The Synthesis of Possible Hydroxylated Metabolites of 2-Chlorophenothiazine Derivatives (1)

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The synthesis of 7-hydroxy, 8-hydroxy and 7,8-dihydroxy prochlorperazines (3a) and perphenazines (3b) is reported. The parent chlorophenothiazines were prepared analogously to previously reported chlorpromazine (3c) metabolite syntheses. The prochlorperazine side chain was introduced in one step using 1-(3-chloropropyl)-4-methylpiperazine and the perphenazine side chain in two steps, first reaction with 1-bromo-3-chloropropane followed by reaction with 1-piperazineethanol. The methoxymethyleneoxy *O*-protective groups were removed under mild conditions using methanolic hydrogen chloride. The preparations of 7-hydroxydesmethylprochlorperazine and 7-hydroxychlorpromazine quaternary methyl iodide are also reported.

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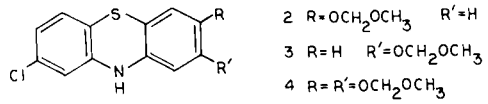
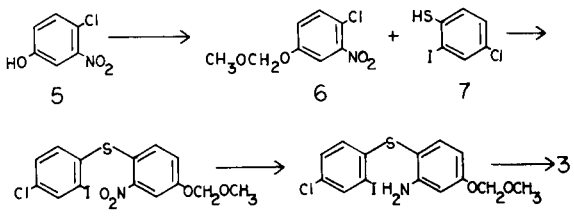
Chlorpromazine, perphenazine and prochlorperazine are major psycholeptic drugs differing in chemical structure by the side chain grouping on the nitrogen of the 2-chlorophenothiazine molecule. Of these three drugs, as well as in comparison with other therapeutically active phenothiazine derivatives, the metabolic pathways of chlorpromazine have been most extensively studied. The major ring hydroxylation route of chlorpromazine metabolism in humans is initiated primarily at the 7 position (4,5) with progressive hydroxylation in part indicated by the occurrence of 7,8-dihydroxychlorpromazine (6) and its subsequent possible biotransformation to an ortho quinone, 7,8-dioxochlorpromazine (7). The existence of minor hydroxylation pathways for this drug originating at the 3 and 8 positions have been postulated from the isolation of the respective hydroxy isomers from urine (8,9). Since similar hydroxylation patterns could be anticipated for perphenazine and prochlorperazine, we synthesized their 7- and 8-hydroxy, 7,8-dihydroxy derivatives, and the 7-hydroxydesmethylprochlorperazine for evaluative and biological studies. We, also, report the preparation of a chlorpromazine derivative of interest namely, the quaternary *N*-methyl iodide of 7-hydroxychlorpromazine.



2,3,4

The three intermediates in common for all the prepared compounds were 2-chloro-7-methoxymethyleneoxyphenothiazine (**2**) from 2-chloro-7-hydroxyphenothiazine (**1**) (10), 2-chloro-7,8-dimethoxymethyleneoxyphenothiazine (**4**) (11), and 2-chloro-8-methoxymethyleneoxyphenothiazine (**3**), prepared according to Scheme I. 4-Chloro-3-

Scheme I



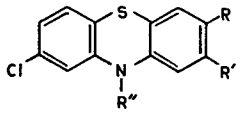
5 6 7

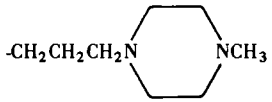
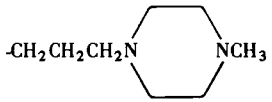
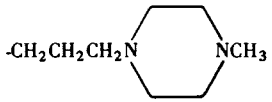
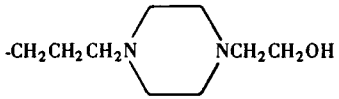
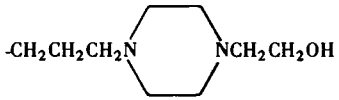
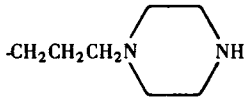
8 9

nitrophenol (**5**) (12) was reacted with chloromethyl methyl ether to give 4-chloro-3-nitromethoxymethyleneoxybenzene (**6**), which was treated in alkaline solution with

Table 1

Chlorophenothiazine Derivatives

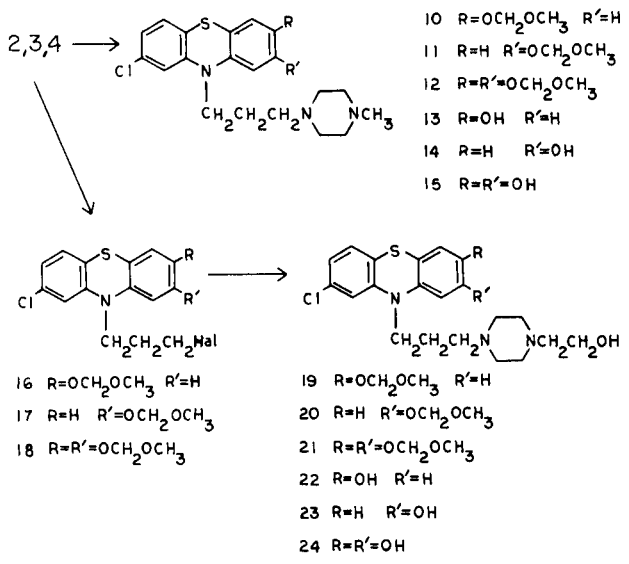


Compound No.	R	R′	R″	Yield	M.p., °C	Molecular Formula	Analyses					
							Calcd.			Found		
							C	H	N	C	H	N
2	-OCH_2OCH_3	-H	-H	39%	130-131	$C_{14}H_{12}ClNO_2S$	57.23	4.12	4.77	57.43	4.16	4.75
3	-H	-OCH_2OCH_3	-H	53%	138-140	$C_{14}H_{12}ClNO_2S$	57.23	4.12	4.77	57.17	4.10	4.64
13	-OH	-H		42%	196-197	$C_{20}H_{24}ClN_3OS$	61.60	6.20	10.78	61.67	6.27	10.68
14	-H	-OH		48%	105-108	$C_{20}H_{24}ClN_3OS$	61.60	6.20	10.78	61.59	6.25	10.84
15	-OH	-OH		59%	198-204	$C_{20}H_{24}ClN_3O_2S \cdot 2HCl$	50.16	5.47	8.78	50.00	5.47	8.83
22	-OH	-H		42%	225-227 dec.	$C_{21}H_{26}ClN_3O_2S \cdot 2HCl \cdot \frac{1}{4}H_2O$	50.70	5.78	8.45	50.72	6.02	8.33
23	-H	-OH		48%	232-234	$C_{21}H_{26}ClN_3O_2S \cdot 2HCl$	51.57	5.73	8.53	50.90	5.74	8.39
24	-OH	-OH		69%	219-222	$C_{21}H_{26}ClN_3O_3S \cdot 2HCl$	49.56	5.54	8.26	49.49	5.62	8.19
26	-OH	-H		12%	190-193	$C_{19}H_{22}ClN_3OS$	60.70	5.90	11.18	60.87	5.93	10.97
28	-OH	-H	-$CH_2CH_2CH_2N(CH_3)_2$	44%	178-179	$C_{17}H_{19}ClN_2OS$	60.98	5.72	8.36	60.92	5.65	8.37
29	-OH	-H	-$CH_2CH_2CH_2N^+(CH_3)_3I^-$	72%	116-119	$C_{18}H_{22}ClIN_2OS \cdot H_2O$	43.69	4.88	5.66	43.43	4.54	5.56

4-chloro-2-iodobenzenethiol (**7**) (11) to give 4-chloro-2-iodo-4′-methoxymethyleneoxy-2′-nitrodiphenylsulfide (**8**). Catalytic hydrogenation of **8** gave 4-chloro-2-iodo-2′-amino-4′-methoxymethyleneoxydiphenylsulfide (**9**). Ring closure to **3** was effected by heating in dimethylformamide with a copper-bronze catalyst.

The prochlorperazine and perpherazine derivatives were prepared as shown in Scheme II. The substituted phenothiazines **2, 3** and **4** were treated with sodium hydride in dimethylsulfoxide, followed by reaction with 2-(3-chloropropyl)-4-methylpiperazine (13) to give the *O*-protected prochlorperazines **10, 11** and **12**. In the perphenazine series, the sodium salts of **2, 3** and **4** were reacted with 1-bromo-3-chloropropane to give the 10-(γ-chloropropyl)-phenothiazines **16, 17** and **18**, mixed with a small amount of the bromopropyl analogs. No attempt was made to separate these and the mixture was used as such in the next reaction with 2-hydroxyethylpiperazine to yield the *O*-protected perphenazines **19, 20** and **21**. The intermediates **10, 11, 12, 19, 20** and **21** were obtained as heavy oils, which were purified either by absorption on silica gel or column chromatography. Attempts were made to prepare salts for characterization by elemental analysis, but failed, as even weak acids promoted removal of the methoxymethylene groups and mixtures with partially deprotected product were obtained. The hydroxyprochlorperazines **13, 14** and **15** and the hydroxyperphenazines **22, 23** and **24** were obtained by treatment of the precursors with methanolic hydrogen chloride. The free base of **13** and **14** is reported while **15, 22, 23** and **24** were isolated as the dihydrochlorides. 7-Hydroxydesmethylprochlorperazine (**26**) was prepared from the intermediate **16** by reaction with an excess of piperazine to give 7-methoxymethyleneoxydesmethylprochlorperazine (**25**) which was unprotected to give **26**, isolated as the free base.

Scheme II



The hydroxychlorpromazine derivatives were prepared according to Scheme III. The previously unreported 7-methoxymethyleneoxychlorpromazine (**27**) was prepared from **2** on reaction with sodium hydride followed by 3-dimethylaminopropyl chloride, in dimethylsulfoxide. Treatment of **27** with methanolic hydrogen chloride gave 7-hydroxychlorpromazine (**28**) (14), which quarternized with methyl iodide to give 7-hydroxychlorpromazine quarternary iodide (**29**) as a hygroscopic hydrate.

Scheme III

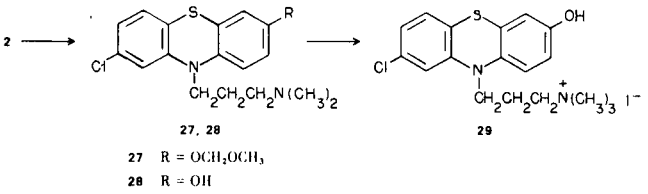


Table II

Absorption Spectra of Hydroxychlorophenothiazine Derivatives

Compound No.	Uv λ max nm (log ε) in ethanol			
13	216 (4.27)	258 (4.40)	316 (3.76)	
14	237 (4.33)	265 (4.36)	316 (3.74)	
15	213 (4.35)	236 (4.40)	258 (4.27)	319 (3.80)
22	214 (4.29)	257 (4.39)	315 (3.69)	
23	212 (4.17)	230 (4.29)	263 (4.32)	317 (3.64)
24	212 (4.32)	233 (4.39)	256 (4.25)	319 (3.78)
26	219 (4.27)	259 (4.43)	318 (3.78)	
29	223 (4.40)	256 (4.43)	310 (3.83)	

The final products are relatively stable in the solid state, the monohydroxy derivatives moderately and the dihydroxy derivatives very unstable in solution, as indicated by color changes through pink and red to purple. In storage and handling exposure to light and air must be avoided.

Physical data are listed in Tables I and II.

EXPERIMENTAL

Melting points were taken on a Thomas-Hoover melting point apparatus in open capillaries and are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Infracord Model 137. Ultraviolet and visible spectra were recorded on a Perkin-Elmer spectrophotometer Model 202. Analyses were performed by Micro-Tech Laboratories, Skokie, Illinois.

2-Chloro-7-methoxymethyleneoxyphenothiazine (**2**).

A mixture of 74 g. (0.34 mole) of **1** (10) and 140 g. (1.02 moles) of anhydrous potassium carbonate in 925 ml. of dimethylformamide was stirred at room temperature under nitrogen for 2 hours. It was cooled and 42.2 g. (0.51 mole) of chloromethyl

methyl ether in 725 ml. of dimethylformamide was added at 8° over 25 minutes. The cooling bath was removed and the mixture stirred for 1 hour. Addition of potassium carbonate and chloromethyl methyl ether was repeated four more times using the same amounts, time and temperature. The reaction mixture was poured into 6 l. of ice water and the product taken up in ethyl acetate. The extracts were washed several times with water and dried. The heavy oil which was obtained on removal of the solvent was chromatographed twice over a silica gel column (600 g.). The product factions were eluted with benzene-ethyl acetate 9:1 and amounted to 39 g. (0.13 mole). The analytical sample was recrystallized from hexane-benzene.

2-Chloro-5-methoxymethyleneoxynitrobenzene (**6**).

This compound was prepared similarly from 4-chloro-3-nitrophenol (**5**) (12). The solid precipitated on addition to ice water and was filtered, washed, air dried and used as such in the next step. From 56 g. (0.32 mole) of **5**, 47 g. (0.22 mole) of **6** was obtained. The analytical sample was crystallized from benzene-hexane to m.p. 28-30°, yield, 68.5%.

Anal. Calcd. for $C_8H_8ClNO_4$: C, 44.15; H, 3.70; N, 6.43. Found: C, 44.13; H, 3.62; N, 6.43.

Subsequent work on similar compounds indicates that higher yields, cleaner products and shorter reaction times were obtained, when the protective group was introduced using sodium hydride in dimethylformamide and all reactants were in equimolar amounts.

4-Chloro-2-iodo-4′-methoxymethyleneoxy-2′-nitrodiphenylsulfide Hemihydrate (**8**).

2-Iodo-4-chlorobenzenethiol (**7**)(11), 27.9 g. (0.103 mole) was dissolved in a mixture of 4.12 g. (0.103 mole) of sodium hydroxide in 92 ml. of 50% ethanol and added to a solution of 22.7 g. (0.103 mole) of **6** in 80 ml. of ethanol. The reaction mixture was stirred and refluxed for 16 hours. It was cooled, the solid filtered, washed with ethanol and dried to give 34.0 g. (75 mmoles) of **8**, yield, 73%. The analytical sample was recrystallized from ethanol to m.p. 116-118°.

Anal. Calcd. for $C_{14}H_{11}ClIO_4S \cdot \frac{1}{2}H_2O$: C, 37.22; H, 2.46; N, 3.12. Found: C, 36.37; H, 2.47; N, 3.10.

4-Chloro-2-iodo-2′-amino-4′-methoxymethyleneoxydiphenylsulfide (**9**).

To a Parr shaker were charged 19.0 g. (39.7 mmoles) of **8**, 480 ml. of ethyl acetate, 4.0 g. of 5% palladium/carbon and 50 psig. of hydrogen. The mixture was shaken for 4 hours, an additional 5.0 g. of catalyst added, and shaking was continued for 21 hours. The catalyst was filtered, extracted with additional hot ethyl acetate, and the combined filtrates were taken to dryness to yield 12.0 g. (71.3%) of **9** as a yellow oil. It was used in the next step without further purification.

2-Chloro-8-methoxymethyleneoxyphenothiazine (**3**).

A mixture of 12.0 g. (28 mmoles) of **9**, 230 ml. of dimethylformamide, 0.40 g. of copper-bronze catalyst, and 5.5 g. of powdered potassium carbonate was stirred and heated at reflux for 3½ hours, cooled, poured into 1 l. of water and extracted with 2 x 700 ml. of ether. The ether was washed with water several times, dried, taken to dryness and the resulting solid crystallized from benzene-hexane to yield 3.33 g. (15 mmoles) of **3**. Another recrystallization gave the analytical sample.

7-Methoxymethyleneoxyprochlorperazine (**10**).

To a stirred solution of 2 g. (7 mmoles) of **2** in 200 ml. of dry dimethylsulfoxide, under nitrogen, was added 0.6 g. (14 mmoles) of 57% sodium hydride in mineral oil. After 4½ hours, 2.6 g. (14 mmoles) of 1-(3-chloropropyl)-4-methylpiperazine (13) dissolved in 25 ml. of dimethylsulfoxide was added and the reaction mixture stirred at 67-70° for 3½ hours. An equal volume of methylene chloride was added and the mixture poured into 2 l. of water. The organic phase was separated and the aqueous phase extracted twice with methylene chloride. The combined extracts were washed five times with water, dried and the solvent evaporated to leave a brown oil. It was chromatographed over silica gel, eluting with 1) benzene, 2) chloroform, and 3) 5 parts of chloroform to 3 parts of 1% concentrated ammonium hydroxide in ethanol. The product was obtained from 3) as a light brown oil. It was dissolved in ether, filtered through 1 cm. of Celite and the solvent removed to leave 2.7 g. (6.2 mmoles) of product **10**, yield, 91%.

8-Methoxymethyleneoxyprochlorperazine (**11**).

This compound was prepared similarly from 1.5 g. (5 mmoles) of **3** and 0.36 g. (8 mmoles) of 1-(3-chloropropyl)-4-methylpiperazine. The crude product was chromatographed over an alumina column (10% water) and eluted with methylene chloride, to give 2.0 g. (4.5 mmoles) of **11** as a light pink oil, yield, 90%.

7,8-Dimethoxymethyleneoxyprochlorperazine (**12**).

This compound was prepared similarly from 3 g. (8.5 mmoles) of **4** (11), 0.74 g. (17.4 mmoles) of sodium hydride (50% in mineral oil) and 3.19 g. (19 mmoles) of 1-(3-chloropropyl)-4-methylpiperazine. The later part of the reaction was heated at 75-80° for 4½ hours. The crude product was absorbed on 100 g. of silica gel, washed with chloroform and liberated with methanol-concentrated ammonium hydroxide 95:5. After removal of the solvent, the product was taken up in benzene, filtered and evaporated to leave 3 g. (6.1 mmoles) of **12** as a red oil, yield, 72%.

7-Hydroxyprochlorperazine (**13**).

To a mixture of 10 ml. of methanol saturated with hydrogen chloride and 130 ml. of methanol was added 2.7 g. (6.2 mmoles) of **10**. The mixture was stirred and refluxed under nitrogen for 1 hour. The solution was concentrated down to 20 ml. and poured into 200 ml. of water, containing 5 ml. of concentrated ammonium hydroxide. The suspension was stirred in an ice bath for 1 hour, the solid was filtered, washed with cold water and air dried overnight. Finally it was dried *in vacuo* over phosphorus pentoxide at 80° for 4 hours to yield 0.93 g. of **13**. From the mother liquor, 0.1 g. more of product was obtained. In all 1.03 g. (2.6 mmoles) was collected.

8-Hydroxyprochlorperazine (**14**).

This compound was prepared similarly from 1.2 g. (2.7 mmoles) of **11** to give 0.52 g. (1.3 mmoles) of product.

7,8-Dihydroxyprochlorperazine Dihydrochloride (**15**).

A solution of 3 g. (6 mmoles) of **12** in 5 ml. of methanolic hydrogen chloride and 75 ml. of methanol was refluxed under nitrogen for 1 hour. The reaction mixture was cooled, treated with sulfur dioxide and evaporated to a glassy residue which was dissolved in 50 ml. of ethanolic sulfur dioxide, treated with charcoal, filtered and concentrated to a suspension. The solid was filtered and the mother liquor concentrated to give a second crop, totalling 1.73 g. (3.5 mmoles) of **15**, after drying *in vacuo* at 78°.

2-Chloro-10-(3-chloropropyl)-7-methoxymethyleneoxyphenothiazine (**16**).

To a solution of 3 g. of **2** in 300 ml. of dimethylsulfoxide was

added 0.9 g. (22 mmoles) of 57% sodium hydride in mineral oil. The mixture was stirred at room temperature, under nitrogen, for 2½ hours. 1-Bromo-3-chloropropane, 4.7 g. (30 mmoles) was added and the mixture stirred and kept at 65-70° for 3½ hours and left at room temperature overnight. An equal volume of methylene chloride was added and the mixture poured into 2 l. of water. The aqueous phase was extracted twice with methylene chloride and the combined extracts were washed five times with water, dried and concentrated to leave a brown oil which was chromatographed on silica gel. The product was eluted with hexane-benzene 1:1 to give 2.4 g. (6.5 mmoles) of **16** as a heavy yellow oil, which was used directly in the next step, yield, 65%.

2-Chloro-10-(3-chloropropyl)-8-methoxymethyleneoxyphenothiazine (**17**).

This compound was prepared similarly from **3**. Reaction temperature for the latter part of the reaction was 75-85°. The product was eluted from a silica gel column with benzene. From 2 g. of **3** (6.8 mmoles), 1.8 g. (4.9 mmoles) of **17** was obtained as an oil, yield, 72%.

2-Chloro-10-(3-chloropropyl)-7,8-dimethoxymethyleneoxyphenothiazine (**18**).

This compound was prepared similarly from **4**. The reaction temperature was 75-80° and the product was eluted from a silica gel column with benzene-ethyl acetate 9:1. From 5 g. (14 mmoles) of **4**, 2.66 g. (6.2 mmoles) of **18** were obtained as a brown oil, yield, 44%.

7-Methoxymethyleneoxyperphenazine (**19**).

To a solution of 2.4 g. (6.5 mmoles) of **16** in 50 ml. of methyl ethyl ketone was added 3.9 g. (30 mmoles) of *N*-β-hydroxyethylpiperazine and 1.7 g. of potassium iodide. The mixture was stirred and refluxed for 20 hours. The solvent was removed and the remaining paste extracted with benzene, the extracts washed several times with water, dried and the solvent evaporated. The remaining oil was chromatographed over a silica gel column. Unreacted starting material eluted with chloroform and product fractions with a mixture of 5 parts of chloroform and 3 parts of 1% concentrated ammonium hydroxide in ethanol. The oil was taken up in ether, filtered and the solvent evaporated to leave 0.8 g. (6.2 mmoles) of **19** as a heavy yellow oil, yield, 26%.

8-Methoxymethyleneoxyperphenazine (**20**).

This compound was prepared similarly from 1.8 g. (4.9 mmoles) of **17**. Reflux time was 65 hours, with two more additions of *N*-β-hydroxyethylpiperazine and potassium iodide after 20 and 42 hours, respectively. The crude product was absorbed on 100 g. of silica in chloroform, washed well on the filter with chloroform and the product liberated with repeated extractions with methanol. After filtration of an ether solution, 1.1 g. (2.5 mmoles) of **20** were obtained as a heavy oil, yield, 50%.

7,8-Dimethoxymethyleneoxyperphenazine (**21**).

This compound was prepared similarly from 2.6 g. (6.2 mmoles) of **18**. Reflux time was 18 hours and purification procedure as for **20**. There resulted 1.6 g. (3.1 mmoles) of **21** as a heavy oil, yield, 50%.

7-Methoxymethyleneoxydesmethylprochlorperazine (**25**).

This compound was prepared similarly from 2.1 g. (5.7 mmoles) of **16**, 1.6 g. (19 mmoles) of anhydrous piperazine and 1 g. of potassium iodide in 30 ml. of refluxing methyl ethyl ketone for 16 hours. There was obtained 0.94 g. (2.2 mmoles) of **25** as a heavy oil, yield, 39%.

7-Hydroxyperphenazine Dihydrochloride ¼ Hydrate (**22**).

A solution of 0.8 g. (1.7 mmoles) of **19** in 5 ml. of saturated methanolic hydrogen chloride and 50 ml. of methanol was refluxed in the dark under nitrogen for 1 hour, cooled and treated with sulfur dioxide. The solvent was removed in vacuum and the glassy solid was dried over phosphorus pentoxide *in vacuo* at room temperature for 40 hours. It was dissolved in 20 ml. of hot 1-butanol, treated with Norite, cooled, and 5 ml. of dry ether added to initiate crystallization. After refrigeration overnight, the solid was filtered, washed with dry ether and dried *in vacuo* over phosphorus pentoxide at 100° for 4 hours to yield 0.43 g. (1 mmole) of **22**.

8-Hydroxyperphenazine Dihydrochloride (**23**).

This compound was prepared similarly from 1.06 g. (2.3 mmoles) of **20**. Recrystallization from 75 ml. of 1-butanol gave 0.39 g. (0.8 mmole) of **23**.

7,8-Dihydroxyperphenazine Dihydrochloride (**24**).

This compound was prepared similarly from 1.6 g. (3 mmoles) of **21**. Recrystallization from 100 ml. of 1-butanol gave in three crops 1.1 g. (2.1 mmoles) of **24**.

7-Hydroxydesmethylprochlorperazine (**26**).

This compound was prepared similarly from 0.82 g. (2 mmoles) of **25** giving 0.08 g. (0.24 mmole) of **26**. The dihydrochloride, which was first isolated could not be crystallized satisfactorily. It was dissolved in 5% sodium bicarbonate solution and the free base extracted with ether and ethyl acetate. The solution was concentrated to dryness, the solid extracted with ether, filtered and concentrated until **26** started to precipitate as a tan solid.

7-Methoxymethyleneoxychlorpromazine (**27**).

A mixture of 24.2 g. (83 mmoles) of **2** and 7.6 g. (179 mmoles) of 57% sodium hydride in mineral oil in 500 ml. of dimethylsulfoxide was stirred under nitrogen at room temperature for 6 hours. A solution of 24.2 g. (200 mmoles) of 3-dimethylaminopropyl chloride in 100 ml. of dimethylsulfoxide was added dropwise over one hour and the resulting mixture stirred at 75-80° for 4 hours. The corresponding work-up is described above for **10**. The crude product was chromatographed over a 600 g. silica gel column, product factions eluted with ethyl acetate-methanol 9:1, combined and the solvent removed. The resulting oil was taken up in hexane, filtered and evaporated to leave **27** as a red oil. 18.8 g. (68 mmoles) was obtained, yield, 60%.

7-Hydroxychlorpromazine (**28**).

A solution of 18 g. (47.5 mmoles) of **27** in 500 ml. of methanol was heated to reflux under nitrogen and treated with 15 ml. of methanolic hydrogen chloride. Refluxing was continued for one hour, followed by cooling and treatment with sulfur dioxide before evaporating to a purple residue. This was taken up in 500 ml. of water containing sulfur dioxide and extracted with ether. The aqueous portion was treated with 4 ml. of 20% sodium hydroxide in portions with cooling. Filtration was followed by further addition of 20% sodium hydroxide to *p*H 8, extraction with ether with readjustment to *p*H 8 as needed. The ether extract was dried and concentrated to obtain 8.9 g. (21 mmoles) of **28** as a tan solid.

7-Hydroxychlorpromazine Methiodide Hydrate (**29**).

A solution of 0.50 g. (1.50 mmoles) of **28** in 55 ml. of acetone

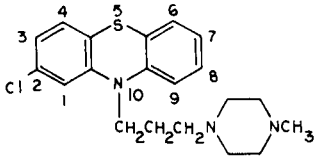
was treated with 0.32 g. (2.25 mmoles) of methyl iodide, in 5 ml. of acetone. The mixture was kept at room temperature for 4 hours and refrigerated for 48 hours. The methiodide was precipitated by addition of 150 ml. of dry ether. The gummy solid was taken up in 10 ml. of acetone and added dropwise to 150 ml. of vigorously stirred ether. A white solid separated immediately and was collected. The hygroscopic product was dried *in vacuo* at 78° for 10 hours to give 0.53 g. (1.1 mmoles) of **29**.

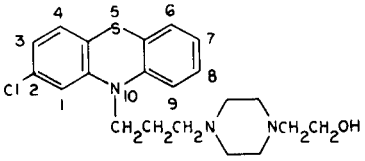
REFERENCES AND NOTES

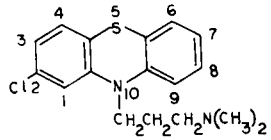
(1) These compounds were prepared under Contract No. ADM-42-74-35 (ER) with the Psychopharmacology Research Branch, National Institute of Mental Health.

(2) Author to whom correspondence should be addressed.

(3a) Prochlorperazine is the generic name for 2-chloro-10-[3-(4-methyl-1-piperazinyl)propyl]phenothiazine. (3b) Perphenazine







is the generic name for 2-chloro-10-[3-[4-(2-hydroxyethyl)piperazinyl]propyl]phenothiazine. (3c) Chlorpromazine is the generic name for 2-chloro-10-(3-dimethylaminopropyl)phenothiazine.

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