Reports of the Academy of Sciences of the USSR

T. T. DUMPIS and Academician of the Academy of Sciences of the Latvian SSR G. Ya. VANAG

1962

SovietRxiv

Abstract

Full Text

Reports of the Academy of Sciences of the USSR
1962. Volume 142, No. 1

CHEMISTRY

T. T. DUMPIS and Academician of the Academy of Sciences of the Latvian SSR G. Ya. VANAG

PREPARATION OF 2-ARYLINDANON-1-OLS-3 BY CATALYTIC HYDROGENATION OF 2-ARYLINDANDIONES-1,3

Many 2-arylindandiones-1,3 (I) are blood anticoagulants and find application in medicine, for example 2-phenylindandione-1,3 (“phenilin”) (1–3), 2-*p*-anisylindandione-1,3 (“anisidone”) (4), 2-oxymethyl-2-phenylindandione-1,3 (“omefin”) (5), 2-α-naphthylindandione-1,3 (6), etc. It was of interest to determine how the physiological action of these substances would change if one carbonyl group were reduced to a hydroxyl group, i.e., if 2-arylindanon-1-ols-3 (II) were obtained.

$$\text{(I)} \xrightarrow{+2H} \text{(II)}; \qquad \text{(III)}$$

$$\text{a) } \mathrm{Ar} = -\mathrm{C_6H_5}; \qquad \text{b) } \mathrm{Ar} = -\text{naphthyl}$$

In the literature, chiefly such arylindanonols are described in which the aryl and hydroxyl groups are attached to one and the same carbon atom (IV); they are obtained from substituted indandiones by the action upon the latter, under certain conditions, of arylmagnesium halides (7,8). Similar indanonols in individual cases may also be obtained by oxidation of the corresponding arylindanones (9,10) or arylindones (11). Arylindanonols may also be obtained by exchange of halogen for a hydroxyl group in halogen-substituted arylindanones (12). Arylindanonols are of interest for the synthesis of derivatives, since, according to literature data, in them the hydroxyl group can readily be replaced by halogen (7,8), and the latter by an amino group (13). According to literature data, aminoindanones and aminoindanols possess physiological activity; they are bronchodilating agents (bronchodilators) and affect blood pressure (14,15); thiosemicarbazones of indanones are also physiologically active (16,17).

We studied the possibility of obtaining 2-arylindanon-1-ols-3 by a new route—catalytic reduction of readily available 2-arylindandiones-1,3. Hydrogenation of 2-phenylindandione-3 (Ia) to 2-phenylindanon-1-ol-3 (IIa) was accomplished at ordinary temperature in alcoholic solution with 1) palladium black, with a yield of recrystallized IIa of 30%, and 2) palladium on barium sulfate, with the same yield.

In the hydrogenation of 2-α-naphthylindandione-1,3 (Ib) to 2-α-naphthylindanon-1-ol-3, it was necessary to raise the reaction temperature. 2-α-Naphthylindanon-1-ol-3 (IIb) was obtained by hydrogenating Ib in alcoholic solution at 60–65° and ordinary pressure: 1) with palladium on barium sulfate, yield of IIb 88.6%; 2) with Raney nickel of grade W-2, yield of IIb 92.5%.

The obtained 2-arylindanon-1-ols-3 (II), unlike the starting 2-arylindandiones-1,3 (I), do not dissolve in sodium carbonate (do not enoliz-

are formed). The structure of II was proved by obtaining the corresponding monoximes (IIIa, b). This confirms that, in the hydrogenation process, one carbonyl group remained unreduced. The presence of a hydroxyl group in 2-phenylindan-1-ol-3-one (IIa) was proved by obtaining the *p*-nitrobenzoate of 2-phenylindan-1-ol-3-one (V)

(IV) (V) (VI)

In 2-α-naphthylindan-1-ol-3-one (IIb), the presence of a hydroxyl group was proved by treatment of IIb with phenyl isocyanate; the phenylurethane of 2-α-naphthylindan-1-ol-3-one (VI) was obtained.

In addition, the structures of IIa and IIb were confirmed by recording IR spectra in the region of double bonds (in the solid state). 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. Thus, in the IR spectrum of solid 2-phenylindandione-1,3 (Ia), according to (18), two carbonyl bands are observed—at 1740 (40) and 1704 cm^{-1} (65)—and bands assigned to the aromatic ring: 1628 (30) and 1580 cm^{-1} (40). In the IR spectrum of the 2-phenylindan-1-ol-3-one (IIa) obtained by us, only one carbonyl band is observed at 1703 cm^{-1} (79), as is observed for 2-substituted indanones-1, for example for 2-phenylindanone-1 (19) at 1705 cm^{-1} and for 2-benzylindanone-1 (20) at 1717 cm^{-1}. In the IR spectrum of IIa the bands assigned to the aromatic ring are retained, at 1650 cm^{-1} (59) and 1588 cm^{-1} (57); in the spectrum of 2-α-naphthylindan-1-ol-3-one (IIb) there is also one carbonyl band at 1687 cm^{-1} (62) and bands assigned to the aromatic ring at 1650 (46) and 1594 cm^{-1} (45). The decrease in the carbonyl-group frequency in IIb can evidently be explained by the presence of hydrogen bonds in the solid state.

In the hydrogenation of 2-substituted indanones-1 to indanols-1, according to literature data, a mixture of stereoisomers is obtained (21). On crystallization of such stereoisomeric indane derivatives, one less soluble isomer is usually isolated, while the other remains in solution (22,11). Such stereoisomers sometimes interconvert on melting (11). The steric structure of the 2-arylindan-1-ol-3-ones obtained by us has not yet been studied.

Experimental Part

2-Phenylindan-1-ol-3-one (IIa). 1) Into a hydrogenation flask (volume 100 ml) are placed 6.66 g (0.03 mole) of 2-phenylindandione-1,3, 70 ml of alcohol, and 0.14 g of palladium black (23). By means of a rubber tube the flask is attached 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 is introduced into the flask. By means of a shaker, the reaction vessel is shaken at room temperature for 7 hr; on the following day the flask is disconnected. The catalyst and unreacted starting product are separated by filtration; the filtrate is diluted with 500 ml of water and 100 ml of saturated sodium chloride solution (to accelerate coagulation). After 4 hr the precipitated resinous product is separated and crystallized from CCl_4. Yield 2 g (30%) of white crystalline IIa, m.p. 119–121°.

2) 3.33 g (0.015 mole) of 2-phenylindandione-1,3 in 50 ml of alcohol with 1.0 g of 5% palladium on barium sulfate (24) are hydrogenated in the apparatus mentioned above at room temperature for 9 hours. In an analogous manner, 2.17 g of the solid reaction product are isolated; after crystallization from CCl_4, 1.0 g (30%) of 2-phenylindanon-1-ol-3 (IIa) is obtained, m.p. 119–121°. In a mixture with the preceding compound it gives no depression of the melting point.

Found %:	C 80.35; H 5.48
$C_{15}H_{12}O_2$. Calculated %:	C 80.36; H 5.36

Oxime (IIIa). 0.56 g (0.0025 mole) of 2-phenylindanon-1-ol-3, 15 ml of alcohol, 0.52 g (0.0075 mole) of $NH_2OH \cdot HCl$, and 1.04 g ($\sim$ 0.0075 mole) of $CH_3COONa \cdot 3H_2O$ are boiled for 3 hours. The hot solution is filtered; the filtrate is cooled and diluted with 100 ml of water. 0.27 g of the oxime is obtained; after crystallization from CCl_4, m.p. 61–64° (decomp.).

Found %:	N 6.05; 5.93
$C_{15}H_{13}O_2N$. Calculated %:	N 5.86

p-Nitrobenzoate (V). 0.68 g (0.003 mole) of phenylindanon-1-ol-3, 1.3 g (0.007 mole) of *p*-nitrobenzoyl chloride, and 10 ml of anhydrous pyridine are boiled for 15 min. On cooling, the whole mass solidifies; it is diluted with 100 ml of a 5% sodium carbonate solution (to remove *p*-nitrobenzoic acid), filtered after 2 hours, and the precipitate on the filter is washed with water. 0.77 g of a brown substance is obtained; after two crystallizations from *n*-butanol, m.p. 242–244°.

Found %:	N 3.38
$C_{22}H_{15}O_5N$. Calculated %:	N 3.75

2-(α-Naphthyl)-indanon-1-ol-3 (IIb). 1) 2.04 g (0.0075 mole) of 2-(α-naphthyl)-indandione-1,3 in 50 ml of alcohol with 0.5 g of 5% palladium on barium sulfate are hydrogenated in the apparatus mentioned above with shaking and simultaneous heating (by means of an infrared lamp) at 60-65° for 12 hours. The next day the catalyst is separated, and the filtrate is diluted with 30 ml of water and 50 ml of saturated sodium chloride solution. After 4 hours the precipitated solid is filtered. 1.82 g of IIb (88.6%) is obtained; after crystallization from a minimal volume of toluene, m.p. 147–150°.

2) 2.04 g (0.0075 mole) of 2-(α-naphthyl)-indandione-1,3 in 50 ml of alcohol with $\sim$ 0.5 g of Raney nickel grade W-2 (25), suspended in absolute alcohol, are hydrogenated at 60-65° for 7 hours. In an analogous manner, 1.9 g (92.5%) of 2-(α-naphthyl)-indanon-1-ol-3 are isolated; after two crystallizations from toluene it gives no depression of the melting point with the preceding compound.

Found %:	C 83.47; 83.17; H 5.22; 5.25
$C_{19}H_{14}O_2$. Calculated %:	C 83.21; H 5.11

Oxime (IIIb). 0.2 g ($\sim$ 0.0007 mole) of 2-(α-naphthyl)-indanon-1-ol-3, 10 ml of alcohol, 0.14 g (0.002 mole) of $NH_2OH \cdot HCl$, and 0.28 g (0.002 mole) of $CH_3COONa \cdot 3H_2O$ are boiled for 5.5 hours, cooled, and diluted with 100 ml of water. The precipitated solid is separated; 0.16 g of a white oxime is obtained; after crystallization from toluene, m.p. 202–204° (decomp.).

Found %:	N 4.99; 4.94
$C_{19}H_{15}O_2N$. Calculated %:	N 4.84

Phenylurethane (VI). 0.17 g of 2-(α-naphthyl)-indanon-1-ol-3 and 0.5 ml of phenyl isocyanate are heated on a boiling water bath for 1.5 hours. The mixture is cooled, and 30 ml of petroleum ether are added to the reaction mixture. The precipitated solid is filtered and washed on the filter with petroleum ether until the disappearance—

of the appearance of the odor of phenyl isocyanate. This gives 0.21 g of phenylurethane VI; after crystallization from toluene, m.p. 143–145° (decomp.).

$C_{26}H_{19}O_3N$.	Found, %:	N 3.55.
	Calculated, %:	N 3.56

Institute of Organic Synthesis
Academy of Sciences of the Latvian SSR

Received
7 IX 1961

REFERENCES CITED

1. G. Ya. Vanag, S. A. Giller, L. S. Geita, Z. D. Bleksmit, V. N. Kovalenko, M. A. Kotovshchikova, *Farmakol. i toksikol.*, No. 6, 23 (1956).
2. Z. D. Bleksmit, M. A. Kotovshchikova, N. V. Martynova, *Vestn. khirurgii*, No. 8, 64 (1958).
3. A. N. Filatov, *Khirurgiya*, 34, No. 1, 43 (1958).
4. K. Lange, E. Perchuk, M. Mal, I. Entsinger, G. Muratov, *RZhKhim.*, *Biokhim.*, No. 31581 (1958).
5. G. Ya. Vanag, M. N. Koptelova, *Izv. AN LatvSSR*, No. 8, 93 (1958).
6. M. Gumińska, M. Eckstein, *Acta Biochim. Polon.*, 3, 323 (1956).
7. R. Weiss, S. Luft, *Monatsh.*, 48, 337 (1927).
8. T. A. Geissmann, V. Tulagin, *Chem. Abstr.*, 36, 1035 (1942).
9. W. v. Müller, Rohde, *Ber.*, 25, 2095 (1892).
10. A. Müller, *Ber.*, 77, 159 (1944).
11. S. Carboni, *Chem. Abstr.*, 46, 482 (1952).
12. R. de Fazi, A. Bauchetti, *Chem. Abstr.*, 41, 7393 (1947).
13. Ch. Courtot, Fayet, Parant, *C. R.*, 186, 371 (1928).
14. R. V. Heinzelmann, *Chem. Abstr.*, 45, 8558 (1951); Pat. USA 2549683; Pat. USA 2549684.
15. N. Levin, B. E. Graham, H. G. Kolloff, *J. Org. Chem.*, 9, 380 (1944).
16. K. Hoffmann, E. Tagmann, *Chem. Abstr.*, 51, 1281 (1957).
17. W. Schuler, R. Meier, *Chem. Abstr.*, 46, 1148 (1952).

18. O. Neiland, in the collection *Cyclic β-Diketones*, Riga, 1961, p. 41.

19. M. L. Josien, N. Fuson, *Bull. Soc. chim. France*, 1952, 389.

20. N. H. Cromwell, R. P. Ayer, *J. Am. Chem. Soc.*, No. 1, 133 (1960).

21. N. Kizhner, *Zhurn. Russk. fiz.-khim. obshch.*, 46, 1411 (1914).

22. E. Bergmann, H. Weiss, *Lieb. Ann.*, 480, 64 (1930).

23. R. Listend, J. Elvidge, M. Volli, J. Wilkinson, *Modern Methods of Research in Organic Chemistry*, IL, 1959, p. 105.

24. *Syntheses of Organic Preparations*, collected volume 4, IL, 1953, p. 409.

25. *Syntheses of Organic Preparations*, collected volume 3, IL, 1952, p. 338.

Note: Figure translations are in progress. See original paper for figures.