Electronic Supplementary Information

Dual aromatase-sulfatase inhibitors based on the Anastrozole template: synthesis, *in vitro* SAR, molecular modelling and *in vivo* activity

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I) Synthesis of Anastrozole: Route (A)†

![Scheme A](image)

**Scheme A.** Reagents and conditions. (i) KCN, TBAB, H$_2$O/CH$_2$Cl$_2$, Δ, 92%; (ii) 4NaH, 4MeI, DMF, 88%; (iii) NaBrO$_3$, NaHSO$_3$, H$_2$O/EtOH; (iv) 1,2,4-triazole, sodium salt, K$_2$CO$_3$, DMF, 69%

(3-Cyanomethyl-5-methyl-phenyl)-acetonitrile I. 1,3-Bis(bromomethyl)-5-methylbenzene (5.00 g, 18.0 mmol), KCN (3.00 g, 42.0 mmol) and tetrabutylammonium bromide (0.200 g, 0.602 mmol) in CH$_2$Cl$_2$ (15 mL) and H$_2$O (5 mL) were refluxed with vigorous stirring for 16 h. Upon cooling, dichloromethane was removed *in vacuo* and the resulting mixture diluted with EtOAc (50 mL). The organic layer was separated and washed with brine (100 mL), dried (MgSO$_4$), filtered and solvent removed *in vacuo* to give yellow residues. Recrystallisation (EtOAc/hexane) gave the title compound as a white solid (2.83 g, 92%), mp 73–75 °C (lit.1 73-74 °C). $\delta$H (270 MHz, CDCl$_3$) 2.37 (3H, s, CH$_3$), 3.71 (4H, s, CH$_2$), 7.06 (1H, s, ArH) and 7.12 (2H, s, ArH); $\delta$C (67.9 MHz, CDCl$_3$) 21.3 (CH$_3$), 23.6 (CH$_2$), 117.8 (C), 124.6 (CH), 128.6 (CH), 130.8 (C) and 140.5 (C); m/z (ES-) 168 ((M - H)$-$, 100%); HRMS (ES+) 171.0915. C$_{11}$H$_{11}$N$_2$ requires 171.0917.

2-[3-(Cyano-dimethyl-methyl)-5-methyl-phenyl]-2-methyl-propionitrile II. To a solution of I (2.70 g, 16.0 mmol) in anhydrous DMF (100 mL) at 0 °C was added cautiously NaH (2.30 g, 96.0 mmol) with stirring under an inert atmosphere. After 15 min, iodomethane (6.60 mL, 96.0 mmol) was added and the resulting suspension was set to stir at room temperature for 12h. The resulting light orange suspension was diluted with EtOAc (50 mL) and washed with distilled H$_2$O (50 mL x 4) and brine (50 mL) and dried (MgSO$_4$). Solvent was removed *in vacuo* to give yellow residues. Recrystallisation (EtOAc/hexane) gave the title compound as a cream solid (2.43 g, 88%), mp 73–75 °C (lit.1 73-75 °C). $\delta$H (270 MHz, CDCl$_3$) 1.72 (12H, s, CH$_3$), 2.39 (3H, s, CH$_3$), 7.06 (1H, s, ArH) and 7.12 (2H, s, ArH); $\delta$C (67.9 MHz, CDCl$_3$) 21.3 (CH$_3$), 23.6 (CH$_2$), 117.8 (C), 124.6 (CH), 128.6 (CH), 130.8 (C) and 140.5 (C); m/z (ES') 168 ((M + Na)$^+$, 100%); HRMS (ES') 227.1541. C$_{15}$H$_{19}$N$_2$ requires 227.1543.

2-[3-(Cyano-dimethyl-methyl)-5-[1,2,4]triazol-1-ylmethyl-phenyl]-2-methyl-propionitrile (Anastrozole). To a biphasic mixture of II (2.40 g, 10.7 mmol) in EtOAc (100 mL) and NaBrO$_3$ (5.00 g, 32.0 mmol) in H$_2$O (150 mL),
at 0 °C, was added a solution of NaHSO₃ (3.50 g, 32.0 mmol) drop wise over 15 minutes. The resulting brown mixture was stirred at room temperature overnight. The phases were separated and the aqueous layer extracted with ethyl acetate (50 mL x 2). The combined organic phases were washed with NaS₂O₃ (aq) (100 mL), distilled H₂O (100 mL x 2) and brine (100 mL), then dried (MgSO₄) and solvent removed in vacuo to give dark yellow residues. To a solution of these residues in anhydrous DMF (10 mL) at 0 °C and under inert conditions was added 1,2,4-triazole, sodium salt (1.72 g, 19.0 mmol). The resulting light brown suspension was stirred at room temperature for 18 h. The reaction mixture was diluted with EtOAc (30 mL) and washed with distilled H₂O (50 mL x 3) and brine (50 mL), dried (MgSO₄), filtered and solvent removed in vacuo to give a yellow oil. Column chromatography (EtOAc) eluted the title compound as a white solid (2.12 g, 69%), mp 77-81 °C (lit.1 81-82 °C) (Found: C, 69.6; H, 6.4; N, 23.9. C₁₇H₁₉N₅ requires C, 69.6; H, 6.5; N, 23.9%).

δH (270 MHz, CDCl₃) 1.71 (12H, s, CH₃), 5.39 (2H, s, CH₂), 7.32 (2H, m, ArH), 7.53 (1H, t, J = 1.7 Hz, ArH), 7.98 (1H, s, C₂H₂N₃) and 8.14 (1H, s, C₂H₂N₃); δH (270 MHz, CDCl₃) 29.2 (CH₃), 37.4 (C), 53.1 (CH₂), 122.2 (CH), 123.9 (C), 124.4 (CH), 136.7 (C), 143.3 (C), 143.5 (CH) and 152.6 (CH); m/z (FAB+) 316 ((M + Na) +, 100%); HRMS (ES +) 294.1700. C₁₇H₂₀N₅ requires 294.1713.

II) Synthesis of Anastrozole: Route (B)†

![Scheme B. Reagents and conditions.](image)

3,5-Bis-bromomethyl-benzoic acid methyl ester III. To a solution of methyl 3,5-dimethylbenzoate (15.0 g, 89.5 mmol) in CCl₄ (150 mL) was added N-bromosuccinimide (16.1 g, 89.5 mmol) and benzoyl peroxide (0.200 g, 0.826 mmol). The resulting light yellow suspension was stirred until a deep orange colouration developed. After cooling to room temperature, the suspension was filtered and the filtrates were evaporated to give a yellow liquid. Column chromatography (EtOAc/hexane 10:90 increasing to 50:50) eluted the title compound as a white crystalline solid (1.99 g, 7%), mp 100-103 °C (lit.¹ 99-101 °C), δ₁H (400 MHz, CDCl₃) 7.60 (1H, t, J = 2.0 Hz, ArH) and 7.97 (2H, d, J = 2.0 Hz, ArH).

3,5-Bis-cyanomethyl-benzoic acid methyl ester IV. Compound III (2.87 g, 8.91 mmol), KCN (1.45 g, 21.4 mmol) and tetrabutylammonium bromide (0.100 g, 0.301 mmol) in CH₂Cl₂ (15 mL) and H₂O (5 mL) were refluxed with vigorous stirring for 4 h. Upon cooling, dichloromethane was removed in vacuo and the resulting mixture diluted with EtOAc (50 mL). The organic layer was separated and washed with brine (100 mL), dried (MgSO₄), filtered and solvent removed in vacuo to give yellow residues. Column chromatography (EtOAc
3,5-Bis-(cyano-dimethyl-methyl)-benzoic acid methyl ester V. To a solution of IV (1.09 g, 5.09 mmol) in anhydrous DMF (20 mL) at 0 °C was added cautiously NaH (0.537 g, 22.4 mmol) with stirring under an inert atmosphere. After 15 min, iodomethane (1.39 mL, 22.4 mmol) was added and the resulting suspension was set to stir at room temperature for 18 h. The reaction mixture was diluted with EtOAc (30 mL) and washed with distilled H₂O (50 mL) and brine (50 mL) and dried (MgSO₄). Solvent was removed and 8.08 (2H, d, J = 2.0 Hz, ArH) and 8.08 (2H, d, J = 2.0 Hz, ArH).

2-[3-(Cyano-dimethyl-methyl)-5-hydroxymethyl-phenyl]-2-methyl-propionitrile VI. To a mixture of V (0.540 g, 2.00 mmol) and LiBH₄ (0.087 g, 0.400 mmol) at room temperature and under inert conditions was added anhydrous THF (10 mL). The resulting yellow solution was set to reflux for 3 h, then cooled to 0 °C and treated drop wise with 1M HCl (aq) until the mixture remained acidic. EtOAc (100 mL) was added and the organic layer was washed with distilled H₂O (50 mL x 3) and brine (50 mL) and dried (MgSO₄). Solvent was removed in vacuo to give dark yellow residues. Column chromatography (EtOAc/hexane 50:50) eluted the title compound as a cream solid (1.33 g, 97%), mp 85–87 °C (lit.¹ 83-85 °C) (Found: C, 71.1; H, 6.8; N, 10.3. C₁₆H₁₈N₂O₂ requires C, 71.1; H, 6.7; N, 10.4%); δ₁H (270 MHz, CDCl₃) 1.75 (12H, s, CH₃), 3.95 (3H, s, COOCH₃), 7.80 (1H, t, J = 1.7 Hz, ArH) [ArCH₂OH signal not found]; m/z (FAB⁺) 396 ((M + H + NBA)+, 25%), 225 ((M – OH)+, 25%), 225 ((M – OH)+, 100).

2-[3-(Cyano-dimethyl-methyl)-5-(3,5-triazole-1-ylmethyl-phenyl)-2-methyl-propionitrile (Anastrozole). To a solution of VI (0.443 g, 1.83 mmol) in anhydrous CH₂Cl₂ (15 mL) at 0 °C under inert conditions was added anhydrous pyridine (0.15 mL, 1.90 mmol) followed by SOCl₂ (0.19 mL, 2.59 mmol). The reaction mixture was stirred at 0 °C for 15 min and then at room temperature for 2 h before subjecting to reflux for 1 h. Upon cooling, the solvent was removed in vacuo to leave white residues which were dissolved in EtOAc (50 mL). The solution was washed with distilled H₂O (50 mL x 3) and brine (50 mL) and dried (MgSO₄), filtered and solvent removed in vacuo to give pale yellow residues. To a solution of these residues in anhydrous DMF (4 mL) at 0 °C and in inert conditions was added 1,2,4-triazole, sodium salt (0.367 g, 3.63 mmol). The resulting light brown suspension was stirred at room temperature for 18 h. The reaction mixture was diluted with EtOAc (30 mL) and washed with distilled H₂O (50 mL x 3) and brine (50 mL), dried (MgSO₄), filtered and solvent removed in vacuo to give a yellow oil. Column chromatography (EtOAc) eluted the title compound as a white solid (0.279 g, 52%). Analytical data corresponds to that obtained by method (A).

Notes and References

1. U. S. Patent 4,935,437
2. Routes are adapted from U.S. Patent 4,935,437 and U.S. Patent RE 36617. Spectroscopic and additional analytical data are provided.

III) Experimental data for 1, 2, 3(a)–(c), 4(a)–(c), 5(a)-(c), 20–23

3-Bromomethyl-5-methyl-benzoic acid methyl ester 1. To a solution of NaBrO₃ (13.8 g, 91.5 mmol) in distilled H₂O (45.8 mL) was added methyl 3,5-dimethylbenzoate (5.00 g, 30.5 mmol) in EtOAc (15.3 mL). To this mixture NaHSO₃ (11.0 g, 91.5 mmol) in distilled H₂O (91.5 mL) was added drop wise with vigorous stirring over 1 h. The reaction mixture was stirred for a further 4 h at room temperature. The organic portion was separated and diluted with EtO (100 mL). This was then washed with saturated Na₂SO₃(aq) (50 mL), distilled H₂O (50 mL x 2), and brine (50 mL). Dried (MgSO₄), filtered and solvent removed in vacuo to leave yellow residues. The residues were dissolved in hexane (50 mL) and the resulting solution cooled to 0 °C for 30 min. A white ppt (3,5-bis-bromomethylbenzoic acid methyl ester) was removed via filtration. The filtrate was reduced in vacuo to a yellow viscous oil. Column chromatography (EtOAc/hexane 10:90) eluted 1 (6.30 g, 85%) as a clear colourless oil. δ₁H (270 MHz, CDCl₃) 2.57 (3H, s, ArCH₃), 3.89 (3H, s, ArCO₂CH₃), 4.47 (2H, s, ArCH₃Br), 7.38 (1H, s, ArH), 7.77 (1H, s, ArH) and 7.84 (1H, s, ArH); m/z (APCI⁺) 245 ([M+Br⁻]+, 100%), 243 ([M+Br⁻+H⁺]+, 90).

3-Cyanomethyl-5-methyl-benzoic acid methyl ester 2. With vigorous stirring a mixture of 1 (19.5 g, 80.1 mmol), KCN (6.26 g, 96.1 mmol) and tetrabutylammonium bromide (1.33 g, 4.00 mmol) with CH₂Cl₂ (100 mL) and distilled H₂O (40 mL) was set to reflux for 24 h. On cooling the organic fraction was separated and washed
with distilled H2O (100 mL x 2) and brine (100 mL). Then dried (MgSO4) and solvent removed in vacuo to leave a red/orange oil. Column chromatography (hexane/EtOAc 50:50) gave 2 (11.39 g, 75%) as a pale yellow solid, mp 56-57 °C. δH (270 MHz, CDCl3) 2.34-3.24 (3H, s, ArCH3), 3.79 (2H, s, ArCH(CN)), 3.89 (3H, s, ArCO2CH3), 7.34 (1H, s, ArH), 7.76 (1H, s, ArH) and 7.79 (1H, s, ArH); m/z (APCI) 188 (([M – H])+, 100%); HRMS (ES+) 190.0867. C11H12NO2 requires 190.0863.

3-(Cyano-dimethyl-methyl)-5-methyl-benzoic acid methyl ester 3(a). Under inert conditions 2 (7.00 g, 37.0 mmol) was dissolved in anhydrous THF (20 mL) to give a yellow solution. With stirring this solution was cooled to 0 °C under inert conditions and NaH (2.22 g, 92.5 mmol) was added gradually and then left to stir at 0 °C for 15 min. Iodomethane (11.6 mL, 81.4 mmol) was then added drop wise. The resulting suspension was left to stir at room temperature for 16 h. Propan-2-ol (5 mL) was carefully added to the reaction mixture followed by CH2Cl2 (50 mL) which was then washed with distilled H2O (50 mL x 2) and brine (50 mL). Dried (MgSO4) and solvent removed in vacuo to leave a red/orange oil. Column chromatography (EtOAc/hexane 0:100) eluted 3(a) as a yellow light brown viscous oil (9.30 g, 75%) and used without further purification.

3-Bromomethyl-5-(1-cyano-cyclobutyl)-benzoic acid methyl ester 4(a). Compound 4(a) was prepared from 3(a) using similar conditions to those described for the synthesis of compound 1. Compound 4(a) was isolated as a light brown viscous oil (9.30 g, 75%) and used without further purification. m/z (APCI+) 298 ([81BrM+H]+, 15%), 296 ([81BrM+H]+, 15), 272 ([79BrM-CN]+, 100), 270 ([79BrM-CN]+, 100). HRMS (ES+) 309.1176. C14H12BrNO2 requires 309.1176.

3-(Cyano-dimethyl-methyl)-5-methyl-benzoic acid methyl ester 3(b). Under inert conditions compound 2 (1.50 g, 7.93 mmol) was dissolved in anhydrous DMF (10 mL) and the solution cooled with stirring to 0 °C. NaH (0.476 g, 19.8 mmol) was carefully added in a resulting in a deep red colouration and evolution of gas. After 15 min at 0 °C, 1,3-dibromopropane (0.960 mL, 9.48 mmol) was added drop wise over 5 min. The reaction was allowed to warm to room temperature and left to stir for 1 h. EtOAc (50 mL) was added to the reaction mixture and this was washed with distilled H2O (50 mL x 4) and brine (50 mL). The organic layer was separated and dried (MgSO4) and solvent removed in vacuo.

3-(1-Cyano-cyclobutyl)-5-methyl-benzoic acid methyl ester 3(b). Under inert conditions compound 2 (0.375 g, 1.91 mmol) was dissolved in anhydrous DMF (10 mL) and the solution cooled with stirring to 0 °C. NaH (0.095 g, 2.35 mmol) was added drop wise over 5 min. The reaction was allowed to warm to room temperature and left to stir for 1 h. EtOAc (50 mL) was then added drop wise. The resulting suspension was left to stir at room temperature for 16 h. Propan-2-ol (5 mL) was carefully added to the reaction mixture followed by CH2Cl2 (50 mL) which was then washed with distilled H2O (50 mL) and brine (50 mL). Dried (MgSO4) and solvent removed in vacuo to leave a red/orange oil. Column chromatography (EtOAc/hexane 30:70) eluted 3(b) as a colourless oil (0.783 g, 43%). δH (270 MHz, CDCl3) 2.34-2.39 (3H, s, ArCH3), 3.79 (3H, s, ArCO2CH3), 7.39 (1H, s, ArH), 7.77 (1H, s, ArH) and 7.85 (1H, s, ArH); m/z (APCI+) 230 ([M - H]–, 22%), 203 ([M - CN]–, 100%); HRMS (ES+) 230.1176. C14H14NO2 requires 230.1176.

3-(I-Cyano-cyclobutyl)-5-methyl-benzoic acid methyl ester 3(c). Under inert conditions compound 2 (1.10 g, 5.69 mmol) was dissolved in anhydrous DMF (10 mL) and the solution cooled with stirring to 0 °C. NaH (0.233 g, 92.8 mmol) was added drop wise over 5 min. The reaction was allowed to warm to room temperature and left to stir for 1 h. EtOAc (50 mL) was then added drop wise. The resulting suspension was left to stir at room temperature for 16 h. Propan-2-ol (5 mL) was carefully added to the reaction mixture followed by CH2Cl2 (50 mL) which was then washed with distilled H2O (50 mL x 2) and brine (50 mL). Dried (MgSO4) and solvent removed in vacuo to leave a red/orange oil. Column chromatography (EtOAc/hexane 30:70) eluted 3(c) as a colourless oil (0.600 g, 35%), (Found: C, 72.3; H, 6.0; N, 6.4. C13H13NO2 requires C, 72.5; H, 6.1; N, 6.5 %). δH (270 MHz, CDCl3) 2.34-2.39 (3H, s, ArCH3), 3.79 (3H, s, ArCO2CH3), 7.39 (1H, s, ArH), 7.77 (1H, s, ArH) and 7.85 (1H, s, ArH); m/z (APCI+) 218 ([M - H]–, 100%), 192 ([M - CN]–, 100); HRMS (ES+) 218.1176. C13H13NO2 requires 218.1176.
mL) and washed with distilled H₂O (50 mL x 3) and brine (50 mL). Dried (MgSO₄) and solvent removed in vacuo to leave dark brown residues. Column chromatography (EtOAc/hexane 15:85 then EtOAc) eluted 5(a) as a brown solid (3.70 g, 60%), mp 78-79 °C. δH (270 MHz, CDCl₃) 1.72 (6H, s, ArC(CH₃)₂CN), 3.90 (3H, s, ArCO₂CH₃), 5.40 (2H, s, ArCH₂Br), 7.60 (1H, s, ArH), 7.85 (1H, s, ArH), 7.98 (1H, s, C₂H₃N₃), 8.07 (1H, s, ArH) and 8.14 (1H, s, C₂H₄N₂); m/z (APCI⁺) 285 ((M + H)⁺, 100%), 216 (45); HRMS (ES⁺) 285.1342. C₁₅H₁₇N₄O₂ requires 285.1346.

3-(1-Cyano-cyclobutyl)-5-[1,2,4]triazol-1-ylmethyl-benzoic acid methyl ester 5(b). Compound 5(b) was prepared from 4(b) using similar conditions to those described for the synthesis of compound 5(a). Column chromatography (EtOAc/hexane 50:50 then EtOAc) eluted 5(b) as a colourless viscous oil (0.410 g, 43%). δH (270 MHz, CDCl₃) 1.99-2.13 (1H, m, CH₂), 2.36-2.50 (1H, m, CH₂), 2.52-2.66 (2H, m, CH₂), 2.77-2.88 (2H, m, CH₂), 3.91 (3H, s, ArCO₂CH₃), 5.39 (2H, s, ArCH₂N), 7.49 (1H, s, ArH), 7.85 (1H, s, ArH), 7.97 (1H, s, C₂H₃N₃), 8.04 (1H, s, ArH) and 8.14 (2H, s, C₂H₄N₃); m/z (APCI⁺) 297 ((M + H)⁺, 100%), 214 (50); HRMS (ES⁺) 297.1335. C₁₆H₁₇N₄O₂ requires 297.1346.

3-(1-Cyano-cyclopropyl)-5-[1,2,4]triazol-1-ylmethyl-benzoic acid methyl ester 5(c). Compound 5(c) was prepared from 4(c) using similar conditions to those described for the synthesis of compound 5(a). Column chromatography (EtOAc/hexane 25:75 then EtOAc) eluted 5(c) as a colourless viscous oil (0.444 g, 59%) (Found: C, 63.5; H, 5.0; N, 19.8. C₁₅H₁₄N₄O₂ requires C, 63.8; H, 5.0; N, 19.9%). δH (270 MHz, CDCl₃) 1.39-1.45 (2H, dd, J = 3.0 & 5.8 Hz, CH₂), 1.76-1.80 (2H, dd, J = 3.0 & 5.8 Hz, CH₂), 3.89 (3H, s, ArCO₂CH₃), 5.38 (2H, s, ArCH₂N), 7.49 (1H, s, ArH), 7.80 (1H, s, ArH), 7.82 (1H, s, ArH), 7.98 (1H, s, C₂H₃N₃) and 8.12 (1H, s, C₂H₄N₃); m/z (APCI⁺) 283 ((M + H)⁺, 100%), 214 (75).

1-Bromo-3-bromomethyl-5-methylbenzene 20. Compound 20 was prepared from 5-bromo-m-xylene (16.76 g, 91.55 mmol) using similar conditions to those described for the synthesis of compound 1. Column chromatography (hexane) eluted 20 as a clear, colourless oil that crystallised on standing to give a white crystalline solid (14.5 g, 54.93 mmol, 60%), mp 57-60 °C. δH (270 MHz, CDCl₃) 2.31 (3H, s, ArCH₃), 4.38 (2H, s, ArCH₂Br), 7.11 (1H, s, ArH), 7.25 (1H, s, ArH) and 7.32 (1H, s, ArH).

(3-Bromo-5-methyl-phenyl)acetonitrile 21. Compound 21 was prepared from 20 (11.25 g, 42.65 mmol) using similar conditions to those described for the synthesis of compound 2. Column chromatography (hexane/CH₂Cl₂ 50:50) eluted 21 as a clear yellow oil (6.63 g, 31.56 mmol, 74%). δH (270 MHz, CDCl₃) 2.31 (3H, s, ArCH₃), 3.66 (2H, s, ArCH₂CN), 7.06 (1H, s, ArH), 7.25 (1H, s, ArH) and 7.27 (1H, s, ArH); m/z (APCI⁺) 212 ([81BrM + H]⁺, 53%), 210 ([79BrM + H]⁺, 55), 185 (80), 183 (76).

2-(3-Bromo-5-methylphenyl)-2-methyl-propionitrile 22. Compound 22 was prepared from 21 (6.0 g, 28.59 mmol) using similar conditions to those described for the synthesis of compound 3(a). Compound chromatography (hexane/CH₂Cl₂ 50:50) eluted 22 as a light yellow oil (5.65 g, 23.73 mmol, 83%). δH (270 MHz, CDCl₃) 1.68 (6H, s, ArC(CH₃)₂CN), 2.33 (3H, s, ArCH₃), 7.20 (1H, s, ArH), 7.26 (1H, s, ArH) and 7.34 (1H, s, ArH); m/z (APCI⁺) 240 ([81BrM + H]⁺, 3%), 238 ([79BrM + H]⁺, 4), 213 ([81BrM – CN]⁺, 100), 211 ([79BrM – CN]⁺, 96), 158 (18).

2-(3-Bromo-5-bromomethyl-phenyl)-2-methylpropionitrile 23. Compound 23 was prepared from 22 (5.06 g, 21.25 mmol) using similar conditions to those described for the synthesis of compound 1. Compound chromatography (hexane/CH₂Cl₂ 50:50) eluted 23 as a colourless viscous oil (3.64 g, 11.48 mmol, 54%). δH (270 MHz, CDCl₃) 1.71 (6H, s, ArC(CH₃)₂CN), 4.41 (2H, s, ArCH₂Br), 7.40-7.41 (1H, t, J = 1.7 Hz, ArH) and 7.48-7.51 (2H, m, ArH); m/z (FAB⁺) 319 ([81BrM + H]⁺, 100%), 317 ([79BrM + H]⁺, 100).