Supporting Information

4-Arylthieno[2,3-*b*]pyridine-2-carboxamides are a new class of antiplasmodial agents

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Figure S1:

3,6-Diamino-4-(3-chlorophenyl)-*N*-(4chlorophenyl)-5-cyanothieno[2,3-*b*]pyridine-2-carboxamide **9a** (KuSaSch018)



3,6-Diamino-*N*-(2-chlorophenyl)-5-cyano-4-(3-fluorophenyl)thieno[2,3-*b*]pyridine-2carboxamide **9b** (KuSaSch022)



3,6-Diamino-*N*-(2-chlorophenyl)-4-(3chlorophenyl)-5-cyanothieno[2,3-*b*]pyridine-2-carboxamide **9c** (KuSaSch027)



3,6-Diamino-4-(3-chlorophenyl)-5-cyano-*N*-(4-fluorophenyl)thieno[2,3-*b*]pyridine-2carboxamide **9d** (KuSaSch028)



3,6-Diamino-*N*-(4-chlorophenyl)-5-cyano-4-(3-methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **9e** (KuSaSch031)



3,6-Diamino-*N*-(2-chlorophenyl)-5-cyano-4-(3-methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **9f** (KuSaSch032)



3,6-Diamino-5-cyano-*N*-(4-fluorophenyl)-4-(3methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **9g** (KuSaSch033)



3,6-Diamino-*N*-(4-chlorophenyl)-5-cyano-4-(3-fluorophenyl)thieno[2,3-*b*]pyridine-2carboxamide **9h** (KuSaSch037)



3,6-Diamino-5-cyano-4-(3-fluorophenyl)-*N*-(4fluorophenyl)thieno[2,3-*b*]pyridine-2carboxamide **9i** (KuSaSch038)



3,6-Diamino-5-cyano-*N*-methyl-4-(3methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **9j** (KuSaSch127)



3,6-Diamino-5-cyano-*N*-heptyl-4-(3methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **9k** (KuSaSch129)



3,6-Diamino-5-cyano-*N*-isopropyl-4-(3methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **91** (KuSaSch131)



3,6-Diamino-5-cyano-*N*-cyclopropyl-4-(3methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **9m** (KuSaSch134)



3,6-Diamino-5-cyano-*N*-(2-morpholinoethyl)-4-(3-methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **9n** (KuSaSch135)



3,6-Diamino-5-cyano-*N*-(2-cyclopropylethyl)-4-(3-methylphenyl)thieno[2,3-*b*]pyridine-2carboxamide **90** (KuSaSch137)



tert-Butyl 4-(3-chloro-4-{3,6-diamino-2-[(3chlorophenyl)carbamoyl]-5-cyanothieno[2,3*b*]pyridin-4-yl}phenyl)piperazine-1carboxylate **9p** (KuSaSch041)



3,6-Diamino-4-[2-chloro-4-(piperazin-1yl)phenyl]-*N*-(3-chlorophenyl)-5cyanothieno[2,3-*b*]-pyridine-2-carboxamide hydrochloride **9q** (KuSaSch043)



3,6-Diamino-4-[2-chloro-4-(pyrrolidin-1yl)phenyl]-*N*-(3-chlorophenyl)-5cyanothieno[2,3-*b*]-pyridine-2-carboxamide **9s** (KuSaSch051)



3,6-Diamino-4-[2-chloro-4-(pyrrolidin-1yl)phenyl]-*N*-(2-chlorophenyl)-5cyanothieno[2,3-*b*]-pyridine-2-carboxamid **9t** (KuSaSch055)



3,6-Diamino-4-(2-chloro-4morpholinophenyl)-*N*-(2-chlorophenyl)-5cyanothieno[2,3-*b*]pyridine-2-carboxamide **9u** (KuSaSch056)



3,6-Diamino-4-(2-chloro-4morpholinophenyl)-*N*-(3-chlorophenyl)-5cyanothieno[2,3-*b*]pyridine-2-carboxamide **9r** (KuSaSch050)



3,6-Diamino-4-(2-chloro-4morpholinophenyl)-*N*-(4-chlorophenyl)-5cyanothieno[2,3-*b*]pyridine-2-carboxamide **9v** (KuSaSch057)



tert-Butyl {2-[(3-chloro-4-{3,6-diamino-2-[(3chlorophenyl)carbamoyl]-5-cyanothieno[2,3*b*]pyridin-4yl}phenyl)(methyl)amino]ethyl}carbamate **9w** (KuSaSch058)



3,6-Diamino-4-(2-chloro-4morpholinophenyl)-5-cyano-*N*-(4fluorophenyl)thieno[2,3-*b*]pyridine-2carboxamide **9x** (KuSaSch059)



tert-Butyl {2-[(3-chloro-4-{3,6-diamino-2-[(4chlorophenyl)carbamoyl]-5-cyanothieno[2,3*b*]pyridin-4yl}phenyl)(methyl)amino]ethyl}carbamate **9y** (KuSaSch060)



3,6-Diamino-4-[2-chloro-4-(pyrrolidin-1yl)phenyl]-*N*-(4-chlorophenyl)-5cyanothieno[2,3-*b*]-pyridine-2-carboxamide **9z** (KuSaSch063)



3,6-Diamino-4-[2-chloro-4-(pyrrolidin-1yl)phenyl]-5-cyano-*N*-(4fluorophenyl)thieno[2,3-*b*]-pyridine-2carboxamide **9aa** (KuSaSch064)



tert-Butyl {2-[(3-chloro-4-{3,6-diamino-5cyano-2-[(4fluorophenyl)carbamoyl]thieno[2,3-*b*]pyridin-4-yl}phenyl)(methyl)amino]ethyl}carbamate **9ac** (KuSaSch073)



3,6-Diamino-4-(2-chloro-4-{[2-(dimethylamino)ethyl](methyl)amino}phenyl)-5-cyano-*N*-(4-fluoro-phenyl)thieno[2,3*b*]pyridine-2-carboxamide **9ab** (KuSaSch067)



tert-Butyl {2-[(3-chloro-4-{3,6-diamino-2-[(2chlorophenyl)carbamoyl]-5-cyanothieno[2,3*b*]pyridin-4yl}phenyl)(methyl)amino]ethyl}carbamate





3,6-Diamino-4-{4-[(2aminoethyl)(methyl)amino]-2-chlorophenyl}-*N*-(3-chlorophenyl)-5-cyano-thieno-[2,3-*b*]pyridine-2-carboxamide hydrochloride **9ae** (KuSaSch075)



3,6-Diamino-4-(2-chloro-4-{[2-(dimethylamino)ethyl](methyl)amino}phenyl)-N-(3-chlorophenyl)-5-cyanothieno[2,3-



tert-Butyl 4-(4-{3-amino-2-[(4chlorophenyl)carbamoyl]-6,7-dihydro-5*H*cyclopenta[*b*]thieno[3,2-*e*]pyridin-4-yl}-3chlorophenyl)piperazine-1-carboxylate **17a** (KuSaSch095)



3-Amino-*N*-(4-chlorophenyl)-4-phenyl-6,7dihydro-5*H*-cyclopenta[*b*]thieno[3,2*e*]pyridine-2-carboxamide **17b** (KuSaSch100)



3-Amino-*N*-(4-fluorophenyl)-4-phenyl-6,7dihydro-5*H*-cyclopenta[*b*]thieno[3,2*e*]pyridine-2-carboxamide **17c** (KuSaSch101)



3-Amino-*N*-(4-chlorophenyl)-4-phenyl-5,6,7,8-tetrahydrothieno[2,3-*b*]quinoline-2carboxamide **17d** (KuSaSch105)







3-Amino-*N*-(4-chlorophenyl)-4-(3methylphenyl)-6,7-dihydro-5*H*cyclopenta[*b*]thieno[3,2-*e*]-pyridine-2carboxamide **17f** (KuSaSch110)



3-Amino-2-[(4-chlorophenyl)carbamoyl]-6methyl-4-(3-methylphenyl)thieno[2,3*b*]pyridine-5-carboxylic acid **17i** (KuSaSch114)



3-Amino-2-[(4-chlorophenyl)carbamoyl]-6methyl-4-phenylthieno[2,3-*b*]pyridine-5carboxylic acid **17j** (KuSaSch115)



tert-Butyl 4-(4-{3-amino-2-[(4chlorophenyl)carbamoyl]-5,6,7,8tetrahydrothieno[2,3-*b*]quinolin-4-yl}-3chlorophenyl)piperazine-1-carboxylate **17k** (KuSaSch118)



tert-Butyl 3-amino-2-[(4chlorophenyl)carbamoyl]-6-methyl-4phenylthieno[2,3-*b*]pyridine-5-carboxylate **17g** (KuSaSch111)



tert-Butyl 3-amino-2-[(4chlorophenyl)carbamoyl]-6-methyl-4-(3methylphenyl)thieno[2,3-*b*]-pyridine-5carboxylate **17h** (KuSaSch112)



tert-Butyl 4-(4-{3-amino-2-[(4chlorophenyl)carbamoyl]-6-methylthieno[2,3b]pyridin-4-yl}-3-chlorophenyl)piperazine-1carboxylate **171** (KuSaSch122)











Figure S4: IR spectrum of **9a** (KuSaSch018).













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Figure S8: IR spectrum of **9e** (KuSaSch031).



Figure S9: APCI-MS spectrum of **9e** (KuSaSch031).







Figure S12: IR spectrum of 9j (KuSaSch127).



Figure S13: APCI-MS spectrum of **9j** (KuSaSch127).





Figure S14: ¹H-NMR spectrum of **9m** (KuSaSch134).



Figure S15: ¹³C-NMR spectrum of **9m** (KuSaSch134).

Figure S16: HSQC-NMR spectrum of **9m** (KuSaSch134). The black circle confirms two protons under one carbon signal.



Figure S17: IR spectrum of **9m** (KuSaSch134).



Figure S18: APCI-MS spectrum of **9m** (KuSaSch134).







Figure S20: ¹³C-NMR spectrum of **9n** (KuSaSch135).



Figure S21: IR spectrum of 9n (KuSaSch135).



Figure S22: APCI-MS spectrum of **9n** (KuSaSch135).







Supporting Information





Figure S25: IR spectrum of **9y** (KuSaSch060).



Figure S26: APCI-MS spectrum of **9y** (KuSaSch060).







Supporting Information








Figure S30: IR spectrum of **9z** (KuSaSch063).



Figure S31: APCI-MS of **9z** (KuSaSch063).



Figure S ²	32+1H_NMR	spectrum	of 9ac	(KuSaSch()73)
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Supporting Information

Figure S33: ¹³C-NMR spectrum of **9ac** (KuSaSch073).



Figure S34: IR spectrum of **9ac** (KuSaSch073).



Figure S35: APCI-MS spectrum of **9ac** (KuSaSch073).







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Figure S38: HSCQ-NMR spectrum of **17a** (KuSaSch095). The black circle confirms 4 protons under a missing signal for two carbons.



Figure S39: IR spectrum of 17a (KuSaSch095).



Figure S40: APCI-MS spectrum of **17a** (KuSaSch095).



Figure S41: ¹H-NMR spectrum of **17b** (KuSaSch100).





Figure S42: ¹³C-NMR spectrum of **17b** (KuSaSch100).

Figure S43: HSQC-NMR spectrum of **17b** (KuSaSch100). The black circle confirms 3 protons under one carbon signal.



Figure S44: IR spectrum of **17b** (KuSaSch100).









Figure S46: ¹H-NMR spectrum of **17e** (KuSaSch107).



Figure S47: ¹³C-NMR spectrum of **17e** (KuSaSch107).

Figure S48: IR spectrum of **17e** (KuSaSch107).







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Figure S50: ¹H-NMR spectrum of **17f** (KuSaSch110).





Figure S52: IR spectrum of **17f** (KuSaSch110).



Figure S53: APCI-MS spectrum of **17f** (KuSaSch110).







Figure S55: ¹³C-NMR spectrum of **17f** (KuSaSch111).



Figure S56: IR spectrum of **17f** (KuSaSch111).







Figure S58: ¹H-NMR spectrum of **17h** (KuSaSch112).



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Figure S59: ¹³C-NMR spectrum of **17h** (KuSaSch112).

Figure S60: IR spectrum of 17h (KuSaSch112).









Figure S62: HPLC chromatogram of **9a** (KuSaSch018) – gradient method (HPLC 3)

Figure S63: HPLC chromatogram of 9a (KuSaSch018) – isocratic method (HPLC 1)





Figure S64: HPLC chromatogram of **9e** (KuSaSch031) – gradient method (HPLC 3)

Figure S65: HPLC chromatogram of 9e (KuSaSch031) – isocratic method (HPLC 1)





Figure S66: HPLC chromatogram of **9m** (KuSaSch134) – gradient method (HPLC 3)

Figure S67: HPLC chromatogram of 9m (KuSaSch134) – isocratic method (HPLC 1)




Figure S68: HPLC chromatogram of 9y (KuSaSch060) – gradient method (HPLC 3)

Figure S69: HPLC chromatogram of 9y (KuSaSch060) – isocratic method (HPLC 1)





Figure S70: HPLC chromatogram of **9ac** (KuSaSch073) – gradient method (HPLC 3)

Figure S71: HPLC chromatogram of **9ac** (KuSaSch073) – isocratic method (HPLC 1)







Figure S73: HPLC chromatogram of 17a (KuSaSch095) – isocratic method (HPLC 1)





Figure S74: HPLC chromatogram of **17b** (KuSaSch100) – gradient method (HPLC 3)

Figure S75: HPLC chromatogram of **17b** (KuSaSch100) – isocratic method (HPLC 1)



1: 254 nm. 4 nm



Figure S77: HPLC chromatogram of **17f** (KuSaSch110) – isocratic method (HPLC 1)







Figure S79: HPLC chromatogram of 17g (KuSaSch111) – isocratic method (HPLC 1)



Sample Availability: Samples of the compounds are not available from the authors.



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