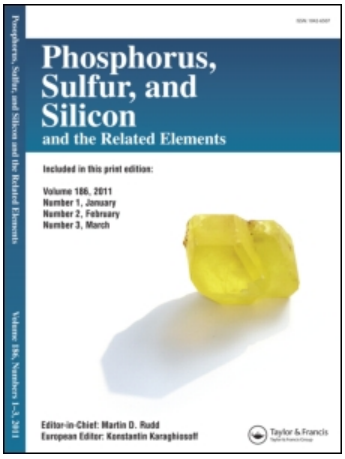

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Reactions with 4,5-DI (*p*-Chlorophenyl)Imidazolidine-2-Thione

Mohie A. F. Sharaf[a]; El-emam H. M. Ezat[a]; Hamdy A. A. Hammouda[a]
[a] Chemistry Department, Faculty of Science, Cairo University, Giza, A.R. Egypt

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REACTIONS WITH 4,5-DI (*p*-CHLOROPHENYL)IMIDAZOLIDINE-2-THIONE

MOHIE A. F. SHARAF, EL-EMAM H. M. EZAT and HAMDY A. A. HAMMOUDA

Chemistry Department, Faculty of Science, Cairo University, Giza, A.R. Egypt

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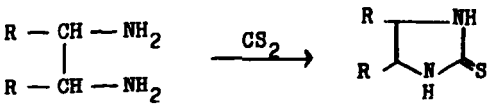
Alkylation of 1 gave the S-alkyl derivatives 3a–c. The S-methyl derivative 3a reacted with amines, with the elimination of methanethiol, to give the 2-amino derivatives 4a–c; with thiosemicarbazide to yield the imidazo [2,1-c]s-triazole 6; and with anthranilic acids to yield the imidazo[2,1-b]quinazolines 8a, b. Compound 3a reacted also with active-methylene compounds to give the ketene aminals 10a–c. Alkylation of 1 with dihaloalkanes afforded the bis compounds 14a, b. In the case of 1,2-dibromoethane, the imidazo[2,1-b]thiazole 13 was obtained. The reaction of 1 with α-halo-ketones led directly to the imidazo[2,1-b]thiazoles 15a–c and 17. However, with halo-acetoacetanilides, the acyclic intermediates 20d–g were isolated.

Key words: Alkylation, ketene aminals, imidazo heterocycles.

The presence of an imidazole nucleus, a biologically accepted pharmacophore, fused to another heterocycle like thiazole, triazole, or quinazoline leads to versatile compounds possessing a wide range of biological activity.[1–6] Continuing our interest[7,8] and searching for compounds for biological studies, it was considered worthwhile to start with a halogen-containing imidazole. This work deals with the synthesis and reactions of the title compound 1. Compound 1 exists essentially in the thione form depicted, as its IR spectrum shows an absorption band at 1270 cm^{-1} (C=S). However, its ability to form thioethers indicates the importance of the thiol or the thiolate anion as reaction intermediates.

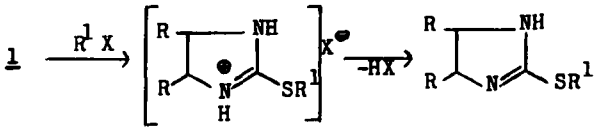
Heating of meso-1,2-di(*p*-chlorophenyl)ethylene diamine[9] with carbon disulfide in refluxing ethanol gave 1 (cf. the synthesis of the 4,5-diphenyl analogue by the fusion of the diamine and thiourea[10]).



1

R = *p*-chlorophenyl in 1 and in all compounds throughout.

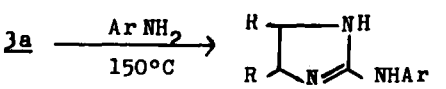
Compound 1 reacted with alkyl halides in absolute ethanol to give the 2-alkylthio-2-imidazolinium halides 2a–c, which on treatment with alkali gave the 2-alkylthio-2-imidazolines 3a–c. Similarly, 1 reacted with 2,4-dinitrochlorobenzene to give 2d and 3d.



2 3

a, R^1= CH_3 ; X = I
b, R^1= C_2H_5 ; X = I
c, R^1= $CH_2C_6H_5$; X = Cl
d, R^1= $C_6H_3(NO_2)_2$-2,4 ; X = Cl

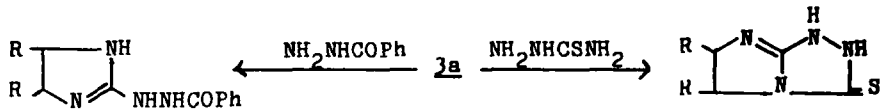
That compound 1 undergoes S-alkylation was evident from the reaction of 3a with some primary amines to afford the 2-amino derivatives 4a–c with the evolution of methanethiol.



4

a, Ar = C_6H_5
b, Ar = $C_6H_4CH_3$-p
c, Ar = $C_6H_4OCH_3$-p

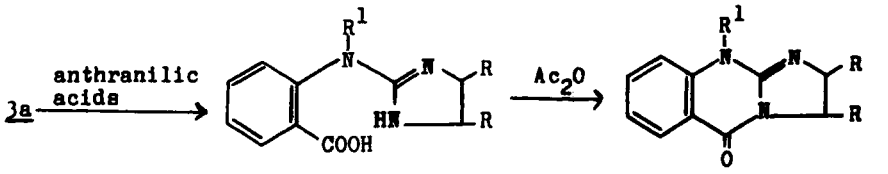
This reaction with amines was extended to various amino compounds to explore its synthetic potential. Heating of 3a with hydrazine hydrate in refluxing ethanol or even at 150°C by refluxing in dimethylformamide gave only traces of methanethiol and no product could be separated. Fusion of 3a with benzhydrazide at 180°C afforded the 2-(β-benzoylhydrazino)-2-imidazoline, 5. The IR spectrum of 5 exhibited a band at 1675 cm^{-1} for the carbonyl group. Trials to cyclize 5 by heating above its melting point or by heating with polyphosphoric acid at 140°C have all failed.



5 6

When 3a was heated with thiosemicarbazide at 180°C, no acyclic intermediate could be isolated, and instead the imidazo[2,1-c]-s-triazole, 6 was obtained. The IR spectrum of 6 showed bands at 3380 cm^{-1} (NH) and 1470 (C=S). Its ^{1}H-NMR spectrum showed signals at δ5.1 ppm (2d, 2H, H-5, H-6), δ5.6 (s, 1H, NH), δ6.8–7.5 (m, 9H, aromatic + NH).

The fusion of 3a with anthranilic acid and N-methylanthranilic acid at 170°C gave the N-(2-imidazolin-2-yl)anthranilic acids, 7a, b, respectively. The IR spectra of 7a, b showed a broad band at 3370–2550 cm^{-1} (OH and NH) and a strong band at 1695 (CO). The ^{1}H-NMR spectrum of 7b showed signals at δ2.3 ppm (s, 3H, CH_3), δ5.3 (s, 2H, H-4, H-5), δ6.7–7.5 (m, 12H, aromatic), δ8.5 (s, 1H, NH) and δ10.3 (s; 1H, COOH).



7

a, $R^1 = H$

b, $R^1 = CH_3$

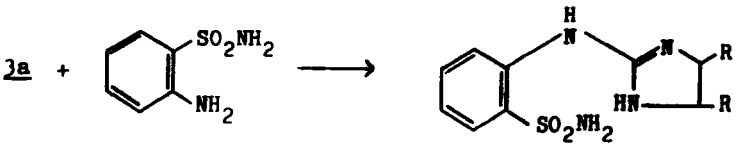
8

a, $R^1 = COCH_3$

b, $R^1 = CH_3$

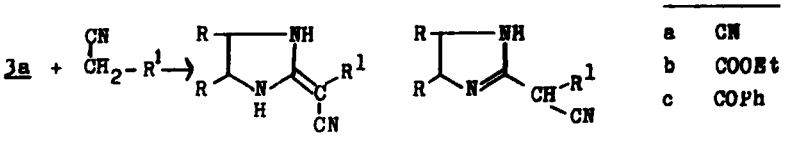
Cyclization of 7a, b was effected by heating with acetic anhydride to get the imidazo[2,1-b]quinazolines 8a, b, respectively. The IR and ^{1}H-NMR spectra of compounds 7 and 8 were in agreement with the assigned structures.

In an analogous manner and aiming to synthesize an imidazo[1,2-b][1,2,4]thiadiazine, compound 3a was heated with orthanilamide at 170–190°C. The product, however, proved by analytical and spectral data to be the acyclic benzenesulfonamide derivative 9.



9

Elimination of the methylmercapto group from 3a was also achieved with active-methylene compounds such as malononitrile, ethyl cyanoacetate and benzoylacetonitrile. Thus, heating of 3a with each of these reagents in refluxing dimethylformamide gave products which, due to the electron-withdrawing effect of the cyano group, can be formulated as the ketene aminals 10a–c, with the 2-alkylidenimidazolidine structure, rather than the 2-alkyl-2-imidazolines 11a–c. This assignment was supported by the spectral data of the products. For instance, the IR spectrum of 10a showed two close peaks for the cyano groups. Its ^{1}H-NMR spectrum showed no signal for the exocyclic methine proton. Ketene aminals are useful synthones reported only in few cases.[11–14]

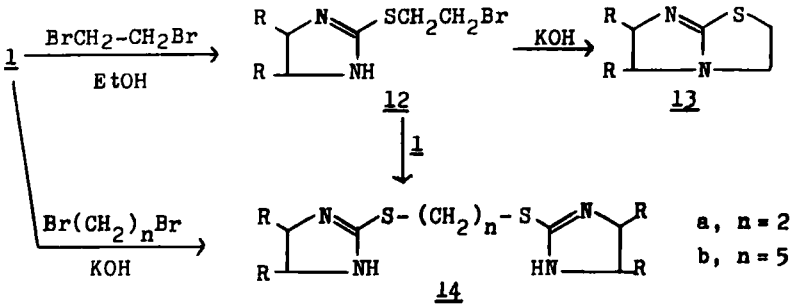


	R^1
a	CN
b	COOEt
c	COPh

10 11

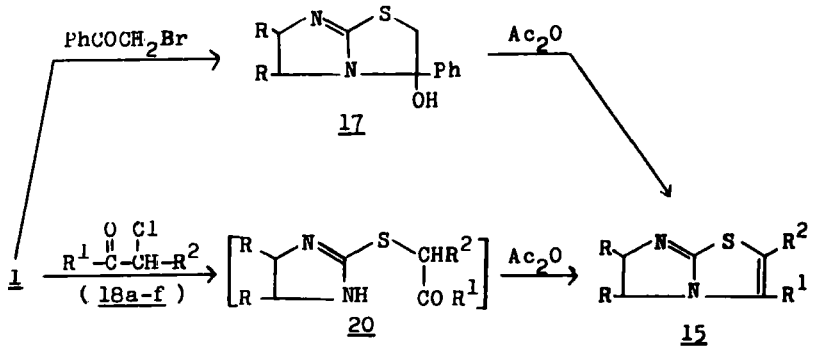
Alkylation of 1 with dihaloalkanes was also tried. With 1,2-dibromoethane, compound 1 either cyclizes or affords a bis compound. When 1 was reacted with an excess of 1,2-dibromoethane in refluxing ethanol, the 2-β-bromoethylthio derivative 12 was obtained in a moderate yield. The latter could be cyclized to the

imidazo[2,1-b]thiazole 13 in presence of alkali. The absence of NH absorption in the IR spectrum of 13 is in support of its structure.

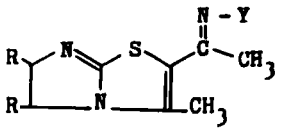


The reaction of 12 with 1 in ethanolic sodium ethoxide gave 1,2-di[4,5-di(*p*-chlorophenyl)-2-imidazolin-2-ylthio]ethane 14a. The molecular symmetry of 14a was clear from its ^{1}H-NMR spectrum which showed a singlet at 3.6 ppm for the equivalent protons of the two methylene groups. Compound 1 similarly reacted with 1,5-dibromopentane to give the bis compound 14b.

Alkylation of 1 with chloroacetone and 3-chloropentane-2,4-dione in refluxing absolute ethanol took place at the sulfur atom with subsequent cyclization to the imidazo[2,1-b]thiazoles 15a, b, respectively. Trials to isolate the acyclic intermediates by conducting the reaction at room temperature have failed and in each case 15 was obtained. The cyclization here may be catalized by the acid (HCl) separated from the reaction. Mercapto heterocycles are known to react with α-haloketones to give directly the fused thiazoles.[15-17] In some instances S-alkylated heterocycles were obtained and these were cyclized by acids to the fused thiazoles.[18]



15,18,20	R^1	R^2
a	CH_3	H
b	CH_3	$COCH_3$
c	Ph	H
d	CH_3	CONHPh
e	CH_3	$CONHC_6H_4CH_3$-p
f	CH_3	$CONHC_6H_4OCH_3$-p
g	$CH_2CONHPh$	H



16

a, Y = OH

b, Y = NHPh

Structure assignment of 15 was based on the fact that the products gave no color with ferric chloride and on elemental and spectral data. For instance, the IR spectra of 15a, b do not show bands for the NH group; that of 15a shows no band for a CO group while that of 15b exhibits a band at 1690 cm^{-1} for the acetyl CO. The ^{1}H-NMR spectrum of 15b shows signals at δ2.1 ppm (s, 3H, CH_3), 2.3 (s, 3H, CH_3), 5.8 (2d J = 3 Hz, 2H, H-5 and H-6) and 6.7–7.1 (m, 8H, aromatic).

Compound 15b gave the oxime 16a and the phenylhydrazone 16b.

Compound 1 reacted with phenacyl bromide under the same conditions to give the 3-hydroxyimidazo[2,1-b]thiazole 17 which on heating with acetic anhydride gave 15c.

In continuation of our previous interest in halogenated acylacetanilides[19,20] the behaviour of 1 towards α-chloro- and γ-bromoacetoacetanilides 18 and 19, respectively is reported here.

Reaction of 1 with 18 in refluxing absolute ethanol gave 15d–f. These are most likely formed via the acid-catalyzed cyclization of the α-(2-imidazolin-2-ylthio)acetoacetanilides 20d–f which could be isolated by conducting the reaction in cold acetone. Similarly, 1 reacted with 19 in cold acetone to give 20g and in refluxing ethanol to give 15g. Assignment of these structures was supported by spectral data. Apparently, the halo-acetoacetanilides behaved towards 1 like a typical α-haloketone where 1 is regarded as a cyclic thiourea (cf. the formation of aminothiazoles from thioureas and α-haloketones[19,21]).

EXPERIMENTAL

Melting points are uncorrected. IR spectra (ν_{max} in cm^{-1}) were recorded (KBr) with a Perkin-Elmer 782 spectrometer. ^{1}H-NMR spectra (chemical shifts in δ ppm against TMS) were taken in DMSO-d_6 (unless otherwise stated) and recorded with a Varian EM 390 90 MHz spectrometer.

4,5-Di(p-chlorophenyl)imidazolidine-2-thione (1): A mixture of 10 g of meso-1,2-di(*p*-chlorophenyl)ethylenediamine[9] and 5 ml of carbon disulfide in 100 ml of EtOH was refluxed until H_2S ceased to evolve (ca. 10 h). The reaction mixture was filtered while hot and the filtrate was left to cool. The crystals that separated were collected (73%) and recrystallized from EtOH to give 1, m.p. 215°C. IR $\tilde{\nu}$ = 3400 (NH), 1270 (C=S). ^{1}H-NMR δ = 5.3 (s, 2H, H-4, H-5), 6.8–7.3 (m, 8H, arom.), 8.7 (s, 2H, NH, exchangeable with D_2O). Anal. Found (Calcd.): C, 55.9 (55.7); H, 3.8 (3.7); N, 8.5 (8.7); S, 9.8 (9.9).

2-Alkylthio-4,5-di(p-chlorophenyl)-2-imidazolinium halides (2a–c): A mixture of 1 (0.01 mol) and the appropriate alkyl halide (0.015 mol) in abs. EtOH (40 ml) was refluxed for 4 h. After concentration and cooling 2a–c were precipitated by Et_2O as colorless crystals in 85–90% yield (cf. Table I). The 2,4-dinitrophenylthio derivative (2d) was similarly obtained from 1 and 2,4-dinitrochlorobenzene.

Formation of 3a–d: A cold solution of 1 g of 2a–d in 10 ml of EtOH was treated with 5 ml of 5% NaOH. Cold water was slowly added while shaking. The colorless crystals were collected and recrystallized to give 3a–d (cf. Table I).

2-Amino-4,5-di(p-chlorophenyl)-2-imidazolines (4a–c): A mixture of 3a (0.01 mol) and the appropriate amine (0.01 mole) was heated at 150°C until no more methanethiol could be detected (ca. 2 h). The product was triturated with petroleum ether, collected and recrystallized to give 4a–c in 50–60% yields.

4a, m.p. 256°C; recrystallized from EtOH, IR $\tilde{\nu}$ = 3390, 3230 (NH), 1635 (C=N). ^{1}H-NMR δ = 5.1 (s, 2H, H-4, H-5), 6.4 (s, 1H, NH), 6.9–7.3 (m, 13H, arom.) and 8.8 (s, 1H, NH). Anal. Found (Calcd.): C, 65.8 (66.0); H, 4.4 (4.5); N, 11.2 (11.0).

4b, m.p. 218°C; recrystallized from aq. EtOH. IR $\tilde{\nu}$ = 3390, 3220 (NH), 1635 (C=N). Anal. Found (Calcd.): C, 67.0 (66.7); H, 4.8 (4.8); N, 10.7 (10.6).

TABLE I

Characterization data of 2 and 3

Compound[a]	M.P. °C	IR ($\bar{\nu}$) NH	IR ($\bar{\nu}$) C=N	Formula	Analysis Calcd. C	Calcd. H	Calcd. N	Found C	Found H	Found N
2a	239	3390	1640	$C_{16}H_{15}N_2SCl_2I$	41.3	3.3	6.0	41.1	3.3	5.8
2b	241	3390	1650	$C_{17}H_{17}N_2SCl_2I$	42.6	3.6	5.8	42.8	3.4	5.7
2c	244	3385	1650	$C_{22}H_{19}N_2SCl_3$	58.7	4.3	6.2	59.0	4.1	6.2
2d	220	3380	1645	$C_{21}H_{15}N_4SO_4Cl_3$	48.0	2.9	10.7	48.1	2.8	10.4
3a*	121	3390	1640	$C_{16}H_{14}N_2SCl_2$	57.0	4.2	8.3	56.8	4.0	8.1
3b	96	3395	1635	$C_{17}H_{16}N_2SCl_2$	58.1	4.6	8.0	58.1	4.8	8.2
3c	158	3400	1640	$C_{22}H_{18}N_2SCl_2$	63.9	4.4	6.8	63.7	4.4	7.0
3d	180	3380	1645	$C_{21}H_{14}N_4SO_4Cl_2$	51.5	2.9	11.4	51.8	2.8	11.2

[a] 2a–d were recrystallized from abs. EtOH; 3a, b from aq. EtOH; 3c, d from aq. dioxan.
*^{1}H-NMR ($CDCl_3$)δ: 2.7 (s, 3H, CH_3), 5.2 (s, 2H, H-4, H-5) 6.8–7.3 (m, 8H, arom.) and 8.8 (s, 1H, NH).

4c, m.p. 212°C; recrystallized from aq. EtOH. IR $\bar{\nu}$ = 3400, 3250 (NH), 1640 (C=N). Anal. Found (Calcd.): C, 63.8 (64.1); H, 4.7 (4.6); N, 10.0 (10.2).

2-(β-Benzoylhydrazino)-4,5-di(p-chlorophenyl)-2-imidazoline (5): A mixture of 0.01 mol of 3a and 0.01 mol of benzhydrazide was heated at 180°C for 1 h, cooled and triturated with petroleum ether to give a yellowish solid (61%). Recrystallization from aq. EtOH gave 5, m.p. 215°C. IR $\bar{\nu}$ = 3380, 3210 (NH), 1675 (CO), 1635 (C=N). Anal. Found (Calcd.): C, 61.8 (62.1); H, 4.1 (4.3); N, 13.1 (13.2).

5,6-Di(p-chlorophenyl)-2,3,5,6-tetrahydro-1H-imidazo[2,1-c]-s-triazole-2-thione (6): Heating equimolar amounts of 3a and thiosemicarbazide exactly as for 5 gave 6 (65%), recrystallized from benzene-benzine, m.p. 194°C. IR $\bar{\nu}$ = 3380, 3300 (NH), 1470 (C=S). ^{1}H-NMR: δ = 5.1 (2d, 2H, H-5, H-6), 5.6 (s, 1H, NH), 6.8–7.5 (m, 9H, arom. + NH). Anal. Found (Calcd.): C, 52.6 (52.9); H, 3.5 (3.3); N, 15.1 (15.4); S, 8.8 (8.8).

2-(o-Carboxyphenylamino)-4,5-di(p-chlorophenyl)-2-imidazolines (7a, b): A mixture of 0.01 mol of 3a and 0.01 mol of anthranilic or N-methylanthranilic acid was heated for 1 h at 170°C. The solid product (70%) was washed with EtOH and recrystallized to give 7a, b, respectively.

7a, m.p. 266°C (EtOH). IR: $\bar{\nu}$ = 3370–2550 (OH and NH), 1695 (CO). Anal. Found (Calcd.): C, 61.7 (62.0); H, 4.2 (4.0); N, 9.9 (9.9).

7b, m.p. 225°C (EtOH). IR: $\bar{\nu}$ = 3360–2550 (OH and NH), 1695 (CO). ^{1}H-NMR: δ = 2.3 (s, 3H, CH_3), 5.3 (s, 2H, H-4, H-5), 6.7–7.5 (m, 12H, arom.), 8.5 (s, 1H, NH), 10.3 (s, 1H, COOH). Anal. Found (Calcd.): C, 62.9 (62.7); H, 4.5 (4.3); N, 9.6 (9.5).

10-Acetyl-2,3-di(p-chlorophenyl)-2,3-dihydroimidazo[2,1-b]quinazolin-5(10H)-one 8a: 0.01 Mol of 3a and 0.01 mol of anthranilic acid were heated at 170°C for 30 min, then acetic anhydride was added and the mixture refluxed for 20 min, cooled and stirred with crushed ice. The solid product obtained was recrystallized from EtOH to give 8a, m.p. 246°C, yield 67%. IR: $\bar{\nu}$ = 1685, 1670 (2CO). ^{1}H-NMR: δ = 1.9 (s, 3H, CH_3), 5.1 (2d, 2H, H-2, H-3), 6.9–7.5 (m, 12H, arom.). Anal. Found (Calcd.): C, 64.1 (64.0); H, 3.9 (3.8); N, 9.5 (9.3).

2,3-Di(p-chlorophenyl)-10-methyl-2,3-dihydroimidazo[2,1-b]quinazolin-5(10H)-one 8b: was prepared from 3a and N-methylanthranilic acid by proceeding just as for 8a, m.p. 239°C (EtOH); yield 80%. IR: $\bar{\nu}$ = 1680 (CO). ^{1}H-NMR: δ = 3.85 (s, 3H, CH_3), 5.2 (2d, 2H, H-2, H-3), 6.9–7.5 (m, 12H, arom.). Anal. Found (Calcd.): C, 65.7 (65.4); H, 4.3 (4.1); N, 9.8 (9.9).

o-[2,3-Di(p-chlorophenyl)-2-imidazolin-2-ylamino]benzenesulfonamide (9): A mixture of 0.01 mol of 3a and 0.01 mol of orthanilamide was heated at 170–190°C for 1 h, cooled and triturated with EtOH and recrystallized from aq. dioxan to give 9 (65%); m.p. 234°C. IR: $\bar{\nu}$ = 3400, 3350, 3290 (NH), 1340, 1160 (SO_2). Anal. Found (Calcd.): C, 54.5 (54.7); H, 3.8 (3.9); N, 12.4 (12.1); S, 6.8 (6.9).

2-Alkylidene-4,5-di(p-chlorophenyl)imidazolidines (10a–c): *General Procedure*: A mixture of 0.01 mol of 3a and 0.01 mol of the active-methylene compound and 30 ml of DMF was refluxed for 5 h, cooled and poured on water. The solid product was filtered off and recrystallized to give 10a–c.

10a was obtained from malononitrile, m.p. 273°C (EtOH), 86%. IR: $\tilde{\nu}$ = 3280 (NH), 2230, 2200 (C≡N). ^{1}H-NMR: δ = 5.4 (s, 2H, H-4, H-5), 6.9–7.3 (m, 8H, arom.), 9.0 (s, 2H, NH exchangeable with D_2O). Anal. Found (Calcd.): C, 60.6 (60.9); H, 3.6 (3.4); N, 15.6 (15.8).

10b was obtained from ethyl cyanoacetate, m.p. 199°C (EtOH), 78%. IR: $\tilde{\nu}$ = 3340 (NH), 2210 (C≡N), 1685 (CO). ^{1}H-NMR: δ = 1.2 (t, 3H, CH_3), 4.1 (q, 2H, CH_2), 5.3 (s, 2H, H-4, H-5), 6.85–7.3 (m, 8H, arom.), 9.0 (s, 2H, NH exchangeable with D_2O). Anal. Found (Calcd.): C, 59.4 (59.7); H, 4.1 (4.3); N, 10.2 (10.4).

10c was obtained from benzoylacetonitrile, m.p. 230°C (aq. dioxan), 70%. IR: $\tilde{\nu}$ = 3440 (NH), 2210 (C≡N), 1670 (CO). ^{1}H-NMR: δ = 5.4 (s, 2H, H-4, H-5), 6.9–7.5 (m, 13H, arom.), 9.0 (s, 2H, NH exchangeable with D_2O). Anal. Found (Calcd.): C, 66.0 (66.4); H, 3.7 (3.9); N, 9.5 (9.7).

2-β-Bromoethylthio-4,5-di(p-chlorophenyl)-2-imidazoline (12): 0.005 Mol of 1 and 0.012 mol of 1,2-dibromoethane were refluxed in 20 ml of EtOH for 5 h. The white solid obtained was collected, stirred in 5% sodium bicarbonate, filtered off and recrystallized from H_2O-DMF (10:1), m.p. 170°C (53%). IR: $\tilde{\nu}$ = 3400 (NH), 3080, 3030, 2970, 2935 (C—H). Anal. Found (Calcd.): C, 47.2 (47.5); H, 3.7 (3.5); N, 6.6 (6.5); S, 7.4 (7.5).

5,6-Di(p-chlorophenyl)-2,3,5,6-tetrahydroimidazo[2,1-b]thiazole (13): 1.5 G of 12 was refluxed in 40 ml of EtOH containing 1.5 g of KOH for 6 h. The solvent was distilled off, the residue washed with water, dried and recrystallized from benzene, m.p. 192°C (52%). IR: $\tilde{\nu}$ = 3075, 3040, 2980, 2935 (C—H). ^{1}H-NMR: δ = 3.85 (m, 4H, $2CH_2$), 5.5 (2d, 2H, H-5, H-6), 6.7–7.1 (m, 8H, arom.). Anal. Found (Calcd.): C, 58.1 (58.5); H, 4.2 (4.0); N, 8.3 (8.0); S, 9.0 (9.2).

1,2-Di[4,5-di(p-chlorophenyl)-2-imidazolin-2-ylthio]ethane (14a)

Method A: To a mixture of 1 (0.01 mol) in EtOH (40 ml) containing sodium ethoxide (0.01 mol) was added 12 (0.01 mol) and the mixture refluxed for 5 h and then concentrated. The solid product was filtered off, stirred in 10% HCl and filtered again from any unchanged 1. The filtrate was basified with NH_4OH and the product was collected and recrystallized from benzene-benzine to give 14a (26%); m.p. 202°C. IR: $\tilde{\nu}$ = 3390 (NH), 3080, 3040, 2970, 2940 (C—H). ^{1}H-NMR: δ = 3.6 (s, 4H, $2CH_2$), 5.1 (s, 2H, NH disappeared after D_2O), 6.0–7.2 (m, 20H, arom. + H-4, H-5). Anal. Found (Calcd.): C, 56.8 (57.2); H, 3.7 (3.9); N, 8.4 (8.3).

Method B: To a solution of 1 (0.01 mol) in 40 ml of EtOH containing 0.6 g of KOH was added 0.005 mol of 1,2-dibromoethane and the mixture refluxed for 5 h, concentrated and poured on water. The product was collected (45%) and recrystallized, m.p. 202°C (no depression with a sample from method A).

1,5-Di[4,5-di(p-chlorophenyl)-2-imidazolin-2-ylthio]pentane (14b): was prepared by Method B, using 1,5-dibromopentane, recrystallized from n-hexane, m.p. 120°C; yield 55%. IR: $\tilde{\nu}$ = 3400 (NH), 3090, 3040, 2990, 2930 (C—H). Anal. Found (Calcd.): C, 59.1 (58.8); H, 4.7 (4.5); N, 8.0 (7.8).

Reaction of 1 with α-halo-ketones: A solution of 0.01 mol of 1 and 0.01 mol of the halo-ketone in 40 ml of abs. EtOH was refluxed for 4 h, cooled and poured on water and basified with NH_4OH. The solid formed was filtered off and recrystallized from aq. EtOH to give 15a, b and 17.

5,6-Di(p-chlorophenyl)-3-methyl-5,6-dihydroimidazo[2,1-b]thiazole (15a): was obtained from chloroacetone in 66% yield, m.p. 162°C. IR: $\tilde{\nu}$ = 3090, 3030, 2960 (C—H). ^{1}H-NMR: δ = 2.1 (s, 3H, CH_3), 5.85 (2d, 2H, H-5 and H-6), 6.7–7.5 (m, 9H, arom. + H-2). Anal. Found (Calcd.): C, 60.1 (59.8); H, 4.1 (3.9); N, 7.6 (7.8).

2-Acetyl-5,6-di(p-chlorophenyl)-3-methyl-5,6-dihydroimidazo[2,1-b]thiazole (15b): was obtained from 3-chloro-2,4-pentanedione in 74% yield, m.p. 176°C. IR: $\tilde{\nu}$ = 1690 (CO). ^{1}H-NMR: δ = 2.1 (s, 3H, CH_3), 2.3 (s, 3H, CH_3), 5.8 (2d, 2H (J = 3 Hz), H-5, H-6), 6.7–7.1 (m, 8H, arom.). Anal. Found (Calcd.): C, 59.3 (59.6); H, 3.8 (4.0); N, 6.7 (6.9).

5,6-Di(p-chlorophenyl)-3-hydroxy-3-phenyl-2,3,5,6-tetrahydroimidazo[2,1-b]thiazole (17): was prepared from phenacyl bromide in 70% yield, m.p. 174°C. IR $\tilde{\nu}$ = 3560–3180 (OH). ^{1}H-NMR: δ = 3.8 (s, 2H, CH_2), 4.1 (s, 1H, exchangeable with D_2O, OH), 5.8 (2d J = 3 Hz, 2H, H-5, H-6), 6.8–7.5 (m, 13H, arom.). Anal. Found (Calcd.): C, 62.3 (62.6); H, 4.0 (4.1); N, 6.3 (6.4).

Dehydration of 17. *Formation of* 15c: 1 G of 17 was heated with 10 ml of acetic anhydride for 30 min, cooled and stirred with crushed ice. The product was collected and recrystallized from AcOH to give 15c, m.p. 190°C. IR $\tilde{\nu}$ = 3085, 3030, 2970. (C—H). Anal. Found (Calcd.): C, 65.0 (65.3); H, 3.9 (3.8); N, 6.6 (6.6).

Formation of the oxime 16a: A solution of 1 g of 15b and 0.2 g of hydroxylamine hydrochloride in 20 ml of AcOH was refluxed for 1 h, cooled and poured on water. The product was recrystallized from aq. DMF to give 16a, m.p. 195°C. IR $\tilde{\nu}$ = 3160 (OH). Anal. Found (Calcd.): C, 57.1 (57.4); H, 3.9 (4.1); N, 10.2 (10.0).

Formation of the phenylhydrazone 16b: A solution of 1 g of 15b and 0.3 g of phenylhydrazine in 25 ml of EtOH was refluxed for 1 h and cooled to give 16b, recrystallized from aq. DMF; m.p. 166°C. IR $\tilde{\nu}$ = 3220 (NH). Anal. Found (Calcd.): C, 63.0 (63.3); H, 4.5 (4.5); N, 11.3 (11.4).

α-[4,5-Di(p-chlorophenyl)-2-imidazolin-2-ylthio]acetoacetanilides (20d–f): A solution of 0.01 mol of 1 and 0.01 mol of 18d–f in 150 ml of acetone was stirred at room temperature. After 30 min white crystals separated. After further 2 h, water was added and the mixture basified with NH_4OH. The product was collected and recrystallized from aq. EtOH to give 20d–f, respectively.

Compound 20d, m.p. 142°C, yield 77%. IR $\tilde{\nu}$ = 3400, 3250 (NH), 1700 (CO), 1660 (CONH). ^{1}H-NMR: δ = 2.1 (s, 3H, CH_3), 4.6 (s, 1H, CH), 5.2 (s, 2H, H-4, H-5), 6.6–7.6 (m, 14H, arom. + NH), 9.5 (s, 1H, CONH). Anal. Found (Calcd.): C, 60.5 (60.2); H, 4.4 (4.3); N, 8.5 (8.4).

Compound 20e, m.p. 156°C, yield 78%. IR $\tilde{\nu}$ = 3400, 3250 (NH), 1700 (CO), 1665 (CONH). Anal. Found (Calcd.): C, 61.2 (60.9); H, 4.4 (4.5); N, 8.0 (8.2).

Compound 20f, m.p. 160°C, yield 75%. IR $\tilde{\nu}$ = 3390, 3250 (NH), 1700 (CO), 1660 (CONH). Anal. Found (Calcd.): C, 59.4 (59.1); H, 4.3 (4.4); N, 7.8 (8.0).

5,6-Di(p-chlorophenyl)-3-methyl-5,6-dihydroimidazo[2,1-b]thiazole-2-carboxanilides (15d–f): A solution of 0.01 mol of 1 and 0.01 mol of 18d–f in 40 ml of abs. EtOH was refluxed for 5 h, cooled and poured on water. Basification with NH_4OH gave a solid which was recrystallized to give 15d–f.

15d, m.p. 250°C (aq. dioxan), yield 71%. IR $\tilde{\nu}$ = 3250 (NH), 1675 (CO). Anal. Found (Calcd.): C, 62.4 (62.5); H, 3.8 (4.0); N, 8.7 (8.8).

15e, m.p. 200°C (aq. EtOH), yield 68%. IR $\tilde{\nu}$ = 3260 (NH), 1675 (CO). ^{1}H-NMR: δ = 2.0 (s, 3H, CH_3), 2.2 (s, 3H, CH_3), 5.85 (2d J = 3 Hz, 2H, H-5 and H-6), 6.7–7.7 (m, 12H, arom.), 9.3 (s, 1H, CONH). Anal. Found (Calcd.): C, 63.0 (63.2); H, 4.5 (4.3); N, 8.5 (8.5).

15f, m.p. 201°C (EtOH), yield 73%. IR $\tilde{\nu}$ = 3265 (NH), 1675 (CO). Anal. Found (Calcd.): C, 61.1 (61.2); H, 4.3 (4.2); N, 8.5 (8.2).

γ-[4,5-Di(p-chlorophenyl)-2-imidazolin-2-ylthio] acetoacetanilide (20g): Prepared as for 20d–f from 1 and 19 in 68% yield; recrystallized from aq. EtOH, m.p. 158°C. IR $\tilde{\nu}$ = 3390, 3280 (NH), 1695 (CO), 1670 (CONH). Anal. Found (Calcd.): C, 59.9 (60.2); H, 4.4 (4.3); N, 8.4 (8.4).

5,6-Di(p-chlorophenyl)-5,6-dihydroimidazo[2,1-b]thiazole-2-acetanilide (15g): Prepared as for 15d–f from 1 and 19 in 76% yield; m.p. 188°C (EtOH). IR $\tilde{\nu}$ = 3275 (NH), 1670 (CO). ^{1}H-NMR: δ = 3.9 (s, 2H, CH_2), 5.3 (2d J = 3 Hz, H-5 and H-6), 6.8–7.5 (m, 9H, arom. + H-2), 9.3 (s, 1H, NH). Anal. Found (Calcd.): C, 62.1 (62.5); H, 4.1 (4.0); N, 8.6 (8.8).

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