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Abstract

Full Text

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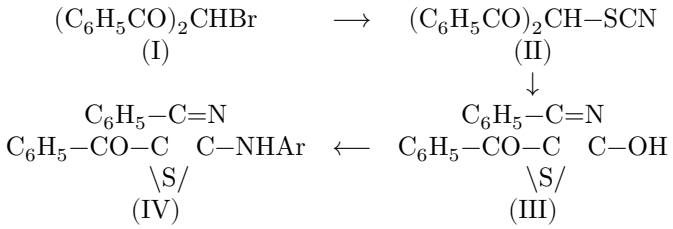
2-Arylamino-4-phenyl-5-benzoylthiazoles

2-Aminothiazoles substituted in the amino group are obtained mainly from N-substituted thioureas and α-haloketones (1-3). Arylaminothiazoles are also formed in the interaction of aromatic amines with α-rhodanoketones (2, 4-10). However, the preparation of ketones of 2-(N-substituted)-aminothiazoles has not been studied.

We have obtained a series of 2-arylamino-4-phenyl-5-benzoylthiazoles (IV) by the interaction of dibenzoylbromomethane (1) with potassium thiocyanate in the presence of aromatic amines in ethyl alcohol solution. The reaction proceeds smoothly, and the corresponding thiazoles (IV) are formed in good yields. It is possible that the reaction proceeds through the intermediate rhodanoketones (II) and oxythiazoles (III), as has been noted (8-10), but so far it has not been possible to isolate them.



$$\mathrm{Ar} = \mathrm{a} - \mathrm{C_6H_5};\ \mathrm{b} - o\text{-};\ \mathrm{v} - m\text{-};\ \mathrm{g} - n\text{-}\mathrm{C_6H_4CH_3};\ \mathrm{d} - n\text{-}\mathrm{C_6H_4};$$

$$\mathrm{e} - n\text{-}\mathrm{C_6H_4OCH_3};\ \mathrm{zh} - n\text{-}\mathrm{C_6H_4COOC_2H_5};\ \mathrm{z} - n\text{-}\mathrm{C_6H_4N{=}NC_6H_5};$$

$$\mathrm{i} - \alpha\text{-}\mathrm{C_{10}H_7}.$$

When hot solutions of equimolar amounts of dibenzoylbromomethane and potassium thiocyanate in ethyl alcohol are mixed, a precipitate of potassium bromide separates, and the solution becomes yellow. The precipitate is filtered off, an aromatic amine is added to the filtrate, and the mixture is boiled under a reflux condenser for several hours. The corresponding 2-arylaminothiazole is obtained

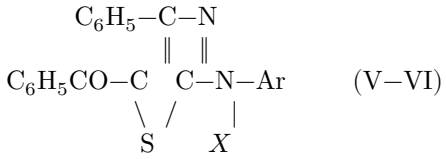
in yields of 40-70% (see Table 1). This is a very convenient method for preparing aromatic ketones of 2-(N-substituted) aminothiazoles.

The structure of 2-anilino-4-phenyl-5-benzoylthiazole (IVa) was proved by an independent synthesis from dibenzoylbromomethane and N-phenylthiourea. A mixed sample of IVa obtained by different routes gives no depression of the melting point.

All the thiazoles obtained are colored from pale yellow to orange-red and have relatively high melting points. They are readily soluble in ethyl alcohol, acetic acid, and dioxane, poorly soluble in ether, and insoluble in water.

Aminothiazoles (IV) in glacial acetic acid solution with sodium nitrite form 2-(N-nitroso-N-arylamino)-4-phenyl-5-benzoylthiazoles (V). These are crystalline orange-colored substances, readily soluble in organic solvents.

On heating aminothiazoles (IV) with acetic anhydride, 2-(N-acetyl-N-arylamino)-4-phenyl-5-benzoylthiazoles (VI) were obtained. These are crystalline substances, slightly yellowish or white in color, soluble in ethyl alcohol and acetic acid, sparingly soluble in ether and chloroform. On heating with dilute alkali followed by acidification, the initial 2-arylamino-4-phenyl-5-benzoylthiazoles (IV) were again obtained.



(V–VI)

V. X = NO; Ar = a $-C_6H_5$; b $-o$-; c $-m$-; d $-n$-$C_6H_4CH_3$; e $-n$-C_6H_4J, m.p. 140° (decomp.); f $-n$-$C_6H_4OCH_3$, m.p. 115° (decomp.).

VI. $X = COCH_3$; Ar = a $-C_6H_5$; b $-o$-; c $-m$-; d $-n$-$C_6H_4CH_3$; e $-n$-C_6H_4J, m.p. 226°; f $-n$-$C_6H_4OCH_3$, m.p. 164-166°; g $-n$-$C_6H_4COOC_2H_5$, m.p. 185°; h $-n$-$C_6H_4N{=}NC_6H_5$, m.p. 231°; i $-\alpha$-$C_{10}H_7$, m.p. 176°.

The structure of the aminothiazoles was also confirmed by IR absorption spectra, recorded on an IKS-14 spectrophotometer for solid substances suspended in paraffin oil.

In all spectra, the absorption maxima of the aromatic (1570-1600 cm^{-1}) and thiazole (about 1510 cm^{-1}) rings ([11]) are clearly visible, as shown for IVd, Vd, and VId (see Fig. 1).

All 2-arylamino-4-phenyl-5-benzoylthiazoles have an absorption maximum near 1550 cm^{-1}, which should be assigned to deformation vibrations of the NH group. This is confirmed by study of the spectra of N,N-disubstituted thiazoles, in which this maximum is absent.

Fig. 1. IR absorption spectra of 2-(p-tolylamino)-4-phenyl-5-benzoylthiazole (IVd), 2-(N-p-tolyl-N-nitrosamino)-4-phenyl-5-benzoylthiazole (Vd), and 2-(N-p-tolyl-N-acetylamino)-4-phenyl-5-benzoylthiazole (VId)

Figure 1: Fig. 1. IR absorption spectra of 2-(p-tolylamino)-4-phenyl-5-benzoylthiazole (IVd), 2-(N-p-tolyl-N-nitrosamino)-4-phenyl-5-benzoylthiazole (Vd), and 2-(N-p-tolyl-N-acetylamino)-4-phenyl-5-benzoylthiazole (VId)

Fig. 1. IR absorption spectra of 2-(*p*-tolylamino)-4-phenyl-5-benzoylthiazole (IVd), 2-(N-*p*-tolyl-N-nitrosamino)-4-phenyl-5-benzoylthiazole (Vd), and 2-(N-*p*-tolyl-N-acetylamino)-4-phenyl-5-benzoylthiazole (VId).

Frequencies of 1606–1610 cm^{-1} may be attributed to absorption of carbonyl groups in aminothiazoles (IV), which, however, are strongly lowered. On substitution of the hydrogen atom in the NH group by a nitroso or acetyl group, the indicated frequencies increase by 20–40 cm^{-1}. In the high-frequency region, aminothiazoles (IV) have two absorption maxima: in the interval 3150 and 3200 cm^{-1}, which should be assigned to the lowered absorption frequencies of the NH group of secondary amines. These maxima are absent in N,N-disubstituted aminothiazoles (V and VI). We ascribe the absorption maximum near 3030 cm^{-1} to the aromatic CH group. It is possible that aminothiazoles (IV) form intermolecular hydrogen bonds.

Experimental Part

2-N-Phenylamino-4-phenyl-5-benzoylthiazole (IVa)

A. From N-phenylthiourea and dibenzoylbromomethane. A solution of 3 g (0.001 mole) of dibenzoylbromomethane ([12]) and 1.5 g (0.01 mole) of N-phenylthiourea in 50 ml of ethyl alcohol is boiled for one hour. After recrystallization from ethyl alcohol, 3.1 g (88%) of yellow crystals (IVa) are obtained. M.p. 196–198°.

Table 1

2-Arylamino-4-phenyl-5-benzoylthiazoles and their derivatives

No.	Compound	Yield, %	Appearance	m.p., °C	Empirical formula	Calculated, %	Found, %
1	IVa	72	Yellow rhombs	195–196	$C_{22}H_{16}ON_2S$	N 7.86 S 8.99	N 7.66 S 8.86

No.	Compound	Yield, %	Appearance	m.p., °C	Empirical formula	Calculated, %	Found, %
2	IV	63	Light-yellow plates	193–194	$C_{23}H_{18}ON_2S$	C 74.56H 4.90N 7.56S 8.66	C 73.92H 4.61N 7.40S 8.59
3	IV	59	Light-yellow plates	162–163	$C_{23}H_{18}ON_2S$	C 74.56H 4.90N 7.56S 8.66	C 74.59H 4.77N 7.46S 8.69
4	IV	67	Yellowish needles	181–182	$C_{23}H_{18}ON_2S$	C 74.56H 4.90N 7.56S 8.66	C 75.09H 4.63N 7.38S 8.69
5	IV	55	Bright-yellow plates	223–224	$C_{22}H_{15}ON_2SJ$	C 54.78H 3.13N 5.81S 6.65J 26.31	C 54.71H 3.17N 5.75S 6.72J 26.42
6	IV	47	Orange plates	177–178	$C_{25}H_{20}O_3N_2S$	C 70.07H 4.70N 6.54S 7.48	C 70.03H 4.71N 6.66S 7.55
7	IVe	68	Yellowish needles	186–187	$C_{23}H_{18}O_2N_2S$	C 71.48H 4.69N 7.25S 8.30	C 71.45H 4.66N 7.04S 8.19
8	IV	44	Orange-red needles	200–201	$C_{28}H_{20}ON_4S$	C 73.02H 4.38N 12.14S 6.94	C 73.03H 4.51N 12.14S 6.98
9	IV	42	Light-yellow prisms	228–229	$C_{26}H_{18}ON_2S$	C 76.87H 4.46N 6.89S 7.89	C 76.96H 4.36N 7.18S 8.06

No.	Compound	Yield, %	Appearance	m.p., °C	Empirical formula	Calculated, %	Found, %
10	Va		Orange plates	142 (decomp.)	$C_{22}H_{15}O_2N_3S$	N 10.90	N 10.97
11	V		Same	123 (decomp.)	$C_{23}H_{17}O_2N_3S$	N 10.52	N 10.59
12	V		Same	113 (decomp.)	$C_{23}H_{17}O_2N_3S$	N 10.52	N 10.69
13	V		Same	143 (decomp.)	$C_{23}H_{17}O_2N_3S$	N 10.52	N 10.63
14	VIa		Yellowish needles	202–203	$C_{24}H_{18}O_2N_2S$	N 7.03S 8.05	N 6.94S 8.07
15	VI		Colorless needles	202–203	$C_{25}H_{20}O_2N_2S$	N 6.79S 7.77	N 6.76S 7.77
16	VI		Colorless needles	146–148	$C_{25}H_{20}O_2N_2S$	N 6.79S 7.77	N 6.25S 7.72
17	VI		Yellowish needles	146–148	$C_{25}H_{20}O_2N_2S$	N 6.79S 7.77	N 6.74S 8.00

Found, %: N 7.59; S 8.91
$C_{22}H_{16}ON_2S$. Calculated, %: N 7.86; S 8.99

B. From dibenzoylbromomethane, potassium thiocyanate, and aniline. To a hot solution of 3 g (0.01 mole) of dibenzoylbromomethane in 50 ml of ethyl alcohol, 1.4 g (0.011 mole) of potassium thiocyanate, dissolved in 50 ml of hot ethyl alcohol, is added, and, with stirring, the mixture is cooled to room temperature. The precipitate that separates is filtered off; the filtrate is boiled with 1.2 g (0.012 mole) of freshly distilled aniline under a reflux condenser for 5 hours. The solution is cooled to −5–0°. After recrystallization from

from ethyl alcohol gives 2.6 g (72%) of 2-N-phenylamino-4-phenyl-5-benzoylthiazole. M.p. 195–196°.

Found, %:	N 7.66; S 8.96
$C_{22}H_{16}ON_2S$. Calculated, %:	N 7.86; S 8.99

A mixture with 2-N-phenylamino-4-phenyl-5-benzoylthiazole obtained by method A gives no depression of the melting point. Other N-substituted thiazoles (IVb–i) were obtained analogously (see Table 1).

2-(N-Phenyl-N-nitrosamino)-4-phenyl-5-benzoylthiazole (Va). To a solution of 0.7 g (0.003 mole) of aminothiazole (IVa) in 10 ml of glacial acetic acid, 0.5 g of sodium nitrite is added. The mixture is diluted with cold water. The precipitate that separates is recrystallized from diethyl ether, giving orange crystals (Va). M.p. 142° (dec.).

Found, %:	N 10.97
$C_{22}H_{15}O_2N_3S$. Calculated, %:	N 10.90

Other N-nitroso derivatives of thiazoles (Vb–e) were obtained analogously (see Table 1).

2-(N-Phenyl-N-acetylamino)-4-phenyl-5-benzoylthiazole (VIa). 0.7 g (0.003 mole) of aminothiazole (IVa) is boiled in 10 ml of acetic anhydride for 20 min. The mixture is cooled and diluted with water. It is recrystallized from ethyl alcohol, giving 0.7 g (85%) of colorless needle-like crystals (VIa). M.p. 202–203°.

Found, %:	N 6.94; S 8.07
$C_{24}H_{18}O_2N_2S$. Calculated, %:	N 7.03; S 8.05

Other N-acetyl derivatives of thiazoles (VIb–i) were obtained analogously (see Table 1).

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