



Soviet-era science, translated into English

CHEMISTRY

R. E. VALTER, Academician of the Academy of Sciences of the
Latvian SSR G. Ya. VANAG

1962

SovietRxiv

View the original and related papers at <https://sovietrxiv.org/items/ru-196201.01771>

Source: Math-Net.Ru and CyberLeninka. Machine translation. Verify with the original.

Abstract

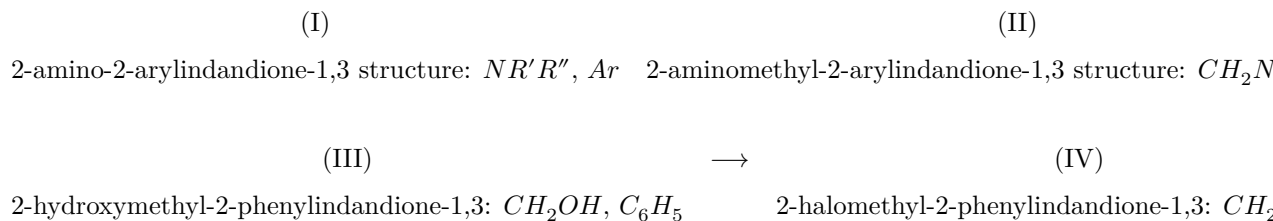
Full Text

CHEMISTRY

R. E. VALTER, Academician of the Academy of Sciences of the Latvian SSR
G. Ya. VANAG

IODOMETHYLATION OF 2-SUBSTITUTED INDANDIONES-1,3

2-Amino-2-arylindandiones-1,3 (I) are physiologically active substances possessing narcotic, anticonvulsant, and anesthetic action ⁽¹⁾. Two of these preparations are already undergoing clinical trials ⁽²⁾. In order to clarify the relationship between chemical structure and physiological activity of aminoindandiones, the study of 2-aminomethyl-2-arylindandiones-1,3 (II) was of interest.

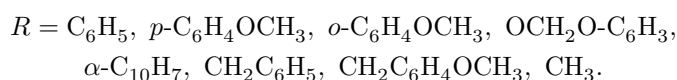
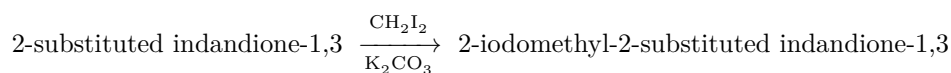


Since β -diketones do not form Mannich bases ⁽³⁾, and the dialkylaminomethylation method developed by Böhme ⁽⁴⁾ can hardly find broader application because of the difficult accessibility of dialkylaminomethyl halides, 2-halomethyl-2-substituted indandiones-1,3 could serve as starting substances for the synthesis of 2-aminomethyl-2-arylindandiones-1,3. 2-Chloromethyl- and 2-bromomethyl-2-phenylindandiones-1,3 (IV, $X = Cl, Br$) were obtained by us* by the action of phosphorus pentachloride or phosphorus and bromine on 2-hydroxymethyl-2-phenylindandione-1,3 (III), which in turn is obtained by the action of formaldehyde on 2-phenylindandione-1,3 ⁽⁵⁾. In view of the low mobility of the chlorine and bromine atoms in the above-mentioned compounds, we were most interested in 2-iodomethyl-2-phenylindandione-1,3 (IV, $X = I$), which, however, could not be obtained by the described route. It was obtained by prolonged heating of 2-chloromethyl-, or better 2-bromomethyl-2-phenylindandione-1,3 with sodium iodide in glacial acetic acid. Thus, its preparation is a complex three-stage synthesis (starting from 2-phenylindandione-1,3).

Subsequently we studied the possibilities of direct iodomethylation of 2-phenylindandione-1,3 with methyl iodide. It turned out that, upon heating 2-phenylindandione-1,3 with an excess of methyl iodide in the presence of potassium carbonate, 2-iodomethyl-2-

* The work is being printed in the Scientific Notes of the Riga Polytechnic Institute.

phenylindandione-1,3. The method is general also for other 2-aryl-, as well as 2-aralkyl- and 2-alkylindandiones-1,3:



It is interesting to note that by this method 2-iodomethyl-2- α -naphthylindandione-1,3 was also obtained; Slovak chemists ⁽⁶⁾ had unsuccessfully attempted to obtain it by the action of methylene iodide on the sodium salt of 2- α -naphthylindandione-1,3 in butanol solution. The authors explain this by steric difficulties, but here, apparently, it is necessary to carry out the reaction at a higher temperature. We heated 2- α -naphthylindandione-1,3 with methylene iodide and potassium carbonate to 140-150°, but under these conditions side processes also occur, since the yield of 2-iodomethyl-2- α -naphthylindandione-1,3 is only 19.5%. By the action of methylene iodide on benzaldehyde in the presence of sodium butylate, the above-mentioned authors obtained 2-iodomethyl-2-phenylindandione-1,3 (identical with that obtained by us), but in only 45% of theory.

By heating with methylene iodide even to 180°, we were unable to obtain the iodomethyl derivatives of 2-xanthryl- and 2-benzhydrylindandiones-1,3, probably owing to bulky substituents, nor of 2-*p*-nitrophenylindandione-1,3. In the latter case this may be explained by the equalized electronic structure of 2-*p*-nitrophenylindandione-1,3 ⁽⁷⁾.

The infrared absorption spectra of 2-iodomethyl-2-substituted indandiones-1,3 in the range 1500-1800 cm⁻¹ (recorded in paraffin oil) have two maxima in the region 1708-1745 cm⁻¹, characterizing the diketone form, and a maximum at about 1595 cm⁻¹, assigned to the aromatic system (Table 1).

Table 1

2,2-Disubstituted indandione-1,3	$\nu_{\text{C=O}}, \text{cm}^{-1}$	$\nu_{\text{arom}}, \text{cm}^{-1}$
2-Methyl-2-phenyl- ⁽⁸⁾	1710(91); 1747(58)	1596(68)
2-Iodomethyl-2-phenyl-	1712(90); 1743(74)	1598(68)

2,2-Disubstituted indandione-1,3	$\nu_{\text{C=O}}, \text{cm}^{-1}$	$\nu_{\text{arom}}, \text{cm}^{-1}$
2-Iodomethyl-2- α - naphthyl-	1709(75); 1743(55)	1594(53)
2-Iodomethyl-2- benzyl-	1708(75); 1745(60)	1597(55)
2-Iodomethyl-2- methyl-	1710(91); 1740(82)	1595(72)

Note. In parentheses—the percent absorption.

Experimental Part

2-Iodomethyl-2-phenylindandione-1,3. 11.1 g (0.05 mole) of 2-phenylindandione-1,3, ground in a mortar with 6.9 g (0.05 mole) of potassium carbonate and 12.1 ml (0.15 mole) of methylene iodide, is heated with a reflux condenser on an oil bath for 1.5 hours at a bath temperature of 180–190°. The end of the reaction is readily determined by the change in the color of the reaction mass: at first it is red; upon completion of the reaction it is yellow or light orange. To the mixture cooled to ~50° about 30 ml of ether is added, and on the second day the precipitate is separated, washed with a small amount of ether, then with warm water, and finally with a small amount of methanol. The yield of 2-iodome-

tyl-2-phenylindandione-1,3: 14.9 g (82.4% of theory). Yellowish crystals with m.p. 189–193°. After recrystallization from acetone or acetic acid, white or light-yellow crystals with m.p. 193–194°.

Found, %: I 35.28, 35.28. $\text{C}_{16}\text{H}_{11}\text{O}_2\text{I}$. Calculated, %: I 35.03.

2-Iodomethyl derivatives of 2-anisyl-, 2-veratryl-, 2-piperonyl-, 2-benzyl-, and 2-*p*-methoxybenzylindandiones-1,3 were obtained analogously. The reaction conditions and constants of the compounds obtained are given in Table 2. In the case—

Table 2

general structure: 2-iodomethyl-2-*R*-indandione-1,3

R	Oil-bath temperature, °C	Yield, %	Solvent for crystallization	M.p., °C	Product color	Empirical formula	I found	I calculated
anisyl	150-160	76.5	Ethanol	130-134	Light-yellow	$C_{17}H_{13}O_3$	42.20	32.37
veratryl	160-170	68.4	Acetic acid	203-205	Yellow	$C_{18}H_{15}O_4$	49.97	30.07
piperonyl	160-170	76.0	Acetic acid	171-173	Yellow	$C_{17}H_{11}O_4$	41.34	31.25
α -naphthyl	140-150	19.5	Acetone	200-202	White	$C_{20}H_{13}O_2$	40.63; 30.71	30.80
benzyl	140-150	66.6	Ethanol	168-170	White	$C_{17}H_{13}O_2$	43.62; 33.66	33.75
<i>p</i> -methoxybenzyl	140-150	52.7	Ethanol	125-127	White	$C_{18}H_{15}O_3$	41.26; 31.33	31.26

of 2-*p*-methoxybenzylindandione-1,3, it is expedient to evaporate the ether filtrate in vacuo, after which an additional amount of 2-iodomethyl-2-*p*-methoxybenzylindandione-1,3 is isolated.

2-Iodomethyl-2-methylindandione-1,3. 6.4 g (0.04 mole) of 2-methylindandione-1,3, dissolved with 5.6 g (0.04 mole) of potassium carbonate and 6.6 ml (0.08 mole) of methylene iodide, are heated for 1.5 h at an oil-bath temperature of 140-150°. To the warm mixture about 50 ml of ether is added, it is thoroughly stirred and immediately filtered. After distilling off the ether in vacuo and cooling the residue in a refrigerator, yellowish crystals of 2-iodomethyl-2-methylindandione-1,3 separate. They are separated and washed with a small amount of ether. Yield 5 g (41.6% of theory). M.p. 95-103°. After recrystallization from a methanol-water mixture (2:1), white crystals with m.p. 102-104° are obtained.

Found, %: I 42.22; 41.91. $C_{11}H_9O_2I$. Calculated, %: I 42.30.

2-Iodomethyl-2- α -naphthylindandione-1,3 was obtained analogously (see Table 2).

Riga Polytechnic Institute

Received
18 XII 1961

CITED LITERATURE

1. *Cyclic β -Diketones*, Riga, 1961, pp. 191 and 359.
2. *Science for Production*, vol. V, Riga, 1960, p. 72 and 86.
3. H. Heilmann, G. Opitz, *Angew. Chem.*, 68, 265 (1956); *Lieb. Ann.*, 604, 213 (1957).
4. H. Böhme, E. Mundlos, G. Keitzer, *Ber.*, 91, 656 (1958).
5. G. Ya. Vanag, E. V. Vanag, Author's Certificate No. 134264, 7 XII 1959.
6. M. Furdik, P. Hrnčiar, V. Vačoková, *Acta Fac. rerum natur. Univ. Comenianae Chim.*, 3, No. 2-3, 117 (1959); *RZhKhim*, 96443 (1960).
7. A. K. Aren, O. Ya. Neilands, G. Ya. Vanag, *DAN*, 132, 115 (1960).
8. Ya. V. Freimanis, G. Ya. Vanag, *ZhOKh*, 30, 3369 (1960).

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

Source: Math-Net.Ru and CyberLeninka. Machine translation. Verify with the original.