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DI-4(3H)-QUINAZOLINON-2-YL DERIVATIVES FROM THE DIACID CHLORIDES OF PINIC AND *sym*-HOMOPINIC ACIDS

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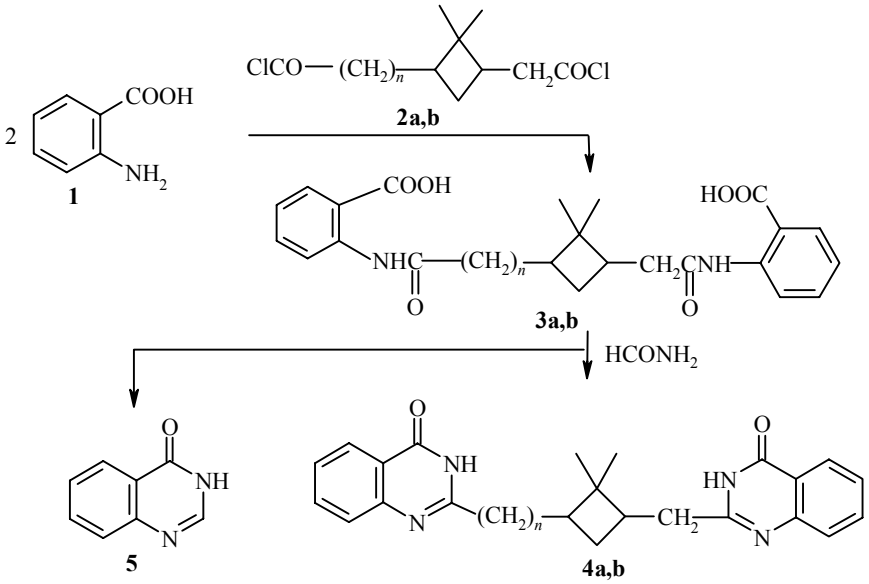
The corresponding diamides have been synthesized by the interaction of the diacid chlorides of cis-2,2-dimethyl-3-carboxycyclobutaneacetic acid (pinic acid) and cis-2,2-dimethylcyclobutane-1,3-diacetic acid (sym-homopinic acid) with two equivalents of anthranilic acid. Treatment of the diamides with formamide gave 2,2-dimethyl-1-[4(3H)-quinazolinon-2-yl]methyl-3-[4(3H)-quinazolinon-2-yl]cyclobutane and 2,2-dimethyl-1,3-di[4(3H)-quinazolinon-2-ylmethyl]cyclobutane respectively.

Keywords: anthranilic acid amides, di-4(3H)-quinazolinon-2-yl derivatives on the basis of pinic and *sym*-homopinic acids.

In continuation of the work [1] on the synthesis of 4(3H)-quinazolinones with a cyclobutylmethyl substituting group in position 2, we have obtained the corresponding diamides **3a,b** by reacting anthranilic acid **1** with the diacid chlorides of *cis*-2,2-dimethyl-3-carboxycyclobutaneacetic (pinic, **2a**) and *cis*-2,2-dimethyl-cyclobutane-1,3-diacetic (*sym*-homopinic **2b**) acids. Heating the amides with formamide (molar ratio compound **3**:$HCONH_2$ 1:7 to 1:9) leads to the 4(3H)-quinazolinones **4a,b** with 4(3H)-quinazolinone **5** as a byproduct.



2–4 a $n = 0$, **b** $n = 1$

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The structures of the compounds synthesized were confirmed by data of IR and ^{1}H NMR spectra.

EXPERIMENTAL

The IR spectra were obtained on a Specord IR 75 spectrometer for suspensions in nujol (1500-1800 cm^{-1}) and in hexachlorobutadiene (2000-3600 cm^{-1}). The frequencies of the stretching vibrations of C–H bonds in the range 2800-3050 cm^{-1} are not indicated. The ^{1}H NMR spectra were taken in DMSO-d_6 on a Bruker WH 90/DS (90 Hz) spectrometer, internal standard was TMS. A check on the purity of products was effected by TLC on Silufol UV 254 plates in the system $CHCl_3$–C_2H_5OH, 9 : 1. Visualization was in UV light or with chlorine and subsequent treatment with KI–benzidine reagent. The initial acid chlorides **2a** and **2b** were obtained by the known procedure of [2, 3]. The methods of [3, 4] were used for the synthesis of the diamides **3a** and **3b**.

Pinic Acid Dianthranilamide (3a). A solution of diacid chloride **2a** (5.12 g, 22.9 mmol) in absolute benzene or dioxane (30 ml) was added slowly with stirring to a solution of anthranilic acid **1** (6.29 g, 45.9 mmol) and triethylamine (6.42 ml, 45.8 mmol) in absolute benzene (dioxane) (100 ml). The reaction mixture was stirred for a further 3 h, the solid was then filtered off, and washed with benzene or dioxane. The filtrate was evaporated on a rotary evaporator with a water-jet pump vacuum, and the residue was recrystallized from acetonitrile. Crystalline diamide **3a** (5.38 g, 55.2%) was obtained; mp 216-217°C. IR spectrum, ν, cm^{-1}: 1697, 1665, 1605, 1583, 1533; 3110, 2600. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 0.91 (3H, s, β-CH_3); 1.27 (3H, s, α-CH_3); 1.66-2.52 (5H, m, $2CH_2$ and CH); 2.83 (1H, t, *J* = 7.0, CH); 7.06 (2H, t, *J* = 8.0, H_{arom}); 7.52 (2H, dt, *J* = 8.0, *J* = 1.5, H_{arom}); 7.90 (2H, dt, *J* = 8.0, *J* = 1.5, H_{arom}); 8.46 (1H, d, *J* = 8.0, H_{arom}); 8.54 (1H, d, *J* = 8.0, H_{arom}); 11.01 (2H, br s, NH); 11.20 (2H, br. s, 2OH). Found, %: C 64.89; H 5.62; N 6.54. $C_{23}H_{24}N_2O_6$. Calculated, %: C 65.08; H 5.70; N 6.60.

***sym*-Homopinic Acid Dianthranilamide (3b).** Compound **3b** was obtained analogously to diamide **3a**. Yield 52.7%; mp 226-228°C (CH_3CN). IR spectrum, ν, cm^{-1}: 1681, 1637, 1599, 1573, 1513; 3320, 2530-2600. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 0.86 (3H, s, β-CH_3); 1.05 (3H, s, α-CH_3); 1.48-2.52 (8H, m, $3CH_2$ and 2CH); 7.11 (2H, t, *J* = 7.0, H_{arom}); 7.51 (2H, dt, *J* = 7.0, *J* = 1.5, H_{arom}); 7.99 (2H, dd, *J* = 7.0, *J* = 1.5, H_{arom}); 8.49 (2H, d, *J* = 7.0, H_{arom}); 8.90 (2H, br. s, NH); 10.89 (2H, br. s, 2OH). Found, %: C 65.61; H 5.89; N 6.35. $C_{24}H_{26}N_2O_6$. Calculated, %: C 65.74; H 5.98; N 6.39.

2,2-Dimethyl-1-[4-(3H)-quinazolinon-2-yl]methyl-3-[4(3H)-quinazolinon-2-yl]cyclobutane (4a). A mixture of diamide **3a** (1.62 g, 3.58 mmol) and formamide (1.5 g, 33.5 mmol) in a flask fitted with a reflux condenser was maintained for 2 h at 175±3°C. The reaction mixture was then cooled, and suspended in water (30 ml) containing sodium bicarbonate (0.50 g, 5.95 mmol). The solid was filtered off, washed with water (3 × 20 ml), dried in the air, and recrystallized from a DMF–H_2O, 3:1 mixture. Compound **4a** (0.95 g, 68.8%) was obtained having mp 306-307°C (decomp.). IR spectrum, ν, cm^{-1}: 1672, 1610, 1564, 1500; 3170, 3120. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm, *J* (Hz): 0.85 (3H, s, β-CH_3); 1.27 (3H, s, α-CH_3); 2.03-2.64 (5H, m, $2CH_2$ and 1CH); 3.14 (1H, t, *J* = 7.0, CH); 7.41-8.16 (8H, m, H_{arom}); 12.01 (1H, s, NH); 12.25 (1H, br. s, NH). Found, %: C 71.59; H 5.65; N 14.39. $C_{23}H_{22}N_4O_2$. Calculated, %: C 71.48; H 5.74; N 14.50.

2,2-Dimethyl-1,3-di[4(3H)-quinazolinon-2-ylmethyl]cyclobutane (4b). Compound **4b** was synthesized analogously to product **4a**. Yield 64.5%; mp 290-292°C (DMF–H_2O, 2:1). IR spectrum, ν, cm^{-1}: 1674, 1612, 1562; 3175, 3123. ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.03 (3H, s, β-CH_3); 1.06 (3H, s, α-CH_3); 1.85-2.89 (8H, m, $3CH_2$, 2CH); 7.38-8.14 (8H, m, H_{arom}); 12.16 (2H, br. s, 2NH). Found, %: C 71.81; H 6.15; N 14.12. $C_{24}H_{24}N_4O_2$. Calculated, %: C 71.98; H 6.04; N 13.99.

4(3H)-Quinazolinone (5). The aqueous solution after isolating compound **4a** was acidified to pH 5-6 with hydrochloric acid and extracted with chloroform (3 × 20 ml). The extract was dried over magnesium sulfate. The solvent was removed in a water pump vacuum, and the residue was recrystallized from acetonitrile. Quinazolinone **5** (0.16 g, 15.3 %) was obtained having mp 210-212°C. A mixing test of product **5** with a known specimen of 4(3H)-quinazolinone [5] gave no depression of melting point. Quinazolinone **5** (0.20 g, 20.3%) was obtained analogously from the aqueous solution after isolating compound **4b**.

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