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X-ray crystallographic data of **34a**.

(1) Unit cell parameters and standard errors

a = 8.14 (1) Å, b = 19.952 (9) Å, c = 11.836 (7) Å, β = 106.57 (7)°, V = 1842 (2) Å

(2) The formula, formula weight, and number of formula units in the unit cell

$2C_9H_8N_2O{\cdot}C_6H_6O_2$, Mw = 402.45, Z = 4

(3) Measured and calculated densities

Dcalc = 1.45 g/cm^3, Dmeas: not measured

(4) Space group

*P*21/a

(5) Data

λ = 1.54178 Å, No. of observed = 1662, No. of measured = 3201

(6) Methods

Collection of intensity data: Diffractometer; Rigaku AFC5R, Scan type; w-2q, Scan rate; 8.0°/min

Structure solution: Direct method (SHELX 86)

Refinement: Full-matrix least-square

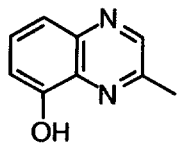
(7) Final R value

R = 0.057, Rw = 0.059

(8) Final difference Fourier map

maximum peak: 0.25 e$^-$/Å^3, minimum peak: -0.28 e$^-$/Å^3

(9) Structure



(10) Tables

(a)Final atomic positional parameters and B (eq) or B (iso)

atom	x	y	z	B(eq) or B(iso)
O(4s)	0.7062(5)	0.4441(2)	0.3522(4)	4.5(2)
O(12b)	0.2497(5)	0.2045(2)	0.3985(3)	4.3(2)
O(12a)	0.4813(6)	0.3506(2)	0.9182(4)	4.7(2)
N(1a)	0.5489(6)	0.2364(2)	0.7997(4)	3.5(2)
N(1b)	0.3161(6)	0.1579(2)	0.2052(4)	3.5(2)
N(4a)	0.6474(6)	0.2552(2)	0.5921(4)	3.8(2)
N(4b)	0.4095(6)	0.2470(2)	0.0489(4)	3.8(2)
C(1s)	0.8394(9)	0.5221(3)	0.5001(5)	3.4(3)
C(2b)	0.3583(8)	0.1362(3)	0.1112(5)	3.9(3)
C(2a)	0.5824(7)	0.1856(3)	0.7392(5)	3.6(3)
C(2s)	0.8541(9)	0.4708(3)	0.4247(5)	3.4(3)
C(3a)	0.6329(8)	0.1964(3)	0.6343(5)	4.1(3)
C(3b)	0.4045(8)	0.1818(3)	0.0337(5)	4.3(3)
C(3s)	1.0149(9)	0.4490(3)	0.4252(5)	3.7(3)
C(5b)	0.3661(7)	0.2710(3)	0.1450(5)	3.1(2)
C(5a)	0.6109(7)	0.3098(3)	0.6524(4)	3.3(3)
C(6b)	0.3686(9)	0.3399(3)	0.1662(6)	4.2(3)
C(6a)	0.6206(8)	0.3746(3)	0.6103(5)	4.0(3)
C(7b)	0.3285(8)	0.3628(3)	0.2635(6)	4.4(3)
C(7a)	0.5841(8)	0.4277(3)	0.6695(5)	4.1(3)
C(8b)	0.2872(8)	0.3181(3)	0.3437(5)	3.8(3)
C(8a)	0.5366(8)	0.4189(3)	0.7740(5)	3.9(3)
C(9b)	0.2840(7)	0.2507(3)	0.3255(5)	3.4(3)
C(9a)	0.5275(8)	0.3562(3)	0.8173(5)	3.6(3)
C(10b)	0.3223(7)	0.2250(3)	0.2236(4)	2.9(2)
C(10a)	0.5631(7)	0.2994(3)	0.7570(4)	3.2(3)

C(11b)	0.355(2)	0.0626(4)	0.088(1)	7.1(5)
C(11a)	0.570(1)	0.1151(4)	0.7806(8)	4.8(4)
H(1a)	0.662(6)	0.154(2)	0.589(4)	4(1)
H(1b)	0.447(7)	0.160(3)	-0.037(5)	7(2)
H(1s)	0.714(7)	0.532(3)	0.503(4)	6(2)
H(2b)	0.400(6)	0.369(2)	0.115(4)	4(1)
H(2a)	0.652(7)	0.384(3)	0.540(4)	5(2)
H(2s)	1.029(6)	0.412(2)	0.373(4)	4(1)
H(3a)	0.588(6)	0.480(2)	0.639(4)	5(1)
H(3b)	0.334(6)	0.415(3)	0.278(4)	5(1)
H(3s)	0.718(7)	0.404(3)	0.319(5)	5(2)
H(4b)	0.264(6)	0.337(2)	0.415(4)	3(1)
H(4a)	0.501(6)	0.457(2)	0.817(4)	4(1)
H(5b)	0.25(1)	0.040(4)	0.088(7)	13(4)
H(5a)	0.464(8)	0.106(3)	0.776(6)	7(2)
H(6b)	0.36(1)	0.051(4)	0.027(6)	9(3)
H(6a)	0.61(1)	0.079(4)	0.735(6)	12(3)
H(7b)	0.43(1)	0.039(4)	0.142(7)	12(3)
H(7a)	0.647(8)	0.107(3)	0.851(6)	8(2)
H(8b)	0.173(7)	0.220(3)	0.447(5)	8(2)
H(8a)	0.47(1)	0.311(3)	0.944(6)	10(2)

(b) Atomic thermal parameters

atom	U11	U22	U33	U12	U13	U23
O(4s)	0.054(3)	0.041(3)	0.069(3)	0.001(2)	0.005(2)	0.014(2)
C(1s)	0.044(5)	0.039(3)	0.050(4)	0.005(3)	0.018(3)	-0.003(3)
C(2s)	0.055(5)	0.029(3)	0.043(3)	-0.003(3)	0.010(3)	0.000(3)
C(3s)	0.061(5)	0.035(3)	0.045(4)	0.003(3)	0.019(3)	-0.008(3)
O(12b)	0.083(3)	0.046(2)	0.047(2)	-0.004(2)	0.039(2)	0.002(2)

N(1b)	0.054(4)	0.038(3)	0.041(3)	0.006(2)	0.013(3)	0.000(2)
N(4b)	0.059(4)	0.047(3)	0.043(3)	0.003(3)	0.020(3)	0.004(3)
C(2b)	0.062(5)	0.043(4)	0.043(4)	0.005(3)	0.012(3)	-0.003(3)
C(3b)	0.068(5)	0.055(4)	0.043(4)	0.009(4)	0.020(4)	-0.001(3)
C(5b)	0.038(4)	0.041(3)	0.040(3)	0.003(3)	0.012(3)	0.001(3)
C(6b)	0.069(5)	0.037(4)	0.061(4)	0.000(3)	0.034(4)	0.005(3)
C(7b)	0.068(5)	0.035(4)	0.071(5)	-0.006(3)	0.031(4)	-0.007(3)
C(8b)	0.056(5)	0.046(4)	0.049(4)	0.000(3)	0.024(3)	-0.010(3)
C(9b)	0.044(4)	0.043(4)	0.043(4)	0.002(3)	0.017(3)	0.000(3)
C(10b)	0.036(4)	0.033(3)	0.041(3)	0.001(3)	0.012(3)	0.001(3)
C(11b)	0.16(1)	0.041(5)	0.069(6)	0.009(6)	0.038(7)	-0.009(5)
O(12a)	0.089(4)	0.047(3)	0.056(3)	0.001(3)	0.042(3)	-0.002(2)
N(1a)	0.052(4)	0.041(3)	0.041(3)	0.001(2)	0.016(3)	0.001(2)
N(4a)	0.064(4)	0.045(3)	0.038(3)	-0.001(3)	0.020(3)	-0.005(2)
C(2a)	0.054(4)	0.038(3)	0.048(4)	0.001(3)	0.016(3)	0.000(3)
C(3a)	0.071(5)	0.042(4)	0.047(4)	0.001(4)	0.024(4)	-0.008(3)
C(5a)	0.048(4)	0.044(4)	0.037(3)	-0.001(3)	0.014(3)	0.002(3)
C(6a)	0.066(5)	0.048(4)	0.040(4)	-0.001(3)	0.020(4)	0.009(3)
C(7a)	0.067(5)	0.039(4)	0.052(4)	-0.001(4)	0.018(4)	0.003(3)
C(8a)	0.064(5)	0.039(4)	0.050(4)	0.001(3)	0.024(4)	-0.002(3)
C(9a)	0.057(5)	0.045(4)	0.040(3)	0.002(3)	0.021(3)	-0.002(3)
C(10a)	0.046(4)	0.037(3)	0.040(3)	0.000(3)	0.010(3)	0.002(3)
C(11a)	0.083(7)	0.036(4)	0.068(6)	-0.005(4)	0.029(5)	0.002(4)

(c) Bond distances

atom	atom	distance	ADC(*)	atom	atom	distance	ADC(*)
O4s	C2s	1.371(7)	1	C2a	C3a	1.431(7)	1
O12b	C9b	1.346(6)	1	C2a	C11a	1.501(9)	1
O12a	C9a	1.355(6)	1	C2s	C3s	1.377(8)	1

N1a	C2a	1.314(6)	1	C5b	C6b	1.399(7)	1
N1a	C10a	1.372(6)	1	C5b	C10b	1.422(7)	1
N1b	C2b	1.328(6)	1	C5a	C6a	1.395(7)	1
N1b	C10b	1.356(6)	1	C5a	C10a	1.415(7)	1
N4a	C3a	1.293(7)	1	C6b	C7b	1.362(8)	1
N4a	C5a	1.382(6)	1	C6a	C7a	1.350(8)	1
N4b	C3b	1.312(7)	1	C7b	C8b	1.411(8)	1
N4b	C5b	1.369(6)	1	C7a	C8a	1.408(8)	1
C1s	C2s	1.385(7)	1	C8b	C9b	1.362(7)	1
C1s	C3s	1.387(8)	76603	C8a	C9a	1.363(7)	1
C2b	C3b	1.418(8)	1	C9b	C10b	1.425(7)	1
C2b	C11b	1.492(9)	1	C9a	C10a	1.413(7)	1

O4s	H3s	0.90(5)	C7a	H3a	1.10(5)
O12b	H8b	1.01(6)	C8b	H4b	0.99(4)
O12a	H8a	0.87(7)	C8a	H4a	1.00(5)
C1s	H1s	1.05(5)	C11b	H5b	0.98(8)
C3a	H1a	1.06(5)	C11b	H6b	0.77(7)
C3b	H1b	1.08(6)	C11b	H7b	0.90(7)
C3s	H2s	0.99(5)	C11a	H5a	0.86(6)
C6b	H2b	0.92(5)	C11a	H6a	0.99(7)
C6a	H2a	0.95(5)	C11a	H7a	0.90(6)
C7b	H3b	1.05(5)			

Distances are in angstroms. Estimated standard deviations in the least significant figure are given in parentheses.

Bond angles

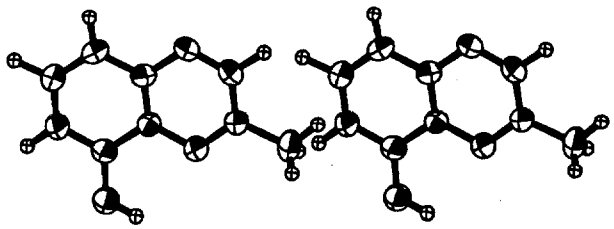
atom	atom	atom	angle	atom	atom	atom	angle
C2a	N1a	C10a	117.0(5)	N4a	C5a	C10a	119.3(5)

C2b	N1b	C10b	116.8(5)	C6a	C5a	C10a	120.5(5)
C3a	N4a	C5a	117.4(5)	C5b	C6b	C7b	119.2(6)
C3b	N4b	C5b	117.0(5)	C5a	C6a	C7a	119.9(6)
C2s	C1s	C3s	120.2(6)	C6b	C7b	C8b	121.2(6)
N1b	C2b	C3b	120.8(5)	C6a	C7a	C8a	120.9(6)
N1b	C2b	C11b	118.5(7)	C7b	C8b	C9b	121.0(6)
C3b	C2b	C11b	120.7(7)	C7a	C8a	C9a	120.2(6)
N1a	C2a	C3a	120.8(5)	O12b	C9b	C8b	124.9(5)
N1a	C2a	C11a	120.1(6)	O12b	C9b	C10b	115.7(5)
C3a	C2a	C11a	119.1(6)	C8b	C9b	C10b	119.4(5)
O4s	C2s	C1s	117.9(6)	O12a	C9a	C8a	117.8(5)
O4s	C2s	C3s	123.0(5)	O12a	C9a	C10a	121.9(5)
C1s	C2s	C3s	119.1(6)	C8a	C9a	C10a	120.3(5)
N4a	C3a	C2a	123.5(6)	N1b	C10b	C5b	122.5(5)
N4b	C3b	C2b	123.5(6)	N1b	C10b	C9b	118.9(5)
C1s	C3s	C2s	120.7(6)	C5b	C10b	C9b	118.6(5)
N4b	C5b	C6b	119.9(5)	N1a	C10a	C5a	119.8(5)
C6b	C5b	C10b	120.7(5)	C5a	C10a	C9a	118.1(5)
N4a	C5a	C6a	120.3(5)				
C2s	O4s	H3s	115(4)	C8a	C7a	H3a	117(3)
C9b	O12b	H8b	116(3)	C7b	C8b	H4b	118(3)
C9a	O12a	H8a	119(5)	C9b	C8b	H4b	121(3)
C2s	C1s	H1s	115(3)	C7a	C8a	H4a	122(3)
C3s	C1s	H1s	124(3)	C9a	C8a	H4a	117(3)
N4a	C3a	H1a	118(3)	C2b	C11b	H5b	116(6)
C2a	C3a	H1a	119(3)	C2b	C11b	H6b	118(6)
N4b	C3b	H1b	120(3)	C2b	C11b	H7b	115(6)
C2b	C3b	H1b	116(3)	H5b	C11b	H6b	96(7)
C1s	C3s	H2s	118(3)	H5b	C11b	H7b	102(7)

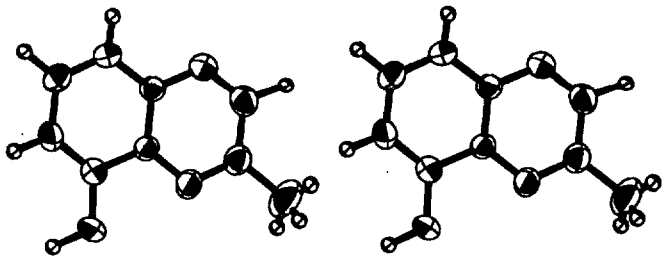
C2s	C3s	H2s	121(3)	H6b	C11b	H7b	108(8)
C5b	C6b	H2b	119(3)	C2a	C11a	H5a	109(5)
C7b	C6b	H2b	122(3)	C2a	C11a	H6a	117(4)
C5a	C6a	H2a	123(3)	C2a	C11a	H7a	112(4)
C7a	C6a	H2a	117(3)	H5a	C11a	H6a	105(6)
C6b	C7b	H3b	118(3)	H5a	C11a	H7a	116(6)
C8b	C7b	H3b	121(3)	H6a	C11a	H7a	98(6)
C6a	C7a	H3a	122(3)				

Angles are in degrees. Estimated standard deviations in the least significant figure are given in parentheses.

The stereo pair of 34a (1)



The stereo pair of 34a (2)



Physical Data of **12–14a,b**, **15b**, **16b–e**, **17b–e**, **18b–e**, **20b,d,e**, **21a–d,f**, **22**, **23**, **32**, **37**, **38**, **42b**, **43b**, **44a,b**, **45b**, **46a,b**, **47b**, **48a–c**, **49b,c**, **50c**, **51**, **52a–j,l,m**, **53**, **54b–d**, **55–61**, **62b,d–67a,b**, **68b–79**, **80b–83b,c,d**, **84–87a,c**, **88a,c–93b,c**, **94–99**, **103**, and **106**.

3-Benzyloxy-2-nitrobenzoic Acid (12). Using a similar procedure to that used for **83a**, the title compound was obtained in 91.2% yield from **11** as colorless crystals after crystallization from isopropyl ether: mp 201–202 °C; ^{1}H NMR (DMSO-d_6) δ 5.30 (2H, s), 7.29–7.47 (5H, m), 7.51–7.70 (3H, m). Anal. ($C_{14}H_{11}NO_5$) C, H, N.

***tert*-Butyl 3-Benzyloxy-2-nitrophenylcarbamate (13).** Using a similar procedure to that used for **6**, the title compound was obtained in 53.8% yield from **12**, DPPA, and *tert*-BuOH as pale yellow crystals after recrystallization from AcOEt: mp 143–144 °C; ^{1}H NMR ($CDCl_3$) δ 1.51 (9H, s), 5.18 (2H, s), 6.76 (1H, d, J = 7.5 Hz), 7.29–7.45 (6H, m), 7.59 (1H, br s), 7.79 (1H, d, J = 7.5 Hz); MS (FAB) m/z 345 (M + 1). Anal. ($C_{18}H_{20}N_2O_5$) C, H, N.

***tert*-Butyl 3-Benzyloxy-*N*-methyl-2-nitrophenylcarbamate (14a).** Following a procedure similar to method A, the title compound was obtained in 92.9% yield from **13** and methyl iodide as pale yellow crystals after recrystallization from hexane: mp 113–115 °C; ^{1}H NMR ($CDCl_3$) δ 1.38 (9H, br s), 3.19 (3H, s), 5.19 (2H, s), 6.87 (1H, br d, J = 7.5 Hz), 7.00 (1H, d, J = 7.5 Hz), 7.31–7.43 (6H, m). Anal. ($C_{19}H_{22}N_2O_5$) C, H, N.

***tert*-Butyl 3-Benzyloxy-*N*-ethyl-2-nitrophenylcarbamate (14b).** Following a procedure similar to method A, the title compound was obtained in 92.8% yield from **27** and ethyl iodide as pale yellow crystals after recrystallization from hexane: mp 88–90 °C; ^{1}H NMR ($CDCl_3$) δ 1.17 (3H, t, J = 7.5 Hz), 1.39 (9H, br s), 3.41–3.80 (2H, m), 5.19 (2H, s), 6.86 (1H, br d, J = 7.5 Hz), 7.01 (1H, d, J = 7.5 Hz), 7.29–7.32 (6H, m); MS (ESI) m/z 373 (M + 1). Anal. ($C_{20}H_{24}N_2O_5$) C, H, N.

3-Benzyloxy-1-ethyl-2-nitroaniline (15b). Using a similar procedure to that used for **15a**, the title compound was obtained in 94.9% yield from **14b** as a yellow oil:

^{1}H NMR ($CDCl_3$) δ 1.30 (3H, t, J = 7.5 Hz), 3.13 (2H, q, J = 7.5 Hz), 5.16 (2H, s), 6.31 (1H, d, J = 7.5 Hz), 6.38 (1H, d, J = 7.5 Hz), 7.21 (1H, t, J = 7.5 Hz), 7.28–7.49 (5H, m). Anal. ($C_{15}H_{16}N_2O_3$) C, H, N.

1-(*N*-Acetyl-*N*-ethyl)-3-benzyloxy-2-nitroaniline (16b). Using a similar procedure to that used for **16a**, the title compound was obtained in 67.3% yield from **15b** and acetyl chloride as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.15 (3H, t, J = 7.5 Hz), 2.18 (3H, S), 3.16–4.10 (2H, m), 5.13 (2H, s), 6.90 (1H, d, J = 7.5 Hz), 7.18 (1H, d, J = 7.5 Hz), 7.33–7.50 (6H, m). Anal. ($C_{17}H_{18}N_2O_4$) C, H, N.

4-Benzyloxy-1-ethyl-2-methyl-1*H*-benzimidazole (17b). Using a similar procedure to that used for **17a**, the title compound was obtained in 34.2% yield from **16b** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.40 (3H, t, J = 7.5 Hz), 2.61 (3H, s), 4.13 (2H, q, J = 7.5 Hz), 5.37 (2H, s), 6.67 (1H, d, J = 7.5 Hz), 6.91 (1H, d, J = 7.5 Hz), 7.09 (1H, t, J = 7.5 Hz), 7.26-7.40 (3H, m), 7.51 (2H, br d, J = 7.5 Hz); MS (FAB) m/z 374 (M + 1). Anal. ($C_{17}H_{18}N_2O$) C, H, N.

1-Ethyl-4-hydroxy-2-methyl-1*H*-benzimidazole (18b). Using a similar procedure to that used for **18a**, the title compound was obtained in 89.9% yield from **17b** as pale brown crystals after crystallization from isopropyl ether: mp 187–190 °C; ^{1}H NMR ($CDCl_3$) δ 1.40 (3H, t, J = 7.5 Hz), 2.68 (3H, s), 4.13 (2H, q, J = 7.5 Hz), 6.81 (1H, d, J = 7.5 Hz), 6.84 (1H, d, J = 7.5Hz), 7.17 (1H, t, J = 7.5 Hz); MS (FAB) m/z 177 (M + 1). Anal. ($C_{10}H_{12}N_2O$) C, H, N.

3-Benzyloxy-1-(*N*-methoxyacetyl-*N*-methyl)-2-nitroaniline (16c). Using a similar procedure to that used for **16a**, the title compound was obtained in 92.7% yield from **15a** and methoxyacetyl chloride as colorless crystals after crystallization from isopropyl ether: mp 111–113 °C; ^{1}H NMR ($CDCl_3$) δ 3.20 (3H, S), 3.34 (3H, S), 3.79 (1H, d, J = 15 Hz), 3.87 (1H, d, J = 15 Hz), 5.22 (2H, s), 6.89 (1H, d, J = 7.5 Hz), 7.13 (1H, d, J = 7.5Hz), 7.29–7.42 (5H, m), 7.45 (1H, t, J = 7.5 Hz); MS (ESI) m/z 331 (M + 1). Anal. ($C_{17}H_{18}N_2O_5$) C, H, N.

4-Benzyloxy-2-methoxymethyl-1-methyl-1*H*-benzimidazole (17c). Using a similar procedure to that used for **17a**, the title compound was obtained in 76.7% yield from **16c** as pale gray crystals after crystallization from isopropyl ether: mp 120–122 °C; ^{1}H NMR ($CDCl_3$) δ 3.38 (3H, s), 3.82 (3H, s), 4.78 (2H, s), 5.38 (2H, s), 6.67 (1H, d, J = 7.5 Hz), 6.93 (1H, d, J = 7.5 Hz), 7.14 (1H, t, J = 7.5 Hz), 7.23-7.39 (3H, m), 7.51 (2H, br d, J = 7.5 Hz); MS (ESI) m/z 283 (M + 1). Anal. ($C_{17}H_{18}N_2O_2$) C, H, N.

4-Hydroxy-2-methoxymethyl-1-methyl-1*H*-benzimidazole (18c). Using a similar procedure to that used for **18a**, the title compound was obtained in 89.9% yield from **17c** as pale gray crystals after crystallization from isopropyl ether: mp 162–163 °C; ^{1}H NMR ($CDCl_3$) δ 3.33 (3H, s), 3.81 (3H, s), 4.81 (2H, s), 6.85 (1H, d, J = 7.5 Hz), 6.87 (1H, d, J = 7.5 Hz), 7.22 (1H, t, J = 7.5 Hz); MS (ESI) m/z 193 (M + 1). Anal. ($C_{10}H_{12}N_2O_2$) C, H, N.

3-Benzyloxy-1-(*N*-ethoxycarbonylacetyl-*N*-methyl)-2-nitroaniline (16d). Using a similar procedure to that used for **16a**, the title compound was obtained in 93.3% yield from **15a** and ethyl malonyl chloride as a yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.24 (3H, t, J = 7.5 Hz), 3.21 (3H, S), 3.23 (2H, S), 4.15 (2H, S), 5.21 (2H, s), 6.99 (1H, d, J = 7.5 Hz), 7.14 (1H, d, J = 7.5 Hz), 7.32–7.52 (6H, m); MS (ESI) m/z 373 (M + 1). Anal. ($C_{19}H_{20}N_2O_6$) C, H, N.

4-Benzyloxy-2-ethoxycarbonylmethyl-1-methyl-1*H*-benzimidazole (17d). Using a similar procedure to that used for **17a**, the title compound was obtained in 31.3% yield from **16d** as colorless crystals after crystallization from diethyl ether: mp 105–106 °C; ^{1}H NMR ($CDCl_3$) δ 1.28 (3H, t, J = 7 Hz), 3.76 (3H, s), 4.06 (2H, s), 4.20 (2H, q, J = 7 Hz), 5.37 (2H, s), 6.69 (1H, d, J = 7.5 Hz), 6.93 (1H, d, J = 7.5 Hz), 7.13 (1H, t, J = 7.5 Hz), 7.25-7.39 (3H, m), 7.50 (2H, br d, J = 7.5 Hz); MS (ESI) m/z 325 (M + 1). Anal. ($C_{19}H_{20}N_2O_3$) C, H, N.

2-Ethoxycarbonylmethyl-4-hydroxy-1-methyl-1*H*-benzimidazole (18d). Using a similar procedure to that used for **18a**, the title compound was obtained in 75.6% yield from **17d** as pale gray crystals after crystallization from diethyl ether: mp 167–170

°C; ^{1}H NMR ($CDCl_3$) δ 1.23 (3H, t, J = 7 Hz), 3.72 (3H, s), 4.13 (2H, s), 4.17 (2H, q, J = 7 Hz), 6.81 (1H, d, J = 7.5 Hz), 6.84 (1H, d, J = 7.5 Hz), 7.19 (1H, t, J = 7.5 Hz); MS (ESI) m/z 235 (M + 1). Anal. ($C_{12}H_{14}N_2O_3$) C, H, N.

1-(*N*-Benzoyl-*N*-methyl)-3-benzyloxy-2-nitroaniline (16e). Using a similar procedure to that used for **16a**, the title compound was obtained in 93.3% yield from **15a** and benzoyl chloride as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 3.37 (3H, S), 5.17 (2H, S), 6.60 (1H, br d, J = 7.5 Hz), 6.93 (1H, d, J = 7.5 Hz), 7.12–7.50 (11H, m). Anal. ($C_{22}H_{20}N_2O_4$) C, H, N.

4-Benzyloxy-1-methyl-2-phenyl-1*H*-benzimidazole (17e). Using a similar procedure to that used for **17a**, the title compound was obtained in 86.0% yield from **16e** as colorless crystals after crystallization from diethyl ether: mp 118–120 °C; ^{1}H NMR ($CDCl_3$) δ 3.85 (3H, s), 5.47 (2H, s), 6.73 (1H, d, J = 7.5 Hz), 6.99 (1H, d, J = 7.5 Hz), 7.17 (1H, t, J = 7.5 Hz), 7.25–7.39 (3H, m), 7.48–7.57 (5H, m), 7.77–7.84 (2H, m). Anal. ($C_{21}H_{18}N_2O$) C, H, N.

4-Hydroxy-1-methyl-2-phenyl-1*H*-benzimidazole (18e). Using a similar procedure to that used for **18a**, the title compound was obtained in 68.5% yield from **17e** as pale gray crystals after crystallization from EtOH: mp 210–211 °C; ^{1}H NMR (DMSO-d_6) δ 3.82 (3H, s), 6.59 (1H, d, J = 7.5 Hz), 7.00 (1H, d, J = 7.5 Hz), 7.07 (1H, t, J = 7.5 Hz), 7.50-7.62 (3H, m), 7.79–7.87 (2H, m). Anal. ($C_{14}H_{12}N_2O$) C, H, N.

4-Hydroxy-2-Methoxy-1-methyl-1*H*-benzimidazole (21a). Using a similar procedure to that used for **18a**, the title compound was obtained in 87.4% yield from **20a** as colorless crystals after crystallization from diethyl ether: mp 226–229 °C; ^{1}H NMR (DMSO-d_6) δ 3.48 (3H, s), 4.08 (3H, s), 6.49 (1H, d, J = 7.5 Hz), 6.76 (1H, d, J = 7.5 Hz), 6.88 (1H, t, J = 7.5 Hz), 9.39 (1H, br s). Anal. ($C_9H_{10}N_2O_2$) C, H, N.

4-Benzyloxy-2-ethoxy-1-methyl-1*H*-benzimidazole (20b). Using a similar procedure to that used for **20a**, the title compound was obtained in 85.1% yield from **19** as colorless crystals after crystallization from hexane–isopropyl ether: mp 99–100 °C; ^{1}H

NMR ($CDCl_3$) δ 1.47 (3H, t, J = 7.5 Hz), 3.51 (3H, s), 4.66 (2H, q, J = 7.5 Hz), 5.40 (2H, s), 6.61 (1H, d, J = 7.5 Hz), 6.75 (1H, d, J = 7.5 Hz), 6.97 (1H, t, J = 7.5 Hz), 7.22–7.38 (3H, m), 7.49 (2H, d, J = 7.5 Hz). Anal. ($C_{17}H_{18}N_2O_2$) C, H, N.

2-Ethoxy-4-hydroxy-1-methyl-1*H*-benzimidazole (21b). Using a similar procedure to that used for **19a**, the title compound was obtained in 72.6% yield from **20b** as colorless crystals after crystallization from hexane–isopropyl ether: mp 164–165 °C; ^{1}H NMR ($CDCl_3$) δ 1.43 (3H, t, J = 6.5 Hz), 3.51 (3H, s), 4.54 (2H, q, J = 6.5 Hz), 6.71 (2H, d, J = 7.5 Hz), 7.03 (1H, t, J = 7.5 Hz), 8.05 (1H, br s). Anal. ($C_{10}H_{12}N_2O_2$) C, H, N.

4-Hydroxy-1-methyl-2-methylamino-1*H*-benzimidazole (21c). Using a similar procedure to that used for **18a**, the title compound was obtained in 73.9% yield from **20c** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 3.09 (3H, s), 3.48 (3H, s), 6.60 (1H, d, J = 7.5 Hz), 6.69 (1H, d, J = 7.5 Hz), 6.98 (1H, t, J = 7.5 Hz); MS (ESI) m/z 178 (M + 1). Anal. ($C_9H_{11}N_3O$) C, H, N.

4-Benzyloxy-2-dimethylamino-1-methyl-1*H*-benzimidazole (20d). Following a procedure similar to method A, the title compound was obtained in 47.5% yield from **20c** and methyl iodide as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 2.99 (6H, s), 3.61 (3H, s), 5.40 (2H, s), 6.60 (1H, d, J = 8 Hz), 6.79 (1H, d, J = 8 Hz), 6.98 (1H, t, J = 8 Hz), 7.29–7.43 (3H, m), 7.50 (2H, d, J = 8 Hz); MS (ESI) m/z 282 (M + 1). Anal. ($C_{17}H_{19}N_3O$) C, H, N.

2-Dimethylamino-4-hydroxy-1-methyl-1*H*-benzimidazole (21d). Using a similar procedure to that used for **18a**, the title compound was obtained in 78.0% yield from **20d** as pale brown crystals after crystallization from isopropyl ether: mp 177–179 °C; ^{1}H NMR ($CDCl_3$) δ 2.93 (6H, s), 3.60 (3H, s), 6.71 (2H, br d, J = 8 Hz), 7.03 (1H, t, J = 8 Hz); MS (ESI) m/z 192 (M + 1). Anal. ($C_{10}H_{13}N_3O$) C, H, N.

(±)-4-Benzyloxy-2-(1-hydroxyethyl)-1-methyl-1*H*-benzimidazole (20e). Using a similar procedure to that used for **8**, the title compound was obtained in 19.4%

yield from **19** and lactic acid as colorless crystals after crystallization from diethyl ether: mp 149–151 °C; ^{1}H NMR (DMSO-d_6) δ 1.57 (3H, t, J = 7.5 Hz), 3.81 (3H, s), 5.03 (1H, quint, J = 7.5 Hz), 5.33 (2H, s), 5.55 (1H, d, J = 7.5 Hz), 6.77 (1H, dd, J = 7.5, 2.5 Hz), 7.07–7.14 (2H, m), 7.29–7.43 (3H, m), 7.50 (2H, d, J = 7.5 Hz); MS (ESI) m/z 283 (M + 1). Anal. ($C_{17}H_{18}N_2O_2$) C, H, N.

2-Acetyl-4-hydroxy-1-methyl-1*H*-benzimidazole (21f). Using a similar procedure to that used for **18a**, the title compound was obtained in 92.5% yield from **20f** as pale brown crystals after crystallization from isopropyl ether: mp 154–155 °C; ^{1}H NMR ($CDCl_3$) δ 2.80 (3H, s), 4.11 (3H, s), 6.83 (1H, d, J = 8.5 Hz), 6.96 (1H, d, J = 8.5 Hz), 7.33 (1H, t, J = 8.5 Hz); MS (ESI) m/z 191 (M + 1). Anal. ($C_{10}H_{10}N_2O_2$) C, H, N.

3-Hydroxy-1-methyl-1,2-phenylenediamine (22). Using a similar procedure to that used for **18a**, the title compound was obtained in 91.8% yield from **15a** as brown solid after crystallization from hexane–isopropyl ether: mp 94–97 °C; ^{1}H NMR (DMSO-d_6) δ 2.68 (3H, d, J = 4.5 Hz), 3.80 (2H, br s), 4.52 (1H, q, J = 4.5 Hz), 5.98 (1H, d, J = 8.5 Hz), 6.13 (1H, d, J = 8.5 Hz), 6.38 (1H, t, J = 8.5 Hz), 8.73 (1H, br s); MS (ESI) m/z 139 (M + 1). Anal. ($C_7H_{10}N_2O$) C, H, N.

3-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-1-methyl-1,2-phenylenediamine (23). Following a procedure similar to method A, the title compound was obtained in 69.8% yield from **22** and **50b** as a brown amorphous solid: ^{1}H NMR (DMSO-d_6) δ ^{1}H NMR ($CDCl_3$) δ 2.24 (3H, s), 2.40 (3H, s), 2.71 (3H, d, J = 5 Hz), 2.79 (3H, d, J = 5 Hz), 3.10 (3H, s), 3.50 (1H, dd, J = 17, 5 Hz), 3.67 (1H, dd, J = 17, 5 Hz), 3.96 (2H, br s), 4.68 (1H, q, J = 5 Hz), 5.03 (2H, s), 6.20 (1H, d, J = 8 Hz), 6.49–6.59 (2H, m), 6.88 (1H, d, J = 15 Hz), 7.22 (1H, d, J = 8 Hz), 7.27 (1H, d, J = 8 Hz), 7.42 (1H, d, J = 15 Hz), 7.63 (2H, d, J = 8 Hz), 7.85 (2H, d, J = 8 Hz), 8.25

(1H, t, J = 5 Hz), 8.48 (1H, q, J = 5 Hz); MS (ESI) m/z 530 (M + 1). Anal. ($C_{30}H_{35}N_5O_4$) C, H, N.

8-Hydroxy-2-methylquinazoline (32). Using a similar procedure to that used for **9**, the title compound was obtained in 71.7% yield from **31** as colorless crystals after crystallization from isopropyl ether: mp 135–137 °C; ^{1}H NMR ($CDCl_3$) δ 2.89 (3H, s), 7.32 (1H, d, J = 7.5 Hz), 7.41 (1H, d, J = 7.5 Hz), 7.49 (1H, t, J = 7.5 Hz), 9.30 (1H, s); MS (FAB) m/z 161 (M + 1). Anal. ($C_9H_8N_2O$) C, H, N.

7-Methoxy-2-methylquinoline (37). Using a similar procedure to that used for **31**, the title compound was obtained in 95.0% yield from **36b** as a colorless oil: ^{1}H NMR ($CDCl_3$) δ 2.61 (3H, s), 4.00 (3H, s), 6.80 (1H, dd, J = 8, 2 Hz), 7.27 (1H, d, J = 2 Hz), 7.52–7.62 (2H, m), 8.47 (1H, d, J = 8 Hz). Anal. ($C_{11}H_{11}NO$) C, H, N.

7-Hydroxy-2-methylquinoline (38). Using a similar procedure to that used for **9**, the title compound was obtained in 81.8% yield from **37** as colorless crystals after crystallization from isopropyl ether: mp 245–246 °C; ^{1}H NMR (DMSO-d_6) δ 2.61 (3H, s), 6.85 (1H, d, J = 8 Hz), 7.30 (1H, d, J = 8 Hz), 7.36 (1H, d, J = 8 Hz), 8.39 (1H, d, J = 8 Hz). Anal. ($C_{10}H_9NO$) C, H, N.

3-Amino-1-(*tert*-butyldiphenylsiloxymethyl)-2,6-dichlorobenzene (44a). Using a similar procedure to that used for **19**, the title compound was obtained in 87.1% yield from **43a** as colorless crystals after crystallization from MeOH: mp 117–118 °C; ^{1}H NMR ($CDCl_3$) δ 1.05 (9H, s), 4.07 (2H, br s), 4.87 (2H, s), 6.66 (1H, d, J = 9 Hz), 7.08 (1H, d, J = 9 Hz), 7.30–7.50 (6H, m), 7.70–7.84 (4H, m). Anal. ($C_{23}H_{25}Cl_2NOSi$) C, H, N.

1-(*tert*-Butyldiphenylsiloxymethyl)-2,6-dichloro-3-[*N*-methyl-*N*-(phthalimidoacetyl)amino]benzene (46a). Following a procedure similar to method A, the title compound was obtained in 88.5% yield from **45a** and methyl iodide as colorless crystals after crystallization from isopropyl ether: mp 167–172 °C; ^{1}H NMR

($CDCl_3$) δ 1.06 (9H, s), 3.20 (3H, s), 4.04 (2H, s), 4.98 (2H, s), 7.31–7.51 (9H, m), 7.65–7.79 (6H, m), 7.80–7.92 (2H, m). Anal. ($C_{34}H_{32}Cl_2N_2O_4Si$) C, H, N.

1-[*tert*-Butyldiphenylsiloxymethyl]-2,6-dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzene (48a). Following a procedure similar to method E, the title compound was obtained in 88.6% yield from **47a** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[23] as pale yellow crystals after crystallization from AcOEt: mp 219–222 °C; ^{1}H NMR ($CDCl_3$) δ 1.05 (9H, s), 3.02 (3H, d, *J* = 5 Hz), 3.21 (3H, s), 3.56 (1H, dd, *J* = 17, 4 Hz), 3.93 (1H, dd, *J* = 17, 5 Hz), 4.91 (1H, d, *J* = 10 Hz), 4.98 (1H, d, *J* = 10 Hz), 6.15 (1H, br d, *J* = 5 Hz), 6.51 (1H, d, *J* = 15 Hz), 6.63 (1H, br s), 7.19–7.28 (2H, m), 7.32–7.48 (6H, m), 7.50–7.60 (3H, m), 7.68–7.78 (6H, m); MS (FAB) *m*/*z* 688 (M + 1). Anal. ($C_{37}H_{39}Cl_2N_3O_4Si$) C, H, N.

2,6-Dimethyl-3-nitrobenzyl alcohol (42b). Using a similar procedure to that used for **82a**, the title compound was obtained in 80.9% yield from **41** as pale yellow crystals after recrystallization from isopropyl ether: mp 100–102 °C; ^{1}H NMR ($CDCl_3$) δ 1.44 (1H, t, *J* = 5 Hz), 2.50 (3H, s), 2.56 (3H, s), 4.82 (2H, d, *J* = 5 Hz), 7.17 (1H, d, *J* = 8 Hz), 7.66 (1H, d, *J* = 8 Hz). Anal. ($C_9H_{11}NO_3$) C, H, N.

1-(*tert*-Butyldiphenylsiloxymethyl)-2,6-dimethyl-3-nitrobenzene (43b). Using a similar procedure to that used for **42a**, the title compound was obtained in 96.2% yield from **42b** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.03 (9H, s), 2.20 (3H, s), 2.38 (3H, s), 5.73 (2H, s), 7.06 (1H, d, *J* = 8 Hz), 7.33–7.49 (6H, m), 7.58–7.73 (5H, m). Anal. ($C_{25}H_{29}NO_3Si$) C, H, N.

3-Amino-1-(*tert*-butyldiphenylsiloxymethyl)-2,6-dichlorobenzene (44b). Using a similar procedure to that used for **19**, the title compound was obtained in 97.8% yield from **43b** as a pale yellow oil: ^{1}H NMR ($CDCl_3$) δ 1.04 (9H, s), 2.09 (3H, s), 2.11 (3H, s), 3.48 (2H, br s), 4.70 (2H, s), 6.58 (1H, d, *J* = 8 Hz), 6.71 (1H, d, *J* = 8 Hz), 7.33–7.48 (6H, m), 7.66–7.73 (4H, m); MS (ESI) *m*/*z* 390 (M + 1). Anal. ($C_{25}H_{31}NOSi$) C, H, N.

1-(*tert*-Butyldiphenylsiloxymethyl)-2,6-dimethyl-3-(*N*-phthalimidoacetyl)aminobenzene (45b). Using a similar procedure to that used for **45a**, the title compound was obtained in 93.6% yield from **44b** and *N*-phthalimidoacetyl chloride as colorless crystal after crystallization from MeCN: mp 207–210 °C; ^{1}H NMR ($CDCl_3$) δ 1.02 (9H, s), 2.12 (3H, s), 2.19 (3H, s), 4.52 (2H, s), 4.70 (2H, s), 6.95 (1H, d, J = 8 Hz), 7.25–7.50 (7H, m), 7.63–7.80 (6H, m), 7.86–7.96 (2H, m); MS (ESI) m/z 577 (M + 1). Anal. ($C_{35}H_{36}N_2O_4Si$) C, H, N.

1-(*tert*-Butyldiphenylsiloxymethyl)-2,6-dimethyl-3-[*N*-methyl-*N*-(*N*-phthalimidoacetyl)amino]benzene (46b). Following a procedure similar to method A, the title compound was obtained in 69.2% yield from **45b** and methyl iodide as colorless crystals after crystallization from AcOEt: mp 180–182 °C; ^{1}H NMR ($CDCl_3$) δ 1.04 (9H, s), 2.21 (3H, s), 2.27 (3H, s), 3.17 (3H, s), 3.82 (1H, d, J = 17 Hz), 4.12 (1H, d, J = 17 Hz), 4.78 (2H, s), 7.09 (1H, d, J = 8 Hz), 7.15 (1H, d, J = 8 Hz), 7.34–7.49 (6H, m), 7.65–7.73 (6H, m), 7.80–7.88 (2H, m); MS (ESI) m/z 591 (M + 1). Anal. ($C_{36}H_{38}N_2O_4Si$) C, H, N.

3-[*N*-Aminoacetyl-*N*-methylamino]-1-[*tert*-butyldiphenylsiloxymethyl]-2,6-dimethylbenzene (47b). Using a similar procedure to that used for **47a**, the title compound was obtained in 93.5% yield from **46b** as a pale yellow amorphous solid: ^{1}H NMR ($CDCl_3$) δ 1.03 (9H, s), 2.02 (3H, s), 2.22 (3H, s), 2.82 (1H, d, J = 17 Hz), 3.09 (1H, d, J = 17 Hz), 3.15 (3H, s), 4.72 (2H, s), 6.92 (1H, d, J = 8 Hz), 7.01 (1H, d, J = 8 Hz), 7.32–7.49 (6H, m), 7.62–7.70 (4H, m); MS (ESI) m/z 461 (M + 1). Anal. ($C_{28}H_{36}N_2O_2Si$) C, H, N.

1-[*tert*-Butyldiphenylsiloxymethyl]-2,6-dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzene (48b). Following a procedure similar to method E, the title compound was obtained in 69.2% yield from **47b** and (*E*)-4-(*N*-methylcarbamoyl)cinnamic acid[23] as pale yellow crystals after crystallization from AcOEt: mp 204–208 °C; ^{1}H NMR ($CDCl_3$) δ 1.05 (9H, s), 2.05 (3H, s), 2.26 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.20 (3H, s), 3.52 (1H, dd, J = 17, 5 Hz), 3.87 (1H, dd, J =

17, 5 Hz), 4.73 (2H, s), 6.16 (1H, br d, J = 5 Hz), 6.51 (1H, d, J = 15 Hz), 6.69 (1H, br t, J = 5 Hz), 6.98 (1H, d, J = 8 Hz), 7.06 (1H, d, J = 8 Hz), 7.35–7.48 (6H, m), 7.51–7.60 (3H, m), 7.65–7.80 (6H, m); MS (ESI) m/z 648 (M + 1). Anal. ($C_{39}H_{45}N_3O_3Si$) C, H, N.

3-[*N*-[(*E*)-3-(6-Acetylaminopyridin-3-yl)acryloylglycyl]-*N*-methylamino]-1-(*tert*-butyldiphenylsiloxymethyl)-2,6-dimethylbenzene (48c). Following a procedure similar to method E, the title compound was obtained in 76.2% yield from **47b** and (*E*)-3-(6-acetamidopyridine-3-yl)acrylic acid[23] as colorless crystals after crystallization from AcOEt: mp 200–202 °C; ^{1}H NMR ($CDCl_3$) δ 1.05 (9H, s), 2.04 (3H, s), 2.21 (3H, s), 2.26 (3H, s), 3.20 (3H, s), 3.52 (1H, dd, J = 17, 5 Hz), 3.87 (1H, dd, J = 17, 5 Hz), 4.73 (2H, s), 6.45 (1H, d, J = 15 Hz), 6.69 (1H, br t, J = 5 Hz), 6.98 (1H, d, J = 8 Hz), 7.07 (1H, d, J = 8 Hz), 7.35–7.47 (6H, m), 7.64–7.71 (4H, m), 7.84 (1H, dd, J = 8, 3 Hz), 8.06 (1H, br s), 8.21 (1H, br d, J = 8 Hz), 8.35 (1H, br s); MS (ESI) m/z 649 (M + 1). Anal. ($C_{38}H_{44}N_4O_4Si$) C, H, N.

2,6-Dimethyl-1-hydroxymethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzene (49b). Using a similar procedure to that used for **49a**, the title compound was obtained in 95.8% yield from **48b** as colorless crystals after crystallization from AcOEt: mp 261–263 °C; ^{1}H NMR (DMSO-d_6) δ 2.27 (3H, s), 2.40 (3H, s), 2.79 (3H, d, J = 5 Hz), 3.08 (3H, s), 3.43 (1H, dd, J = 17, 5 Hz), 3.65 (1H, dd, J = 17, 5 Hz), 4.53 (2H, d, J = 5 Hz), 4.88 (1H, t, J = 5 Hz), 6.89 (1H, d, J = 15 Hz), 7.15 (2H, s), 7.41 (1H, d, J = 15 Hz), 7.64 (2H, d, J = 8 Hz), 7.85 (2H, d, J = 8 Hz), 8.21 (1H, br t, J = 5 Hz), 8.48 (1H, br d, J = 8 Hz); MS (ESI) m/z 410 (M + 1). Anal. ($C_{23}H_{27}N_3O_4$) C, H, N.

3-[*N*-[(*E*)-3-[6-Acetylaminopyridin-3-yl]acryloylglycyl]-*N*-methylamino]-1-hydroxymethyl-2,6-dimethylbenzene (49c). Using a similar procedure to that used for **49a**, the title compound was obtained in 97.7% yield from **48c** as colorless crystals after crystallization from AcOEt: mp 215–216 °C; ^{1}H NMR (DMSO-d_6) δ 2.27 (3H, s), 2.40 (3H, s), 2.79 (3H, d, J = 5 Hz), 3.08 (3H, s), 3.43 (1H, dd, J =

17, 5 Hz), 3.65 (1H, dd, J = 17, 5 Hz), 4.53 (2H, d, J = 5 Hz), 4.88 (1H, t, J = 5 Hz), 6.89 (1H, d, J = 15 Hz), 7.15 (2H, s), 7.41 (1H, d, J = 15 Hz), 7.64 (2H, d, J = 8 Hz), 7.85 (2H, d, J = 8 Hz), 8.21 (1H, br t, J = 5 Hz), 8.48 (1H, br d, J = 8 Hz); MS (ESI) m/z 411 (M + 1). Anal. ($C_{22}H_{26}N_4O_4$) C, H, N.

3-[*N*-[(*E*)-3-[6-Acetylaminopyridin-3-yl]acryloylglycyl]-*N*-methylamino]-1-chloromethyl-2,6-dimethylbenzene (50c). Using a similar procedure to that used for **50b**, the title compound was obtained in 91.4% yield from **48c** as pale yellow crystals after crystallization from AcOEt–hexane: mp 218–221 °C; ^{1}H NMR (DMSO-d_6) δ 2.11 (3H, s), 2.28 (3H, s), 2.43 (3H, s), 3.09 (3H, s), 3.41 (1H, dd, J = 17, 5 Hz), 3.60 (1H, dd, J = 17, 5 Hz), 4.84 (2H, s), 6.76 (1H, d, J = 15 Hz), 7.21 (1H, d, J = 8 Hz), 7.27 (1H, d, J = 8 Hz), 7.37 (1H, d, J = 15 Hz), 7.98 (1H, dd, J = 8, 2 Hz), 8.11 (1H, d, J = 8 Hz), 8.17 (1H, t, J = 5 Hz), 8.17 (1H, br t, J = 5 Hz), 8.47 (1H, d, J = 2 Hz); MS (ESI) m/z 429 (M + 1). Anal. ($C_{22}H_{25}ClN_4O_3$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylbenzoxazole (51). Following a procedure similar to method A, the title compound was obtained in 85.7% yield from **50a** and 4-hydroxy-2-methylbenzoxazole as a colorless amorphous solid; ^{1}H NMR ($CDCl_3$) δ 2.61 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.28 (3H, s), 3.67 (1H, dd, J = 17, 4 Hz), 3.94 (1H, dd, J = 17, 5 Hz), 5.58 (1H, d, J = 10 Hz), 5.61 (1H, d, J = 10 Hz), 6.15 (1H, br d, J = 5 Hz), 6.52 (1H, d, J = 15 Hz), 6.68 (1H, br s), 6.93 (1H, d, J = 7.5 Hz), 7.16 (1H, d, J = 7.5 Hz), 7.21–7.35 (3H, m), 7.46–7.62 (3H, m), 7.76 (2H, d, J = 7.5 Hz); MS (FAB) m/z 581 (M + 1). Anal. ($C_{29}H_{26}Cl_2N_4O_5$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-1,2-dimethyl-1*H*-benzimidazole (52a). Following a procedure similar to method A, the title compound was obtained in 85.7% yield from **9** and **50a** as a colorless amorphous solid; ^{1}H NMR ($CDCl_3$) δ 2.58 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.28 (3H, s), 3.61–3.72 (4H, m), 3.93

(1H, dd, J = 17, 5 Hz), 5.52 (1H, d, J = 10 Hz), 5.58 (1H, d, J = 10 Hz), 6.20 (1H, br d, J = 5 Hz), 6.52 (1H, d, J = 15 Hz), 6.70 (1H, br s), 6.88 (1H, d, J = 7.5 Hz), 6.98 (1H, d, J = 7.5 Hz), 7.22 (1H, t, J = 7.5 Hz), 7.30 (1H, d, J = 8 Hz), 7.48 (1H, d, J = 8 Hz), 7.51–7.62 (3H, m), 7.77 (2H, d, J = 7.5 Hz); MS (FAB) m/z 594 (M + 1). Anal. ($C_{30}H_{29}Cl_2N_5O_4$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-1-ethyl-2-methyl-1*H*-benzimidazole (52b). Following a procedure similar to method A, the title compound was obtained in 81.2% yield from **18a** and **50a** as a colorless amorphous solid; ^{1}H NMR ($CDCl_3$) δ 1.40 (3H, t, J = 7 Hz), 2.58 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.28 (3H, s), 3.68 (1H, dd, J = 17, 4 Hz), 3.94 (1H, dd, J = 17, 5 Hz), 4.15 (2H, q, J = 7 Hz), 5.52 (1H, d, J = 10 Hz), 5.58 (1H, d, J = 10 Hz), 6.20 (1H, br d, J = 5 Hz), 6.52 (1H, d, J = 15 Hz), 6.70 (1H, br t, J = 5 Hz), 6.86 (1H, d, J = 7.5 Hz), 6.99 (1H, d, J = 7.5 Hz), 7.22 (1H, t, J = 7.5 Hz), 7.31 (1H, d, J = 8 Hz), 7.48 (1H, d, J = 8 Hz), 7.51–7.62 (3H, m), 7.76 (2H, d, J = 7.5 Hz); MS (FAB) m/z 608 (M + 1). Anal. ($C_{31}H_{31}Cl_2N_5O_4$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-ethyl-1-methyl-1*H*-benzimidazole (52c). Following a procedure similar to method A, the title compound was obtained in 74.8% yield from **18b** and **50a** as a colorless amorphous solid; ^{1}H NMR ($CDCl_3$) δ 1.36 (3H, t, J = 7 Hz), 2.93 (2H, q, J = 7 Hz), 3.02 (3H, d, J = 4 Hz), 3.27 (3H, s), 3.66 (1H, dd, J = 17, 4 Hz), 3.73 (3H, s), 3.93 (1H, dd, J = 17, 5 Hz), 5.53–5.64 (2H, m), 6.17 (1H, br s), 6.52 (1H, d, J = 15 Hz), 6.68 (1H, br t, J = 5 Hz), 6.86 (1H, d, J = 8 Hz), 6.98 (1H, d, J = 8 Hz), 7.21 (1H, t, J = 8 Hz), 7.30 (1H, d, J = 8 Hz), 7.46 (1H, d, J = 8 Hz), 7.54 (2H, d, J = 8 Hz), 7.59 (1H, d, J = 15 Hz), 7.75 (2H, d, J = 8 Hz); MS (FAB) m/z 608 (M + 1). Anal. ($C_{31}H_{31}Cl_2N_5O_4$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-ethyl-1-methyl-

1*H*-benzimidazole Hydrochloride (64c). Following a procedure similar to method B, the title compound was obtained in 92.8% yield from **64c** as a colorless amorphous solid; ^{1}H NMR (DMSO-d_6) δ 1.27–1.37 (3H, m), 2.78 (3H, d, J = 5 Hz), 3.12 (2H, q, J = 7.5 Hz), 3.15 (3H, s), 3.84 (1H, dd, J = 17, 4 Hz), 3.95 (3H, s), 4.15 (1H, dd, J = 17, 5 Hz), 5.53 (1H, d, J = 10 Hz), 5.60 (1H, d, J = 8 Hz), 6.86–6.92 (1H, m), 7.37–7.49 (2H, m), 7.49–7.78 (4H, m), 7.78–7.91 (4H, m), 8.38 (1H, br t, J = 5 Hz), 8.52 (1H, br s). Anal. ($C_{31}H_{31}Cl_2N_5O_4$•HCl) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-1-methyl-2-phenyl-1*H*-benzimidazole (52d). Following a procedure similar to method A, the title compound was obtained in 78.2% yield from **18e** and **50a** as a colorless amorphous solid; ^{1}H NMR ($CDCl_3$) δ 2.98 (3H, d, J = 5 Hz), 3.25 (3H, s), 3.66 (1H, dd, J = 17, 5 Hz), 3.82 (3H, s), 3.93 (1H, dd, J = 17, 5 Hz), 5.66 (2H, s), 6.24 (1H, br q, J = 5 Hz), 6.51 (1H, d, J = 15 Hz), 6.71 (1H, br t, J = 5 Hz), 6.93 (1H, d, J = 8 Hz), 7.08 (1H, d, J = 8 Hz), 7.25–7.34 (2H, m), 7.43–7.61 (7H, m), 7.68–7.79 (4H, m). Anal. ($C_{35}H_{31}Cl_2N_5O_4$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methoxy-1-methyl-1*H*-benzimidazole (52e). Following a procedure similar to method A, the title compound was obtained in 78.2% yield from **21a** and **50a** as colorless crystals after crystallization from ether: mp 244–249 °C; ^{1}H NMR ($CDCl_3$) δ 3.02 (3H, d, J = 5 Hz), 3.27 (3H, s), 3.53 (3H, s), 3.67 (1H, dd, J = 17, 5 Hz), 3.93 (1H, dd, J = 17, 5 Hz), 5.64 (2H, s), 6.29 (1H, br q, J = 5 Hz), 6.53 (1H, d, J = 15 Hz), 6.70 (1H, br t, J = 5 Hz), 6.82–6.90 (2H, m), 7.11 (1H, t, J = 8 Hz), 7.30 (1H, d, J = 8 Hz), 7.46 (1H, d, J = 8 Hz), 7.53 (2H, d, J = 8 Hz), 7.58 (1H, d, J = 15 Hz), 7.76 (2H, d, J = 8 Hz); MS (ESI) m/z 610 (M + 1). Anal. ($C_{30}H_{29}Cl_2N_5O_5$) C, H, N.

4-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methoxy-1-

methyl-1*H*-benzimidazole (52f). Following a procedure similar to method A, the title compound was obtained in 72.9% yield from **21a** and **50b** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.35 (3H, s), 2.51 (3H, s), 3.03 (3H, d, J = 5 Hz), 3.25 (3H, s), 3.55 (3H, s), 3.64 (1H, dd, J = 17, 5 Hz), 3.88 (1H, dd, J = 17, 5 Hz), 4.19 (3H, s), 5.41 (2H, s), 6.15 (1H, br s), 6.53 (1H, d, J = 15 Hz), 6.72 (1H, br s), 6.81–6.89 (2H, m), 7.02–7.18 (3H, m), 7.50–7.62 (3H, m), 7.75 (2H, d, J = 8 Hz); MS (ESI) *m/z* 570 (M + 1). Anal. ($C_{32}H_{35}N_5O_5$) C, H, N.

4-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-ethoxy-1-methyl-1*H*-benzimidazole (52g). Following a procedure similar to method A, the title compound was obtained in 70.1% yield from **21b** and **50b** as colorless crystals after crystallization from MeCN: mp 226–231 °C; ^{1}H NMR ($CDCl_3$) δ 1.43 (3H, t, J = 7 Hz), 2.32 (3H, s), 2.50 (3H, s), 3.00 (3H, d, J = 5 Hz), 3.24 (3H, s), 3.53 (3H, s), 3.61 (1H, dd, J = 17, 5 Hz), 3.87 (1H, dd, J = 17, 5 Hz), 4.59 (2H, q, J = 7 Hz), 5.41 (2H, s), 6.23 (1H, q J = 5 Hz), 6.52 (1H, d, J = 15 Hz), 6.72 (1H, br t, J = 5 Hz), 6.80–6.89 (2H, m), 7.02–7.17(3H, m), 7.52 (2H, d, J = 8 Hz), 7.56 (1H, d, J = 15 Hz), 7.74 (2H, d, J = 8 Hz); MS (ESI) *m/z* 584 (M + 1). Anal. ($C_{33}H_{37}N_5O_5$) C, H, N.

4-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methoxymethyl-1-methyl-1*H*-benzimidazole (52h). Following a procedure similar to method A, the title compound was obtained in 77.8% yield from **18c** and **50b** as colorless crystals after crystallization from MeCN: mp 232–235 °C; ^{1}H NMR (DMSO-d_6) δ 2.28 (3H, s), 2.40 (3H, s), 2.79 (3H, d, J = 5 Hz), 3.10 (3H, s), 3.28 (3H, s), 3.49 (1H, dd, J = 17, 5 Hz), 3.67 (1H, dd, J = 17, 5 Hz), 3.78 (3H, s), 4.63 (2H, s), 5.34 (2H, s), 6.87 (1H, d, J = 15 Hz), 6.92 (1H, d, J = 8 Hz), 7.13–7.33 (4H, m), 7.42 (1H, d, J = 15 Hz), 7.62 (2H, d, J = 8 Hz), 7.84 (2H, d, J = 8 Hz), 8.26 (1H, br t, J = 5 Hz), 8.48 (1H, br q, J = 5 Hz); MS (ESI) *m/z* 584 (M + 1). Anal. ($C_{32}H_{35}N_5O_5$) C, H, N.

4-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-ethoxycarbonylmethyl-1-methyl-1*H*-benzimidazole (52i). Following a procedure similar to method A, the title compound was obtained in 73.5% yield from **18d** and **50b** as colorless crystals after crystallization from diethyl ether–MeCN: mp 132–140 °C; ^{1}H NMR (DMSO-d_6) δ 1.19 (3H, t, J = 8 Hz), 2.29 (3H, s), 2.40 (3H, s), 2.79 (3H, d, J = 5 Hz), 3.12 (3H, s), 3.49 (1H, dd, J = 17, 5 Hz), 3.67 (1H, dd, J = 17, 5 Hz), 3.72 (3H, s), 4.09 (2H, s), 4.11 (2H, q, J = 8 Hz), 5.33 (2H, s), 6.89 (1H, d, J = 16 Hz), 6.92 (1H, d, J = 8 Hz), 7.13–7.33 (4H, m), 7.42 (1H, d, J = 16 Hz), 7.63 (2H, d, J = 8 Hz), 7.84 (2H, d, J = 8 Hz), 8.25 (1H, br t, J = 5 Hz), 8.48 (1H, br q, J = 5 Hz); MS (ESI) m/z 626 (M + 1). Anal. ($C_{35}H_{39}N_5O_6$) C, H, N.

2-Acethyl-4-[[2,6-dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-1-methyl-1*H*-benzimidazole (52j). Following a procedure similar to method A, the title compound was obtained in 74.3% yield from **21f** and **50b** as colorless crystals after crystallization from MeCN: mp 234–236 °C; ^{1}H NMR (DMSO-d_6) δ 2.32 (3H, s), 2.45 (3H, s), 2.67 (3H, s), 2.79 (3H, d, J = 5 Hz), 3.12 (3H, s), 3.50 (1H, dd, J = 17, 5 Hz), 3.67 (1H, dd, J = 17, 5 Hz), 4.04 (3H, s), 5.38 (2H, s), 6.88 (1H, d, J = 16 Hz), 7.08 (1H, d, J = 8 Hz), 7.25–7.47 (5H, m), 7.63 (2H, d, J = 8 Hz), 7.85 (2H, d, J = 8 Hz), 8.25 (1H, br t, J = 5 Hz), 8.47 (1H, br q, J = 5 Hz); MS (ESI) m/z 582 (M + 1). Anal. ($C_{33}H_{35}N_5O_5$) C, H, N.

4-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-1-methyl-2-methylamino-1*H*-benzimidazole (52l). Following a procedure similar to method A, the title compound was obtained in 41.3% yield from **21c** and **50b** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 2.29 (3H, s), 2.40 (3H, s), 2.98 (3H, s), 3.03 (3H, s), 3.22 (3H, s), 3.53 (3H, br s), 3.66 (1H, d, J = 17 Hz), 3.87 (1H, d, J = 17 Hz), 5.27 (2H, s), 6.57 (1H, d, J = 15 Hz), 6.80–6.89 (2H, m), 7.06–7.16 (3H, m),

7.50–7.61 (3H, m), 7.75 (2H, d, J = 8 Hz); MS (ESI) m/z 569 (M + 1). Anal. ($C_{32}H_{36}N_6O_4$) C, H, N.

4-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-dimethylamino-1-methyl-1*H*-benzimidazole (52m). Following a procedure similar to method A, the title compound was obtained in 93.6% yield from **21d** and **50b** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.34 (3H, s), 2.50 (3H, s), 2.95 (6H, s), 3.01 (3H, d, J = 5 Hz), 3.23 (3H, s), 3.58–3.68 (4H, m), 3.88 (1H, dd, J = 17, 5 Hz), 5.42 (2H, s), 6.20 (1H, br d, J = 5 Hz), 6.52 (1H, t, J = 15 Hz), 6.72 (1H, br t, J = 5 Hz), 6.80–6.90 (2H, m), 7.01–7.17 (3H, m), 7.50–7.60 (2H, m), 7.75 (2H, d, J = 8 Hz); MS (ESI) m/z 583 (M + 1). Anal. ($C_{33}H_{38}N_6O_4$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2,3-dimethylbenzo[*b*]furan (53). Following a procedure similar to method A, the title compound was obtained in 86.5% yield from 2,3-dimethylbenzo[*b*]furan-7-ol and **50a** as colorless crystals after crystallization from MeCN: mp 237–238 °C; ^{1}H NMR (DMSO-d_6) δ 2.10 (3H, s), 2.32 (3H, s), 2.77 (3H, d, J = 5 Hz), 3.13 (3H, s), 3.50 (1H, dd, J = 17, 5 Hz), 3.76 (1H, dd, J = 17, 4 Hz), 5.43 (2H, s), 6.85 (1H, t, J = 15 Hz), 7.01 (1H, d, J = 8 Hz), 7.05–7.18 (2H, m), 7.40 (1H, d, J = 15 Hz), 7.63 (2H, d, J = 8 Hz), 7.73 (2H, d, J = 8 Hz), 7.77 (1H, d, J = 8 Hz), 7.85 (2H, d, J = 8 Hz), 8.32 (1H, br t, J = 5 Hz), 8.49 (1H, br q, J = 5 Hz). Anal. ($C_{31}H_{29}Cl_2N_3O_5$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoline Hydrochloride (54b). Following a procedure similar to method B, the title compound was obtained in 94.8% yield from **62b** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 2.30 (3H, s), 2.48 (3H, s), 2.99 (3H, s), 3.12 (3H, br s), 3.28 (3H, s), 3.80 (1H, d, J = 17 Hz), 3.88 (1H, d, J = 17 Hz), 5.39 (1H, d, J = 10 Hz), 5.49 (1H, d, J = 10 Hz), 6.61 (1H, d, J = 15 Hz), 7.19–7.28 (2H, m), 7.40–

7.53 (3H, m), 7.66 (1H, d, J = 8 Hz), 7.75–7.97 (5H, m), 8.90 (1H, d, J = 8 Hz). Anal. ($C_{33}H_{34}N_4O_4$•HCl) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-3-[6-(*N*-methylcarbamoyl)pyridin-3-yl]acryloylglycyl]amino]benzyl]oxy]-2-methylquinoline Dihydrochloride (54c). Following a procedure similar to method B, the title compound was obtained in 90.3% yield from **62c** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 3.00 (3H, s), 3.13 (3H, s), 3.25 (3H, s), 3.85 (3H, d, J = 16 Hz), 4.21 (1H, d, J = 16 Hz), 5.53 (1H, d, J = 10 Hz), 5.64 (1H, d, J = 10 Hz), 6.85 (1H, d, J = 16 Hz), 7.41–7.62 (4H, m), 7.73 (1H, d, J = 8 Hz), 7.78–7.88 (2H, m), 8.33 (2H, br s), 8.80 (1H, d, J = 8 Hz), 9.00 (1H, br s). Anal. ($C_{30}H_{27}Cl_2N_5O_4$•2HCl) C, H, N.

8-[[2,6-Dimethyl -3-[*N*-methyl-*N*-[(*E*)-3-[6-(*N*-methylcarbamoyl)pyridin-3-yl]acryloylglycyl]amino]benzyl]oxy]-2-methylquinoline Dihydrochloride (54d). Following a procedure similar to method B, the title compound was obtained in 81.3% yield **62d** as a colorless amorphous solid: ^{1}H NMR (DMSO-d_6) δ 2.29 (3H, s), 2.48 (3H, s), 2.82 (3H, d, J = 5 Hz), 2.92 (3H, s), 3.13 (3H, s), 3.55 (1H, dd, J = 17, 4 Hz), 3.75 (1H, dd, J = 17, 5 Hz), 5.41–5.54 (2H, m), 7.05 (1H, d, J = 15 Hz), 7.31 (1H, d, J = 8 Hz), 7.39 (1H, d, J = 8 Hz), 7.49 (1H, d, J = 15 Hz), 7.81–8.00 (4H, m), 8.05 (1H, d, J = 8 Hz), 8.15 (1H, dd, J = 8, 2 Hz), 8.35 (1H, br t, J = 5 Hz), 8.74–8.84 (2H, m), 8.98 (1H, br s). Anal. ($C_{32}H_{33}N_5O_4$•2HCl) C, H, N.

5-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylisoquinoline (55). Following a procedure similar to method A, the title compound was obtained in 41.3% yield from **27** and **50a** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.69 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.31 (3H, s), 3.70 (1H, dd, J = 17, 4 Hz), 3.99 (1H, dd, J = 17, 5 Hz), 5.47 (1H, d, J = 10 Hz), 5.51 (1H, d, J = 10 Hz), 6.16 (1H, br d, J = 5 Hz), 6.53 (1H, d, J = 15 Hz), 6.69 (1H, br t, J = 4 Hz), 7.19 (1H, d, J = 7.5 Hz), 7.40 (1H, d, J = 8 Hz), 7.45–7.64 (6H), 7.72–7.80 (3H), 9.15 (1H, s); MS (FAB) m/z 591 (M + 1). Anal. ($C_{31}H_{28}Cl_2N_4O_4$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinazoline (56). Following a procedure similar to method A, the title compound was obtained in 82.0% yield from **32** and **50a** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.90 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.28 (3H, s), 3.67 (1H, dd, J = 18, 4 Hz), 3.93 (1H, dd, J = 18, 4 Hz), 5.63 (2H, s), 6.20 (1H, br d, J = 5 Hz), 6.52 (1H, d, J = 16 Hz), 6.68 (1H, br t, J = 4 Hz), 7.33 (1H, d, J = 7.5 Hz), 7.41–7.62 (7H), 7.77 (2H, d, J = 8 Hz), 9.31 (1H, s); MS (FAB) m/z 592 (M + 1). Anal. ($C_{30}H_{27}Cl_2N_5O_4$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoxaline (63a). Following a procedure similar to method A, the title compound was obtained in 85.8% yield from **34a** and **50a** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.77 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.28 (3H, s), 3.67 (1H, dd, J = 17, 4 Hz), 3.94 (1H, dd, J = 17, 4 Hz), 5.62 (2H, s), 6.20 (1H, br d, J = 5 Hz), 6.53 (1H, d, J = 16 Hz), 6.69 (1H, br t, J = 4 Hz), 7.29–7.38 (2H, m), 7.49–7.80 (8H, m), 8.74 (1H, s); MS (FAB) m/z 592 (M + 1). Anal. ($C_{30}H_{27}Cl_2N_5O_4$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoxaline Hydrochloride (57a). Following a procedure similar to method B, the title compound was obtained in 85.3% yield from **63a** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 2.89 (3H, s), 2.98 (3H, s), 3.29 (3H, s), 3.19 (1H, d, J = 17 Hz), 4.00 (1H, d, J = 17 Hz), 5.65 (2H, s), 6.62 (1H, d, J = 15 Hz), 7.44–7.63 (6H, m), 7.75–7.91 (4H, m), 8.92 (1H, s). Anal. ($C_{30}H_{27}Cl_2N_5O_4$•HCl) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-3-methylquinoxaline (58). Following a procedure similar to method A, the title compound was obtained in 88.9% yield from **34b** and **50a** as a colorless amorphous

solid: ^{1}H NMR ($CDCl_3$) δ 2.78 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.28 (3H, s), 3.69 (1H, dd, J = 17, 4 Hz), 3.93 (1H, dd, J = 17, 5 Hz), 5.57 (2H, s), 6.68 (1H, br d, J = 5 Hz), 6.52 (1H, d, J = 15 Hz), 6.68 (1H, br t, J = 4 Hz), 7.27 (1H, overlapped with $CDCl_3$), 7.35 (1H, d, J = 9 Hz), 7.49–7.79 (8H, m), 8.73 (1H, s).; MS (FAB) m/z 592 (M + 1). Anal. ($C_{30}H_{27}Cl_2N_5O_4$) C, H, N.

7-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoline (59). Following a procedure similar to method A, the title compound was obtained in 79.3% yield from **38** and **50a** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.76 (3H, s), 3.03 (3H, d, J = 5 Hz), 3.29 (3H, s), 3.69 (1H, dd, J = 17, 4 Hz), 4.00 (1H, dd, J = 17, 5 Hz), 5.40 (1H, d, J = 10 Hz), 5.48 (1H, d, J = 10 Hz), 6.68 (1H, br d, J = 5 Hz), 6.53 (1H, d, J = 15 Hz), 6.70 (1H, br t, J = 4 Hz), 7.20 (2H, d, J = 8 Hz), 7.37 (1H, d, J = 8 Hz), 7.50–7.63 (5H, m), 7.69 (1H, d, J = 8 Hz), 7.77 (2H, d, J = 8 Hz), 8.00 (1H, d, J = 8 Hz); MS (FAB) m/z 591 (M + 1). Anal. ($C_{30}H_{27}Cl_2N_5O_4$) C, H, N.

2-[[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]methyl]-6-methylpyridine (60). Following a procedure similar to method A, the title compound was obtained in 47.8% yield from 2-hydroxymethyl-2-methylpyridine and **50a** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.02 (6H, s), 3.02 (3H, d, J = 5 Hz), 3.23 (3H, s), 3.59 (1H, d, J = 17, 4 Hz), 3.89 (1H, dd, J = 17, 5 Hz), 5.03 (2H, s), 5.82 (2H, s), 6.15 (1H, br d, J = 5 Hz), 6.51 (1H, d, J = 15 Hz), 6.62 (1H, br t, J = 5 Hz), 7.30 (1H, d, J = 8 Hz), 7.35–7.48 (2H, m), 7.51–7.62 (4H, m), 7.76 (2H, d, J = 8 Hz), 8.32 (1H, d, J = 5 Hz); MS (FAB) m/z 555 (M + 1). Anal. ($C_{28}H_{28}Cl_2N_4O_4$) C, H, N.

3-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-(2,5-dimethylpyrrolyl)pyridine (61). Following a procedure similar to method A, the

title compound was obtained in 53.9% yield from 3-hydroxy-2-(2,5-dimethylpyrrolyl)pyridine and **50a** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.02 (6H, s), 3.02 (3H, d, J = 5 Hz), 3.23 (3H, s), 3.59 (1H, d, J = 17, 4 Hz), 3.89 (1H, dd, J = 17, 5 Hz), 5.03 (2H, s), 5.82 (2H, s), 6.15 (1H, br d, J = 5 Hz), 6.51 (1H, d, J = 15 Hz), 6.62 (1H, br t, J = 5 Hz), 7.30 (1H, d, J = 8 Hz), 7.35–7.48 (2H, m), 7.51–7.62 (4H, m), 7.76 (2H, d, J = 8 Hz), 8.32 (1H, d, J = 5 Hz); MS (FAB) m/z 620 (M + 1). Anal. ($C_{32}H_{31}Cl_2N_5O_4$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoline (62b). Following a procedure similar to method A, the title compound was obtained in 74.8% yield from 8-hydroxy-2-methylquinoline and **50b** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.37 (3H, s), 2.52 (3H, s), 2.72 (3H, s), 3.00 (3H, d, J = 5 Hz), 3.26 (3H, s), 3.63 (1H, dd, J = 17, 4 Hz), 3.88 (1H, dd, J = 17, 5 Hz), 5.35 (2H, s), 6.22 (1H, br d, J = 5 Hz), 6.52 (1H, d, J = 15 Hz), 6.75 (1H, br s), 7.08 (1H, d, J = 8 Hz), 7.18 (1H, d, J = 8 Hz), 7.22–7.32 (2H, m), 7.41–7.61 (5H, m), 7.73 (2H, d, J = 8 Hz), 8.04 (1H, d, J = 8 Hz); MS (FAB) m/z 551 (M + 1). Anal. ($C_{33}H_{34}N_4O_4$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-3-[6-(*N*-methylcarbamoyl)pyridin-3-yl]acryloylglycyl]amino]benzyl]oxy]-2-methylquinoline (62d). Following a procedure similar to method C, the title compound was obtained in 80.2% yield **83c** and methylamine hydrochloride as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.37 (3H, s), 2.53 (3H, s), 2.74 (3H, s), 3.05 (3H, d, J = 5 Hz), 3.27 (3H, s), 3.64 (1H, dd, J = 17, 4 Hz), 3.90 (1H, dd, J = 17, 5 Hz), 5.36 (2H, s), 6.61 (1H, d, J = 15 Hz), 6.77 (1H, br t, J = 5 Hz), 7.07 (1H, d, J = 8 Hz), 7.18 (1H, d, J = 8 Hz), 7.22–7.33 (2H, m), 7.40–7.49 (5H, m), 7.60 (2H, d, J = 15 Hz), 7.91–7.80 (2H, m), 8.03 (1H, d, J = 8 Hz), 8.20 (1H, d, J = 8 Hz), 8.63 (1H, d, J = 2 Hz); MS (FAB) m/z 552 (M + 1). Anal. ($C_{32}H_{33}N_5O_4$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoxaline (63b). Following a procedure similar to method A, the title compound was obtained in 89.7% yield from **34a** and **50b** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.34 (3H, s), 2.51 (3H, s), 2.77 (3H, s), 3.02 (3H, d, J = 5 Hz), 3.27 (3H, s), 3.65 (1H, dd, J = 17, 4 Hz), 3.88 (1H, dd, J = 17, 5 Hz), 5.35 (2H, s), 6.17 (1H, br d, J = 5 Hz), 6.53 (1H, d, J = 15 Hz), 6.71 (1H, br t, J = 5 Hz), 7.09 (1H, d, J = 8 Hz), 7.19 (1H, d, J = 8 Hz), 7.30 (1H, d, J = 8 Hz), 7.51–7.61 (3H, m), 7.67 (1H, t, J = 8 Hz), 7.72–7.79 (3H, m), 8.75 (1H, s); MS (ESI) m/z 552 (M + 1). Anal. ($C_{32}H_{33}N_5O_4$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-3-[6-(*N*-methylcarbamoyl)pyridin-3-yl)acryloylglycyl]amino]benzyl]oxy]-2-methylquinoxaline (63c). Following a procedure similar to method C, the title compound was obtained in 82.0% yield from **79** and methylamine hydrochloride as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.34 (3H, s), 2.52 (3H, s), 2.77 (3H, s), 3.04 (3H, d, J = 5 Hz), 3.28 (3H, s), 3.64 (1H, dd, J = 17, 5 Hz), 3.89 (1H, dd, J = 17, 5 Hz), 5.34 (2H, s), 6.61 (1H, d, J = 15 Hz), 6.76 (1H, br t, J = 5 Hz), 7.10 (1H, d, J = 8 Hz), 7.19 (1H, d, J = 8 Hz), 7.31 (1H, d, J = 8 Hz), 7.60 (1H, d, J = 15 Hz), 7.67 (1H, t, J = 8 Hz), 7.75 (1H, d, J = 8 Hz), 7.91–8.00 (2H, m), 8.20 (1H, d, J = 8 Hz), 8.61 (1H, d, J = 2 Hz), 8.73 (1H, s); MS (ESI) m/z 553 (M + 1). Anal. ($C_{31}H_{32}N_6O_4$) C, H, N.

2,6-Dichloro-1-hydroxymethyl-3-[*N*-methyl-*N*-(*N*-phthalimidoacetyl)amino]benzene (65a). Using a similar procedure to that used for **49a**, the title compound was obtained in 63.8% yield from **46a** as colorless crystals after crystallization from MeOH: mp 237–240 °C; ^{1}H NMR ($CDCl_3$) δ 2.24 (1H, t, J = 7 Hz), 3.21 (3H, s), 4.09 (2H, s), 5.04 (1H, d, J = 7 Hz), 7.43 (1H, d, J = 8 Hz), 7.48 (1H, d, J = 8 Hz), 7.67–7.75 (2H, m), 7.80–7.88 (2H, m). Anal. ($C_{18}H_{14}Cl_2N_2O_4$) C, H, N.

2,6-Dimethyl-1-hydroxymethyl-3-[*N*-methyl-*N*-(*N*-phthalimidoacetyl)amino]benzene (65b). Using a similar procedure to that used for **49a**, the title compound was obtained in 65.4% yield from **46a** as colorless crystals after crystallization from AcOEt: mp 241–243 °C; ^{1}H NMR ($CDCl_3$) δ 2.47 (3H, s), 2.48 (3H, s), 3.20 (3H, s), 3.81 (1H, d, J = 17 Hz), 4.18 (1H, d, J = 17 Hz), 4.83 (2H, s), 7.14 (1H, d, J = 8 Hz), 7.19 (1H, d, J = 8 Hz), 7.68–7.75 (2H, m), 7.80–7.88 (2H, m); MS (ESI) m/z 353 (M + 1). Anal. ($C_{20}H_{20}N_2O_4$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-(*N*-phthalimidoacetyl)amino]benzyl]oxy]-2-methoxy-1-methyl-1*H*-benzimidazole (66). Using a similar procedure to that used for **68a**, the title compound was obtained in 67.9% yield from **65a** and **21a** as colorless crystals after crystallization from MeCN: mp 199–201 °C; ^{1}H NMR ($CDCl_3$) δ 3.24 (3H, s), 3.53 (3H, s), 4.10 (2H, s), 4.20 (3H, s), 5.63–5.74 (2H, m), 6.80–6.88 (2H, m), 7.10 (1H, t, J = 8 Hz), 7.43–7.55 (2H, m), 7.67–7.76 (2H, m), 7.80–7.90 (2H, m); MS (ESI) m/z 553 (M + 1). Anal. ($C_{27}H_{22}Cl_2N_4O_5$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-methyl-*N*-(*N*-phthalimidoacetyl)amino]benzyl]oxy]-2-methylquinoxaline (67a). Using a similar procedure to that used for **68a**, the title compound was obtained in 72.3% yield from **65a** and **34a** as colorless crystals after crystallization from MeOH: mp 218–219 °C; ^{1}H NMR ($CDCl_3$) δ 2.78 (3H, s), 3.24 (3H, s), 4.10 (2H, s), 5.63 (1H, d, J = 10 Hz), 5.71 (1H, d, J = 10 Hz), 7.33 (1H, br d, J = 7.5 Hz), 7.50 (1H, d, J = 8 Hz), 7.54 (1H, d, J = 8 Hz), 7.63 (1H, t, J = 7.5 Hz), 7.69–7.78 (3H, m), 7.82–7.90 (2H, m), 8.73 (1H, s); MS (ESI) m/z 535 (M + 1). Anal. ($C_{27}H_{20}Cl_2N_4O_4$) C, H, N.

4-[[2,6-Dimethyl-3-[*N*-methyl-*N*-(*N*-phthalimidoacetyl)amino]benzyl]oxy]-2-methylquinoxaline (67b). Using a similar procedure to that used for **68a**, the title compound was obtained in 72.3% yield from **65b** and **34a** as colorless crystals after crystallization from AcOEt: mp 124–127 °C; ^{1}H NMR ($CDCl_3$) δ 2.50 (3H, s), 2.54 (3H, s), 2.76 (3H, s), 3.22 (3H, s), 3.96 (1H, d,

J = 17 Hz), 4.20 (1H, d, *J* = 17 Hz), 5.37 (1H, d, *J* = 10 Hz), 7.20–7.35 (3H, m), 7.61–7.77 (4H, m), 7.81–7.89 (2H, m), 8.74 (1H, s); MS (ESI) *m/z* 495 (M + 1). Anal. ($C_{29}H_{26}N_4O_4$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-methyl-*N*-(*N*-phthalimidoacetyl)amino]benzyl]oxy]-2-methylquinoline (68b). Using a similar procedure to that used for **68a**, the title compound was obtained in 63.9% yield from **65b** and 8-hydroxy-2-methylquinoline as colorless crystals after crystallization from MeOH: mp 117–119 °C; ^{1}H NMR ($CDCl_3$) δ 2.51 (3H, s), 2.57 (3H, s), 2.73 (3H, s), 3.22 (3H, s), 3.96 (1H, d, *J* = 17 Hz), 4.19 (1H, d, *J* = 17 Hz), 5.38 (1H, d, *J* = 10 Hz), 5.43 (1H, d, *J* = 10 Hz), 7.17–7.32 (4H, m), 7.37–7.48 (2H, m), 7.67–7.74 (2H, m), 7.80–7.89 (2H, m), 8.02 (1H, d, *J* = 8 Hz). Anal. ($C_{30}H_{27}N_3O_4$) C, H, N.

8-[[3-(*N*-Aminoacetyl-*N*-methylamino)-2,6-dichlorobenzyl]oxy]-2-methoxy-1-methyl-1*H*-benzimidazole (69). Using a similar procedure to that used for **47a**, the title compound was obtained in 78.1% yield from **66** as a pale yellow amorphous solid: ^{1}H NMR ($CDCl_3$) δ 3.00 (1H, d, *J* = 15 Hz), 3.10 (1H, d, *J* = 15 Hz), 3.21 (3H, s), 4.16 (3H, s), 5.62 (2H, s), 6.78–6.88 (2H, m), 7.09 (1H, t, *J* = 8 Hz), 7.23 (1H, d, *J* = 8 Hz), 7.43 (1H, d, *J* = 8 Hz); MS (ESI) *m/z* 423 (M + 1). Anal. ($C_{19}H_{20}Cl_2N_4O_3$) C, H, N.

8-[[3-(*N*-Aminoacetyl-*N*-methylamino)-2,6-dichlorobenzyl]oxy]-2-methylquinoxaline (70a). Using a similar procedure to that used for **47a**, the title compound was obtained in 91.2% yield from **67a** as a pale yellow amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.79 (3H, s), 3.00 (1H, d, *J* = 17 Hz), 3.11 (1H, d, *J* = 17 Hz), 3.22 (3H, s), 5.62 (2H, s), 7.23–7.33 (2H, m), 7.49 (1H, d, *J* = 8 Hz), 7.64 (1H, t, *J* = 7.5 Hz), 7.78 (1H, br d, *J* = 7.5 Hz), 8.75 (1H, s); MS (FAB) *m/z* 405 (M + 1). Anal. ($C_{19}H_{18}Cl_2N_4O_2$) C, H, N.

8-[[3-(*N*-Aminoacetyl-*N*-methylamino)-2,6-dimethylbenzyl]oxy]-2-methylquinoxaline (70b). Using a similar procedure to that used for **47a**, the title compound was obtained in 93.3% yield from **67b** as a pale yellow amorphous solid: ^{1}H

NMR ($CDCl_3$) δ 2.32 (3H, s), 2.51 (3H, s), 2.78 (3H, s), 2.68 (3H, s), 2.93 (1H, d, *J* = 17 Hz), 3.16 (1H, d, *J* = 17 Hz), 3.22 (3H, s), 5.34 (2H, s), 7.06 (1H, d, *J* = 8 Hz), 7.16 (1H, d, *J* = 8 Hz), 7.29 (1H, d, *J* = 8 Hz), 7.65 (1H, t, *J* = 8 Hz), 7.76 (1H, d, *J* = 8 0 Hz), 8.74 (1H, s); MS (FAB) *m/z* 405 (M + 1). Anal. ($C_{19}H_{18}Cl_2N_4O_2$) C, H, N.

8-[[3-(*N*-Aminoacetyl-*N*-methylamino)-2,6-dichlorobenzyl]oxy]-2-methylquinoline (71a). Using a similar procedure to that used for **47a**, the title compound was obtained in 91.2% yield from **68a** as pale brown crystals after crystallization from diethyl ether: mp 145–149°C; ^1H NMR ($CDCl_3$) δ 2.76 (3H, s), 2.96 (1H, d, *J* = 16 Hz), 3.10 (1H, d, *J* = 16 Hz), 3.21 (3H, s), 5.66 (2H, s), 7.20–7.50 (6H, m), 8.02 (1H, d, *J* = 8 Hz). Anal. ($C_{20}H_{19}Cl_2N_3O_2$) C, H, N.

8-[[3-(*N*-Aminoacetyl-*N*-methylamino)-2,6-dimethylbenzyl]oxy]-2-methylquinoxaline (71b). Using a similar procedure to that used for **47a**, the title compound was obtained in 89.7% yield from **68b** as a pale yellow amorphous solid: ^1H NMR ($CDCl_3$) δ 2.32 (3H, s), 2.51 (3H, s), 2.78 (3H, s), 2.68 (3H, s), 2.93 (1H, d, *J* = 17 Hz), 3.16 (1H, d, *J* = 17Hz), 3.22 (3H, s), 5.34 (2H, s), 7.06 (1H, d, *J* = 8 Hz), 7.16 (1H, d, *J* = 8 Hz), 7.29 (1H, d, *J* = 8 Hz), 7.65 (1H, t, *J* = 8 Hz), 7.76 (1H, d, *J* = 8 Hz), 8.74 (1H, s); MS (FAB) *m/z* 365 (M + 1). Anal. ($C_{21}H_{24}N_4O_2$) C, H, N.

4-[[2,6-Dichloro-3-[*N*-[(*E*)-4-(*N*,*N*-dimethylcarbamoyl)cinnamamidoacetyl]-*N*-methylamino]benzyl]oxy]-2-methoxy-1-methyl-1*H*-benzimidazole (72). Following a procedure similar to method E, the title compound was obtained in 71.2% yield from **69a** and (*E*)-4-(*N*,*N*-dimethylcarbamoyl)cinnamic acid[23] as a colorless amorphous solid: ^1H NMR ($CDCl_3$) δ 2.98 (3H, br s), 3.11 (3H, br s), 3.27 (3H, s), 3.53 (3H, s), 3.65 (1H, dd, *J* = 17, 5 Hz), 3.93 (1H, dd, *J* = 17, 5 Hz), 4.18 (3H, s), 5.63 (2H, s), 6.50 (1H, d, *J* = 15 Hz), 6.55 (1H, br t, *J* = 5 Hz), 6.80–6.87 (2H, m), 7.10 (1H, t, *J* = 8 Hz), 7.30 (1H, d, *J* = 8 Hz), 7.38–7.61 (6H, m); MS (ESI) *m/z* 624 (M + 1). Anal. ($C_{31}H_{31}Cl_2N_5O_5$) C, H, N.

4-[[3-[*N*-[(*E*)-3-(6-Acetamidopyridin-3-yl)acryloylglycyl]-*N*-methylamino]-2,6-dichlorobenzyl]oxy]-2-methoxy-1-methyl-1*H*-

benzimidazole (73a). Following a procedure similar to method E, the title compound was obtained in 75.7% yield from **69a** and (*E*)-3-(6-acetamidopyridin-3-yl)acrylic acid[23] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.21 (3H, s), 3.28 (3H, s), 3.53 (3H, s), 3.66 (1H, dd, *J* = 17, 4 Hz), 3.95 (1H, dd, *J* = 17, 5 Hz), 4.19 (3H, s), 5.66 (2H, s), 6.46 (1H, d, *J* = 15 Hz), 6.68 (1H, br t, *J* = 5 Hz), 6.80–6.88 (2H, m), 7.10 (1H, t, *J* = 8 Hz), 7.29 (1H, d, *J* = 8 Hz), 7.44–7.56 (2H, m), 7.83 (1H, dd, *J* = 17, 4 Hz), 8.07 (1H, br s), 8.20 (1H, d, *J* = 8 Hz), 8.35 (1H, br s); MS (ESI) *m/z* 611 (M + 1). Anal. ($C_{29}H_{28}Cl_2N_6O_5$) C, H, N.

4-[[3-[*N*-[(*E*)-3-(6-Acetamidopyridin-3-yl)acryloylglycyl]-*N*-methylamino]-2,6-dimethylbenzyl]oxy]-2-methoxy-1-methyl-1*H*-benzimidazole (73b). Following a procedure similar to method A the title compound was obtained in 63.7% yield from **21a** and **50c** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.21 (3H, s), 2.33 (3H, s), 2.50 (3H, s), 3.26 (3H, s), 3.54 (3H, s), 3.62 (1H, dd, *J* = 17, 5 Hz), 3.88 (1H, dd, *J* = 17, 5 Hz), 4.19 (3H, s), 5.40 (2H, s), 6.47 (1H, d, *J* = 15 Hz), 6.72 (1H, br t, *J* = 5 Hz), 6.81–6.89 (2H, m), 7.03–7.18 (3H, m), 7.51 (1H, d, *J* = 15 Hz), 7.84 (1H, dd, *J* = 8, 2 Hz), 8.11 (1H, br s), 7.21 (1H, br d, *J* = 8 Hz), 8.36 (1H, br s); MS (ESI) *m/z* 571 (M + 1). Anal. ($C_{31}H_{34}N_6O_5$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-[(*E*)-4-(*N*,*N*-dimethylcarbamoyl)cinnamamidoacetyl]-*N*-methylamino]benzyl]oxy]-2-methylquinoxaline (74a). Following a procedure similar to method E, the title compound was obtained in 66.1% yield from **70a** and (*E*)-4-(*N*,*N*-dimethylcarbamoyl)cinnamic acid[23] as colorless crystals after crystallization from isopropyl ether: mp 110–114 °C; ^{1}H NMR ($CDCl_3$) δ 2.77 (3H, s), 2.98 (3H, br s), 3.11 (3H, br s), 3.27 (3H, s), 3.67 (1H, dd, *J* = 17, 4 Hz), 3.95 (1H, dd, *J* = 17, 5 Hz), 5.62 (2H, s), 6.51 (1H, d, *J* = 15 Hz), 6.68 (1H, br t, *J* = 5 Hz), 7.28–7.36 (2H, m), 7.42 (2H, d, *J* = 8 Hz), 7.48–7.70 (5H, m), 7.76 (1H, d, *J* = 8 Hz), 8.74 (1H, s). Anal. ($C_{31}H_{29}Cl_2N_5O_4$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-[(*E*)-4-(*N*,*N*-dimethylcarbamoyl)cinnamamidoacetyl]-*N*-methylamino]benzyl]oxy]-2-methylquinoxaline (74b). Following a procedure similar to method E, the title compound was obtained in 66.1% yield from **70b** and (*E*)-4-(*N*,*N*-dimethylcarbamoyl)cinnamic acid[23] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.31 (3H, s), 2.50 (3H, s), 2.73 (3H, s), 2.98 (3H, br s), 3.11 (3H, s), 3.26 (3H, s), 3.63 (1H, dd, *J* = 17, 4 Hz), 3.87 (1H, dd, *J* = 17, 5 Hz), 5.34 (2H, s), 6.50 (1H, d, *J* = 15 Hz), 6.68 (1H, br t, *J* = 5 Hz), 7.08 (1H, d, *J* = 8 Hz), 7.18 (1H, d, *J* = 8 Hz), 7.30 (1H, d, *J* = 8 Hz), 7.41 (2H, d, *J* = 8 Hz), 7.48–7.60 (5H, m), 7.65 (1H, t, *J* = 8 Hz), 7.75 (1H, d, *J* = 8 Hz), 8.73 (1H, s); MS (ESI) *m*/*z* 566 (M + 1). Anal. ($C_{33}H_{35}N_5O_4$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-4-(2-oxo-pyrrolidin-1-yl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoxaline (75a). Following a procedure similar to method E, the title compound was obtained in 74.5% yield from **70a** and (*E*)-4-(2-oxo-pyrrolidin-1-yl)cinnamic acid[23] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.12–2.25 (2H, m), 2.63 (2H, t, *J* = 7.5 Hz), 2.78 (3H, s), 3.28 (3H, s), 3.65 (1H, dd, *J* = 17, 4 Hz), 3.85–4.00 (3H, m), 5.62 (2H, s), 6.43 (1H, d, *J* = 15 Hz), 6.59 (1H, br t, *J* = 4 Hz), 7.29–7.38 (2H, m), 7.48–7.70 (7H, m), 7.78 (1H, d, *J* = 8 Hz), 8.73 (1H, s); MS (FAB) *m*/*z* 618 (M + 1). Anal. ($C_{32}H_{29}Cl_2N_5O_4$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-methyl-*N*-[(*E*)-4-(2-oxo-pyrrolidin-1-yl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoxaline (75b). Following a procedure similar to method E, the title compound was obtained in 92.7% yield from **70b** and (*E*)-4-(2-oxo-pyrrolidin-1-yl)cinnamic acid[23] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.11–2.23 (2H, m), 2.34 (3H, s), 2.50 (3H, s), 2.62 (2H, t, *J* = 7.5 Hz), 2.77 (3H, s), 3.26 (3H, s), 3.64 (1H, dd, *J* = 17, 5 Hz), 3.81–3.91 (3H, m), 5.35 (2H, s), 6.42 (1H, d, *J* = 15 Hz), 6.64 (1H, br s), 7.10 (1H, d, *J* = 8 Hz), 7.19 (1H, d, *J* = 8 Hz), 7.30 (1H, d, *J* = 8 Hz), 7.48–7.57 (3H, m), 7.62–7.70

(3H, m), 7.75 (1H, d, J = 8 Hz), 8.74 (1H, s); MS (FAB) m/z 578 (M + 1). Anal. ($C_{34}H_{35}N_5O_4$) C, H, N.

8-[[3-[*N*-[(*E*)-4-(Acetamido)cinnamidoacetyl]-*N*-methylamino]-2,6-dichlorobenzyl]oxy]-2-methylquinoxaline (77a). Following a procedure similar to method E, the title compound was obtained in 84.7% yield from **70a** and (*E*)-4-(acetamido)cinnamic acid as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.15 (3H, s), 2.76 (3H, s), 3.26 (3H, s), 3.64 (1H, dd, J = 17, 4 Hz), 3.92 (1H, dd, J = 17, 5 Hz), 5.61 (2H, s), 6.39 (1H, d, J = 15 Hz), 6.61 (1H, br t, J = 4 Hz), 7.28–7.35 (2H, m), 7.40–7.58 (6H, m), 7.62–7.71 (2H, m), 7.78 (1H, d, J = 8 Hz), 8.74 (1H, s); MS (FAB) m/z 592 (M + 1). Anal. ($C_{30}H_{27}Cl_2N_5O_4$) C, H, N.

8-[[3-[*N*-[(*E*)-4-(Acetamido)cinnamidoacetyl]-*N*-methylamino]-2,6-dichlorobenzyl]oxy]-2-methylquinoxaline Hydrochloride (76a). Following a procedure similar to method B, the title compound was obtained in 89.5% yield from **77a** as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 2.17 (3H, s), 2.91 (3H, s), 3.29 (3H, s), 3.69 (1H, d, J = 17 Hz), 3.98 (1H, d, J = 17 Hz), 5.62 (2H, s), 6.43 (1H, d, J = 15 Hz), 7.40–7.59 (8H, m), 7.87 (1H, br t, J = 8 Hz), 7.95 (1H, br d, J = 8 Hz), 8.90 (1H, s). Anal. ($C_{30}H_{27}Cl_2N_5O_4$•HCl) C, H, N.

8-[[3-[*N*-[(*E*)-3-(6-Acetylaminopyridine-3-yl)acryloylglycyl]-*N*-methylamino]-2,6-dimethylbenzyl]oxy]-2-methylquinoxaline (77b). Following a procedure similar to method E, the title compound was obtained in 84.7% yield from **70b** and (*E*)-3-(6-acetamidopyridin-3-yl)acrylic acid[23] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.22 (3H, s), 2.35 (3H, s), 2.51 (3H, s), 2.77 (3H, s), 3.27 (3H, s), 3.64 (1H, dd, J = 17, 5 Hz), 3.87 (1H, dd, J = 17, 5 Hz), 5.35 (2H, s), 6.47 (1H, d, J = 15 Hz), 6.71 (1H, br t, J = 5 Hz), 7.10 (1H, d, J = 8 Hz), 7.19 (1H, d, J = 8 Hz), 7.31 (1H, d, J = 8 Hz), 7.51 (1H, d, J = 15 Hz), 7.67 (1H, t, J = 8 Hz), 7.76 (1H, d, J = 8 Hz), 7.85 (1H, d, J = 8 Hz), 8.07 (1H, br s), 7.21 (1H, br d, J = 8 Hz), 8.36 (1H, br s), 8.74 (1H, s); MS (ESI) m/z 553 (M + 1). Anal. ($C_{31}H_{32}N_6O_4$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-[(*E*)-3-(6-ethoxycarbonylpyridin-3-yl)acryloylglycyl]-*N*-methylamino]benzyl]oxy]-2-methylquinolxaine (78). Following a procedure similar to method E, the title compound was obtained in 81.5% yield from **70b** and (*E*)-3-(6-ethoxycarbonylpyridin-3-yl)acrylic acid[23] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 1.45 (3H, t, *J* = 7.5 Hz), 2.33 (3H, s), 2.51 (3H, s), 2.77 (3H, s), 3.27 (3H, s), 3.64 (1H, dd, *J* = 17, 5 Hz), 3.89 (1H, dd, *J* = 17, 4 Hz), 4.49 (2H, q, *J* = 7.5 Hz), 5.35 (2H, s), 6.63 (1H, d, *J* = 15 Hz), 6.78 (1H, br t, *J* = 5 Hz), 7.10 (1H, d, *J* = 8 Hz), 7.20 (1H, d, *J* = 8 Hz), 7.31 (1H, d, *J* = 8 Hz), 7.60 (1H, d, *J* = 15 Hz), 7.67 (1H, t, *J* = 8 Hz), 7.76 (1H, d, *J* = 8 Hz), 7.92 (1H, dd, *J* = 8, 3 Hz), 8.14 (1H, d, *J* = 8 Hz), 8.74 (1H, br s), 8.85 (1H, d, *J* = 3 Hz); MS (ESI) *m/z* 568 (M + 1). Anal. ($C_{32}H_{33}N_5O_5$) C, H, N.

8-[[3-[*N*-[(*E*)-3-(6-Carboxypyridin-3-yl)acryloylglycyl]-*N*-methylamino]-2,6-dimethylbenzyl]oxy]-2-methylquinoxaline (79). Using a similar procedure to that used for **83a**, the title compound was obtained in 90.3% yield from **78** as a pale yellow amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.36 (3H, s), 2.51 (3H, s), 2.78 (3H, s), 3.28 (3H, s), 3.66 (1H, dd, *J* = 17, 5 Hz), 3.90 (1H, dd, *J* = 17, 5 Hz), 5.35 (2H, s), 6.68 (1H, d, *J* = 15 Hz), 6.83 (1H, br t, *J* = 5 Hz), 7.10 (1H, d, *J* = 8 Hz), 7.20 (1H, d, *J* = 8 Hz), 7.31 (1H, d, *J* = 8 Hz), 7.58–7.70 (2H, m), 7.77 (1H, d, *J* = 8 Hz), 8.02 (1H, dd, *J* = 8, 2 Hz), 8.21 (1H, d, *J* = 8 Hz), 8.70 (1H, br d, *J* = 2 Hz), 8.75 (1H, s); MS (ESI) *m/z* 540 (M + 1). Anal. ($C_{30}H_{29}N_5O_5$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-3-(3-pyridinyl)acryloylglycyl]amino]benzyl]oxy]-2-methylquinoline (80b). Following a procedure similar to method E, the title compound was obtained in 87.8% yield from **71a** and (*E*)-3-(3-pyridyl)acrylic acid as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.72 (3H, s), 3.27 (3H, s), 3.67 (1H, dd, *J* = 17, 4 Hz), 3.95 (1H, dd, *J* = 17, 5 Hz), 5.65 (2H, s), 6.57 (1H, d, *J* = 15 Hz), 6.77 (1H, br t, *J* = 4 Hz), 7.21–7.64 (8H, m), 7.80 (1H, dt, *J* = 8, 1 Hz), 8.03 (1H, d, *J* = 8 Hz), 8.57 (1H, dd, *J* = 5, 1 Hz), 8.72 (1H, d, *J* = 1 Hz). Anal. ($C_{28}H_{24}Cl_2N_4O_3$) C, H, N.

8-[[3-[*N*-[(*E*)-Cinnamamidoacetyl]-*N*-methylamino]-2,6-dichlorobenzyl]oxy]-2-methylquinoline Hydrochloride (81a). Following a procedure similar to method B, the title compound was obtained in 92.1% yield from **80a** as a pale yellow amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 3.09 (3H, s), 3.21 (3H, s), 3.91 (2H, s), 5.59 (1H, d, J = 10 Hz), 5.79 (1H, d, J = 10 Hz), 6.59 (1H, d, J = 16 Hz), 7.28–7.69 (8H, m), 7.72 (1H, br d, J = 8 Hz), 7.81–8.03 (3H, m), 8.98 (1H, d, J = 8 Hz). Anal. ($C_{29}H_{25}Cl_2N_3O_3$•HCl) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-3-(3-pyridinyl)acryloylglycyl]amino]benzyl]oxy]-2-methylquinoline Dihydrochloride (81b). Following a procedure similar to method B, the title compound was obtained in 89.2% yield from **80b** and (*E*)-3-(3-pyridyl)acrylic acid as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$–CD_3OD) δ 2.90 (3H, s), 3.15 (3H, s), 3.60 (1H, dd, J = 16, 5 Hz), 3.92 (1H, dd, J = 16, 5 Hz), 5.64 (2H, s), 7.08 (1H, d, J = 15 Hz), 7.53 (1H, d, J = 15 Hz), 7.77–8.00 (7H, m), 8.43–8.59 (2H, m), 8.77 (1H, d, J = 8 Hz), 8.90–9.08 (2H, m). Anal. ($C_{28}H_{24}Cl_2N_4O_3$•HCl) C, H, N.

8-[[2,6-Dichloro-3-[*N*-[(*E*)-4-(methoxycarbonyl)cinnamamidoacetyl]-*N*-methylamino]benzyl]oxy]-2-methylquinoline (82a). Following a procedure similar to method E, the title compound was obtained in 92.3% yield from **71a** and (*E*)-4-(methoxycarbonyl)cinnamic acid as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.74 (3H, s), 3.27 (3H, s), 3.64 (1H, dd, J = 17, 4 Hz), 3.87–4.00 (4H, m), 5.60–5.70 (2H, m), 6.57 (1H, d, J = 15 Hz), 6.75 (1H, br t, J = 5 Hz), 7.24–7.63 (11H, m), 8.03 (1H, m). Anal. ($C_{31}H_{27}Cl_2N_3O_5$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-[(*E*)-3-(6-ethoxycarbonylpyridin-3-yl)acryloylglycyl]-*N*-methylamino]benzyl]oxy]-2-methylquinoline (82b). Following a procedure similar to method E, the title compound was obtained in 83.5% yield from **71a** and (*E*)-3-(6-ethoxycarbonylpyridin-3-yl)acrylic acid[23] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 1.45 (3H, t, J = 7.5 Hz), 2.72 (3H, s), 3.27 (3H, s), 3.70 (1H, dd, J = 17, 5 Hz), 3.94 (1H, dd, J = 17, 5 Hz), 4.49 (2H, q, J = 7.5 Hz),

5.59–5.70 (2H, m), 6.66 (1H, d, J = 15 Hz), 6.80 (1H, br t, J = 5 Hz), 7.22–7.35 (3H, m), 7.37–7.53 (3H, m), 7.60 (1H, d, J = 15 Hz), 7.91 (1H, m), 8.02 (1H, d, J = 8 Hz), 8.12 (1H, d, J = 8 Hz), 8.84 (1H, m). Anal. ($C_{31}H_{28}Cl_2N_4O_5$) C, H, N.

8-[[2,6-Dimethyl-3-[*N*-[(*E*)-3-(6-ethoxycarbonylpyridin-3-yl)acryloylglycyl]-*N*-methylamino]benzyl]oxy]-2-methylquinoline (82c). Following a procedure similar to method E, the title compound was obtained in 88.2% yield from **71b** and (*E*)-3-(6-ethoxycarbonylpyridin-3-yl)acrylic acid[23] as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 1.45 (3H, t, J = 7.5 Hz), 2.38 (3H, s), 2.53 (3H, s), 2.72 (3H, s), 3.26 (3H, s), 3.64 (1H, dd, J = 18, 4 Hz), 3.90 (1H, dd, J = 18, 4 Hz), 4.49 (2H, q, J = 7.5 Hz), 5.36 (2H, s), 6.64 (1H, d, J = 16 Hz), 6.78 (1H, br t, J = 5 Hz), 7.08 (1H, d, J = 8 Hz), 7.18 (1H, d, J = 8 Hz), 7.23–7.33 (2H, m), 7.39–7.49 (2H, m), 7.61 (1H, d, J = 16 Hz), 7.92 (1H, dd, J = 8, 2 Hz),8.03 (1H, d, J = 8 Hz), 8.13 (1H, d, J = 8 Hz), 8.84 (1H, d, J = 2 Hz); MS (ESI) m/z 567 (M + 1). Anal. ($C_{33}H_{34}N_4O_5$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-[(*E*)-3-(methoxycarbonyl)cinnamamidoacetyl]-*N*-methylamino]benzyl]oxy]-2-methylquinoline (82d). Following a procedure similar to method E, the title compound was obtained in 83.1% yield from **71a** and (*E*)-3-(methoxycarbonyl)cinnamic acid as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.72 (3H, s), 3.27 (3H, s), 3.65 (1H, dd, J = 17, 4 Hz), 3.85–4.01 (4H, m), 5.65 (2H, s), 6.55 (1H, d, J = 15 Hz), 6.68 (1H, br t, J = 5 Hz), 7.20–7.36 (3H, m), 7.36–7.54 (4H, m), 7.54–7.70 (2H, m), 7.95–8.06 (2H, m), 8.20 (1H, br s). Anal. ($C_{31}H_{27}Cl_2N_3O_5$) C, H, N.

8-[[3-[*N*-[(*E*)-3-(6-Carboxypyridin-3-yl)acryloylglycyl]-*N*-methylamino]-2,6-dichlorobenzyl]oxy]-2-methylquinoine (83b). Using a similar procedure to that used for **83a**, the title compound was obtained in 86.6% yield from **82b** as a colorless amorphous solid: ^{1}H NMR (DMSO-d_6) δ 2.58 (3H, s), 3.13 (3H, s), 3.50 (1H, dd, J = 17, 5 Hz), 3.80 (1H, dd, J = 17, 5 Hz), 5.46 (1H, d, J = 10

Hz), 5.53 (1H, d, J = 10 Hz), 6.95 (1H, d, J = 15 Hz), 7.30–7.57 (5H, m), 7.78 (2H, br s), 8.02 (1H, d, J = 8 Hz), 8.10 (1H, d, J = 8 Hz), 8.20 (1H, d, J = 8 Hz), 8.45 (1H, br t, J = 5 Hz), 8.85 (1H, s). Anal. ($C_{29}H_{24}Cl_2N_4O_5$) C, H, N.

8-[[3-[*N*-[(*E*)-3-(6-Carboxypyridin-3-yl)acryloylglycyl]-*N*-methylamino]-2,6-dimethylbenzyl]oxy]-2-methylquinoine (83c). Using a similar procedure to that used for **83a**, the title compound was obtained in 80.4% yield from **82c** as a colorless amorphous solid: ^{1}H NMR (DMSO-d_6) δ 2.33 (3H, s), 2.46 (3H, s), 2.61 (3H, s), 3.13 (3H, s), 3.51 (1H, dd, J = 17, 5 Hz), 3.71 (1H, dd, J = 17, 5 Hz), 5.25–5.37 (2H, m), 7.00 (1H, d, J = 15 Hz), 7.25 (1H, d, J = 8 Hz), 7.37 (1H, d, J = 8 Hz), 7.37–7.57 (5H, m), 8.00 (1H, d, J = 8 Hz), 8.08 (1H, d, J = 8 Hz), 8.21 (1H, d, J = 8 Hz), 8.33 (1H, br t, J = 5 Hz), 8.78 (1H, br s); MS (ESI) m/z 539 (M + 1). Anal. ($C_{31}H_{30}N_4O_5$) C, H, N.

8-[[3-[*N*-[(*E*)-3-Carboxycinnamamidoacetyl-*N*-methylamino]-2,6-dichlorobenzyl]oxy]-2-methylquinoline (83d). Using a similar procedure to that used for **83a**, the title compound was obtained in 84.6% yield from **82d** as colorless crystals after crystallization from MeCN: mp 162–164 °C; ^{1}H NMR (DMSO-d_6) δ 2.70 (3H, s), 3.26 (3H, s), 3.65 (1H, d, J = 16 Hz), 4.00 (1H, d, J = 16 Hz), 5.58 (2H, s), 6.60 (1H, d, J = 16 Hz), 7.20–7.68 (9H, m), 8.00 (1H, d, J = 7.5 Hz), 8.06 (1H, d, J = 8 Hz), 8.20 (1H, br s); MS (FAB) m/z 578 (M + 1). Anal. ($C_{30}H_{25}Cl_2N_3O_5$) C, H, N.

8-[[2,6-Dichloro-3-[*N*-methyl-*N*-[(*E*)-3-(*N*-methylcarbamoyl)cinnamamidoacetyl]amino]benzyl]oxy]-2-methylquinoline (84). Following a procedure similar to method C, the title compound was obtained in 74.8% yield from **83d** and methylamine hydrochloride as a colorless amorphous solid: ^{1}H NMR ($CDCl_3$) δ 2.70 (3H, s), 2.99 (3H, br s), 3.25 (3H, s), 3.66 (3H, br dd, J = 16, 4 Hz), 3.95 (3H, br dd, J = 16, 4 Hz), 5.65 (2H, s), 6.45–6.60 (2H, m), 6.50 (1H, m), 7.21–7.69 (9H, m), 7.75 (1H, d, J = 8 Hz), 7.87 (1H, br s), 8.04 (1H, d, J = 8 Hz). Anal. ($C_{31}H_{28}Cl_2N_4O_4$) C, H, N.