RESEARCH IN THE IMIDAZOLE SERIES

LXIX.* SYNTHESIS OF NAPHTH[1,2-d]IMIDAZO[3,2-b]THIAZOLE DERIVATIVES FROM 2-CHLORONAPHTH[1,2-d]IMIDAZOLE

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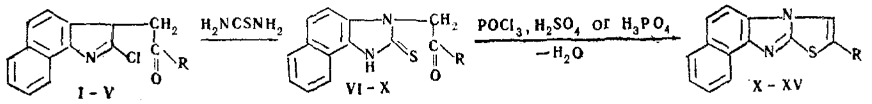
2-Alkyl(aryl, heteryl)-substituted naphth[1,2-d]imidazo[3,2-b]thiazoles were synthesized by the reaction of 2-chloro-3-acylmethylnaphth[1,2-d]imidazoles with thiourea and subsequent cyclization of the 2-mercapto-3-acylmethylnaphth[1,2-d]imidazoles.

In developing our research in [2-5], we have studied the replacement of a chlorine atom by a mercapto group in a number of 2-chloro-3-acylmethylnaphth[1,2-d]imidazoles (I-V), which, as in the case of 2-chlorobenzimidazole [5, 6], proceeds readily under the influence of thiourea, and 2-mercapto-3-acylmethylnaphth[1,2-d]imidazoles (VI-X, Table 1) are obtained.

A study of the IR spectra of these compounds and of 2-mercaptonaphth[1,2-d]imidazole demonstrated that they exist as thiones in the solid state.

When VI-X are treated with concentrated H_2SO_4 in the cold or on heating in $POCl_3$ or concentrated H_3PO_4, they readily split out a water molecule and are converted to 2-substituted naphth[1,2-d]imidazo-[3,2-b]thiazoles (XI-XV, Table 1),



EXPERIMENTAL

The 2-chloro-3-pivalylmethyl(phenacyl, p-methoxyphenacyl, p-bromophenacyl)naphth[1,2-d]imidazoles (I-IV) were obtained by the method in [7].

2-Chloro-3-(α-acetothienyl)naphth[1,2-d]imidazo[3,2-b]thiazole (V). This compound was obtained in 60% yield by the reaction of 2-chloronaphth[1,2-d]imidazole [8] with 2-bromoacetothienone by the method in [7] and had mp 196-197° (dec., from aqueous dioxane). Found: C 62.6; H 3.4; N 8.5; Cl 10.4; S 9.8%. $C_{17}H_{11}N_2ClOS$. Calculated: C 62.6; H 3.4; N 8.6; Cl 10.8; S 9.8%.

2-Mercapto-3-acylmethylnaphth[1,2-d]imidazoles (VI-X, Table 1). A solution of 0.01 mole of I-V and 0.02 mole of thiourea in 30 ml of ethanol (I) or dimethylformamide (DMF) (II-V) was refluxed for 2 h, cooled, and poured into water. The mixture was neutralized with ammonium hydroxide, and the precipitate was removed by filtration and washed with water. The compounds were purified for analysis by crystallization from ethanol–DMF (VI, VIII), methanol–DMF (IX), DMF (VII), and aqueous DMF (X).

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*See [1] for communication XLVIII.

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TABLE 1. 3-Acylmethyl-2-mercaptonaphth[1,2-d]imidazoles (VI-X) and 2-Alkyl(aryl, heteryl)naphth[1,2-d]imidazo[3,2-d]thiazoles (XI-XV)

Compound	R	Mp, °C (dec.)	Empirical formula	Found, %				Calculated, %				Yield, %
				C	H	N	S	C	H	N	S	
VI	*t*-C_4H_9	305—307	$C_{17}H_{18}N_2OS$[a]	68,0	6,0	9,7	10,6	68,4	6,1	9,4	10,8	83
VII	C_6H_5	290—292	$C_{19}H_{14}N_2OS$[a]	71,8	4,6	8,8	9,9	71,7	4,4	8,8	10,1	83
VIII	$C_6H_4OCH_3$-*p*	295—297	$C_{20}H_{16}N_2O_2S$[a]	68,7	5,0	7,6	9,0	68,9	4,6	8,0	9,2	83
IX	C_6H_4Br-*p*	295—297	$C_{19}H_{19}BrN_2OS$[b]	57,2	3,3	7,1	8,2	57,4	3,3	7,1	8,1	96
X	C_4H_3S[c]	308—310	$C_{17}H_{12}N_2OS_2 \cdot 0{,}5\ H_2O$	61,3	4,3	8,4	19,6	61,2	3,9	8,4	19,2	71
XI	*t*-C_4H_9	131—132	$C_{17}H_{16}N_2S$	72,8	5,8	10,0	11,4	72,8	5,8	10,0	11,4	86
XII	C_6H_5	222—223	$C_{19}H_{12}N_2S \cdot 0{,}5\ H_2O$	73,9	4,2	8,7	10,0	73,8	4,2	8,7	10,4	90
XIII	$C_6H_4OCH_3$-*p*	188—190	$C_{19}H_{14}N_2OS$	72,8	4,4	9,8	8,2	72,7	4,3	9,7	8,5	88
XIV	C_6H_4Br-*p*	231—233	$C_{19}H_{11}BrN_2S$[d]	60,5	3,3	7,4	8,5	60,2	2,9	7,4	8,5	90—94
XV	C_4H_3S	174—175	$C_{17}H_{10}N_2S_2 \cdot 0{,}5\ H_2O$	65,1	3,8	8,5	20,4	64,7	3,5	8,9	20,3	95

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a) Infrared spectra (recorded from mineral oil suspensions with a UR-10 spectrometer), cm^{-1}: VI 1720 (CO), 3130 (NH); VII 1690 (CO), 3100 (NH); VIII 1680 (CO), 3160 (NH). b) Found: Br 19.9%. Calculated: Br 20.1%. c) C_4H_3S is 2-thienyl. d) Found: Br 20.8%. Calculated: Br 21.1%.

2-Alkyl(aryl)naphth[1,2-d]imidazo[3,2-b]thiazoles (XI-XV, Table 1). A) A mixture of 0.01 mole of VII, IX, or X in 30 ml of $POCl_3$ was refluxed for 1 h, and the $POCl_3$ was removed by vacuum distillation. The residue was decomposed with water, the mixture was neutralized with ammonium hydroxide, and the precipitate (XII, XIV, XV) was removed by filtration and washed with water.

B) A mixture of 0.005 mole of VI in 15 ml of 85% H_3PO_4 was refluxed for 1 h, cooled, and poured into water. The mixture was neutralized with ammonia, and the precipitated XI was removed by filtration and washed with warm water.

C) A solution of 0.005 mole of VIII or IX in 15-20 ml of concentrated H_2SO_4 was allowed to stand at 18-20° for 1-3 h. It was then poured into water and worked up as in experiment B to give XIII and XIV.

The properties of XI-XV are as follows: they are colorless, light-yellow (XII-XIV) or light-brown (XV) crystalline substances that are only slightly soluble in most organic solvents. The compounds were purified for analysis by crystallization from ethanol (XIII), ethanol–DMF (1 : 1) (XII, XIV), and aqueous dioxane (XI, XV).

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