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Chemical structures I-III

Figure 1: Chemical structures I-III

Abstract

Full Text

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2-PHENYL-4-AZABENZ-(*f*)-INDANDIONE-1,3–A NEW REPRESENTATIVE OF HETEROCYCLIC ANALOGS OF INDANDIONE-1,3

Recently, the attention of chemists has been increasingly attracted by compounds containing a cyclopentanedione-1,3 grouping in the molecule. In particular, derivatives of indandione-1,3 have shown themselves to be new analytical reagents, blood anticoagulants, rodenticides, and narcotics and sleeping agents of a new type (1).

To elucidate the relationship between the structure of indandione-1,3 derivatives and their biological activity, and to obtain compounds of a new type, we undertook a study of the possibilities for synthesizing derivatives of indandione-1,3 containing a heteroatom in the ring—in particular, azaindandiones-1,3. The literature contains several fragmentary data on azaindandiones-1,3. Zincke and Wünschheimer (2), by decomposition of 1,3,4-triketo-2,2-dichloroquinoline, obtained 2-chloro-4-azaindandione-1,3. Using the Claisen condensation of the dimethyl ester of quinoline acid with methyl acetate, Bittner (3) synthesized the methyl ester of 4-azaindandione-1,3-carboxylic-2 acid. Fels (4), by rearrangement of benzalcinhomeride, obtained 2-phenyl-5-azaindandione-1,3, and the formation of the N-oxide of 2-methyl-4-azaindandione-1,3 upon treatment of nicotinic acid N-oxide with propionic anhydride was noted by Beinh and Saxton (5).

We tested the synthesis of 2-arylazaindandiones-1,3 using anhydrides of heterocyclic *o*-dicarboxylic acids and found it to be of little promise because of the thermal instability of such anhydrides. We chose another route of synthesis using lactones (6–10). As the starting compound we used the lactone of 2-oxymethylquinolinecarboxylic-3 acid (I), obtained from *o*-aminobenzaldehyde and tetronic acid (11).

Lactone I condenses with benzaldehyde on boiling in acetic anhydride with formation of 1-keto-3-benzalfuro-(3,4-*b*)-quinoline (II). Compound II, with structural formulas IV–VII

Figure 2: structural formulas IV–VII

sodium methylate, rearranges into the sodium salt of 2-phenyl-4-azabenz-(*f*)-indandione-1,3 (III), which under the action of acids is converted into 2-phenyl-4-azabenz-indandione-1,3 (2-phenyl-β-quinindandione-1,3). This compound is also formed in the condensation of I with benzaldehyde by the Shapiro method ([9], [10]), but in lower yield. 2-Phenyl-4-azabenz-(*f*)-indandione-1,3 (IV) is sparingly soluble in organic solvents, with the exception of dimethylformamide, is insoluble in water, and has a high melting point. In the infrared region of the spectrum it is characterized by intense absorption at 1538 and 1553 cm^{-1}. On the basis of these data, we consider the existence of 2-phenyl-4-azabenz-(*f*)-indandione-1,3 more probable not in the diketone form and not in the enol form, but in the partially ionized form IV. The spectra of 2-phenyl-4-azabenz-(*f*)-indandione-1,3 and its sodium salt, recorded in the ultraviolet region of the spectrum for $2 \cdot 10^{-5} M$ alcoholic solutions, are very similar to one another. This indicates that, at the concentrations studied, IV is completely ionized and dissolves in ethyl alcohol only insofar as it is ionized. The sodium salt (III) forms with copper, nickel, and cobalt ions sparingly soluble, high-melting intramolecular complexes. We have obtained the copper complex (V) in pure form. The orange-red salts of the alkaline-earth metals (Mg, Ca, Sr, Ba), and the bright-red zinc, cadmium, and manganese salts of IV are somewhat soluble in water and, under the action of acids, are converted into IV. On interaction of aqueous solutions of III with hydrolyzing metal salts (Al, Fe, Cr), IV is also formed.

With diazomethane, IV forms N-methylbetaine of 2-phenyl-4-azabenz-(*f*)-indandione-1,3 (VI). Bromination with N-bromosuccinimide gives 2-bromo-2-phenyl-4-azabenz-(*f*)-indandione-1,3 (VII). On interaction of VII with gaseous methylamine in dioxane solution, a mixture of various products was obtained, which has not yet been studied in detail.

Experimental Part

1-Keto-3-benzalfuro-(3,4-b)-quinoline (II). 1.85 g (0.01 g-mol.) of the lactone of 2-oxymethylquinolinecarboxylic-3 acid and 1.06 g (0.01 g-mol.) of freshly distilled benzaldehyde are boiled in 4 ml of acetic anhydride with a reflux condenser for 3 hours. A further 1.06 g of benzaldehyde is added and boiling is continued for another 4 hours. On cooling, yellow needles precipitate. Yield 2.08 g (77%) of II; m.p. 212–215°. The substance is difficultly soluble in alcohol, ether, and water, and readily soluble in dioxane. After crystallization from a mixture of dioxane and ethanol, m.p. 215–216°.

Found, %: N 5.23. $C_{18}H_{11}O_2N$. Calculated, %: N 5.13.

IR spectrum (absorption in % in parentheses): 1578 (34); 1620 (44); 1666 (26); 1784 (75).

2-Phenyl-4-azabenz-(*f*)-indandione-1,3 (IV). Method A. To a suspension of 2.08 g of II in 15 ml of abs. methanol, an equimolar amount of sodium methylate in 15 ml of abs. methanol is added. The reaction mixture assumes an orange-red color and becomes homogeneous. After 15–20 min, 3–4 ml of glacial acetic acid is added, and 2-phenyl-4-azabenz-(*f*)-indandione-1,3 (IV) is precipitated. Yield 1.49 g (72%). Small dark-red crystals, difficultly soluble in all ordinary organic solvents. After crystallization from dimethylformamide, m.p. $\sim 350^\circ$.

Found, %: N 5.05. $C_{18}H_{11}O_2N$. Calculated, %: N 5.13.

IR spectrum: 1494 (55); 1538 (83); 1553 (88); 1619 (37); 1668 (44). UV spectrum ($\lambda_{\max}$ and ε (in parentheses)): 243 (37000); 253 (37500); 307 (18800); 318 (22900); 396 (14900).

Method B. A mixture of 1.85 g (0.01 g-mol.) of the lactone of 2-oxymethylquinolinecarboxylic-3 acid, 1.06 g (0.01 g-mol.) of freshly distilled benzaldehyde, and 5.5 g (0.068 g-mol.) of abs. ethyl acetate is heated, and 1.5 ml of liquid is immediately distilled off. A solution of 0.013 g-mol. of sodium methylate in 10 ml of abs. methanol is added, and another 3 ml of liquid is distilled off. The orange-red reaction mixture is boiled with a reflux condenser for 3 hours. After addition of glacial acetic—

of acetic acid a dark-red precipitate forms. Yield 0.52 g (19%). The compound is identical with IV obtained by method A.

Sodium salt of 2-phenyl-4-azabenz-(f)-indandione-1,3 (III). 0.28 g of IV is suspended in 2 ml of absolute methanol, and an equimolar amount of sodium methylate in 2 ml of absolute methanol is added. The mixture is slightly heated and the hot orange-red solution is filtered. On cooling in a refrigerator, orange-red crystals of the sodium salt (III) are formed, which do not change on heating in a capillary to 380°. It dissolves better in methanol than in water.

Found, %: N 4.54. $C_{18}H_{10}O_2NNa$. Calculated, %: N 4.76

IR spectrum: 1495 (86); 1531 (92); 1600 (43); 1629 (56). UV spectrum: 236 (43700); 252 (40800); 307 (20500); 381 (25000); 396 (16600).

Copper complex (V) was obtained by mixing aqueous solutions of III and cupric chloride. The yield is quantitative. The complex is insoluble in water and in ordinary organic solvents, and is not decomposed by acetic or hydrochloric acid. After crystallization from dimethylformamide, small brown crystals are formed, with m.p. ~375°.

Found, %: N 4.84. $C_{36}H_{20}O_4N_2Cu$. Calculated, %: N 4.61

IR spectrum: 1493 (92); 1551 (99); 1575 (86); 1620 (63); 1663 (74).

N-Methylbetaine of 2-phenyl-4-azabenz-(f)-indandione-1,3 (VI). To a suspension of 0.14 g of IV in 2 ml of ether is added a solution of diazomethane (from 0.12 g of N-nitrosomethylurea) in ether. Nitrogen is evolved, and the finely crystalline suspension is converted into fluffy flakes. The yield is almost quantitative. The substance dissolves in hot dimethylformamide and pyridine, and does not dissolve in alkali. After crystallization from dimethylformamide, dark-red crystals with m.p. ~290° are obtained.

Found, %: N 4.96. $C_{19}H_{13}O_2N$. Calculated, %: N 4.88

IR spectrum: 1496 (65); 1553 (64); 1567–79 (93–90); 1623 (77); 1654 (67).

2-Bromo-2-phenyl-4-azabenz-(f)-indandione-1,3 (VII). To a suspension of 1.67 g (0.0061 g-mol.) of IV in 4 ml of dimethylformamide is added 1.33 g (0.0075 g-mol.) of N-bromosuccinimide. Within 15 min the dark-red reaction mixture is converted into a light-yellow solution, which is poured onto ice—white flakes of VII are formed. After crystallization from benzene with the addition of petroleum ether, the yield is 1.53 g (71%), m.p. 152–153°.

Found, %: N 4.13; Br 22.86
$C_{18}H_{10}O_2NBr$. Calculated, %: N 3.98; Br 22.69

IR spectrum: 1475 (62); 1575 (67); 1721 (91); 1750 (69).

IR spectra were recorded in the range 1480–1800 cm^{-1} on an IKS-12 spectrophotometer for suspensions of the substances in Vaseline oil. UV spectra were recorded on an SF-4 for $2 \cdot 10^{-5}$ M alcoholic solutions.

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