4-[10-(Methoxybenzyl)-9-anthryl]phenol derivatives
as new antitubercular agents#

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Dedicated to Dr. Nitya Anand on the occasion of his 80th birthday
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Abstract
A series of 4-[10-(methoxybenzyl)-9-anthryl]phenyloxyalkylamine derivatives was prepared by
aminoalkylation of 4-[10-(methoxybenzyl)-9-anthryl]phenols obtained by Friedel-Crafts reaction
of 9-anthryl(methoxyphenyl)methanols. The title compounds were tested against Mycobacterium
tuberculosis H37Rv and showed antitubercular activity in the range of 12.5–25 µg/mL.

Keywords: 9-Anthryl(methoxyphenyl)methanols, aminopropan-2-ols, Friedel-Crafts reaction, antitubercular agents

Introduction

Tuberculosis (TB) is a growing global health problem because of lack of proper therapeutic
agents for its remedy.1 There is another serious and alarming problem due to the resurgence of
TB especially for the synergy with global human immunodeficiency virus (HIV) and the
emergence of multi-drug-resistant (MDR) strains.2 Thus, there is an urgent need for developing
new anti-tubercular drugs which will effectively kill MDR strains, less toxic, shortened duration
of therapy, rapid mycobactericidal mechanism of action in the intracellular environment.

Halogen derivatives of benzo[h]chromene and benzo[a]anthracenes are known for antitumor,
antimicrobial and other biological activities.3 Benzophenone derivatives also possess
antimycobacterial activity.3 In our recent paper,4 we have described that diaryloxymethano-
phenanthrenes with basic amino substituents could serve as a lead for antitubercular agents. With
this knowledge at hand, we became interested in methoxybenzyl- and hydroxyphenyl-substituted
anthracene derivatives carrying a basic amino side chain and in studying the effect on the growth of *M. tuberculosis*. These compounds are sufficiently hydrophobic, a requirement for good antitubercular activity. Thus, we chose N-[2-[4-[10-(methoxybenzyl)-9-anthryl]phenoxy]alkyl]amines 8 as targets for developing antitubercular agents. The synthesis and biological evaluation of a series of compounds of the structural prototype 8 is the subject of this paper.

Retrosynthetic analysis of N-[2-[4-[10-(methoxybenzyl)-9-anthryl]phenoxy]alkyl]amines 8 requires 4-[10-(methoxybenzyl)-9-anthryl]phenols 5 as precursors obtainable by Friedel-Crafts alkylation of 9-anthryl(methoxyphenyl)methanols 4,5 which in turn, can be synthesized by the addition of bromoanisole-derived Grignard reagents 2 to anthracene-9-carbaldehyde 3 (Scheme 1).

![Scheme 1. Retrosynthesis of target compounds 8.](image)

**Results and Discussion**

**Chemistry**
The reaction of Grignard reagents 2a–c derived from bromoanisoles 1a–c with anthracene-9-carbaldehyde 3 furnished 9-anthryl(methoxyphenyl)methanols 4a–c in 60–75% yield (Scheme 2). Subsequent Friedel-Crafts alkylation of 9-anthryl(methoxyphenyl)methanols 4a–c with phenol in the presence of AlCl₃/SnCl₄ or conc. H₂SO₄ provided 4-[10-(methoxybenzyl)-9-anthryl]phenols 5a–c. In the case of the 4-methoxy-substituted compound 5c a sideproduct 4-[9-anthryl(4-methoxyphenyl)methyl] phenol 6c was isolated as well (Scheme 2).

Upon Lewis acid complexation or protonation of 4-[10-(methoxybenzyl)-9-anthryl]phenols 5a–c the formation of a cationic intermediate is presumed, which undergoes electrophilic substitution at phenol. The reaction of 9-anthryl(4-methoxyphenyl)methanol 4c with phenol in the presence of conc. H₂SO₄ is assumed to proceed via the cationic intermediate 7c as resembled by resonance structures such as 9-anthryl(4-methoxyphenyl)methyl cation and 1-(4-methoxybenzyldiene)-9,10-dihydroanthracen-9-yl cation (Scheme 3) giving rise to the formation of 4-[10-(4-methoxybenzyl)-9-anthryl]phenol 5c and 4-[9-anthryl(4-methoxyphenyl)methyl]phenol 6c as major and minor products, respectively.
Both isomers 5c and 6c were characterized by $^1$H NMR spectra: The methylene group of 5c gives rise to a singlet at $\delta$ 4.85 (2H), the $^1$H NMR spectrum of 6c exhibits two singlets (1H each) at $\delta$ 6.97 (methine proton) and $\delta$ 8.44 (10-H of the anthracene moiety). The mass spectra of both isomers are characteristic as well: 5c gives rise to a peak $m/z$ 283, assigned to the [10-(4-hydroxyphenyl)-9-anthryl]methyl cation, whereas the fragment ion $m/z$ 213 of 6c is attributed to the (4-hydroxyphenyl)(4-methoxyphenyl)methyl cation.

Scheme 2. Synthesis of 4-[10-(methoxybenzyl)-9-anthryl]phenols 5a−c via 9-anthryl(methoxyphenyl)methanols 4a−c, and formation of 4-[9-anthryl(4-methoxyphenyl)methyl]phenol 6c.

Scheme 3. Resonance structures of carbocation intermediate 7c; formation of phenols 5c and 6c.

The target as possible antitubercular agents were the aminoalkoxy derivatives 8. The reaction of 5a−c with different alkylamine hydrochlorides in the presence of K$_2$CO$_3$ and acetone led to the formation of compounds 8 in good yields (Scheme 4). By treatment of amines 8 with ethanolic hydrogen chloride the corresponding salts 8·HCl were prepared. The salts 8·HCl were tested and found active against M. tuberculosis with MIC in the range of 12.5–25 µg/mL (Table 1). Therefore, N-[4-[10-(methoxybenzyl)-9-anthryl]phenoxy]alkylamine derivatives were selected as active the pharmacophore, and further synthetic transformations were performed.
Table 1. *In vitro* antitubercular activity of 8·HCl and 10 against *M. tuberculosis* H$_{37}$R$_{v}$

<table>
<thead>
<tr>
<th>MIC [µg/mL]</th>
<th>Compound</th>
<th>Agar dilution Method</th>
<th>BACTEC Method</th>
<th>MABA Method</th>
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<td>8aa·HCl</td>
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<td>n.a.</td>
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<tr>
<td>8ab·HCl</td>
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<td>n.a.</td>
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<tr>
<td>8ac·HCl</td>
<td>25</td>
<td>12.5</td>
<td>12.5</td>
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<tr>
<td>8ad·HCl</td>
<td>25</td>
<td>n.d.</td>
<td>12.5</td>
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<tr>
<td>8bc·HCl</td>
<td>25</td>
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<td>12.5</td>
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<tr>
<td>8bd·HCl</td>
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<td>n.a.</td>
<td>n.a.</td>
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<tr>
<td>8ca·HCl</td>
<td>25</td>
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<td>12.5</td>
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<tr>
<td>8cb·HCl</td>
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<tr>
<td>8cc·HCl</td>
<td>25</td>
<td>n.d.</td>
<td>12.5</td>
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<tr>
<td>8cd·HCl</td>
<td>25</td>
<td>12.5</td>
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<td>10bb</td>
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<td>10cf</td>
<td>n.a.</td>
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n.a.: not active at 25 µg/mL; n.d.: not determined.

We were interested to study the effect of 3-amino-2-hydroxy-1-propoxy substituents attached to the [(methoxybenzyl)anthryl]phenyl pharmacophore. Towards this objective, phenols 5a–c were treated with epichlorohydrin in the presence of K₂CO₃ to furnish the epoxides 9a–c in good yields (58–87%). The epoxides 9a–c, in turn, reacting with commercially available amines afforded a variety of 1-aminopropan-2-ol derivatives 10 (Scheme 5).


Biology
The in vitro activity of the products against M. tuberculosis H₃₇Rv was determined by agar micro dilution technique, standard BACTEC radiometric growth assay and micro almar blue assay (MABA). These compounds were tested at different concentrations to evaluate the antitubercular activity of products 8·HCl and 10 (Table 1).

The 10-(methoxybenzyl)-substituted anthracenes were synthesized and tested to study the effect of 2-, 3-, and 4-methoxy substituents on the antitubercular activity. It is noteworthy that all anthracene derivatives 8aa·HCl, 8ab·HCl and 10aa–ad with o-methoxybenzyl groups showed no antitubercular activity at 25µg/mL, whereas the m- and p-methoxybenzyl-substituted derivatives except 8bd·HCl, 10bb, 10be, 10cd, and 10cf showed activity in the range of 12.5–25 µg/mL. This is possibly due to better exposed m- and p-methoxy substituents on the anthracene skeleton. Thus, anthracenes with p- and m-methoxybenzyl groups at position 10 and alkylaminoalkoxyphenyl substituents attached to position 9 exhibit a better antitubercular activity in vitro.

Summary
The analysis of in vitro data for the compounds 8·HCl and 10 clearly suggests that these classes of compounds are indeed antitubercular. We are reporting for the first time that substituted
anthracenes with methoxybenzyl at 9-position and hydroxyphenyl with alkylaminohydrochloride chains at 10-position might be a suitable pharmacophore for developing antitubercular agents. A rational and logical design of a compound retaining the antitubercular activity with lower value of MIC may be a favorable molecule. Syntheses of the compounds and their biological evaluation towards this direction are currently underway.

**Experimental Section**

**General Procedures.** All the reactions were monitored by thin layer chromatography over silica gel coated TLC plates. The spots on TLC were visualized by spraying the plates with 2% CeSO$_4$ in 2 N H$_2$SO$_4$ and warming on a hot plate or in an oven at about 100 °C. For column chromatography silica gel 60–120 mesh was used. IR spectra were recorded on Perkin Elmer 881 or FT IR 820/PC instrument. Electron impact mass spectra (EI-MS) were recorded on JEOL (Japan) /D-300 instrument, and FAB mass spectra were recorded on JEOL SX 102/DA-6000 mass using Argon /Xenon (6 KV, 10 MA) as the FAB gas. $^1$H and $^{13}$C NMR spectra were recorded on a Bruker Advance DPX 200 MHz spectrometer using TMS as internal reference. Elemental analyses were carried out on a Carlo ERBA-1108 analyzer. Commercially available grades of organic solvents of adequate purity were used. Acetone after heating at reflux with KMnO$_4$ for 4 h was distilled and stored in a bottle over dry K$_2$CO$_3$. Benzene was refluxed over freshly cut sodium metal pieces and kept over molecular 3 Å sieves. Tetrahydrofuran is dried over calcium sulphate and refluxed over lithium aluminum hydride; peroxides were removed by passage through a column of alumina, followed by distillation and storage over molecular sieves 3Å.

9-Anthryl(2-methoxyphenyl)methanol (4a). To a solution of 2-bromoanisol 1a (8.98 mL, 72.63 mmol) in dry THF (20 mL) was added magnesium (1.97 g, 82.28 mmol), and the mixture was stirred at room temperature for 2h. To the Grignard reagent 2a thus formed was added anthracene-9-carbaldehyde 3 (5 g, 24.2 mmol) in THF (25 mL), and the reaction mixture was stirred for 3–4 h. After quenching with saturated aq. NH$_4$Cl (ca. 20 mL) THF was removed in vacuo. The mixture was extracted three times with ethyl acetate, the extract was washed with brine and dried over sodium sulfate. After concentration of the product solution the residue was chromatographed on silica gel with 10% ethyl acetate in hexane ($R_f$ = 0.7) furnishing 4a (4.5 g, 60%) as a yellow semi solid. IR (neat): 3262, 1593, 1456, 1237, 1035 cm$^{-1}$. $^1$H NMR (200 MHz, CDCl$_3$): $\delta$ 8.43 (1H, s), 8.42 (2H, d, $J$ = 8.6 Hz), 7.94 (2H, d, $J$ = 8.4 Hz), 7.39–7.30 (7H, m), 6.86 (1H, t, $J$ = 7 Hz), 6.63 (1H, d, $J$ = 7 Hz), 6.57 (1H, d, $J$ = 7 Hz), 4.08 (1H, s), 3.81 (3H, s). $^{13}$C NMR (50 MHz, CDCl$_3$): $\delta$ 158.0, 132.3, 131.4, 130.9, 129.6, 128.9, 126.5, 125.9, 125.3, 121.1, 111.0, 69.4, 55.9. MS (FAB): $m/z$ (%) 314 (100) [M$^+$], 297 (90) [M –OH]. Anal. Calcd for C$_{22}$H$_{18}$O$_2$ (314.38): C, 84.99; H, 5.80. Found: C, 84.99; H, 5.80.

9-Anthryl(3-methoxyphenyl)methanol (4b). As described for 4a, 3-bromoanisol 1b (9.19 mL,
72.5 mmol) in dry THF (25 mL), magnesium (1.97 g, 82.0 mmol) and anthracene-9-carbaldehyde 3 (5 g, 24.2 mmol) in THF (25 mL) furnished 4b (5.75 g, 75%) as a yellow semi solid, Rf = 0.7 (10% ethyl acetate/hexane). IR (neat): ν ~ 3409, 1599, 1488, 1256, 1045, 760 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.46 (1H, s), 8.34 (2H, d, J = 8.3 Hz), 8.01 (2H, d, J = 8.2 Hz), 7.46–7.35 (4H, m), 7.17 (1H, t, J = 7.8 Hz), 7.06 (1H, s), 6.86 (1H, d, J = 7.6 Hz), 6.75 (1H, d, J = 7.6 Hz), 3.72 (3H, s), 2.62 (1H, d, J = 3.8 Hz). MS (FAB): m/z (%) 314 (100) [M⁺], 297 (90) [M – OH]. Anal. Calcd for C₂₂H₁₈O₂ (314.38): C, 84.05; H, 5.77. Found: C, 84.19; H, 5.81.

9-Anthryl(4-methoxyphenyl)methanol (4c). As described for 4a, 4-bromoanisol 1c (16.15 g, 0.086 mol) in dry THF (20 mL), magnesium (2.06 g, 0.086 mol) and anthracene-9-carbaldehyde 3 (5.94 g, 0.028 mol) in THF (25 mL) furnished 4c (6.0 g, 66%) as a yellow semisolid. Rf = 0.7 (10% ethyl acetate/hexane). IR (neat): ν ~ 3510, 2362, 1604, 1507, 1242, 1169, 732 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.46 (1H, s), 8.36 (2H, d, J = 9 Hz), 8.03 (1H, d, J = 7.8 Hz), 8.01 (1H, d, J = 9 Hz), 7.47–7.34 (5H, m), 7.27 (1H, d, J = 9 Hz), 6.79 (2H, d, J = 10 Hz), 3.74 (3H, s), 2.64 (1H, d, J = 5.4 Hz). MS (EI): m/z (%) 314 (100) [M⁺], 297 (90) [M – OH], 107 (20) [OCH₃C₆H₅]. Anal. Calcd for C₂₂H₁₈O₂ (314.38): C, 84.05; H, 5.77. Found: C, 84.22; H, 5.78.

4-[10-(2-Methoxybenzyl)-9-anthryl]phenol (5a). To a solution of carbinol 4a (3.0 g, 9.55 mmol) and phenol (3.15 mL, 38.22 mmol) in dry benzene (40 mL) was added a catalytic amount of conc. H₂SO₄, and the mixture was heated at 80 °C for 1h. After cooling, the reaction mixture was neutralized with saturated aq. NaHCO₃ and extracted with ethyl acetate. The concentrated extract was subjected to column chromatography on silica gel and elution with 15% ethyl acetate in hexane (Rf = 0.6) furnishing 5a (2.6 g, 69%) as a white solid; mp 115 °C (dichloromethane). IR (KBr): ν ~ 3441, 1599, 1490, 1232 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.16 (2H, d, J = 8.2 Hz), 7.74 (2H, d, J = 7.6 Hz), 7.41–7.24 (6H, m), 7.23 (1H, d, J = 8Hz), 7.05 (2H, d, J = 8Hz), 6.90 (1H, d, J = 8 Hz), 6.46 (1H, d, J = 7 Hz), 5.20 (1H, bs), 4.98 (2H, s), 4.06 (3H, s). MS (FAB): m/z (%) 390 (100) [M⁺], 297 (60) [M – C₆H₄OH], 121 (30) [OCH₃C₆H₄CH₂]. Anal. Calcd for C₂₈H₂₂O₂ (390.47): C, 86.13; H, 5.68. Found: C, 86.51; H 5.91.

4-[10-(3-Methoxybenzyl)-9-anthryl]phenol (5b). As described for 5a, 4b (3.83 g, 12.19 mmol) and phenol (4.02 g, 48.79 mmol) furnished 5b (2.69 g, 56%) as white solid; mp 108 °C (dichloromethane), Rf = 0.6 (15% ethyl acetate/hexane). IR (KBr): ν ~ 3414, 1601, 1440, 1379, 1253, 1141, 1037, 757 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.23 (2H, d, J = 8.6 Hz), 7.77 (2H, d, J = 8 Hz), 6.90 (1H, d, J = 8 Hz), 6.61 (1H, t, J = 7 Hz), 6.46 (1H, d, J = 7 Hz), 5.20 (1H, bs), 4.98 (2H, s), 4.06 (3H, s). MS (FAB): m/z (%) 390 (100) [M⁺], 283 (40) [M – OCH₃C₆H₅]. Anal. Calcd for C₂₈H₂₂O₂ (390.47): C, 87.22; H, 5.89.

4-[10-(4-Methoxybenzyl)-9-anthryl]phenol (5c). As described for 5a, 4c (2.85 g, 9.07 mmol) and phenol (1.28 g, 18.61 mmol) furnished 5c (1.6 g, 55%) as a white solid; mp 194 °C (dichloromethane); Rf = 0.6 (15% ethyl acetate/hexane). ¹H NMR (200 MHz, CDCl₃): δ 9.04 (1H, s), 8.15 (2H, d, J = 8.7 Hz), 7.72 (2H, d, J = 8.7 Hz), 7.3 (2H, t, J = 6.9 Hz), 7.22 (2H, d, J = 8 Hz).
= 8.1 Hz), 7.16 (2H, d, J = 8.4 Hz), 7.02 (2H, d, J = 8.4 Hz), 6.98 (2H, d, J = 8.4 Hz), 6.64 (2H, d, J = 8.4 Hz), 4.85 (2H, s), 3.58 (3H, s). 13C NMR (50 MHz, CDCl3): δ 157.2, 156.2, 136.6, 132.4, 131.8, 130.0, 129.5, 129.1, 128.5, 127.4, 125.0, 124.2, 124.1, 115.0, 113.3, 54.6, 32.2. MS (FAB): m/z (%) 390 (100) [M +], 297 (10) [M –C₆H₄OH], 283 (30) [M –OCH₃C₆H₄].


4-[9-Anthryl(4-methoxyphenyl)methyl]phenol (6c). To a solution of carbinol 4a (2.85 g, 9.07 mmol) and phenol (1.28 g, 13.61 mmol) in dry benzene (40 mL) was added a catalytic amount of conc. H₂SO₄, and the mixture was heated at 80 °C for 1h. After cooling, the reaction mixture was neutralized with saturated aq. NaHCO₃ and extracted with ethyl acetate. The concentrated extract was subjected to column chromatography on silica gel and elution with 15% ethyl acetate in hexane furnishing 5c (Rₓ = 0.6) and 6c (Rₓ = 0.5) as a brown solid (100 mg, 5%); mp 78 °C (dichloromethane).

IR (KBr): ν ~ 3431, 1605, 1507, 1443, 1245, 1172, 1028 cm⁻¹. 1H NMR (200 MHz, CDCl₃): δ 8.44 (1H, s), 8.14 (2H, d, J = 9 Hz), 8.00 (2H, d, J = 8.5 Hz), 7.45–7.20 (4H, m), 7.14–6.90 (4H, m), 6.97 (1H, s), 6.77 (2H, d, J = 8 Hz), 6.69 (2H, d, J = 8 Hz), 3.75 (3H, s). MS (FAB): m/z (%) 390 (100) [M +], 297 (40) [M –C₆H₄OH].


N-[2-[(4-[10-(2-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]-N,N-dimethylamine (8aa). A mixture of 5a (0.99 g, 2.56 mmol), anhydrous K₂CO₃ (1.769 g, 12.8 mmol), 1-(2-chloroethyl)-dimethylamine hydrochloride (0.554 g, 3.846 mmol) and dry acetone (50 mL) was heated at reflux for 7 h. K₂CO₃ was filtered off and acetone was distilled off. The residue was extracted with ethyl acetate, the extract was washed with water, brine and dried over anhydrous Na₂SO₄. Column chromatography on silica gel and elution with 35% ethylacetate in hexane (Rₓ = 0.4) furnished 8aa (1.1 g, 93%) as a brown solid; mp 112 °C. IR (KBr): ν ~ 3440, 1633, 769 cm⁻¹. 1H NMR (200 MHz, CDCl₃): δ 8.19 (2H, d, J = 8.4 Hz), 7.40 (2H, d, J = 8 Hz), 7.40–7.20 (7H, m), 7.12 (2H, d, J = 8 Hz), 6.90 (1H, d, J = 7 Hz), 6.53 (1H, t, J = 7 Hz), 6.36 (1H, d, J = 7 Hz), 4.98 (2H, s), 4.22 (2H, t, J = 6.2 Hz), 4.07 (3H, s), 2.84 (2H, t, J = 6.2 Hz), 2.41 (6H, s). MS (FAB): m/z (%) 462 (100) [M +], 390 (10) [M –CH₂CH₂N(CH₃)₂], 354 (10) [M –OCH₃C₆H₄].

2-[4-[(2-Methoxybenzyl)-9-anthryl]phenoxy]ethanol hydrochloride (8aa·HCl). Product 8aa was dissolved in absolute ethanol (20 mL) and ethanolic HCl was added dropwise until the pH of the mixture was acidic. After removing ethanol the residue was recrystallized from a mixture of absolute ethanol and dry ether to give 8aa·HCl (1.2 g, 95%) as a brown solid; mp 134 °C. Anal. Calcd for C₃₂H₃₂ClNO₂ (498.05): C, 77.17; H, 6.48; N, 2.81. Found: C, 76.20; H, 6.66; N 2.45.

N-[2-[(4-[10-(2-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]-N,N-diethylamine (8ab). As described for 8aa, 5a (0.99 g, 2.56 mmol), anhydrous K₂CO₃ (1.769 g, 12.8 mmol), 1-(2-chloroethyl)diethylamine hydrochloride (0.661 g, 3.846 mmol) and dry acetone (20 mL) furnished 8ab (1.05 g, 83%) as a yellow solid, mp 144 °C (dichloromethane). Rₓ = 0.5 (50% ethyl acetate/hexane). IR (KBr): ν 2927, 1507, 1244, 759 cm⁻¹. 1H NMR (200 MHz, CDCl₃): δ 8.09 (2H, d, J = 8.6 Hz), 7.66 (2H, d, J = 8 Hz), 7.36–7.26 (7H, m), 7.14 (2H, d, J = 8.6 Hz), 6.90 (1H, d, J = 7.5 Hz), 6.53 (1H, t, J = 7 Hz), 6.38 (1H, d, J = 7 Hz), 4.91 (2H, s), 4.12 (2H, t, J =
6.2 Hz), 3.98 (3H, s), 2.91 (2H, t, J = 6.2 Hz), 2.64 (4H, q, J = 7.2 Hz), 1.06 (6H, t, J = 7 Hz). MS (FAB): m/z (%) 490 (100) [M⁺], 390 (20) [M –CH₂CH₂N(CH₂CH₃)₂].

2-[4-[10-(2-Methoxybenzyl)-9-anthryl]phenoxy]-N,N-diethylenamine hydrochloride (8ab·HCl). As described for 8aa·HCl, product 8ab was converted into 8ab·HCl (1.272 g, 94%), as a brown solid; mp 154 °C. Anal. Calcd for C₃₄H₃₆ClNO₂ (526.11): C, 77.62; H, 6.90; N, 2.66. Found: C, 77.99; H, 7.10; N, 2.90.

N-[2-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]-N,N-dimethylamine (8ba). As described for 8aa, 5b (250 mg, 0.64 mmol), anhydrous K₂CO₃ (0.44 g, 3.2 mmol), 1-(2-chloroethyl)dimethylamine hydrochloride (0.144 g, 0.96 mmol) and dry acetone (50 mL) furnished 8ba. 160 mg, 54%) as a white solid; mp 122 °C. Rₕ = 0.6 (60% ethyl acetate/hexane). IR (KBr): ν ~ 2934, 1601, 1451, 1243, 1175, 1035 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.25 (2H, d, J = 8.6 Hz), 7.73 (2H, d, J = 8.4 Hz), 7.45–7.27 (6H, m), 7.16 (1H, s), 7.14 (2H, d, J = 8 Hz), 6.74 (2H, d, J = 8 Hz), 6.72 (1H, d, J = 8.2 Hz), 5.03 (2H, s), 4.22 (2H, t, J = 7 Hz), 3.69 (3H, s), 2.84 (2H, t, J = 7 Hz), 2.41 (6H, s). MS (FAB): m/z (%) 462 (100) [M⁺], 390 (50) [M –CH₂CH₂N(CH₃)₂].

2-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]-N,N-diethylenamine hydrochloride (8ba·HCl). As described for 8aa·HCl, product 8ba yielded 8ba·HCl. (190 mg, 94%) as a white solid; mp 131 °C. Anal. Calcd for C₃₂H₃₂ClNO₂ (498.05): C, 77.17; H, 6.48; N, 2.81. Found: C, 77.11; H, 6.95; N, 2.85.

N-[2-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]-N,N-diethylamine (8bb). As described for 8aa, 5b (400 mg, 1.02 mmol), anhydrous K₂CO₃ (709 mg, 5.12 mmol), 1-(2-chloroethyl)diethylamine hydrochloride (0.144 g, 0.96 mmol) and dry acetone (20 mL) furnished 8bb, 400 mg, 80%) as a white solid; mp 115 °C. Rₕ = 0.5 (60% ethyl acetate/hexane). IR (KBr): ν ~ 2932. 1597, 1507, 1454, 1240, 1038 cm –¹. ¹H NMR (200 MHz, CDCl₃): δ 8.25 (2H, d, J = 8.6 Hz), 7.72 (2H, d, J = 8.4 Hz), 7.45–7.27 (6H, m), 7.16 (1H, s), 7.14 (2H, d, J = 8 Hz), 6.74 (2H, d, J = 8 Hz), 6.72 (1H, d, J = 8.1 Hz), 5.03 (2H, s), 4.19 (2H, t, J = 7 Hz), 3.70 (3H, s), 2.98 (2H, t, J = 7 Hz), 2.72 (4H, q, J = 7 Hz), 1.15 (6H, t, J = 7 Hz). MS (FAB): m/z (%) 490 (70) [M⁺], 390 (20) [M –CH₂CH₂N(CH₂)₄].

2-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]-N,N-diethylenamine hydrochloride (8bb·HCl). As described for 8aa·HCl, product 8bb yielded 8bb·HCl. (450mg, 98%) as a yellow solid; mp 126 °C. Anal. Calcd for C₃₂H₃₂ClNO₂ (526.11): C, 77.62; H, 6.90; N, 2.66. Found: C, 77.99; H, 7.04; N, 2.80.

1-[2-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]pyrrolidine (8bc). As described for 8aa, 5b (400 mg, 1.02 mmol), anhydrous K₂CO₃ (709 mg, 5.13 mmol), 1-(2-chloroethyl)pyrrolidine hydrochloride (265 mg, 1.53 mmol) and dry acetone (20 mL) yielded 8bc (400 mg, 80%) as a yellow solid; mp 131 °C (dichloromethane). Rₕ =0.6 (50% ethyl acetate/hexane). IR (KBr): ν 2926, 1507, 1246, 756 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.25 (2H, d, J = 8.6 Hz), 7.72 (2H, d, J = 8.4 Hz), 7.45–7.27 (6H, m), 7.16 (1H, s), 7.14 (2H, d, J = 8 Hz), 6.74 (2H, d, J = 8 Hz), 6.72 (1H, d, J = 8.2 Hz), 5.03 (2H, s), 4.26 (2H, t, J = 7 Hz), 3.70 (3H, s), 3.01 (2H, J = 7 Hz), 2.71–2.68 (4H, m), 1.90–1.82 (4H, m). MS (FAB): m/z (%) 488 (40) [M⁺], 390 (20) [M –CH₂CH₂N(CH₂)₄, 98 (100) [CH₂CH₂N(CH₂)₄].
1-[2-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]pyrrolidine hydrochloride (8bc·HCl). As described for 8aa·HCl, product 8bc afforded 8bc·HCl. (444 mg, 90%) as a brown solid; mp 141 °C. Anal. Calcd for C₃₄H₃₄ClNO₂ (524.09): C, 77.92; H, 6.54; N, 2.67. Found: C, 78.02; H, 6.87; N, 2.83.

1-[2-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]piperidine (8bd). As described for 8aa, 5b (400 mg, 1.02 mmol), anhydrous K₂CO₃ (709 mg, 1.54 mmol), 1-(2-chloroethyl)piperidine hydrochloride (250 mg, 1.54 mmol) and dry acetone (50 mL) gave 8bd (460 mg, 90%) as a yellow solid; mp 138 °C (dichloromethane). Rᵣ = 0.6 (50% ethylacetate/hexane). IR (KBr): ν ~ 2929, 1507, 1246, 755 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.25 (2H, d, J = 8.6 Hz), 7.73 (2H, d, J = 8.4 Hz), 7.16 (1H, s), 7.14 (2H, d, J = 8 Hz), 6.74 (2H, d, J = 8 Hz), 6.72 (1H, d, J = 8.2 Hz), 5.03 (2H, s), 4.25 (2H, t, J = 7 Hz), 3.70 (3H, s), 2.87 (2H, t, J = 7Hz), 2.61–2.56 (4H, m), 1.70–1.48 (6H, m). MS (FAB): m/z (%) 502 (100) [M⁺], 390 (10) [M – CH₂CH₂N(CH₂)₅].

1-[2-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]piperidine hydrochloride (8bd·HCl). As described for 8aa·HCl, product 8bd afforded 8bd·HCl (480 mg, 89%) as a yellow solid; mp 145 °C. Anal. Calcd for C₃₅H₃₆ClNO₂ (538.12): C, 78.12; H, 6.74; N, 2.60. Found: C, 78.19; H, 7.01; N, 2.87.

N-[2-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]–N,N-dimethylamine (8ca). As described for 8aa, 5c (250 mg, 0.641 mmol), anhydrous K₂CO₃ (443 mg, 3.205 mmol), 1-(2-chloroethyl)dimethylamine hydrochloride (138 mg, 0.961 mmol) and dry acetone (30 mL) furnished 8ca (200 mg, 67%) as a white solid; mp 110 °C (dichloromethane). Rᵣ = 0.6 (40% ethylacetate/hexane). IR (KBr): ν 3468, 2930, 2361, 1241, 778 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.26 (2H, d, J = 8.8 Hz), 7.74 (2H, d, J = 8.8 Hz), 7.14 (2H, d, J = 8 Hz), 7.09 (2H, d, J = 8 Hz), 6.77 (2H, d, J = 8 Hz), 5.00 (2H, s), 4.23 (2H, t, J = 6 Hz), 3.73 (3H, s), 2.85 (2H, t, J = 6 Hz), 2.42 (6H, s). MS (FAB): m/z (%) 461 (100) [M⁺], 390 (20) [M – CH₂CH₂N(CH₃)₂].

N-[2-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]–N,N-dimethylamine hydrochloride (8ca·HCl). As described for 8aa·HCl, product 8ca afforded 8ca·HCl (295 mg, 92%), as a white solid; mp 119 °C. Anal. Calcd for C₃₂H₃₆ClNO₂ (498.05): C, 77.17; H, 6.48; N, 2.81. Found: C, 77.13; H, 6.85; N, 2.84.

N-[2-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]–N,N-diethylamine (8cb). As described for 8aa, compound 5c (300 mg, 0.796 mmol), anhydrous K₂CO₃ (532 mg, 3.845 mmol), 1-(2-chloroethyl)diethylamine hydrochloride (198 mg, 1.154 mmol) and dry acetone (20 mL) gave 8cb (370 mg, 99%) as a yellow solid; mp 129 °C (dichloromethane). Rᵣ = 0.6 (65% ethylacetate/hexane) IR (KBr): ν 3459, 2962, 2361, 1507, 1239, 778 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.26 (2H, d, J = 8.6 Hz), 7.74 (2H, d, J = 8.8 Hz), 7.47–7.28 (6H, m), 5.00 (2H, s), 4.20 (2H, t, J = 6 Hz), 3.73 (3H, s), 2.99 (2H, t, J = 6 Hz), 2.71 (4H, q, J = 6 Hz), 1.13 (6H, t, J = 7 Hz). MS (FAB): m/z (%) 489 (50) [M⁺], 390 (100) [M – CH₂CH₂N(CH₂CH₃)₂].
N-[2-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]-N,N-dietethylamine hydrochloride (8cb·HCl). As described for 8aa·HCl, product 8cb afforded 8cb·HCl, (380 mg, 90%) as a white solid; mp 135 °C. Anal. Calcd for C_{34}H_{36}ClNO_{2} (526.11): C, 77.62; H, 6.90; N, 2.66. Found: C, 77.20; H, 7.05; N, 2.58.

1-[2-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]pyrrolidine (8cc). As described for 8aa, compound 5c (300 mg, 0.769 mmol), anhydrous K_{2}CO_{3} (532 mg, 3.84 mmol), 1-(2-chloroethyl)pyrrolidine hydrochloride (195 mg, 1.154 mmol) and dry acetone (30 mL) yielded 8cc (300 mg, 80%) as a yellow solid; mp 138 °C (dichloromethane). R_{f} = 0.5 (50% ethylacetate/hexane). IR (KBr): ν 2938, 2360, 1510, 1244, 1035 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.25 (2H, d, J = 8.6 Hz), 7.73 (2H, d, J = 8.8 Hz), 7.47–7.28 (6 H, m), 7.15 (2H, d, J = 8 Hz), 7.09 (2H, d, J = 8 Hz), 6.76 (2H, d, J = 8.8 Hz), 4.99 (2H, s), 4.26 (2H, t, J = 6 Hz), 3.72 (3H, s), 3.00 (2H, t, J = 6 Hz), 2.71–2.70 (4H, m), 1.89–1.82 (4H, m); MS (FAB): m/z (%) 487 (40) [M⁺], 390 (100) [M – CH₂CH₂N(CH₂)₄].

1-[2-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]pyrrolidine hydrochloride (8cc·HCl). As described for 8aa·HCl, product 8cc afforded 8cc·HCl., (360 mg, 89%) as a white solid; mp 143 °C. Anal. Calcd for C_{34}H_{34}ClNO_{2} (524.09): C, 77.92; H, 6.54; N, 2.67. Found: C, 77.99; H, 6.73; N, 2.60.

1-[2-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]piperidine (8cd). As described for 8aa, 5c (300 mg, 0.769 mmol), anhydrous K_{2}CO_{3} (532 mg, 3.845 mmol), 1-(2-chloroethyl)piperidine hydrochloride (212 mg, 1.154 mmol) and dry acetone (30 mL) furnished 8cd (310 mg, 80%) as a yellow solid; mp 152 °C (dichloromethane). R_{f} = 0.6 (55% ethylacetate/hexane). IR (KBr): ν 2935, 1607, 1510, 1245, 1036, 756 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.26 (2H, d, J = 8.6 Hz), 7.73 (2H, d, J = 8.8 Hz), 7.47–7.28 (6H, m), 7.14 (2H, d, J = 8 Hz), 7.09 (2H, d, J = 8 Hz), 6.76 (2H, d, J = 8 Hz), 4.99 (2H, s), 4.25 (2H, t, J = 6 Hz), 3.72 (3H, s), 2.87 (2H, t, J = 6 Hz), 2.61–2.55 (4H, m), 1.69–1.42 (6H, m). MS (FAB): m/z (%) 501 (100) [M⁺], 416 (10) [M –N(CH₂)₅], 390 (30) [M –CH₂CH₂N(CH₂)₃].

1-[2-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]ethyl]piperidine hydrochloride (8cd·HCl). As described for 8aa·HCl, product 8cd afforded 8cd·HCl., (380 mg, 91%) as a yellow solid; mp 159 °C. Anal. Calcd for C_{35}H_{36}ClNO₂ (538.12): C, 78.12; H, 6.74; N, 2.60. Found: C, 78.99; H, 6.99; N, 2.57.

2-[4-[10-(2-Methoxybenzyl)-9-anthryl]phenoxy]methyl)oxirane (9a). A mixture of compound 5a (2 g, 5.12 mmol), anhydrous K_{2}CO_{3} (2.52 g, 18.23 mmol) and epichlorohydrin (75 mL) was heated at reflux for 12 h. K_{2}CO_{3} was filtered off and epichlorohydrin was removed in vacuo. The residue was extracted with ethyl acetate, the extract was washed with water, brine and dried (Na₂SO₄). Column chromatography on silica gel and elution with 20% ethylacetate in hexane (R_f = 0.6) furnished 9a (1.97 g, 86%) as a white solid; mp 190 °C (dichloromethane). IR (KBr): ν 2952, 2312, 1620, 1520, 1252, 786 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.17 (2H, d, J = 8.6 Hz), 7.71 (2H, d, J = 7.6 Hz), 7.41–7.27 (7H, m), 7.14 (2H, d, J = 8.6 Hz), 7.00 (1H, d, J = 7.5 Hz), 6.61 (1H, t, J = 7 Hz), 6.46 (1H, d, J = 7 Hz), 4.98 (2H, s), 4.36 (2H, dd, J = 7, 3.2 Hz), 4.15 (1H, d, J = 6 Hz), 4.06 (3H, s), 3.4 (1H, m), 2.98 (1H, m), 2.84 (1H, m). MS (FAB):
m/z (%) 446 (100) [M⁺], 391 (30) [M –CH₂CH₂O], 339 (10) [M –OCH₃C₆H₄]. Anal. Caled for C₃₁H₂₆O₃ (446.54): C, 83.38; H, 5.87. Found: C, 82.99; H, 6.05.

2-[[4-[[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]methyl]oxirane (9b). As described for 9a, compound 5b (2.68 g, 6.87 mmol), anhydrous K₂CO₃ (4.6 g, 33.3 mmol) and epichlorohydrin (75 mL) furnished 9b (1.80 g, 58%) as a white solid; mp 182 °C (dichloromethane). R_f = 0.6 (20% ethylacetate/hexane). IR (KBr): ν ~ 2929, 2360, 1615, 1525, 1247, 782 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.25 (2H, d, J = 8.6 Hz), 7.69 (2H, d, J = 8.4 Hz), 7.44–7.31 (6H, m), 7.18 (1H, s), 7.16 (1H, d, J = 8 Hz), 7.12 (1H, d, J = 8 Hz), 6.73 (2H, d, J = 8 Hz), 6.72 (1H, d, J = 8.2 Hz), 5.03 (2H, s), 4.36 (2H, dd, J = 9, 3.2 Hz), 4.11 (1H, dd, J = 9, 3.4 Hz), 3.70 (3H, s), 3.4 (1H, m), 2.97 (1H, m), 2.83 (1H, m). MS (FAB): m/z (%) 446 (100) [M⁺], 391 (30) [MCH₂CH₂O], 326 (15) [M –OCH₃C₆H₄]. Anal. Caled for C₃₁H₂₆O₃ (446.54): C, 83.38; H, 5.87. Found: C, 83.49; H, 6.15.

2-[[4-[[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]methyl]oxirane (9c). As described for 9a, compound 5c (1.30 g, 3.33 mmol), anhydrous K₂CO₃ (2.3 g, 16.65 mmol) and epichlorohydrin (75 mL) furnished 9c (1.3 g, 87%) as a white solid; mp 171 °C (dichloromethane). R_f = 0.6 (20% ethylacetate/hexane). IR (KBr): ν ~ 2927, 2362, 1608, 1510, 1244, 1033, 761 cm⁻¹. ¹H NMR (200 MHz, CDCl₃): δ 8.26 (2H, d, J = 8.6 Hz), 7.71 (2H, d, J = 7.6 Hz), 7.42–7.26 (6H, m), 7.27 (2H, d, J = 8 Hz), 7.16 (2H, d, J = 8 Hz), 6.76 (2H, d, J = 8 Hz), 5.00 (2H, s), 4.35 (2H, dd, J = 6.2, 3.2 Hz), 4.11 (1H, dd, J = 9, 3.4 Hz), 3.73 (3H, s), 3.45 (1H, m), 2.97 (1H, m), 2.82 (1H, m). MS (FAB): m/z (%) 446 (100) [M⁺], 391 (25) [M –CH₂CH₂O], 326 (15) [M –OCH₃C₆H₄CH₂]. Anal. Caled for C₃₁H₂₆O₃ (446.54): C, 83.38; H, 5.87. Found: C, 83.49; H, 6.15.

1-[[4-[[10-(2-Methoxybenzyl)-9-anthryl]phenoxy]-3-pyrrolidin-1-ylpropan-2-ol (10aa). A mixture of 9a (300 mg, 0.672 mmol), pyrrolidine (71 mg, 1.00 mmol) in ethanol (10 mL) was heated at reflux for 7 h. Ethanol was removed, and the residue was extracted with ethyl acetate. The extract was washed with brine and dried. Column chromatography on silica gel and elution with 90% ethyl acetate in hexane (R_f = 0.4) furnished 10aa (300 mg, 86%) as a white solid; mp 138 °C (dichloromethane), IR (KBr): ν ~ 3420, 2929, 1560, 1440, 1382, 1245, 1152, 760 cm⁻¹. ¹H NMR (200 MHz, DMSO-d₆): δ 8.17 (2H, d, J = 8.8 Hz), 7.71 (2H, d, J = 8.6 Hz), 7.41–7.27 (7H, m), 7.14 (2H, d, J = 8 Hz), 7.00 (1H, d, J = 8 Hz), 6.61 (1H, d, J = 7 Hz), 6.46 (1H, d, J = 7 Hz), 4.98 (2H, s), 4.20–4.12 (3H, m), 4.05 (3H, s), 3.74 (1H, bs), 3.00–2.60 (6H, m), 1.86–1.84 (4H, m). MS (FAB): m/z (%) 518 (100) [M⁺], 390 (30) [M –CH₂CHOHCH₂N(CH₂)₄]. Anal. Caled for C₃₅H₃₅NO₃ (517.66): C, 81.21; H, 6.81; N, 2.71. Found: C, 80.99; H, 7.01; N, 3.00.

1-[[4-[[10-(2-Methoxybenzyl)-9-anthryl]phenoxy]-3-piperidin-1-ylpropan-2-ol (10ab). As described for 10aa, 9a (300 mg, 0.672 mmol) and piperidine (0.104 mL, 1.05 mmol) in ethanol (10 mL) was heated at reflux for 7 h. Ethanol was removed, and the residue was extracted with ethyl acetate. The extract was washed with brine and dried. Column chromatography on silica gel and elution with 90% ethyl acetate in hexane (R_f = 0.4) furnished 10ab (340 mg, 83%) as a white solid; mp 174 °C (dichloromethane), IR (KBr): ν ~ 2929, 2862, 1245, 1045, 775 cm⁻¹. ¹H NMR (200 MHz, DMSO-d₆): δ 8.17 (2H, d, J = 8.8 Hz), 7.71 (2H, d, J = 8.6 Hz), 7.41–7.27 (7H, m), 7.14 (2H, d, J = 8 Hz), 7.00 (1H, d, J = 8 Hz), 6.61 (1H, d, J = 7 Hz), 6.46 (1H, d, J = 7 Hz), 4.98 (2H, s), 4.20–4.12 (3H, m), 4.05 (3H, s), 3.74 (1H, bs), 3.00–2.60 (6H, m), 1.86–1.84 (4H, m). MS (FAB): m/z (%) 532 (100) [M⁺], 391 (20) [M –
CH₂CHOHCH₂N(CH₂)₅. Anal. Calcd for C₃₆H₃₇NO₃ (531.68): C, 81.32; H, 7.01; N, 2.63. Found: C, 82.19; H, 7.15; N, 2.99.

1-[4-[10-(2-Methoxybenzyl)-9-anthryl]phenoxy]-3-(4-methylpiperazin-1-yl)propan-2-ol (10ac). A mixture of 9a (300 mg, 0.672 mmol) and N-methylpiperazine (0.11 mL, 1.00 mmol) in ethanol (20 mL) was heated at reflux for 7 h. Ethanol was removed, and the residue was extracted with ethyl acetate. The extract was washed with brine and dried. Column chromatography on silica gel and elution with 5% methanol in chloroform (R_f = 0.4) furnished 10ac (210 mg, 57%) as a white solid; mp 170 °C (dichloromethane). IR (KBr): ν ≈ 2932, 2362, 1509, 1244, 1172, 1034, 740 cm⁻¹. ¹H NMR (200 MHz, DMSO-d₆): δ 8.17 (2H, d, J = 8.6 Hz), 7.71 (2H, d, J = 8.6 Hz), 7.41–7.27 (7H, m), 7.14 (2H, d, J = 8.8 Hz), 6.61 (1H, t, J = 7 Hz), 6.46 (1H, t, J = 7 Hz), 4.98 (2H, s), 4.20–4.07 (3H, m), 4.06 (3H, s), 2.77–2.40 (10H, m), 2.60 (1H, bs), 2.23 (3H, s). MS (FAB): m/z (%) 546 (100) [M + CH₂CHOHCH₂N(CH₂)₄NCH₃]. Anal. Calcd for C₃₆H₃₈N₂O₃ (546.70): C, 79.09; H, 7.01; N, 5.12. Found: C, 79.33; H, 7.15; N, 5.19.

1-(Cyclohexylamino)-3-{4-[10-(2-Methoxybenzyl)-9-anthryl]phenoxy}propan-2-ol (10ad). A mixture of 9a (300 mg, 0.672 mmol), cyclohexylamine (100 mg, 1.00 mmol) in ethanol (20 mL) was heated at reflux for 7 h. Ethanol was removed, and the residue was extracted with ethyl acetate. The extract was washed with brine and dried. Column chromatography on alumina and elution with 5% methanol in chloroform (R_f = 0.4) furnished 10ad (330 mg, 90%) as a white solid; mp 155 °C (dichloromethane), IR (KBr): ν ≈ 3434, 2378, 1650, 1212, 1048, 1161 cm⁻¹. ¹H NMR (200 MHz, DMSO-d₆): δ 8.17 (2H, d, J = 8.6 Hz), 7.71 (2H, d, J = 8.4 Hz), 7.41–7.27 (7H, m), 7.14 (2H, d, J = 8 Hz), 7.00 (1H, d, J = 7.5 Hz), 6.61 (1H, t, J = 7 Hz), 6.46 (1H, d, J = 8 Hz), 5.00 (2H, s), 4.19–4.17 (3H, m), 4.09 (3H, s), 3.00 (1H, d, J = 6 Hz), 2.95 (1H, m), 2.5 (1H, m), 2.00 (1H, bs), 1.99 (1H, d, J = 7 Hz), 1.70 (1H, d, J = 7 Hz), 1.50 (1H, d, J = 7 Hz), 1.40–1.10 (8H, m). MS (FAB): m/z (%) 546 (100) [M⁺], 390 (25) [M – CH₂CHOHCH₂NHCH(CH₂)₅]. Anal. Calcd for C₃₇H₃₉N₂O₃ (545.71): C, 81.43; H, 7.20; N, 2.57. Found: C, 81.34; H, 7.17; N, 2.69.

1-{{4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy}}-3-pyrrolidin-1-ylpropan-2-ol (10ba). As described for 10aa a mixture of 9b (300 mg, 0.672 mmol), pyrrolidine (71 mg, 1.00 mmol) in ethanol (10 mL) furnished 10ba (300 mg, 86%) as a white solid; mp 142 °C (dichloromethane); R_f = 0.4 (90% ethyl acetate/hexane). IR (KBr): ν ≈ 3429, 2928, 1595, 1446, 1379, 1244, 1161, 1035, 765 cm⁻¹. ¹H NMR (200 MHz, DMSO-d₆): δ 8.37 (2H, d, J = 8.8 Hz), 7.62 (2H, d, J = 8.6 Hz), 7.53 (2H, t, J = 7.6 Hz), 7.42 (2H, d, J = 8 Hz), 7.34 (2H, t, J = 7.6 Hz), 7.21 (1H, s), 7.17 (1H, d, J = 8 Hz), 7.11 (1H, d, J = 8 Hz), 6.76 (2H, d, J = 7 Hz), 6.66 (1H, d, J = 7 Hz), 5.05 (2H, s), 4.94 (1H, d, J = 4 Hz), 4.05–3.99 (2H, m), 3.66 (3H, s), 2.54–2.49 (6H, m), 1.70–1.60 (4H, m). MS (FAB): m/z (%) 518 (100) [M⁺], 390 (25) [M – CH₂CHOHCH₂NHCH(CH₂)₃]. Anal. Calcd for C₃₅H₃₅NO₃ (517.66): C, 81.21; H, 6.81; N, 2.71. Found: C, 81.69; H, 7.11; N, 3.03.

1-{{4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy}}-3-piperidin-1-ylpropan-2-ol (10bb). As described for 10aa, a mixture of 9b (300 mg, 0.671 mmol), piperidine (74 mg, 0.874 mmol) in ethanol (20 mL) furnished 10bb (300 mg, 84%) as a white solid; mp 149 °C. R_f = 0.4 (5% 765 cm⁻¹. ¹H NMR (200 MHz, DMSO-d₆): δ 8.37 (2H, d, J = 8.8 Hz), 7.62 (2H, d, J = 8.6 Hz), 7.53 (2H, t, J = 7.6 Hz), 7.42 (2H, d, J = 8 Hz), 7.34 (2H, t, J = 7.6 Hz), 7.21 (1H, s), 7.17 (1H, d, J = 8 Hz), 7.11 (1H, d, J = 8 Hz), 6.76 (2H, d, J = 7 Hz), 6.66 (1H, d, J = 7 Hz), 5.05 (2H, s), 4.94 (1H, d, J = 4 Hz), 4.05–3.99 (2H, m), 3.66 (3H, s), 2.54–2.49 (6H, m), 1.70–1.60 (4H, m). MS (FAB): m/z (%) 518 (100) [M⁺], 390 (25) [M – CH₂CHOHCH₂NHCH(CH₂)₃]. Anal. Calcd for C₃₅H₃₅NO₃ (517.66): C, 81.21; H, 6.81; N, 2.71. Found: C, 81.69; H, 7.11; N, 3.03.
methanol/chloroform). IR (KBr): $\tilde{\nu}$ 2929, 1596, 1449, 1247, 1161, 1037, 768 cm$^{-1}$. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 8.36 (2H, d, $J = 8.8$ Hz), 7.62 (2H, d, $J = 8.8$ Hz), 7.52 (2H, t, $J = 8$ Hz), 7.48 (2H, t, $J = 8$ Hz), 7.43 (2H, t, $J = 8.2$ Hz), 7.29 (1H, s), 7.26 (1H, d, $J = 8$ Hz), 7.14 (1H, d, $J = 8$ Hz), 6.75 (2H, d, $J = 8.2$ Hz), 6.71 (1H, d, $J = 8$ Hz), 5.04 (2H, s), 4.99 (1H, m), 4.14–4.02 (4H, m), 3.62 (3H, s), 3.30–3.25 (4H, m), 1.52–1.48 (6H, m). MS (FAB): $m/z$ (%) 532 (100) [M +], 390 (30) [M – CH$_2$CHOHCH$_2$N(CH$_2$)$_5$]. Anal. Calcd for C$_{36}$H$_{37}$NO$_3$ (531.68): C, 81.32; H, 7.01; N, 2.63. Found: C, 80.99; H, 7.05; N, 2.99.

1-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]-3-(4-methylpiperazin-1-yl)propan-2-ol (10bc). As described for 10ac, a mixture of 9b (300 mg, 0.672 mmol), N-methylpiperazine (101 mg, 1.00 mmol) in ethanol (20 mL) furnished 10bc (160 mg, 43%) as a white solid; mp 140 °C. $R_f = 0.4$ (5% methanol/chloroform). IR (KBr): $\tilde{\nu}$ 2932, 1605, 1448, 1383, 1243, 1147, 1041 cm$^{-1}$. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 8.36 (2H, d, $J = 8.8$ Hz), 7.63–7.28 (8H, m), 7.20 (1H, s), 7.16 (1H, d, $J = 8$ Hz), 7.10 (1H, d, $J = 8$ Hz), 6.74 (2H, d, $J = 8$ Hz), 6.66 (1H, d, $J = 8$ Hz), 5.03 (2H, s), 4.92 (1H, m), 3.90–3.00 (5H, m), 3.63 (3H, s), 2.53 (3H, s), 2.48–2.44 (8H, m). MS (FAB): $m/z$ (%) 547 (100) [M +], 390 (40) [M – CH$_2$CHOHCH$_2$N(CH$_2$)$_4$NCH$_3$]. Anal. Calcd for C$_{36}$H$_{38}$N$_2$O$_3$ (546.70): C, 79.09; H, 7.01; N, 5.12. Found: C, 79.55; H, 6.00; N, 5.22.

1-[4-[10-(3-Methoxybenzyl)-9-anthryl]phenoxy]-3-morpholin-4-ylpropan-2-ol (10bd). As described for 10aa, 9b (300 mg, 0.672 mmol), morpholine (87 mg, 1.00 mmol) in ethanol (10 mL) gave 10bd (300 mg, 83%) as a white solid; mp 177 °C. $R_f = 0.4$ (90% ethyl acetate/hexane). IR (KBr): $\tilde{\nu}$ 3446, 2936, 1606, 1512, 1452, 1243, 1116, 1042, 764 cm$^{-1}$. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 8.25 (2H, d, $J = 8.6$ Hz), 7.71 (2H, d, $J = 8.8$ Hz), 7.44–7.24 (7H, m), 7.16 (2H, d, $J = 8$ Hz), 6.71 (3H, m), 5.04 (2H, s), 4.17–4.13 (3H, m), 3.80–3.75 (4H, m), 3.69 (3H, s), 2.74–2.50 (6H, m), 1.54 (1H, bs); MS (FAB): $m/z$ (%) 534 (100) [M +], 390 (30) [M – CH$_2$CHOHCH$_2$N(CH$_2$)$_4$O]. Anal. Calcd for C$_{35}$H$_{35}$NO$_4$ (533.66): C, 78.77; H, 6.61; N, 2.62. Found: C, 78.00; H, 7.01; N, 2.68.

1-(4-Benzylpiperazin-1-yl)-3-[4-[10-(3-methoxybenzyl)-9-anthryl]phenoxy]propan-2-ol (10be). As described for 10aa, a mixture of 9b (300 mg, 0.671 mmol), N-Benzylpiperidine (177 mg, 1.00 mmol) in ethanol (10 mL) furnished 10be (250 mg, 59%) as a brown solid; mp 147 °C. $R_f = 0.4$ (5% methanol/chloroform). IR (KBr): $\tilde{\nu}$ 3422, 2934, 1604, 1452, 1243, 1116, 1042, 767 cm$^{-1}$. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 8.37 (2H, d, $J = 8.8$ Hz), 7.64–7.09 (16H, m), 6.76 (2H, d, $J = 7$ Hz), 6.67 (1H, d, $J = 7.8$ Hz), 5.04 (2H, s), 4.91 (1H, m), 4.14–3.99 (4H, m), 3.66 (3H, s), 2.74–2.50 (6H, m), 1.54 (1H, bs); MS (FAB): $m/z$ (%) 624 (100) [M +2], 390 (30) [M – CH$_2$CHOHCH$_2$N(CH$_2$)$_4$NCH$_2$C$_6$H$_5$]. Anal. Calcd for C$_{42}$H$_{42}$N$_2$O$_3$ (622.79): C, 81.00; H, 6.80; N, 4.50. Found: C, 81.29; H, 7.00; N, 3.99.

1-[4-[10-(4-Methoxybenzyl)-9-anthryl]phenoxy]-3-piperidin-1-ylpropan-2-ol (10cb). As described for 10ac, a mixture of 9c (300 mg, 0.673 mmol), piperidine (85 mg, 1.008 mmol) in ethanol (20 mL) furnished 10cb (225 mg, 62%) as a white solid; mp 194 °C (dichloromethane); $R_f = 0.4$ (5% methanol in chloroform). IR (KBr): $\tilde{\nu}$ 2927, 2857, 1240, 1033, 761 cm$^{-1}$. $^1$H NMR (200 MHz, DMSO-$d_6$): $\delta$ 8.37 (2H, d, $J = 8.8$ Hz), 7.61 (2H, d, $J = 8.6$ Hz), 7.52 (2H, t, $J = 7$ Hz), 7.41 (2H, d, $J = 8$ Hz), 7.34 (2H, d, $J = 7$ Hz), 7.18 (2H, d, $J = 8.6$ Hz), 4.99 (2H, s), 4.98
(1H, m), 4.02–3.96 (2H, m), 3.71 (3H, s), 3.68–3.64 (4H, m), 1.52–1.22 (6H, m). MS (FAB): m/z (%) 532 (100) [M⁺], 390 (30) [M –CH₂CHOHCH₂N(CH₂)₃]. Anal. Calcd for C₃₆H₃₇NO₃ (531.68): C, 81.32; H, 7.01; N, 2.63. Found: C, 81.93; H, 7.61; N, 2.32.

1-[4-{10-(4-Methoxybenzyl)-9-anthryl}phenoxy]-3-(4-methylpiperazin-1-yl)propan-2-ol (10cc). As described for 10ac, a mixture of 9c (300 mg, 0.672 mmol), N-methylpiperazine (0.11 mL, 1.00 mmol) in ethanol (20 mL) furnished 10cc (210 mg, 57%) as a white solid; mp 173 °C (dichloromethane); Rf = 0.4 (5% methanol in chloroform). IR (KBr): ν ~ 2932, 2362, 1509, 1244, 1172, 1034 cm⁻¹. 1H NMR (200 MHz, DMSO-d₆): δ 8.37 (2H, d, J = 8.6 Hz), 7.61 (2H, d, J = 8.6 Hz), 7.52 (2H, t, J = 7 Hz), 7.41 (2H, d, J = 8 Hz), 7.34 (2H, d, J = 7 Hz), 7.18 (2H, d, J = 8.6 Hz), 7.07 (2H, d, J = 8.8 Hz), 6.80 (2H, t, J = 7 Hz), 4.99 (2H, s), 4.98 (1H, m), 4.03–3.97 (4H, m), 3.70 (3H, s), 3.68–3.66 (8 H, m), 2.15 (3H, s). MS (FAB): m/z (%) 546 (100) [M⁺], 433 [M –CH₂N(CH₂)₄NCH₃], 390 {30) [M –CH₂CHOHCH₂N(CH₂)₄NCH₃]. Anal. Calcd for C₃₆H₃₈N₂O₃ (546.70): C, 79.09; H, 7.01; N, 5.12. Found: C, 78.87; H, 6.25; N, 5.20.

1-[4-{10-(4-Methoxybenzyl)-9-anthryl}phenoxy]-3-morpholin-4-ylpropan-2-ol (10cd). As described for 10aa, 9c (300 mg, 0.672 mmol), morpholine (87 mg, 1.00 mmol) in ethanol (10 mL) furnished 10cd (215 mg, 60%) as a white solid; mp 196 °C (dichloromethane); Rf = 0.4 (90% ethyl acetate/hexane). IR (KBr): ν ~ 2928, 2361, 1244, 1034, 769 cm–¹. 1H NMR (200 MHz, DMSO-d₆): δ 8.37 (2H, d, J = 8.6 Hz), 7.61 (2H, d, J = 8.6 Hz), 7.55 (2H, t, J = 6.6 Hz), 7.41 (2H, d, J = 8.6 Hz), 7.33 (2H, t, J = 6.6 Hz), 7.18 (2H, d, J = 8.8 Hz), 6.78 (2H, d, J = 8.8 Hz), 4.99 (2H, s), 4.10–3.90 (3H, m), 3.66–3.54 (4H, m), 3.65 (3H, s), 3.49–3.26 (6H, m). MS (FAB): m/z (%) 533 (100) [M⁺], 433 [M –CH₂CHOHCH₂N(CH₂)₄NCH₃]. Anal. Calcd for C₃₅H₃₅NO₄ (533.66): C, 78.77; H, 6.61; N, 2.62. Found: C, 78.87; H, 6.25; N, 5.20.

1-(Cyclopropylamino)-3-{4-[10-(4-methoxybenzyl)-9-anthryl]phenoxy}propan-2-ol (10cf). As described for 10ad, a mixture of 9c (300 mg, 0.672 mmol), cyclopropylamine (57 mg, 1.00 mmol) in ethanol (10 mL) furnished 10cf (129 mg, 38%) as a white solid; mp 136 °C (dichloromethane); Rf = 0.4 (90% ethyl acetate/hexane). IR (KBr): ν ~ 3400, 2364, 1611, 1244, 1034 cm–¹. 1H NMR (200 MHz, DMSO-d₆): δ 8.26 (2H, d, J = 8.6 Hz), 7.71 (2H, d, J = 8.6 Hz), 7.14 (4H, m), 7.14 (4H, d, J = 8 Hz), 6.76 (2H, d, J = 8 Hz), 6.74 (2H, d, J = 8 Hz), 5.00 (2H, s), 4.21–4.14 (2H, m), 3.79–3.75 (1H, m), 3.73 (3H, s), 3.05–2.98 (2H, m), 2.2 (1H, m), 0.53–0.44 (4H, m). MS (FAB): m/z (%) 503 (100) [M⁺], 433 (50) [M – CH₂NHCH(CH₂)₂], 390 (30) [M – CH₂CHOHCH₂NCH(CH₂)₂]. Anal. Calcd for C₃₅H₃₁NO₃ (489.60): C, 80.95; H, 6.38; N, 2.86. Found: C, 81.00; H, 6.31; N, 2.98.

**Agar micro dilution method.** Twofold dilutions of each test compound were added to 7H10 agar, and *M. tuberculosis* H₃₇R₇ Rv was used as test organism. MIC is the concentration of the compound that completely inhibits the growth and colony forming ability of *M. tuberculosis*.

In a 24 well plate 3 mL middle brook 7H11 agar medium with OADC supplement was dispensed in each well. The test compound was added to the middle brook medium agar before in duplicate so that the final concentration of the test compound in each well was 25, 12.5, 6.25,
3.125 and 1.56 µg/mL, respectively. The known CFU of the H\textsubscript{37}R\texttextsubscript{v} culture was dispensed on top of agar in each well in a negative pressure biosafety hood. The plates were then incubated at 37 °C CO\textsubscript{2} incubator. The concentration at which complete inhibition of colonies was observed was taken as MIC of test drug.

**BACTEC Method.** A stock solution of the test compounds in DMSO (1mg/mL) was prepared and sterilized by passage through 0.22 µm filters. 50 µL were added to 4 mL radiometric 7H12 broth (BACTEC 12B; Becton Dickinson Diagnostic Instrument System US) to achieve the final concentrations. Controls received 50 µL DMSO. Isoniazid and rifampin (Sigma Chemical Co. St. Louis, MO) were included as positive drug control. In the BACTEC method, 10\textsuperscript{4} to 10\textsuperscript{5} CFU/mL of *M. tuberculosis* H\textsubscript{37}R\textsubscript{v} was inoculated in 4 mL fresh BACTEC 12B broth containing the test compounds. An additional control was inoculated with 1:100 dilution of the inoculum to represent 1% of the bacterial population. (10\textsuperscript{2} to 10\textsuperscript{3} CFU/mL). The vials were incubated at 37 °C, and GI readings were recorded daily until the GI in 1:100 control had reached 30. The concentration of the drug producing final GI reading lower than those in 1:100 control was considered to have inhibited more than 90% of the bacteria and was defined as the MIC.

**Micro almar blue assay (MABA).** *M. tuberculosis*, H\textsubscript{37}R\textsubscript{a} was used as a suitable surrogate for the virulent H\textsubscript{37}R\textsubscript{v} strain. The standard antitubercular agents Rifamycin, isoniazid, *p*-amino-salicylic acid, ethambutol and ethionamide were taken as positive controls. A compound is considered active only if it shows inhibition greater than or equal to 90%.

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**References**


