282. Synthesis of 1- and 5-Aryl-2,4-benzothiazepines

25th Communication on Seven-membered Heterocycles[1])

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(23.VI.77)

Summary

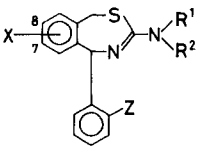
α-Aryl-*o*-xylyl dibromides **1** reacted with thioureas to give the mono-isothiouronium salts **2**, bis-isothiouronium salts **4** being formed as by-products in some cases. Compounds **2**, which readily reacted with water or alcohols to form **3**, were cyclized with Na_2CO_3 in anhydrous acetone to yield 5-aryl-2,4-benzothiazepines **5**, **6** and **7**, but the 2′-chlorophenyl-derivative **2l** exceptionally cyclized to the cyclobutene **20**. The 1-aryl-2,4-benzothiazepines **14**, **15** and **16** were prepared unequivocally by acid-catalysed cyclizations of thioureas **13** and **19**.

In an extension of work on fused 7-membered ring compounds, a series of 5- and 1-aryl-substituted 2,4-benzothiazepines *(Tables 1* and *2)* has been prepared. 2,4-Benzothiazepines had previously received little attention [2–4], and no 5- or 1-aryl substituted derivatives had been reported.

1. 5-Aryl-2,4-benzothiazepines. – For the preparation of the 5-aryl series *(Scheme 1)*, thioureas reacted preferentially with *α*-aryl-*o*-xylyl dibromides **1** at the unsubstituted methylene group to give the isothiouronium salts **2**. *Pifferi et al.* [5] had reported that the sodium salt of *N*-hydroxyurethane also reacted at the unsubstituted methylene group of *α*-substituted *o*-xylyl dibromides. With *N,N′*-dialkylthioureas, both mono- and bis-isothiouronium salts, **2** and **4**, were formed in about 60% and 40% yields respectively, the latter either as oils which could be removed by decantation or as solids which could be filtered off. The solutions thus obtained were used directly for cyclization, because of the lability of the benzhydryl bromine atom of the intermediate **2** which underwent partial alcoholysis or hydrolysis on attempted isolation or purification. With cyclic thioureas, the bis-isothiouronium salts, if formed at all, were present usually in amounts of less than 2%, and the mono-substituted intermediates **2** were usually precipitated in analytically pure form during addition of the thiourea to the dibromide in dry acetone solution. The use of moist acetone for the preparation of these intermediates **2** gave mixtures with the benzhydrols **3**. The bromides **2** could be easily converted into the benzhydrol derivatives **3** by heating in water or alcohols. With cyclic thiourea derivatives **2**,

[1]) 24th Communication [1].

Table 1. *5-Aryl-2,4-benzothiazepines*



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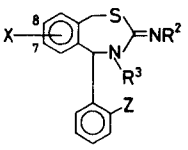

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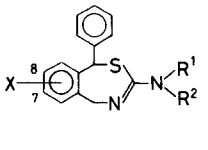
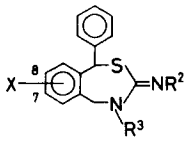
Compound	X	Z	R^1	R^2	R^3	Salt or base	M.p.(°C)	Solvent[a])
5a	H	H	H	H	–	$(CO_2H)_2$	225–229 dec.	1
5b	H	H	CH_3	CH_3	–	Base	186–189	2
5c	7-Cl	H	H	H	–	$(CO_2H)_2$	200–201 dec.	1
5d	7-Cl	H	CH_3	CH_3	–	HBr	252–254 dec.	2
6	H	H	–	CH_3	CH_3	HBr	234–235 dec.	3
7a	H	H	–	$-(CH_2)_2-$		Base	210–213	4
7b	H	H	–	$-(CH_2)_3-$		HCl	280–281	3
7c	H	H	–	$-(CH_2)_4-$		HBr	254–256 dec.	5
7d	8-Cl	H	–	$-(CH_2)_3-$		Base	155–157	6
7e	H	CH_3	–	$-(CH_2)_3-$		HBr	264–270	1
7f	H	F	–	$-(CH_2)_3-$		HCl	258–262	3

[a]) 1: methanol; 2: acetone/methanol; 3: 2-propanol; 4: dioxan; 5: methanol/2-propanol; 6: acetone/ether.

Table 2. *1-Aryl-2,4-benzothiazepines*



14

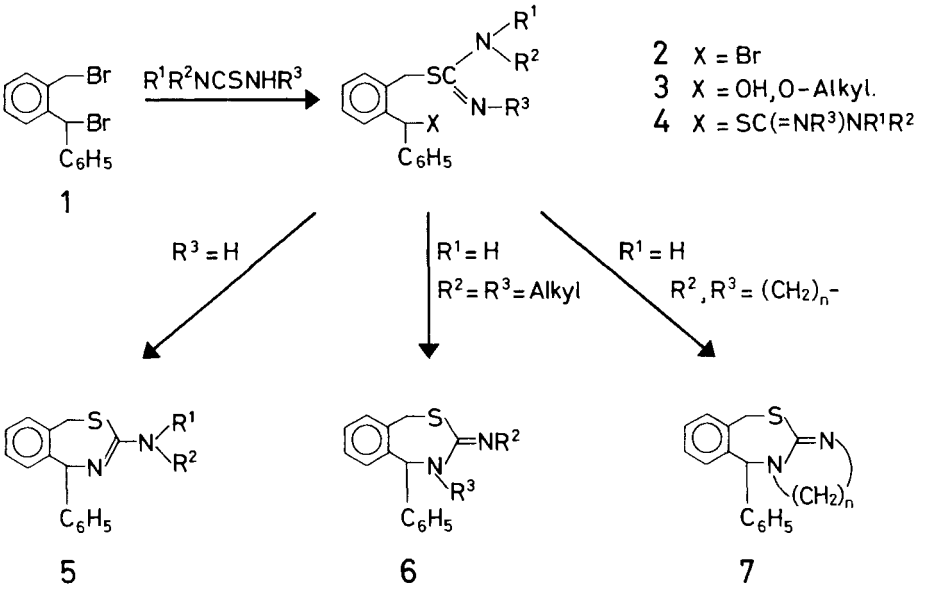


15 , 16

Compound	X	R^1	R^2	R^3	Salt or base	M.p.(°C)	Solvent[a])
14a	H	H	H	–	$(CO_2H)_2$	186–189	1
14b	H	CH_3	H	–	HCl	194–195	2
14c	H	CH_3	CH_3	–	HCl	198–202	2
14d	7-Cl	CH_3	H	–	HCl	192–193 dec.	3
14e	8-Cl	$C_6H_5CH_2CH_2$	H	–	HCl	175–177	3
15a	H	–	H	CH_3	HCl	210–212	3
15b	H	–	CH_3	CH_3	HCl	189–190 dec.	3
15c	7-Cl	–	CH_3	CH_3	HCl	196–198 dec.	3
15d	8-Cl	–	CH_3	CH_3	HCl	140–145 dec.	3
16a	H	–	$-(CH_2)_2-$		HCl[b])	175–176 dec.	3
16b	H	–	$-(CH_2)_3-$		HCl	213–216 dec.	3

[a]) 1: ethanol/ether; 2: acetone/methanol; 3: 2-propanol.
[b]) + 1 mol 2-propanol.

Scheme 1



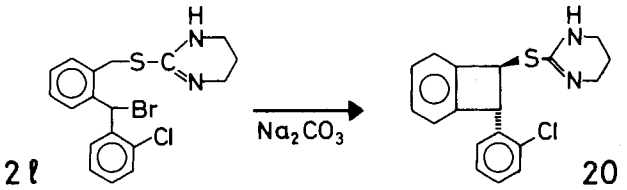
alcoholysis in methanol was usually slow enough to enable pure bromides to be isolated.

Care had to be taken in the preparation of these bromides **2** for NMR. spectral measurement. The hydrolysis takes place readily at room temperature in DMSO containing traces of moisture, and the spectra thus obtained may represent those of the benzhydrols **3** rather than **2**. The differences between these substances are clearly shown in the spectra by the positions of the H–C(2*a*) and 2 H–C(1*a*) protons. With *a*-phenyl-*o*-xylyl dibromide (**1**) the H–C(2*a*) appears as a singlet at 7.0 ppm and the 2 H–C(1*a*) appear as two doublets at 4.75 and 4.95 ppm, $J =$ 12 Hz, probably due to restricted rotation of the $-CH_2Br$ group. In the isothiouronium salts **2**, the H–C(2*a*) still appears as a singlet at 7.0 ppm, and the 2 H–C(1*a*) appear as a singlet at 4.85 ppm. In the benzhydrols **3**, the H–C(2*a*) appears as a singlet at 6.0 ppm, with the 2 H–C(1*a*) as a singlet at 4.85 ppm.

The isothiouronium salts **2** could be cyclized to 5-aryl-2,4-benzothiazepines **5**, **6** or **7**[2]) in anhydrous acetone containing anhydrous sodium carbonate [3]. Some of these are shown in *Table 1*. Other inorganic bases, *e.g.* disodium hydrogen phosphate, or organic solvents, *e.g.* alcohols, acetonitrile, gave inferior yields. The cyclic products obtained differed from the isomeric 1-aryl-2,4-benzothiazepines **14**, **15** or **16** *(Scheme 2)*, prepared by an unequivocal route, thus confirming that thioureas react with *a*-aryl-*o*-xylyl dibromides preferentially at the unsubstituted methylene group.

In the cyclization of the 2′-chlorophenyl-isothiouronium salt **21** an unusual reaction occurred. The main product, obtained in 85% yield, which had a correct

[2]) Compounds **7** were wrongly reported in some patents as 1-aryl-2,4-benzothiazepine derivatives [6].



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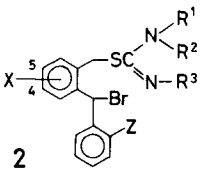
elemental analysis for the expected 2,4-benzothiazepine, had an NMR. spectrum which showed two methine protons, in place of the expected two H–C(1) and one H–C(5) protons for the thiazepine ring. X-ray crystal structure analysis showed the compound to be the benzocyclobutene derivative **20**, with the substituents in the *trans* position [7]. The reason for the unusual course of the reaction in this case is not clear, for with both the 2′-methyl- and 2′-fluoro-analogues **2j** and **2k** *(Table 3)*, only the expected 2,4-benzothiazepines **7e** and **7f** *(Table 1)* were isolated.

Table 3. *Thiourea and isothiouronium intermediates*



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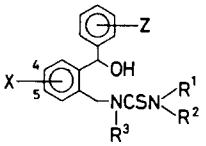
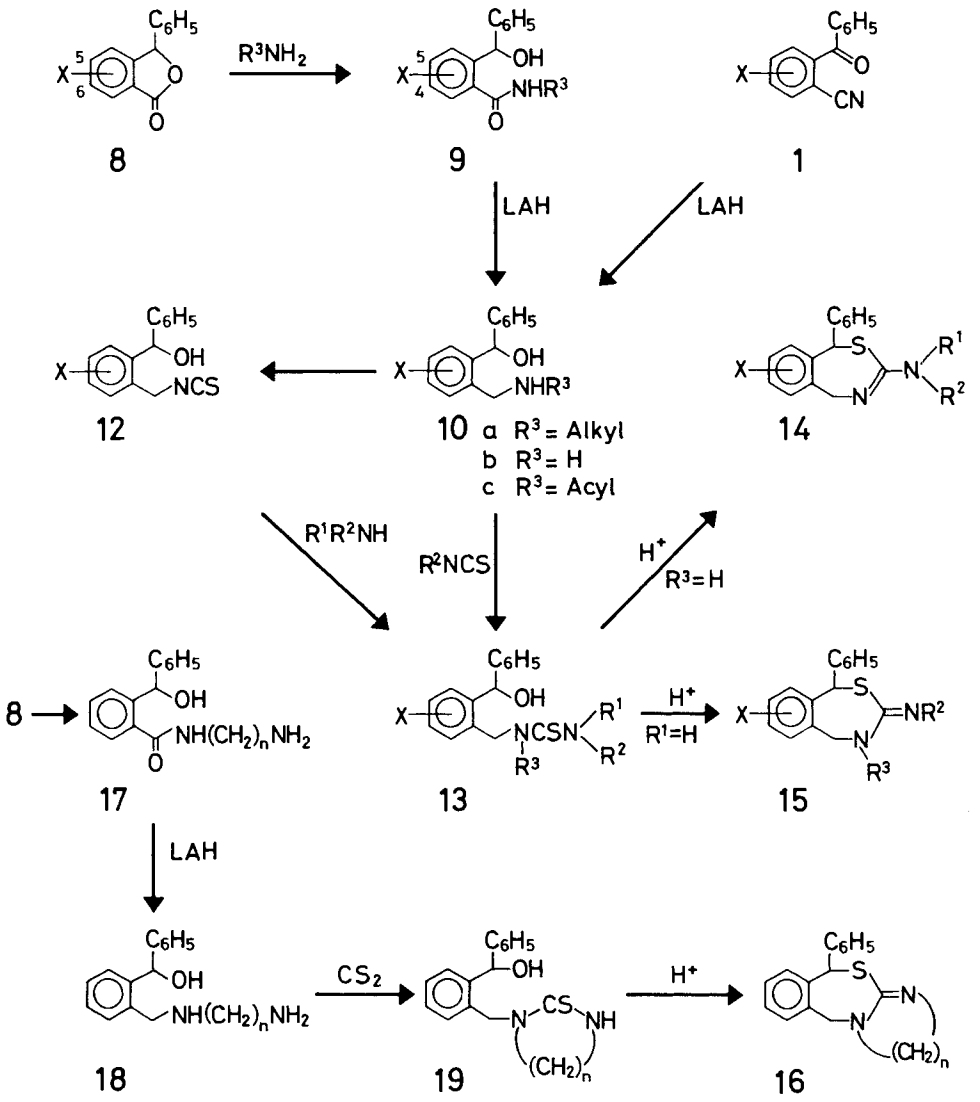


13 , 19

Compound	X	Z	R^1	R^2	R^3	M.p.(°C)	Solvent[a])
2a	H	H	H	H	H	–	
2b	H	H	CH_3	CH_3	H	–	–
2c	4-Cl	H	H	H	H	–	–
2d	4-Cl	H	CH_3	CH_3	H	190–191	pptd
2e	H	H	H	CH_3	CH_3	–	–
2f	H	H	H	$-(CH_2)_2-$		165–173	1
2g	H	H	H	$-(CH_2)_3-$		175–177	pptd
2h	H	H	H	$-(CH_2)_4-$		165–167	pptd
2i	5-Cl	H	H	$-(CH_2)_3-$		176–179 dec.	pptd
2j	H	CH_3	H	$-(CH_2)_3-$		165–167	pptd
2k	H	F	H	$-(CH_2)_3-$		153–161	pptd
2l	H	Cl	H	$-(CH_2)_3-$		174–177 dec.	pptd
13a	H	H	H	H	H	144–147	2
13b	H	H	CH_3	H	H	175–178	3
13c	H	H	CH_3	CH_3	H	153–156	4
13d	5-Cl	H	CH_3	H	H	152–154	5
13e	4-Cl	H	$C_6H_5CH_2CH_2$	H	H	97–101	6
13f	H	H	H	H	CH_3	182–184	3
13g	H	H	H	CH_3	CH_3	141–144	8
13h	5-Cl	H	H	CH_3	CH_3	98–102	6
13i	4-Cl	H	H	CH_3	CH_3	127–132	7
19a	H	H	H	$-(CH_2)_2-$		129–131	8
19b	H	H	H	$-(CH_2)_3-$		156–159	8

[a]) 1: methanol; 2: acetone/ether; 3: 2-ethoxyethanol/water; 4: benzene; 5: ether; 6: diisopropyl ether; 7: methylene chloride/ether; 8: 2-propanol.

Scheme 2



2. 1-Aryl-2,4-benzothiazepines. – These compounds were prepared as shown in *Scheme 2*, and some are described in *Table 2*. 3-Phenylphthalides **8** reacted with amines to give the amides **9**, which were reduced to the corresponding amino-methylbenzhydrols **10**. This method was unsuitable for phthalides containing a halogen atom at position 5 or 6, because of partial dehalogenation with lithium aluminium hydride (LAH). For halogenated intermediates **10a** or **10b** (X = Cl) the routes described by *Freter et al.* [8] were used. Thus compounds **10b** were produced without loss of halogen by LAH reduction of the halogenated cyanobenzophenones

11. When secondary amines in this series were required, mono-acylation of **10b** to give **10c** was followed by LAH reduction to **10a**, which proceeded without loss of halogen. Both **10a** and **10b** reacted with isothiocyanates to give the thioureas **13**. For compounds **13** in which both R^1 and R^2 were alkyl, **10b** was converted into the isothiocyanate **12**, and this reacted with secondary amines to give **13**. In contrast to the series described in *Scheme 1*, it was possible in this series to produce, unequivocally, 2,4-benzothiazepines **15** in which the substituents R^2 and R^3 could be varied independently (*e.g.* **15a**).

For the preparation of cyclic thioureas **19**, the phthalides **8** reacted with diamines to give the amides **17**, which were reduced to the diamines **18**, and these were cyclized with carbon disulfide.

The thioureas **13** and **19**, some of which are shown in *Table 3*, were cyclized by suspension in glacial acetic acid and addition of freshly prepared dry ethanolic HCl. The reactions were complete in about 3 hours at or below room temperature. In the presence of moisture or on warming, isoindolines were formed as by-products, presumably by preferential attack of the benzhydryl carbenium ion on the unprotonated thiourea nitrogen rather than the sulfur atom.

3. NMR. spectroscopy of 1-aryl and 5-aryl-benzo-2,4-thiazepines. – In the NMR. spectra of the 1-aryl- and 5-aryl-benzo-2,4-thiazepines, the H–C(1) and the H–C(5) appeared at 6.4–6.5 ppm in both series, while the 2 H–C(5) and the 2 H–C(1) appeared as two doublets with geminal coupling, but in different positions according to whether the methylene group was attached to the nitrogen or sulfur atom.

In the *unsubstituted* tricyclic tetrahydropyrimido[2,1-*c*][2,4]-benzothiazepine [2], which has no phenyl group in the 7-membered ring, the 2 H–C(5) and the 2 H–C(1) appeared as singlets at 4.9 and 4.65 ppm respectively, the latter being practically at the same position as the singlet due to the 2 H–C(1*a*) of benzylisothiouronium chloride. In the salts of the 1-phenyl derivatives **14**, **15**, **16**, the 2 H–C(5) appeared at *ca.* 4.7 and 5.3 ppm, $J = 16$ Hz (for the free base *ca.* 4.3 and 5.0 ppm), whereas in the salts of the 5-aryl derivatives **5** and **6** they appeared at *ca.* 4.1 and 4.4 ppm, $J = 15$ Hz (for the free base *ca.* 3.5 and 3.8 ppm). In the case of **7**, these protons were obscured under a multiplet between 3.2 and 4.2 ppm.

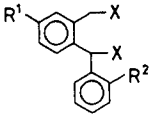
Thus, NMR. spectroscopy provides the means for a ready classification of all our benzo-2,4-thiazepines as either 5-aryl or 1-aryl derivatives. X-ray structure determination of **7b** and **16b** confirmed the structures and showed that the aryl groups were axial to the 7-membered ring [9].

Experimental part

General. – NMR. spectra were recorded in DMSO-d_6 with TMS as an internal standard, using a *Varian* T-60 high resolution NMR. spectrophotometer. Abbreviations: *s* = singlet, *d* = doublet, *t* = triplet, *m* = multiplet, br. = broad; chemical shift in δ values (ppm), coupling constants in Hz. Microanalytical results were within $\pm 0.4\%$ of the theoretical values. Further abbreviations: RT. = room temperature, HV. = high vacuum.

α-(2-Bromomethylphenyl)phenylmethyl bromides **1** *(Table 4).* A solution of phosphorus tribromide (1 mol) in dry $CHCl_3$ (150 ml) was added dropwise over 1 h to a cooled solution of the 2-hydroxymethyl-

Table 4. *Intermediate diols and dibromides*



X	R^1	R^2	M.p.(°C)	Solvent[a])
OH	Cl	H	(not isolated)	–
Br	Cl	H	b.p. 178–180/0.6 Torr	–
OH	H	Cl	68–72	1
Br	H	Cl	83–86	2
OH	H	F	94–96	3
Br	H	F	(not isolated)	–
OH	H	CH_3	106–107	4
Br	H	CH_3	69–72	5
Br	H	H	36–38[b])	2

[a]) 1: toluene; 2: 40/60° petroleum ether; 3: toluene/hexane; 4: ether; 5: methylene chloride/hexane.
[b]) B.p. 170°/0.2 Torr [5].

benzhydrol[3]) (1 mol) in dry $CHCl_3$ (1 l). The mixture was stirred 4 days at RT., poured onto ice (1 kg), the $CHCl_3$ layer was washed with water (3 × 200 ml), dried over Na_2SO_4 and evaporated. The residue was either distilled in HV., crystallized from light petroleum, or used without further purification. Yields: 85–95%.

2-[2-(α-Bromophenylmethyl)-phenylmethylthio]-1,4,5,6-tetrahydropyrimidine hydrobromide (**2g**). A solution of propylenethiourea (5.8 g, 0.05 mol) in warm dry acetone (500 ml) was added dropwise over 1 h to a well-stirred solution of **1** (17 g, 0.05 mol) in dry acetone (150 ml). The suspension was stirred for 1 h more, filtered, and the product was washed with dry acetone to give 19.5 g (85%) of white crystals, m.p. 175–177°. – NMR.: 1.9 (br. *m*, 2 H–C(5)); 3.45 (br. *m*, 2 H–C(4), 2 H–C(6)); 4.8 (*s*, 2 H–C(1α)); 7.0 (*s*, H–C(2α)). $C_{18}H_{20}Br_2N_2S$.

Compounds **2d** and **2f** to **2l** were prepared similarly *(Table 3)*.

6-Phenyl-3,4,6,11-tetrahydro-2H-pyrimido[2,1-c][2,4]benzothiazepine (**7b**). A suspension of **2g** (86 g, 0.19 mol), anhydrous Na_2CO_3 (40 g, 0.38 mol) and anhydrous Na_2SO_4 (20 g) in dry acetone (2l) was stirred at 20° for 18 h, then heated to gentle reflux for 96 h, and allowed to cool. The inorganic salts were filtered off, the filtrate was evaporated, and the residue taken up in toluene and washed with water. The base was extracted into 2N HCl, the aqueous layer made alkaline with 2N Na_2CO_3, and the base extracted into toluene, washed with water and dried. The extract was concentrated to give 34.1 g (62%) of white prisms, m.p. 163–167°. – NMR.: 1.8 (br. *m*, 2 H–C(3)); 3.2–3.7 (br. *m*, 2 H–C(2), 2 H–C(4), 2 H–C(11)); 5.6 (*s*, H–C(6)).

Hydrochloride, from 2-propanol, m.p. 280–281° (dec.). – NMR.: 1.8 (br. *m*, 2 H–C(3)); 3.2–4.2 (br. *m*, 2 H–C(2), 2 H–C(4), 2 H–C(11)); 6.4 (*s*, H–C(6)). $C_{18}H_{19}ClN_2S$.

Compounds **5d**, and **7a–7f** were prepared similarly *(Table 1)*.

4-Methyl-3-methylimino-5-phenyl-1,3,4,5-tetrahydro-2,4-benzothiazepine hydrobromide (**6**). A solution of *N,N'*-dimethylthiourea (7.8 g, 0.075 mol) in dry acetone (150 ml) was added dropwise over 45 min to a stirred solution of **1** (26.0 g, 0.076 mol) in dry acetone (70 ml), and the mixture was stirred for a further 3 h. The oil which solidified was filtered off, dried, and gave 12 g (0.022 mol) bis-isothiouronium salt **4** (R^1=H, R^2=R^3=CH_3), m.p. 207° (dec.), $C_{20}H_{28}Br_2N_4S_2$. The filtrate containing **2e** (calc. 0.031 mol) was diluted with dry acetone to 440 ml, anhydrous Na_2CO_3 (7 g, 0.066 mol) and anhydrous Na_2SO_4 (5 g) were added, and after being stirred 45 min at 20°, the mixture was gently refluxed for 48 h. It was then worked up as described for **7b**. The hydrobromide (5.2 g, 12%) crystallized from 2-propanol,

[3]) The intermediate diols were prepared by methods analogous to those described [10] [11]. New compounds are described in *Table 4*.

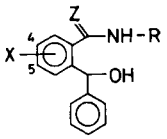
m.p. 234–235° (dec.). – NMR.: 3.05 (*s*, $H_3C-N(4)$); 3.65 (*s*, $H_3C-N=$); 4.1 and 4.4 (2 *d*, $J=15$, 2 H–C(1)); 6.5 (*s*, H–C(1)). $C_{17}H_{19}BrN_2S$.

Compounds **5a–5c** were prepared similarly *(Table 1)*.

trans-*2-{[7-(2-Chlorophenyl)-bicyclo[4.2.0]octa-1,3,5-trienyl-8]-thio}-1,4,5,6-tetrahydropyrimidine hydrochloride* (**20**). A suspension of **21** (12.3 g, 0.025 mol), anhydrous Na_2CO_3 (5.3 g, 0.05 mol) and anhydrous Na_2SO_4 (5 g) in dry acetone (250 ml) was stirred 3 h at 20° and then heated for 24 h under reflux. The product was worked up as described for **7b**. The hydrochloride crystallized first from acetone (7.8 g, 85%), then from 2-propanol, in white plates m.p. 184–186°. – NMR.: 1.7 (br. *m*, 2 H–C(5)); 3.2 (unclear *t*, 2 H–C(4), 2 H–C(6)); 4.85 and 5.05 (2 *d*, $J=4$, H–C(7'), H–C(8')). $C_{18}H_{18}Cl_2N_2S$. Free base (from ether/petrolether) m.p. 102–105°. $C_{18}H_{17}ClN_2S$.

N-Substituted-2-(α-hydroxyphenylmethyl)benzamides **9** *and* **17** *(Table 5)*. These compounds were prepared by a method analogous to that described by *Freter & Götz* [8]. A solution of the 3-phenylphthalide (0.1 mol) and the amine (0.5 mol) in dry toluene/ether (1:1, 400 ml) was stirred at RT. until TLC. showed absence of the phthalide. The mixture was evaporated to dryness below 50° in a rotary film evaporator, last traces of less volatile amines being removed azeotropically with toluene. The residual oils were triturated with dry ether to give white crystalline solids in yields of 80–96%. These substances, being labile, were not recrystallized.

Table 5. *Intermediate amides and aminomethylbenzhydrols*



Compound No.	X	Z	R	Salt	M.p.(°C)	Solvent[a])
9	4-Cl	O	CH_3	–	122–123	–
17	H	O	$-(CH_2)_2NH_2$	–	105–108	–
	H	O	$-(CH_2)_3NH_2$	–	93–97	–
10	4-Cl	H_2	H	HCl	203–205	1
	4-Cl	H_2	CH_3	HCl	147–149	2
18	H	H_2	$-(CH_2)_2NH_2$	$2(CO_2H)_2 \cdot H_2O$	190–192 dec.	3
	H	H_2	$-(CH_2)_3NH_2$	$2(CO_2H)_2 \cdot H_2O$	195–198 dec.	3

[a]) 1: acetone/2-propanol; 2: diisopropyl ether/2-propanol; 3: aqueous methanol.

2-(Substituted aminomethyl)-α-phenylbenzenemethanol salts **10** *and* **18** *(Table 5)*. These compounds were prepared by methods analogous to those described [8] [10]. a) A suspension of the benzamide **9** or **17** (0.1 mol) in dry THF (250 ml) was added dropwise over 2 h to a stirred, refluxing suspension of LAH (9 g, 0.24 mol) in dry THF (300 ml). After 4–8 h heating under reflux, the mixture was left overnight and was decomposed carefully by dropwise addition of saturated K_2CO_3 solution (54 ml). The suspension was filtered, the residue washed with THF, and the combined filtrate and washings were evaporated to dryness. The residual oil was taken up in 2N acetic acid, washed with CH_2Cl_2, the acid layer was made alkaline with 2N NaOH and the product was extracted into CH_2Cl_2 and evaporated. Oxalic acid salts were prepared by adding the theoretical quantity of oxalic acid dihydrate in methanol. Hydrochlorides were prepared by adding the theoretical quantity of dry ethanolic HCl to a 2-propanol solution of the base. Yields, 50–90%.

b) Alternatively, the crude *N*-acylated derivatives **10c** of the aminomethylbenzhydrols **10b** were reduced with LAH to **10a**, as described above.

Preparation of thioureas **13** *and* **19** *(Table 3)*. a) The amine **10a** or **10b** (0.1 mol) in benzene (200 ml) was treated dropwise with a solution of the isothiocyanate (0.105 mol) in benzene (50 ml) and left at 20° overnight. The solution was evaporated to dryness, the residue was dissolved in CH_2Cl_2, washed with 2N acetic acid, water, and dried. After evaporation, the residual oil was crystallized. Yields,

80–90%. Compounds **13a**, **13b**, **13d–13i** were prepared by this method. In the cases of **13a** and **13f**, the benzoyl derivatives were hydrolysed to the thioureas in 2N NaOH.

b) A solution of 2-aminomethylbenzhydrol · HCl (**10b**, X = H, 0.02 mol) in water (50 ml) was added dropwise to a stirred, ice-cooled mixture of carbon disulfide (0.02 mol) and NaOH (0.04 mol) in water (10 ml) over 15 min. After 5 h stirring at 20°, ethyl chloroformate (0.02 mol) was added dropwise and the mixture was stirred overnight. The isothiocyanate **12** (X = H) was extracted into ether, washed with N HCl, water, dried over Na_2SO_4, purified by elution with ether/hexane 1:1 on 360 g 60-mesh silica gel, and on evaporation gave a homogeneous oil (60%). This oil in absolute benzene (50 ml) was treated with dimethylamine (0.012 mol) and left at 20° overnight, when **13c** crystallized in 80% yield.

c) The free bases of the diamines **18** (0.05 mol) in 2-propanol (500 ml) were treated dropwise with carbon disulfide (0.1 mol), and the suspensions were heated for 18 h under reflux. The solvent was evaporated, and the residual oils in CH_2Cl_2 were washed with 2N acetic acid, water, dried and evaporated. The residual oily solids crystallized from ethyl acetate to give **19** in *ca.* 50% yields.

*11-Phenyl-3,4,6,11-tetrahydro-2*H*-pyrimido[2,1-c][2,4]benzothiazepine hydrochloride* (**16a**). A solution of **19b** (2.7 g, 0.008 mol) in glacial acetic acid (50 ml) and freshly prepared ethanolic HCl (10 ml) was kept at 0–5° for 3 h, and then at RT. for 2 h. TLC. showed absence of starting material. The solvent was evaporated, the residue was dissolved in absolute ethanol, treated with charcoal, filtered and evaporated. On trituration with dry acetone, the residual oil gave white granular crystals (2.6 g, 96%), m.p. 213–216° from 2-propanol. – NMR.: 1.8 (br. *m*, 2 H–C(3)); 2.8–3.7 (br. *m*, 2 H–C(2), 2 H–C(4)); 4.65, 5.45 (2 *d*, *J* = 16, 2 H–C(6)); 6.5 (*s*, H–C(11)). $C_{18}H_{19}ClN_2S$.

Compounds **14a–14e**, **15a–15d**, and **16b** were prepared similarly *(Table 2)*.

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