Supporting Information

5-Amino-2-Aroylquinolines as Highly Potent Tubulin Polymerization Inhibitors

Chih-Ying Nien, Yun-Ching Chen, Ching-Chuan Kuo, Hsing-Pang Hsieh, Chi-Yen Chang, Jian-Sung Wu, Su-Ying Wu, Jing-Ping Liou, Jang-Yang Chang

College of Pharmacy, Taipei Medical University, Taipei 110, Taiwan, Republic of China. National Institute of Cancer Research, National Health Research Institutes, Tainan 704, Taiwan, Republic of China. Division of Biotechnology and Pharmaceutical Research, National Health Research Institutes, Miaoli 350, Taiwan, Republic of China. Division of Hematology/Oncology, Department of Internal Medicine, National Cheng Kung University Hospital, Tainan 704, Taiwan, Republic of China.

Contents:

General. (A) **Chemistry.** Nuclear magnetic resonance (^{1}H NMR) spectra were obtained with Bruker DRX-500 spectrometer (operating at 500 MHz), with chemical shift in parts per million (ppm, δ) downfield from TMS as an internal standard. High-resolution mass spectra (HRMS) were measured with a JEOL (JMS-700) electron impact (EI) mass spectrometer. Elemental analyses were performed on an Elementar vario EL Ⅲ analyzer. Elemental analyses were found to be within ± 0.4% of the theoretical values. Purity of tested compounds was > 95%. Flash column chromatography was done using silica gel (Merck Kieselgel 60, No. 9385, 230-400 mesh ASTM). All reactions were carried out under an atmosphere of dry nitrogen.

(B) **Biology. (a) Materials.** Regents for cell culture were obtained from Gibco-BRL Life Technologies (Gaitherburg, MD). Microtubule-associated protein (MAP)-rich tubulin was purchased from Cytoskeleton, Inc. (Denver, CO). [^{3}H]Colchicine (specific activity, 60-87 Ci/mmol) was purchased from PerkinElmer Life Sciences (Boston, MA).

(b) Cell Growth Inhibitory Assay. Human oral epidermoid carcinoma KB cells, non small cell lung carcinoma H460 cells, colorectal carcinoma HT29 cells, and stomach carcinoma MKN45 cells were maintained in RPMI-1640 medium supplied with 5% fetal bovine serum. KB-VIN10 cells were maintained in growth medium supplemented with 10 nM vincristine, generated from vincristine-driven selection, and displayed overexpression of P-gp170/MDR. Cell in logarithmic phase were cultured at a density of 5000 cells/mL/well in a 24-well plate. KB-VIN10 cells were cultured in drug-free medium for 3 days prior to use. The cells were exposed to various concentrations of the test drugs for 72 h. The methylene blue dye assay was used to evaluate the effect of the test compounds on cell growth as described previously.[1] The IC_{50} value resulting from 50% inhibition of cell growth was calculated graphically as a comparison with the control. Compounds were examined in at least three independent experiments, and the values shown for these compounds are the mean and standard deviation of these data.

(c) Tubulin Polymerization in Vitro Assay.[2,3] Turbidimetric assays of microtubules were performed as described by Bollag et al.[4] In brief, microtubule-associated protein (MAP)-rich tubulin (from bovine brain, Cytoskeleton, Denver, C.O.) had been dissolved in reaction buffer (100

mM PIPES (pH 6.9), 2 mM $MgCl_2$, 1 mM GTP) in preparing of 4 mg/mL tubulin solution. Tubulin solution (240 μg MAP-rich tubulin per well) was placed in 96-well microtiter plate in the presence of test compounds or 2% (v/v) DMSO as vehicle control. The increase in absorbance was measured at 350 nm in a PowerWave X Microplate Reader (BIO-TEK Instruments, Winooski, VT) at 37 °C and recorded every 30 s for 30 min. The area under the curve (AUC) used to determine the concentration that inhibited tubulin polymerization to 50% (IC_{50}). The AUC of the untreated control and 10μM of colchicine was set to 100% and 0% polymerization, respectively, and the IC_{50} was calculated by nonlinear regression in at least three experiments.

(d) Tubulin Competition-Binding Scintillation Proximity Assay.[5-7] This assay was performed in a 96-well plate. In brief, 0.08 (micro)M of [^{3}H]colchicine was mixed with the test compound and 0.5 (micro)g special long-chain biotin-labeled tubulin (0.5 μg) and then incubated in 100 μl of reaction buffer (80 mM PIPES, pH 6.8, 1 mM EGTA, 10% glycerol, 1 mM $MgCl_2$, and 1 mM GTP) for 2h at 37°C. Then eighty (micro) g of Streptavidin-labeled SPA beads were added to each reaction mixture. Then the radioactive counts were directly measured by a scintillation counter.

Table 3. Elemental analyses of compounds **5-17**

Compd	formula	calculated			found		
		%C	%H	%N	%C	%H	%N
5	$C_{19}H_{17}NO_4 \cdot H_2O$	66.85	5.61	4.10	66.53	5.82	4.05
6	$C_{19}H_{17}NO_4$	70.58	5.30	4.33	70.62	5.11	4.69
7	$C_{19}H_{17}NO_4$	70.58	5.30	4.33	70.71	5.42	4.12
8	$C_{19}H_{17}NO_4 \cdot 0.75\ H_2O$	67.75	5.54	4.16	67.36	5.42	4.28
9	$C_{19}H_{17}NO_4 \cdot 0.5\ H_2O$	68.66	5.46	4.21	68.79	5.32	4.51
10	$C_{19}H_{17}NO_4$	70.58	5.30	4.33	70.83	5.19	4.12
11	$C_{19}H_{17}NO_4 \cdot H_2O$	66.85	5.61	4.10	66.31	5.92	3.82
12	$C_{20}H_{19}NO_5$	67.98	5.42	3.96	68.12	5.31	3.78
13	$C_{20}H_{19}NO_5$	67.98	5.42	3.96	67.60	5.23	4.12
14	$C_{20}H_{19}NO_5 \cdot H_2O$	64.68	5.70	3.77	64.99	5.68	3.42
15	$C_{20}H_{20}N_2O_5 \cdot 0.25H_2O$	64.42	5.54	7.51	64.11	5.61	7.25
16	$C_{19}H_{17}NO_5$	67.25	5.05	4.13	67.02	5.16	4.49
17	$C_{20}H_{20}INO_4$	51.63	4.33	3.01	51.92	4.16	3.12

Spectral Data and Procedure of compounds **5-8**, **10-11**, **13-14**, **16-17**, **26-29**, and **31-32**

2-(3',4',5'-Trimethoxybenzoyl)quinoline (**5**)

The title compound was obtained in 64% overall yield from 3,4,5-trimethoxyphenylmagnesium bromide and 2-quinolinecarboxaldehyde (**18**) in a similar manner as described for the preparation of **9**; TLC (EtOAc : *n*-hexane = 2 : 3), R_f 0.35, mp 158 - 159 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 6H), 3.97 (s, 3H), 7.64 (s, 2H), 7.69 – 7.66 (m, 1H), 7.81 - 7.78 (m, 1H), 7.92 (d, J = 8.1 Hz, 1H), 8.11 (d, J = 8.6 Hz, 1H) , 8.20 (d, J = 8.3 Hz, 1H), 8.36 (d, J = 8.5 Hz, 1H). MS (EI) *m/z*: 323 (M^+, 100%). HRMS (EI) for $C_{19}H_{17}NO_4$ (M^+): calcd, 323.1157; found, 323.1158. Anal. ($C_{19}H_{17}NO_4 \cdot H_2O$) C, H, N.

3-(3',4',5'-Trimethoxybenzoyl)quinoline (6)

The title compound was obtained in 70% overall yield from 3,4,5-trimethoxyphenylmagnesium bromide and 3-quinolinecarboxaldehyde (**19**) in a similar manner as described for the preparation of **9**;

TLC (EtOAc : *n*-hexane = 1 : 1), R_f 0.33, mp 107 - 109 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.88 (s, 6H), 3.97 (s, 3H), 7.11 (s, 2H), 7.65 (t, *J* = 7.5 Hz, 1H), 7.86 (t, *J* = 7.6 Hz, 1H), 7.94 (d, *J* = 8.1 Hz, 1H), 8.20 (d, *J* = 8.5 Hz, 1H) , 8.58 (s, 1H), 9.30 (s, 1H). MS (EI) *m/z*: 323 (M^+, 100%). HRMS (EI) for $C_{19}H_{17}NO_4$ (M^+): calcd, 323.1158; found, 323.1164. Anal. ($C_{19}H_{17}NO_4$) C, H, N.

4-(3',4',5'-Trimethoxybenzoyl)quinoline (**7**)

The title compound was obtained in 62% overall yield from 3,4,5-trimethoxyphenylmagnesium bromide and 4-quinolinecarboxaldehyde (**20**) in a similar manner as described for the preparation of **9**; TLC (EtOAc : *n*-hexane = 3 : 2), R_f 0.31, mp 109 - 110 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.78 (s, 6H), 3.94 (s, 3H), 7.09 (s, 2H), 7.41 (d, *J* = 4.2 Hz, 1H), 7.55 (t, *J* = 7.6 Hz, 1H), 7.77 (d, *J* = 7.6 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H) , 8.20 (d, *J* = 8.4 Hz, 1H), 9.03 (d, *J* = 4.2 Hz, 1H). MS (EI) *m/z*: 323 (M^+, 100%). HRMS (EI) for $C_{19}H_{17}NO_4$ (M^+): calcd, 323.1158; found, 323.1152. Anal. ($C_{19}H_{17}NO_4$) C, H, N.

5-(3',4',5'-Trimethoxybenzoyl)quinoline (**8**)

The title compound was obtained in 66% overall yield from 3,4,5-trimethoxyphenylmagnesium bromide and 5-quinolinecarboxaldehyde (**21**) in a similar manner as described for the preparation of **9**; TLC (EtOAc : *n*-hexane = 2 : 3), R_f 0.27, mp 145 - 147 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.82 (s, 6H), 3.95 (s, 3H), 7.11 (s, 2H), 7.46 (dd, *J* = 4.2, 8.7 Hz, 1H), 7.70 (d, *J* = 6.9 Hz, 1H), 7.76 (t, *J* = 7.7 Hz, 1H), 8.29 (d, *J* = 8.4 Hz, 1H) , 8.50 (d, *J* = 8.5 Hz, 1H), 8.98 (d, *J* = 3.2 Hz, 1H). MS (EI) *m/z*: 323 (M^+, 100%). HRMS (EI) for $C_{19}H_{17}NO_4$ (M^+): calcd, 323.1156; found, 323.1148. Anal. ($C_{19}H_{17}NO_4 \cdot 0.75\ H_2O$) C, H, N.

7-(3',4',5'-Trimethoxybenzoyl)quinoline (**10**)

The title compound was obtained in 58% overall yield from 3,4,5-trimethoxyphenylmagnesium bromide and 7-quinolinecarboxaldehyde in a similar manner as described for the preparation of **9**; TLC (EtOAc : *n*-hexane = 1 : 1), R_f 0.25, mp 149 - 151 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 6H), 3.95 (s, 3H), 7.14 (s, 2H), 7.52 (dd, *J* = 4.2, 8.3 Hz, 1H), 7.95 (d, *J* = 8.5 Hz, 1H), 8.00 – 8.02 (m, 1H), 8.24 (d, *J* = 8.2 Hz, 1H) , 8.48 (s, 1H), 9.00 – 9.01 (m, 1H). MS (EI) *m/z*: 323 (M^+, 100%). HRMS (EI) for $C_{19}H_{17}NO_4$ (M^+): calcd, 323.1158; found, 323.1166. Anal. ($C_{19}H_{17}NO_4$) C, H, N.

8-(3',4',5'-Trimethoxybenzoyl)quinoline (**11**)

The title compound was obtained in 57% overall yield from 3,4,5-trimethoxyphenylmagnesium bromide and 8-quinolinecarboxaldehyde (**24**) in a similar manner as described for the preparation of **9**; TLC (EtOAc : *n*-hexane = 1 : 1), R_f 0.30, mp 153 - 155 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.75 (s, 6H), 3.91 (s, 3H), 7.12 (s, 2H), 7.44 (dd, *J* = 4.1, 8.2 Hz, 1H), 7.63 (t, *J* = 7.5 Hz, 1H), 7.73 (t, *J* = 6.8 Hz, 1H), 7.96 (d, *J* = 8.1 Hz, 1H) , 8.22 (d, *J* = 8.1 Hz, 1H), 8.89 (d, *J* = 2.9 Hz, 1H). MS (EI) *m/z*: 323 (M^+, 100%). HRMS (EI) for $C_{19}H_{17}NO_4$ (M^+): calcd, 323.1158; found, 323.1162. Anal. ($C_{19}H_{17}NO_4 \cdot H_2O$) C, H, N.

6-Methoxy-2-(3',4',5'-trimethoxybenzoyl)quinoline (**12**)

The title compound was obtained in 68% overall yield from 3,4,5-trimethoxyphenylmagnesium bromide and 6-methoxy-2-quinolinecarboxaldehyde (**27**) in a similar manner as described for the preparation of **9**; TLC (EtOAc : *n*-hexane = 3 : 2), R_f 0.37, mp 143 - 145 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.91 (s, 3H), 3.96 (s, 3H), 3.98 (s, 3H), 7.15 (d, J = 2.7 Hz, 1H), 7.44 (dd, J = 4.0, 9.1 Hz, 1H), 7.64 (s, 2H), 8.06 – 8.12 (m, 1H), 7.96 (d, J = 8.1 Hz, 1H) , 8.22 (d, J = 8.5 Hz, 1H). MS (EI) *m/z*: 353 (M^+, 100%). HRMS (EI) for $C_{20}H_{19}NO_5$ (M^+): calcd, 353.1263; found, 353.1262. Anal. ($C_{20}H_{19}NO_5$) C, H, N.

8-Methoxy-4-(3',4',5'-trimethoxybenzoyl)quinoline (**13**)

The title compound was obtained in 43 % overall yield from 3,4,5-trimethoxyphenylmagnesium bromide and 8-methoxy-4-quinolinecarboxaldehyde (**32**) in a similar manner as described for the preparation of **9**; TLC (EtOAc : *n*-hexane = 2 : 1), R_f 0.25, mp 162.5 – 164.1 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.77 (s, 6H), 3.94 (s, 3H), 4.13 (s, 3H), 7.06 (s, 2H), 7.11 (d, J = 7.6 Hz, 1H), 7.38 (d, J = 8.4 Hz, 1H), 7.43 (d, J = 4.1 Hz, 1H), 7.47 (t, J = 8.1 Hz, 1H). MS (EI) *m/z*: 353 (M^+, 100%). HRMS (EI) for $C_{20}H_{19}NO_5$ (M^+): calcd, 353.1264; found, 353.1268. Anal. ($C_{20}H_{19}NO_5$) C, H, N.

2-Methoxy-6-(3',4',5'-trimethoxybenzoyl)quinoline (**14**)

To a mixture of 6-(3',4',5'-trimethoxybenzoyl)quinoline (**9**) (0.20 g, 0.62 mmole) and dichloromethane (2 mL), *m*-chloroperbenzoic acid (0.16 g, 0.93 mmol) was added at 0 ^{o}C and then stirred at ambient temperature for 12 h. The reaction mixture was treated with 10% sodium sulfite, saturated $NaHCO_3$, brine, and extracted with EtOAc (10mL x 2). The combined organic layers were dried over $MgSO_4$ and evaporated in vacuum to give a residue with further purification. The residue was dissolved in CH_2Cl_2 (3mL) and treated with phosphoryl chloride (0.6 mL) followed by heating up to 50^{o}C for 12h. The reaction mixture was evaporated and concentrated in vacuum to give crude residue, which was subject to sodium methoxide (0.12g, 2.1 mmol) in methanol (3mL) and heated at reflux. After 3h, the reaction mixture was extracted with EtOAc (10mL x 3) and basified with $NaHCO_3$. The combined organic layers were dried over $MgSO_4$ and evaporated to give a residue, which was purified by silica gel chromatography (EtOAc : *n*-hexane = 3 : 1) and recrystallized (CH_3OH) to afford the desired compound **14**, yield 51%; R_f 0.45, mp 182 - 183 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.87 (s, 6H), 3.96 (s, 3H), 4.06 (s, 3H), 6.82 (d, J = 5.3 Hz, 1H), 7.11 (s, 2H), 8.12 (s, 2H), 8.65 (s, 1H), 8.85 (d, J = 5.3 Hz, 1H). MS (EI) *m/z*: 353 (M^+, 100%). HRMS (EI) for $C_{20}H_{19}NO_5$ (M^+): calcd, 353.1263; found, 353.1262. Anal. ($C_{20}H_{19}NO_5 \cdot H_2O$) C, H, N.

6-(3',4',5'-trimethoxybenzoyl)-1-methylquinoline N-oxide (**16**)

To a mixture of 6-(3',4',5'-trimethoxybenzoyl)quinoline (**9**) (0.2 g, 0.62 mmol) and dichloromethane (2 mL), *m*-chloroperbenzoic acid (0.16 g, 0.93 mmol) was added at 0°C. The reaction mixture was stirred at ambient temperature for 16 h and then washed with 10% sodium sulfite, saturated $NaHCO_3$ and extracted with CH_2Cl_2 (3 x 20 ml). The combined organic layer dried

over $MgSO_4$ and evaporated to afford the desired product **16**, yield 95%; TLC (EtOAc : *n*-hexane = 9 : 1), R_f 0.30, mp 175 - 176 °C. ^{1}H NMR (500 MHz, $CDCl_3$): δ 3.86 (s, 6H), 3.96 (s, 3H), 7.07 (s, 2H), 7.39 (dd, *J* = 6.2, 8.2 Hz, 1H), 7.83 (d, *J* = 8.4 Hz, 1H), 8.11 (d, *J* = 8.3 Hz, 1H), 8.29 (s, 1H), 8.62 (d, *J* = 5.9 Hz, 1H), 8.85 (d, *J* = 8.9 Hz, 1H). MS (EI) *m/z*: 339 (M^+, 100%). HRMS (EI) for $C_{19}H_{17}NO_5$ (M^+): calcd, 339.1107; found, 339.1106. Anal. ($C_{19}H_{17}NO_5$) C, H, N.

6-(3',4',5'-trimethoxybenzoyl)-1-methylquinolinium iodide (17)

To a solution of **9** (0.1g, 0.3 mmol) and CH_3I (0.1 mL, 1.54 mmol) was stirred at room temperature for 16 h. The reaction mixture was evaporated and concentrated by vacuum to afford the desired **17**, yield 91%; TLC (CH_2Cl_2 : CH_3OH = 2 : 1), R_f 0.30, mp 187 - 188 °C. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.88 (s, 6H), 3.98 (s, 3H), 5.03 (s, 3H), 7.08 (s, 2H), 8.25 (dd, *J* = 5.8, 8.3 Hz, 1H), 8.49 (d, *J* = 9.0 Hz, 1H), 8.57 - 8.54 (m, 1H), 8.59 (s, 1H), 9.06 (d, *J* = 8.4 Hz, 1H), 10.52 (d, *J* = 5.6 Hz, 1H). MS (EI) *m/z*: 338 (M^+, 100%). HRMS (EI) for $C_{20}H_{20}NO_4^+$ (M-127): calcd, 338.1392; found, 338.1392. Anal. ($C_{20}H_{20}INO_4$) C, H, N.

6-Methoxy-2-methyl-5-nitroquinoline (26)

The 6-methoxy-2-methylquinoline (**25**) (0.5 g, 2.89 mmol) was added to 65% nitric acid (2 mL) and 95% sulfuric acid (2 mL) at 0 ℃ in portion. After stirring for 3 h, the reaction mixture was quenched and extracted by water and CH_2Cl_2. The organic layers were combined and evaporated to give a residue, which was purified by flash chromatography (EtOAc : *n*-hexane = 1 : 2) to give the desired compound **26**, yield 75%. TLC (EtOAc : *n*-hexane = 1 : 2), R_f 0.40. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.72 (s, 3H), 4.05 (s, 3H), 7.39 (d, *J* = 8.8 Hz, 1H), 7.52 (d, *J* = 9.4 Hz, 1H), 7.95 (d, *J* = 8.8 Hz, 1H), 8.15 (d, *J* = 9.4 Hz, 1H).

6-Methoxy-2-quinolinecarboxaldehyde (27)

To a stirred mixture of selenium dioxide (3.20 g, 28.86 mmol) and **25** (1 g, 5.77 mmol) in *p*-xylene (20 mL) was heated at reflux for 16h. The reaction mixture was filtered through a pad of celite and then evaporated the filtrate to give a residue that was purified by silica gel flash column chromatography (EtOAc : *n*-hexane = 2 : 3) to afford the desired compound **27**, yield 72%. R_f 0.45. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.98 (s, 3H), 7.14 (d, *J* = 2.5 Hz, 1H), 7.47 (dd, *J* = 2.5, 9.2 Hz, 1H), 7.8 (d, *J* = 8.4 Hz, 1H), 8.13 – 8.19 (m, 2H), 10.19 (s, 1H).

6-Methoxy-5-nitro-2-quinolinecarboxaldehyde (28)

To a stirred suspension of SeO_2 (2.29g, 20.6 mmol) and **26** (0.9g, 4.13 mmol) in 1,4-dioxane (40 mL) was heated at reflux for 48h. The reaction mixture was filtered through a pad of celite and then evaporated the filtrate to give a residue that was purified by silica gel flash column chromatography (EtOAc: *n*-hexane = 2 : 3) to afford the desired compound **28**, yield 72%. R_f 0.26. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.13 (s, 3H), 7.69 (d, *J* = 9.5 Hz, 1H), 8.11 (d, *J* = 8.1 Hz, 1H), 8.20 (d, *J* = 8.2 Hz, 1H), 8.41 (d, *J* = 9.5 Hz, 1H), 10.17 (s, 1H).

6-Methoxy-5-nitro-2-(3',4',5'-trimethoxybenzoyl)quinoline (29)

The title compound was obtained in 57 % overall yield from 3,4,5-trimethoxy phenylmagnesium bromide and 6-methoxy-5-nitro-2-quinolinecarboxaldehyde (**28**) in a similar manner as described for the preparation of **9**. ^{1}H NMR (500 MHz, $CDCl_3$) δ 3.90 (s, 3H), 3.97 (s, 3H), 4.12 (s, 3H), 7.55 (s, 2H), 7.66 (d, *J* = 9.4, 1H), 8.22 (d, *J* = 8.9 Hz, 1H), 8.26 (d, *J* = 8.9 Hz, 1H), 8.35 (d, *J* = 9.4 Hz, 1H).

8-Methoxy-4-methylquinoline (31)

To a stirred solution of *o*-anisidine (**30**) (0.92 mL, 8.1 mmol) and ferric chloride (1.3g, 8.1 mmol) in acetic acid (10 mL), the methyl vinyl ketone (0.76 mL, 8.9 mmol) was added dropwise over 15 min at room temperature. The reaction mixture was heated to 70 ^{o}C for one hour followed by the addition of zinc chloride (1.1g, 8.1 mmol) heating at reflux for another 2h. The reaction mixture was cooled, filtered, basified with 10 % NaOH solution, extracted with ethyl acetate (3 x 20 ml), dried over Na_2SO_4 and evaporated to give the desired product **31**, yield 60 %. TLC (EtOAc : *n*-hexane = 2 : 1), R_f 0.26. ^{1}H NMR (500 MHz, $CDCl_3$) δ 2.57 (s, 3H), 3.99 (s, 3H), 6.95 (d, *J* = 7.6 Hz, 1H), 7.15 (d, *J* = 4.1 Hz, 1H), 7.39 - 7.36 (m, 1H), 7.45 (d, *J* = 8.6 Hz, 1H), 8.70 (d, *J* = 4.2 Hz, 1H).

8-Methoxy-4-quinolinecarboxaldehyde (32)

To a stirred mixture of selenium dioxide (0.64g, 5.77 mmol) and **31** (0.2g, 1.16 mmol) in *p*-xylene (10 mL) was heated at reflux for 16h. The reaction mixture was filtered through a pad of celite and then evaporated the filtrate to give a residue that was purified by silica gel flash column chromatography (EtOAc : *n*-hexane = 2 : 1) to afford the desired compound **32**, yield 68%. R_f 0.23, ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.12 (s, 3H), 7.16 (d, *J* = 7.8 Hz, 1H), 7.68 - 7.64 (m, 1H), 7.83 (d, *J* = 4.1 Hz, 1H), 8.55 (d, *J* = 8.6 Hz, 1H), 9.20 (d, *J* = 4.1 Hz, 1H), 10.53 (s, 1H).

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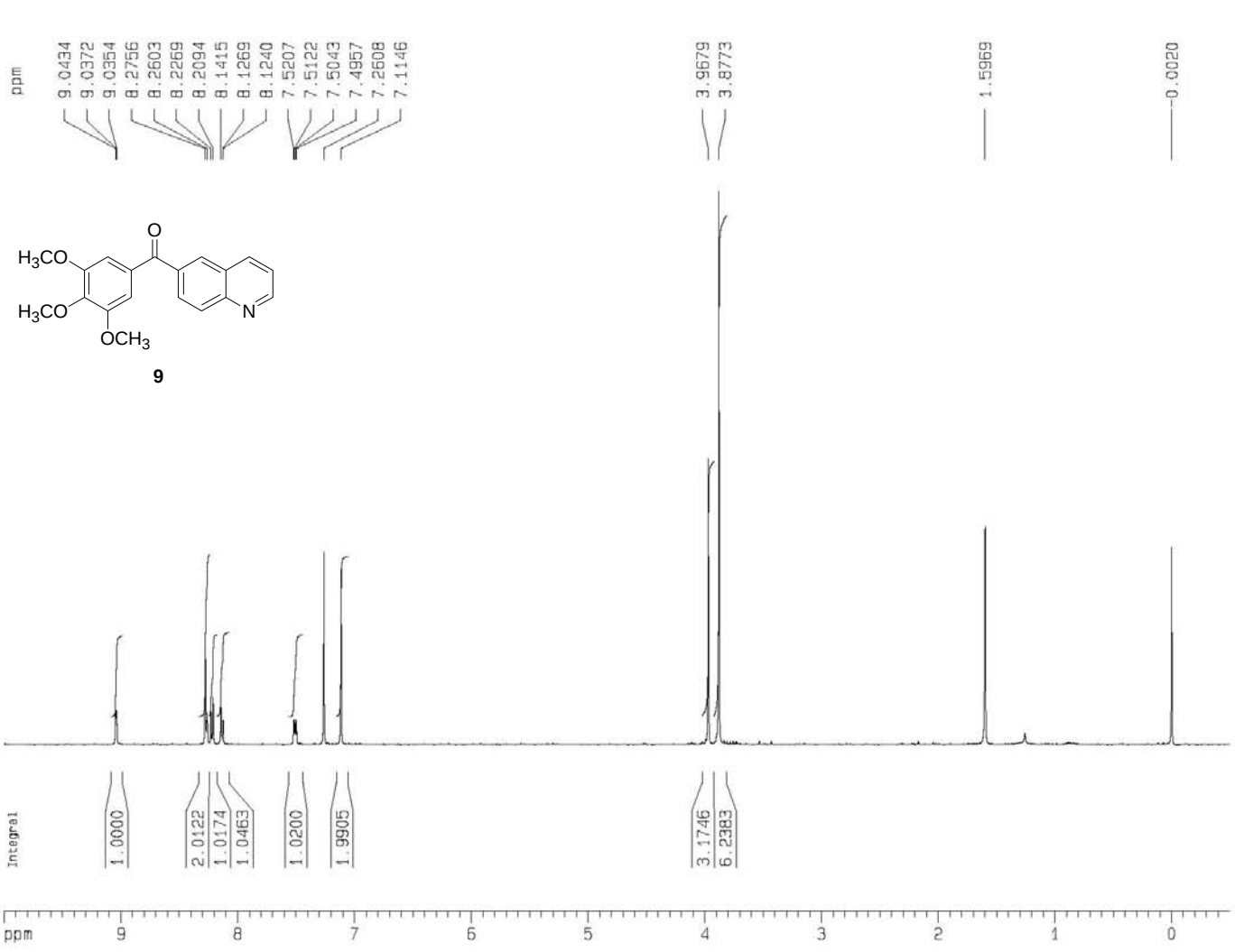

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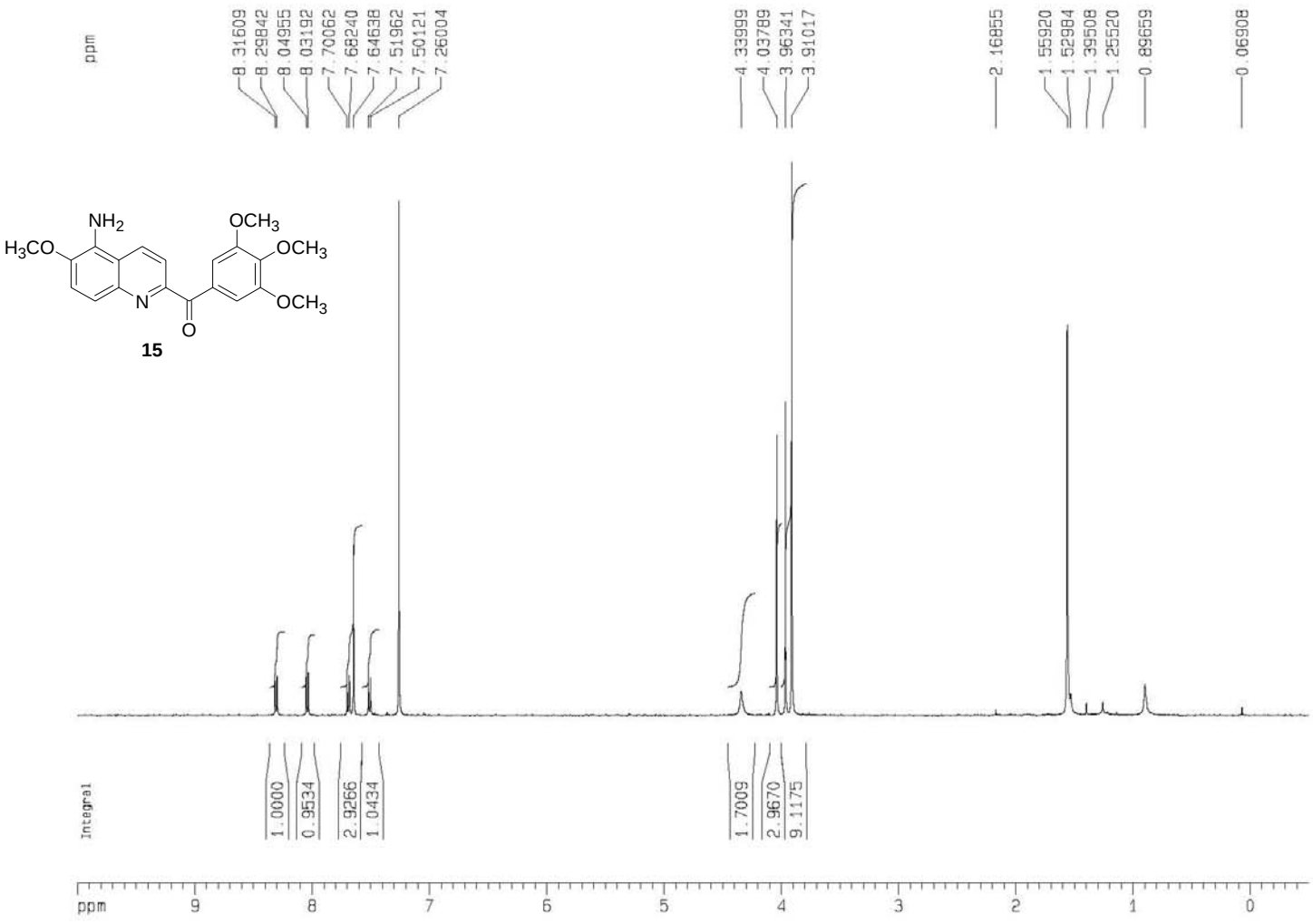

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SI 16384
SF 500.1300136 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

1D NMR plot parameters
CX 22.00 cm
CY 10.00 cm
F1P 10.000 ppm
F1 5001.30 Hz
F2P -0.500 ppm
F2 -250.06 Hz
PPMCM 0.47727 ppm/cm
HZCM 238.69839 Hz/cm

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