Regioselective synthesis of *N*-acyl- and *N*-alkyldioxolo[4,5-*b*]phenothiazines

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Abstract

We describe the preparation of new substituted dioxolo[4,5-*b*]phenothiazines by two slightly different reaction sequences. N-Arylation of [1,3]benzodioxol-5-amine with organolead or organobismuth reagents afforded *N*-aryl[1,3]benzodioxol-5-amines; subsequent Bernthsen thionation gave rise to phenothiazine ring formation and was followed by N-acylation. On the other hand, [1,3]benzodioxol-5-amine was first N-alkylated, the resulting *N*-alkyl[1,3]benzodioxol-5-amines were N-phenylated, before Bernthsen the final tetracyclic thionation furnished product.

Keywords: Dioxolophenothiazines, arylation, Bernthsen thionation, N-acylation.

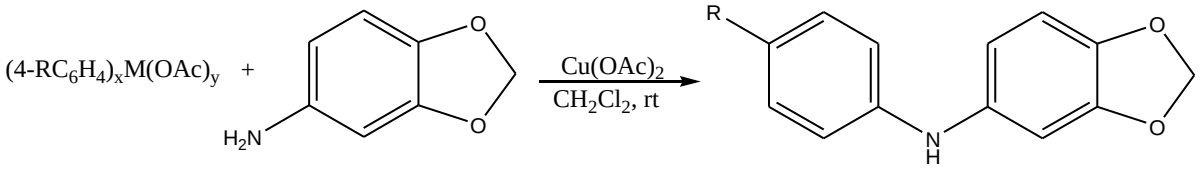
Introduction

The phenothiazines, exemplified by chlorpromazine, are the largest and most widely investigated class of neuroleptic agents.[1] The important feature of these compounds is that the amino group is separated from the nitrogen atom of the phenothiazine ring by a carbon chain. Although a wide range of derivatives has been described,[2]the number of polycyclic systems bearing a phenothiazine ring has remained relatively small. We have previously reported the preparation of new tetracycle derivatives bearing a pyrazole[3] or a cyclopentane[4] ring fused to a phenothiazine moiety. We are now involved in the preparation of N-substituted tetracycles featuring a dioxole ring fused to the phenothiazine moiety.

Results and Discussion

To our knowledge, there are a few syntheses of dioxolo[4,5-*b*] phenothiazines,[5] which have been prepared in only four steps using Ullmann coupling of the *N*-aryl[1,3]benzodioxol-5-amines intermediates. Our synthetic approach is based on N-arylation of aromatic primary amines with different organolead or organobismuth reagents in the presence of a copper catalyst.[6] The resulting *N*-aryl[1,3]benzodioxol-5-amines were subjected to Bernthsen thionation [7] to yield the corresponding phenothiazines.

The first key step is the synthesis of the diarylamines 3a-d from [1,3]benzodioxol-5-amine 2 by copper catalysis. Ullmann reaction gave only poor yields of desired products.[8] A modified procedure[9] using organometallic reagents improved the yield of this N-arylation step. With *p*-tolyllead(IV) triacetate 1a and (4-methoxyphenyl)lead(IV) triacetate 1b[10] the corresponding coupling products *N*-(4-methylphenyl)[1,3]benzodioxol-5-amine 3a and *N*-(4-methoxyphenyl)[1,3]benzodioxol-5-amine 3b were obtained (Scheme 1). Similarly, the *N*-aryl[1,3]benzodioxol-5-amines 3c-d were prepared using the arylbismuth reagents 1c-d.[11]



x = 1; M = Pb; y = 3
1a: R=CH_3
1b: R=OCH_3

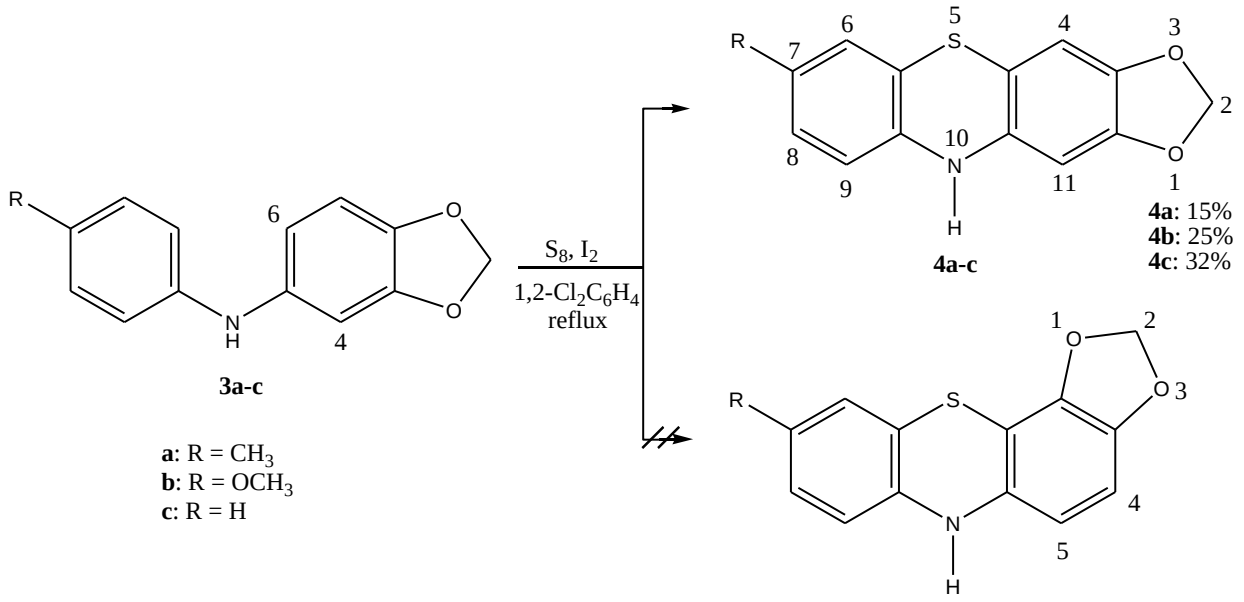
x = 3; M = Bi; y = 2
1e: R = H
1d: R = Cl

2

3a: R = CH_3, 40%
3b: R = OCH_3, 66%
3c: R = H, 54%
3d: R = Cl, 41%

Scheme 1

Subsequently, Bernthsen thionation [12] of diarylamines 3a-d with sulfur and iodine in *o*-dichlorobenzene brought about conversion into phenothiazine derivatives. Usually, this cyclization reaction gives rise to mixtures of isomers owing to two possible cyclization sites in the [1,3]benzodioxol moiety; thus, cyclization of compounds 3 is expected togive the linear [*b*]fused phenothiazine isomer (cyclization at position 6) and the angular [*a*]fused isomer (cyclization at position 4) (Scheme 2). When applied to compounds 3a-c, the thionation reaction turned out to be regioselective and led to single isomers, the linear dioxolo[4,5-*b*]phenothiazines 4a-c. Under the same conditions the reaction of the chloro derivative 3d was unsuccessful, leading to many side products of polymerization.

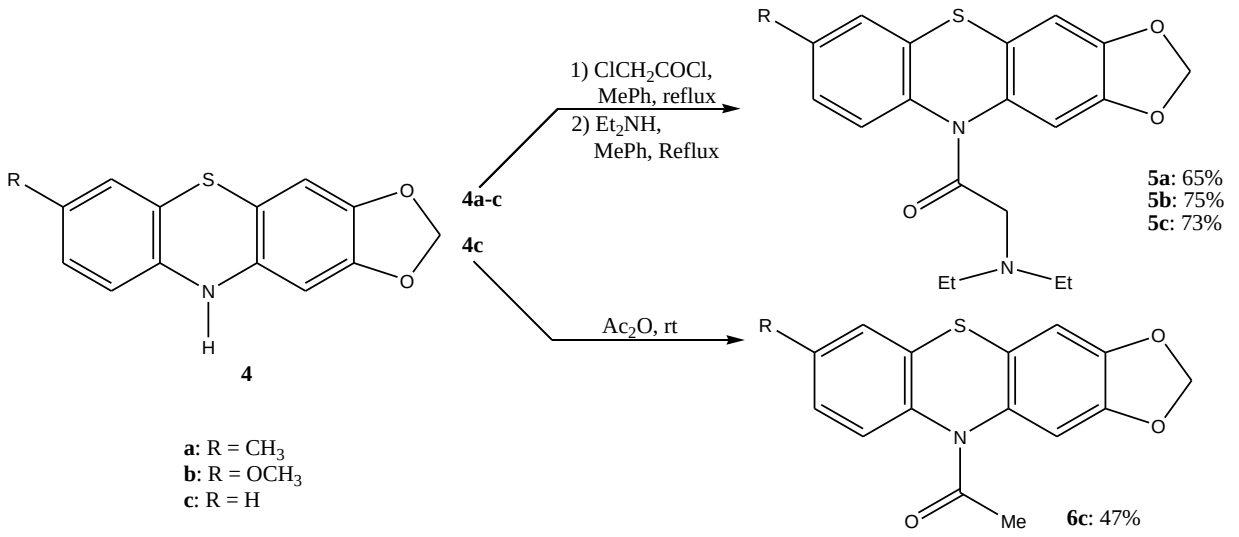


a: R = CH_3
b: R = OCH_3
c: R = H

Scheme 2

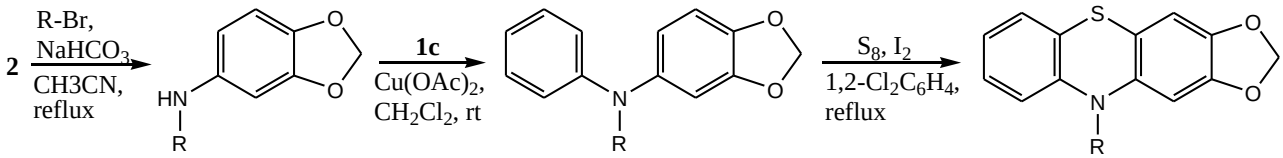
The assignment of the linearly fused tetracyclic structure was unambiguously supported by the ^{1}H NMR spectra, in particular, by the evaluation of the multiplet pattern of the C-ring proton signals: In the case of [*b*] fusion each 4-H and 11-H are expected to resonate as singlets, whereas in the case of [*a*] fusion, two doublets (AB quartet) would be expected for 4-H and 5-H (Scheme 2). In fact, the former pattern was observed, for example the two singlets at δ 6.43 and 6.61 prove the linear fused structure of 10*H*-[1,3]dioxolo[4,5-*b*]phenothiazine 4c.

The next step involved the conversion of the phenothiazines 4 into N-acyl and N-alkylaminoalkyl derivatives; usually, the preparation of the latter can be achieved with phase transfer catalysis and provides good results when applied to phenothiazine derivatives,[13] but did not work with tetracycles 4. Acylation of 4a-c with chloroacetylchloride, followed by condensation with diethylamine furnished the corresponding *N*-(2-diethylaminoacetyl) derivatives 5a-c (Scheme 3). Acetic anhydride converted 4c into 10-acetyl-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazine 6c.



Scheme 3

Previously described preparative procedures for direct N-amino alkylation of dioxolophenothiazines[5a,b] using sodium amide in xylene or sodium hydride in DMSO and *N*,*N*-dimethylaminoalkyl halides proved not successful and no recovered material was obtained. We also attempted direct N-alkylation of the *N*-aryl[1,3]benzodioxol-5-amines 3a-d before phenothiazine cyclization but the desired products were not obtained. Therefore, we changed the strategy: In the first step, the aromatic amine 2 was mono-alkylated with different alkyl halides in the presence of sodium hydrogen carbonate in acetonitrile.[14] 1-Bromobutane and 1-bromo-3-methylbutane gave *N*-butyl- and *N*-isopentyl[1,3]benzodioxol-5-amines 7a and 7b, respectively. The amines 7c and 7d were prepared in the same way. Subsequently, the reaction of *N*-alkyl[1,3]benzodioxol-5-amines 7a-d with triphenylbismuth(V) diacetate 1c provided the corresponding *N*-alkyl-*N*-phenyl[1,3]benzodioxol-5-amines 8a-d (Scheme 4).



Scheme 4

Under Bernthsen's condition only two arylamines, 8a and 8b were cyclized to linear fused tetracyclic products, 9a and 9b. By contrast, the arylamines, 8c and 8d only led to degradation products.

Conclusions

In conclusion, this report describes the preparation of a new class of tetracyclic heterocycles, *N*-acyl- and *N*-alkyl-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazines, employing organometalic reagents for N-arylation and Bernthsen thionation condition for phenothiazine ring closure. Currently, further studies are in progress to explore the scope of this approach for the synthesis of other heterocycles.

Experimental Section

General Procedures. ^{1}H and ^{13}C NMR spectra were measured on a BRUKER AC 400 MHz spectrometer. Chemical shifts were recorded as units relative to tetramethylsilane as the internal standard. Separations by chromatography were performed on silica gel (Merck, 70 -230 mesh). 4-Tolyllead(IV) triacetate 1a, 4-methoxyphenyllead(IV) triacetate 1b, triphenylbismuth(V) diacetate 1c and tris(4-chlorophenyl)bismuth(V) diacetate 1d were prepared according to reported procedures.[10,11] [1,3]benzodioxol-5-amine 2 was commercially available (JANSSEN) and was used as received.

N-(4-Methylphenyl)[1,3]benzodioxol-5-amine (3a). To a solution of [1,3]benzodioxol-5-amine 2 (1g, 7.3 mmol) in dry CH_2Cl_2 (40 mL) at rt were slowly added *p*-tolyllead(IV) triacetate 1a (3.8 g, 8 mmol) and copper(II) acetate (0.13 g, 0.7 mmol). The mixture was stirred at rt for 4 h . Next, CH_2Cl_2 (20mL) was added to the solution, and the resulting mixture was filtered. The insoluble part was washed with CH_2Cl_2 (2 x 20 mL), and the organic layers were dried and evaporated to give a crude reaction product, which was purified by chromatography on silica gel with CH_2Cl_2 as the eluant. A white powder 3a was obtained (0.66 g, 40%), mp 102 ^{o}C. ^{1}H-NMR (DMSO-d_6): δ 2.20 (s, CH_3), 5.92 (s, 2H), 6.48 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.62 (d, *J* = 2.2 Hz, 1H), 6.77 (d, *J* = 8.3 Hz, 1H), 6.86 (d, *J* = 8.1 Hz, 2H), 6.99 (d, *J* = 8.1 Hz, 2H), 7.74 (s, NH); ^{13}C-NMR (DMSO-d_6): δ 20.29, 99.97, 100.65, 108.57, 109.60, 116.35, 127.83, 129.61, 138.71, 140.80, 141.98, 147.75. Anal. Calcd. for $C_{14}H_{13}NO_2$: C, 73.99; H, 5.76; N, 6.16. Found: C, 74.23; H, 5.37; N, 5.90.

***N*-(4-Methoxyphenyl)[1,3]benzodioxol-5-amine (3b).** As described above, 2 (1g, 7.3 mmol) and (4-methoxyphenyl)lead(IV) triacetate 1b (3.93 g, 8 mmol) gave orange needles of 3b (1.2 g, 66%), mp 81 ^{o}C. ^{1}H-NMR (DMSO-d_6): δ 3.69 (s, OCH_3), 5.90 (s, 2H), 6.35 (dd, *J* = 8.1, 2.2 Hz, 1H), 6.52 (d, *J* = 2.2 Hz, 1H), 6.69 (d, *J* = 8.2 Hz, 1H), 6.86 (d, *J* = 8.9 Hz, 2H), 6.99 (d, *J* = 8.9

Hz, 2H), 7.60 (s, NH); ^{13}C-NMR (DMSO-d_6) δ 55.17, 98.66, 100.45, 108.13, 108.50, 114.73, 119.02, 137.38, 139.92, 140.12, 147.71, 153.24. Anal. Calcd. for $C_{14}H_{13}NO_3$: C, 69.12; H, 5.39; N, 5.76. Found: C, 69.51; H, 5.74; N, 5.92.

***N*-Phenyl[1,3]benzodioxol-5-amine (3c).** As described above, 2 (1g, 7.3 mmol) and triphenylbismuth(V) diacetate 1c (1.5 g, 2.7 mmol) gave 3c (0.84 g, 54%), mp 83 ºC. ^{1}H-NMR ($CDCl_3$): δ 5.92 (s, 2H), 6.54 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.69 (d, *J* = 2.2 Hz, 1H), 6.73 (d, *J* = 8.2 Hz, 1H), 6.85 (m, 1H), 6.92 (m, 2H), 7.22 (m, 2H); ^{13}C-NMR ($CDCl_3$): δ 101.14, 102.60, 108.62, 113.00, 116.27, 120.06, 129.39, 137.31, 142.92, 144.70, 148.26. Anal. Calcd. for $C_{13}H_{11}NO_2$: C, 73.22; H, 5.20; N, 6.57. Found: C, 73.30; H, 4.95; N, 6.82.

N-(4-Chlorophenyl)[1,3]benzodioxol-5-amine (3d). As described above, 2 (1g, 7.3 mmol) and tris(4-chlorophenyl)bismuth(V) diacetate 1d (1.8 g, 2.7 mmol) gave a white powder 3d (0.27 g, 41%), mp 78 ºC. ^{1}H-NMR (DMSO-d_6): δ 5.96 (s, 2H), 6.54 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.68 (dd, *J* = 8.2, 2.2 Hz, 1H), 6.82 (d, *J* = 8.3 Hz, 1H), 6.92 (d, *J* = 8.2 Hz, 2H), 7.19 (d, *J* = 8.8 Hz, 2H), 8.05 (s, NH); ^{13}C-NMR (DMSO-d_6): δ 100.90, 101.49, 108.64, 111.70, 116.54, 121.69, 128.96, 137.13, 141.87, 143.96, 147.86. Anal. Calcd. for $C_{13}H_{10}NO_2Cl$: C, 63.04; H, 4.07; N, 5.66. Found: C, 63.30; H, 4.35; N, 5.96.

7-Methyl-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazine (4a). A mixture of *N*-(4-methylphenyl)[1,3]benzodioxol-5-amine 3a (0.5 g, 2.2 mmol), sulphur (0.15 g, 4.6 mmol), and one iodine crystal was refluxed under nitrogen in dry *o*-dichlorobenzene (4 mL) during 6 h. The mixture was extracted with Et_2O (15 mL), filtered and concentrated. The resulting oil was chromatographed on silica gel with toluene to elute first the solvent (*o*-dichlorobenzene), and next a red powder 4a (80 mg, 15%), mp 184 ºC. ^{1}H-NMR (DMSO-d_6): δ 2.13 (s, CH_3), 5.90 (s, 2H), 6.40 (s, 1H), 6.57 (d, *J* = 8.0 Hz, 1H), 6.60 (s, 1H), 6.75 (br s, 1H), 6.80 (br d, *J* = 7.9 Hz, 1H), 8.28 (s, NH); ^{13}C-NMR (DMSO-d_6): δ 20.03, 96.95, 101.06, 106.55, 106.65, 114.19, 116.67, 126.50, 128.01, 130.75, 137.80, 140.49, 142.30, 147.03, Anal. Calcd. for $C_{14}H_{11}NO_2S$: C, 65.35; H, 4.31; N, 5.44. Found: C, 65.51; H, 4.78; N, 5.63.

7-Methoxy-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazine (4b). As described above, *N*-(4-methoxyphenyl)[1,3]benzodioxol-5-amine 3b (0.5 g, 2 mmol) gave after chromatography with ethyl acetate as eluant a yellow powder 4b (140 mg, 25%), mp 186 ºC. ^{1}H-NMR (DMSO-d_6): δ 3.65 (s, OCH_3), 5.90 (s, 2H), 6.39 (s, 1H), 6.60 (m, 2H), 6.61 (s, 1H), 6.62 (br s, 1H), 8.19 (s, NH), ^{13}C-NMR (DMSO-*d6*): δ 55.47, 96.87, 101.04, 106.21, 106.51, 111.58, 113.21, 114.95, 118.04, 136.51, 138.31, 142.17, 147.10, 154.69. Anal. Calcd. for $C_{14}H_{11}NO_3S$: C, 61.52; H, 4.06; N, 5.12. Found: C, 61.87; H, 3.81; N, 5.30.

10*H*-[1,3]Dioxolo[4,5-*b*]phenothiazine (4c). As described above, *N*-phenyl[1,3]benzodioxol-5-amine 3c (0.5 g, 2.3 mmol), sulphur (0.15 g, 4.6 mmol) gave after chromatography with toluene as eluant a white powder 4c (180 mg, 32%), mp 202 ºC. ^{1}H-NMR (DMSO-d_6): δ 5.91 (s, 2H), 6.43 (s, 1H), 6.61 (s, 1H), 6.68 (dd, *J* = 7.9, 1.0 Hz, 1H), 6.76 (td, *J* = 7.6, 1.1 Hz, 1H), 6.92 (dd, *J* = 7.6, 1.0 Hz, 1H), 6.99 (td, *J* = 7.7, 1.1 Hz, 1H), 8.42 (s, NH). ^{13}C-NMR (DMSO-d_6): δ 97.09,101.11, 106.55, 106.73, 114.35, 116.79, 121.83, 126.27, 127.59, 137.48, 142.54, 143.03,

147.11. Anal. Calcd. for $C_{13}H_9NO_2S$: C, 64.18; H, 3.73; N, 5.76. Found: C, 64.51; H, 4.02; N, 5.93.

2-Diethylamino-1-(7-methyl-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazin-10-yl)ethan-1-one (5a). To a solution of 7-methyl-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazine 4a (0.18 g, 0.7 mmol) and toluene (7 mL) was added chloroacetyl chloride (5.7 mg, 0.5 mmol), and the mixture was kept at 35 ºC under stirring during 45 min. The solution was concentrated, and to the residual viscous oil a solution of *N*,*N*-diethylamine (2 mL) in toluene (4 mL) was added. The solution was refluxed 2 h under stirring and evaporated to yield a brown oil (170 mg, 65%). ^{1}H-NMR (DMSO-d_6): δ 0.92 (t, *J* = 7.1 Hz, 6H), 2.32 (s, CH_3), 2.65 (q, *J* = 7.1 Hz, 4H), 3.40 (s, 2H), 6.07 (br s, 2H), 7.08 (s, 1H), 7.18 (br d, *J* = 8.1 Hz, 1H), 7.24 (s, 1H), 7.34 (br s, 1H), 7.48 (d, *J* = 8.1 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 11.38, 20.44, 47.50, 54.10, 102.24, 107.36, 108.18, 124.74, 126.65, 127.93, 127.93, 132.47, 132.76, 136.16, 136.79, 146.27, 147.12, 168.18. Anal. Calcd. for $C_{20}H_{22}N_2O_3S$: C, 64.84; H, 5.99; N, 7.56. Found: C, 65.03; H, 5.74; N, 7.80.

2-Diethylamino-1-(7-methoxy-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazin-10-yl)ethan-1-one (5b). As described above, from 4b (0.18 g, 0.7 mmol) after work up a brown oil 5b (200 mg, 75%) was obtained. ^{1}H-NMR (DMSO-d_6): δ 0.80 (t, *J* = 7.1 Hz, 6H), 2.44 (q, *J* = 7.1 Hz, 4H), 3.31 (s, 2H), 3.76 (s, OCH_3), 6.08 (br s, 2H), 6.91 (dd, *J* = 8.7, 2.6 Hz, 1H), 7.06 (d, *J* = 2.4 Hz, 1H), 7.09 (s, 1H), 7.25 (s, 1H), 7.46 (d, *J* = 8.7 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 12.10, 46.88, 54.65, 55.73, 102.21, 107.36, 108.19, 112.35, 113.21, 124.68, 127.83, 131.83, 132.48, 133.61, 146.15, 147.10, 157.38, 169.42. Anal. Calcd. for $C_{20}H_{22}N_2O_4S$: C, 62.16; H, 5.74; N, 7.25. Found: C, 62.47; H, 5.85; N, 7.41.

2-Diethylamino-1-(10*H*-[1,3]dioxolo[4,5-*b*]phenothiazin-10-yl)ethan-1-one (5c). As described above, 4c (0.1 g, 0.7 mmol) gave a red oil 5c (180 mg, 73%). ^{1}H -NMR (DMSO-d_6): δ 0.81 (t, *J* = 7.0 Hz, 6H), 2.45 (br q, *J* = 6.6 Hz, 4H), 3.36 (s, 2H), 6.05 (s, 2H), 7.13 (s, 1H), 7.28 (t, *J* = 7.5 Hz, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.37 (td, *J* = 7.5, 1.2 Hz, 1H), 7.53 (dd, *J* = 7.7, 1.0 Hz, 1H), 7.59 (d, *J* = 7.7 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 11.95, 46.83, 54.57, 102.23, 107.35, 108.28, 124.60, 126.85, 127.21, 127.21, 127.72, 132.50, 132.85, 138.92, 146.12, 147.09, 169.08. Anal. Calcd. for $C_{19}H_{20}N_2O_3S$: C, 64.02; H, 5.66; N, 7.86. Found: C, 64.29; H, 5.91; N, 8.01.

10-Acetyl-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazine (6c). A mixture of 4c (0.2 g, 0.8 mmol) in acetic anhydride (5mL) was stirred at rt during 8 h . The solution was filtrated and evaporated to yield a red oil 6c (0.107, 47%) was left. ^{1}H-NMR (DMSO-d_6): δ 2.11 (s, CH_3), 6.06 (s, 2H), 7.13 (s, 1H), 7.26 (br s, 1H), 7.29 (t, *J* = 7.5 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 1H), 7.54 (d, *J* = 7.5 Hz, 1H), 7.56 (m, 1H); ^{13}C-NMR (DMSO-d_6) δ 21.31, 102.24, 107.27, 108.47, 124.55, 126.68, 127.24, 127.38, 127.70, 132.74, 132.74, 139.08, 146.14, 147.10, 172.23. Anal. Calcd. for $C_{15}H_{11}NO_3S$: C, 63.14; H, 3.89; N, 4.91. Found: C, 63.22; H, 4.02; N, 4.96.

***N*-Butyl[1,3]benzodioxol-5-amine (7a).** To a solution of 2 (2g, 14.6 mmol) in dry acetonitrile (30 mL) was added 1-bromobutane (2.2 g, 16 mmol) and $NaHCO_3$ (1.3 g, 15.4 mmol). The solution was refluxed under stirring during 8 h , neutralised with HCl (2*N*, 7 mL) and methylene chloride (20 mL) was added. The organic phase was separated, washed twice with water (40 mL) and evaporated. The residue was dissolved in MeOH (20 mL), acidified with H_2SO_4 (3 mL),

filtrated, and the filtrate was concentrated to 5 mL volume. The mixture was neutralized with $NaHCO_3$ (1.5 g, 17.9 mmol) and dissolved in methylene chloride (20 mL). The organic phase was separated, washed twice with water (20 mL) and evaporated to give a yellow oil 7a (1.6 g, 58%). ^{1}H-NMR (DMSO-d_6): δ 0.90 (t, J = 7.3 Hz, 3H), 1.40 (m, 2H), 1.49 (m, 2H), 2.90 (t, J = 7.0 Hz, 2H), 5.20 (br s, NH), 5.81 (s, 2H), 5.95 (dd, J = 8.3, 2.3 Hz, 1H), 6.24 (d, J = 2.3 Hz, 1H), 6.63 (d, J = 8.3 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 13.89, 19.89, 30.95, 43.44, 94.93, 99.89, 102.96, 108.46, 137.73, 145.16, 147.78. Anal. Calcd. for $C_{11}H_{15}NO_2$: C, 68.37; H, 7.82; N, 7.25. Found: C, 68.15; H, 7.94; N, 6.98.

***N*-Isopentyl[1,3]benzodioxol-5-amine (7b).** As described above, 1-bromo-3-methylbutane (2.4 g, 16 mmol) and $NaHCO_3$ (1.3 g, 15.4 mmol) gave a yellow oil 7b (1.8 g, 61 %). ^{1}H-NMR (DMSO-d_6): δ 0.89 (d, J = 6.6 Hz, 6H), 1.66 (m, 1H), 1.42 (m, 2H), 2.98 (t, J = 7.3 Hz, 2H), 5.86 (s, 2H), 6.14 (dd, J = 8.4, 1.5 Hz, 1H), 6.40 (d, J = 1.6 Hz, 1H), 6.70 (d, J = 8.4 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 22.34, 25.27, 37.00, 43.23, 96.49, 100.21, 105.35, 108.38, 139.47, 142.27, 147.73. Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.17; H, 8.74; N, 6.36.

***N*-Isopropyl[1,3]benzodioxol-5-amine (7c).** As described above, 2-bromopropane (1.97 g, 16 mmol) and $NaHCO_3$ (2.2 g, 26.3 mmol) gave an orange oil 7c (1.2 g, 47%). ^{1}H-NMR (DMSO-d_6): δ 1.08 (d, J = 6.3 Hz, 6H), 3.42 (hept, J = 6.3 Hz, 1H), 4.98 (s, NH), 5.83 (s, 2H), 5.96 (dd, J = 8.4, 2.3 Hz, 1H), 6.24 (d, J = 2.2 Hz, 1H), 6.63 (d, J = 8.3 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 22.56, 43.81, 95.94, 99.92, 103.86, 108.58, 137.65, 144.17, 147.85. Anal. Calcd. for $C_{10}H_{13}NO_2$: C, 67.02; H, 7.31; N, 7.82. Found: C, 67.25; H, 7.48; N, 8.19.

***N*-(1-Methylbutyl)[1,3]benzodioxol-5-amine (7d).** As described above, 2-bromopentane (2.4 g, 16 mmol) and $NaHCO_3$ (1.3 g, 15.4 mmol) gave a yellow oil 7d (1.6 g, 52 %). ^{1}H -NMR (DMSO-d_6): δ 0.87 (t, J = 7.3 Hz, 3H), 1.04 (d, J = 6.3 Hz, 3H), 1.33 (m, 2H), 1.45 (m, 2H), 3.27 (m, 1H), 5.08 (br s, NH), 5.81 (s, 2H), 5.97 (dd, J = 8.2, 2.1 Hz, 1H), 6.24 (d, J = 2.1 Hz, 1H), 6.62 (d, J = 8.3 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 14.15, 18.95, 20.39, 38.62, 47.96, 95.47, 99.95, 103.78, 108.62, 137.65, 144.23, 147.87. Anal. Calcd. for $C_{12}H_{17}NO_2$: C, 69.54; H, 8.27; N, 6.76. Found: C, 69.81; H, 7.98; N, 6.90.

***N*-Butyl-*N*-phenyl[1,3]benzodioxol-5-amine (8a).** To a solution of 7a (1g, 5.2 mmol) in dry CH_2Cl_2 (30 mL) at rt were slowly added triphenylbismuth(V) diacetate 1c (1 g, 1.8 mmol) and copper(II) acetate (0.09 g, 0.5 mmol). The mixture was stirred at rt during 4 h. Next, CH_2Cl_2 (20mL) was added, and the resulting mixture was filtered. The insoluble part was washed with CH_2Cl_2 (2 x 20 mL), and the organic layers were dried and evaporated to give a crude reaction product, which was purified by chromatography on silica gel with toluene as the eluent. A yellow oil was recovered, yielding 0.30 g (22 %) of 8a. ^{1}H-NMR (DMSO-d_6): δ 0.87 (t, J = 7.4 Hz, 3H), 1.31 (m, 2H), 1.52 (m, 2H), 3.56 (t, J = 7.6 Hz, 2H), 6.01 (s, 2H), 6.56 (dd, J = 8.3, 2.2 Hz, 1H), 6.68 (d, J = 2.0 Hz, 1H), 6.69 (m, 2H), 6.70 (m, 1H), 6.89 (d, J = 8.3 Hz, 1H), 7.14 (m, 2H); ^{13}C-NMR (DMSO-$d6$): δ 13.86, 19.67, 29.18, 51.52, 101.21, 106.82, 108.75, 115.95, 118.10, 118.36, 129.89, 141.64, 143.82, 148.11, 148.66. Anal. Calcd. for $C_{17}H_{19}NO_2$: C, 75.81; H, 7.11; N, 5.20. Found: C, 76.03; H, 7.45; N, 5.47.

***N*-Isopentyl-*N*-phenyl[1,3]benzodioxol-5-amine (8b).** As described above, 7b (1g, 4.8 mmol) and triphenylbismuth(V) diacetate 1c (1.1 g, 1.9 mmol) gave an orange oil 8b (0.45 g, 33%). ^{1}H-NMR (DMSO-d_6): δ 0.88 (d, *J* = 6.6 Hz, 6H), 1.61 (m, 1H), 1.44 (td, *J* = 7.8, 6.7 Hz, 2H), 3.58 (t, *J* = 7.6 Hz, 2H), 6.02 (s, 2H), 6.56 (dd, *J* = 8.3, 2.2 Hz, 1H), 6.68 (m, 1H), 6.69 (d, *J* = 2.2 Hz, 1H), 6.71 (m, 2H), 6.90 (d, *J* = 8.2 Hz, 1H), 7.15 (m, 2H); ^{13}C-NMR (DMSO-d_6): δ 22.53, 25.64, 35.73, 50.19, 101.22, 106.84, 108.76, 115.82, 118.06, 118.40, 129.02, 141.59, 143.85, 148.11, 148.56. Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.51; H, 7.80; N, 5.12.

***N*-Isopropyl-*N*-phenyl-[1,3]benzo-dioxol-5-amine (8c).** As described above, 7c (1g, 5.6 mmol) and triphenylbismuth(V) diacetate 1c (1.2 g, 2.2 mmol) gave a pale yellow oil 8c (0.54 g, 38%).^{1}H-NMR (DMSO-d_6): δ 1.07 (d, *J* = 6.5 Hz, 6H), 4.24 (hept, *J* = 6.5 Hz, 1H), 6.05 (s, 2H), 6.50 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.54 (d, *J* = 8.1 Hz, 1H), 6.61 (d, *J* = 2.1 Hz, 1H), 6.65 (m, 1H), 6.94 (m, 2H), 7.11 (m, 2H); ^{13}C-NMR (DMSO-d_6): δ 20.75, 47.14, 101.43, 108.65, 110.53, 115.24, 117.30, 118.70, 128.96, 137.12, 145.21, 148.07, 148.65. Anal. Calcd. for $C_{16}H_{17}NO_2$: C, 75.27; H, 6.71; N, 5.49. Found: C, 75.53; H, 6.39; N, 5.79.

***N*-(1-Methylbutyl)-*N*-phenyl[1,3]benzodioxol-5-amine (8d).** As described above, 7d (1g, 4.8 mmol) and triphenylbismuth(V) diacetate 1c (1.1 g, 1.9 mmol) gave a brown oil 8d (0.20 g, 15%).^{1}H-NMR (DMSO-d_6): δ 0.88 (t, *J* = 7.2 Hz, 3H), 1.08 (d, *J* = 6.6 Hz, 3H), 1.22 (m, 2H), 1.36 (m, 2H), 4.06 (m, 1H), 6.02 (s, 2H), 6.50 (dd, *J* = 8.2, 2.1 Hz, 1H), 6.56 (m, 2H), 6.58 (d, *J* = 2.0 Hz, 1H), 6.65 (m, 1H), 6.92 (d, *J* = 8.2 Hz, 1H), 7.11 (m, 2H); ^{13}C-NMR (DMSO-d_6): δ 13.91, 18.45, 19.52, 37.02, 51.81, 101.20, 108.42, 109.84, 115.57, 117.35, 121.97, 128.76, 137.59, 144.79, 147.89, 148.74. Anal. Calcd. for $C_{18}H_{21}NO_2$: C, 76.29; H, 7.47; N, 4.94. Found: C, 76.34; H, 7.63; N, 5.22.

10-Butyl-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazine (9a). A solution of 8a (0.30 g, 1.1 mmol), sulphur (0.07 g, 2.2 mmol), and one iodine crystal was refluxed under nitrogen in dry *o*-dichlorobenzene (2 mL) during 8 h. The mixture was extracted with Et_2O (10 mL), filtered and concentrated. The resulting oil was chromatographed on silica gel with Et_2O to elute first the solvent (*o*-dichlorobenzene) followed by a viscous green oil 8a (0.07 g, 21%).^{1}H-NMR (DMSO-d_6): δ 0.89 (t, *J* = 7.4 Hz, 3H), 1.40 (m, 2H), 1.66 (m, 2H), 3.81 (t, *J* = 6.8 Hz, 2H), 5.95 (s, 2H), 6.72 (s, 1H), 6.73 (s, 1H), 6.92 (br t, *J* = 7.5 Hz, 1H), 6.98 (br d, *J* = 7.9 Hz, 1H), 7.12 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.18 (td, *J* = 7.8, 1.5 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 13.64, 19.44, 28.95, 46.70, 98.97, 101.46, 107.18, 114.58, 115.93, 122.36, 124.94, 127.01, 127.52, 140.17, 142.88, 145.84, 147.67. Anal. Calcd. for $C_{17}H_{17}NO_2S$: C, 68.20; H, 5.72; N, 4.68. Found: C, 68.33; H, 5.87; N, 4.49.

10-Isopentyl-10*H*-[1,3]dioxolo[4,5-*b*]phenothiazine (9b). A solution of 8b (0.45 g, 1.6 mmol), sulphur (0.1 g, 3.2 mmol) and one iodine crystal was refluxed under nitrogen in dry *o*-dichlorobenzene (3 mL) during 8 h. The mixture was extracted as described above and chromatographed to yield a red oil 9b (0.14 g, 28%). ^{1}H-NMR (DMSO-d_6): δ 0.89 (d, *J* = 6.3 Hz, 6H), 1.55 (q, *J* = 7.8, 6.7 Hz, 2H), 1.68 (m, 1H), 3.78 (t, *J* = 7.1 Hz, 2H), 5.90 (s, 2H), 6.53 (s, 1H), 6.66 (s, 1H), 6.92 (m, 1H), 6.98 (d, *J* = 8.2 Hz, 1H), 7.12 (dd, *J* = 7.6, 1.5 Hz, 1H), 7.18 (td,

J = 7.7, 1.5 Hz, 1H); ^{13}C-NMR (DMSO-d_6): δ 22.66, 26.31, 36.18, 46.12, 98.54, 101.50, 107.68, 115.56, 115.56, 122.45, 126.06, 127.31, 127.45, 140.62, 143.17, 146.30, 147.82. Anal. Calcd. for $C_{18}H_{19}NO_2S$: C, 68.98; H, 6.11; N, 4.47. Found: C, 69.18; H, 6.35; N, 4.24.

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