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10-Aminoacylphenothiazines

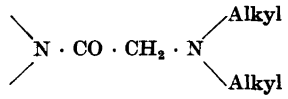
I. Aminoacetyl and Aminopropionyl Derivatives

RICHARD DAHLBOM and TORSTEN EKSTRAND

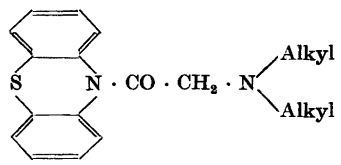
Centrallaboratoriet, AB Astra, Södertälje, Sweden

Aminoalkyl derivatives of phenothiazine have been made the object of exhaustive chemical [1-5] and pharmacological [6,7] investigations, which have shown that compounds of this type have some outstanding pharmacological properties. In particular, they are very potent antihistamine agents; but also their spasmolytic and local anesthetic activities are in some cases rather high.

According to the literature no corresponding aminoacylphenothiazines seem to have been prepared. Since compounds containing the general grouping

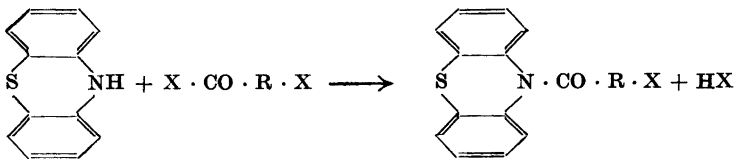


have shown very interesting properties [8,9] especially as local anesthetics (Xylocaine), we decided to synthesise the corresponding 10-phenothiazine derivatives, *viz.*



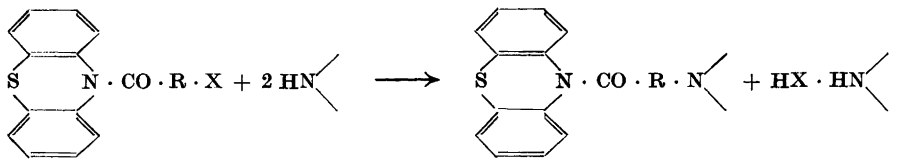
As even these simple compounds had rather promising properties and were easy to prepare, we considered it worth while making a more exhaustive investigation involving varying both the amino component and the intermediate chain. A preliminary communication on this work has already been published [10] and this paper gives a more detailed report on the chemical and pharmacological properties of the compounds we have prepared.

Phenothiazine reacted readily with haloacyl halides when heated under reflux in benzene or toluene until hydrogen halide was no longer evolved, forming the corresponding 10-haloacylphenothiazines in good yields.



In this way we have treated phenothiazine with chloroacetyl chloride, α-bromopropionyl bromide, β-chloropropionyl chloride and α,β-dibromopropionyl chloride.

The haloacylphenothiazines thus formed were treated with a number of different primary and secondary amines, giving the desired 10-aminoacylphenothiazines.



In a few cases some complications occurred. When, for example, 10-chloroacetylphenothiazine was treated with β-hydroxydiethylamine, the expected amount of amine hydrochloride separated but apparently the hydroxyaminoacyl compound initially formed was not stable and decomposed at about the same rate as it was produced, since only phenothiazine separated (in theoretical yield) from the reaction mixture. We also attempted to prepare the desired compound by the addition of ethylene oxide to 10-ethylaminoacetylphenothiazine, but even in this case only phenothiazine was formed. It should be added, that 10-chloroacetylphenothiazine, 10-ethylaminoacetylphenothiazine, and 10-diethylaminoacetylphenothiazine are all quite stable compounds. Phenothiazine, however, was formed even when we tried to prepare the hydroxy compound under very mild conditions (room temperature). Attempts to prepare other hydroxyaminoacylphenothiazines by the same two routes were also unsuccessful. No attempts were made to isolate the hydroxyaminoacyl moiety of the molecule, but since there is a possibility that it may form a heterocyclic compound, we shall investigate this reaction more fully at a later date.

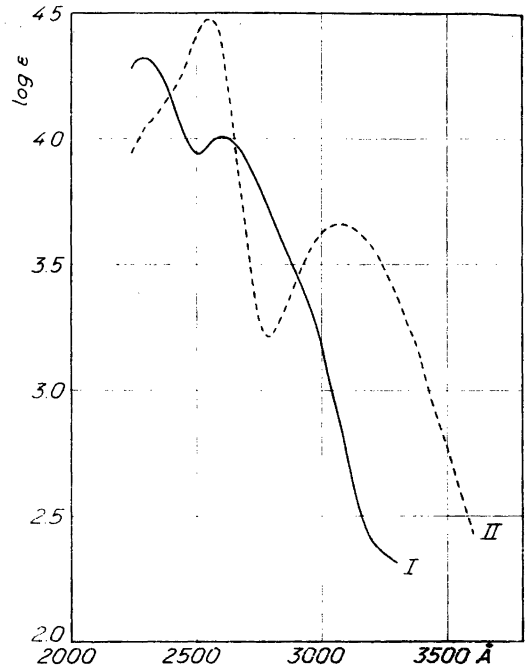


Fig. 1. The absorption spectra of 10-(α-diethylaminopropionyl)-phenothiazine (I) and 10-(β-piperidinopropyl)-phenothiazine (II) in abs. ethanol (concentrations ca. $5 \times 10^{-5} M$)

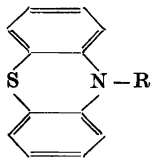
The reaction between α,β-dibromopropionylphenothiazine and amines invariably yielded the bisamino compounds, even when the halocompound was used in excess.

It is known that the CO-group in acid amides can be reduced to $—CH_2—$ by lithium aluminium hydride [11,12]. As the corresponding reduction of aminoacylphenothiazines might provide a rather easy route to the aminoalkylphenothiazines, we attempted reductions of this type. We found, however, that aminoacylphenothiazines when treated with lithium aluminium hydride in ether at room temperature were split instantaneously into phenothiazine and the corresponding aminoalcohol.

ULTRA-VIOLET ABSORPTION SPECTRA

We have not been able to find in the literature any data on the UV-absorption of 10-substituted phenothiazines. For control and comparison purposes we have measured the absorption of a number of 10-aminoalkyl- and 10-

Table 1. 10-Alkyl- and 10-acylphenothiazines.



R	E^1_{max}		E^2_{max}	
	λ Å	log ε	λ Å	log ε
$-C_2H_5$	2 560	4.55	3 100	3.64
$-C_3H_7$	2 550	4.53	3 080	3.66
$-CH_2 \cdot CH_2 \cdot N(CH_2 \cdot CH_2)_2O$	2 550	4.51	3 080	3.65
$-CH_2 \cdot CH(CH_3) \cdot N(CH_2)_3$	2 550	4.48	3 080	3.66
$-CO \cdot CH_3$	2 290	4.38	2 600	4.05
$-CO \cdot CH_2 \cdot N(CH_2)_4$	2 300	4.30	2 600	4.01
$-CO \cdot CH_2 \cdot N(C_2H_5)_2$	2 290	4.30	2 600	4.00
$-CO \cdot CH(CH_3) \cdot N(C_2H_5)_2$	2 290	4.32	2 600	4.01
$-CO \cdot CH(N(C_2H_5)_2) \cdot CH_2 \cdot N(C_2H_5)_2$	2 300	4.43	2 600	4.00

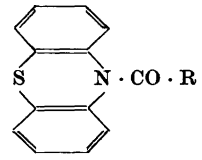
aminoacylphenothiazines. The measurements were made with a Beckman Model DU spectrophotometer using calibrated cells, and absolute ethanol as solvent throughout. The alkyl compounds were prepared by methods previously described [4,13]—. It was found, that all the alkyl compounds gave almost identical spectra, and the same was the case with the acyl compounds. However the two types were distinctly different as is shown in Fig. 1. The wavelengths of the maxima and the extinction coefficients are detailed in Table 1. As expected, the spectra of the alkyl compounds are very similar to the spectrum of unsubstituted phenothiazine [14].

PHARMACOLOGY

The compounds have been subjected to pharmacological tests *, for local anesthetic activity (rabbit cornea, Xylocaine-HCl being used as a standard). Antihistaminic activity and the effects on spasms induced by acetylcholine and $BaCl_2$ were determined on isolated guinea pig small intestine (standard, diphenhydramine-HCl). The results of these tests are summarised in Table 2.

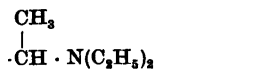
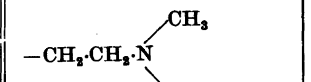
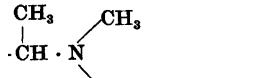
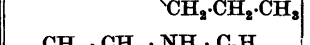
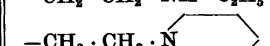
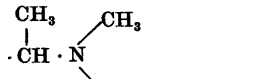
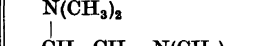
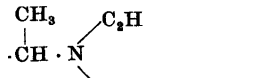
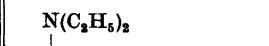
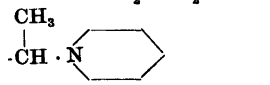
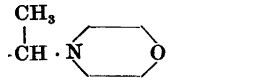
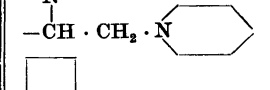
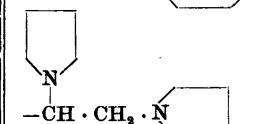
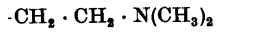
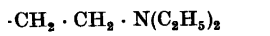
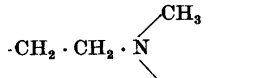
Local anesthetic effect. All the compounds possessed a marked activity, usually superior to that of Xylocaine. A variation of the intermediate chain in the order acetyl-, α-propionyl-, β-propionyl-increased the activity. The propionyl derivatives with two amino groups were even more active. Pyrrolidine appears to be the most favourable amino component. Unfortunately the α,β-bispyrrolidino-propionylphenothiazine was not soluble enough to be tested.

Table 2. Some pharmacological properties of 10-aminoacylphenothiazines.



R	Local anesthetic activity	Effect in reducing the spasm produced by		
		Acetylcholine	$BaCl_2$	Histamine
$-CH_2 \cdot N(CH_3)_2$	1.25	1.33		0.1
$-CH_2 \cdot N(C_2H_5)_2$	1.75	2.3	1.45	0.2
$-CH_2 \cdot N(CH_3)(C_2H_5)$	1.8	2.2	2	0.5
$-CH_2 \cdot N(CH_3)(CH_2 \cdot CH_2 \cdot CH_3)$	1.75	1.9	1.8	0.03
$-CH_2 \cdot N(C_2H_5)(CH_2 \cdot CH_2Cl)$		3.3	0.5	0.05
$-CH_2 \cdot NH \cdot C_2H_5$	2	2.0	0.15	0.08
$-CH_2 \cdot NH$ 		0.33	0.2	0.005
$-CH_2 \cdot N$ 	0.13	4	1	0.22
$-CH_2 \cdot N$ 		0.07		0.05
$-CH_2 \cdot N$ 	2.5	3	3	0.33
$-CH(CH_3) \cdot N(CH_3)_2$	3	1.6	1.1	0.06

* Acknowledgement is made to Dr. S. Wiedling of Astra's Biological Department for performing these tests. The pharmacological data will later be discussed by Dr. Wiedling in a wider context.

	3	12	6.6	0.1		3.1	9	1.3	0.07
	2	6.5	1.5	0.2		4	3.3	2.4	0.17
							7	2.6	0.25
	4	6	7	0.3		7	18	20	0.25
						8	1.0		0.0075
		11	7.7	0.06		9	1.0		0.027
	4	1.25	1.2	0.08					
		0.06		0.03			0.15		0.005
	2.5	2.2	3	0.11			0.3	0.8	0.007
	2.9	12	5	0.2	Atropine sulphate		30		
	5	7.5	1.2	0.1	Papaverine-HCl			0.33	
	2.5	14	1	0.18	Xylocaine-HCl	1.0			
					Diphenhydramine-HCl		1.0	1.0	1.0

Antihistaminic effect. All the compounds were inferior to diphenhydramine, the bisamino compounds having a substantially weaker effect.

Antispasmodic effect. Some of the compounds had outstanding spasmolytic properties. Against spasm induced by $BaCl_2$ some of the derivatives were comparable with, or superior to previously known antispasmodics. The propionyl compounds were somewhat superior to the acetyl compounds and the bisamino derivatives had a weak effect. The highest antispasmodic activity was exhibited by β-pyrrolidino-propionylphenothiazine.

EXPERIMENTAL

Halogenoacylphenothiazines

10-Chloroacetylphenothiazine (I). To a solution of phenothiazine (19.9 g, 0.1 mole) in boiling benzene (100 ml), chloroacetyl chloride (17.0 g, 0.15 mole) was added in por-

tions. The mixture was refluxed for two hours, most of the solvent was evaporated and the residue cooled in ice water. The precipitate which formed (21 g) was collected and recrystallised twice from ethanol. M. p. 115—116.5°.

$C_{14}H_{10}ClNOS$ (275.8)	Calc.	Cl 12.9	N 5.08	S 11.6
	Found	» 13.0	» 5.16	» 11.9

10-(α-Bromopropionyl)-phenothiazine (II). This compound was prepared in the same way as described above from phenothiazine (10.0 g) and α-bromopropionyl bromide (16.0 g) by refluxing in toluene (50 ml) for three hours. The crude product (12.8 g) was recrystallised twice from ethanol. M. p. 147.5—148.5°.

$C_{15}H_{12}BrNOS$ (334.2)	Calc.	Br 23.9
	Found	» 23.8

10-(β-Chloropropionyl)-phenothiazine (III), was prepared similarly from phenothiazine (10.0 g) and β-chloropropionyl chloride [15] (7.5 g) by refluxing for five hours in benzene (70 ml). The crude product (13.4 g) was recrystallised from methanol. M. p. 142—143°.

$C_{15}H_{12}ClNOS$ (289.8)	Calc.	Cl 12.2
	Found	» 12.2

10-(α,β-Dibromopropionyl)-phenothiazine (IV). From phenothiazine (26.0 g) and α,β-dibromopropionyl chloride [16] (48.0 g) by refluxing in toluene (260 ml) for three hours. Yield 49.0 g. M. p. 135—135.5° after recrystallisation from ether.

$C_{15}H_{11}Br_2NOS$ (413.1)	Calc.	C 43.6	H 2.68	Br 38.7
	Found	» 43.5	» 2.85	» 38.7

Aminoacylphenothiazines

The compounds described below were all prepared in essentially the same way. The halogenoacyl phenothiazine (1 mole) was dissolved in benzene or toluene and heated under reflux with excess of the appropriate amine (usually 2.6 mole). In some cases when the amine was rather volatile it was found advantageous to carry out the reaction in a sealed bottle. The hydrohalide of the amine was separated and the filtrate extracted with *N* hydrochloric acid. The extract was made alkaline with sodium carbonate solution and the precipitated base, which usually soon solidified, collected and recrystallised. In some cases when it was impossible to obtain the base in crystalline form it was converted to the hydrochloride by extracting the oil with ether and precipitating the hydrochloride by the addition of a dry ethereal solution of hydrogen chloride.

10-(Dimethylaminoacetyl)-phenothiazine. Dimethylamine (24.0 g) and 10-chloroacetylphenothiazine (I) (41.4 g) in benzene (100 ml) were shaken in a sealed bottle for eight hours. After isolation as described above the product (41.0 g) was recrystallised twice from ethanol, and then had m. p. 148.5—150° *.

* In the preliminary communication on this compound, the m. p. was erroneously given as 114.5 — 116.

$C_{16}H_{16}N_2OS$ (284.4)	Calc.	C 67.6	H 5.67	S 11.3
	Found	» 67.4	» 5.69	» 11.1

10-(Diethylaminoacetyl)-phenothiazine, prepared by boiling diethylamine (49.5 g) and I (69 g) in benzene (250 ml) for four hours. Yield 57.6 g. Recrystallised from light petroleum (40—60°), m. p. 58—59°.

$C_{18}H_{20}N_2OS$ (312.4)	Calc.	C 69.2	H 6.45	N 8.97
	Found	» 68.9	» 6.45	» 8.94

10-(Methylethylaminoacetyl)-phenothiazine. Methylethylamine [17] (1.5 g) and I (2.8 g) were heated at 100° in toluene (25 ml) for seven hours. The crude product (2.7 g) was recrystallised from light petroleum-ethanol (1 : 1). M. p. 113—115°.

$C_{17}H_{18}N_2OS$ (298.4)	Calc.	C 68.4	H 6.08
	Found	» 68.4	» 6.11

10-(Methylpropylaminoacetyl)-phenothiazine. From methylpropylamine [17] (1.9 g) and I (2.8 g) by refluxing in toluene (25 ml) for five hours. Yield 2.8 g. Recrystallised from light petroleum. M. p. 80—81°.

$C_{18}H_{20}N_2OS$ (312.4)	Calc.	C 69.2	H 6.45
	Found	» 69.1	» 6.34

10-(β-Chloroethyl-ethylaminoacetyl)-phenothiazine. β-Chloroethylethylamine hydrochloride [18] (7.2 g) was suspended in water (100 ml) and the mixture made alkaline with ammonia. The precipitated base was extracted with toluene (3 × 15 ml), the toluene solution dried, I (5.5 g) added and the mixture was heated at 50° for five hours. As the crude product did not crystallise it was converted to the hydrochloride. Yield 1.8 g. Recrystallised from light petroleum-ethanol (1 : 1). M. p. 190—191° (dec.). The low yield in this synthesis may be due to the instability of the chloroalkylamine.

$C_{18}H_{19}ClN_2OS \cdot HCl$ (383.3)	Calc.	Cl 18.5	N 7.31
	Found	» 18.5	» 7.28

10-(Ethylaminoacetyl)-phenothiazine, was prepared from ethylamine (5.4 g) and I (13.8 g) in benzene (50 ml) by heating in a sealed bottle to 80° for two hours. The crude base (12.2 g) was crystallised from light petroleum. M. p. 95—96°.

$C_{16}H_{16}N_2OS$ (284.4)	Calc.	C 67.6	H 5.67
	Found	» 67.9	» 5.85

10-(Cyclohexylaminoacetyl)-phenothiazine. Cyclohexylamine (40 ml) and I (27.6 g) in benzene (200 ml) were shaken in a sealed bottle at room temperature for ten hours. In this case the base could not be extracted with hydrochloric acid owing to the low solubility of its hydrochloride. The reaction mixture was filtered and evaporated to

dryness, yielding 39.5 g of product which was recrystallised from light petroleum-ethanol (1 : 1). M. p. 124—126°.

$C_{20}H_{22}N_2OS$ (338.5)	Calc.	C	71.0	H	6.55
	Found	»	70.3	»	6.71

10-(Piperidylacetyl)-phenothiazine. Piperidine (14.5 g) and I (17.7 g) were refluxed in benzene (75 ml) for three hours, and the product (17.1 g), recrystallised from ethanol, had m. p. 164—165°.

$C_{19}H_{20}N_2OS$ (324.4)	Calc.	C	70.3	H	6.21
	Found	»	70.3	»	6.23

10-(Morpholinoacetyl)-phenothiazine. Morpholine (11.3 ml) and I (13.8 g) in benzene (30 ml) were refluxed for four hours. The product (14.9 g) was recrystallised from light petroleum-acetone (1 : 1), m. p. 141—142°.

$C_{18}H_{18}N_2O_2S$ (326.4)	Calc.	C	66.2	H	5.56	N	8.58
	Found	»	66.2	»	5.50	»	8.68

10-(Pyrrolidinoacetyl)-phenothiazine. Pyrrolidine (1.85 g) and I (2.76 g) were refluxed in toluene (25 ml) for four hours, and the product (1.7 g) recrystallised from light petroleum-ethanol (5 : 1), m. p. 142—142.5°.

$C_{18}H_{18}N_2OS$ (310.4)	Calc.	C	69.6	H	5.84	N	9.03
	Found	»	69.5	»	5.83	»	9.10

10-(α-Dimethylaminopropionyl)-phenothiazine. α-Bromopropionylphenothiazine, II, (33.4 g) and dimethylamine (17.0 g) were heated in benzene (100 ml) at 85° over night, and the product (24.3 g) recrystallised from acetone — light petroleum (1 : 1.5). M. p. 98.5—100°.

$C_{17}H_{18}N_2OS$ (298.4)	Calc.	C	68.4	H	6.08	N	9.39
	Found	»	68.0	»	6.15	»	9.30

10-(α-Diethylaminopropionyl)-phenothiazine. Diethylamine (19.0 g) and II (33.4 g) were refluxed for five hours in toluene (100 ml). Yield 32.8 g. Recrystallised from ethanol. M. p. 100.5—101.5°.

$C_{19}H_{22}N_2OS$ (326.5)	Calc.	C	69.9	H	6.79
	Found	»	69.8	»	6.70

From this compound the hydrobromide (m. p. 200—201°, dec.) and hydrochloride (m. p. 200—201°, dec.) have also been prepared.

10-(α-Methylethylaminopropionyl)-phenothiazine. Methylethylamine (1.5 g) and II (3.3 g) were heated in toluene (25 ml) at 80° for seven hours, giving 3.0 g of product of m. p. 67—69° after recrystallisation from light petroleum.

$C_{18}H_{20}N_2OS$ (312.4)	Calc.	C	69.2	H	6.45
	Found	»	69.3	»	6.33

10-(α-Methylpropylaminopropionyl)-phenothiazine. Methylpropylamine (1.9 g) and II (3.4 g) were refluxed in toluene (25 ml) for five hours. The oily base was converted to the hydrochloride (0.8 g) which crystallised from acetone. M. p. 188—190°.

$C_{19}H_{22}N_2OS \cdot HCl$ (362.9)	Calc.	C	62.9	H	6.39
	Found	»	62.9	»	6.52

10-[α-(β'-Chloroethylethylamino)-propionyl]-phenothiazine. This compound was prepared from the free base from β-chloroethylethylamine hydrochloride (7.2 g) and II (6.7 g) by refluxing for five hours in toluene (45 ml). The hydrochloride (1.0 g) was recrystallised from ethanol, m. p. 188—189°.

$C_{19}H_{21}ClN_2OS \cdot HCl$ (397.4)	Calc.	C	57.4	H	5.58	N	7.05
	Found	»	56.8	»	5.75	»	7.06

10-(α-Piperidinopropionyl)-phenothiazine. Piperidine (30 ml) and II (33.4 g) in toluene (100 ml) were heated over night to 85° in a sealed bottle. The crude base (35.0 g) was crystallised from 60 % ethanol. M. p. 110—111°.

$C_{20}H_{22}N_2OS$ (338.5)	Calc.	C	71.0	H	6.57
	Found	»	70.9	»	6.57

10-(α-Morpholinopropionyl)-phenothiazine. Morpholine (11.3 ml) and II (16.7 g) were refluxed in benzene for two hours and the product (17.0 g) had m. p. 123—124° after recrystallisation from ether.

$C_{19}H_{20}N_2O_2S$ (340.4)	Calc.	C	67.0	H	5.92	N	8.23
	Found	»	67.2	»	5.85	»	8.35

10-(α-Pyrrolidinopropionyl)-phenothiazine. Pyrrolidine (1.85 g) and II (3.34 g) were refluxed in toluene (25 ml) for four hours. The crude base (2.7 g) was recrystallised from light petroleum. M. p. 94.5—95.5°.

$C_{19}H_{20}N_2OS$ (324.4)	Calc.	C	70.3	H	6.21	N	8.64
	Found	»	70.0	»	6.03	»	8.69

10-(β-Dimethylaminopropionyl)-phenothiazine. Dimethylamine (2.3 g) and β-chloropropionylphenothiazine, III, (5.8 g) were heated in toluene (100 ml) at 100° over night. The product (5.8 g) after recrystallisation from light petroleum had m. p. 90.5—91.5°.

$C_{17}H_{18}N_2OS$ (298.4)	Calc.	C	68.4	H	6.08	N	9.39
	Found	»	67.8	»	6.14	»	9.24

10-(β-Diethylaminopropionyl)-phenothiazine, prepared from diethylamine (9.5 g) and III (14.5 g) by refluxing in toluene (100 ml) for three hours. After recrystallisation from light petroleum m. p. 44.5—45.5°. Yield 15.0 g.

$C_{19}H_{22}N_2OS$ (326.5)	Calc.	C 69.9	H 6.79	N 8.58
	Found	» 70.2	» 6.86	» 8.45

10-(β-Methylethylaminopropionyl)-phenothiazine. Methylethylamine (1.5 g) and III (2.9 g) were heated in toluene (25 ml) to 100° for seven hours. The product (2.7 g) after recrystallisation from light petroleum had m. p. 58—60°.

$C_{18}H_{20}N_2OS$ (312.4)	Calc.	C 69.2	H 6.45	N 8.97
	Found	» 69.5	» 6.38	» 9.07

10-(β-Methylpropylaminopropionyl)-phenothiazine. From methylpropylamine (1.9 g) and III (2.9 g) by refluxing in toluene (25 ml) for five hours. As the base did not solidify and the hydrochloride also was oily, in this case the oxalate was prepared. Yield 2.7 g. M. p., after recrystallisation from acetone, 145—146°.

$C_{19}H_{22}N_2OS \cdot (COOH)_2$ (416.5)	Calc.	C 60.6	H 5.81	N 6.73
	Found	» 60.5	» 5.76	» 6.79

10-(β-Ethylaminopropionyl)-phenothiazine. Ethylamine (15.4 ml) and III (29.1 g) were heated in benzene (100 ml) to 100° for three hours. The crude base (29.8 g) was recrystallised from acetone. M. p. 108—110°.

$C_{17}H_{18}N_2OS$ (298.4)	Calc.	C 68.4	H 6.08	
	Found	» 68.5	» 6.15	

10-(β-Piperidinopropionyl)-phenothiazine. Piperidine (4.4 g) and III (5.8 g) were refluxed for four hours in toluene (50 ml). The product, (6.5 g) after recrystallisation from 50 % ethanol, had m. p. 97—99°.

$C_{20}H_{22}N_2OS$ (338.5)	Calc.	C 71.0	H 6.57	N 8.28
	Found	» 70.9	» 6.49	» 8.21

10-(β-Pyrrolidinopropionyl)-phenothiazine. Pyrrolidine (2.78 g) and III (4.3 g) were refluxed in toluene (25 ml) for four hours. The crude base (4.5 g) was recrystallised from light petroleum-ethanol (5 : 1). M. p. 108—109°.

$C_{19}H_{20}N_2OS$ (324.4)	Calc.	C 70.3	H 6.21	N 8.64
	Found	» 70.5	» 6.33	» 8.66

10-[α,β-Bis(dimethylamino)-propionyl]-phenothiazine. Dimethylamine (4.5 g) and 10-(α,β-dibromopropionyl)-phenothiazine, IV, (10.2 g) were heated with toluene (100 ml)

in a sealed bottle to 110° for three hours. The product (8.1 g) recrystallised from light petroleum had m. p. 80—81°.

$C_{19}H_{23}N_3OS$ (341.5)	Calc.	C 66.8	H 6.79	N 12.3
	Found	» 67.0	» 6.89	» 12.1

10-[α,β-Bis(diethylamino)-propionyl]-phenothiazine was prepared from diethylamine (36.5 g) and IV (41.3 g) by refluxing in toluene (400 ml) for three hours. The free base (36.7 g) was recrystallised from ethanol. M. p. 107—108°.

$C_{23}H_{31}N_3OS$ (397.6)	Calc.	C 69.5	H 7.86	N 10.6
	Found	» 69.6	» 7.98	» 10.5

10-[α,β-Bis(piperidino)-propionyl]-phenothiazine was prepared from piperidine (6.4 g) and IV (6.2 g) by refluxing in toluene (60 ml) for two hours. The crude base (7.7 g) was recrystallised from acetone. M. p. 136.5—137.5°.

$C_{25}H_{31}N_3OS$ (421.6)	Calc.	C 71.2	H 7.41	N 9.97
	Found	» 71.5	» 7.53	» 9.91

10-[α,β-Bis(pyrrolidino)-propionyl]-phenothiazine. Pyrrolidine (3.7 g) and IV (4.1 g) were refluxed in toluene (40 ml) for three hours. The base (2.5 g) was recrystallised from light petroleum. M. p. 102—104°.

$C_{23}H_{27}N_3OS$ (393.5)	Calc.	C 70.2	H 6.93	N 10.7
	Found	» 70.3	» 7.15	» 10.2

SUMMARY

The synthesis of 29 10-aminoacetyl- and 10-aminopropionyl-phenothiazines is described. Most of the compounds are powerful local anesthetics and some of them show outstanding spasmolytic properties. The absorption spectra of some 10-aminoacyl- and 10-aminoalkyl-phenothiazines have been determined.

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