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# SYNTHESIS OF 2-(2-HYDROXYBENZYL)PHTHALAZIN-1(2H)-ONES

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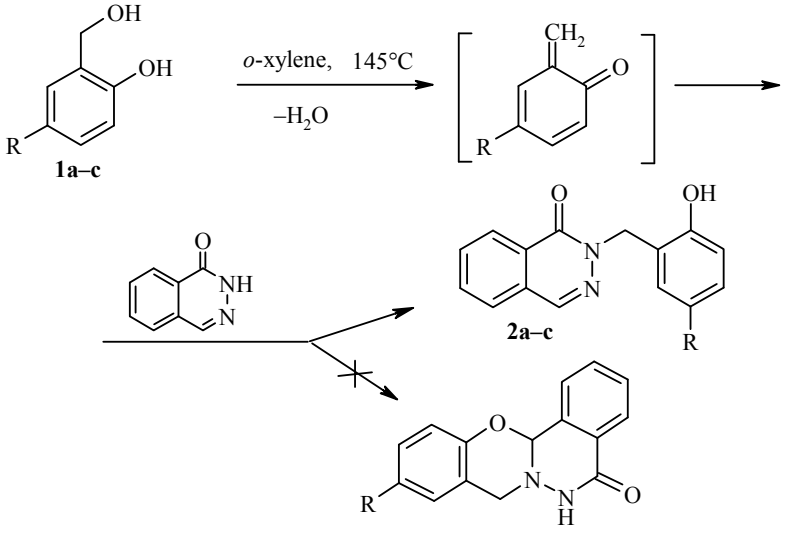
It is known that reaction of naphthalene series *o*-methylenequinones, generated *in situ* from 1-dimethylaminomethyl-2-naphthol, and phthalazin-1(2H)-ones form the Diels-Alder heteroreaction adducts 5,15*a*-dihydro-6H,8H-naphtho[1',2':5,6]oxazino[2,3-*a*]phthalazin-5-ones [1]. At the same time, in the case of *o*-methylenequinones generated from the salicyl alcohols **1a-c**, there are obtained, rather than the expected 6H,8H-phthalazino[1,2-*b*][1,3]benzoxazines, the products of Michael 1,4-addition, i.e. the 2-(2-hydroxybenzyl)phthalazin-1(2H)-ones **2a-c**.




**a** R = H, **b** R = Br, **c** R = COMe

The IR spectra of compounds **2a-c** show the presence of carbonyl stretching bands for the heterocycle fragments in the range 1628-1632 $cm^{-1}$. The hydroxyl group corresponds to a broad absorption band in the range 2800-3300 $cm^{-1}$. The retention of intense C=N stretching bands at 1582 $cm^{-1}$ also provides an evidence about the

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formation of acyclic compounds. The $^1$H NMR spectra show the hydroxyl group proton at 9.52-10.32 ppm and the proton on the carbon of the azomethine fragment as a singlet at 8.24-8.29 ppm [2].

IR spectra were recorded on a Shimadzu FTIR-8400S spectrometer for KBr tablets. $^1$H NMR spectra were obtained on a Bruker AM-400 spectrometer (400 MHz) using TMS as internal standard and mass spectra on a Finnigan Trace DSQ instrument with ionization energy 70 eV. Elemental analysis was carried out on a Euro Vector EA-3000 CHNS autoanalyzer.

**2-(2-Hydroxybenzyl)phthalazin-1(2H)-one (2a)**. A mixture of salicyl alcohol **1a** (1 g, 8.1 mmol) and phthalazin-1(2H)-one (1.18 g, 8.1 mmol) in *o*-xylene (30 ml) was refluxed with stirring for 40 h. Solvent was removed *in vacuo*, the residue was purified by column chromatography on silica gel (eluent dichloromethane), and then recrystallized from methanol. Compound **2a** (0.93 g, 46%) was obtained as colorless crystals; mp 157-158ºC. IR spectrum, ν, cm$^{-1}$: 3300-2800 (OH), 1628 (C=O), 1582 (C=N), 1485, 1454, 1439, 1373, 1331, 1242, 1180, 1088, 764, 733, 687. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 5.39 (2H, s, $CH_2$); 6.89 (1H, dd, *J* = 8.07, 7.34, H-5'); 7.00 (1H, d, *J* = 8.80, H-3'); 7.25 (1H, t, *J* = 8.07, H-4'); 7.49 (1H, d, *J* = 8.80, H-6'); 7.68 (1H, d, *J* = 8.07, H-5); 7.77-7.84 (2H, m, H-6,7); 8.24 (1H, s, H-4); 8.42 (1H, d, *J* = 8.07, H-8); 9.52 (1H, s, OH). Mass spectrum (EI), *m/z* ($I_{rel}$, %): 252 $[M]^+$ (100), 235 $[M\text{-}OH]^+$ (35), 207 $[M\text{-}OH\text{-}CO]^+$ (17), 146 $[C_8H_6N_2O]^+$ (53), 132 $[C_8H_6NO]^+$ (84), 121 $[C_7H_7NO]^+$ (97), 118 $[C_7H_6N_2]^+$ (20), 107 $[C_7H_7O]^+$ (25), 89 $[C_7H_6]^+$ (72), 77 $[C_6H_5]^+$ (44). Found, %: C 71.29; H 4.88; N 10.98. $C_{15}H_{12}N_2O_2$. Calculated, %: C 71.42; H 4.79; N 11.10.

**2-(5-Bromo-2-hydroxybenzyl)phthalazin-1(2H)-one (2b)** was prepared similarly to compound **2a** from 5-bromosalicyl alcohol (**1b**) (1 g, 4.9 mmol) and phthalazin-1(2H)-one (0.72 g, 4.9 mmol) in *o*-xylene (30 ml) to give colorless crystals (1.06 g, 65%); mp 186-187ºC (toluene). IR spectrum, ν, cm$^{-1}$: 3300-2800 (OH), 1628 (C=O), 1605 (C=C), 1582 (C=N), 1481, 1443, 1373, 1331, 1242, 1169, 814, 764, 687. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 5.33 (2H, s, $CH_2$); 6.86 (1H, d, *J* = 8.07, H-3'); 7.31 (1H, d, *J* = 8.07, H-4'); 7.60 (1H, s, H-6'); 7.75-8.03 (3H, m, H-5,6,7); 8.29 (1H, s, H-4); 8.46 (1H, d, *J* =7.34, H-8); 9.65 (1H, s, OH). Mass spectrum (EI, for $^{79}$Br isotope), *m/z* ($I_{rel}$, %): 330 $[M]^+$ (8), 313 $[M\text{-}OH]^+$ (3), 285 $[M\text{-}OH\text{-}CO]^+$ (2), 199 $[C_7H_6BrNO]^+$ (27), 146 $[C_8H_6N_2O]^+$ (26), 132 $[C_8H_6NO]^+$ (100), 118 $[C_7H_6N_2]^+$ (18), 104 (21), 89 $[C_7H_6]^+$ (68), 77 $[C_6H_5]^+$ (52). Found, %: C 54.52; H 3.30; N 8.41. $C_{15}H_{11}BrN_2O_2$. Calculated, %: C 54.40; H 3.35; N 8.46.

**2-(5-Acetyl-2-hydroxybenzyl)phthalazin-1(2H)-one (2c)** was prepared similarly to compound **2a** from 5-acetylsalicyl alcohol (**1c**) (1 g, 6 mmol) and phthalazin-1(2H)-one (0.88 g, 6 mmol) in *o*-xylene (30 ml) to give colorless crystals (1.04 g, 59%); mp 158-159ºC (ethanol). IR spectrum, ν, cm$^{-1}$: 3300-2800 (OH), 1674 (C=O acetyl), 1632 (C=O), 1601 (C=C), 1582 (C=N), 1427, 1362, 1327, 1288, 1238, 1107, 841, 759, 690. $^1$H NMR spectrum, δ, ppm (*J*, Hz): 2.53 (3H, s, $CH_3$); 5.37 (2H, s, $CH_2$); 6.96 (1H, d, *J* = 8.24, H-3'); 7.71 (1H, dd, *J* = 7.33, *J* = 0.92, H-5); 7.79 (1H, td, *J* = 7.33, *J* = 1.83, H-7); 7.82 (1H, td, *J* = 7.33, *J* = 1.83, H-6); 7.84 (1H, dd, *J* = 8.24, *J* = 2.29, H-4'); 8.10 (1H, d, *J* = 2.29, H-6'); 8.26 (1H, s, H-4); 8.40 (1H, dd, *J* = 7.79, *J* = 0.92, H-8); 10.32 (1H, s, OH). Mass spectrum (EI), *m/z* ($I_{rel}$, %): 294 $[M]^+$ (22), 277 $[M\text{-}OH]^+$ (4), 249 $[M\text{-}OH\text{-}CO]^+$ (4), 163 $[C_9H_9NO_2]^+$ (40), 148 $[C_9H_8O_2]^+$ (36), 146 $[C_8H_6N_2O]^+$ (22), 133 (38), 132 $[C_8H_6NO]^+$ (100), 118 $[C_7H_6N_2]^+$ (15), 105 (22), 89 $[C_7H_6]^+$ (60), 77 $[C_6H_6]^+$ (47). Found, %: C 69.46; H 4.66; N 9.42. $C_{17}H_{14}N_2O_3$. Calculated, %: C 69.38; H 4.79; N 9.52.

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