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Abstract

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PREPARATION OF 2-ARALKYLINDANON-1-OLS-3 BY CATALYTIC HYDROGENATION OF 2-ARYLIDENEINDANDIONES-1,3

Recently, in a series of papers $^{(1-3)}$, we studied the selective hydrogenation of 2-arylideneindandiones-1,3 (I) with sodium hydrosulfite (dithionite) ($Na_2S_2O_4 \cdot 2H_2O$) and developed a method for obtaining 2-aralkylindandiones-1,3 (II):

$$\text{(I)} \quad \text{2-arylideneindandione-1,3 structure} \quad \xrightarrow{+\,2\text{H}} \quad \text{(II)} \quad \text{2-aralkylindandione-1,3 structure}$$

The latter are homologs of 2-arylindandiones-1,3, among which physiologically active substances are known, for example 2-phenylindandione-1,3 (phenylin), used in medicine as a blood anticoagulant $^{(4-6)}$. It turned out that, among the 2-aralkylindandiones-1,3 (II) obtained by us, some also possess anticoagulant action $^{(7)}$.

In the present work the catalytic hydrogenation of 2-arylideneindandiones-1,3 (I) has been studied. It was found that under certain conditions it is possible to add 4 hydrogen atoms to the molecule of 2-arylideneindandione-1,3 (I), with formation of 2-aralkylindanon-1-ols-3 (III):

$$\text{(I)} \quad \text{2-arylideneindandione-1,3 structure} \quad \xrightarrow{+\,4\text{H}} \quad \text{(III)} \quad \text{2-aralkylindanon-1-ol-3 structure}$$

(IV) (V) (VI)

a) Ar = $-C_6H_5$, c) Ar = $-C_6H_3(OCH_3)_2$;
b) Ar = $-C_6H_4OCH_3$, d) Ar = $-C_{10}H_7$.

The structure of the 2-aralkylindanon-1-ols-3 (III) was proved by obtaining the corresponding oximes (IV) and phenylurethanes (V). The reaction conditions for obtaining III depend strongly on the Ar radical and on the catalyst used. Under other conditions, it is possible to obtain both the corresponding indandiones-1,3 (II) and indandiols-1,3, which will be reported separately.

2-Benzylindanon-1-ol-3 (IIIa) was obtained by hydrogenation of 2-benzalindandione-1,3 (Ia) at ordinary pressure: a) at room temperature with skeletal nickel catalyst, grade W-2 ([23]), yield 97.2%; b) at 60–65° with palladium black, yield 76.5%; c) at room temperature with palladium on barium sulfate, yield 95.2%; d) under the same conditions with Adams' catalyst, yield 75.6%.

To confirm the structures, IR spectra in the region of double bonds (in the solid state) were recorded for IIIa and IIIb. It is known from the literature that the diketo form of indandione-1,3 derivatives is characterized by a split peak in the interval 1705–1770 cm^{-1} and by a frequency of 1580–1600 cm^{-1}. The first interval characterizes two carbonyl groups, and the second the aromatic system. In the IR spectrum of IIIa and IIIb only one carbonyl band is observed: for IIIa at 1681 cm^{-1} (90), and for IIIb at 1703 cm^{-1} (64); the bands assigned to the aromatic ring remain: for IIIa at 1595 cm^{-1} (79), and for IIIb at 1503 cm^{-1} (48) and 1603 cm^{-1} (40.5). According to literature data, the carbonyl bands of indanone-1 are at 1698 cm^{-1} ([9]), and those of 2-benzylindanon-1 at 1717 cm^{-1} ([10]). The decrease in the frequency of the carbonyl group in IIIa can evidently be explained by the presence of hydrogen bonds in the solid state.

By hydrogenation of 2-anisalindandione-1,3 (Ib) at ordinary pressure and room temperature with Adams' catalyst, 2-*p*-methoxybenzylindanon-1-ol-3 (IIIb) was obtained in 81.6% yield. In an analogous manner, by hydrogenation of 2-veratralindandione-1,3 (Iv), 2-(3′,4′-dimethoxybenzyl)-indanon-1-ol-3 (IIIv) was obtained in 64.9% yield.

2-(α-Naphthyl)-indandione-1,3 (Ig) is hydrogenated with skeletal nickel at room temperature. 2-α-Naphthylmethylindanon-1-ol-3 (IIIg) was obtained in 71.8% yield. All the 2-aralkylindanon-1-ols-3 (III) obtained, in contrast to 2-aralkylindandiones-1,3 (II), do not dissolve in sodium carbonate (do not enolize).

The method described is a new method for obtaining indanon-1-ols-3. In the literature, indanon-1-ols-3 with a tertiary hydroxyl group (type VI) have chiefly been described; they are obtained from substituted indandiones-1,3 by treating the latter under certain conditions with Grignard reagents ([11],[12]). In individual cases, indanonols can also be obtained by oxidation of the corresponding indanones ([13]–[15]) or by replacing halogen with a hydroxyl group in halogen-substituted indanones ([16]). The indanonols obtained may be of interest for the synthesis of a number of derivatives. Thus, it is known that in compounds VI the hydroxyl group can be replaced by halogen, and the latter by an amino group ([11],[17]). Aminoindanones, aminoindanols, and aminoindanes possess physiological activity; for example, they are used as bronchodilating preparations (bronchodilators) ([18]–[21]). Hydrogenation of 2-substituted indanones-1 to the corresponding indanols-1 gives a mixture of stereoisomers ([16]); when the products are purified by crystallization, one (less soluble) isomer is usually isolated from such stereoisomers, while the second remains in the mother liquor (^{22}). The steric structure of the 2-aralkylindanon-1-ols-3 (III) obtained by us has not yet been studied.

Experimental Part

2-Benzylindanon-1-ol-3 (IIIa). a) In a hydrogenation flask (volume 300 ml) are placed 3.51 g (0.015 mole) of 2-benzalindandione-1,3, 100 ml of alcohol, and ~1 g of skeletal nickel (grade W-2) (^{23}), suspended in absolute alcohol. By means of a rubber tube, the flask is connected to the lower end of a reflux condenser, the upper end of which is connected to a gasometer with hydrogen. A stream of hydrogen is used to displace the air from the system through the side arm of the flask, after which the side arm is tightly closed with a stopper through which a thermometer has been inserted. With the aid of a shaker, the reaction vessel is shaken at room temperature (17-19°) for 7 h. On the next day the flask is disconnected from the hydrogen source and the catalyst is separated by filtration. The filtrate is diluted with 400 ml of water; the precipitate that separates out

after 2 hours, it is filtered. Yield 3.47 g (97.2%) of IIIa, after crystallization from CCl_4, m.p. 99-101°. b) 3.04 g of benzalindandione in 50 ml of alcohol with 0.05 g of palladium black (^{24}) is hydrogenated in the apparatus mentioned, with heating of the reaction mixture (using an infrared lamp), for 7 hours at 60-65°. After cooling, 2.37 g (76.5%) of IIIa is isolated in the same manner. M.p. 99-101°. c) 3.51 g of benzalindandione in 50 ml of alcohol with 1.0 g of 5% palladium on barium sulfate (^{25}) is hydrogenated at room temperature for 8.5 hours. In the same manner, 3.4 g (95.2%) of IIIa is isolated, m.p. 99-101°. d) 3.51 g of benzalindandione in 50 ml of alcohol with 0.03 g of Adams catalyst (^{24}) is hydrogenated at room temperature for 7 hours. Yield 2.7 g (75.6%) of IIIa, after crystallization from CCl_4, m.p. 99-101°.

Found, %:	C 80.74; 80.67; H 5.82; 6.06
$C_{16}H_{14}O_2$. Calculated, %:	C 80.67; H 5.88

Oxime (IVa). 0.48 g (0.002 mole) of 2-benzylindanon-1-ol-3, 10 ml of alcohol, 0.28 g (0.004 mole) of $NH_2OH \cdot HCl$, and 0.56 g (0.004 mole) of $CH_3COONa \cdot 3H_2O$ are boiled for 3 hours. The hot solution is filtered; after cooling, the filtrate is diluted with 40 ml of water. The precipitated solid is separated. 0.42 g of white oxime is obtained; after crystallization from methanol-water (1:1), m.p. 165-167°.

Found, %:	N 5.27
$C_{16}H_{15}O_2N$. Calculated, %:	N 5.53

Phenylurethane (Va). 1.0 g of IIIa and 0.5 ml of phenyl isocyanate are heated on a boiling water bath for 30 min. The mixture is cooled, the precipitated solid is filtered off, and washed on the filter with petroleum ether until the odor of phenyl isocyanate disappears. 1.1 g of white phenylurethane is obtained; after two crystallizations from CCl_4, m.p. 158–160°.

Found, %:	N 4.04
$C_{23}H_{19}O_3N$. Calculated, %:	N 3.92

2-(p-Methoxybenzyl)indanon-1-ol-3 (IIIb). 3.96 g (0.015 mole) of 2-anisalindandione-1,3 (Ib) in 50 ml of alcohol with 0.03 g of Adams catalyst is hydrogenated at room temperature for 7 hours. On the next day the catalyst is removed, the filtrate is diluted with 450 ml of water, and, to accelerate coagulation of the precipitated product, 50 ml of saturated sodium chloride solution is added. The mixture is filtered, giving 3.28 g (81.6%) of white IIIb; after two crystallizations from dilute methanol (1:1), m.p. 108–110°.

Found, %:	C 76.10; H 6.20
$C_{17}H_{16}O_3$. Calculated, %:	C 76.12; H 5.97

Oxime (IVb). 0.54 g (0.002 mole) of the obtained IIIb, 12 ml of alcohol, 0.28 g (0.004 mole) of $NH_2OH \cdot HCl$, and 0.56 g (0.004 mole) of $CH_3COONa \cdot 3H_2O$ are boiled for 3.5 hours. The mixture is cooled, diluted with 150 ml of water, and filtered. 0.51 g of white oxime is obtained; after two crystallizations from benzene, m.p. 156–159°.

Found, %:	N 4.89
$C_{17}H_{17}O_3N$. Calculated, %:	N 4.95

Phenylurethane (Vb). From 0.54 g (0.002 mole) of IIIb and 0.5 ml of phenyl isocyanate, on heating for 1 hour, analogously to Va, 0.79 g of phenylurethane 2-*p*-methoxybenzylindanon-1-ol-3 (Vb) is obtained; after two crystallizations from CCl_4, m.p. 161.5–163.5° (decomp.).

Found, %:	N 3.70
$C_{24}H_{21}O_4N$. Calculated, %:	N 3.62

2-(3′,4′-Dimethoxybenzyl)indanon-1-ol-3 (IIIc). 4.41 g (0.015 mole) of 2-veratralindandione-1,3 (Ic) in 50 ml of alcohol with 0.04 g of Adams catalyst is hydrogenated at room temperature for 9 hours. Analogously—

…as in the preceding case, 2.9 g (64.9%) of 2-(3′,4′-dimethoxybenzyl)-indan-1-ol-3-one are isolated; after two crystallizations from CCl_4, m.p. 103–105°.

Found, %: C 72.65; H 6.23
$C_{18}H_{18}O_4$. Calculated, %: C 72.48; H 6.04

Oxime (IVb). 0.45 g (~ 0.0015 mole) of 2-(3′,4′-dimethoxybenzyl)-indan-1-ol-3-one, 10 ml of alcohol, 0.21 g (0.003 mole) of $NH_2OH \cdot HCl$, and 0.42 g (0.003 mole) of $CH_3COONa \cdot 3H_2O$ are boiled for 3 hours. Analogously to IVb, 0.36 g of oxime is isolated; after two crystallizations from CCl_4, m.p. 92–95° (decomp.).

Found, %: N 4.86
$C_{18}H_{19}O_4N$. Calculated, %: N 4.47

Phenylurethane (Vb). From 0.3 g of 2-(3′,4′-dimethoxybenzyl)-indan-1-ol-3-one, analogously to Va, 0.45 g of phenylurethane is obtained; after two crystallizations from CCl_4, m.p. 154–156°.

Found, %: N 3.65
$C_{25}H_{23}O_5N$. Calculated, %: N 3.36

2-(α-Naphthylmethyl)-indan-1-ol-3-one (IIIg). 4.26 g (0.015 mole) of 2-α-naphthylindandione-1,3 (Ig) in 100 ml of alcohol with ~ 1 g of skeletal nickel (grade W-2) are hydrogenated at room temperature for 7 hours. Analogously to IIIb, 3.1 g (71.8%) of 2-α-naphthylmethylindan-1-ol-3-one are isolated; after two crystallizations from methanol, m.p. 153–155°.

Found, %: C 83.56; H 5.56
$C_{20}H_{16}O_2$. Calculated, %: C 83.33; H 5.56

Oxime (IVg). 0.29 g of 2-(α-naphthylmethyl)-indan-1-ol-3-one, 10 ml of alcohol, 0.14 g of $NH_2OH \cdot HCl$, and 0.28 g of $CH_3COONa \cdot 3H_2O$ are boiled for 3 hours. Analogously to IVb, 0.63 g of oxime is obtained; after two crystallizations from methanol, m.p. 187–190°.

Found, %: N 4.34
$C_{20}H_{17}O_2N$. Calculated, %: N 4.62

Phenylurethane (Vg). 0.58 g (~ 0.002 mole) of 2-(α-naphthylmethyl)-indan-1-ol-3-one and 0.5 ml of phenyl isocyanate are heated for 1 hour analogously to Va, giving 0.2 g of phenylurethane; after crystallization from toluene, m.p. 193–194° (decomp.).

Found, %: N 3.57
$C_{27}H_{21}O_3N$. Calculated, %: N 3.44

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