Synthesis of Tetracyclic and Pentacyclic Phenothiazines *via* Benzotriazole Methodology

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Treatment of 10-(benzotriazol-1-yl)alkylphenothiazine with electron-rich alkenes in the presence of zinc bromide gave tetracyclic phenothiazines **4** and **9** as well as pentacyclic phenothiazines **5**, which have potential use in the pharmaceutical industry.

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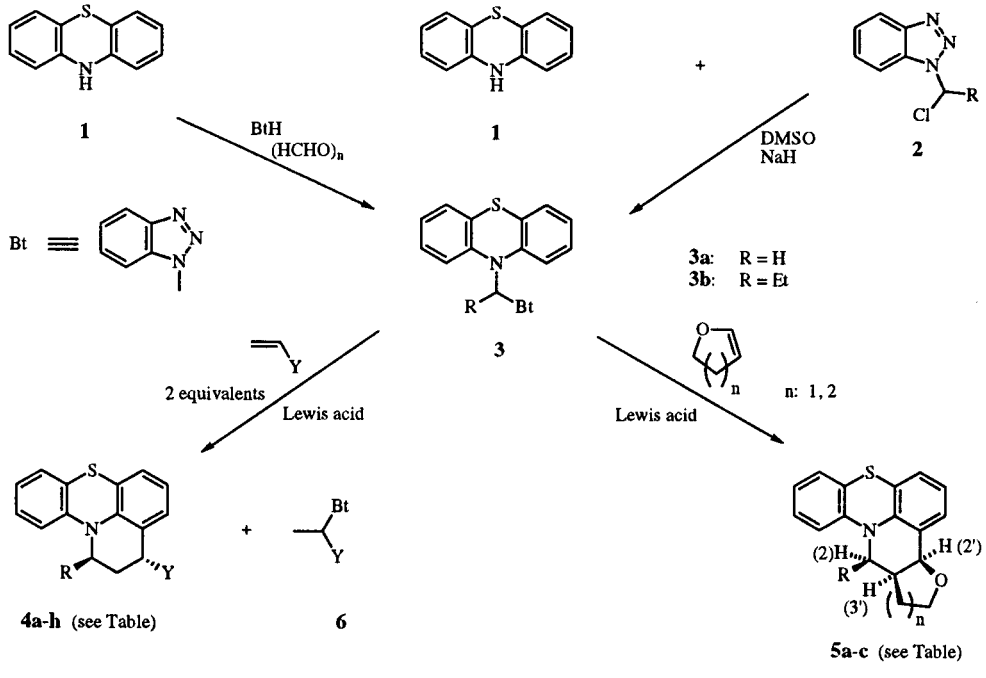
Introduction.

Phenothiazine derivatives are important because of their biological activities. For example, chlorpromazine has been used over the past 40 years for its sedative and antipsychotic properties [1]. Phenothiazine derivatives are often synthesized by direct alkylation or acylation of phenothiazine [2-5]. Tetracyclic phenothiazines of type **4** have previously been prepared by i) reactions of phenothiazine with malonic esters followed by Friedel-Crafts cyclization [4,6]; ii) Michael addition of phenothiazine with acrylonitrile or an α,β-unsaturated ester, followed by hydrolysis and Friedel-Crafts reaction [7,8]. Pentacyclic phenothiazines of type **5**, to the best of our knowledge, have not been reported. Our previous work showed that 1-(*N*-arylamino)methylbenzotriazoles reacted with double or triple bonds to form tetrahydroquinolines [9-12], 1,2-dihydroquinolines [13] and quinolinium salts [13]. Three examples of the application of this methodology to phenothiazine ring extension were included: 10-(benzotriazol-1-yl)-methylphenothiazine with (i) 2-methyl-1,3-butadiene gave 9-methyl-9-vinyl-9,10,11,12-tetrahydropyrido[3,2,1-*kl*]-1,4-phenothiazine [9]; (ii) vinyl ether gave 3-ethoxy-(2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine [10]; and (iii) *N*-vinyl-2-pyrrolidinone to give 1-(2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazin-3-yl)-2-pyrrolidinone [11]. We now report further syntheses of tetracyclic and pentacyclic phenothiazines using benzotriazole methodology.

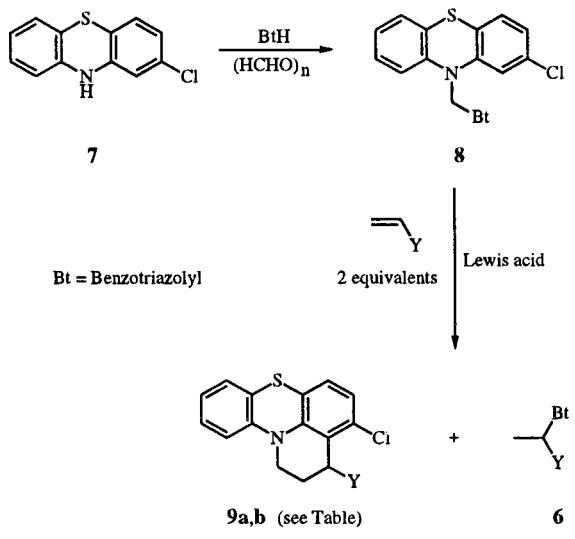
Results and Discussion.

10-(Benzotriazol-1-yl)methylphenothiazine (**3a**) and 2-chloro-10-(benzotriazol-1-yl)methylphenothiazine (**8**) were prepared as previously reported [9]. Although a similar method failed to give 10-[α-alkyl-α-(benzotriazol-1-yl)]methylphenothiazine (**3b**), compound **3b** was made by reacting 1-(α-chloropropyl)benzotriazole with phenothiazine anion. Attempts to purify **3b** on silica gel led to decomposition, but crude **3b** could be used as formed directly in the next step.

Scheme 1



Scheme 2



7 8 9a,b (see Table) 6

Table

Preparation of Tetracyclic Phenothiazines **4a-h**, **9a,b** and Pentacyclic Phenothiazines **5a-c**

Compound	R	Y or n	Yield (%)
4a	H	1-pyrrolidonyl	71
4b	H	$N(Me)COCH_3$	80
4c	H	OEt	70
4d	H	$OC_{12}H_{25}$	75
4e	H	OPh	60
4f	Et	$N(Me)COCH_3$	65 [a]
4g	Et	1-pyrrolidonyl	75 [a]
4h	Et	OEt	52 [a]
9a	--	1-pyrrolidonyl	79
9b	--	OEt	65
5a	H	1	59
5b	H	2	54
5c	Et	1	72 [a]

[a] Yield for two steps.

Reactions of 10-(benzotriazol-1-yl)methylphenothiazine **3a** with the electron rich alkenes *N*-vinylpyrrolidone, *N*-methyl-*N*-vinylacetamide, vinyl ethyl ether, vinyl dodecyl ether, and vinyl phenyl ether in the presence of zinc bromide gave the corresponding tetracyclic phenothiazines **4a-e** (Scheme 1 and Table). In these reactions **3** → **4**, two equivalents of alkene were needed because one equivalent was consumed by the benzotriazolyl anion which was formed simultaneously to generate by-product of type **6**.

Treatment of **3a** with the cyclic vinyl ethers, 2,3-dihydrofuran and 3,4-2*H*-dihydropyran gave exclusively the *cis*-fused pentacyclic phenothiazines **5a** and **5b**, respectively. The *cis* relationship of H-2' and H-3' were determined by NOE experiments: irradiation H-2' of **5a** at 4.50 ppm, H-3' at 2.45-2.55 ppm showed positive NOE, and a similar result was found for **5b**. The assignments were further supported by the H-2'/H-3' coupling constants in the ^1H nmr: 4.9 Hz for **5a** and 1.5 Hz for **5b**, which were consistent with previous reports [14-16].

Similarly, **3b** was treated with *N*-methyl-*N*-vinylacetamide, *N*-vinylpyrrolidone, vinyl ethyl ether and 2,3-dihydrofuran, under the above conditions to give tetracyclic phenothiazines **4f-h** and pentacyclic phenothiazine **5c**, respectively. From the ^1H nmr of **4g**, the ring 4-position CH proton (α to the pyrrolidonyl group) is assigned to the signal at 5.48 ppm. This signal is a double-doublet with J = 6.6 and 10.5 Hz. This indicates that there is one axial-axial coupling and thus that the pyrrolidonyl group is equatorial. The proton of the ring 2-position CH to which the ethyl group is attached is assigned to the signal at 4.22-4.26 ppm and this signal is a mutiplet with J < 5.0 Hz. This shows the absence of axial-axial coupling, and therefore the ethyl group is axial. This demonstrates the ethyl group is *trans* to the pyrrolidonyl group. Similarly, **4f** and **4h** both have *trans* configurations, although minor amount of the *cis* isomer of **4f** was also detected in the ^1H nmr spectra.

In compound **5c**, the two rings are *cis*-fused, as demonstrated by NOE experiments and the coupling constant of H-2' and H-3' of 5.2 Hz. Irradiation of H-2' at 4.46 ppm, H-3' at 2.69-2.80 ppm showed a positive NOE. Irradiation of H-3' at 2.69-2.80 ppm, both H-2' and the proton (H-2) of the ring 2-position CH to which the ethyl group is attached showed positive effects. The above experiments indicate that these three protons are all *cis* and both H-2' and H-2 are axial. Therefore, the ethyl group is *trans* to the H-3'.

Compound **8** was reacted with vinyl ethyl ether and *N*-vinylpyrrolidinone under similar conditions to give 71% and 65% of the expected tetracyclic phenothiazines **9a,b**, respectively. Compounds **4a-h**, **9a,b** and **5a-c** have all been characterized by ^1H, ^{13}C nmr and CHN analyses.

In conclusion, we have successfully prepared tetracyclic phenothiazines **4** and **9**, and pentacyclic phenothiazines **5** from the reaction of 10-(benzotriazol-1-yl)alkylphenothiazine **3** with electron-rich alkenes in the presence of zinc bromide. These compounds have potential use in the pharmaceutical industry.

EXPERIMENTAL

Melting points were determined using a Koefler hot stage apparatus, and are uncorrected. The ^1H nmr and ^{13}C nmr spectra

were recorded on a Gemini 300 nmr spectrometer (300 MHz and 75 MHz respectively) in chloroform-*d* with tetramethylsilane (for ^1H) and chloroform-*d* (for ^{13}C) as the internal reference. Microanalyses were performed on a Carlo Erba 1106 elemental analyzer.

Compound **3a,b** was prepared by the literature procedure [9].

10-(Benzotriazol-1-yl)methylphenothiazine (**3a**).

This compound was obtained as a white solid (65%) from benzene, mp 170-171° (lit [9] mp 168-169°); ^1H nmr: δ 8.01 (d, J = 8.2 Hz, 1H), 7.53 (d, J = 7.9 Hz, 1H), 7.30-7.42 (m, 2H), 7.03-7.18 (m, 6H), 6.98 (t, J = 7.2 Hz, 2H), 6.64 (s, 2H); ^{13}C nmr: δ 146.4, 142.6, 132.3, 127.7, 127.6, 126.6, 124.2, 119.9, 117.0, 110.5, 62.6.

10-(α-Benzotriazol-1-yl)propylphenothiazine (**3b**).

This compound was obtained as a mixture which contains Bt-1 and Bt-2 isomers and directly used for the next step; ^1H nmr: δ 8.02-8.08 (m, 1H, from Bt-1 isomer), 7.95-8.01 (m, 2H, from Bt-2 isomer), 6.95-7.50 (m, 11H), 6.15-6.40 (m, 1H), 2.55-2.85 (m, 2H), 0.95-1.15 (m, 3H); ^{13}C nmr: δ 146.4 [Bt-1 isomer], 142.7, 132.8, 131.0, 127.3, 127.2, 126.6, 125.1, 124.4, 123.8, 123.1, 121.0, 119.9, 118.5, 110.4, 81.4 [Bt-2 isomer], 65.9 [Bt-1 isomer], 29.6 [Bt-2 isomer], 26.7 [Bt-1 isomer], 10.3 [Bt-2 isomer], 10.1 [Bt-1 isomer].

2-Chloro-10-(benzotriazol-1-yl)methylphenothiazine (**8**).

This compound was obtained as a white solid (60%) from benzene, mp 149-150°; ^1H nmr: δ 8.02 (d, J = 8.1 Hz, 1H), 7.50 (d, J = 8.1 Hz, 1H), 7.33-7.42 (m, 2H), 7.03-7.18 (m, 5H), 7.01 (t, J = 7.2 Hz, 2H), 6.63 (s, 2H); ^{13}C nmr: δ 146.4, 144.0, 142.0, 133.5, 132.3, 128.2, 127.8, 127.6, 126.6, 125.3, 124.6, 124.3, 124.2, 120.1, 117.4, 110.2, 62.4.

Anal. Calcd. for $C_{19}H_{13}ClN_4S$: C, 62.55; H, 3.59; N, 15.36. Found: C, 62.71; H, 3.52; N, 15.39.

General Procedure for the Preparation of Phenothiazine Derivatives **4**, **5** and **9**.

N-(1-Benzotriazolylalkyl)phenothiazine **3** or **8** (2 mmoles), alkene (4 mmoles) and anhyd zinc bromide (20 mg) in dry methylene chloride (30 ml) were stirred at rt for 48 hours. After the reaction was complete, the mixture was washed with aqueous sodium hydroxide (2 *N*, 2 x 15 ml) and water (2 x 15 ml), and extracted with ethyl acetate (3 x 20 ml). The combined organic layers were dried over anhyd sodium sulfate. After removal of the solvent under vacuum, the residue was purified by column chromatography on silica gel to give pure products.

1-(2,3-Dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazin-3-yl)-2-pyrrolidinone (**4a**).

This compound was obtained as a white solid (71%) from ethyl acetate, mp 160-161° (lit [11] mp 149-152°); ^1H nmr: δ 7.08-7.20 (m, 2H), 6.90-7.03 (m, 2H), 6.70-6.89 (m, 3H), 5.37-5.43 (m, 1H), 3.65-3.85 (m, 2H), 3.04-3.26 (m, 2H), 2.52 (t, J = 8.1 Hz, 2H), 2.15-2.37 (m, 2H), 1.92-2.10 (m, 2H); ^{13}C nmr: δ 175.5, 144.0, 142.1, 127.5, 127.1, 126.6, 125.6, 122.7, 122.3, 122.2, 122.0, 120.6, 112.7, 47.9, 44.2, 43.6, 31.2, 25.7, 18.2.

N-(2,3-Dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazin-3-yl)-*N*-methyl acetamide (**4b**).

This compound was obtained as a white solid (71%) from ethyl acetate, mp 127-128°; ^1H nmr: δ 7.06-7.20 (m, 2H), 6.70-7.03 (m, 5H), 5.91-6.00 (m, 0.7H) [4.95-5.05 (m, 0.3H)], 3.69-3.89 (m, 2H), 2.68 (s, 3H), 2.20-2.38 (m, 5H); ^{13}C nmr: δ 171.5 [171.1], 144.2, 142.7, 127.5, 127.1 [126.9], 126.4, 125.7 [124.7], 122.9, 122.6, 122.2 [122.1], 112.7 [112.6], 50.1 [55.4], 44.4 [44.8], 31.6 [28.5], 25.3 [26.7], 22.2 [21.6].

Anal. Calcd. for $C_{18}H_{18}N_2OS$: C, 69.65; H, 5.85; N, 9.03. Found: C, 69.34; H, 6.12; N, 8.90.

3-Ethoxy-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine (**4c**).

This compound was obtained as an oil [10] (70%); ^1H nmr: δ 6.77-7.13 (m, 7H), 4.31 (s, 1H), 3.78 (t, J = 9.6 Hz, 1H), 3.48-3.65 (m, 3H), 2.25-2.35 (m, 1H), 2.05-2.15 (m, 1H), 1.20 (t, J = 6.9 Hz, 3H); ^{13}C nmr: δ 144.1, 141.2, 128.7, 127.4, 127.2, 126.9, 123.4, 122.6, 121.4, 121.3, 120.0, 113.1, 72.2, 63.3, 40.9, 27.0, 15.5.

3-Dodecyloxy-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine (**4d**).

This compound was obtained as an oil (75%); ^1H nmr: δ 6.95-7.15 (m, 4H), 6.77-6.92 (m, 3H), 4.29 (t, J = 3.0 Hz, 1H), 3.75-3.85 (m, 1H), 3.44-3.59 (m, 3H), 2.08-2.22 (m, 1H), 2.05-2.15 (m, 1H), 1.11-1.65 (m, 20H), 0.88 (t, J = 6.9 Hz, 3H); ^{13}C nmr: δ 144.1, 141.1, 128.7, 127.3, 127.1, 126.8, 123.6, 122.5, 121.5, 121.3, 120.0, 113.0, 99.6, 72.3, 68.1, 65.3, 41.0, 31.9, 29.9, 29.6, 29.5, 29.4, 29.3, 26.9, 26.2, 22.7, 19.8, 14.1.

Anal. Calcd. for $C_{27}H_{37}NOS$: N, 3.31. Found: N, 3.01.

3-Phenoxy-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine (**4e**).

This compound was obtained as an oil (60%); ^1H nmr: δ 7.22-7.36 (m, 2H), 6.75-7.16 (m, 10H), 5.29 (s, 1H), 3.72-3.84 (m, 1H), 3.60-3.69 (m, 1H), 2.38-2.54 (m, 1H), 2.15-2.30 (m, 1H); ^{13}C nmr: δ 157.2, 144.0, 141.5, 129.6, 128.5, 127.5, 127.4, 127.0, 122.7, 121.9, 121.5, 121.4, 120.2, 116.7, 113.0, 71.4, 40.9, 26.1.

Anal. Calcd. for $C_{21}H_{17}NOS$: C, 76.13; H, 5.13; N, 4.22. Found: C, 76.17; H, 5.44; N, 4.17.

N-(1-Ethyl-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazin-3-yl)-*N*-methylacetamide (**4f**).

This compound was obtained as a white solid (65%) from ethyl acetate, mp 122-124°; ^1H nmr: δ 6.86-7.20 (m, 7H), 6.03 (t, J = 8.2 Hz, 0.75H) [5.09 (t, J = 8.0 Hz, 0.25H)], 4.15-4.35 (m, 1H), 2.57 (s, 2.25H) [2.53 (s, 0.75H)], 2.28 (s, 2.25H) [2.17 (s, 0.75H)], 2.00-2.15 (m, 2H), 1.60-1.79 (m, 2H), 1.02 (t, J = 7.2 Hz, 3H); ^{13}C nmr: δ 171.5 [171.1], 145.6, 142.7, 127.8, 127.5, 126.9, 126.4, 126.3, 124.7, 123.7, 122.6, 122.2, 113.8, 54.5, 47.5, 31.6, 27.3, 25.3, 22.2, 10.9.

Anal. Calcd. for $C_{20}H_{22}N_2OS$: C, 70.97; H, 6.55; N, 8.28. Found: C, 71.08; H, 6.90; N, 8.37.

1-(1-Ethyl-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazin-3-yl)-2-pyrrolidinone (**4g**).

This compound was obtained as a white solid (75%) from ethyl acetate, mp 145-147°; ^1H nmr: δ 7.12-7.23 (m, 2H), 7.00-7.10 (m, 1H), 6.70-6.92 (m, 4H), 5.45-5.55 (m, 1H), 4.20-4.35 (m, 1H), 3.05-3.17 (m, 1H), 2.88-2.90 (m, 1H), 2.47 (t, J = 7.7 Hz, 2H), 1.68-2.21 (m, 6H), 1.02 (t, J = 7.1 Hz, 3H); ^{13}C nmr: δ 175.5, 145.3, 142.0, 127.9, 127.5, 126.7, 126.2, 125.1, 125.0, 123.1, 122.6, 122.4, 113.9, 54.0, 45.7, 43.4, 31.3, 28.0, 25.2, 18.1, 10.7.

Anal. Calcd. for $C_{21}H_{22}N_2OS$: C, 71.97; H, 6.33; N, 7.99. Found: C, 71.92; H, 6.74; N, 8.29.

1-Ethyl-3-ethoxy-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine (**4h**).

This compound was obtained as an oil (52%); ^{1}H nmr: δ 6.79-7.17 (m, 7H), 4.31-4.40 (m, 1H), 3.41-3.47 (m, 2H), 2.41-2.45 (m, 1H), 1.67-1.97 (m, 2H), 1.25-1.40 (m, 2H), 1.10 (t, J = 9.6 Hz, 3H), 0.90 (t, J = 7.2 Hz, 3H); ^{13}C nmr: δ 143.8, 142.6, 127.9, 127.8, 127.7, 127.6, 127.1, 127.0, 124.8, 122.6, 121.1, 115.4, 72.2, 63.0, 49.5, 33.0, 25.4, 15.3, 9.3.

Anal. Calcd. for $C_{19}H_{21}NOS$: N, 4.50. Found: N, 4.37.

1-(10-Chloro-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazin-3-yl)-2-pyrrolidinone (**9a**).

This compound was obtained as a white solid (71%) from ethyl acetate, mp 179-181°; ^{1}H nmr: δ 6.98-7.03 (m, 2H), 6.76-6.96 (m, 4H), 5.37-5.43 (m, 1H), 3.65-3.85 (m, 2H), 3.16-3.26 (m, 1H), 3.04-3.14 (m, 1H), 2.52 (t, J = 7.9 Hz, 2H), 2.16-2.37 (m, 2H), 1.95-2.10 (m, 2H); ^{13}C nmr: δ 175.6, 145.2, 141.4, 133.5, 127.7, 127.6, 126.7, 125.9, 122.7, 122.6, 122.5, 120.6, 113.2, 47.9, 44.4, 43.6, 31.2, 25.6, 18.3.

Anal. Calcd. for $C_{19}H_{17}ClN_2OS$: C, 63.95; H, 4.80; N, 7.85. Found: C, 63.64; H, 4.75; N, 7.80.

10-Chloro-3-ethoxy-2,3-dihydro-1*H*-pyrido[3,2,1-*kl*]phenothiazine (**9b**).

This compound was obtained as an oil (65%); ^{1}H nmr: δ 6.80-7.01 (m, 6H), 4.31 (s, 1H), 3.75 (t, J = 9.6 Hz, 1H), 3.48-3.69 (m, 3H), 2.25-2.35 (m, 1H), 2.05-2.15 (m, 1H), 1.20 (t, J = 6.9 Hz, 3H); ^{13}C nmr: δ 145.9, 141.1, 134.0, 129.6, 128.0, 127.9, 124.5, 122.9, 122.6, 120.6, 120.4, 114.2, 72.7, 64.2, 41.7, 27.5, 16.2.

Anal. Calcd. for $C_{17}H_{16}ClNOS$: C, 64.24; H, 5.08; N, 4.41. Found: C, 63.95; H, 5.00; N, 4.69.

1,2,13,13a-Tetrahydro-3*aH*-furo[2',3':4,5]pyrido[3,2,1-*kl*]phenothiazine (**5a**).

This compound was obtained as a solid (60%) from ether, mp 130-131°; ^{1}H nmr: δ 7.25 (d, J = 7.9 Hz, 1H), 7.02-7.18 (m, 3H), 6.82-6.98 (m, 3H), 4.50 (d, J = 4.9 Hz, 1H), 3.98-4.08 (m, 1H), 3.80-3.90 (m, 2H), 3.27 (t, J = 12.5 Hz, 1H), 2.45-2.55 (m, 1H), 2.28-2.40 (m, 1H), 1.76-1.88 (m, 1H); ^{13}C nmr: δ 145.2, 141.1, 129.6, 127.5, 127.4, 126.4, 123.5, 123.3, 123.1, 122.7, 122.3, 113.5, 75.4, 65.8, 46.1, 34.5, 29.4.

Anal. Calcd. for $C_{17}H_{15}NOS$: C, 72.57; H, 5.37; N, 4.98. Found: C, 72.58; H, 5.24; N, 5.00.

2,3,14,14a-Tetrahydro-1*H*,4*aH*-pyrano[2',3':4,5]pyrido[3,2,1-*kl*]-phenothiazine (**5b**).

This compound was obtained as a solid (60%) from ether, mp 174-175°; ^{1}H nmr: δ 7.00-7.18 (m, 4H), 6.85-6.95 (m, 3H), 4.41 (d, J = 1.5 Hz, 1H), 3.86-3.97 (m, 2H), 3.68 (td, J = 9.5, 2.3 Hz, 1H), 3.45-3.55 (m, 1H), 2.25-2.29 (m, 1H), 1.88-1.94 (m, 3H), 1.51-1.55 (m, 1H);^{13}C nmr: δ 144.2, 141.8, 129.1, 127.4, 127.2, 127.1, 123.4, 122.5, 122.3, 122.1, 119.8, 113.3, 73.2, 67.2, 45.4, 31.2, 25.2, 22.2.

Anal. Calcd. for $C_{18}H_{17}NOS$: C, 73.22; H, 5.76; N, 4.74. Found: C, 73.09; H, 5.81;N,4.86.

13-Ethyl-1,2,13,13a-tetrahydro-3*aH*-furo[2',3':4,5]pyrido-[3,2,1-*kl*]phenothiazine (**5c**).

This compound was obtained as a solid (72%) from ether, mp 164-166°; ^{1}H nmr: δ 7.30 (d, J = 7.9 Hz, 1H), 7.02-7.25 (m, 3H), 6.82-7.01 (m, 3H), 4.47 (d, J = 5.2 Hz, 1H), 4.06-4.14 (m, 1H), 3.85-4.02 (m, 2H), 2.69-2.80 (m, 1H), 2.30-2.45 (m, 1H), 1.95-2.13 (m, 1H), 1.40-1.70 (m, 2H), 0.96 (t, J = 7.0 Hz, 3H); ^{13}C nmr: δ 146.4, 138.5, 128.5, 127.8, 127.5, 126.3, 125.5, 124.6, 122.6, 122.1, 114.2, 114.1, 74.6, 66.1, 57.8, 40.0, 28.5, 21.0, 11.7.

Anal. Calcd. for $C_{19}H_{19}NOS$: C, 73.75; H, 6.19; N, 4.53. Found: C, 73.67; H, 6.18; N, 4.76.

REFERENCES AND NOTES

[1] M. Gordon, P. N. Craig and C. L. Zirkle, In Molecular Modification in Drug Design. Adv. Chem. Ser. Vol **45**, ACS, Washington, D. C., 1964, pp 140-147.

[2] H. Gilman, R. D. Nelson and J. F. Champaigne, Jr., *J. Am. Chem. Soc.*, **74**, 4205 (1952).

[3] H. E. Zaugg, L. R. Swett and G. R. Stone, *J. Org. Chem.*, **23**, 1389 (1958).

[4] M. Harfenist, R. Blumfeld, T. Capiris and E. Magnien, *J. Org. Chem.*, **27**, 3977 (1962).

[5] S. J. Schmolka and H. Zimmer, *Synthesis*, 29 (1984).

[6] M. Harfenist, *J. Org. Chem.*, **27**, 4326 (1962).

[7] E. F. Godefroi and E. L. Wittle, *J. Org. Chem.*, **21**, 1163 (1956).

[8] M. Harfenist and E. Magnien, *J. Am. Chem. Soc.*, **80**, 6080 (1958).

[9] A. R. Katritzky and M. F. Gordeev, *J. Org. Chem.*, **58**, 4049 (1993).

[10] A. R. Katritzky, B. Rachwal and S. Rachwal, *J. Org. Chem.*, **60**, 2588 (1995).

[11] A. R. Katritzky, B. Rachwal and S. Rachwal, *J. Org. Chem.*, **60**, 3993 (1995).

[12] A. R. Katritzky, D. Nichols, M. Qi and B. Yang, *J. Heterocyclic Chem.*, **34**, 1259 (1997).

[13] A. R. Katritzky, D. Semenzin, B. Yang and D. M. P. Pleynet, *J. Heterocyclic Chem.*, in press (1998).

[14] A. R. Katritzky, G. Qiu and B. Yang, *J. Org. Chem.*, **62**, 8210 (1997).

[15] A. R. Katritzky, G. Qiu and B. Yang, *Synthesis*, 704 (1998).

[16] T. Kametani, H. Takeda, Y. Suzuki, H. Kasai and T. Honda, *Heterocycles*, **24**, 3385 (1986).