Synthesis and Structure Determination of Isomeric 7- and 8-Chloro-1,5-benzodiazepine Derivatives

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Reaction of 4-chloro-1,2-benzenediamine with 3,3-dimercapto-1-phenyl-2-propen-1-one afforded, as expected, a mixture of 7-chloro and 8-chloro-1,3-dihydro-4-phenyl-2*H*-1,5-benzodiazepine-2-thione. After separation of the two components and further reaction, their structure was established by chemical degradation of 7-chloro-2-(2-diethylaminoethylthio)-4-phenyl-3*H*-1,5-benzodiazepine to 5-chloro-1,3-dihydro-1-methyl-2*H*-benzimidazol-2-one. The structure was also confirmed by single X-ray analysis of 7-chloro-2-(2-diethylaminoethylthio)-4-phenyl-3*H*-1,5-benzodiazepine.

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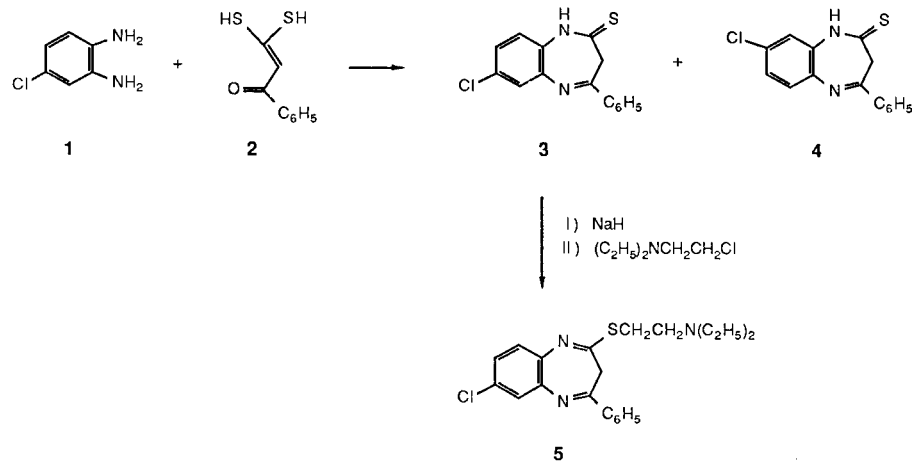
As an extension of our research on the derivatives of 1,5-benzodiazepines [1a-e], it seemed interesting to us to study whether the introduction at position 7 of electron-withdrawing groups, particularly of a chlorine atom, could give compounds having enhanced pharmacodynamic activity, in analogy to 7-chloro-1,4-benzodiazepine derivatives [2].

To this end, we synthesized the versatile intermediate 7-chloro-1,3-dihydro-4-phenyl-2*H*-1,5-benzodiazepine-2-thione (**3**). This compound was obtained, together with the expected 8-chloro isomer **4**, by reacting 4-chloro-1,2-benzenediamine (**1**) with 3,3-dimercapto-1-phenyl-2-propen-1-one (**2**) in boiling xylene (Scheme 1), following our previously reported method [1c,3]. By this route, a crude product containing compounds **3** and **4** in approximately 1:1 ratio (tlc) was obtained, from which the less soluble **3** was isolated, with a 41% yield, upon crystallization from ethyl acetate. Pure **4** was isolated, although in poorer yield, by working up of the mother liquor. Compound **3** was then alkylated, through sulphide anion generation with sodium hydride followed by quenching with 2-chloro-*N*,*N*-diethylethanamine, to yield 7-chloro-2-(2-diethylaminoethylthio)-4-phenyl-3*H*-1,5-benzodiazepine (**5**). The unequivocal structure assignment of compounds **3** and **4** presented considerable difficulties. Indeed elemental analyses, as well as ir and ^{1}H nmr spectra of both compounds, could only confirm that we had obtained the expected compounds, without defining the position of the chlorine atom.

The ^{13}C nmr spectra were not run, also on the basis of the spectra of chloro derivatives of 1,3-dihydro-2*H*-1,5-benzodiazepin-2-one reported by Bernardini *et al.* [4],

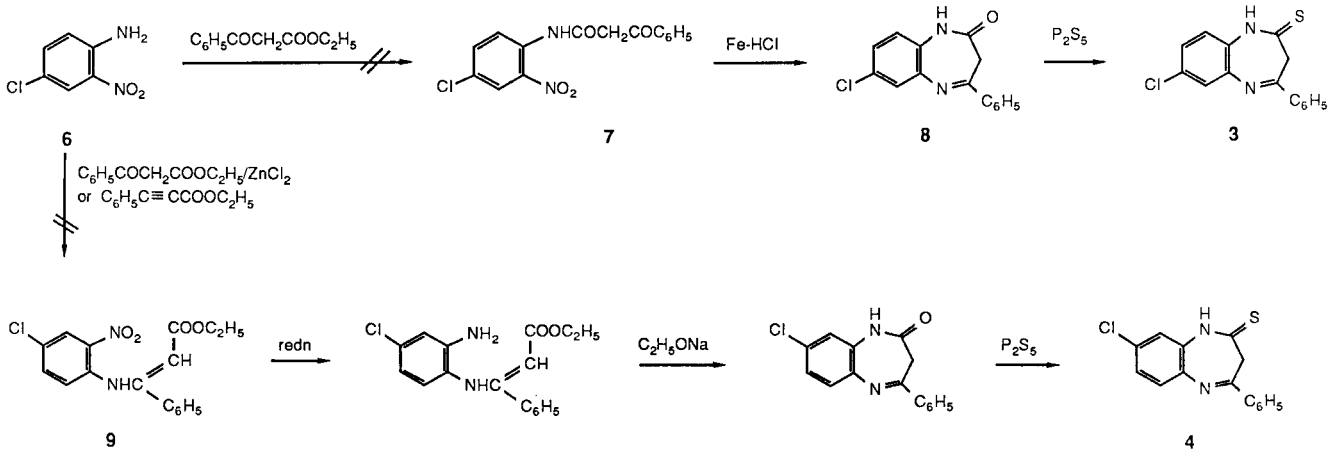
Scheme 1



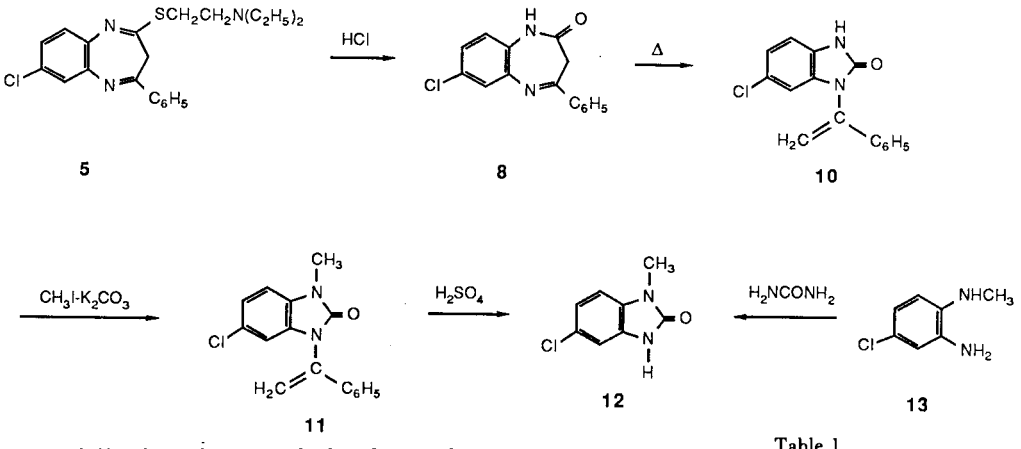
1 2 3 4

5

Scheme 2



Scheme 3



from which it appears difficult to distinguish the chemical shifts, due to the overcrowding of the aromatic carbon atoms signals.

Attempts to unequivocally prepare compound **3**, according to the routes described in the publications of Sexton [5], Davoll [6] and Pennini *et al.* [7], and compound **4**, based on the procedures published by Israel *et al.* [8] (Scheme 2) were unsuccessful.

By melting 4-chloro-2-nitrobenzenamine (**6**) at 150° with ethyl 3-oxo-3-phenylpropanoate to yield *N*-(4-chloro-2-nitrophenyl)-3-oxo-3-phenylpropanamide (**7**) utilizing a procedure of Staskun [9] for an analogous compound and following the reaction by tlc, we noted no transformation of the reagents.

On the other hand, attempts to obtain ethyl 3-(4-chloro-2-nitrophenylamino)-3-phenyl-2-propenoate (**9**) by conjugate addition of 4-chloro-2-nitrobenzenamine (**6**) to ethyl 3-phenyl-2-propynoate or by condensation of ethyl 3-oxo-3-phenylpropanoate with the same benzenamine in boiling dry ethanol in the presence of anhydrous zinc chloride, following a procedure described by Israel [8], gave no conversion of the reagents.

Table 1

Summary of Crystal and Intensity Data Collection for Compound **5**.

Formula	$C_{21}H_{24}N_3SCl$
M.W.	385.96
Unit cell	orthorhombic
a	8.330(6) Å
b	15.469(2)
c	32.052(6)
V	4130 Å^3
Space group	$Pca2_1$
Z	8 (2 independent molecules in the asymmetric unit)
D_{calc}	1.24 g cm^{-3}
Crystal dimensions	0.05 x 0.24 x 0.37 mm
F(000)	1632
λ	1.5418 Å
μ (Cu-Kα)	26.41 cm^{-1}
θ range	1-65°
Unique reflections collected	3582
Observed reflections used	1584 with $I > 2.5\sigma_I$
R	0.079
R_w	0.103

Given these failures to unequivocally obtain isomers **3** and **4** starting from readily available materials, we attempted to elucidate their structure by chemical degradation (Scheme 3).

Acidic hydrolysis of the thioether **5** gave 7-chloro-1,3-dihydro-4-phenyl-2*H*-1,5-benzodiazepin-2-one (**8**), mp 224-226° after crystallization from ethanol or ethyl acetate. This compound was described by Clifford *et al.* [10] as having mp 230° (crystallization solvent not specified) and by Chmilenko *et al.* [11] with mp 234°, after crystallization from ethanol.

On melting compound **8** at 240°, 6-chloro-1,3-dihydro-1-(1-phenylethen-1-yl)-2*H*-benzimidazol-2-one (**10**) was formed, *via* an [1,3]-sigmatropic rearrangement, in analogy with the results of M. Israel *et al.* for similar compounds [8,12-14].

Compound **10** was methylated to 6-chloro-1,3-dihydro-3-methyl-1-(1-phenylethen-1-yl)-2*H*-benzimidazol-2-one (**11**), which, on treatment with hot sulphuric acid, gave 5-chloro-1,3-dihydro-1-methyl-2*H*-benzimidazol-2-one (**12**).

The physico-chemical and spectroscopic characteristics (mp, ir, ^{1}H nmr) of compound **12** obtained by this procedure were identical with those of **12** prepared by melting 4-chloro-*N*^{1}-methyl-1,2-benzenediamine (**13**) with urea [15].

As further confirmation, we prepared in analogous way the isomer 6-chloro-1,3-dihydro-1-methyl-2*H*-benzimidazol-2-one [15], which showed mp, ir and ^{1}H nmr different from those of compound **12**.

On the basis of the results exposed above and since the rearrangement **8** → **10** occurs without cleavage of nitrogen-carbon bonds of the fused benzenic ring (and such a chance is unlikely in the following reactions) we could confirm the assigned structures for compounds **3** and **4**.

In parallel with this chemical approach, one of us (F.G.) established the structure of the thioether **5**, as a base, by single crystal X-ray analysis.

Figure 1 shows a perspective view of the two independent molecules of **5**, whose structure was fully confirmed. Crystal and intensity data collection are given in Table 1, atomic parameters in Table 2. The most flexible parts of molecules, *i.e.* the thioalkylamino chains, show, in the crystal, a notable effect of disorder at their terminal segments (See Experimental). This disorder, which can be essentially described in terms of a rotational freedom around the C(23) - N(24) bonds of both independent molecules, is mainly responsible of the marked decay of reflection intensity as a function of the θ angle. By taking into account the resulting poor accuracy of the atomic parameters, only a selection of bond lengths, valency and torsion angles is given in Table 3.

The main conformational features exhibited by the two independent molecules are those found in the crystal structure of *N*,*N*-diethyl-*N*-methyl-2-[[4-[4-(phenylthio)-phenyl]-3*H*-1,5-benzodiazepin-2-yl]thio]ethanaminium iodide (tibezonium iodide) [16].

Table 2

Fractional atomic coordinates and isotropic (equivalent for chlorine and sulfur atoms) thermal parameters of the non-hydrogen atoms with e.s.d.'s in parentheses.

$$Beq = 4/3\ \Sigma_i\Sigma_j a_i \cdot a_j J^3_{ij}$$

Atom	x	y	z	Biso/Beq (Å^2)
Cl	0.4254(8)	0.9561(3)	0.2445	10.8(2)
S	0.4356(5)	0.4402(2)	0.3338(1)	7.2(1)
N(1)	0.432(1)	0.5873(6)	0.2896(3)	4.9(2)

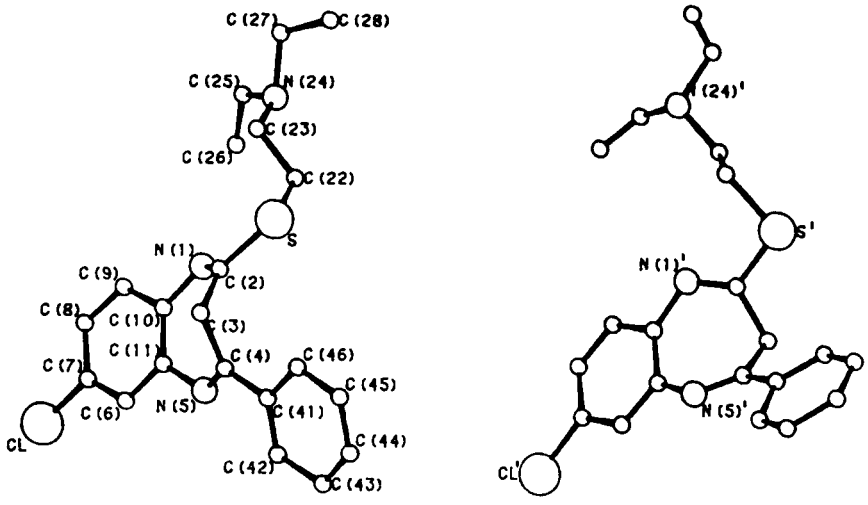


Figure 1. Perspective view of the two independent molecules of compound **5** with the atom-labelling scheme.

Table 2 (continued)

Atom	x	y	z	Biso/Beq (Å²)
C(2)	0.455(2)	0.5567(8)	0.3256(4)	6.1(3)
C(3)	0.487(2)	0.6101(9)	0.3633(4)	6.8(4)
C(4)	0.336(2)	0.6560(8)	0.3739(4)	5.3(3)
N(5)	0.293(1)	0.7158(6)	0.3483(3)	5.6(2)
C(6)	0.369(2)	0.8243(9)	0.2985(4)	6.2(3)
C(7)	0.436(2)	0.8482(8)	0.2624(4)	6.1(3)
C(8)	0.502(2)	0.7921(9)	0.2344(4)	6.4(3)
C(9)	0.499(2)	0.7060(9)	0.2451(4)	6.7(3)
C(10)	0.438(2)	0.6773(9)	0.2849(4)	6.0(3)
C(11)	0.377(2)	0.7367(7)	0.3114(3)	4.3(3)
C(22)	0.370(2)	0.3952(9)	0.2843(4)	6.7(4)
C(23)	0.508(2)	0.3788(10)	0.2563(5)	7.4(4)
N(24)	0.452(2)	0.3425(8)	0.2178(4)	9.5(4)
C(25)	0.470(3)	0.3856(16)	0.1826(9)	16.2(8)
C(26)	0.379(4)	0.4587(16)	0.1794(8)	16.8(9)
C(27)	0.542(3)	0.2609(13)	0.2044(7)	12.6(6)
C(28)	0.492(3)	0.1882(15)	0.2285(8)	16.0(0)
C(41)	0.243(2)	0.6379(7)	0.4109(4)	5.2(3)
C(42)	0.127(2)	0.6969(9)	0.4219(4)	6.8(4)
C(43)	0.030(2)	0.6767(9)	0.4589(5)	7.2(4)
C(44)	0.064(2)	0.6019(11)	0.4795(6)	9.3(5)
C(45)	0.177(2)	0.5438(10)	0.4674(6)	8.4(4)
C(46)	0.272(2)	0.5605(8)	0.4318(4)	6.5(3)
Cl′	0.4007(8)	−0.4518(3)	0.5640(2)	11.3(2)
S′	0.4354(5)	0.0554(2)	0.4690(1)	6.1(1)
N(1)′	0.429(1)	−0.0792(6)	0.5187(3)	4.9(2)
C(2)′	0.414(1)	−0.0509(7)	0.4819(4)	4.6(3)
C(3)′	0.367(2)	−0.1055(8)	0.4455(4)	5.0(3)
C(4)′	0.518(1)	−0.1635(7)	0.4372(4)	4.5(3)
N(5)′	0.563(1)	−0.2223(6)	0.4623(3)	5.7(2)
C(6)′	0.479(2)	−0.3206(8)	0.5128(4)	5.7(3)
C(7)′	0.408(2)	−0.3423(9)	0.5512(4)	6.3(3)
C(8)′	0.351(2)	−0.2779(9)	0.5767(4)	6.6(4)
C(9)′	0.361(2)	−0.1948(8)	0.5648(4)	5.5(3)
C(10)′	0.424(1)	−0.1705(7)	0.5267(4)	4.4(3)
C(11)′	0.483(1)	−0.2371(8)	0.5003(4)	4.7(3)
C(22)′	0.490(2)	0.0991(8)	0.5204(4)	5.4(3)
C(23)′	0.346(2)	0.1173(10)	0.5467(5)	7.7(4)
N(24)′	0.398(2)	0.1543(9)	0.5877(4)	8.8(4)
C(25)′	0.308(5)	0.1074(17)	0.6201(11)	22.0(13)
C(26)′	0.327(3)	0.0346(15)	0.6368(8)	15.5(8)
C(27)′	0.346(4)	0.2505(17)	0.5858(10)	19.2(10)
C(28)′	0.417(6)	0.2914(25)	0.6062(14)	31.1(20)
C(41)′	0.624(2)	−0.1427(8)	0.4004(4)	5.4(3)
C(42)′	0.738(2)	−0.2021(9)	0.3885(4)	6.5(3)
C(43)′	0.844(2)	−0.1889(10)	0.3551(5)	7.8(4)
C(44)′	0.822(2)	−0.1135(9)	0.3311(5)	7.5(4)
C(45)′	0.709(2)	−0.0554(9)	0.3416(5)	7.4(4)
C(46)′	0.607(2)	−0.0720(8)	0.3761(4)	6.1(3)

Table 3

Selected bond lengths (Å), valency and torsion angles (°). The e.s.d.'s on bond lengths range from 0.01 to 0.02 Å, and those on the angles are estimated to be about 2°.

Bond lengths

	Unprimed molecule	Primed molecule
Cl - C(7)	1.76	1.74
N(1) - C(10)	1.40	1.44
N(1) - C(2)	1.26	1.26
C(2) - C(3)	1.49	1.49
C(3) - C(4)	1.48	1.57
C(4) - N(5)	1.29	1.27
N(5) - C(11)	1.41	1.41
C(10) - C(11)	1.35	1.42
C(2) - S	1.83	1.71
S - C(22)	1.82	1.84

Valency angles

	Unprimed molecule	Primed molecule
C(10) - N(1) - C(2)	118	120
N(1) - C(2) - C(3)	124	124
C(2) - C(3) - C(4)	107	104
C(3) - C(4) - N(5)	116	122
C(4) - N(5) - C(11)	124	122
N(5) - C(11) - C(10)	124	124
C(11) - C(10) - N(1)	127	127
N(1) - C(2) - S	119	123
S - C(2) - C(3)	116	112
C(2) - S - C(22)	106	99

Torsion angles

	Unprimed molecule	Primed molecule
C(10) - N(1) - C(2) - C(3)	0	9
N(1) - C(2) - C(3) - C(4)	70	−71
C(2) - C(3) - C(4) - N(5)	−69	68
C(3) - C(4) - N(5) - C(11)	2	−2
C(4) - N(5) - C(11) - C(10)	43	−40
N(5) - C(11) - C(10) - N(1)	−1	3
C(11) - C(10) - N(1) - C(2)	−40	35
N(1) - C(2) - S - C(22)	−4	2
N(5) - C(4) - C(41) - C(42)	−12	18

Owing to the rigid boat conformation of the diazepine ring, the molecule achieves conformational chirality. The two enantiomers, which are contained in the same asymmetric unit of the crystal, interchange by ring reversal.

EXPERIMENTAL

Melting points were determined in open capillaries on a Buchi melting point apparatus and are uncorrected. Infrared spectra were recorded on a Perkin Elmer 297 spectrophotometer. The ^1H nmr spectra were recorded on a Hitachi Perkin Elmer R-24A spectrometer at 60 MHz with TMS or DSS as internal standard. The purity of the products was checked by tlc (Kieselgel GF 254, Merck, layer thickness 0.25 mm). Column chromatography was performed with Kieselgel 60 Merck.

7-Chloro-1,3-dihydro-4-phenyl-2*H*-1,5-benzodiazepine-2-thione (**3**) and 8-Chloro-1,3-dihydro-4-phenyl-2*H*-1,5-benzodiazepine-2-thione (**4**).

A mixture of 4-chloro-1,2-benzenediamine (**1**, 14.2 g, 0.1 mole) and 3,3-dimercapto-1-phenyl-2-propen-1-one [17] (**2**, 19.6 g, 0.1 mole) in xylene (200 ml) was stirred at reflux for 3 hours under nitrogen. After cooling, the precipitate was filtered, dried and washed with hot water to remove unreacted **1**. The crude was mainly constituted by an approximately 1:1 mixture (tlc, carbon tetrachloride/ethyl acetate, 95:5) of **3** and **4** having R_f = 0.55 and 0.70 respectively. Crystallization of the mixture from ethyl acetate (2.5 l), afforded **3** (11.7 g, 41%), mp 244°; ir (nujol): 3125 (NH), 1575, 1520 (C=N, aromatic C=C), 1090 (CCl) cm^{-1}; nmr (DMSO-d_6): δ 12.9 (bs, 1H, NH), 8.5-8.0 (m, 2H, aromatics in 2 and 6 of phenyl in 4), 7.7-7.2 (m, 6H, other aromatics), 4.0 (s, 2H, CH_2).

Anal. Calcd. for $C_{15}H_{11}ClN_2S$: C, 62.82; H, 3.86; N, 9.76; S, 11.20. Found: C, 63.13; H, 3.76; N, 10.07; S, 11.54.

Repeated evaporations of the mother liquor separated mixtures of **3** and **4**. The final residue was crystallized from methanol to afford **4** (0.8 g, 3%), mp 227°; ir (nujol): 3125 (NH), 1610, 1535 (C=N, aromatic C=C), 1095 (CCl) cm^{-1}; nmr (DMSO-d_6): δ 12.9 (bs, 1H, NH), 8.5-8.1 (m, 2H, aromatics in 2 and 6 of phenyl in 4), 7.7-7.2 (m, 6H, other aromatics), 4.0 (s, 2H, CH_2).

Anal. Calcd. for $C_{15}H_{11}ClN_2S$: C, 62.82; H, 3.86; N, 9.76; S, 11.20. Found: C, 63.03; H, 3.98; N, 9.92; S, 11.48.

7-Chloro-2-(2-diethylaminoethylthio)-4-phenyl-3*H*-1,5-benzodiazepine (**5**).

A mixture of 7-chloro-1,3-dihydro-4-phenyl-2*H*-1,5-benzodiazepine-2-thione (**3**, 2.87 g, 0.01 mole) and sodium hydride (50%, 0.5 g, 0.01 mole) in dry benzene (200 ml) was stirred at reflux for 30 minutes; then a solution of 2-chloro-*N*,*N*-diethylethanamine (2.02 g, 0.015 mole) in dry benzene (10 ml) was added and the mixture stirred at reflux for 10 hours. After cooling, sodium chloride was filtered off and the solution evaporated to dryness under reduced pressure. The residue was dissolved with petroleum ether and filtered. The solvent was removed under reduced pressure and the residual oil heated at 50° - 0.2 mm/Hg for 2 hours, to remove 2-chloro-*N*,*N*-diethylethanamine still present. Compound **5** was obtained as an oil (3.2 g, 83%) pure in tlc (eluent was the upper layer of a mixture butanol/water/acetic acid 4:5:1). Crystallization from petroleum ether afforded 2.4 g of **5** (62%), mp 60-61°; nmr (deuteriochloroform): δ 8.2-7.9 (m, 2H, aromatics in 2 and 6 of phenyl in 4), 7.6-7.1 (m, 6H, other aromatics), 3.35 (s, 2H, CH_2 of the benzodiazepine), 3.4-2.9 (m, 2H, CH_2S), 2.8-2.5 (m, 2H, CH_2CH_2N), 2.5 (q, 4H, ethylic CH_2), 1.0 (t, 6H, CH_3).

Anal. Calcd. for $C_{21}H_{24}ClN_3S$: C, 65.35; H, 6.27; N, 10.89; S, 8.31. Found: C, 65.01; H, 6.57; N, 10.84; S, 8.71.

Compound **5** hydrochloride was prepared in a conventional manner and crystallized from ethyl acetate, mp 170°; ir (nujol): 2380 (NH^+), 1590, 1570 (NH^+, C=N), 1080 (CCl) cm^{-1}.

Anal. Calcd. for $C_{21}H_{24}ClN_3S \cdot HCl$: C, 59.71; H, 5.96; N, 9.94; S, 7.57. Found: C, 60.04; H, 5.85; N, 9.98; S, 7.91.

7-Chloro-1,3-dihydro-4-phenyl-2*H*-1,5-benzodiazepin-2-one (**8**).

A suspension of 7-chloro-2-(2-diethylaminoethylthio)-4-phenyl-3*H*-1,5-benzodiazepine (**5**, 24.7 g, 0.064 mole) in 1*N* hydrochloric acid (320 ml) was stirred for 6 hours at 20/25°; then the solid was filtered and rinsed with 5% acqueous solution of sodium hydrogencarbonate, to yield crude **8**, (16.88 g, 97%), pure by tlc (carbon tetrachloride/ethyl acetate, 6:4), mp 216-220°. After crystallization from ethyl acetate or ethanol, **8** showed mp 224-226° (lit mp 230° [10], 234° [11]); ir (nujol): 3100 (NH), 1675 (CO), 1080 (CCl) cm^{-1}; nmr (DMSO-d_6): δ 11.3 (s, 1H, NH), 8.3-7.9 (m, 2H, aromatics in 2 and 6 of phenyl in 4), 7.8-7.1 (m, 6H, other aromatics), 3.6 (s, 2H, CH_2).

Anal. Calcd. for $C_{15}H_{11}ClN_2O$: C, 66.50; H, 4.09; N, 10.34; Cl, 13.09. Found: C, 66.76; H, 4.23; N, 10.55; Cl, 13.44.

6-Chloro-1,3-dihydro-1-(1-phenylethen-1-yl)-2*H*-benzimidazol-2-one (**10**).

7-Chloro-1,3-dihydro-4-phenyl-2*H*-1,5-benzodiazepin-2-one (**8**, 2.0 g, 0.0074 mole) was heated at 240-245° for 40 minutes. After cooling, the brownish vitreous mass was ground with a few 95% ethanol to give a crystalline solid, which after filtration and recrystallization from ethanol yielded **10** (1.2 g, 60%), mp 212-213°; ir (nujol): 3100 (NH), 1705 (CO), 1070 (CCl), 950 (C=CH_2) cm^{-1}; nmr (DMSO-d_6): δ 12-11 (bb, 1H, NH), 7.6 (s, 5H, aromatics of phenyl), 7.5-6.85 (m, 3H, aromatics of benzimidazolone), 6.3 and 5.75 (2s, 2H, olefinics).

Anal. Calcd. for $C_{15}H_{11}ClN_2O$: C, 66.50; H, 4.09; N, 10.34; Cl, 13.09. Found: C, 66.27; H, 4.11; N, 10.30; Cl, 12.84.

6-Chloro-1,3-dihydro-3-methyl-1-(1-phenylethen-1-yl)-2*H*-benzimidazol-2-one (**11**).

A mixture of 6-chloro-1,3-dihydro-1-(1-phenylethen-1-yl)-2*H*-benzimidazol-2-one (**10**, 0.90 g, 0.0033 mole), anhydrous potassium carbonate (0.46 g, 0.0033 mole) and methyl iodide (0.75 ml, 0.012 mole) in dimethyl sulfoxide (6 ml) was stirred at 45° for 16 hours. After cooling, the mixture was poured into water and the solid thus formed, filtered, washed with water, dried and then purified by column chromatography (silica gel, 5% methanol in benzene) to give **11** (0.78 g, 83%), mp 148-150° (unchanged after crystallization from ethyl acetate/hexane); ir (nujol): 1700 (CO), 1600 (C=C), 1065 (CCl), 950 (C=CH_2) cm^{-1}; nmr (deuteriochloroform): δ 7.55 (s, 5H, aromatics of phenyl), 7.3-6.9 (m, 3H, aromatics of benzimidazolone), 6.15 and 5.7 (2s, 2H, olefinics), 3.55 (s, 3H, CH_3).

Anal. Calcd. for $C_{16}H_{13}ClN_2O$: C, 67.49; H, 4.60; N, 9.48; Cl, 12.45. Found: C, 67.30; H, 4.64; N, 9.63; Cl, 12.68.

5-Chloro-1,3-dihydro-1-methyl-2*H*-benzimidazol-2-one (**12**).

A suspension of 6-chloro-1,3-dihydro-3-methyl-1-(1-phenylethen-1-yl)-2*H*-benzimidazol-2-one (**11**, 0.36 g, 0.00126 mole) in 12*N* sulphuric acid (2 ml), was stirred at 135° for 25 minutes. After cooling at 90°, the mixture was diluted with water (0.5 ml) and kept at 90° for 4 hours. After cooling, the mixture was poured into water and let standing overnight. The precipitate was collected, dried and crystallized from chloroform/petroleum ether to give **12** (0.20 g, 87%), mp 236-237° (lit 225-227° [15]); ir (nujol): 3100 (NH), 1740 (CO), 1680 (NH), 1070 (CCl) cm^{-1}; nmr (DMSO-d_6): δ 12-10 (bb, 1H, NH), 7.25 (s, 3H, aromatics), 3.4 (s, 3H, CH_3).

This compound has been also prepared according to the method described by Ricci *et al.* [15], by melting an equimolar mixture of 4-chloro-N^1-methyl-1,2-benzenediamine (**13**) and urea at 160° under nitrogen. Crystallization from ethyl acetate of the product thus formed, afforded **12** in 25% yield with mp 236-237°.

Anal. Calcd. for $C_8H_7ClN_2O$: C, 52.62; H, 3.86; N, 15.34; Cl, 19.11. Found: C, 52.79; H, 3.88; N, 15.40; Cl, 19.41.

6-Chloro-1,3-dihydro-1-methyl-2*H*-benzimidazol-2-one.

This compound was prepared according to Ricci *et al.* [15], by melting an equimolar mixture of 4-chloro-N^2-methyl-1,2-benzenediamine hydrochloride and urea at 170-175° under nitrogen. Crystallization of the product thus formed from ethyl acetate yielded the desired product (63%), mp 228-230° (lit 224-226° [15]); ir (nujol): 3200 (NH), 1710 (CO), 1610 (NH), 1070 (CCl) cm^{-1}; nmr (DMSO-d_6): δ 12-10 (bb, 1H, NH), 7.4 (s, 1H, aromatic in 7), 7.2 (s, 2H, aromatics in 4 and 5), 3.4 (s, 3H, CH_3).

Attempt to Obtain *N*-(4-Chloro-2-nitrophenyl)-3-oxo-3-phenylpropanamide (**7**).

An equimolar mixture of 4-chloro-2-nitrobenzenamine (**6**) and ethyl 3-oxo-3-phenylpropanoate was heated at 150° for 18 hours. No transfor-

mation of the reagents was observed (tlc: petroleum ether/ethyl acetate 7:3).

Attempts to Obtain Ethyl 3-(4-Chloro-2-nitrophenylamino)-3-phenyl-2-propenoate (**9**).

Method A.

A mixture of 4-chloro-2-nitrobenzenamine (**6**, 0.43 g, 0.0025 mole) and ethyl 3-phenyl-2-propynoate (0.405 ml, 0.0025 mole) in benzene or 95% ethanol (5 ml) was stirred at reflux for 50 hours. No transformation of the reagents was noted (tlc, benzene).

Method B.

An equimolar mixture of 4-chloro-2-nitrobenzenamine (**6**) and ethyl 3-phenyl-2-propynoate was heated at 80° for 20 hours and then at 120° for 15 hours. Also in this case no transformation of the reagents was noted.

Method C.

A solution of ethyl 3-oxo-3-phenylpropanoate (26 ml, 0.15 mole), 4-chloro-2-nitrobenzenamine (17.25 g, 0.10 mole), anhydrous zinc chloride (0.50 g) in dry ethanol (250 ml) was stirred at reflux for 18 hours without obtaining transformation of the reagents (tlc, petroleum ether/ethyl acetate 7:3).

X-Ray Crystal Structure Analysis of **5**.

Very thin, pale yellow single crystals were obtained by evaporation of a chloroform solution. The intensity data were collected on an Enraf-Nonius CAD4 diffractometer by the ω/θ scan technique, using the Ni-filtered Cu-Kα radiation. Lattice parameters, approximately measured from Weissenberg photographs, were refined by a least-squares fit of 25 well-centered high-angle reflections (Table 1). Three standard reflections, periodically monitored, showed no significant variation of the experimental conditions. Lorentz and polarization but no absorption corrections were applied. Systematic absences were consistent with the space groups Pca2, and Pbcm. Both were tested in structure determination trials, the former resulting to be the correct option. The structure was solved by direct methods using the P10 formula of the computer program SIR [18], based on the estimates of triple-phase structure invariants by means of their second representation. The E-map with the highest figure of merit showed all non-hydrogen atoms except those forming the terminal parts of thioalkylamino chains, which were located, with some difficulty, in a following difference Fourier synthesis. All H-atoms were given calculated positions and thermal parameters 10% greater than those of the bonded atoms. The methyl H-atoms were put in a staggered conformation. The H-atoms were included in structure factors calculations but not refined. Full-matrix least-squares refinement proceeded to convergence by minimizing Σ w $(\Delta F)^2$, where w = $1/\sigma^2$ (F_o).

The unfavourable ratio of the number of parameters to the number of observed reflections prevented the thermal parameters from being refined anisotropically, except those concerning chlorine and sulphur atoms. 228 parameters were refined for 1584 reflections. A final difference Fourier synthesis showed several peaks less than 0.4 e Å^{-3} in the region of the terminals of thioalkylamino chains. Their presence gives further evidence, in addition to the particularly high values of the thermal parameters, of a positional disorder of these molecular segments.

The final discrepancy indices $R = \Sigma \mid F_o \mid - \mid F_c \mid / \Sigma \mid F_o \mid$ and $R_w = [\Sigma w(\mid F_o \mid - \mid F_c \mid)^2 / \Sigma w \mid F_o \mid ^2]^{1/2}$ are presented, with other pertinent crystallographic data, in Table 1. Atomic scattering factors were taken from ref [19]. Calculations of refinement, Fourier maps and molecular geometry were performed by the Enraf-Nonius system of programs (SDP). Lists of hydrogen parameters, anisotropic thermal parameters of chlorine and sulphur atoms, and observed and calculated structure factors can be obtained by one of the authors (F. G.).

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