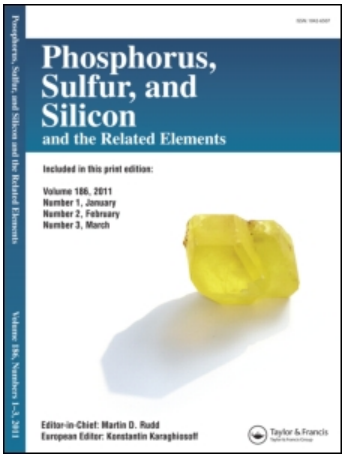

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RING TRANSFORMATION OF 3-(2-OXOPROPYL)-2(3H)-BENZOTHIAZOLONE IN REACTION WITH PRIMARY AMINE

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RING TRANSFORMATION OF 3-(2-OXOPROPYL)-2(3H)-BENZOTHIAZOLONE IN REACTION WITH PRIMARY AMINE

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New 3-alkyl-1,3-dihydro-1-(2-mercaptophenyl)-4-methyl-2H-imidazolin-2-ones and the products of their oxidation-the corresponding disulfides are synthesized by ring transformation of 3-(2-oxopropyl)-2(3H)-benzothiazolone in reaction with primary amines. The supposed reaction mechanism is disscused. This reaction is a suitable one-stage method for the synthesis of 3,4-substituted 2H-imidazolones containing a 2-mercaptophenyl group.

Keywords: 3-Substituted-2(3H)-benzothiazolone, ring transformation, 3-alkyl-1-(2-mercaptophenyl)-4-methyl-2H-imidazolin-2-ones

INTRODUCTION

The chemistry of 1,3-dihydro-2H-imidazol-2-ones has received particular attention because of the broad pharmacological activity of these compounds such as cardiotonic[1,2], anticonvulsant[3], histaminergic[4] and other activities[5,6].

The two main pathways for the synthesis of 1,3-dihydro-2H-imidazol-2-ones entail either reactions of condensation of α-substituted ketones and ketimines with different reagents such as isocyanates[7], potassium cyanate[8], ureas[9], alkyl carbamates[10], cyanogen bromide[11], carbon dioxide, ammonia with potassium cyanate[12] and cyclocondensation of

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some substituted ureas[13,14]. 2H-imidazol-2-ones have also been obtained by reaction of ring transformation of the oxazole ring in substituted 2H-oxazol-2-ones[15,16], 2-aminooxazolium and 2-amino oxazolium salt[17], containing a phenacyl group in position 3.

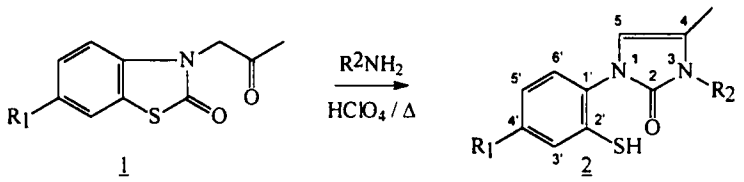
The synthesis of 1,3-dihydro-1-(2-hydroxyphenyl)-3,4-disubstituted-2H- imidazol-2-ones by ring transformation of 3-(2-oxoalkyl-,aryl)-2(3H)-benzoxazolones in a reaction with primary amines has been also reported in a previous paper[18]. No similar interaction with 2(3H)-benzothiazolones has been described.

In the present paper we report a ring transformation in 2(3H)-benzothiazolones, containing a 2-oxopropyl group at position 3, to 1,3-dihydro-2H-imidazol-2-ones by treatment with primary amines. As we reported [19,20] earlier, these compounds react with hydrazines and hydroxylamine only at the more reactive carbonyl group of the 2-oxopropyl substituent giving the corresponding hydrazones, azines or oximes.

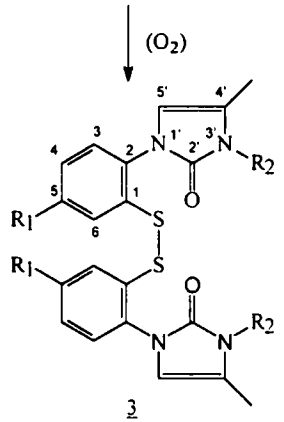
RESULTS AND DISCUSSION

The reaction was carried out at 60–90° C with excess of primary amines such as methylamine, ethylamine, n-propylamine, i-butyl amine, cyclohexylamine and benzylamine in perchloric acid for 7 to 48 h. The obtained 3-alkyl 1,3-dihydro-1-(2-mercaptophenyl)-4-methyl-2H-imidazolin-2-ones **2** were partially oxidized to the corresponding disulfides **3** (Scheme 1).

Much longer time is needed for the completion of the reaction if it is carried out at r.t. Thus, in the case of n-propylamine, heating of the reaction mixture at 60–70°C shortens the reaction time from 40 to 10 h. With weak nucleophiles, as aniline, no product was obtained a even after reflux for 40 h. The media of the reaction was chosen after a series of experiments which have been carried out with 6-bromo-3-(2-oxopropyl)-2(3H)-benzothizolone and n-propyl amine in solvents such as amine, amine/perchloric acid, amine/water, amine/ethanol, amine /THF. Purest products for shortest reaction time and in highest yield were obtained in amine/perchloric acid (89% yield) and amine/water (76% yield). The reaction proceeded easier and with higher yields in the presence of electronaccepting substituent at position 6 of the benzene ring.



Comp.	R_1	R_2
2a, **3a**	6-Br	CH_3
2b, **3b**	6-NO_2	CH_3
2c, **3c**	6-Br	CH_2CH_3
2d, **3d**	6-NO_2	CH_2CH_3
2e, **3e**	6-Br	$CH_2CH_2CH_3$
2f, **3f**	6-NO_2	$CH_2CH_2CH_3$
2g, **3f**	6-Br	$CH_2CH(CH_3)_2$
2h, **3h**	6-NO_2	$CH_2CH(CH_3)_2$
2i, **3i**	6-Br	C_6H_{11}
2j, **3j**	6-NO_2	C_6H_{11}
2k, **3k**	6-Br	$CH_2C_6H_5$
2l, **3l**	6-NO_2	$CH_2C_6H_5$
3m	6-H	$CH_2CH_2CH_3$
3n	6-H	$CH_2CH(CH_3)_2$



SCHEME 1

Carrying out the reaction in a pressure tube (air free conditions) lead to increase of the yields of compounds **2** and decrease of those of the disulfides **3**. In all the cases compounds **3** were more stable, easier to isolate and purify than the thiophenol forms **2**. The insolubility of **3** in dilute alkaline solutions was used for their separation from **2**. The compounds **2g** and **2f** were also obtained by reduction of the corresponding disulfides **3** with sodium tetrahydroborate in dioxane.

The reaction conditions and the data of the compounds are listed in ***Table 1–4***. The structures of all compounds were confirmed by their elemental analysis, IR, ^{1}H-NMR spectra and in some cases (**2h, 3h**) by mass spectra. In the IR spectra of compounds **2** and **3** two bands were observed in the 1630–1695 cm^{-1} region: an intensive band for carbonyl group at the 1670–1695 cm^{-1} and a weaker band at 1650–1630 cm^{-1} for carbon-carbon double bond from the imidazolone cycle. In addition, in the IR spectra of

compounds **2** (nujol) a weak band at 2450–2550 cm^{-1} for SH was observed. ^{1}H-NMR spectra of the compounds **2** and **3** reveal, besides the signals for aromatic protons and those for the protons of alkyl substituent at position 3, the protons of the methyl group at 2.11 ppm and a signal for the methyne proton from the imidazolone cycle at 6.04 ppm appearing as a doublet because of the allylic coupling of 1.3 Hz. In the ^{1}H-NMR-spectra of the compounds **2** an exchangeable (with D_2O) singlet for the proton from thiophenol group at 4.21–4.84 ppm, was observed.

The transformation of the thiazolone into the imidazolone ring seems to proceed with an initial attack of the amine at the more reactive carbonyl group of the oxopropyl substituent, followed by a rearrangement of the intermediate as shown in ***Scheme 2***.

TABLE I 3-Alkyl-1,3-dihydro-4-(2-mercaptophenyl)-1-methyl-2H-imidazole-2-ones **2a-2l**

Comp.	*Reaction*		*Method*	*Yield (%)*	*M.p. (°C)*
	Temp. (°C)	*Time (h)*			
2a	90	10	A	50	151–153
2b	70	9	A	65	170–173
2c	40–45	9	C	80	105–107
2d	40–45	14	C	82	131–134
2e	60–70	8	A	52	109–111
	60	12	C	89	
2f	80	6	A	42	118–121
2g	70–75	16	A	26	112–114
	60	10	C	70	
2h	70	8	A	52	113–116
2i	90–100	38	B	20	115–117
	70–80	48	C	88	
2j	70	20	A	10	125–127
	70–80	20	C	26	
2k	70	25	B	19	100–102
	70–80	20	C	72	
2l	70	22	A	43	125–128

TABLE II Bis-[2-(3-alkyl-1, 3-dihydro-4-methyl-2H-imidazol-2-onyl)phenyl]disulfide **3a-3n**

Comp.	*Reaction*		*Method*	*Yield (%)*	*M.p. (°C)*	*Bruto formula (M.W.)*	*Analysis, % C,H,N Calc./Found*
	Temp.(°C).	*Time(h)*					
3a	90	10	A	25	210–212	$C_{22}H_{20}Br_2N_4O_2S_2$	44.30, 3.38, 9.40
						596.32	44.67, 3.35, 8.77
3b	70	9	A	22	217–219	$C_{22}H_{20}N_6O_6S_2$	50.0, 3.81, 15.90
						528.55	50.37, 4.13, 15.51
3c	40–45	9	C	8	155–158	$C_{24}H_{24}Br_2N_4O_2S_2$	46.17, 3.87, 8.97
						624.41	46.67, 4.15, 8.50
3d	40–45	14	C	11	190–195	$C_{24}H_{24}N_6O_6S_2$	51.79, 4.35, 15.10
						556.51	52.08, 4.88, 15.53
3e	60–70	8	A	18	176–178	$C_{26}H_{28}Br_2N_4O_2S_2$	47.86, 4.33, 8.59
	60	12	C	6		652.46	47.56, 4.18, 8.21
3f	80	6	A	51	222–224	$C_{26}H_{28}N_6O_6S_2$	53.41, 4.83, 14.37
						584.66	53.24, 4.80, 14.17
3g	70–75	16	A	62	161–163	$C_{28}H_{32}Br_2N_4O_2S_2$	49.42, 4.74, 8.23
	60	10	C	10		680.52	49.71, 4.84, 7.65

Comp.	*Reaction*		*Method*	*Yield (%)*	*M.p. (°C)*	*Bruto formula (M.W.)*	*Analysis, % C,H,N Calc./Found*
	Temp.(°C).	*Time(h)*					
3h	70	8	A	40	210–212	$C_{28}H_{32}N_6O_6S_2$	54.89, 5.12, 13.72
						612.72	55.12, 5.06, 12.08
3i	90–100	38	B	70	202–205	$C_{32}H_{36}Br_2N_4O_2S_2$	52.46, 4.95, 7.65
	70–80	48	C	5		732.59	52.80, 4.40, 7.38
3j	70	20	A	74	233–235	$C_{32}H_{36}N_6O_6S_2$	57.82, 5.46, 12.64
	70–80	20	C	60		664.79	57.57, 5.36, 12.43
3k	70	25	B	72	175–177	$C_{34}H_{28}Br_2N_4O_2S_2$	54.56, 3.77, 7.48
	70–80	20	C	14		748.53	55.35, 4.07, 7.28
3l	70	22	A	39	204–206	$C_{34}H_{28}N_6O_6S_2$	12.35
						680.75	11.75
3m	95–100	12	B	45	117–119	$C_{26}H_{29}N_4O_2S_2$	63.28, 5.88, 11.35
						493.66	63.68, 5.54, 11.75
3n	95–100	20	B	31	161–165	$C_{28}H_{33}N_4O_2S_2$	64.49, 6.33, 10.75
						521.77	64.11, 5.93, 10.36

TABLE III Spectral Data of Compounds **2a-21**

Comp.	*IR, (cm^{-1}), (nujol)*	*^{1}H-NMR, ppm, ($CDCl_3$)*
2a	2450, 1660, 1630	2.11 (d, 3H, J=1.3 Hz, CH_3), 3.26 (s, 3H, NCH_3), 4.29 (s, 1H, SH), 6.1 (d, 1H, J=1.3 Hz, H-5), 7.43 (d, 1H, $J_{6'-5'}$=8.7 Hz, H-6′), 8.08 (dd, 1H, $J_{5'-3'}$=2.6 Hz, $J_{5'-6'}$= 8.7 Hz, H-5′), 8.36 (d, 1H, $J_{3'-5'}$=2.5 Hz, H-3′)
2b	2480, 1690, 1650, 1520, 340	2.15 (d, 3H, J=1.3 Hz, CH_3), 3.30 (s, 3H, NCH_3), 4.69 (s, 1 H, SH), 6.21 (d, 1 H, J=1.3 Hz, H-5), 7.43 (d, 1 H, $J_{6'-5'}$=8.7 Hz, H-6′), 8.08 (dd, 1H, $J_{5'-3'}$=2.6 Hz, $J_{5'-6'}$=8.7 Hz, H-5′), 8.36 (d, 1H, $J_{3'-5'}$=2.5 Hz, H-3′)
2c	2460, 1660, 1630	1.29 (t, 3H, CH_2CH_3), 2.12 (d, 3H, J=1.3 Hz, CH_3), 3.7–3.78 (q, 2H, NCH_2), 4.36 (s, 1H, SH), 6.08 (d, 1H, J=1.3 Hz, H-5), 7.1 (d, 1H, $J_{6'-5'}$=8.4 Hz, H-6′), 7.33 (dd, 1H, $J_{5'-3'}$=2.2 Hz, $J_{5'-6'}$= 8.4 Hz, H-5′), 7.60 (d, 1H, $J_{3'-5'}$=2.2 Hz, H-3′)
2d	2480, 1675, 1640, 1520, 1340	1.32 (t, 3H, CH_2CH_3), 2.17 (d, 3H, J=1.3 Hz, CH_3), 3.69–3.78 (q, 2H, NCH_2), 4.79 (s, 1H, SH), 6.21 (d, 1H, J=1.3 Hz, H-5), 7.44 (d, 1H, $J_{6'-5'}$=8.8 Hz, H-6′), 8.08 (dd, 1H, $J_{5'-3'}$=2.6 Hz, $J_{5'-6'}$=8.8 Hz, H-5′), 8.36 (d, 1H, $J_{3'-5'}$=2.5 Hz, H-3′)
2e	2500, 1680, 1640	0.97 (t, 3H, CH_2CH_3), 1.65–1.77 (m, 2H, CH_2CH_3), 2.11 (d, 3H, J=1.3 Hz, CH_3), 3.64 (t, 1H, NCH_2), 4.41 (s, 1H, SH), 6.09 (d, 1H, J=1.3 Hz, H-5), 7.11 (d, 1H, $J_{6'-5'}$=8.4 Hz, H-6′) 7.34 (dd, 1H, $J_{5'-3'}$=2.2 Hz, $J_{5'-6'}$=8.5 Hz, H-5′), 7.61 (d, 1H, $J_{3'-5'}$=2.2 Hz, H-3′)
2f	2460, 1670, 1630, 1520, 1340	0.99 (t, 3H, CH_2CH_3), 1.67–1.81 (m, 2H, CH_2CH_3), 2.15 (d, 3H, J=1.3 Hz, CH_3), 3.66 (t, 1H, NCH_2), 4.78 (s, 1H, SH), 6.09 (d, 1H. J=1.3 Hz, H-5), 7.43 (d, 1H, $J_{6'-5'}$=8.7 Hz, H-6′), 8.21 (dd, 1H, $J_{5'-3'}$=2.6 Hz, $J_{5'-6'}$=8.8 Hz, H-5′), 8.35 (d, 1H, $J_{3'-5'}$=2.6 Hz, H-3′)
2g	2500, 1680, 1640	0.96 (d, 6H, $CH(CH_3)_2$), 2.06–2.17 (m, 4H, CH_3, $CHCH_2$), 2.1 (d, 3H, J=1.3 Hz, CH_3), 3.48 (d, 2H, NCH_2), 4.41 (s, 1H, SH), 6.10 (d, 1H, J=1.3 Hz, H-5), 7.1 (d, 1H, $J_{6'-5'}$=8.4 Hz, H-6′), 7.34 (dd, 1H, $J_{5'-3'}$=2.2 Hz, $J_{5'-6'}$= 8.5 Hz, H-5′), 7.61 (d, 1H, $J_{3'-5'}$=2.2 Hz, H-3′)
2h[a]	2480, 1670, 1645, 1520, 1345	1.02 (d, 6H, $CH(CH_3)_2$), 2.08–2 22 (m, H, CH_3, $CHCH_2$), 2.17 (d, 3H, J=1.3 Hz, CH_3), 3.54 (d, 2H, NCH_2), 4.84 (s, 1H, SH), 6.25 (d, 1H, J=1.3 Hz, H-5), 7.46 (d, 1H, $J_{6'-5'}$=8.8 Hz, H-6′), 8.09 (dd, 1H, $J_{5'-3'}$=2.6 Hz, $J_{5'-6'}$=8.8 Hz, H-5′), 8.38 (d, 1H, $J_{3'-5'}$=2.5 Hz, H-3′)

Comp.	*IR, (cm^{-1}), (nujol)*	*^{1}H-NMR, ppm, ($CDCl_3$)*
2i	2420, 1670, 1635	1.20–2.13 (m, 10H, 5C$\underline{H}_2$-cyclohexyl), 2.16 (d, 3H, J=1.2 Hz, CH_3), 3.82–3.93 (tt, 1H, NC$\underline{H}$), 4.21 (s, 1H, S$\underline{H}$), 6.07 (d, 1H, J=1.2 Hz, H-5), 7.05 (d, 1H, $J_{6'-5'}$=8.4 Hz, H-6′), 7.33 (dd, 1H, $J_{5'-3'}$=2.2 Hz, $J_{5'-6'}$= 8.5 Hz, H-5′), 7.6 (d, 1H, $J_{3'-5'}$=2.2 Hz, H-3′)
2j	2530, 1665, 1630, 1520, 1340	1.21–2.19 (m, 10H, 5C$\underline{H}_2$-cyclohexyl), 2.18 (d, 3H, J=1.2 Hz, CH_3), 3.81–3.94 (tt, 1H, NC$\underline{H}$), 4.82 (s, 1H, S$\underline{H}$), 6.17 (d, 1H, J=1.2 Hz, H-5), 7.43 (d, 1H, $J_{6'-5'}$=8.7 Hz, H-6′), 8.07 (dd, 1H, $J_{5'-3'}$=2.6 Hz, $J_{5'-6'}$=8.7 Hz, H-5′), 8.35 (d, 1H, $J_{3'-5'}$ =2.5 Hz, H-3′)
2k	2500, 1680, 1650	2.01 (d, 3H, J=1.4 Hz, CH_3), 4.33 (s, 1H, S$\underline{H}$), 4.92 (s, 2H, NC$\underline{H}_2$), 6.12 (d, 1H, J=1.6 Hz, H-5), 7.15 (d, 1H, $J_{6'-5'}$=8.4 Hz, H-6′), 7.27–7.33 (m, 5H, arom.), 7.37 (dd, H, $J_{5'-3'}$=2.2 Hz, $J_{5'-6'}$= 8.4 Hz, H-5′), 7.64 (d, H, $J_{3'-5'}$ =2.2 Hz, H-3′)
2l	2480, 1680, 1650, 1520, 1340	2.04 (d, 3H, J=1.3 Hz, CH_3), 4.69 (s, 1H, S$\underline{H}$), 4.94 (s, 2H, NC$\underline{H}_2$), 6.23 (d, 1H, J=1.3 Hz, H-5), 7.29–7.35 (m, 5H, arom.), 7.46 (d, 1H, $J_{6'-5'}$=8.7 Hz, H-6′), 8.08 (dd, 1H, $J_{5'-3'}$=2.6 Hz, $J_{5'-6'}$ =8.7 Hz, H-5′), 8.37 (d, 1H, $J_{3'-5'}$=2.5 Hz, H-3′)

a. mass spectrum (70 cV) [m/z (%)]

2h 307 (M^+, 100); 292 (4.99); 264 (21.6); 251 (81.1); 210 (17); 207 (28.15); 181 (89.76); 161 (51.46); 135 (29.7).

TABLE IV Spectral Data of Compounds **3a-3n**

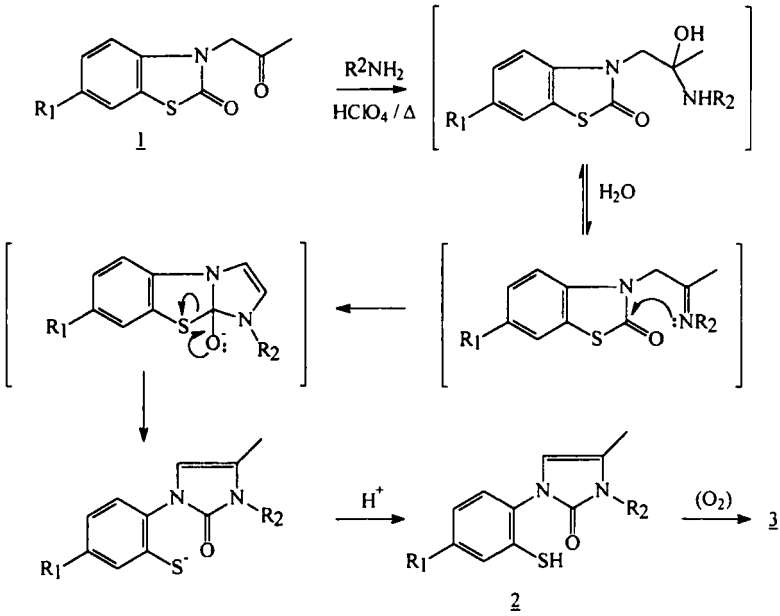
Comp.	*IR, (cm^{-1}), (nujol)*	*^{1}H-NMR, ppm, ($CDCl_3$)*
3a	1685, 1640	2. 1 (d, 6H, J=1.3 Hz, $2CH_3$), 3.24 (s, 6H, $2NCH_3$), 6.06 (d, 2H, J=1.3 Hz, 2H-5′), 7.06 (d, 2H, J_{3-4}=8.4 Hz, 2H-3), 7.2 (dd, 2H, J_{4-6}=2.2 Hz, J_{4-3}=8.4 Hz, 2H-4), 7.76 (d, 2H, J_{6-4}=2.2 Hz, 2H-6)
3b	1695, 1650, 1525, 1345	2.12 (d, 6H, J=1.3 Hz, $2CH_3$), 3.27 (s, 6H, $2NCH_3$), 6.15 (d, 2H, J=1.3 Hz, 2H-5′), 7.35 (d, 2H, J_{3-4}=8.7 Hz, 2H-3), 8.08 (dd, 2H, J_{4-6}=2.5 Hz, J_{4-3}=8.7 Hz, 2H-4), 8.56 (d, 2H, J_{6-4}=5 Hz, 2H-6)
3c	1690, 1640	
3d	1695, 1645, 1530, 1350	1.30 (t, 6H, $2CH_2C\underline{H}_3$), 2.14 (d, 6H, J=1.3 Hz, $2CH_3$), 3.69–3.78 (q, 4H, $2NC\underline{H}_2$), 6.13 (d, 2H, J=1.3 Hz, 2H-5′), 7.35 (d, 2H, J_{3-4}=8.7 Hz, 2H-3), 8.08 (dd, 2H, J_{4-6}=2.5 Hz, J_{4-3}=8.7 Hz, 2H-4), 8.56 (d, 2H, J_{6-4}=2.5 Hz, 2H-6)
3e	1685, 1640	0.97 (t, 6H, $2CH_2C\underline{H}_3$), 1.64–1.79 (m, 4H, $2C\underline{H}_2CH_3$), 2.11 (d, 6H, J =1.3 Hz, $2CH_3$), 3.62 (t, 4H, $2NC\underline{H}_2$), 6.04 (d, 2H, J=1.3 Hz, 2H-5′), 7.07 (d, 2H, J_{3-4}=8.4 Hz, 2H-3) 7.37 (dd, 2H, J_{4-6}=2.2 Hz, J_{4-3}=8.4 Hz, 2H-4), 7.76 (d, 2H, J_{6-4}=2.2 Hz, 2H-6)
3f	1690,1645, 1520, 1340	1.02 (t, 6H, $2CH_2C\underline{H}_3$), 1.73–1.79 (m, 4H, $2C\underline{H}_2CH_3$), 2.17 (d, 6H, J=1.3 Hz, $2CH_3$), 3.67 (t, 4H, $2NC\underline{H}_2$), 6.16 (d, 2H, J=1.3 Hz, 2H-5′), 7.34 (d, 2H, J_{3-4}=8.7 Hz, 2H-3), 8.15 (dd, 2H, J_{4-6}=2.5 Hz, J_{4-3}=8.7 Hz, 2H-4), 8.57 (d, 2H, J_{6-4}=2.5 Hz, 2H-6)
3g	1690, 1640	0.97 (d, 12H, $CH(C\underline{H}_3)_2$), 2.06–2.14 (m, 2H, $2C\underline{H}CH_2$), 2.1 (d, 6H, J=1.3 Hz, $2CH_3$), 3.46 (d, 4H, $2NC\underline{H}_2$), 6.05 (d, 2H, J=1.3 Hz, 2H-5′), 7.07 (d, 2H, J_{3-4}=8.4 Hz, 2H-3), 7.37 (dd, 2H, J_{4-6}=2.2 Hz, J_{4-3}= 8.5 Hz, 2H-4), 7.76 (d, 2H, J_{6-4}=2.2 Hz, 2H-6)
3h[a]	1695, 1650, 1530, 1345	1.02 (d, 12H, $CH(C\underline{H}_3)_2$), 2.08–2 22 (m, 2H, $2C\underline{H}CH_2$), 2.16 (d, 6H, J=1.3 Hz, $2CH_3$), 3.5 (d, 4H, $2NC\underline{H}_2$), 6.16 (d, 2H, J=1.3 Hz, 2H-5′), 7.37 (d, 2H, J_{3-4}=8.8 Hz, 2H-3), 8.1 (dd, 2H, J_{4-6}=2.5 Hz, J_{4-3}=8.7 Hz, 2H-4), 8.56 (d, 2H, J_{6-4}=2.5 Hz, 2H-6)
3i	1690, 1640	1.24–2.20 (m, 20H, $10C\underline{H}_2$-cyclohexyl), 2.15 (d, 6H, J=1.3 Hz, $2CH_3$) 3.79–3.92 (tt, 2H, $NC\underline{H}$), 5.99 (d, 2H, J=1.3 Hz, 2H- 5′), 7.05 (d, 2H, J_{3-4}=8.4 Hz, 2H-3), 7.36 (dd, 2H, J_{4-6}=2.2 Hz, J_{4-3}= 8.5 Hz, 2H-4), 7.75 (d, 2H, J_{6-4}=2.2 Hz, 2H-6)

Comp.	*IR, (cm^{-1}), (nujol)*	*^{1}H-NMR, ppm, ($CDCl_3$)*
3j	1680,1650, 1530, 1340	1.22–2.28 (m, 20H, 10C$\underline{H}_2$-cyclohexyl), 2.19 (d, 6H, J=1.1 Hz, 2CH_3) 3.82–3.94 (tt, 2H, NC$\underline{H}$), 6.17 (d, 2H, J=1.2 Hz, 2H- 5′), 7.34 (d, 2H, J_{3-4}=8.7 Hz, 2H-3), 8.09 (dd, 2H, J_{4-6}=2.6 Hz, J_{4-3}=8.7 Hz, 2H-4), 8.57 (d, 2H, J_{6-4}=2.6 Hz, 2H-6)
3k	1685, 1640	2.0 (d, 6H, J=1.3 Hz, 2CH_3), 4.91 (s, 4H, 2NC$\underline{H}_2$), 6.09 (d, 2H, J=1.3 Hz, 2H-5′), 7.12 (d, 2H, J_{3-4}=8.4 Hz, 2H-3), 7.27- 7.34 (m, 10H, arom.) 7.4 (dd, 2H, J_{4-6}=2.2 Hz, J_{4-3}= 8.5 Hz, 2H-4), 7.81 (d, 2H, J_{6-4}=2.2 Hz, 2H-6)
3l	1670, 1640, 1520, 1345	2.03 (d, 6H, J=1.4 Hz, 2CH_3), 4.91 (s, 4H, 2NC$\underline{H}_2$), 6.19 (d, 2H, J=1.4 Hz, 2H-5′), 7.12 (d, 2H, J_{3-4}=8.4 Hz, 2H-3), 7.27- 7.36 (m, 10H, 2 arom.), 7.39 (d, 2H, J_{3-4}=8.7 Hz, 2H-3), 8.1 (dd, 2H, J_{4-6}=2.5 Hz, J_{4-3}=8.7 Hz, 2H-4), 8.56 (d, 2H, J_{6-4}=2.5 Hz, 2H-6)
3m	1680, 1640	0.96 (t, 6H, 2CH_2C$\underline{H}_3$), 1.64–1.73 (m, 4H, 2C$\underline{H}_2$CH_3), 2.1 (d, 6H, J=1.3 Hz, 2CH_3), 3.62 (t, 4H, 2NC$\underline{H}_2$), 6.06 (d, 2H, J=1.3 Hz, 2H-5′), 7.22–7.68 (m, 8H, arom.)
3n	1680, 1640	0.94 (d, 12H, CH(C$\underline{H}_3$)$_2$), 2.07–2.17 (m, 2H, 2C$\underline{H}$CH_2), 2.09 (d, 6H, J=1.4 Hz, 2CH_3), 3.47 (d, 4H, 2NC$\underline{H}_2$), 6.06 (s, 2H, J=1.4 Hz, 2H-5′), 7.19–7.68 (m, 8H, arom.)

a. mass spectrum (70 eV) [m/z (%)]

3h 612.4 (M^+, 2 28); 307 (71.79); 249 (25.30); 207 (100); 181(30); 161(54.5); 135 (10.19).

The described reaction is a suitable one-stage method for the synthesis of 1,3-dihydro-a 2H-imidazol-2-ones containing a mercaptophenyl group and the corresponding disulfides.



SCHEME 2

EXPERIMENTAL

Melting points were determined on a Boetius hot-stage microscope and are uncorrected. IR spectra were recorded on a Specord 71 IR spectrometer (Carl Zeiss, Germany) in nujol (NaCl plate) and in chloroform (NaCl cell). H-NMR spectra of compounds **2f, 2h, 3i, 3l** were taken on a Varian instrument (300 MHz) and those of the other compounds on a Bruker AC 250 spectrometer with TMS as internal standard. Chemical shifts δ are reported in ppm. The reactions were followed by TLC (silica gel 60 F_{254}, Merck), using hexane/ethylacetate (3:2) solvent system for compounds ***2a-e, g***, and ***3a-e, g*** and toluene/chloroform/ethylacetate (3:2:1) solvent system for the rest. Mass spectra were obtained with a Varian MAT 311A mass spectrometer using the direct inlet system (70 eV).

3-(2-Oxopropyl)-2(3H)-benzothiazolones were synthesized according to a known procedure[19].

3-Alkyl-1,3-dihydro-1-(2-mercaptophenyl)-4-methyl-2H-imidazol-2-ones 2a-21 and bis[2-(3-alkyl-1,3-dihydro-4-methyl-2H-imidazol-2-onyl)phenyl] disulfide 3a-3n

General procedure

Method A

The corresponding amine (72–80 mmol) was added dropwise to a stirring solution of 6-bromo-3-(2-oxopropyl)-2(3H)-benzothiazolone or 6-nitro-3-(2-oxopropyl)-2(3H)-benzothiazolone (4 mmol) in 70–72% perchloric acid (40mmol) with cooling (ice bath). The mixture was stirred and heated at 60–90°C for 8–40 h until complete consumption of the starting material (TLC)was observed. After cooling and neutralizing of the reaction mixture with 5% hydrochloric acid a precipitate or oil of the disulfides *3* was formed. When an oil was obtained, it solidified after cooling for several hours in a refrigerator. The precipitates were filtered, washed with water and dried. The acidification of the filtrate with hydrochloric acid to pH 1 led to the corresponding thiophenols **2**. The precipitate of compounds **2** was filtered, washed with water to pH 7 and dried in a vacuum dryer.

Method B

The corresponding amine (72–80 mmol) was added dropwise to a stirring solution of 3-(2-oxopropyl)-2(3H)-benzothiazolone or 6-bromo-3-(2-oxopropyl)-2(3H)-benzothiazolone (4 mmol) in 70–72% perchloric acid (40 mmol) with cooling (ice bath). The mixture was stirred and heated at 60–90° C for 10–30 h until complete consumption of the starting material (TLC)was observed. After cooling and acidifying to pH 1 the oil formed was extracted with chloroform or methylene chloride. The organic phase was separated and stirred with 5% sodium hydroxide for 5–10 min., washed with water and dried over Na_2SO_4. The solvent was the removed under vacuum and the residue was recrystallized to give the disulfides **3**. The corresponding thiophenols **2** were isolated after acidification of the alkaline filtrate using 5% a hydrochloric acid. The precipitates of **2** were filtered, washed with water and dried in a vacuum dryer.

Method C

The reaction mixture prepared as in method A was heated at 60–85° C for 10–30 h in a pressure tube (Aldrich) with threaded type A plug until no starting material was observed (TLC). After cooling, the reaction mixture was poured into an equal volume of cold water and was acidified with 10% hydrochloric acid. The precipitate obtained was a mixture of both compounds, thiophenols **2** and disulfides **3** (TLC). It was filtered, washed with water and treated with 5% sodium hydroxide. The insoluble disulfide **3** was filtered, washed with water and dried. The precipitate of thiophenols **2** obtained after acidification of the alkaline filtrate was filtered, washed with water and dried in a vacuum dryer.

Reduction of the disulfides **3e** and **3k** to the thiophenols **2e** and **2k**.

Sodium tetrahydroborate (1.3 mmol) was added to a solution of the corresponding disulfides **3**(0.25 mmol) in dry dioxane (6 ml). The conversion of disulfides **3** was accomplished within 2h reflux (TLC). The reaction mixture was cooled and the inorganic precipitate filtered, The thiophenols **2e** or **2k** were isolated after evaporation of dioxane in a vacuum.

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