UNIVERSITAT DE BARCELONA

Novel multi-target directed ligands as drug candidates against Alzheimer's disease

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Unidad de Química Farmacéutica

NOVEL MULTI-TARGET DIRECTED LIGANDS AS DRUG CANDIDATES AGAINST ALZHEIMER'S DISEASE

Nuclear Magnetic Resonance Spectroscopy (^{1}H and ^{13}C spectrum)

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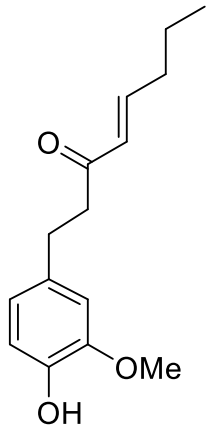
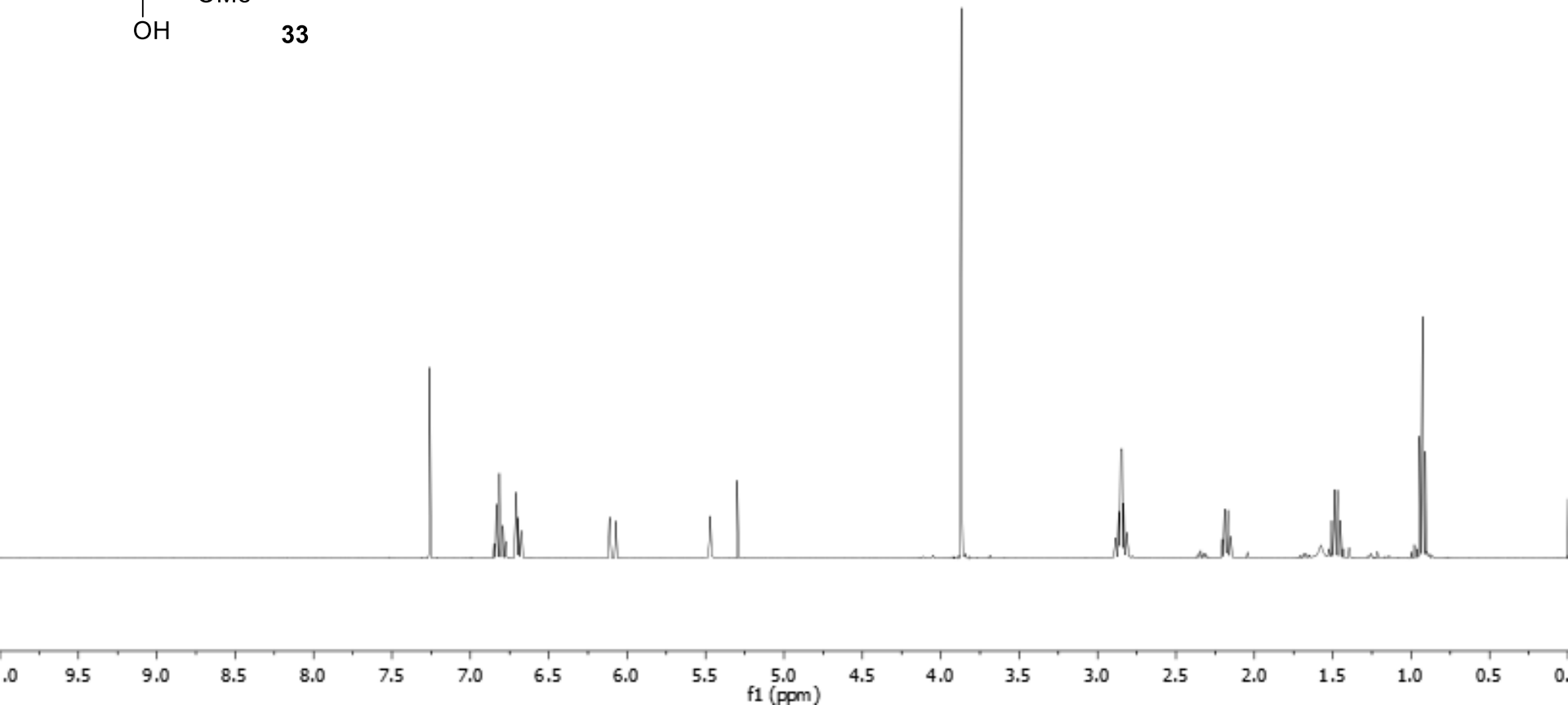
Barcelona, 2017

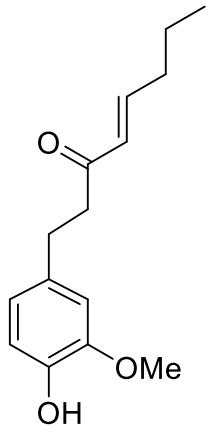
1-(4-hydroxy-3-methoxyphenyl)oct-4-en-3-one, **33** – ^{1}H NMR (400 MHz, $CDCl_3$)



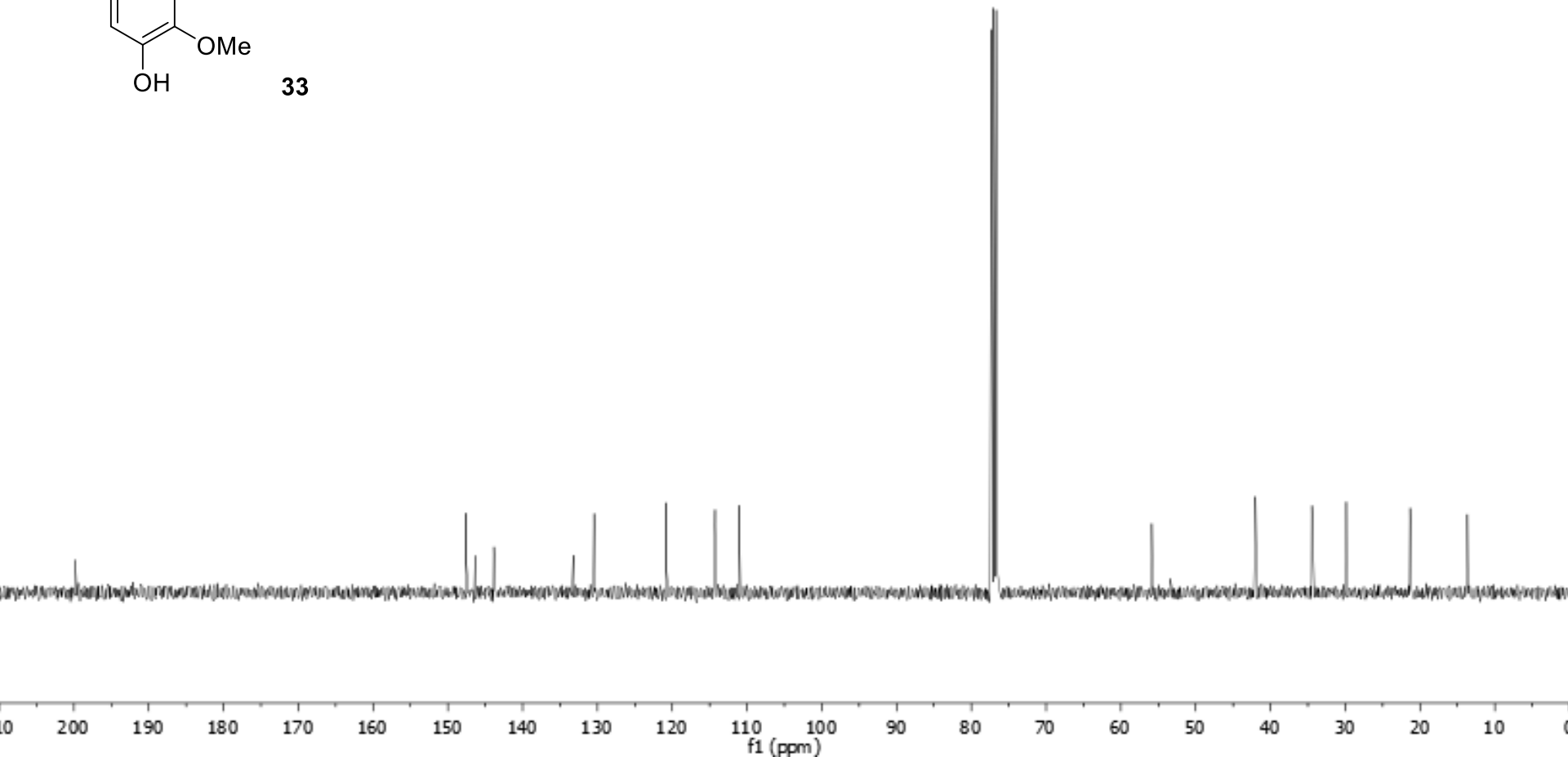
33



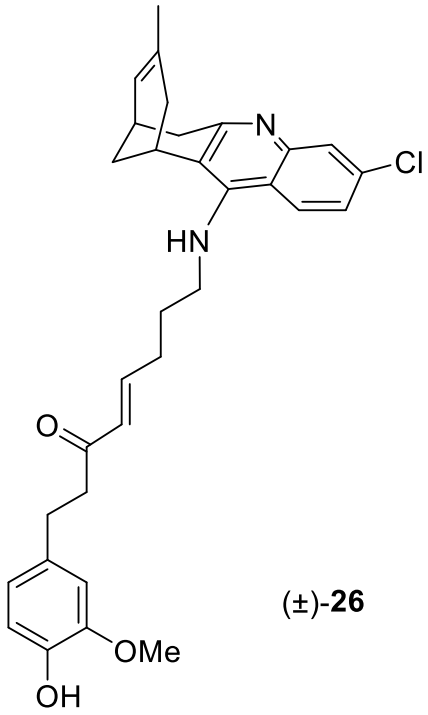
1-(4-hydroxy-3-methoxyphenyl)oct-4-en-3-one, **33** – ^{13}C NMR (100.6 MHz, $CDCl_3$)



33

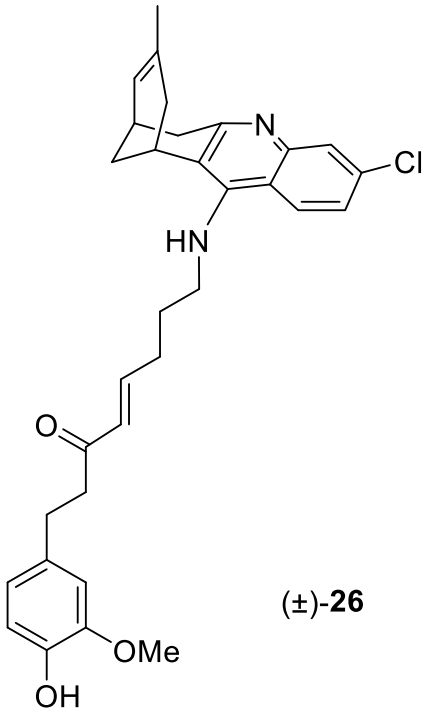


(±)-8-[(3-Chloro-6,7,10,11-tetrahydro-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]-1-(4-hydroxy-3-methoxyphenyl)oct-4-en-3-one, (±)-**26** – ^{1}H NMR (400 MHz, $CDCl_3$)



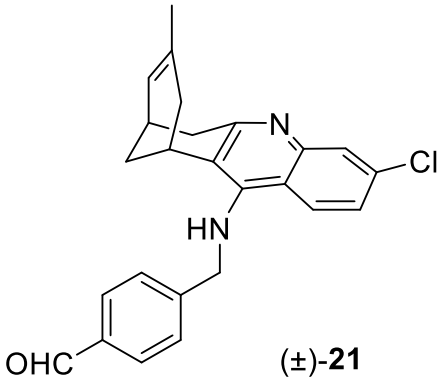
(±)-**26**

(±)-8-[(3-Chloro-6,7,10,11-tetrahydro-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]-1-(4-hydroxy-3-methoxyphenyl)oct-4-en-3-one, (±)-**26** – ^{13}C NMR (100.6 MHz, CD_3OD)

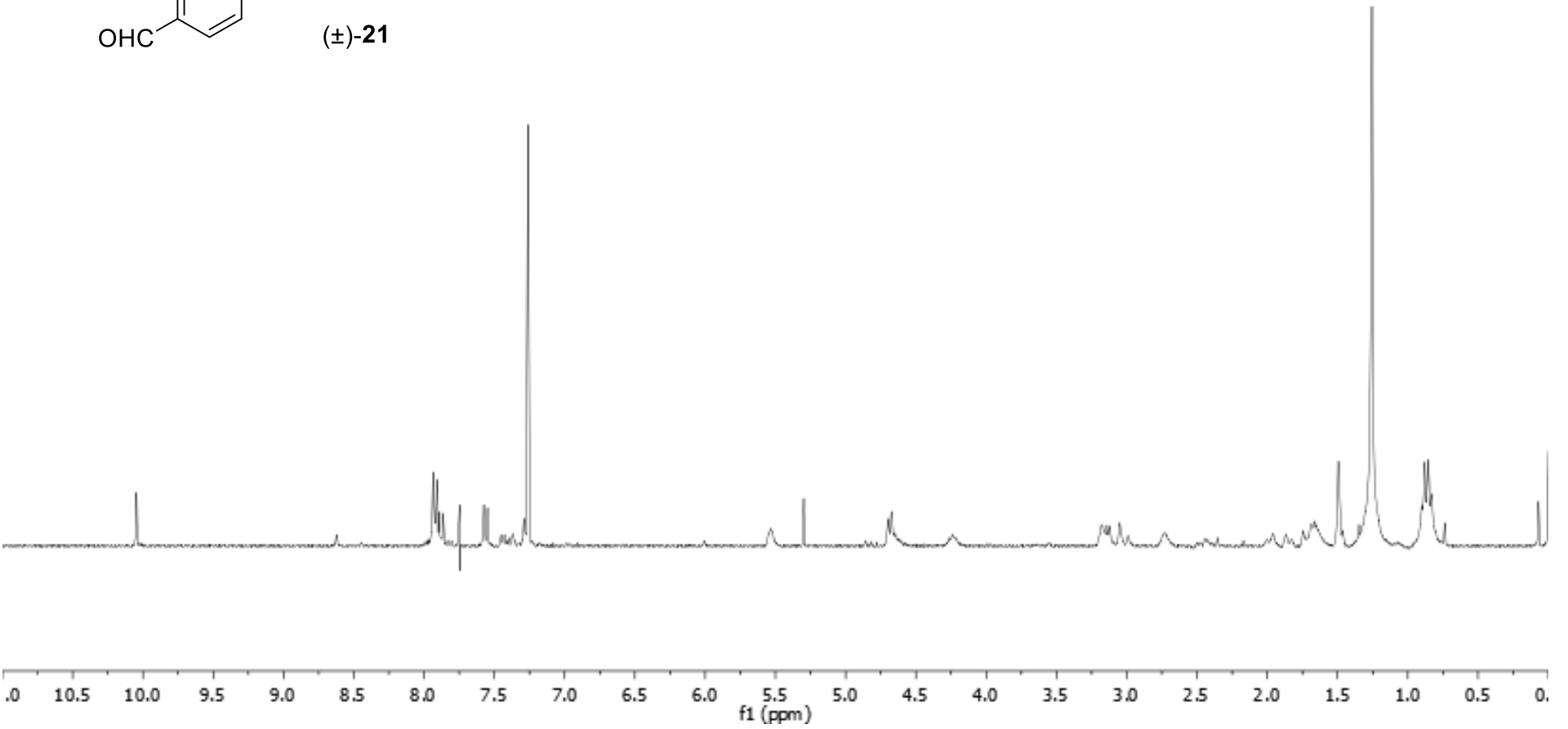


(±)-**26**

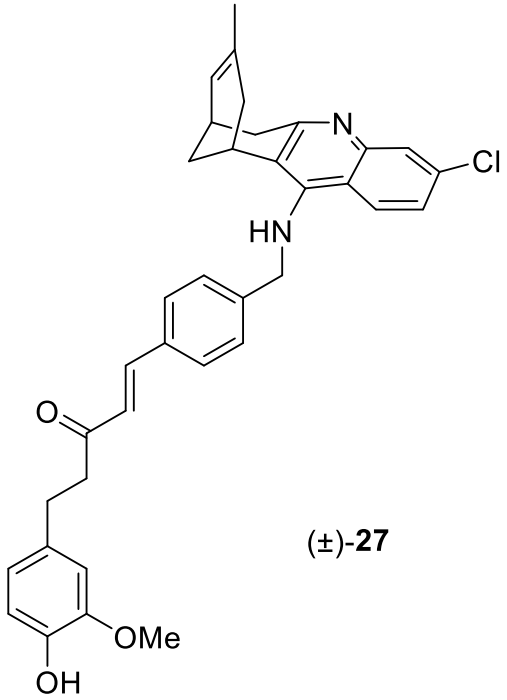
(±)-4-{[(3-Chloro-6,7,10,11-tetrahydro-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]methyl}benzaldehyde, (±)-**21** – ^{1}H NMR (300 MHz, $CDCl_3$)



(±)-**21**



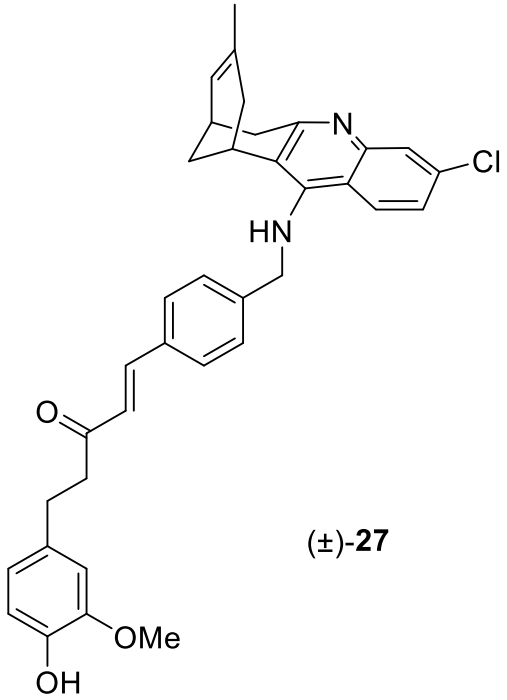
(±)-{4-{[(3-chloro-6,7,10,11-tetrahydro-9-methyl-7,11-methanocyclooocta[*b*]quinolin-12-yl)amino]methyl}phenyl}-5-(4-hydroxy-3-methoxyphenyl)pent-1-en-3-one, (±)-**27** – ^{1}H NMR (400 MHz, $CDCl_3$)



(±)-**27**

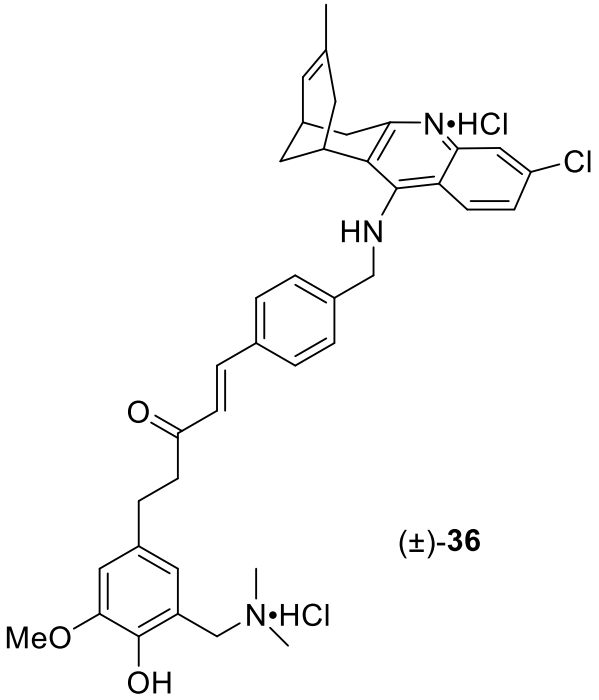
(±)-{4-{[(3-chloro-6,7,10,11-tetrahydro-9-methyl-7,11-methanocyclooocta[*b*]quinolin-12-yl)amino]methyl}phenyl}-5-(4-hydroxy-3-methoxyphenyl)pent-1-en-3-one, (±)-**27** –

^{13}C NMR (100.6 MHz, $CDCl_3$)



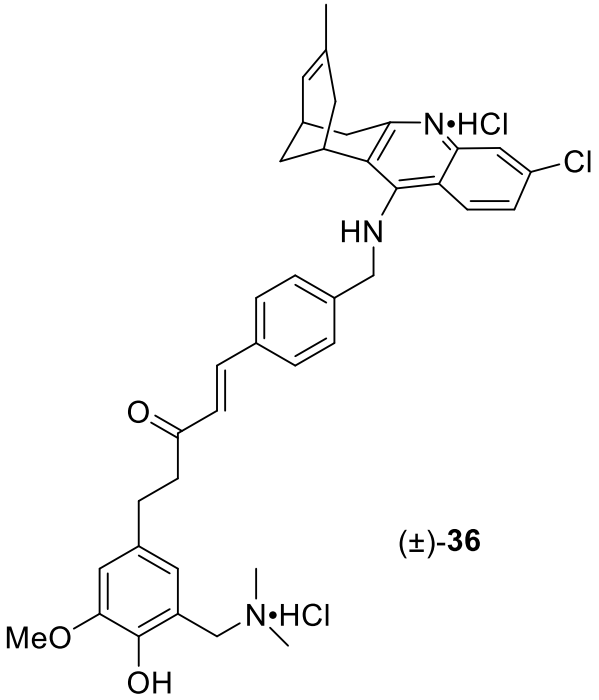
(±)-**27**

(±)-1-{4-{[(3-chloro-6,7,10,11-tetrahydro-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]methyl}phenyl}-5-[3-(dimethylamino)methyl-4-hydroxy-5-methoxyphenyl]pent-1-en-3-one, (±)-**36** – ^{13}C NMR (500 MHz, CD_3OD)



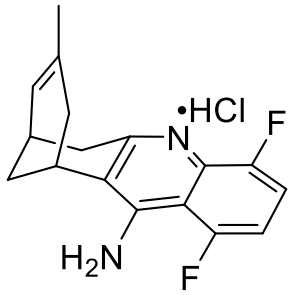
(±)-**36**

(±)-1-{4-{[(3-chloro-6,7,10,11-tetrahydro-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]methyl}phenyl}-5-[3-(dimethylamino)methyl-4-hydroxy-5-methoxyphenyl]pent-1-en-3-one, (±)-**36** – ^{13}C NMR (125.8 MHz, CD_3OD)



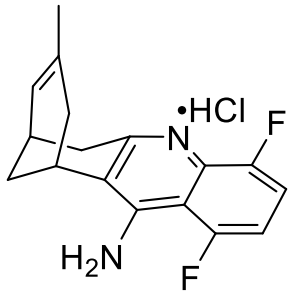
(±)-**36**

(±)-12-amine-1,4-difluoro-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*]quinoline, (±)-**39a** – ^{1}H NMR (400 MHz, CD_3OD)



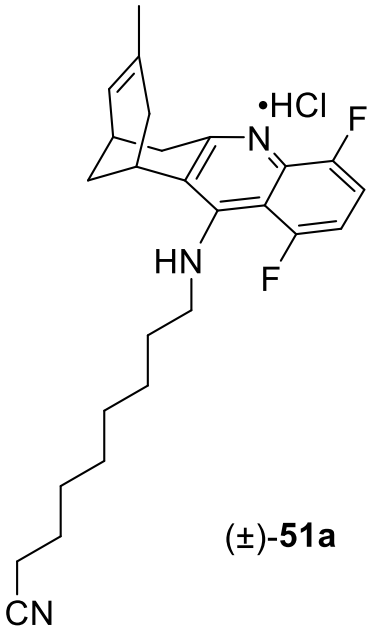
(±)-**39a**

(±)-12-amine-1,4-difluoro-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*]quinoline, (±)-**39a** – ^{13}C NMR (100.6 MHz, CD_3OD)



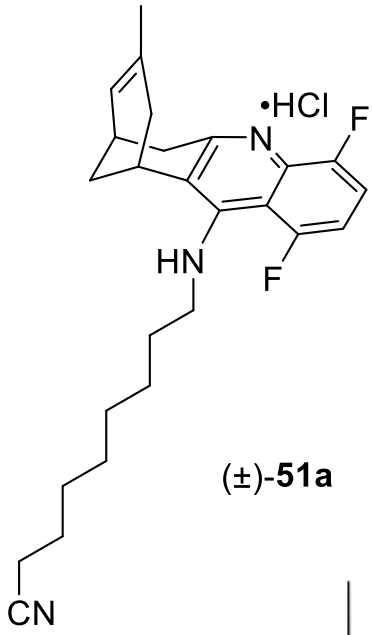
(±)-**39a**

(±)-9-[(1,4-difluoro-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*]quinolin-12-yl)amino]nonanenitrile, (±)-**51a** – ^{1}H NMR (400 MHz, CD_3OD)



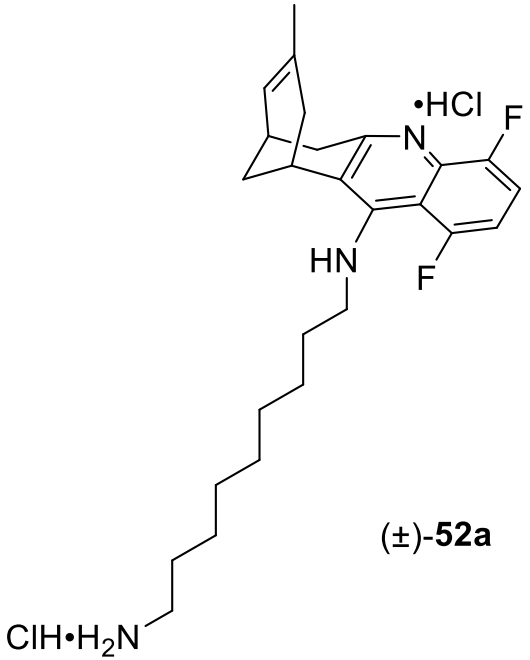
(±)-**51a**

(±)-9-[(1,4-difluoro-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*]quinolin-12-yl)amino]nonanenitrile, (±)-**51a** – ^{13}C NMR (100.6 MHz, CD_3OD)



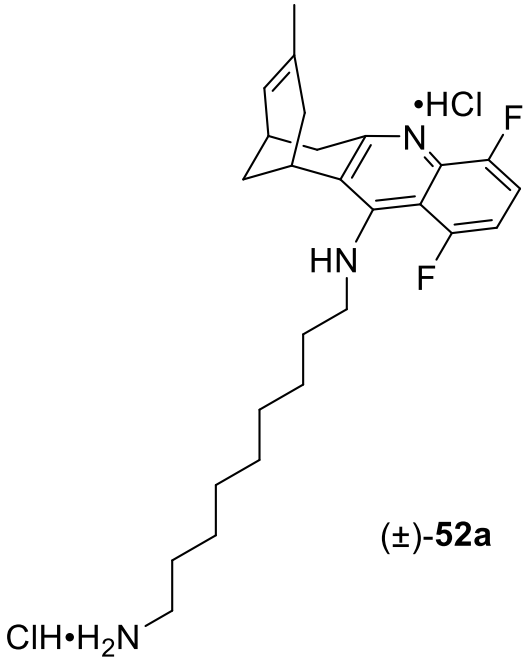
(±)-**51a**

(±)-*N*-(1,4-difluoro-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*]quinolin-12-yl)nonane-1,9-diamine, (±)-**52a** – ^{1}H NMR (400 MHz, CD_3OD)



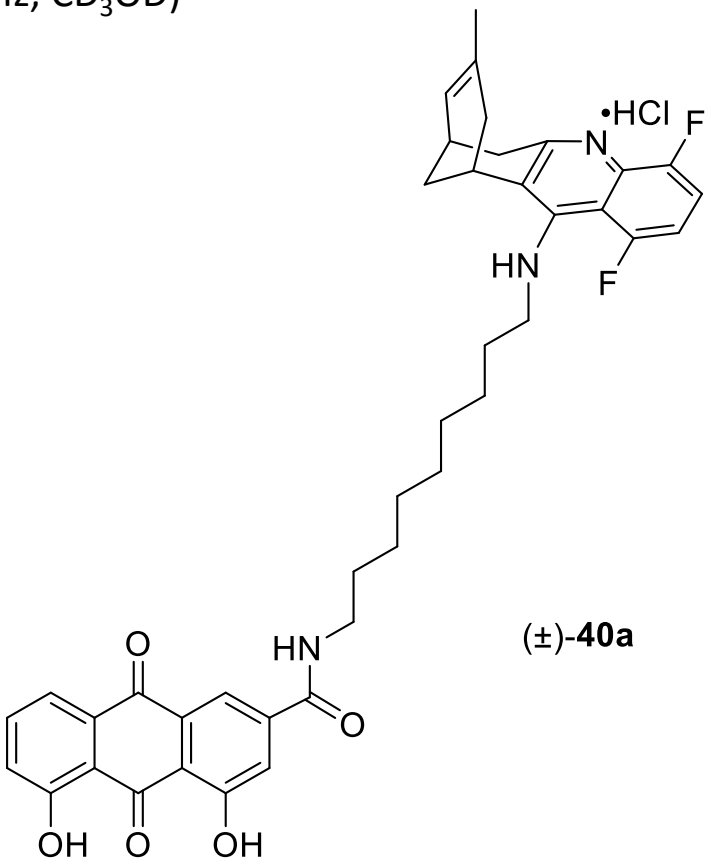
(±)-**52a**

(±)-*N*-(1,4-difluoro-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*]quinolin-12-yl)nonane-1,9-diamine, (±)-**52a** – ^{13}C NMR (100.6 MHz, CD_3OD)



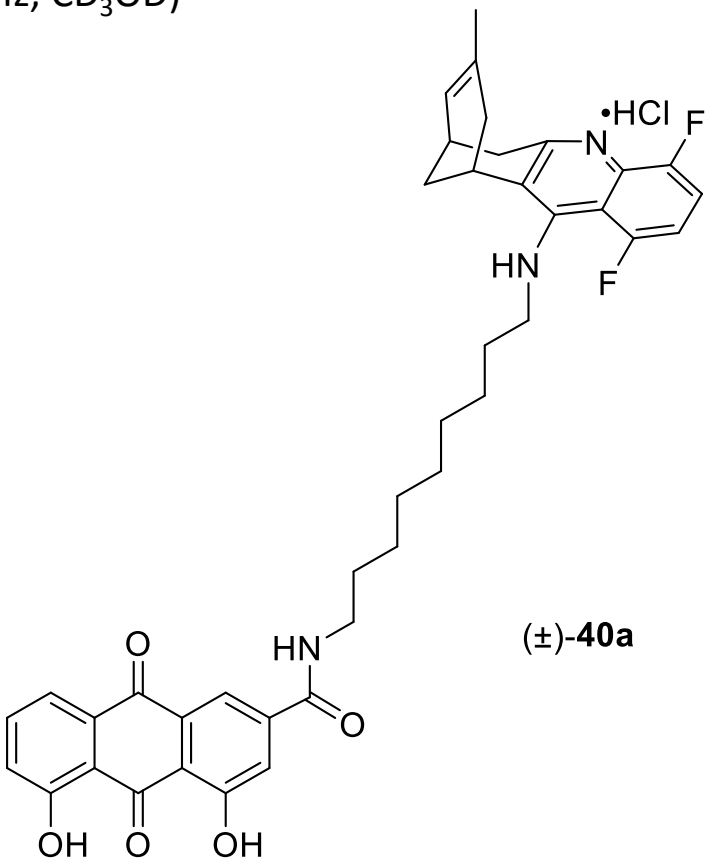
(±)-**52a**

(±)-*N*-{9-[(1,4-difluoro-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*]quinolin-12-yl)amino]nonyl}-9,10-dihydro-4,5-dihydroxy-9,10-dioxoanthracene-2-carboxamide, (±)-**40a** – ^{1}H NMR (400 MHz, CD_3OD)



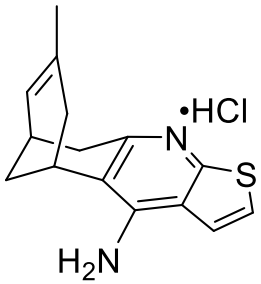
(±)-**40a**

(±)-*N*-{9-[(1,4-difluoro-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*]quinolin-12-yl)amino]nonyl}-9,10-dihydro-4,5-dihydroxy-9,10-dioxoanthracene-2-carboxamide (±)-**40a** – ^{13}C NMR (100.6 MHz, CD_3OD)



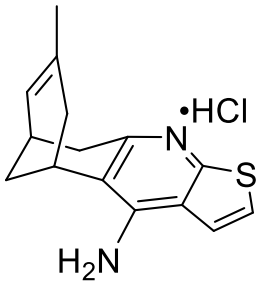
(±)-**40a**

(±)-4-amine-5,6,9,10-tetrahydro-7-methyl-5,9-methanocycloocta[*b*]thieno[2,3-*e*]pyridine, (±)-**39b** – ^{1}H NMR (400 MHz, CD_3OD)



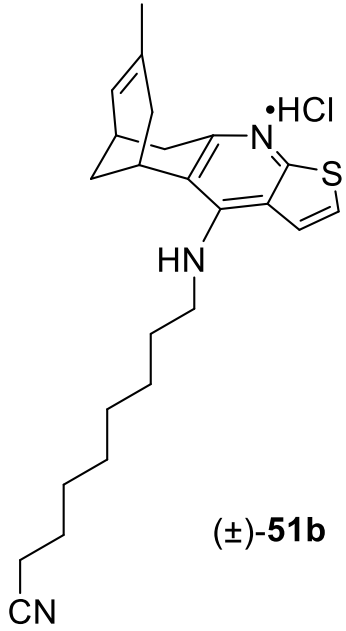
(±)-**39b**

(±)-4-amine-5,6,9,10-tetrahydro-7-methyl-5,9-methanocycloocta[*b*]thieno[2,3-*e*]pyridine, (±)-**39b** – ^{13}C NMR (100.6 MHz, CD_3OD)



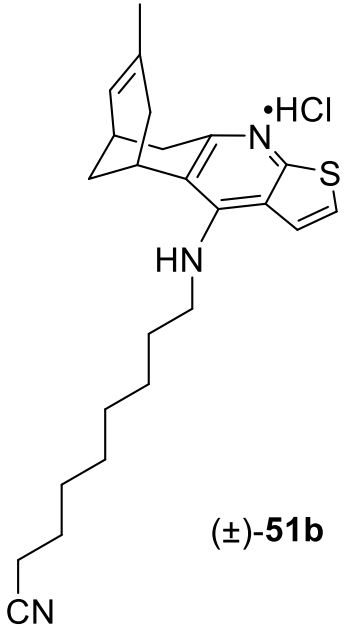
(±)-**39b**

(±)-9-[(7-methyl-5,6,9,10-tetrahydro-5,9-methanocycloocta[*b*]thieno[3,2-*e*]pyridin-4-yl)amino]nonanenitrile, (±)-**51b** – ^{1}H NMR (400 MHz, CD_3OD)



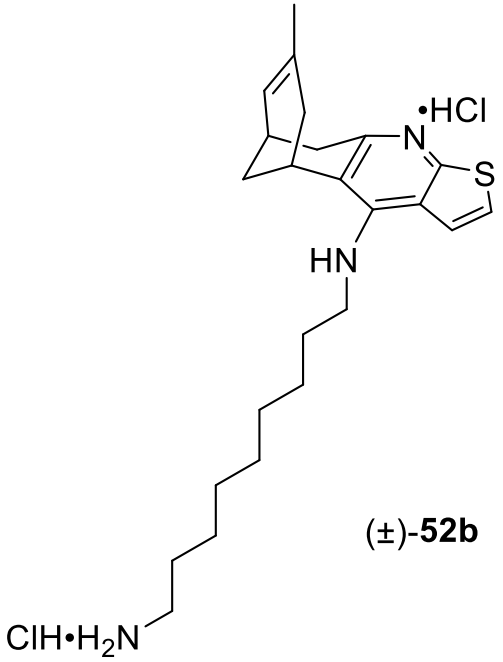
(±)-**51b**

(±)-9-[(7-methyl-5,6,9,10-tetrahydro-5,9-methanocycloocta[*b*]thieno[3,2-*e*]pyridin-4-yl)amino]nonanenitrile, (±)-**51b** – ^{13}C NMR (100.6 MHz, CD_3OD)



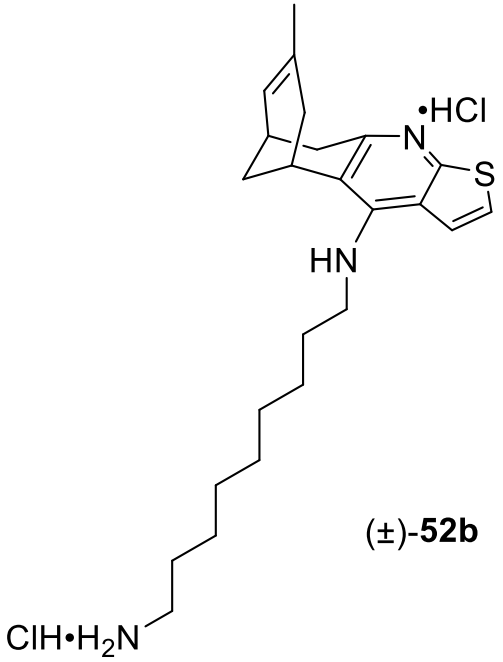
(±)-**51b**

(±)-*N*-(5,6,9,10-tetrahydro-7-methyl-5,9-methanocycloocta[*b*]thieno[3,2-*e*]pyridin-4-yl)nonane-1,9-diamine, (±)-**52b** – ^{1}H NMR (400 MHz, CD_3OD)



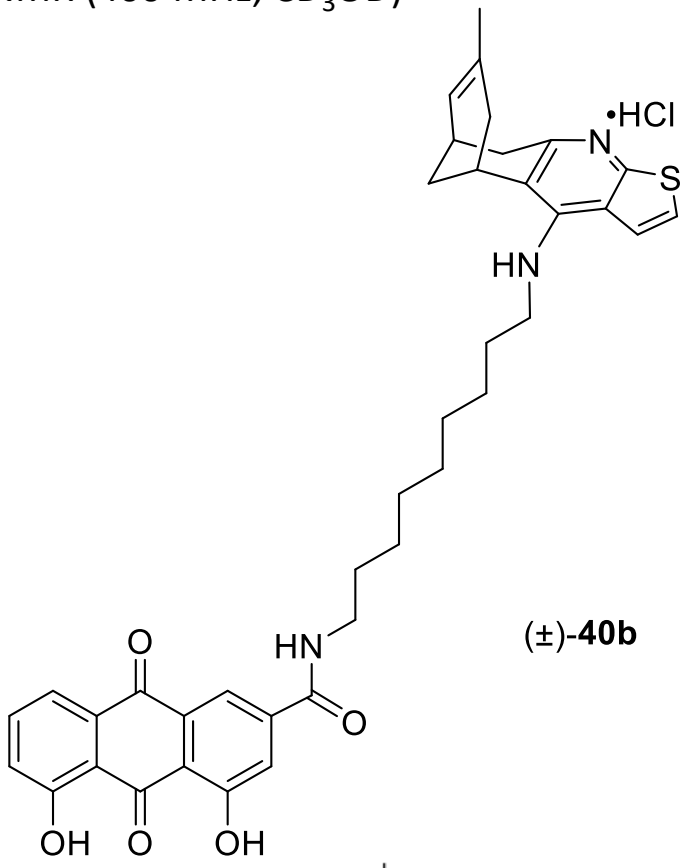
(±)-**52b**

(±)-*N*-(5,6,9,10-tetrahydro-7-methyl-5,9-methanocycloocta[*b*]thieno[3,2-*e*]pyridin-4-yl)nonane-1,9-diamine, (±)-**52b** – ^{13}C NMR (100.6 MHz, CD_3OD)



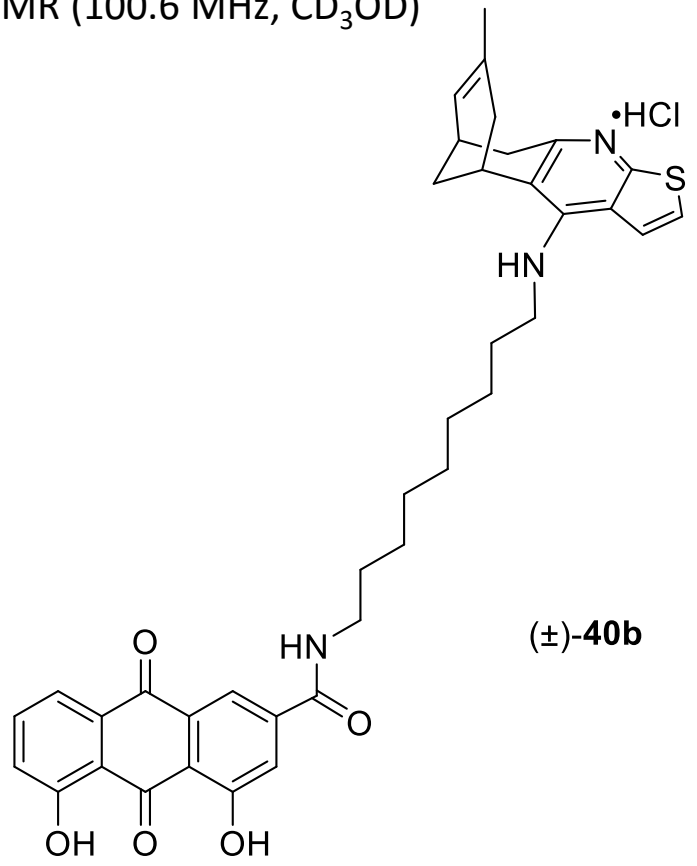
(±)-**52b**

(±)-9,10-dihydro-4,5-dihydroxy-9,10-dioxo-*N*-{9-[(5,6,9,10-tetrahydro-7-methyl-5,9-methanocycloocta[*b*]thieno[3,2-*e*]pyridin-4-yl)amino]nonyl}anthracene-2-carboxamide, (±)-**40b** – ^{1}H NMR (400 MHz, CD_3OD)



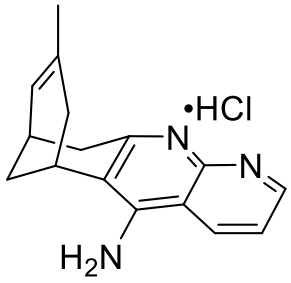
(±)-**40b**

(±)-9,10-dihydro-4,5-dihydroxy-9,10-dioxo-*N*-{9-[(5,6,9,10-tetrahydro-7-methyl-5,9-methanocycloocta[*b*]thieno[3,2-*e*]pyridin-4-yl)amino]nonyl}anthracene-2-carboxamide, (±)-**40b** – ^{13}C NMR (100.6 MHz, CD_3OD)



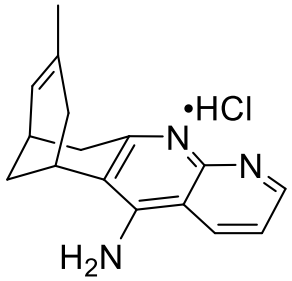
(±)-**40b**

(±)-5-amine-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*][1,8] naphthyridine, (±)-**39c** – ^{1}H NMR (400 MHz, CD_3OD)



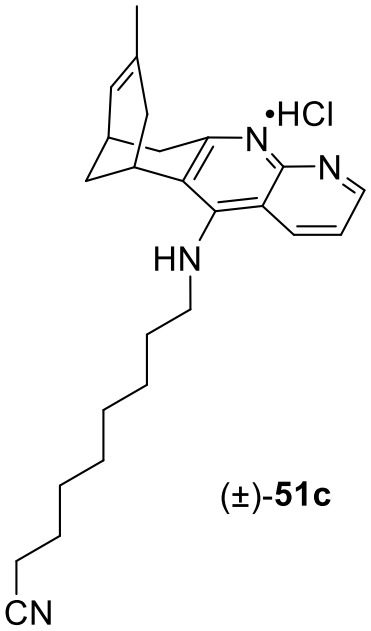
(±)-**39c**

(±)-5-amine-6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*][1,8] naphthyridine, (±)-**39c** – ^{13}C NMR (100.6 MHz, CD_3OD)



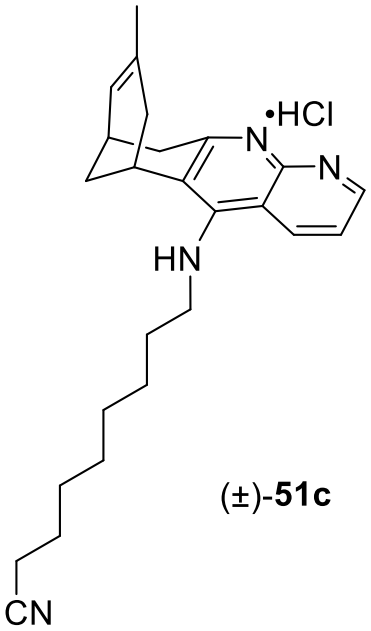
(±)-**39c**

(±)-9-[(6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*][1,8]naphthyridin-5-yl)amino]nonanenitrile, (±)-**51c** – ^{1}H NMR (400 MHz, CD_3OD)



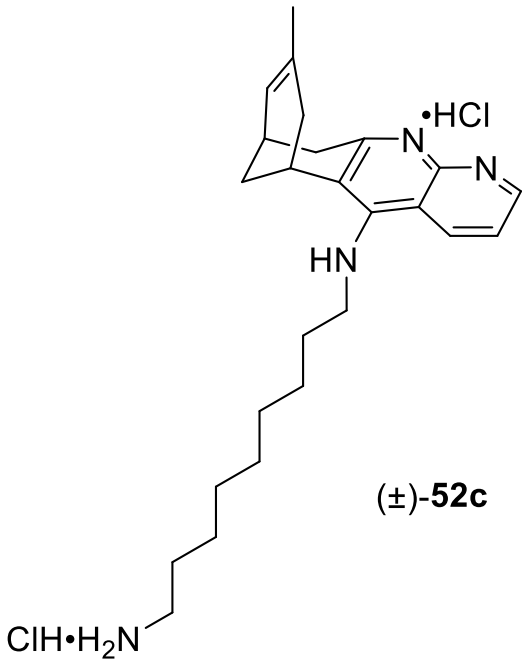
(±)-**51c**

(±)-9-[(6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*][1,8]naphthyridin-5-yl)amino]nonanenitrile, (±)-**51c** – ^{13}C NMR (100.6 MHz, CD_3OD)



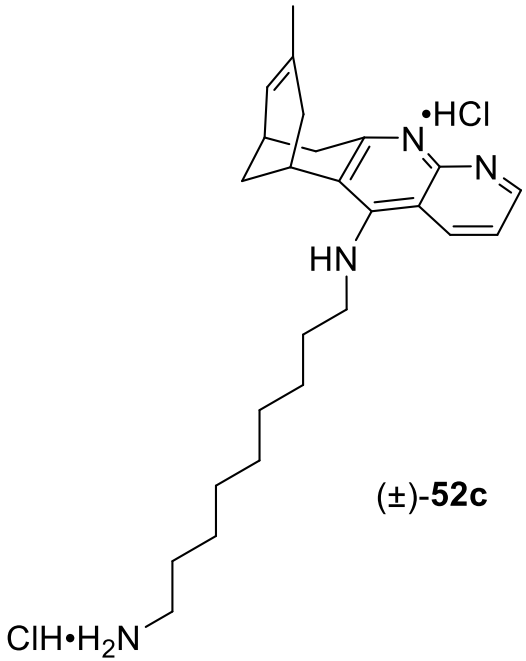
(±)-**51c**

(±)-*N*-(6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*][1,8]naphthyridin-5-yl)-1,9-diaminononane, (±)-**52c** – ^{1}H NMR (400 MHz, CD_3OD)



(±)-**52c**

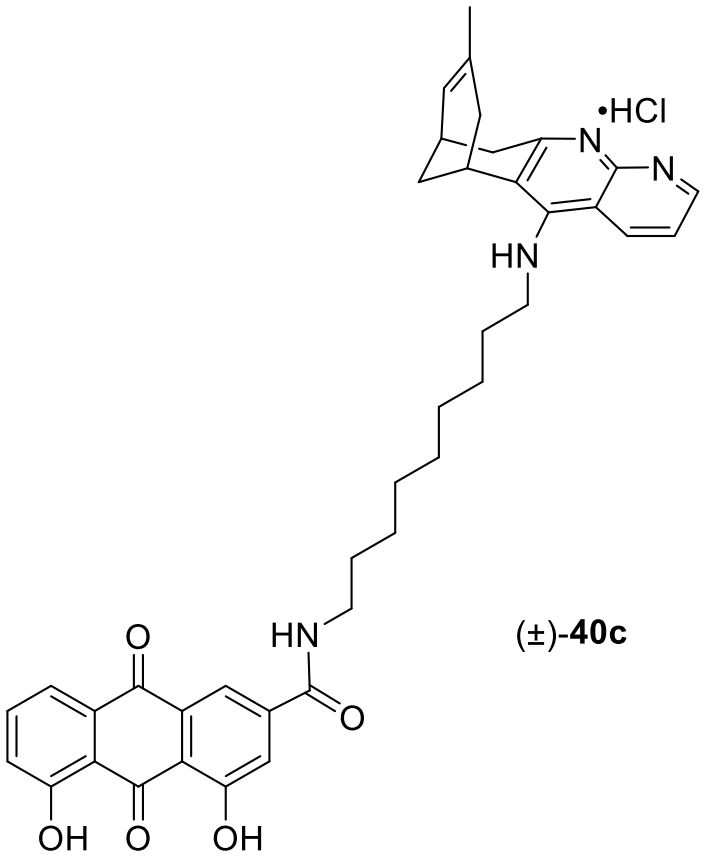
(±)-*N*-(6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*][1,8]naphthyridin-5-yl)-1,9-diaminononane, (±)-**52c** – ^{13}C NMR (100.6 MHz, CD_3OD)



(±)-**52c**

(±)-*N*-{9-[(6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*][1,8]naphthyridin-5-yl)amino]nonyl}-9,10-dihydro-4,5-dihydroxy-9,10-dioxoanthracene-2-carboxamide,

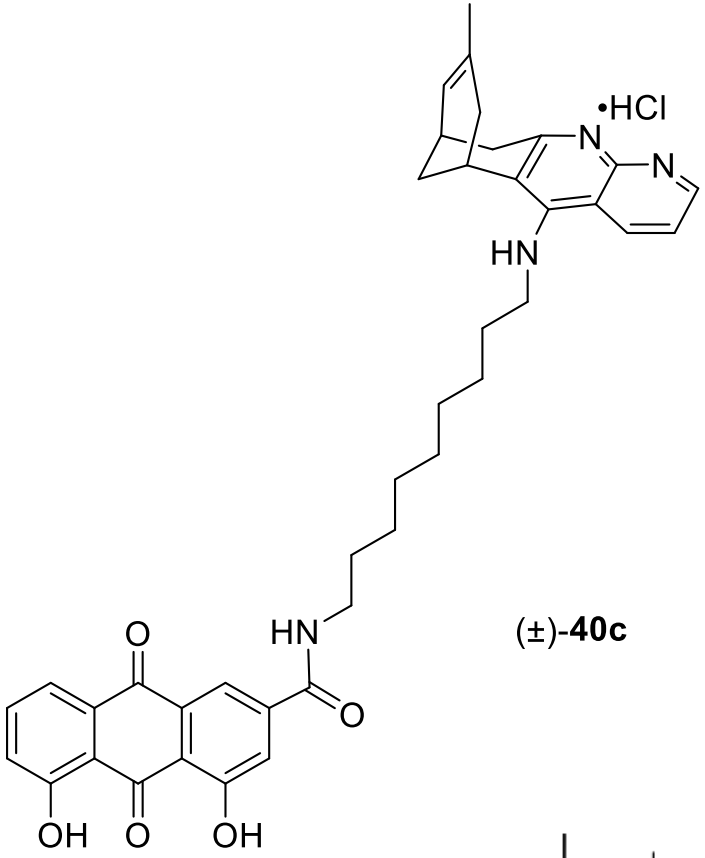
(±)-**40c** – ^{1}H NMR (400 MHz, CD_3OD)



(±)-**40c**

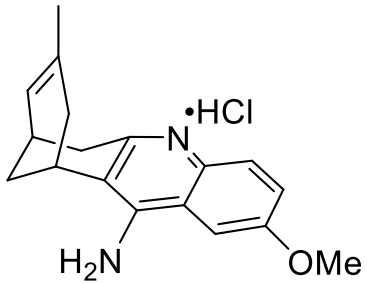
(±)-*N*-{9-[(6,7,10,11-tetrahydro-8-methyl-6,10-methanocycloocta[*b*][1,8]naphthyridin-5-yl)amino]nonyl}-9,10-dihydro-4,5-dihydroxy-9,10-dioxoanthracene-2-carboxamide,

(±)-**40c** – ^{13}C NMR (100.6 MHz, CD_3OD)



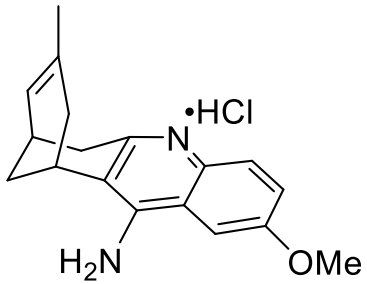
(±)-**40c**

(±)-6,7,10,11-tetrahydro-2-methoxy-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-amine, (±)-**39d** – ^{1}H NMR (400 MHz, CD_3OD)



(±)-**39d**

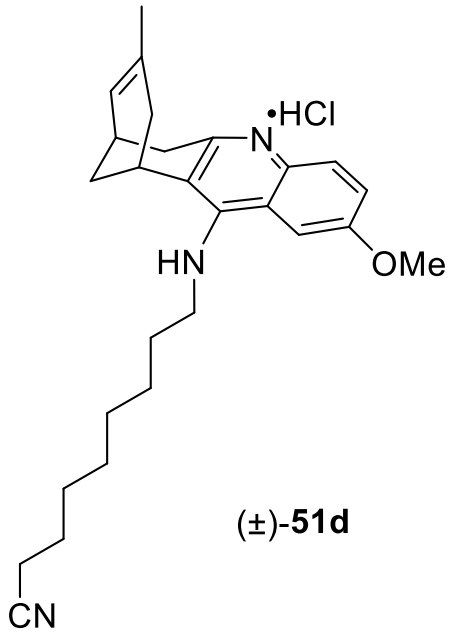
(±)-6,7,10,11-tetrahydro-2-methoxy-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-amine, (±)-**39d** – ^{13}C NMR (100.6 MHz, CD_3OD)



(±)-**39d**

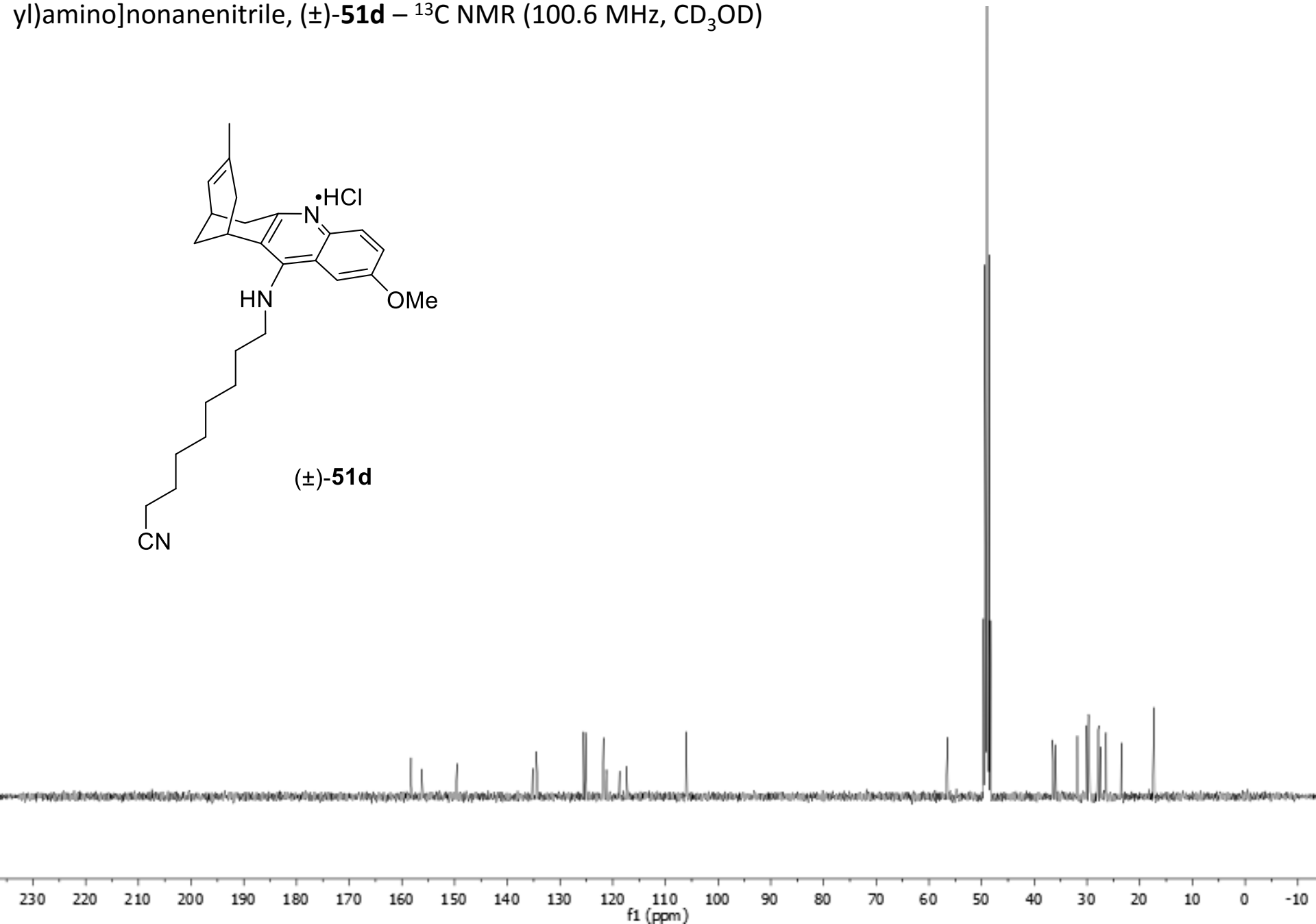
(±)-9-[(6,7,10,11-tetrahydro-2-methoxy-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]nonanenitrile, (±)-**51d** –

^{1}H NMR (400 MHz, CD_3OD)

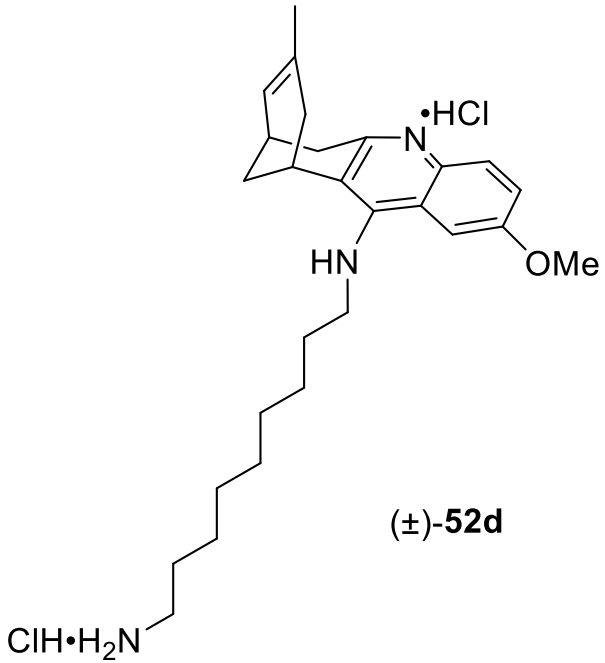


(±)-**51d**

(±)-9-[(6,7,10,11-tetrahydro-2-methoxy-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]nonanenitrile, (±)-**51d** – ^{13}C NMR (100.6 MHz, CD_3OD)

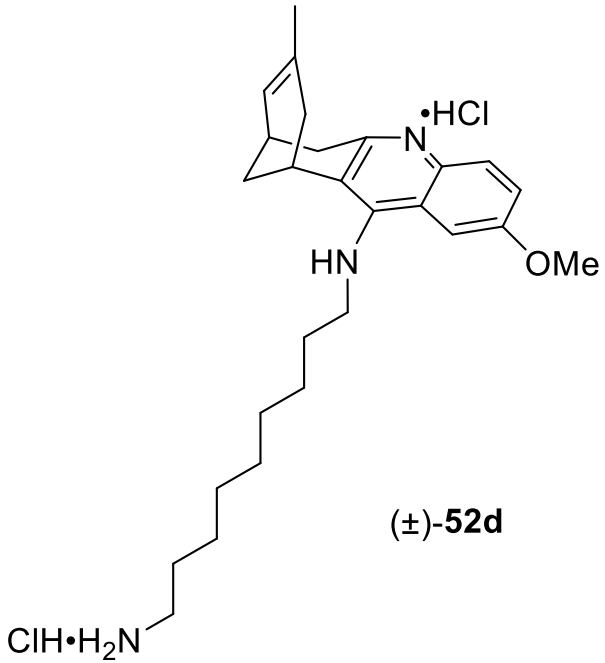


(±)-*N*-(6,7,10,11-tetrahydro-2-methoxy-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)nonane-1,9-diamine, (±)-**52d** – ^{1}H NMR (400 MHz, CD_3OD)



(±)-**52d**

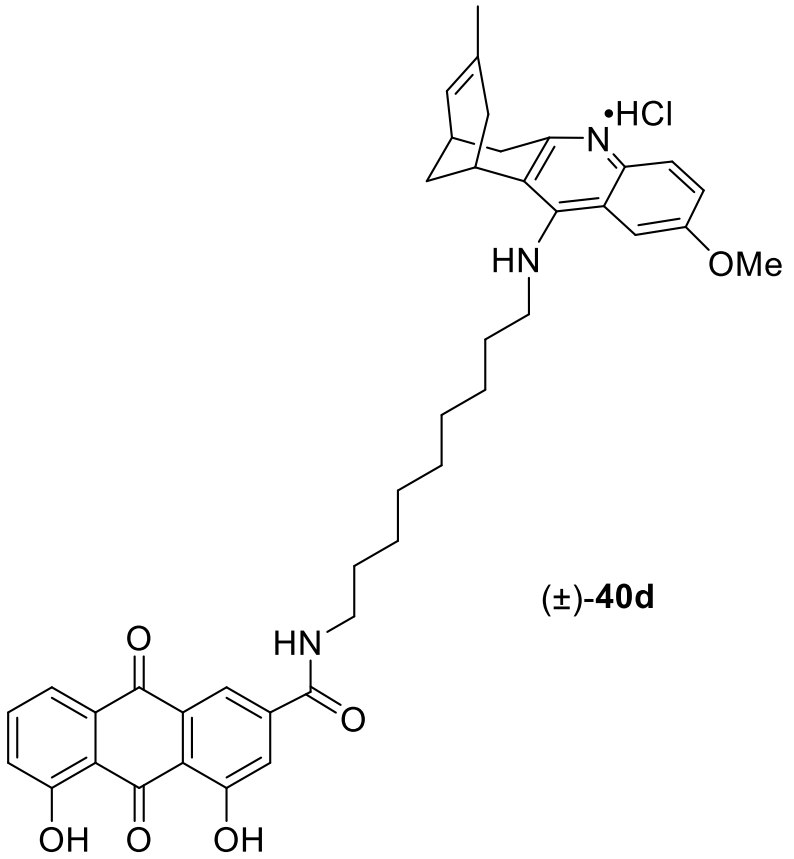
(±)-*N*-(6,7,10,11-tetrahydro-2-methoxy-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)nonane-1,9-diamine, (±)-**52d** – ^{13}C NMR (100.6 MHz, DMSO-d_6)



(±)-**52d**

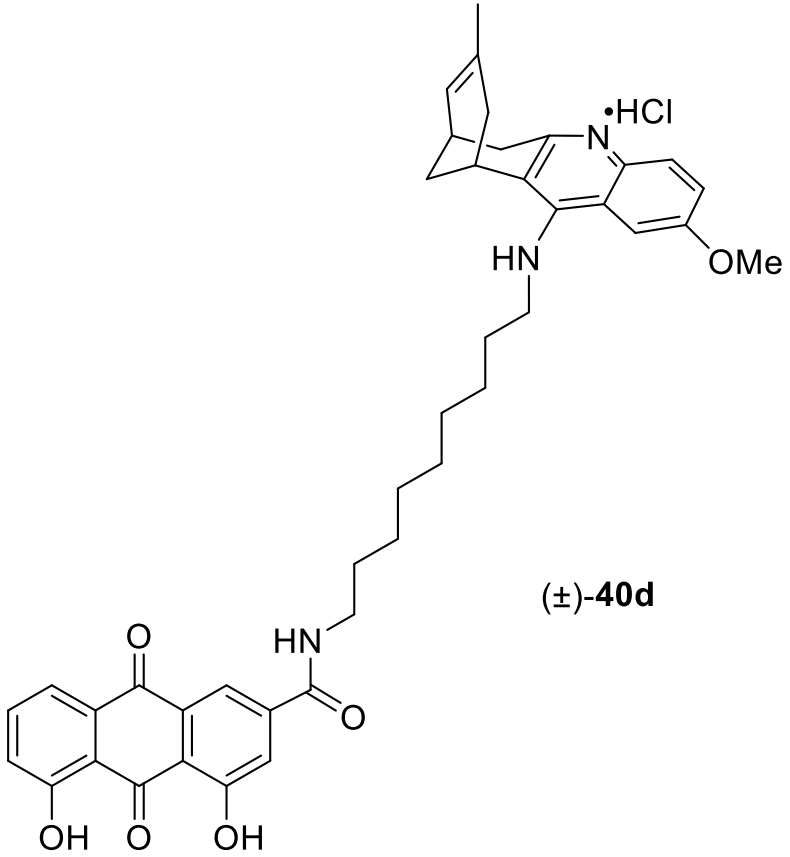
(±)-9,10-dihydro-4,5-dihydroxy-9,10-dioxo-*N*-{9-[(6,7,10,11-tetrahydro-2-methoxy-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]nonyl}anthracene-2-carboxamide, (±)-**40d** –

^{1}H NMR (400 MHz, CD_3OD)

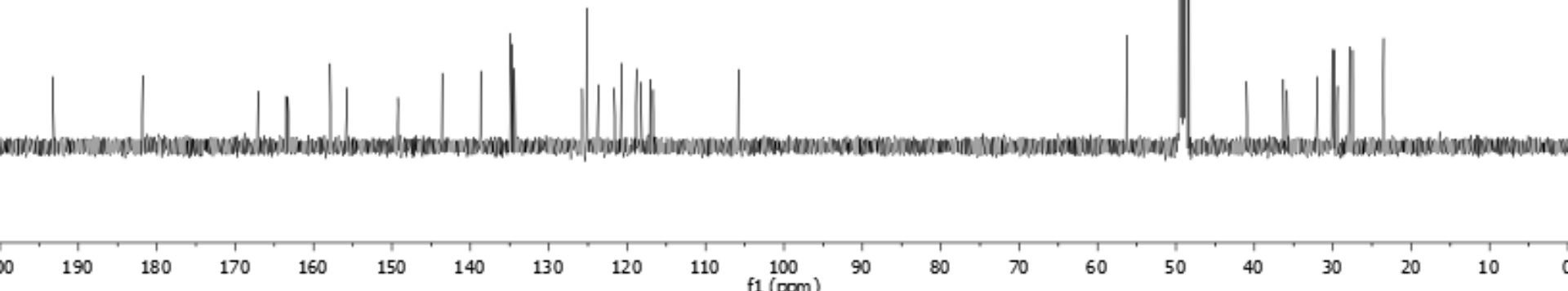


(±)-**40d**

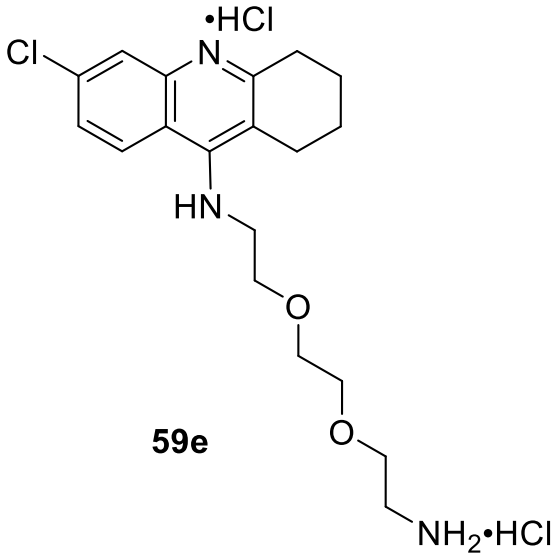
(±)-9,10-dihydro-4,5-dihydroxy-9,10-dioxo-*N*-{9-[(6,7,10,11-tetrahydro-2-methoxy-9-methyl-7,11-methanocycloocta[*b*]quinolin-12-yl)amino]nonyl}anthracene-2-carboxamide,
(±)-**40d** – ^{13}C NMR (100.6 MHz, CD_3OD)



(±)-**40d**

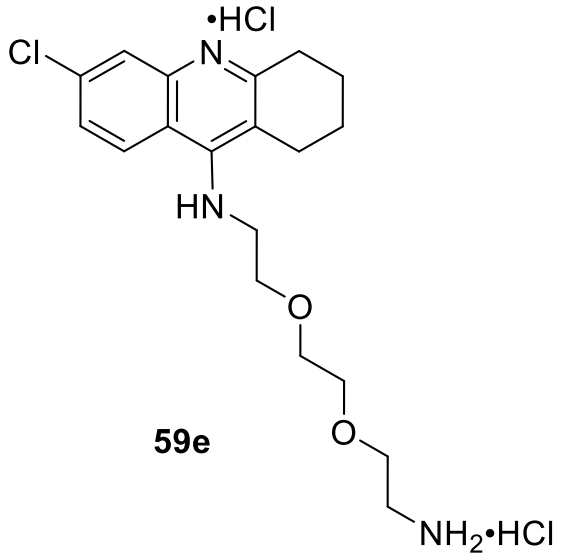


N-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-3,6-dioxaoctane-1,8-diamine, **59e** – ^{1}H NMR (400 MHz, CD_3OD)



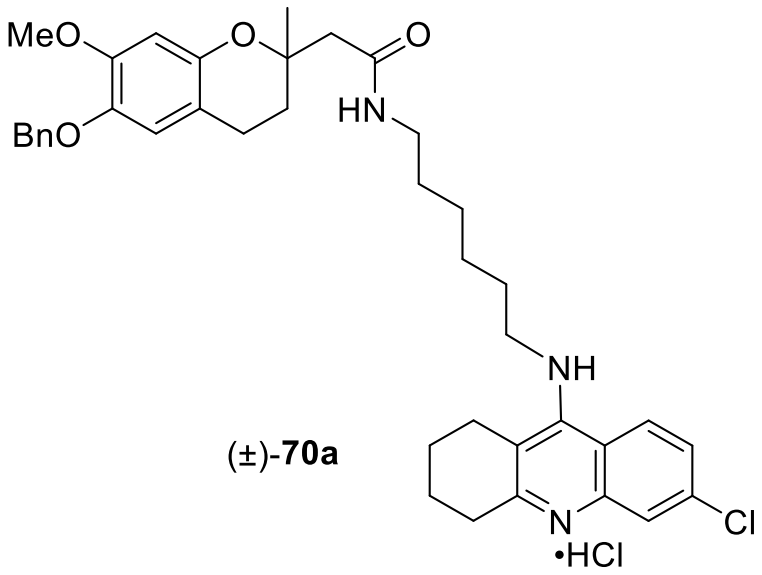
59e

N-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-3,6-dioxaoctane-1,8-diamine, **59e** – ^{13}C NMR (100.6 MHz, CD_3OD)



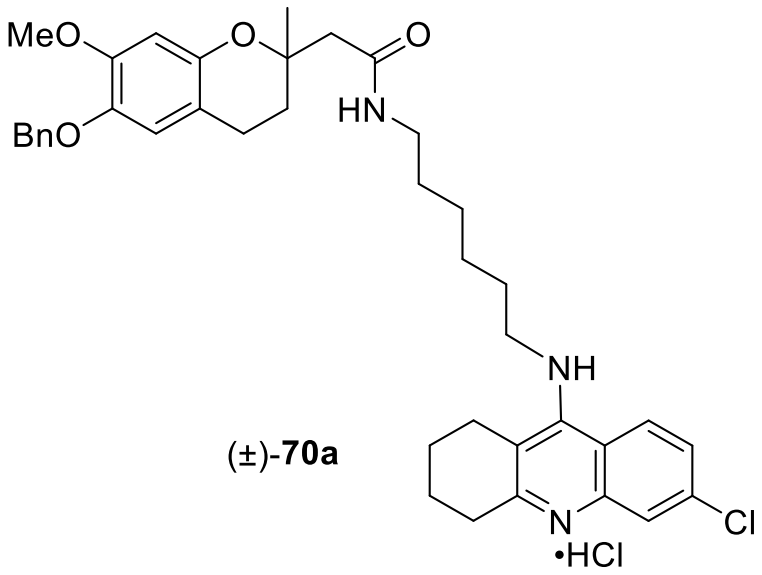
59e

(±)-*N*-{6-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]hexyl}-2-(6-benzyloxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**70a** – ^{1}H NMR (400 MHz, CD_3OD)



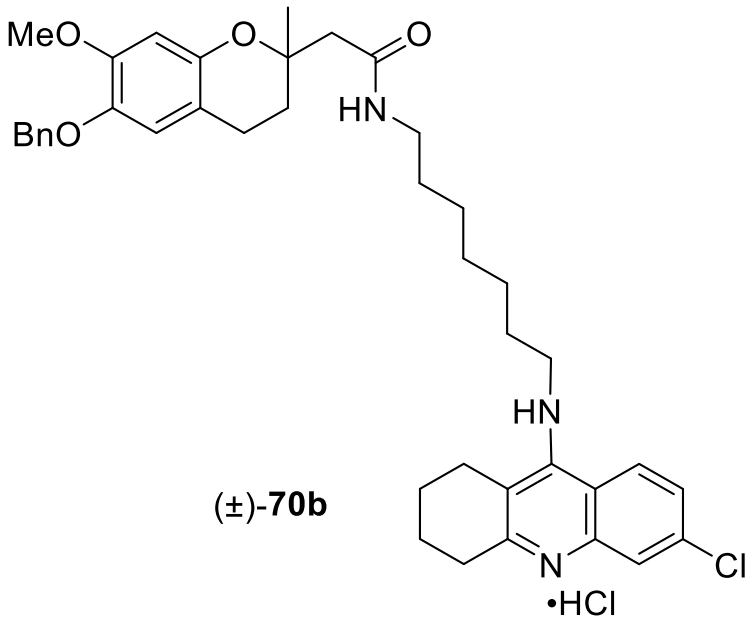
(±)-**70a**

(±)-*N*-{6-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]hexyl}-2-(6-benzyloxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**70a** – ^{13}C NMR (100.6 MHz, CD_3OD)



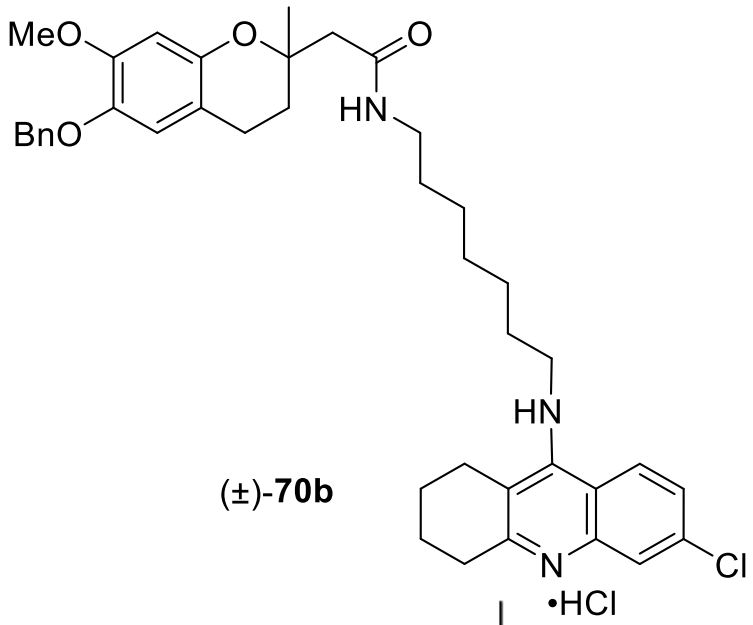
(±)-**70a**

(±)-*N*-{7-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]heptyl}-2-(6-benzyloxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**70b** – ^{1}H NMR (400 MHz, CD_3OD)



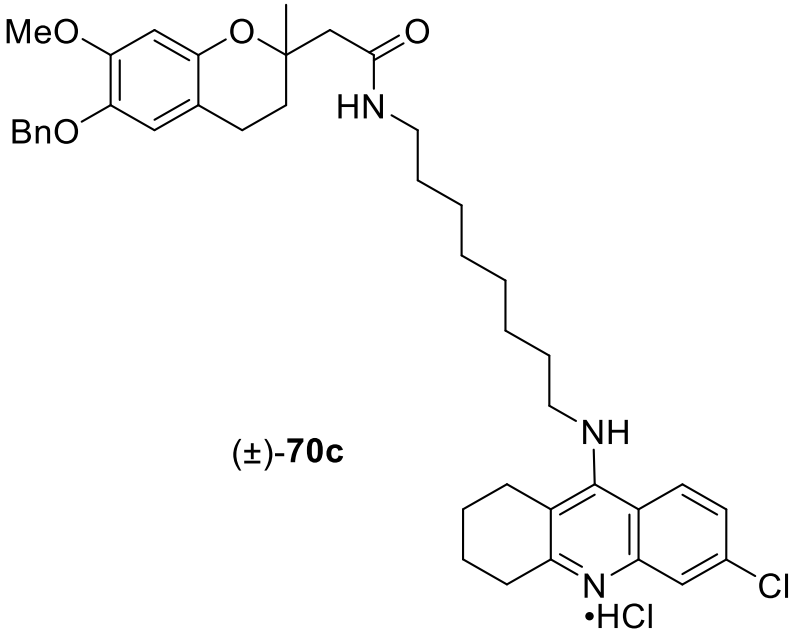
(±)-**70b**

(±)-*N*-{7-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]heptyl}-2-(6-benzyloxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**70b** – ^{13}C NMR (100.6 MHz, CD_3OD)



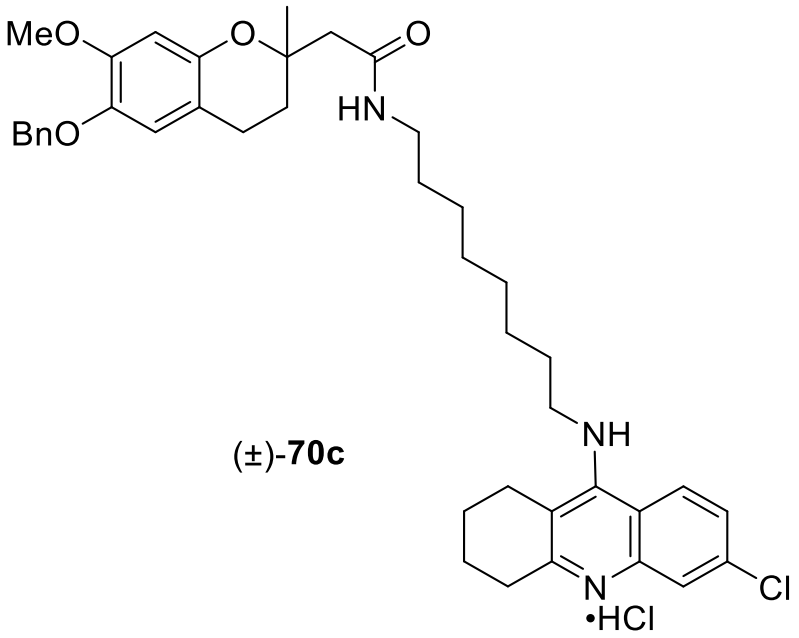
(±)-**70b**

(±)-*N*-{8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]octyl}-2-(6-benzyloxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**70c** – ^{1}H NMR (400 MHz, CD_3OD)



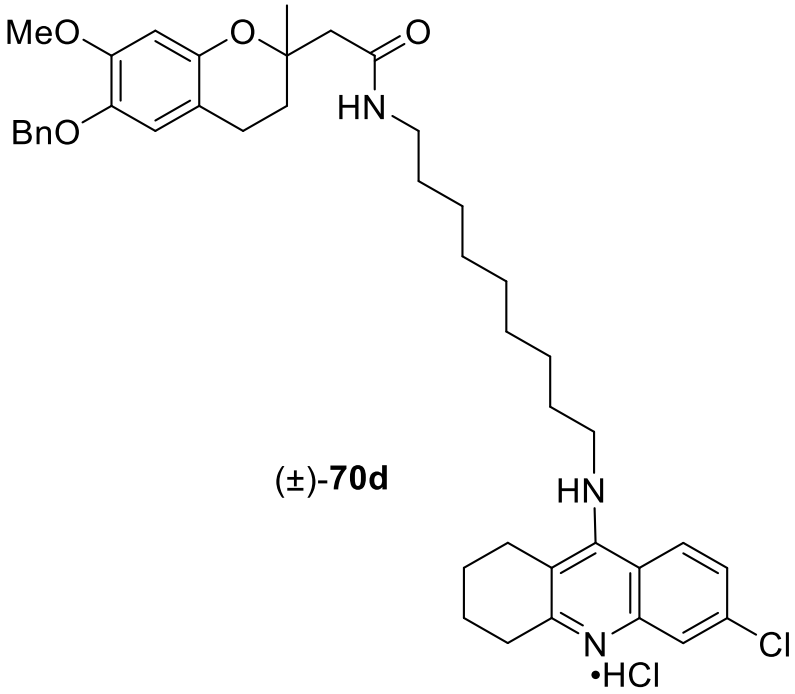
(±)-**70c**

(±)-*N*-{8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]octyl}-2-(6-benzyloxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**70c** – ^{13}C NMR (100.6 MHz, CD_3OD)



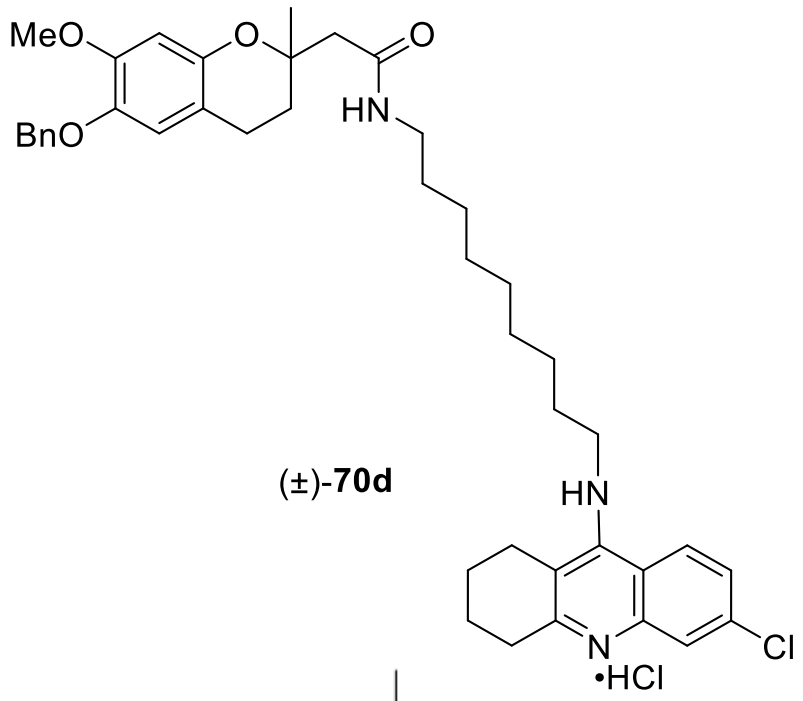
(±)-**70c**

(±)-*N*-{9-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]nonyl}-2-(6-benzyloxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**70d** – ^{1}H NMR (400 MHz, CD_3OD)



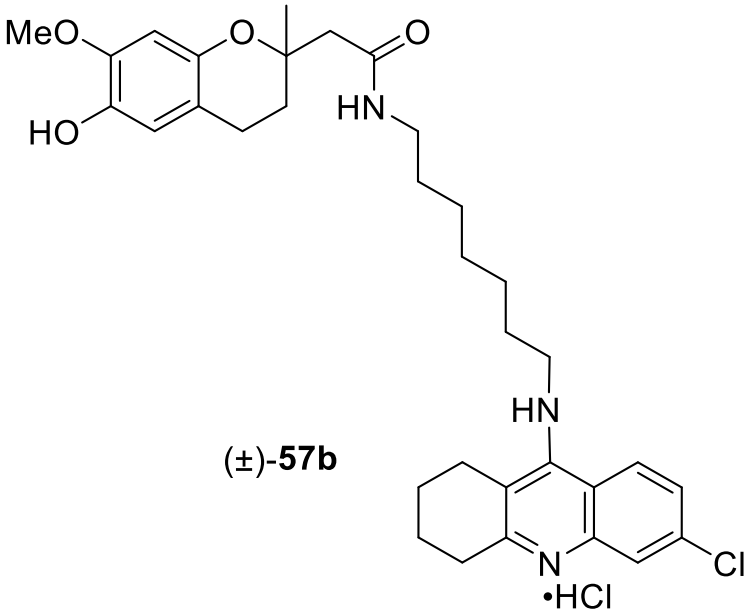
(±)-**70d**

(±)-*N*-{9-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]nonyl}-2-(6-benzyloxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**70d** – ^{13}C NMR (100.6 MHz, CD_3OD)



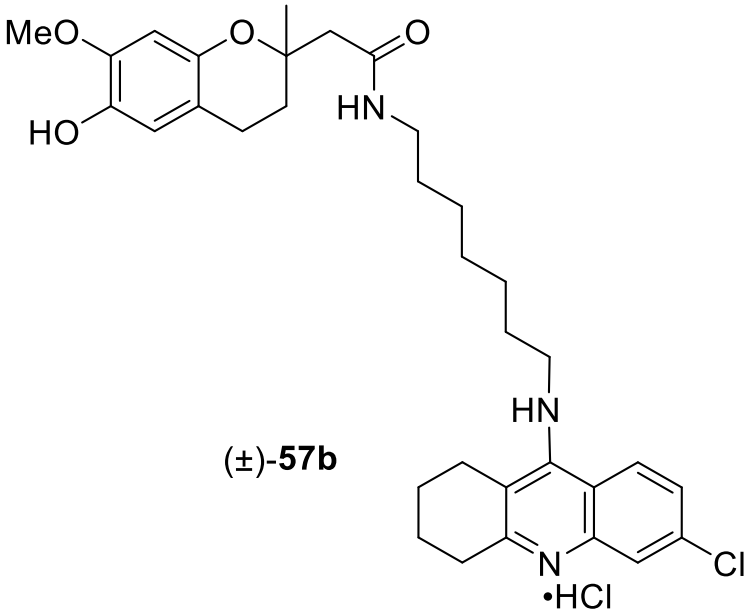
(±)-**70d**

(±)-*N*-{7-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]heptyl}-2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**57b** – ^{1}H NMR (400 MHz, CD_3OD)



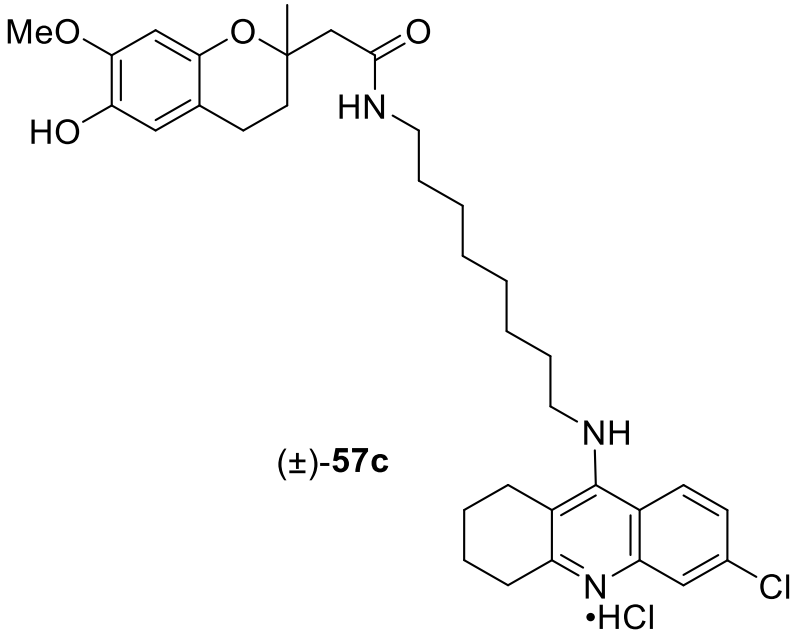
(±)-**57b**

(±)-*N*-{7-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]heptyl}-2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**57b** – ^{13}C NMR (100.6 MHz, CD_3OD)



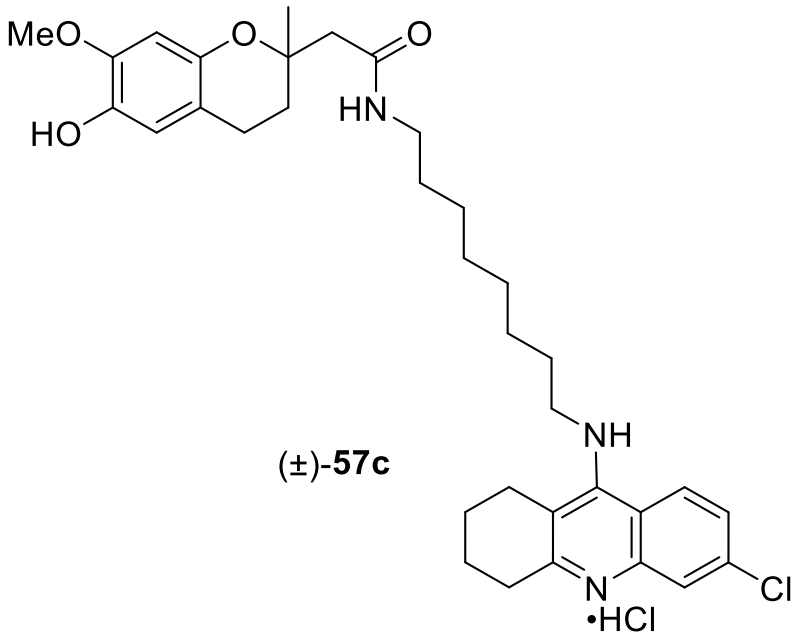
(±)-**57b**

(±)-*N*-{8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]octyl}-2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**57c** – ^{1}H NMR (400 MHz, CD_3OD)



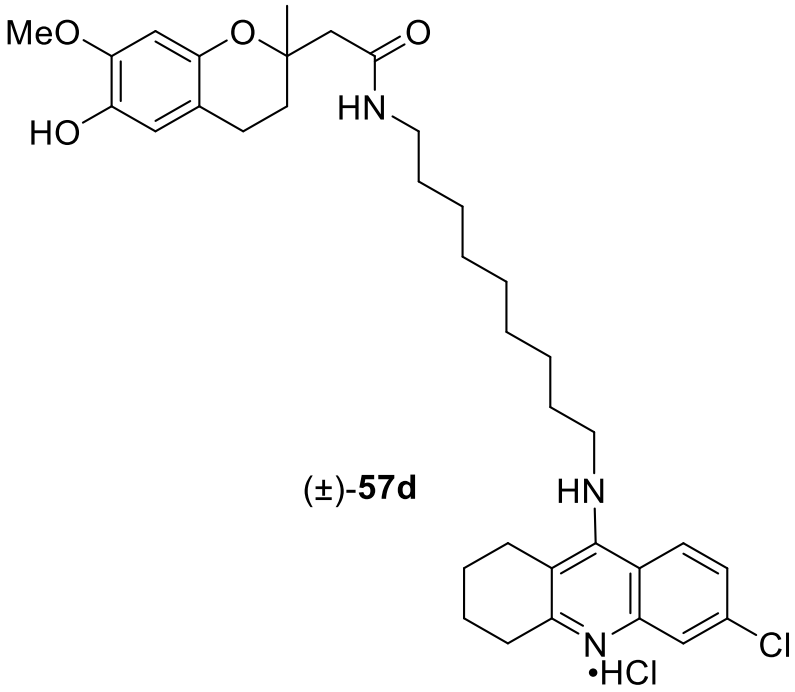
(±)-**57c**

(±)-*N*-{8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]octyl}-2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**57c** – ^{13}C NMR (100.6 MHz, CD_3OD)



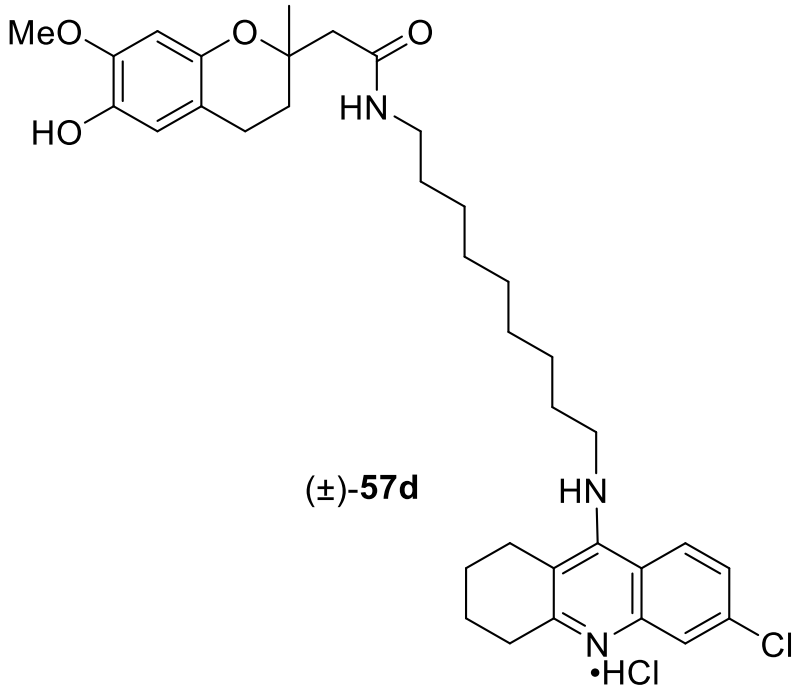
(±)-**57c**

(±)-*N*-{9-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]nonyl}-2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**57d** – ^{1}H NMR (400 MHz, CD_3OD)



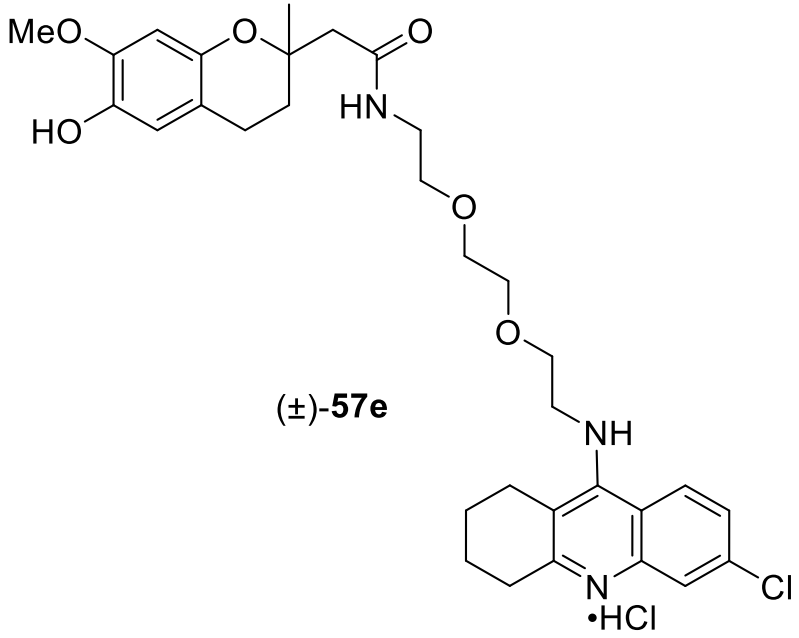
(±)-**57d**

(±)-*N*-{9-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]nonyl}-2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**57d** – ^{13}C NMR (100.6 MHz, CD_3OD)



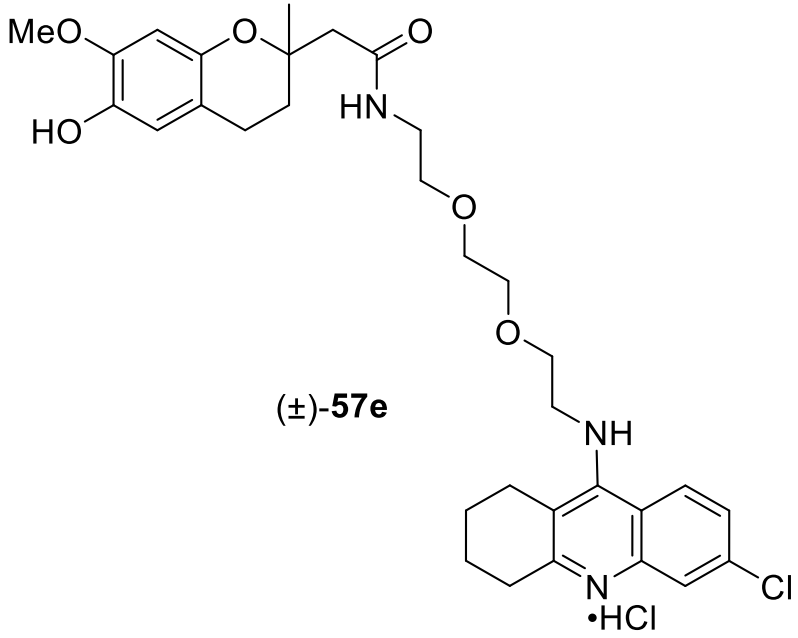
(±)-**57d**

(±)-*N*-{8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-3,6-dioxaoctyl}-2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**57e** – ^{1}H NMR (400 MHz, CD_3OD)



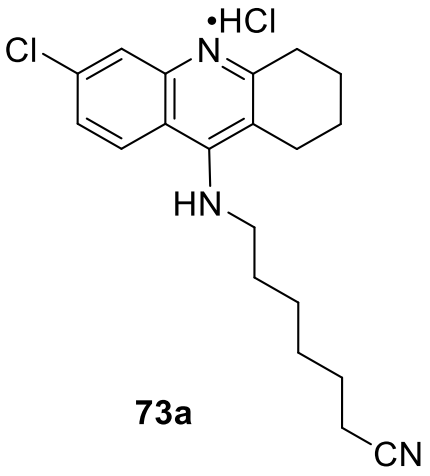
(±)-**57e**

(±)-*N*-{8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-3,6-dioxaoctyl}-2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)acetamide, (±)-**57e** – ^{13}C NMR (100.6 MHz, CD_3OD)

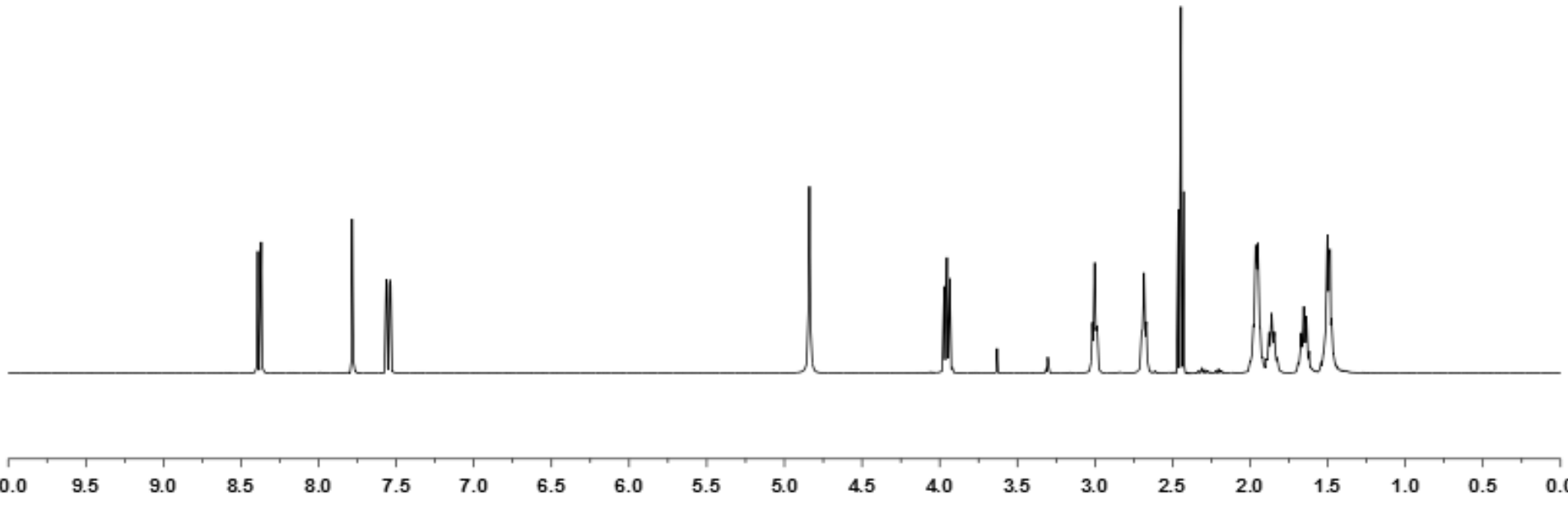


(±)-**57e**

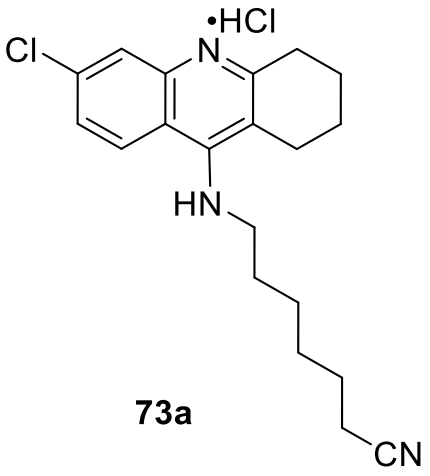
7-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]heptanenitrile, **73a** – ^{1}H NMR (400 MHz, CD_3OD)



73a

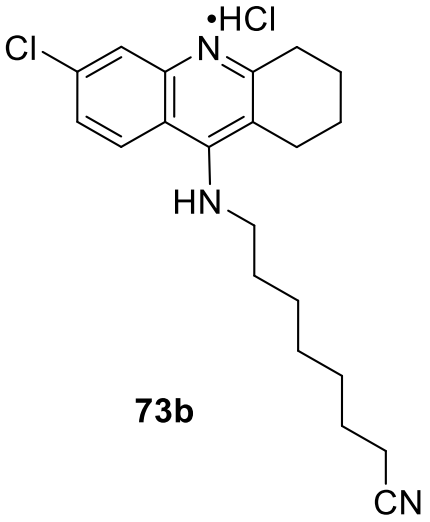


7-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]heptanenitrile, **73a** – ^{13}C NMR (100.6 MHz, CD_3OD)

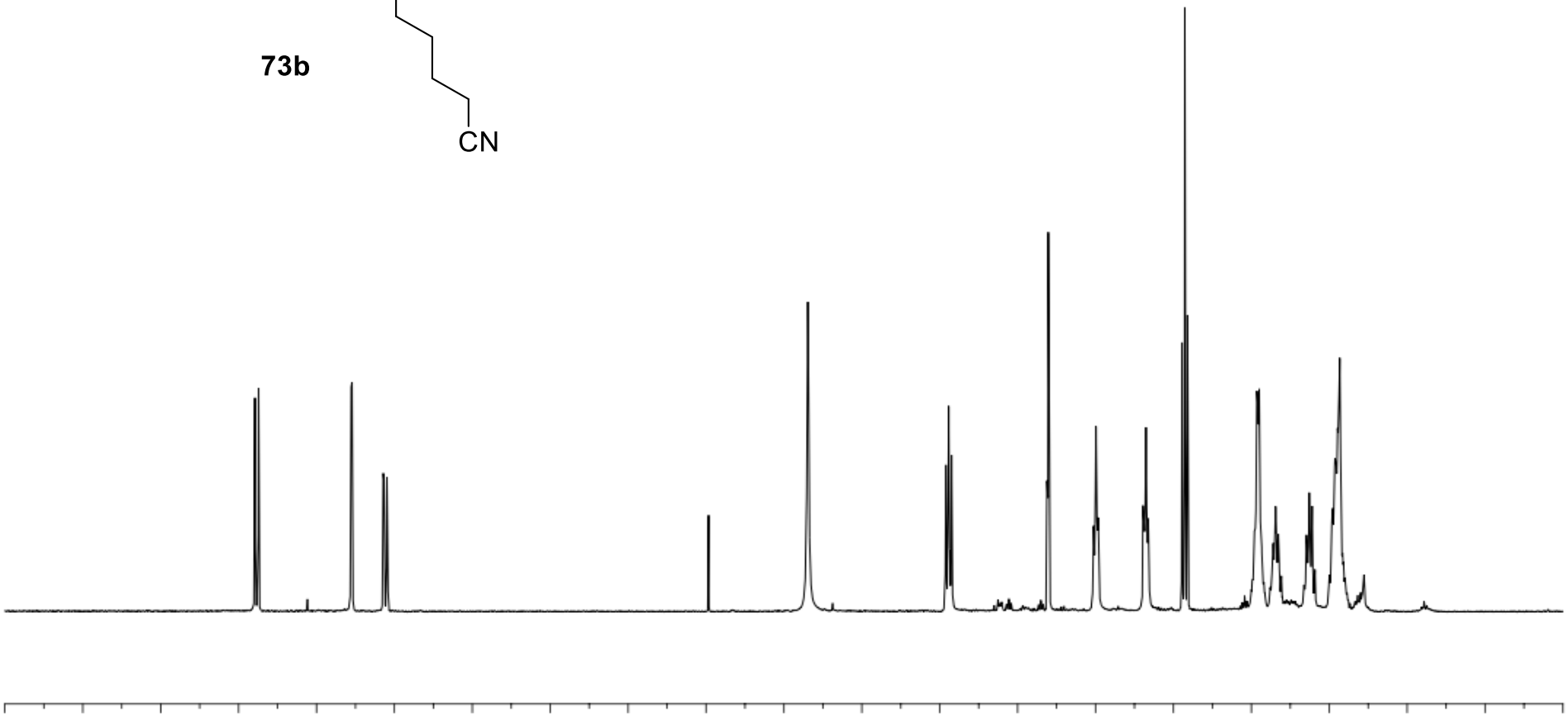


73a

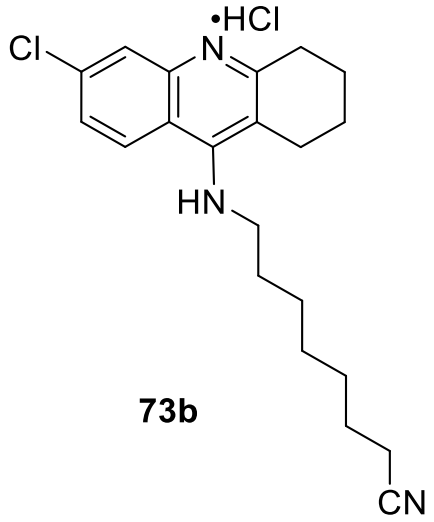
8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]octanenitrile, **73b** – ^{1}H NMR (400 MHz, CD_3OD)



73b

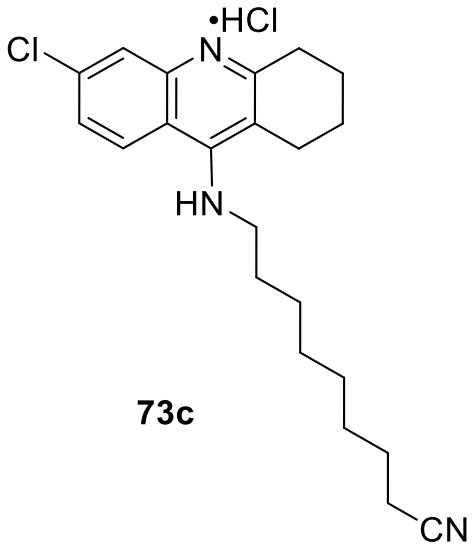


8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]octanenitrile, **73b** – ^{13}C NMR (100.6 MHz, CD_3OD)



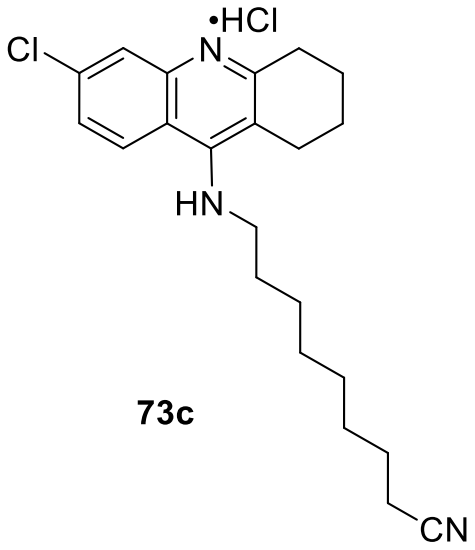
73b

9-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]nonanenitrile, **73c** – ^{1}H NMR (400 MHz, CD_3OD)



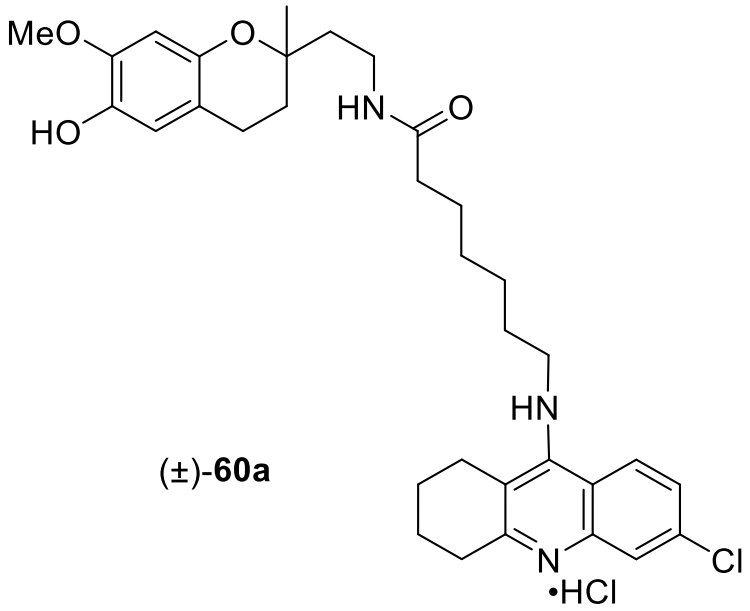
73c

9-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]nonanenitrile, **73c** – ^{13}C NMR (100.6 MHz, CD_3OD)



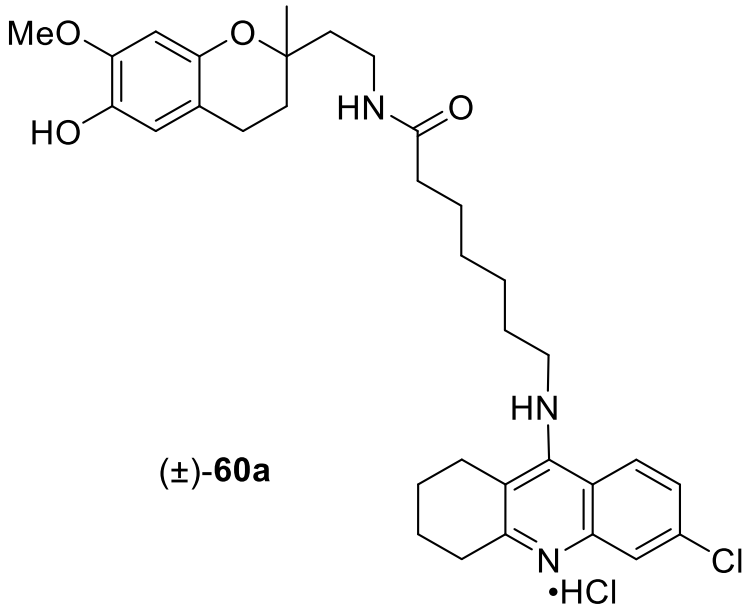
73c

(±)-7-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]heptanamide, (±)-**60a** – ^{1}H NMR (400 MHz, CD_3OD)



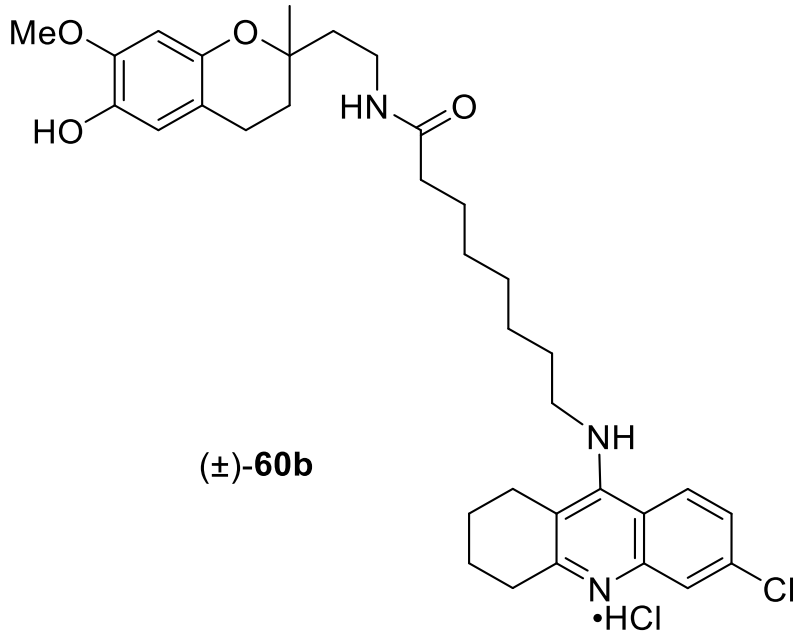
(±)-**60a**

(±)-7-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]heptanamide, (±)-**60a** – ^{13}C NMR (100.6 MHz, CD_3OD)



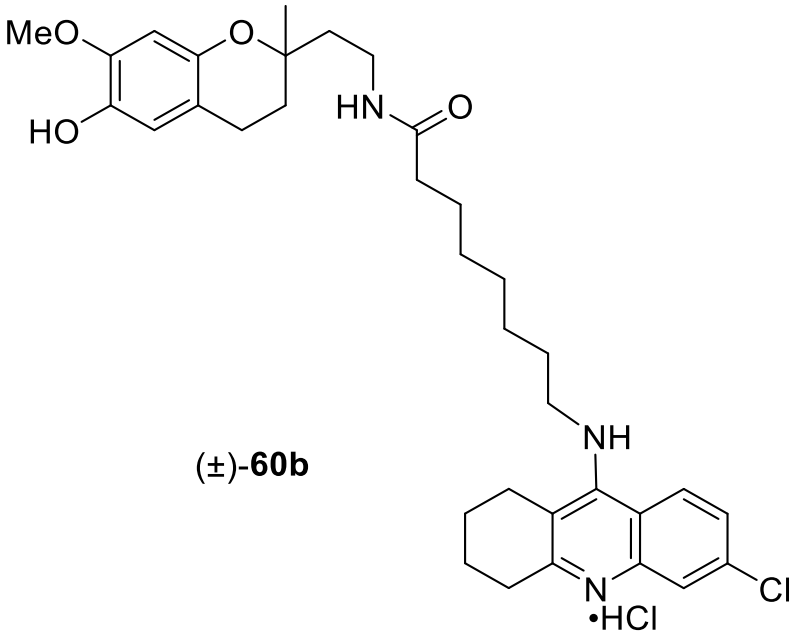
(±)-**60a**

(±)-8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]octanamide, (±)-**60b** – ^{1}H NMR (400 MHz, CD_3OD)



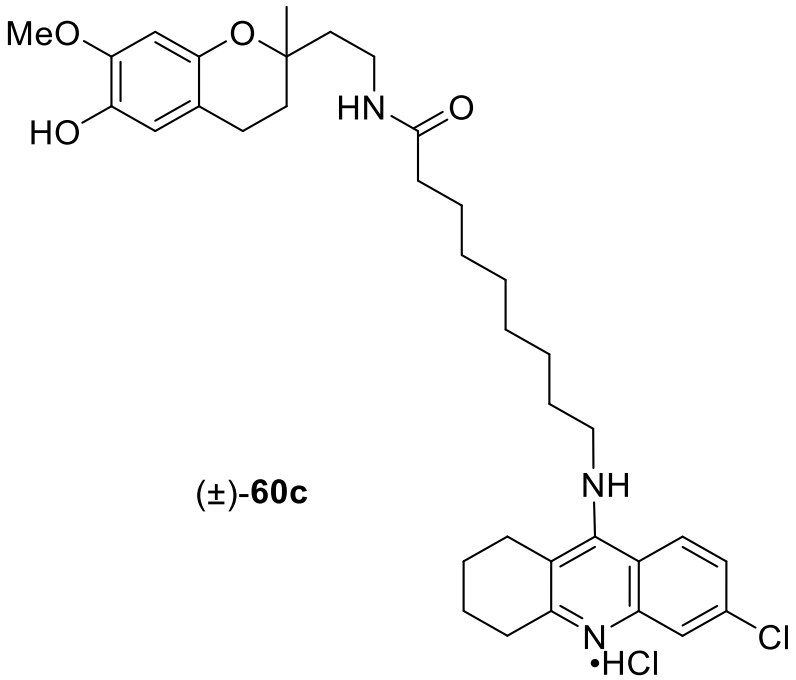
(±)-**60b**

(±)-8-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]octanamide, (±)-**60b** – ^{13}C NMR (100.6 MHz, CD_3OD)



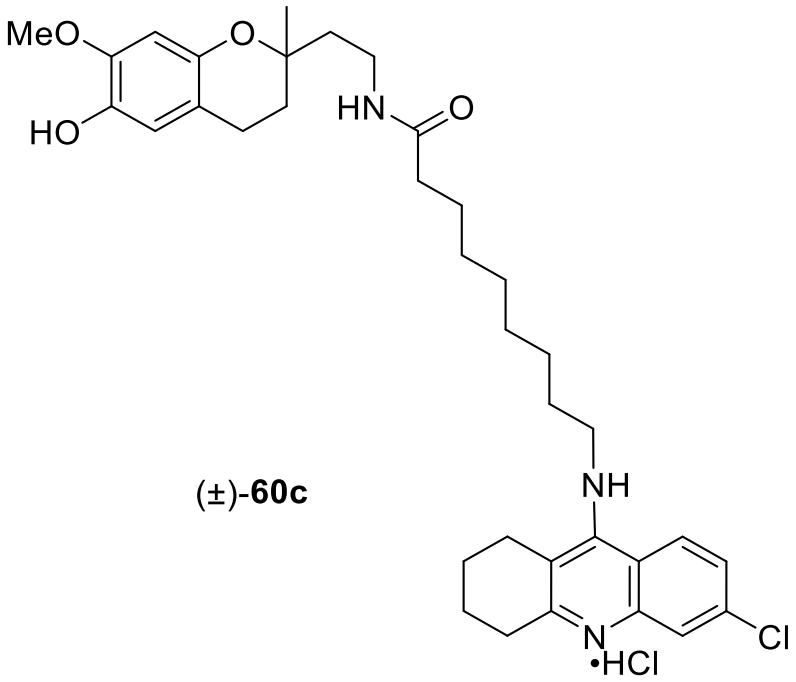
(±)-**60b**

(±)-9-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]nonanamide, (±)-**60c** – ^{1}H NMR (400 MHz, CD_3OD)



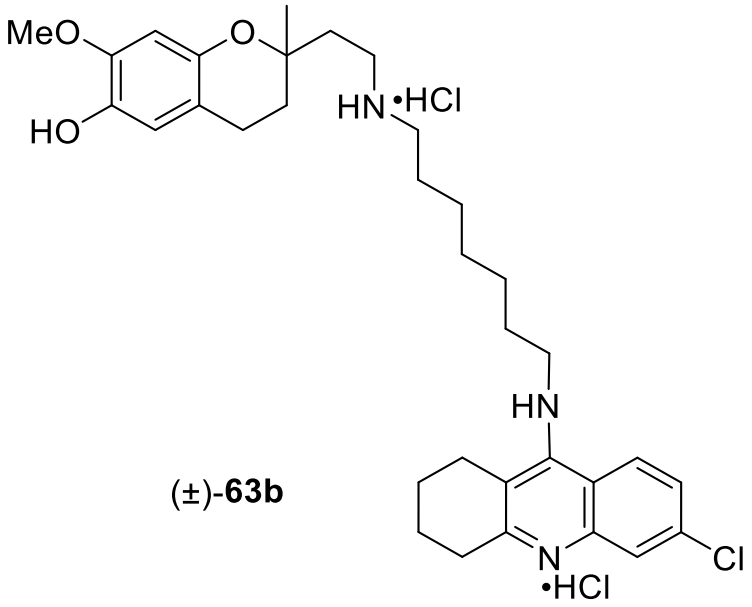
(±)-**60c**

(±)-9-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]nonanamide, (±)-**60c** – ^{13}C NMR (100.6 MHz, CD_3OD)



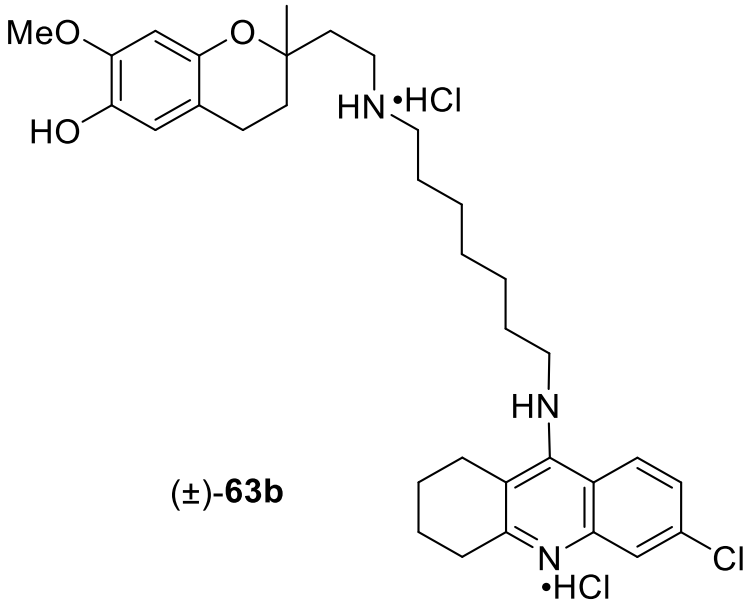
(±)-**60c**

(±)-*N*-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]heptane-1,7-diamine, (±)-**63b** – ^{1}H NMR (400 MHz, CD_3OD)



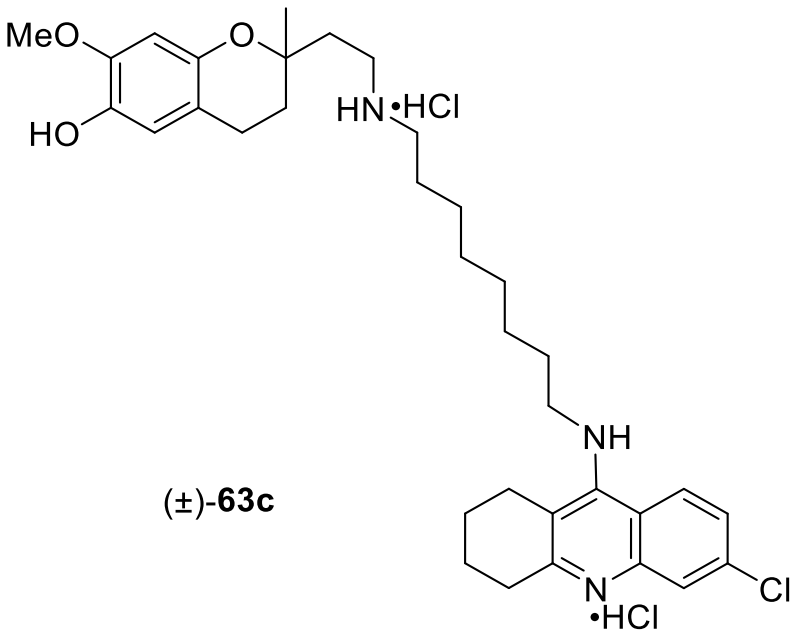
(±)-**63b**

(±)-*N*-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]heptane-1,7-diamine, (±)-**63b** – ^{13}C NMR (100.6 MHz, CD_3OD)



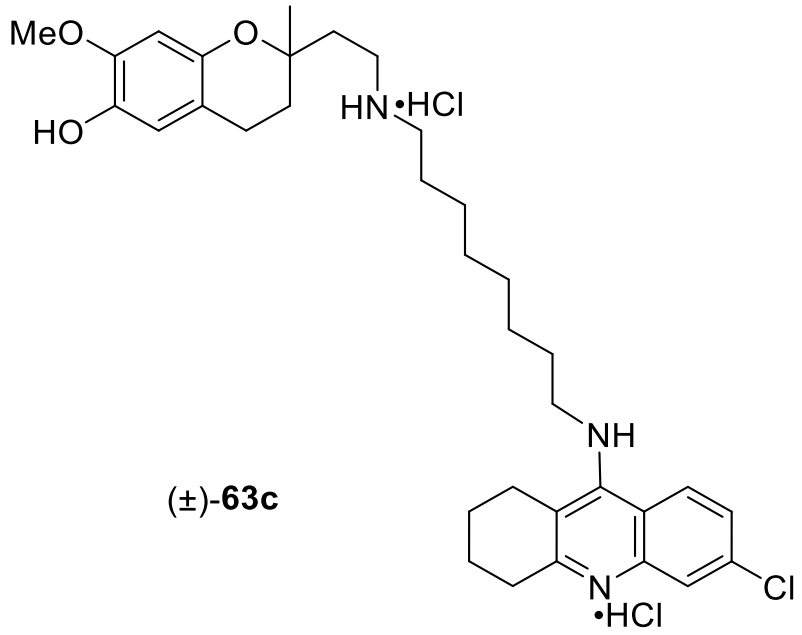
(±)-**63b**

(±)-*N*-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]octane-1,8-diamine, (±)-**63c** – ^{1}H NMR (400 MHz, CD_3OD)



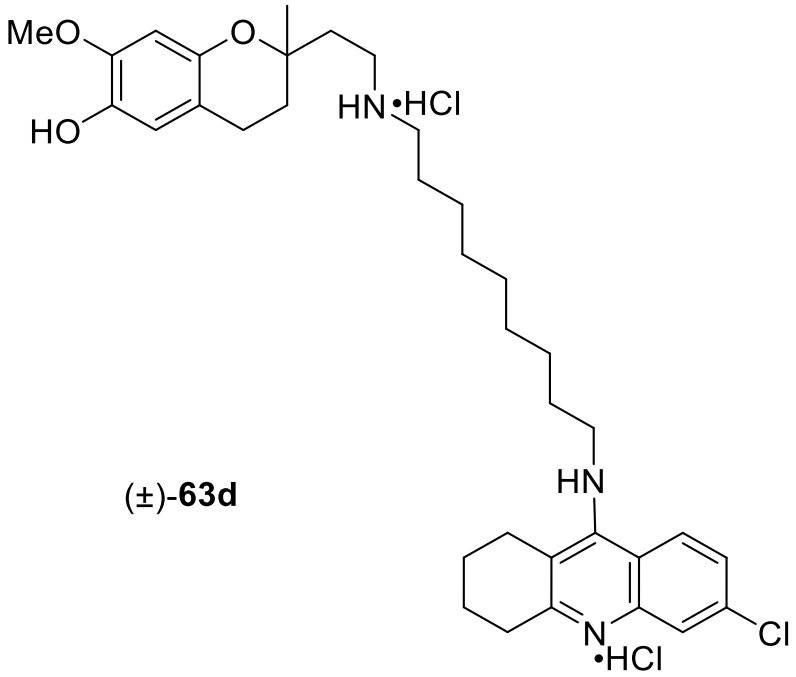
(±)-**63c**

(±)-*N*-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]octane-1,8-diamine, (±)-**63c** – ^{13}C NMR (100.6 MHz, CD_3OD)



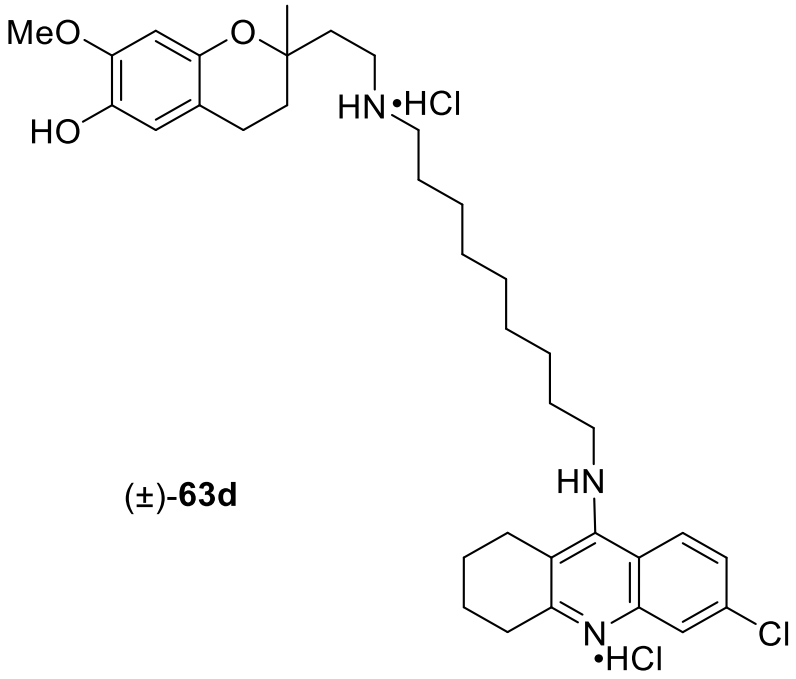
(±)-**63c**

(±)-*N*-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]nonane-1,9-diamine, (±)-**63d** – ^{1}H NMR (400 MHz, CD_3OD)



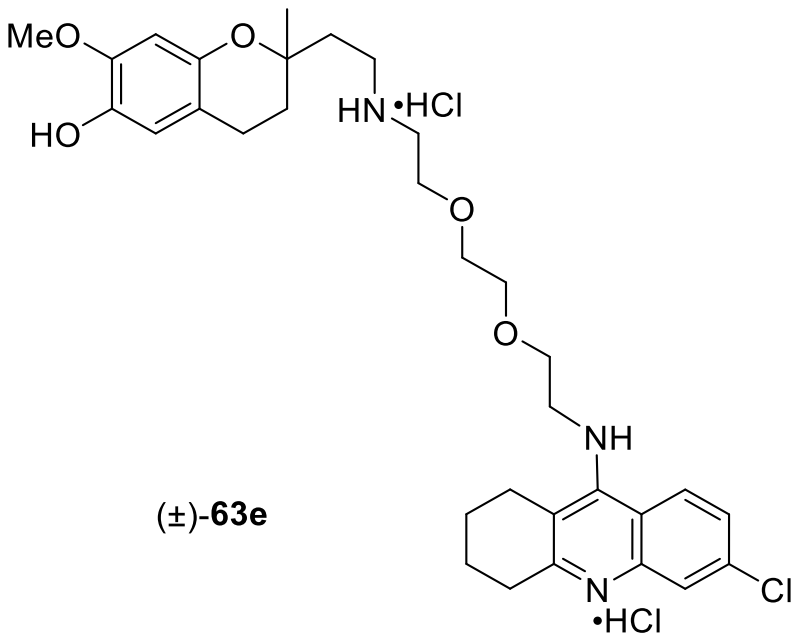
(±)-**63d**

(±)-*N*-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]nonane-1,9-diamine, (±)-**63d** – ^{13}C NMR (100.6 MHz, CD_3OD)



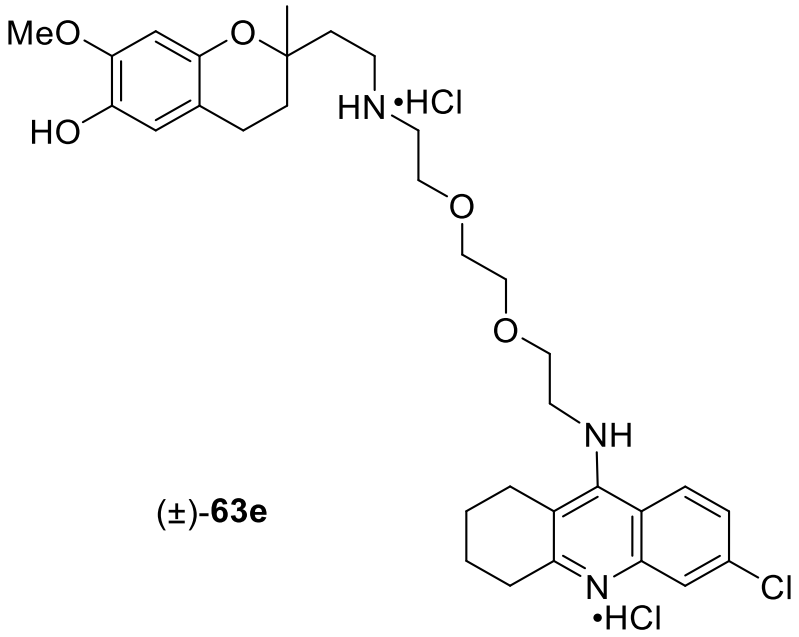
(±)-**63d**

(±)-*N*-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]-3,6-dioxaoctane-1,8-diamine, (±)-**63e** – ^{1}H NMR (400 MHz, CD_3OD)



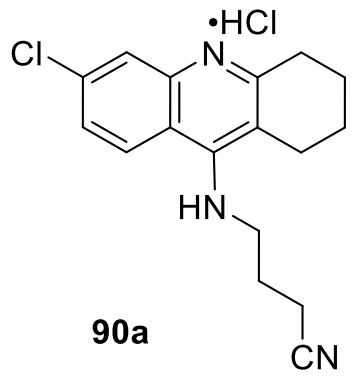
(±)-**63e**

(±)-*N*-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-[2-(6-hydroxy-7-methoxy-2-methylchroman-2-yl)ethyl]-3,6-dioxaoctane-1,8-diamine, (±)-**63e** – ^{13}C NMR (100.6 MHz, CD_3OD)



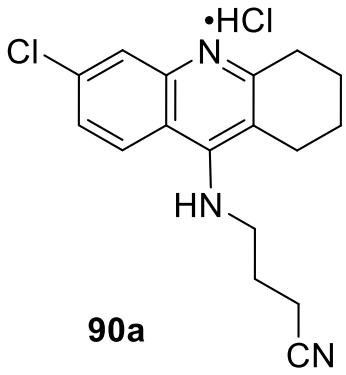
(±)-**63e**

4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]butanenitrile, **90a** – ^{1}H NMR (400 MHz, CD_3OD)



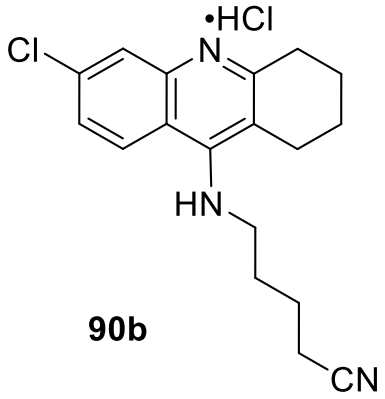
90a

4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]butanenitrile, **90a** – ^{13}C NMR (100.6 MHz, CD_3OD)



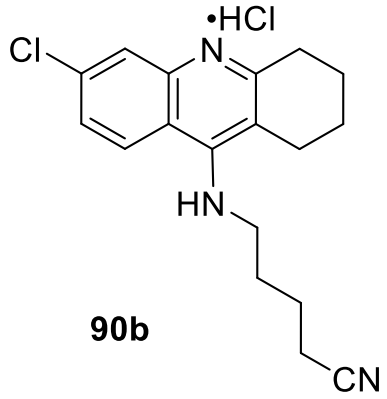
90a

5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]pentanenitrile, **90b** – ^{1}H NMR (400 MHz, CD_3OD)



90b

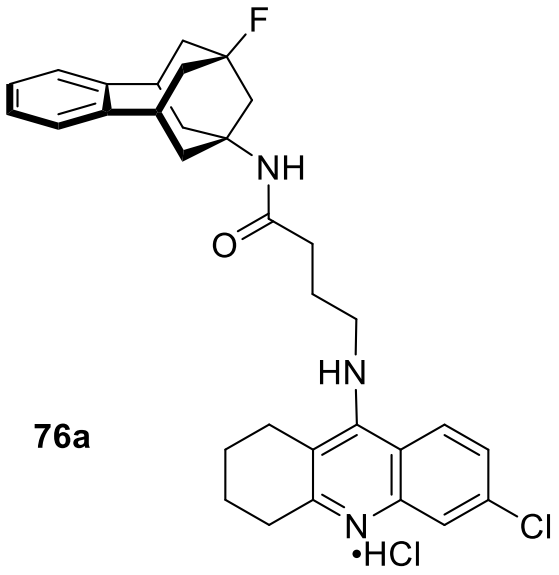
5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]pentanenitrile, **90b** – ^{13}C NMR (100.6 MHz, CD_3OD)



90b

4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)butanamide, **76a** –

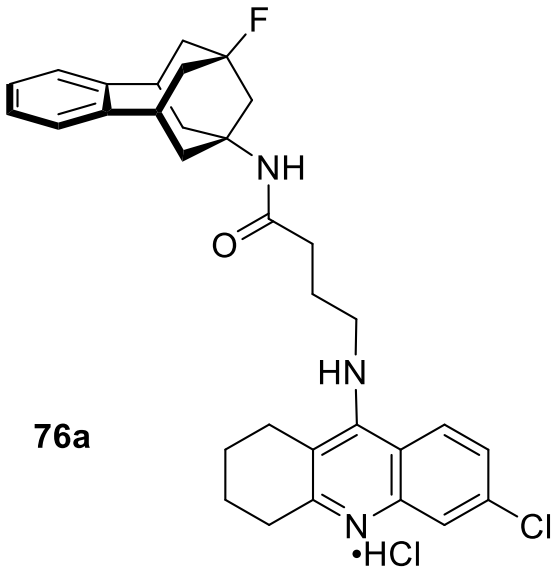
^{1}H NMR (400 MHz, CD_3OD)



76a

4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)butanamide, **76a** –

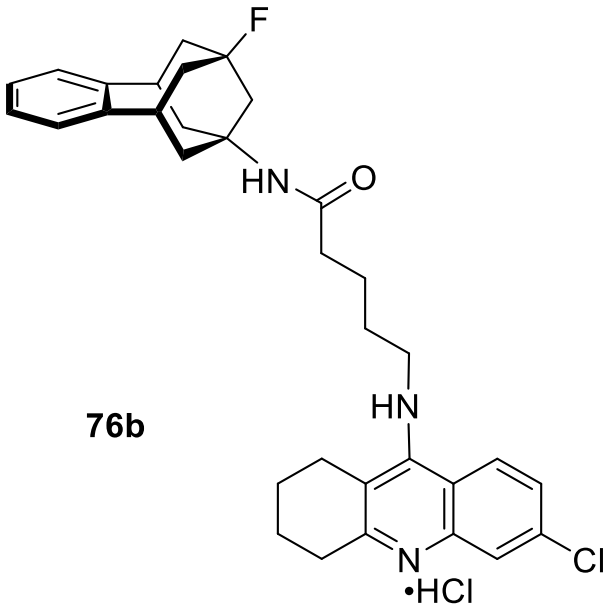
^{1}H NMR (400 MHz, CD_3OD)



76a

5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)pentanamide, **76b** –

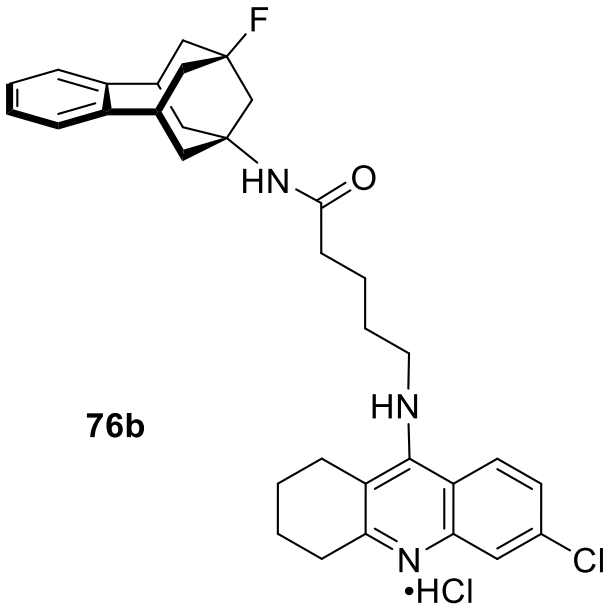
^{1}H NMR (400 MHz, CD_3OD)



76b

5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]-*N*-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)pentanamide, **76b** –

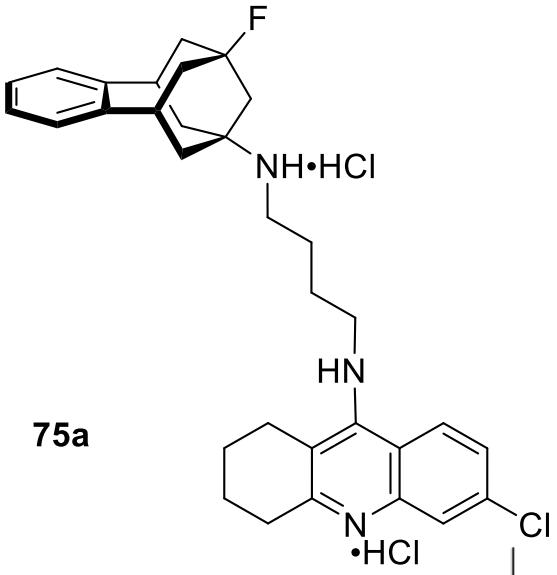
^{13}C NMR (100.6 MHz, CD_3OD)



76b

N-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)butane-1,4-diamine,

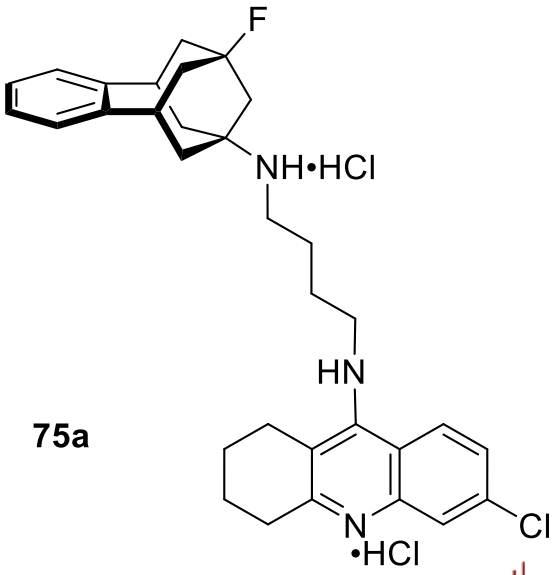
75a – ^{1}H NMR (400 MHz, CD_3OD)



75a

N-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)butane-1,4-diamine,

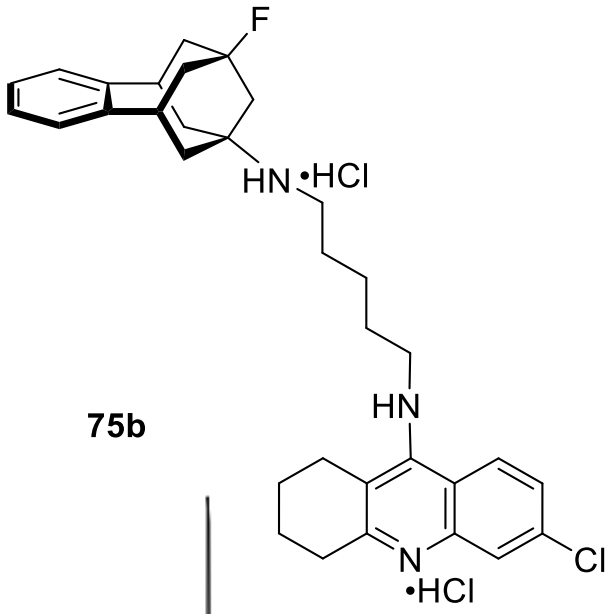
75a – ^{13}C NMR (100.6 MHz, CD_3OD)



75a

N-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)pentane-1,5-diamine,

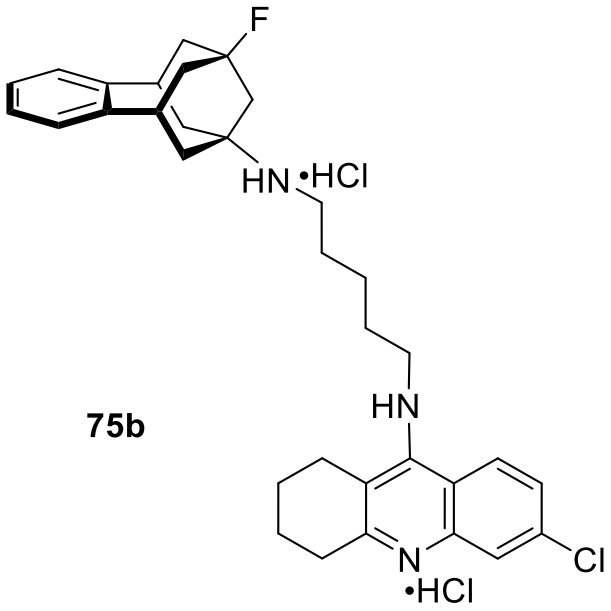
75b – ^{1}H NMR (400 MHz, CD_3OD)



75b

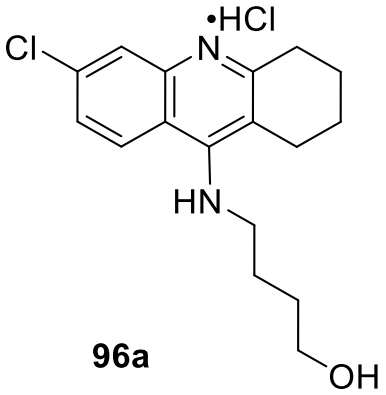
N-(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)-*N'*-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)pentane-1,5-diamine,

75b – ^{13}C NMR (100.6 MHz, CD_3OD)



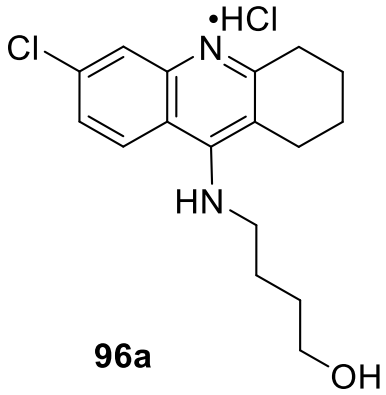
75b

4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]butan-1-ol, **96a** – ^{1}H NMR (400 MHz, CD_3OD)



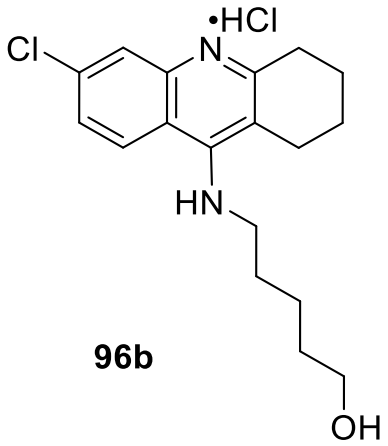
96a

4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]butan-1-ol, **96a** – ^{13}C NMR (100.6 MHz, CD_3OD)



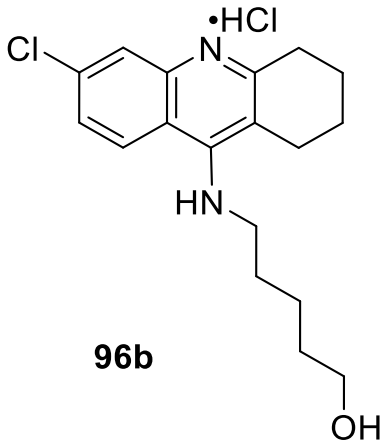
96a

5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]pentan-1-ol, **96b** – ^{1}H NMR (400 MHz, CD_3OD)



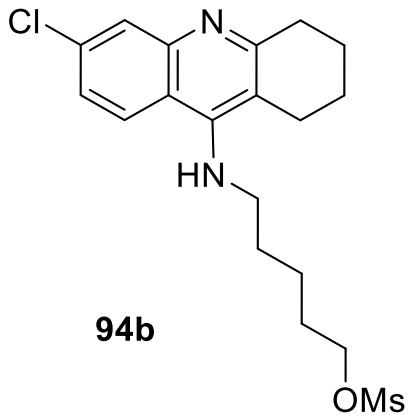
96b

5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]pentan-1-ol, **96b** – ^{13}C NMR (100.6 MHz, CD_3OD)



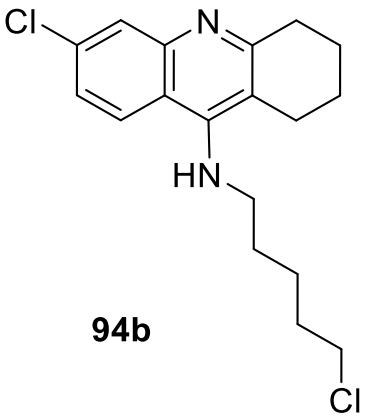
96b

5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]pentyl methanesulfonate, **94b** – ^{1}H NMR (400 MHz, $CDCl_3$)

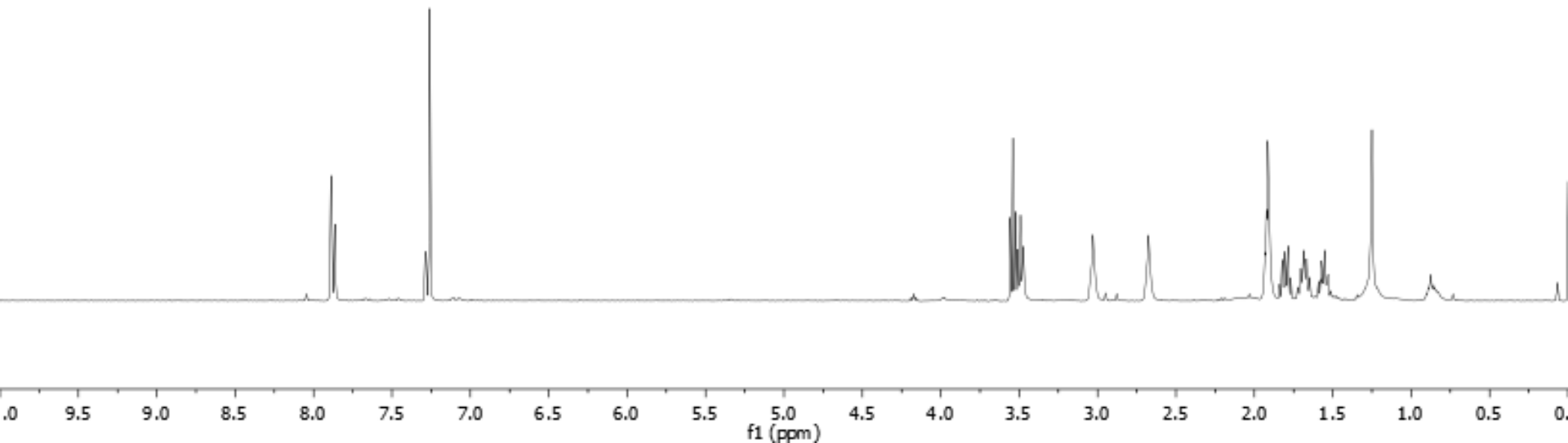


94b

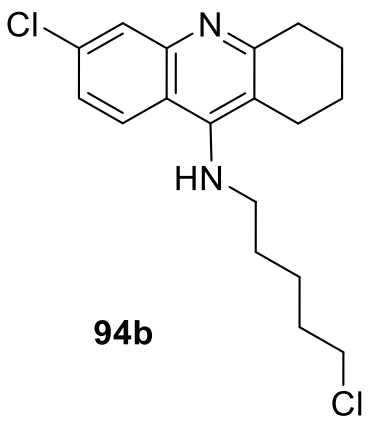
6-chloro-*N*-(5-chloropentyl)-1,2,3,4-tetrahydroacridin-9-amine, **97** – ^{1}H NMR (400 MHz, $CDCl_3$)



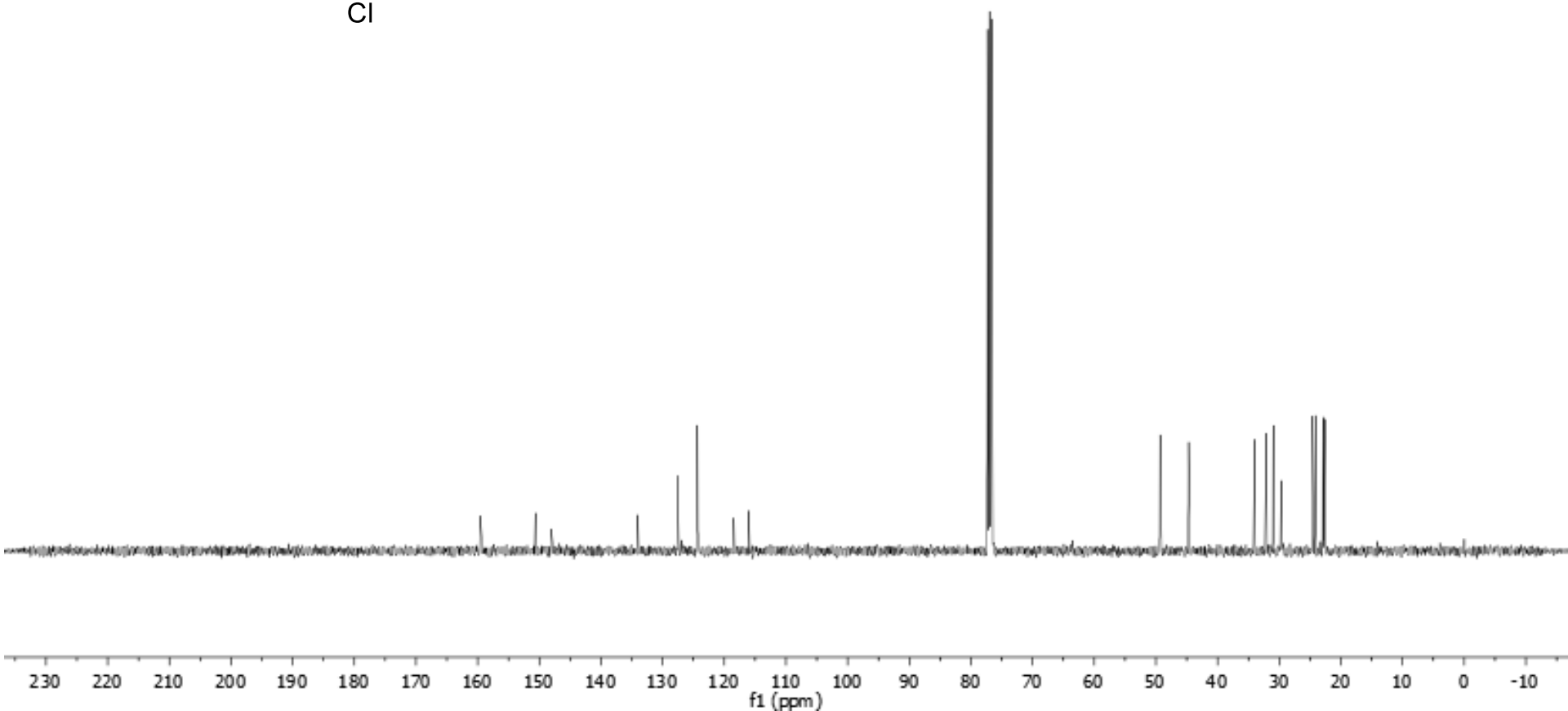
94b



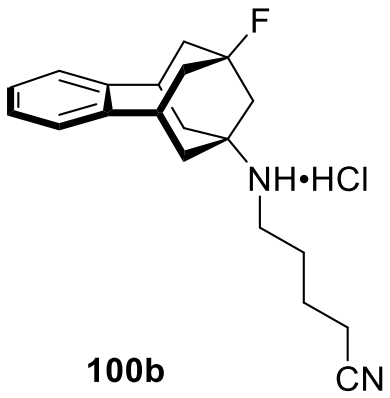
6-chloro-*N*-(5-chloropentyl)-1,2,3,4-tetrahydroacridin-9-amine, **97** – ^{13}C NMR (100.6 MHz, $CDCl_3$)



94b



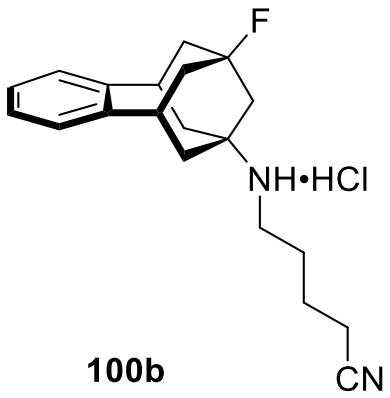
5-[(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)amino]pentanenitrile, **100b** – ^{1}H NMR (400 MHz, CD_3OD)



100b

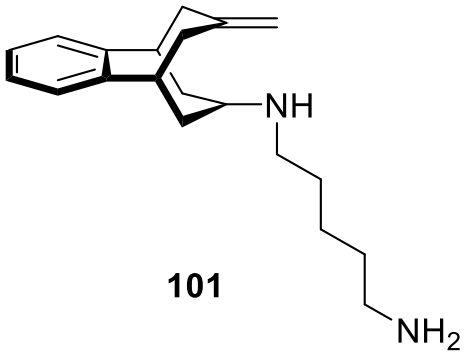
5-[(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)amino]pentanenitrile,

100b – ^{13}C NMR (100.6 MHz, CD_3OD)

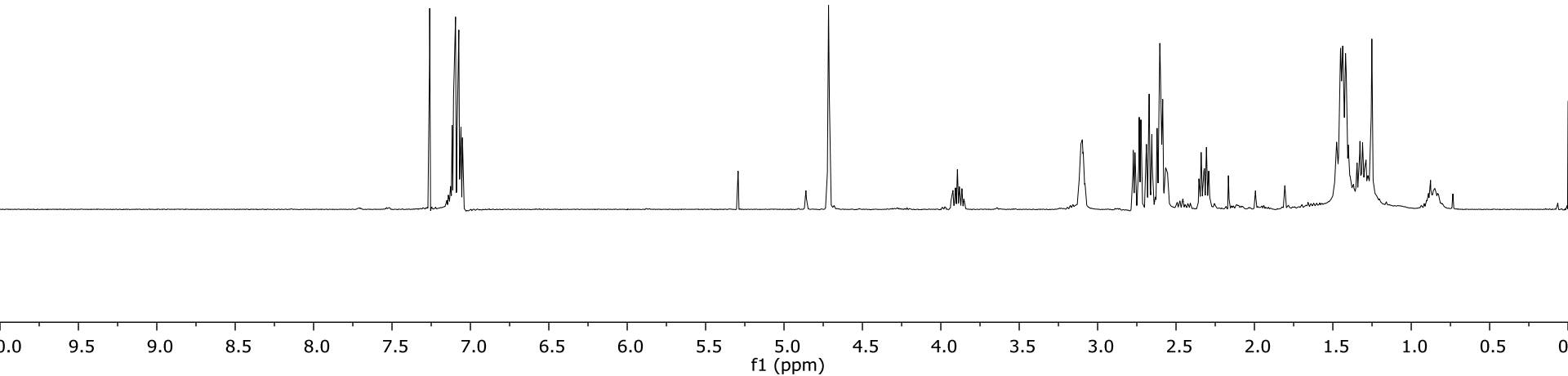


100b

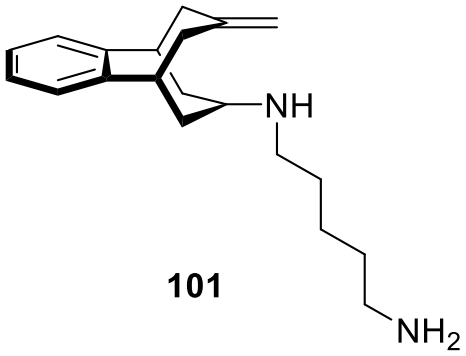
N-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)pentane-1,5-diamine, **99b** – ^{1}H NMR (400 MHz, $CDCl_3$)



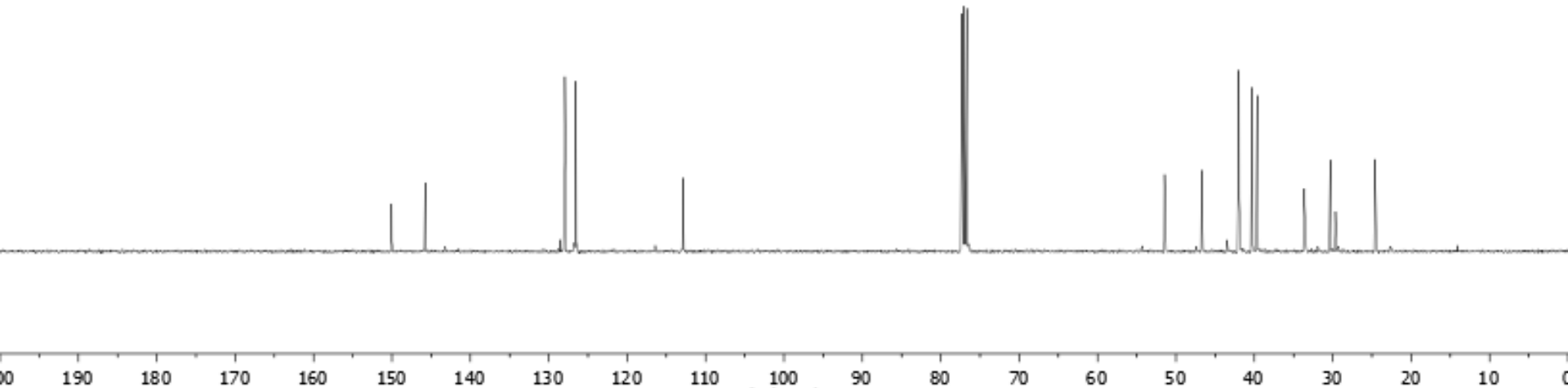
101



N-(9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-7-yl)pentane-1,5-diamine, **99b** – ^{13}C NMR (100.6 MHz, $CDCl_3$)

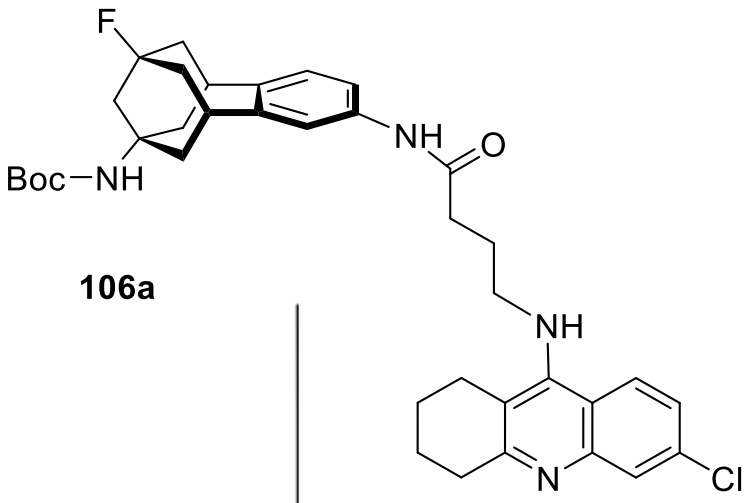


101



N-{7-[(*tert*-butyloxycarbonyl)amino]-9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-2-yl}-4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]butanamide,

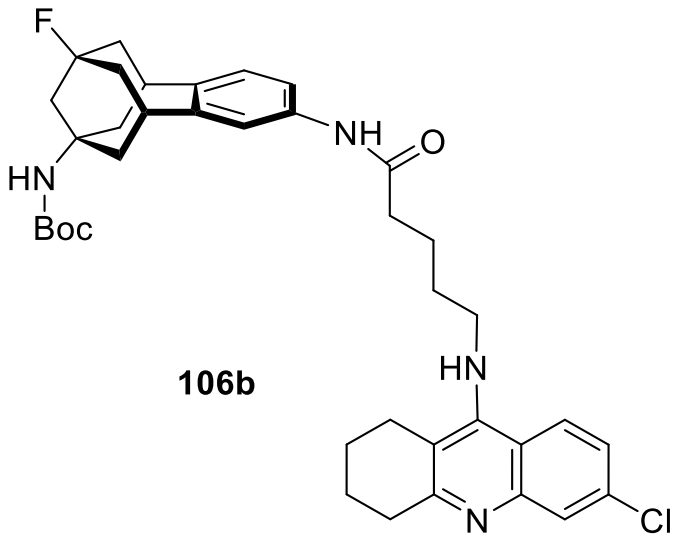
106a – ^{1}H NMR (400 MHz, $CDCl_3$)



106a

N-{7-[(*tert*-butyloxycarbonyl)amino]-9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-2-yl}-5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]pentanamide,

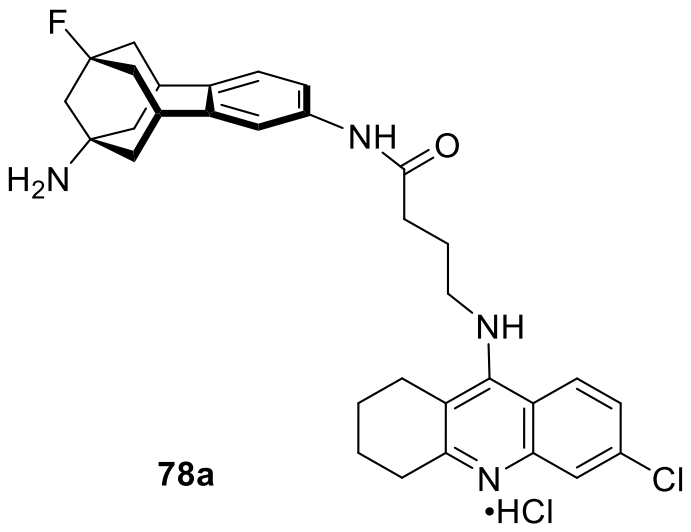
106b – ^{1}H NMR (400 MHz, $CDCl_3$)



106b

N-(7-amino-9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-2-yl)-4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]butanamide,

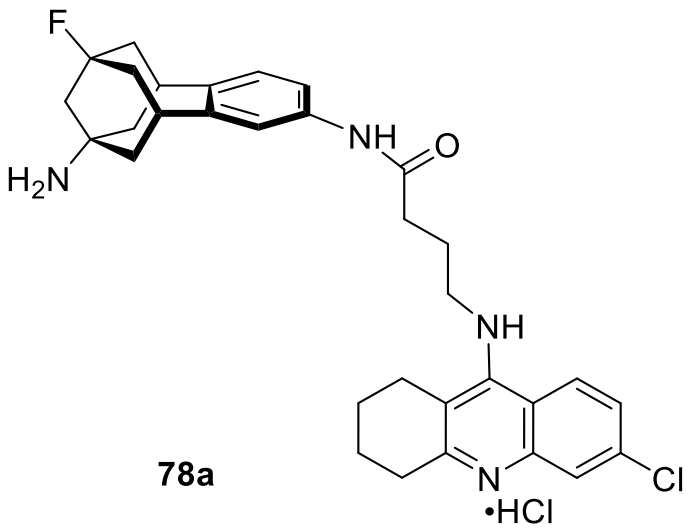
78a – ^{1}H NMR (400 MHz, CD_3OD)



78a

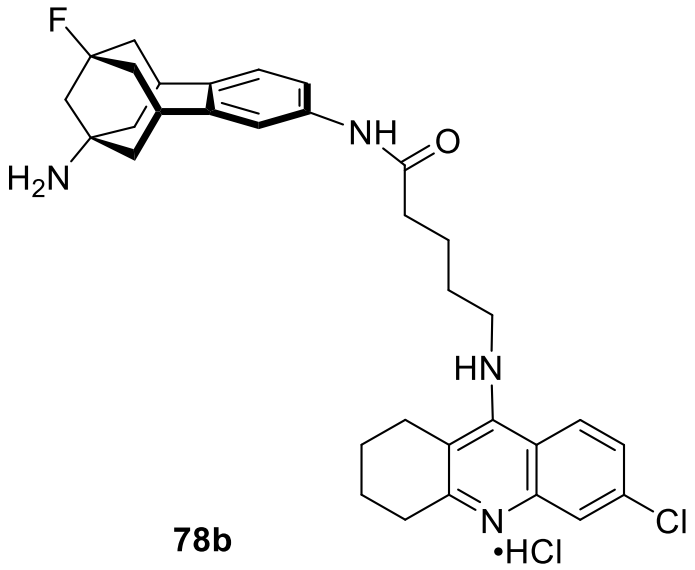
N-(7-amino-9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-2-yl)-4-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]butanamide, **78a** –

^{13}C NMR (100.6 MHz, CD_3OD)



78a

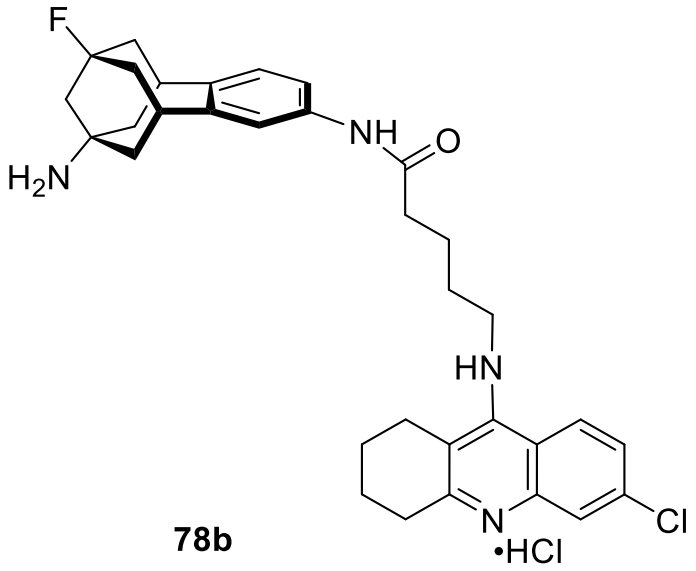
N-(7-amino-9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-2-yl)-5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]pentanamide, **78b** – ^{1}H NMR (400 MHz, CD_3OD)



78b

N-(7-amino-9-fluoro-7*H*-5,6,8,9,10,11-hexahydro-5,9:7,11-dimethanobenzo[9]annulen-2-yl)-5-[(6-chloro-1,2,3,4-tetrahydroacridin-9-yl)amino]pentanamide, **78b** –

^{13}C NMR (100.6 MHz, CD_3OD)



78b