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Abstract

Full Text

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Academician of the Academy of Sciences of the Latvian SSR G. Ya. Vanag, E. Yu. Gudrinietse,
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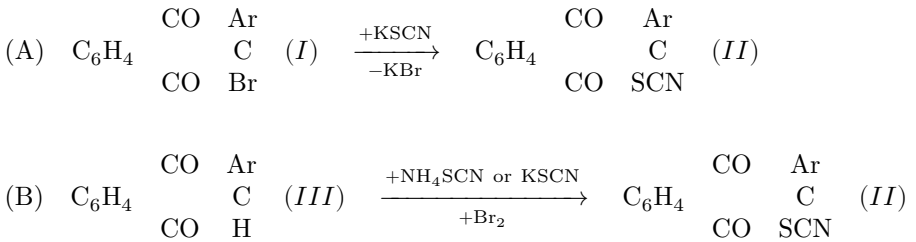
THIOCYANATION OF 2-ARYLINDANDIONES-1,3

Thiocyanate compounds are often used as intermediates for obtaining many sulfur-containing derivatives, for example: mercaptans, sulfides, disulfides, sulfonic acids, and other compounds ([1–4]). But many thiocyanate derivatives are also important in their own right: they possess physiological activity—they lower blood pressure ([5, 6]), act bacteriostatically ([7]), and are used as insecticides, in the manufacture of dyes, and in the vulcanization of rubber ([8]).

Thiocyanate derivatives of β-diketones have been studied very little, and thiocyanatoindandiones are completely unknown. Since halogenation, nitration, and sulfonation of indandiones-1,3 generally proceed readily, it was of interest to carry out their thiocyanation as well. Some data on the thiocyanation of compounds at an active methylene group are already available in the literature ([9, 10]).

As is known, 2-phenylindandione-1,3 is an active blood anticoagulant and is used in the Soviet Union under the name "phenylin." It turned out that 2-chloro-, 2-bromo-, 2-nitro-, and 2-oximethylphenylindandiones-1,3 are also active blood anticoagulants ([11]). It was therefore important to establish the influence of the thiocyanate group on the anticoagulant action of phenylin.

2-Thiocyanato-2-phenylindandione-1,3 (II) was prepared by us in two ways: by the exchange reaction of 2-bromo-2-phenylindandione-1,3 (I, Ar = C_6H_5) with potassium thiocyanate and by direct thiocyanation of 2-phenylindandione-1,3 (III, Ar = C_6H_5) with potassium or ammonium thiocyanate and bromine. The latter reaction proceeds well at +2° in methanol or at 20° in glacial acetic acid.



$$\begin{aligned} \text{Ar} &= \text{C}_6\text{H}_5 \\ &= \text{C}_6\text{H}_4{-}\text{NO}_2\text{-n} \\ &= \text{C}_6\text{H}_4{-}\text{OCH}_3\text{-n} \\ &= \text{C}_{10}\text{H}_7{-} \end{aligned}$$

The best results are obtained by the exchange reaction according to scheme A, and also by direct thiocyanation in methanol according to scheme B. The drawback of the po-

of the latter method is only that indandiones-1,3 are sparingly soluble in methanol. In thiocyanation in glacial acetic acid the yields are not so constant; the formation of yellow by-products is sometimes observed.

2-Thiocyano-2-arylindandiones are white or slightly yellowish crystalline substances. They are stable in an acidic medium; under the action of alkalis they split off the thiocyanate group with formation of enolate salts of the corresponding arylindandiones. According to preliminary studies carried out by M. N. Koptelova, 2-thiocyano-2-phenylindandione-1,3 is more active as a blood anticoagulant than 2-phenylindandione-1,3 itself.

Experimental Part

2-Thiocyano-2-phenylindandione-1,3 (II Ar = C_6H_5). a) To a warm solution of 5 g (0.0166 mole) of 2-bromo-2-phenylindandione-1,3 in 20 ml of abs. ethanol, 1.8 g (0.0185 mole) of potassium thiocyanate in 20 ml of methanol is added. Already on mixing the two warm solutions a white crystalline precipitate separates. The mixture is heated on a water bath for 30 min, then allowed to cool; the precipitate is separated and washed with water. Yield 4.5 g (98%) of 2-thiocyano-2-phenylindandione-1,3, m.p. 123–124°. After crystallization from methanol or glacial acetic acid, 3.9 g (85%) of white crystals was obtained. M.p. 124–126°.

$\text{C}_{16}\text{H}_9\text{O}_2\text{SN}$.	Found %:	N 5.06
	Calculated %:	N 5.02

b) 7 g (0.0315 mole) of 2-phenylindandione-1,3 and 5.75 g (0.0755 mole) of ammonium thiocyanate are dissolved with heating in 1100 ml of methanol; the solution is cooled to +2°, and over the course of 30 min a solution of 1.93 ml of bromine (0.0377 mole) in 25 ml of methanol saturated with ammonium bromide is added to it. During the reaction the red color of the solution changes to yellow-pink. Toward the end of the reaction the solution is gradually diluted with water. Yield 8.4 g (95.5%) of 2-thiocyano-2-phenylindandione-1,3; after crystallization from methanol, 7.4 g (84%). M.p. 125–126°.

$C_{16}H_9O_2SN$.	Found %:	N 4.74
	Calculated %:	N 5.02

c) 1 g (0.045 mole) of 2-phenylindandione-1,3 and 0.82 g (0.0108 mole) of ammonium thiocyanate or 1 g of potassium thiocyanate are dissolved with heating in 100 ml of glacial acetic acid; the solution is cooled to 20°, and over the course of 30 min a solution of 0.28 ml (0.0054 mole) of bromine in 15 ml of glacial acetic acid is added. Toward the end of the reaction the red solution becomes almost decolorized. On gradual dilution of the solution with water, 2-thiocyano-2-phenylindandione-1,3 separates. Yield 1.0–1.15 g (87–92%), m.p. 123–124°; after crystallization from methanol, 0.9–1.05 g (72–84%), m.p. 124–126°.

$C_{16}H_9O_2SN$.	Found %:	N 4.82
	Calculated %:	N 5.02

2-Thiocyano-2-phenylindandione-1,3 dissolves in acetone; on heating it dissolves in methanol, ethanol, and glacial acetic acid; it is sparingly soluble in ether and insoluble in water. In caustic soda it dissolves with a red coloration; from the solution the sodium salt of 2-phenylindandione-1,3 precipitates. The same salt is formed as the main product also on treatment with alcoholic alkali, but at the same time a small amount of a yellow substance with the odor of mercaptans is formed. On heating in abs. ethanol with dry caustic soda, chiefly this yellow substance is formed.

In concentrated sulfuric acid, 2-thiocyano-2-phenylindandione-1,3 dissolves with a yellowish coloration; then a rapidly passing violet coloration appears, and the solution darkens. On dilution with water

a new substance with the former nitrogen content precipitates. On heating with concentrated hydrochloric acid, 2-rhodan-2-phenylindandione-1,3 is not changed.

2-Rhodan-2-*p*-nitrophenylindandione-1,3 (II Ar = C_6H_4–NO_2-*p*).
a) To a solution of 1.2 g (0.0035 mole) of 2-bromo-2-*p*-nitrophenylindandione-1,3 in 10 ml of dioxane there is added a solution of 0.4 g (0.0041 mole) of potassium rhodanide in 10 ml of a mixture of dioxane with methanol (1 : 1), and the mixture is boiled for 20 min. After dilution with water, 0.8 g (72%) of a yellow precipitate separates, m.p. 119–122°. Recrystallization from glacial acetic acid gives pale-yellow crystals of 2-rhodan-2-*p*-nitrophenylindandione-1,3, m.p. 126–128°.

b) To a solution of 2 g (0.0075 mole) of 2-*p*-nitrophenylindandione-1,3 and 1.36 g (0.0178 mole) of ammonium rhodanide in 435 ml of glacial acetic acid at 20°, 0.46 ml of bromine (0.0089 mole) in 25 ml of glacial acetic acid is added dropwise, and the procedure is then as in the preparation of

2-rhodan-2-phenylindandione-1,3 by method b). Yield of crude product 1.5 g (62%), m.p. 128°.

c) To a solution of 1 g (0.0037 mole) of 2-*p*-nitrophenylindandione-1,3 and 0.84 g (0.0086 mole) of potassium rhodanide in 250 ml of glacial acetic acid, a solution of 0.22 ml (0.0043 mole) of bromine in 15 ml of glacial acetic acid is added dropwise, and the procedure is then as above. Yield of 2-rhodan-2-*p*-nitrophenylindandione-1,3 recrystallized from glacial acetic acid: 0.65 g (53.7%), m.p. 127–128°.

$C_{16}H_8O_4SN_2$. Found, %: N 8.27
Calculated, %: N 8.61

2-Rhodan-2-anisylindandione-1,3 (II Ar = C_6H_4–OCH_3-*p*).
To a solution of 0.94 g (0.0037 mole) of 2-anisylindandione-1,3 and 0.68 g (0.0089 mole) of ammonium rhodanide in 60 ml of glacial acetic acid at 20°, over the course of 30 min, a solution of 0.27 ml (0.0045 mole) of bromine in 5 ml of glacial acetic acid is added. The red solution is almost decolorized. Dilution with water gives 1.1 g (96%) of yellowish crystals. After crystallization from methanol the yield is 0.85 g (74%) of 2-rhodan-2-anisylindandione-1,3. White crystals, m.p. 138–140°.

$C_{17}H_{11}O_3SN$. Found, %: N 4.33; 4.59
Calculated, %: N 4.53

2-Rhodan-2-α-naphthylindandione-1,3 (IIAr = $C_{10}H_7$-α).
From 1.5 g (0.0055 mole) of 2-α-naphthylindandione-1,3 and 1 g (0.0131 mole) of ammonium rhodanide in 250–300 ml of glacial acetic acid, by the action of 0.33 ml (0.0066 mole) of bromine in 10 ml of glacial acetic acid at 20°, 1.7 g (94%) of yellowish 2-rhodan-2-α-naphthylindandione-1,3 was obtained, m.p. 127°. After crystallization from methanol–yellowish crystals, m.p. 126–127°. Readily soluble in benzene and chloroform.

$C_{20}H_{11}O_2SN$. Found, %: N 4.16; 4.19
Calculated, %: N 4.25

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