decarboxylation of **1** was carried out according to *Hubacher*[21]. A solution of **1** (1.0 g, 3.5172 mol) in freshly redistilled quinoline (5 ml) was heated under reflux. Then $Cu(OAc)_2 \cdot H_2O$ (50 mg) was added and heating was continued for 45 min. After cooling the reaction mixture was diluted with ether (30 ml) and filtered. The filtrate was extracted with 3 N HCl (5 × 15 ml), washed with water and dried over anhydrous $MgSO_4$. Evaporation of the solvent afforded a crude sample of ketone **4**. Yield 0.82 g (97%), m. p. 131.0 – 134.5 °C. This was extracted with 5% NaOH, filtered, and the filtrate was acidified with dilute HCl giving **4** (0.71 g, 84%). Vacuum (ca. 1 torr) sublimation at 160 °C, followed by crystallization from methanol afforded TLC-pure, colourless crystals of **4**, m. p. 134.1 – 135.2 °C. – TLC: R_F(B) 0.66 (conc. H_2SO_4 → yellow), R_B 1.29. – UV/VIS (EtOH): λ_{max} (lg ε) = 204 (4.49), 238 (4.12), 256 (4.18), λ_{min} = 223 (4.07), 358 nm (4.33); (0.01 N KOH) λ_{max} (lg ε) = 209 (4.33), 251 (4.07), 358 (4.33), λ_{min} = 228 (3.25), 288 nm (3.18). – IR (N, HCB): 3175 sb (OH), 2953 m, 2865 m, 2805 w (iPr), 1629 s (C=O), 1601 s, 1594 s, 1582 s, 1570 s, 1506 m (aromat.), 1470 w, 1447 m, 1384 m, 1352 w, 1348 w, 1328 s, 1312 s, 1302 s, 1284 s, 1238 m, 1166 m, 1117 w, 1081 m, 982 m, 908 m, 833 s, 799 m, 757 w, 726 s, 703 m, 689 w, 670 cm^{-1} w. – IR (1,2-dichloroethane, saturated solution, 1700 – 2000 cm^{-1} region): 1722, 1767, 1815, 1896, 1958 cm^{-1}. – ^1H NMR ([D_6]acetone/TMS int.): δ = 1.23 (d, J = 7 Hz; 6H, $CH(CH_3)_2$), 3.34 (sept, J = 6.5 Hz; 1H, $CH(CH_3)_2$), 6.94 (d, J = 8 Hz; 1H, 5-H), 7.39 – 7.76 (m; 7H, 2,6,2',3',4',5',6'-H).

$C_{16}H_{16}O_2$ (240.3) Calcd. C 79.97 H 6.71 Found C 79.89 H 7.15

2-Hydroxy-3-isopropylanthraquinone (**5**): A solution of **1** (1.04 g, 3.6558 mmol) in conc. (96%) H_2SO_4 (40 ml) was heated at 110 °C for 50 min. The reddish-brown reaction mixture was poured onto water (300 ml). The yellow, amorphous precipitate was coagulated by heating to the boiling point and then filtered off and washed with water. This gave a lemon-yellow, crude mass of compound **5** (0.78 g, 80%). Column chromatography on silica gel 40 (70 – 230 mesh, Merck

No. 10180, mobile phase C) gave TLC-pure **5**. Crystallization from dilute methanol afforded yellow crystals of **5**, m. p. 256.2–257.0°C. – TLC: R_F(B) 0.68 (conc. H_2SO_4 → reddish), R_B 1.45. – UV (EtOH): λ_{max} (lg ε) = 205 (4.38), 239 (4.25), 245 (4.25), 278 (4.63), 385.5 (3.44), λ_{min} = 227 (4.13), 243 (4.23), 253 (4.06), 360 nm (3.39). – UV/VIS (0.01 N KOH): λ_{max} (lg ε) = 207 (4.33), 249 (4.42), 315 (4.47), 486 (3.66), λ_{min} = 218 (3.73), 273 (3.91), 387 nm (3.10). – IR (N, HCB): 3371 s (OH), 3061 w, 3009 w (aromat.), 2961 w, 2859 w (iPr), 1666 s (9-C=O), 1648 m (10-C=O), 1579 s, 1569 s, 1544 w, 1503 w (aromat.), 1466 w, 1449 w, 1423 w, 1328 s, 1303 s, 1265 s, 1247 s, 1175 w, 1131 w, 1099 w, 1045 w, 960 w, 910 w, 883 w, 855 w, 753 m, 730 w, 708 s, 658 cm^{-1} w. – ^1H NMR ([D_6]DMSO/HMDS ext.): δ = 1.42 (d, J = 7 Hz; 6H, CH(CH_3)$_2$), 3.46 (sept, J = 7 Hz; 1H, CH(CH$_3$)$_2$), 7.72 (s; 1H, 1-H), 7.96–8.46 (m; 5H, 4,5,6,7,8-H).

$C_{17}H_{14}O_3$ (266.3) Calcd. C 76.68 H 5.30 Found C 76.44 H 5.13

3,3-Bis(4-hydroxy-3-isopropylphenyl)phthalide (**6**): Conc. (96%) H_2SO_4 (25 ml) was added dropwise during 5 min to a stirred, ice-cooled solution of **1** (1.15 g, 4.0448 mmol) and 2-isopropylphenol (1.6 g, 11.7478 mmol) in ether (40 ml). The colour changed from a light orange-brown to a deep reddish-orange. After additional stirring for 15 min, the reaction mixture was poured onto water (200 ml). The organic layer was washed with water and then extracted with 5% $NaHCO_3$ aq. (4 × 20 ml). The combined alkaline extracts were acidified with dilute HCl, giving unreacted **1** (0.25 g). The ethereal solution was washed with water and the solvent was evaporated. The resulting solid was subjected to a steam-distillation until the phenolic odour of 2-isopropylphenol disappeared. Non-volatile material was then extracted with 5% NaOH, filtered and the filtrate was acidified with dilute (1:1) HCl. This gave a crude sample of compound **6**, yield 1.23 g (76%). Further purification was effected by PLC (silica gel H acc. to Stahl, mobile phase D). Elution of "the phthalide band" with ether and evaporation of the solvent left a TLC-pure sample of **6**, yield 0.79 g (49%). Several crystallizations from dilute methanol gave colourless crystals of **6**, m. p. 158.1–159.2°C. – TLC: R_F(B) 0.54 (conc. H_2SO_4 → red colour), R_B 1.23. – UV (EtOH): λ_{max} (lg ε) = 203 (4.99), 278 (3.78), λ_{min} = 262 nm (3.63). – UV/VIS (0.01 N KOH): λ_{max} (lg ε) = 209 (4.56), 284 (3.82), 382 (3.98), 571 (4.77), λ_{min} = 260 (3.75), 335 (3.53), 429 nm (3.11). – IR (N, HCB): 3422 m (OH), 3202 mb (OH), 3022 w (aromat.), 2975 m, 2867 w (iPr), 1726 s (γ-lactone), 1604 w, 1498 m (aromat.), 1466 m, 1428 m, 1416 m, 1375 w, 1361 w, 1332 m, 1288 m, 1264 s, 1227 m, 1191 w, 1173 m, 1160 m, 1124 w, 1032 w, 993 w, 983 w, 872 w, 867 w, 855 w, 793 w, 783 w, 763 w, 742 m, 713 cm^{-1} w. – ^1H NMR ([D_6]acetone/TMS int.): δ = 1.12 (d, J = 6.5 Hz; 12H, 3'- and 3''-CH(CH_3)$_2$, 3.25 (sept. J = 7 Hz; 2H, 3'- and 3''-CH(CH$_3$)$_2$), 6.72–7.01 (m; 4H, 5',6',5'',6''-H), 7.15 (d, J = 2 Hz; 2',2''-H), 7.45–7.92 (m; 4H, 4,5,6,7-H), 8.58 (s; ca. 0.6H, 4'- and 4''-OH).

$C_{26}H_{26}O_4$ (402.5) Calcd. C 77.59 H 6.51 Found C 77.59 H 7.06

3-(4-Hydroxy-5-isopropyl-2-methylphenyl)-3-(4-hydroxy-3-isopropylphenyl)phthalide (**7**): A mixture of **1** (1.0 g, 3.5172 mmol) and conc. (96%) H_2SO_4 (34 ml) was stirred at room temperature for 16 min. Then a finely pulverized 2-isopropyl-5-methylphenol (thymol) (1.5 g, 10.2606 mmol) was added and the resulting mixture was stirred for 15 min. The reaction mixture was then poured onto water (300 ml). The separated oily mass was subjected to a steam-distillation until the thymolic odour disappeared. The non-volatile solid was filtered off and extracted with hot, 5% NaOH aq. The resulting extract was acidified with dilute (1:1) HCl. This gave an amorphous, almost colourless sample of compound **7**, yield 0.67 g (39%). Further purification by PLC (silica gel 60 $PF_{254+366}$, mobile phase C), followed by crystallization from dilute methanol, afforded TLC-pure, colourless crystals of **7**, m. p. 263.8–264.8°C. – TLC: R_F(B) 0.60 (conc. H_2SO_4 → red), R_B 1.15. – UV (EtOH): λ_{max} (lg ε) = 204 (4.98), 279 (3.74), λ_{min} = 263 nm (3.57). – UV/VIS (0.01 N KOH): λ_{max} (lg ε) = 209 (4.60), 301 (4.10), 389 (4.04), 582 (4.60), λ_{min} = 260 (3.79), 332 (3.61), 443 nm (3.41). – IR (N, HCB): 3460 m (OH), 3200 mb (OH), 2972 m,

2930 w, 2868 w (Me and iPr), 1734 s (γ-lactone), 1614 w, 1597 w, 1511 m, 1505 m (aromat.), 1471 m, 1430 s, 1383 w, 1363 w, 1343 m, 1294 m, 1275 s, 1265 s, 1255 m, 1174 m, 1127 m, 1108 w, 1098 w, 1092 w, 1084 w, 1047 w, 936 w, 899 w, 864 w, 821 m, 748 m, 712 w, 698 w, 676 cm^{-1} w. – ^1H NMR ([D_6]acetone/TMS int.): δ = 0.94 – 1.18 (m; 12H, 5′- and 3″-$CH(CH_3)_2$), 1.98 (s; 3H, 2′-CH_3), 2.99 – 3.40 (m; 2H, 5′- and 3″-$CH(CH_3)_2$), 6.72 (s; 1H, 3′-H), 6.81 – 7.07 (m; 4H, 6′,2″,5″,6″-H), 7.46 – 7.94 (m; 4H, 4,5,6,7-H), 8.49 (s; ca. 0.7H, Ar^1OH), 10.37 (s; 1H, Ar^2OH).

$C_{27}H_{28}O_4$ (416.5) Calcd. C 77.86 H 6.78 Found C 77.83 H 6.73

4-(4-Hydroxy-3-isopropylphenyl)-1(2H)-phthalazinone (**8**): Hydrazine hydrate (0.1 ml, 2.0575 mmol) was added to a solution of **1** (0.5 g, 1.7586 mmol) in butanol (15 ml) and the mixture was heated under reflux for 2 h. Evaporation in vacuo of volatile components afforded a crude, crystalline sample of compound **8** (0.49 g, 99%). The previously stated[1] work-up procedure, followed by crystallization from dilute ethanol yielded TLC-pure, colourless crystals of **8**, m. p. 274.8 – 275.6 °C. – TLC: R_F(B) 0.62 (conc. H_2SO_4 → yellow), R_B 1.29. – UV (EtOH): λ_{max} (lg ε) = 208 (4.70), 306 (3.98), λ_{min} = 280 nm (3.90). – IR (N, HCB): 3217 sb (OH), 2957 w, 2857 w (iPr), 1639 s (C=O), 1601 s, 1576 m, 1537 w, 1505 w, 1481 w (aromat.), 1461 m, 1431 m, 1387 m, 1352 m, 1330 m, 1302 w, 1284 m, 1243 m, 1185 w, 1161 m, 1119 w, 1074 w, 846 m, 823 w, 799 w, 794 w, 781 m, 765 w, 723 w, 692 w, 664 cm^{-1} w. – ^1H NMR ([D_6]DMSO/HMDS ext.): δ = 1.37 (d, J = 7 Hz; 6H, $(CH_3)_2CH$), 3.44 (sept, J = 7.5 Hz; 1H, $CH(CH_3)_2$), 7.13 (d, J = 10.5 Hz; 1H, 5′-H), 7.32 – 7.49 (m; 2H, 2′,6′-H), 7.81 – 8.11 (m; 3H, 5,6,7-H), 8.39 – 8.57 (m; 1H, 8-H), 9.91 (s; ca. 0.23H, 4′-OH), 12.92 (s; ca. 0.23H, 2-H).

$C_{17}H_{16}N_2O_2$ (280.3) Calcd. C 72.84 H 5.75 N 9.99 Found C 72.90 H 5.52 N 10.22

4-(4-Hydroxy-3-isopropylphenyl)-2-phenyl-1(2H)-phthalazinone (**9**): Phenylhydrazine (99%, 0.21 ml, 2.1089 mmol) was added to a solution of **1** (0.5 g, 1.7586 mmol) in butanol (15 ml) and the mixture was refluxed for 2 h. Evaporation of volatile components afforded 0.625 g (99.7%) of crude, partly crystalline, brownish phthalazinone **9**. The solid was washed with methanol and then crystallized from dilute ethanol, giving TLC-pure, colourless crystals of **9**. After drying in vacuo at 150 °C for 2 days the crystals melted at 224.0 – 225 °C, then solidified and remelted at 228.0 – 230.0 °C. – TLC: R_F(B) 0.56 (conc. H_2SO_4 → yellow), R_B 1.27. – UV (EtOH): λ_{max} (lg ε) = 207 (4.68), 312.5 (4.06), λ_{min} = 282 nm (3.91). – IR (N, HCB): 3264 sb (OH), 2967 w, 2817 w (iPr), 1641 s (C=O), 1631 (C=N), 1604 m, 1572 m, 1535 w, 1501 m, 1490 m (aromat.), 1449 w, 1422 w, 1363 w, 1339 m, 1328 s, 1302 s, 1273 m, 1229 m, 1174 m, 1133 m, 1074 w, 1026 w, 990 w, 891 w, 863 w, 827 m, 782 m, 775 w, 756 m, 730 m, 716 m, 688 s, 659 cm^{-1} m. – ^1H NMR: ([D_6]DMSO/HMDS ext.): δ = 1.36 (d, J = 6.5 Hz; 6H, $CH(CH_3)_2$), 3.44 (sept. J = 7 Hz; 1H, $CH(CH_3)_2$), 7.14 (d, J = 8 Hz; 1H, 5′-H), 7.40 – 8.17 (m; 10H, 5,6,7,2′,6′,2″,3″,4″,5″,6″-H), 8.44 – 8.67 (m; 1H, 8-H), 9.96 (s; ca. 0.26H, 4′-OH).

$C_{23}H_{20}N_2O_2$ (356.4) Calcd. C 77.51 H 5.66 N 7.86 Found C 77.63 H 5.57 N 7.65

2-(3-Bromo-4-hydroxy-5-isopropylbenzoyl)benzoic Acid (**10**): A solution of **1** (0.87 g, 3.06 mmol) in dilute (3:1) acetic acid was treated with bromine (0.527 g, 3.3 mmol). The mixture was heated to the boiling point and then left overnight. Concentration, followed by addition of water (100 ml) gave 1.10 g (99%) of brownish acid **10**. Crystallization from dilute ethanol afforded TLC-pure, colourless crystals of **10**, m. p. 201.7 – 202.8 °C. – TLC: R_F(A) 0.48 (conc. H_2SO_4 → yellow), R_B 1.33. – UV(EtOH): λ_{max} (lg ε) = 215 (4.51), 287 (4.15), λ_{min} = 254 nm (3.75). – UV/VIS (0.01 N KOH): λ_{max} (lg ε) = 211 (4.46), 255 (4.06), 351 (4.38), λ_{min} = 243 (4.03), 286 nm (3.69). – IR (N, HCB): 3419 m (OH), 3084 w (aromat.), 2982 m, 2934 w, 2879 m (iPr), 2690 mb, 2581 mb, 2549 mb (COOH), 1691 s (COOH), 1660 s (C=O), 1586 s (aromat.), 1471 m, 1464 m, 1456 m, 1424 m; 1385 w, 1365 w (iPr), 1299 s (OH), 1266 m, 1252 s, 1204 m, 1157 s, 1118 m,

1083 m, 992 m; 937 mb (COOH), 903 w, 813 w, 793 m, 770 m, 763 m, 713 m, 671 cm^{-1} m. – ^{1}H-NMR ([D$_6$]acetone/TMS int.): δ = 1.17 (d, *J* = 7 Hz; 6H, CH(CH_3)$_2$), 3.33 (sept, *J* = 7 Hz, 1H, CH(CH$_3$)$_2$), 7.34 – 7.81 (m; 5H, 3,4,5,2',6'-H), 8.01 – 8.12 (m; 1H, 6-H).

$C_{17}H_{15}BrO_4$ (363.2) Calcd. C 56.22 H 4.15 Br 22.00 Found C 56.30 H 4.60 Br 22.33

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[60/82]