

Supporting Information

**Synthesis and Mechanism of Action Studies of a Series of Norindenoisoquinoline
Topoisomerase I Poisons Reveal an Inhibitor with a Flipped Orientation in the Ternary
DNA-Enzyme-Inhibitor Complex As Determined by X-Ray Crystallographic Analysis**

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Elemental Analyses

(3,4-Dimethoxybenzylidene)-(2,2-dimethoxyethyl)amine (9). Anal. Calcd for C₁₃H₁₉NO₄·0.1CHCl₃: C, 59.34; H, 7.22; N, 5.28. Found: C, 59.21; H, 7.26; N, 5.36.

(3,4-Dimethoxybenzyl)-(2,2-dimethoxyethyl)amine (10). Anal. Calcd for C₁₃H₂₁NO₄: C, 61.16; H, 8.29; N, 5.49. Found: C, 61.45; H, 8.46; N, 5.23.

2,3,8,9-Tetramethoxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (13). Anal. Calcd for C₂₀H₂₀NO₄Cl·1.85H₂O: C, 59.00; H, 5.87; N, 3.44. Found: C, 58.98; H, 5.72; N, 3.49.

2,3-Dimethoxy-8,9-methylenedioxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (14). Anal. Calcd for C₁₉H₁₆NO₄Cl·0.85H₂O: C, 61.17; H, 4.78; N, 3.75. Found: C, 61.19; H, 4.77; N, 3.56.

(3,4-Methylenedioxybenzylidene)-(2,2-dimethoxyethyl)amine (15). Anal. Calcd for C₁₂H₁₅NO₄: C, 60.75; H, 6.37; N, 5.90. Found: C, 60.99; H, 6.59; N, 5.69.

(3,4-Methylenedioxybenzyl)-(2,2-dimethoxyethyl)amine (16). Anal. Calcd for C₁₂H₁₇NO₄: C, 60.24; H, 7.16; N, 5.85. Found: C, 60.16; H, 7.25; N, 5.61.

8,9-Dimethoxy-2,3-methylenedioxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (18). Anal. Calcd for C₁₉H₁₆NO₄Cl·0.7H₂O: C, 61.61; H, 4.74; N, 3.78. Found: C, 61.40; H, 4.98; N, 3.75.

2,3-Methylenedioxy-7,8-methylenedioxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (19). Anal. Calcd for C₁₈H₁₂NO₄Cl·0.85H₂O: C, 60.55; H, 3.87; N, 3.92. Found: C, 60.56; H, 3.96; N, 3.93.

7,8,9-Trimethoxy-2,3-methylenedioxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride

(20). Anal. Calcd for C₂₀H₁₈NO₅Cl·1.9H₂O: C, 56.92; H, 5.21; N, 3.32. Found: C, 56.92; H, 5.02; N, 3.29.

(3,4,5-Trimethoxybenzylidene)-(2,2-dimethoxyethyl)amine (21). Anal. Calcd for C₁₄H₂₁NO₅·0.35 CHCl₃: C, 53.02; H, 6.62; N, 4.31. Found: C, 52.73; H, 6.67; N, 4.17.

(3,4,5-Trimethoxybenzyl)-(2,2-dimethoxyethyl)amine (22). Anal. Calcd for C₁₄H₂₃NO₅: C, 58.93; H, 8.12; N, 4.91. Found: C, 58.66; H, 8.17; N, 4.63.

2,3,4,7,8-Pentamethoxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (23). Anal. Calcd for C₂₁H₂₂NO₅Cl·1.6H₂O: C, 58.29; H, 5.87; N, 3.24. Found: C, 58.32; H, 5.77; N, 3.05.

2,3,4-Trimethoxy-7,8-methylenedioxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride

(24). Anal. Calcd for C₂₀H₁₈NO₅Cl·0.45H₂O: C, 60.73; H, 4.81; N, 3.54. Found: C, 60.74; H, 4.89; N, 3.48.

2,3,4,7,8,9-Hexamethoxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (25). Anal. Calcd for C₂₂H₂₄NO₆Cl·1.95H₂O: C, 56.34; H, 6.00; N, 2.99. Found: C, 56.36; H, 5.94; N, 2.92.

(2,5-Dimethoxybenzylidene)-(2,2-dimethoxyethyl)amine (27). Anal. Calcd for C₁₃H₁₉NO₄: C, 61.64; H, 7.56; N, 5.53. Found: C, 61.84; H, 7.63; N, 5.51.

(2,5-Dimethoxybenzyl)-(2,2-dimethoxyethyl)amine (28). Anal. Calcd for C₁₃H₂₁NO₄: C, 61.16; H, 8.29; N, 5.49. Found: C, 61.48; H, 8.39; N, 5.18.

1,4,7,8-Tetramethoxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (29). Anal. Calcd for C₂₀H₂₀NO₄Cl·1.7H₂O: C, 59.39; H, 5.83; N, 3.46. Found: C, 59.22; H, 5.53; N, 3.72.

1,4-Dimethoxy-7,8-methylenedioxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride

(30). Anal. Calcd for C₁₉H₁₆NO₄Cl·0.5H₂O: C, 62.22; H, 4.67; N, 3.82. Found: C, 62.01; H, 4.83; N, 3.54.

(2,3,4-Trimethoxybenzylidene)-(2,2-dimethoxyethyl)amine (32). Anal. Calcd for C₁₄H₂₁NO₅: C, 59.35; H, 7.47; N, 4.94. Found: C, 59.67; H, 7.55; N, 4.88.

(2,3,4-trimethoxybenzyl)-(2,2-dimethoxyethyl)amine (33). Anal. Calcd for C₁₄H₂₃NO₅: C, 58.93; H, 8.12; N, 4.91. Found: C, 59.16; H, 8.24; N, 4.64.

1,2,3,7,8-Pentamethoxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (34). Anal. Calcd for C₂₁H₂₂NO₅Cl·1.8H₂O: C, 57.81; H, 5.91; N, 3.21. Found: C, 57.91; H, 5.84; N, 2.96.

1,2,3-Trimethoxy-7,8-methylenedioxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (35). Anal. Calcd for C₂₀H₁₈NO₅Cl·0.15H₂O: C, 61.51; H, 4.72; N, 3.59. Found: C, 61.81; H, 4.85; N, 3.29.

1,2,3,7,8,9-Hexamethoxy-11*H*-indeno[1,2-*c*]isoquinoline Hydrochloride (36). Anal. Calcd for C₂₂H₂₄NO₆Cl·1.4H₂O: C, 57.56; H, 5.88; N, 3.05. Found: C, 57.50; H, 5.98; N, 3.16.