

Visual Detection of Formaldehyde by Highly Selective Fluorophore Labeling via Gold(III) Complex-Mediated Three-Component Coupling Reaction

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Supporting Information

General Procedure

All reagents were commercially available and used without further purification. Milli-Q[®] water used as reaction solvent and HPLC mobile phase were deionised using a Milli-Q[®] Gradient A10 system (Millipore, Billerica, USA). Flash column chromatography was performed using silica gel 60 (230-400 mesh, ASTM). ¹H and ¹³C NMR spectra were recorded on Bruker DPX-400, DPX-600, Varian Unity Inova 400 NB and 500 NB spectrometers. The chemical shifts are expressed in ppm and coupling constants are given in Hz. Data for ¹H NMR are recorded as follows: chemical shift (δ , ppm), multiplicity (s, singlet; br s, broad singlet; d, doublet; dd, double doublet; t, triplet; td, triplet of doublets; m, multiplet), coupling constant (Hz), integration. Data for ¹³C NMR are reported in terms of chemical shift (δ , ppm). Low resolution mass spectra (MS) and high resolution mass spectra (HR-MS) were obtained on Waters Micromass Q-ToF 2TM with positive ESI in terms of mass to charge ratio (m/z). Microplate reader results were obtained with a BMG FLUOstar Galaxy Multi-functional Microplate Reader.

ESI-MS Analysis of Propargylamine Formation in A3-Coupling Reaction

The mass spectrometer was performed over an m/z range of 100-1000 on Waters Micromass Q-ToF 2TM with positive ESI, and the raw spectra were deconvoluted by the MassLynx 4.1 Transform Program (Waters, Manchester, UK). Desolvation and source temperatures were 150 °C and 80 °C, respectively. Operating conditions optimized for the detection of reaction mixture were as the followings: capillary voltage 3 kV, sample cone voltage 30 V, extraction voltage 4 V and collision cell voltage 10 eV.

HPLC Conditions for Model Reaction Study

Waters 2695 HPLC Separation Module equipped with XTerra MS C18 (5 μ m, 4.6 mm x 100 mm) Column and Waters 2998 Photodiode Array (PDA) Detector was used for separation. The flow rate was 0.6 mL/min. The injection volume was 10 μ L. The PDA detector wavelength was set to 254 nm.

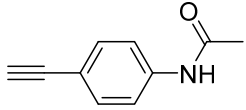
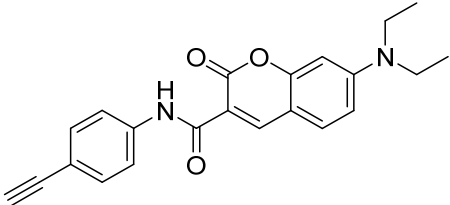
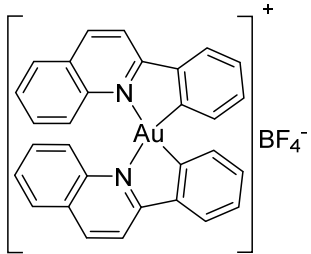

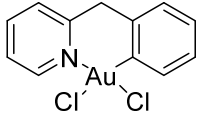
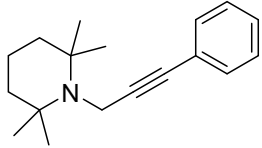
Mobile phase A was made of Milli-Q[®] water. Mobile phase B was made of acetonitrile. The initial conditions for separation were 30% B for 3 min, followed by a linear gradient to 70% B by 3 min. The composition was maintained for 4 min, followed by a linear gradient to 100% B by 1 min. The composition was maintained for 3 min, followed by a linear gradient to 30% B by 2 min. The composition was maintained for 2 min.

LC-MS/MS Conditions for Propargylamine 5a

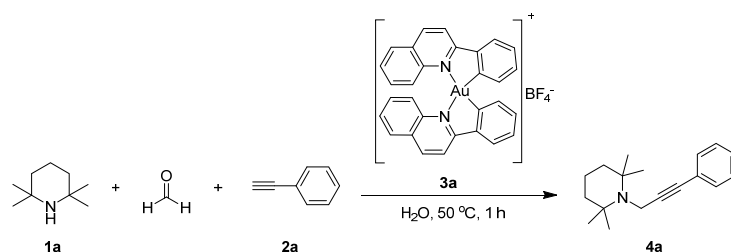
LC-MS/MS analyses were performed by using a hybrid Q-TOF mass spectrometer (AB Sciex 4000 QTRAP) equipped with an ionspray source and an Agilent 1200 LC. The flow rate was 0.5 mL/min.

Mobile phase A was made of HCOOH-NH₄OOCH water solution. Mobile phase B was made of acetonitrile. The initial conditions for separation were 100% B for 1 min, followed by a linear gradient to 80% B by 19 min and followed by a linear gradient to 100% B by 18 min. The composition was maintained for 2 min.

Literature References of Compounds

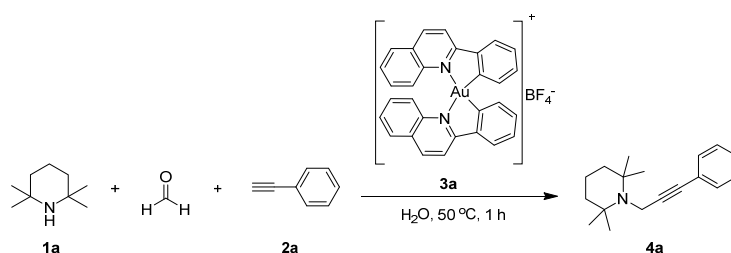
 <p style="text-align: center;">2b</p>	<p>W. K. Chan, C. M. Ho, M. K. Wong and C. M. Che, <i>J. Am. Chem. Soc.</i>, 2006, 128, 14796–14797.</p>
 <p style="text-align: center;">2c</p>	<p>M. Maldonado-Domínguez, R. Arcos-Ramos, M. Romero, B. Flores-Pérez, R. Santillan, P. G. Lacroix, I. Malfant and N. Farfán, <i>New J. Chem.</i>, 2014, 38, 260–268.</p>
 <p style="text-align: center;">3a</p>	<p>H. M. Ko, K. K. Y. Kung, J. F. Cui and M. K. Wong, <i>Chem. Comm.</i>, 2013, 49, 8869–8871.</p>
 <p style="text-align: center;">3b</p>	<p>E. C. Constable and T. A. Leese, <i>J. Organomet. Chem.</i>, 1989, 363, 419–424.</p>
 <p style="text-align: center;">3c</p>	<p>M. A. Cinellu, A. Zucca, S. Stoccoro, G. Minghetti, M. Manassero and M. Sansoni, <i>J. Chem. Soc., Dalton Trans.</i>, 1995, 2865–2872.</p>
 <p style="text-align: center;">4a</p>	<p>P. H. Li and L. Wang, <i>Tetrahedron</i>, 2007, 63, 5455–5459.</p>

Procedure for A3-coupling Reaction of Formaldehyde in 1 h

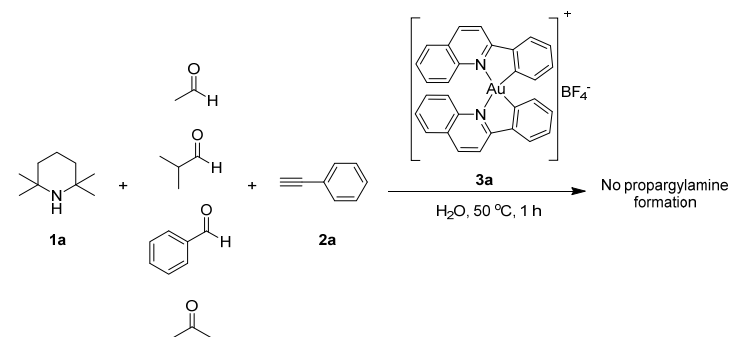


A mixture of formaldehyde (0.1 mmol), 2,2,6,6-tetramethylpiperidine **1a** (0.11 mmol), phenylacetylene **2a** (0.15 mmol) and bis-cyclometallated gold(III) complex **3a** (0.01 mmol) in water (600 μ L) was stirred at 50 °C for 1 h. Then, the mixture was extracted with dichloromethane (10 mL \times 3). The combined organic layer was dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography using ethyl acetate/n-hexane as eluent to give propargylamine **4a** in 6% isolated yield.

Procedure for Study of Selectivity of 2,2,6,6-Tetramethylpiperidine 1a for Formaldehyde

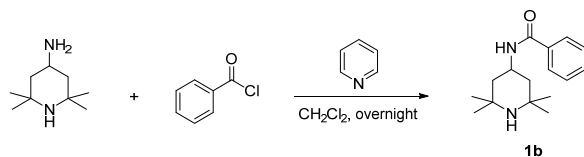


A mixture of formaldehyde (0.1 mmol), 2,2,6,6-tetramethylpiperidine **1a** (0.11 mmol), phenylacetylene **2a** (0.15 mmol) and bis-cyclometallated gold(III) complex **3a** (0.01 mmol) in water (600 μ L) was stirred at 50 °C for 1 h. Then, the mixture was extracted with dichloromethane (600 μ L). The organic layer was analyzed by ESI-MS for the formation of propargylamine **4a**.



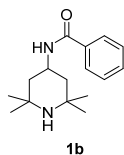
The reaction was repeated with acetaldehyde, isobutyraldehyde, benzaldehyde and acetone instead of formaldehyde, respectively. ESI-MS analysis of the reaction mixtures showed no propargylamine formation for acetaldehyde, isobutyraldehyde, benzaldehyde and acetone.

Procedure for Synthesis of 1b



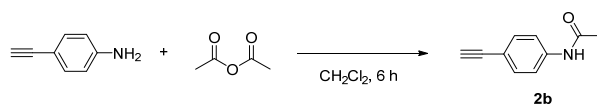
A mixture of 4-amino-2,2,6,6-tetramethylpiperidine (6 mmol), benzoyl chloride (3 mmol) and pyridine (3 mmol) was stirred in dichloromethane (20 mL) under nitrogen atmosphere at room temperature for overnight. After reaction, the mixture was concentrated under reduced pressure. The residue was purified by flash column chromatography using methanol/ethyl acetate as eluent to give amine **1b** in 84% isolated yield.

Characterization Data of 1b



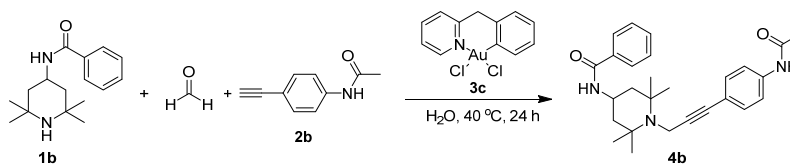
White powder; analytical TLC (silica gel 60) (40% methanol/ethyl acetate), $R_f = 0.45$; ¹H NMR (400 MHz, CDCl₃) δ 7.76 (d, $J = 7.2$ Hz, 2H), 7.48 (t, $J = 7.3$ Hz, 1H), 7.41 (t, $J = 7.6$ Hz, 2H), 6.05 (d, $J = 7.2$ Hz, 1H), 4.41-4.51 (m, 1H), 1.99 (dd, $J = 6.2$ Hz, 2H), 1.29 (s, 6H), 1.14 (s, 6H), 1.04 (t, $J = 12.2$ Hz, 2H); ¹³C NMR (100 MHz, CDCl₃) δ 166.70, 134.75, 131.34, 128.51, 126.75, 51.24, 45.20, 43.05, 34.82, 28.42; ESI-MS m/z 261 [M+H]⁺; HRMS (ESI) for C₁₆H₂₅N₂O, calcd. 261.1961, found 261.1960.

Procedure for Synthesis of 2b



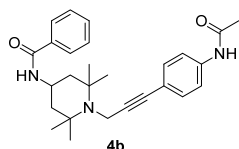
A mixture of 4-ethynylaniline (2.5 mmol) and acetic anhydride (3.3 mmol) in dichloromethane (5 mL) was stirred at room temperature for 6 h. After evaporation of solvent, the residue was purified by flash column chromatography using ethyl acetate/n-hexane as eluent to afford alkyne **2b** in 95% yield.

Procedure for Synthesis of **4b**



A mixture of formaldehyde (1 mmol), amine **1b** (1.1 mmol), alkyne **2b** (1.5 mmol) and cyclometallated gold(III) complex **3c** (0.01 mmol) in water (1 mL) was stirred at 40 °C for 24 h. After reaction, the mixture was extracted with ethyl acetate (15 mL \times 3). The combined organic layer was dried over anhydrous MgSO₄, filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography using ethyl acetate/n-hexane as eluent to give propargylamine **4b** in 36% yield.

Characterization Data of **4b**



White powder; analytical TLC (silica gel 60) (70% ethyl acetate/n-hexane), R_f = 0.57; ¹H NMR (400 MHz, CD₃OD) δ 7.81 (d, J = 7.2 Hz, 2H), 7.50 (d, J = 8.1 Hz, 3H), 7.44 (t, J = 7.0 Hz, 2H), 7.29 (d, J = 8.1 Hz, 2H), 4.36-4.42 (m, 1H), 3.63 (s, 2H), 2.11 (s, 3H), 1.79 (d, J = 10.0 Hz, 2H), 1.56 (t, J = 12.2 Hz, 2H), 1.32 (s, 6H), 1.25 (s, 6H); ¹³C NMR (100 MHz, CDCl₃) δ 171.65, 169.76, 139.59, 136.07, 132.82, 132.57, 129.52, 128.36, 120.86, 120.80, 92.69, 82.19, 57.37, 43.35, 34.22, 33.99, 23.89, 22.39; ESI-MS m/z 432 [M+H]⁺; HRMS (ESI) for C₂₇H₃₄N₃O₂, calcd. 432.2646, found 432.2649.

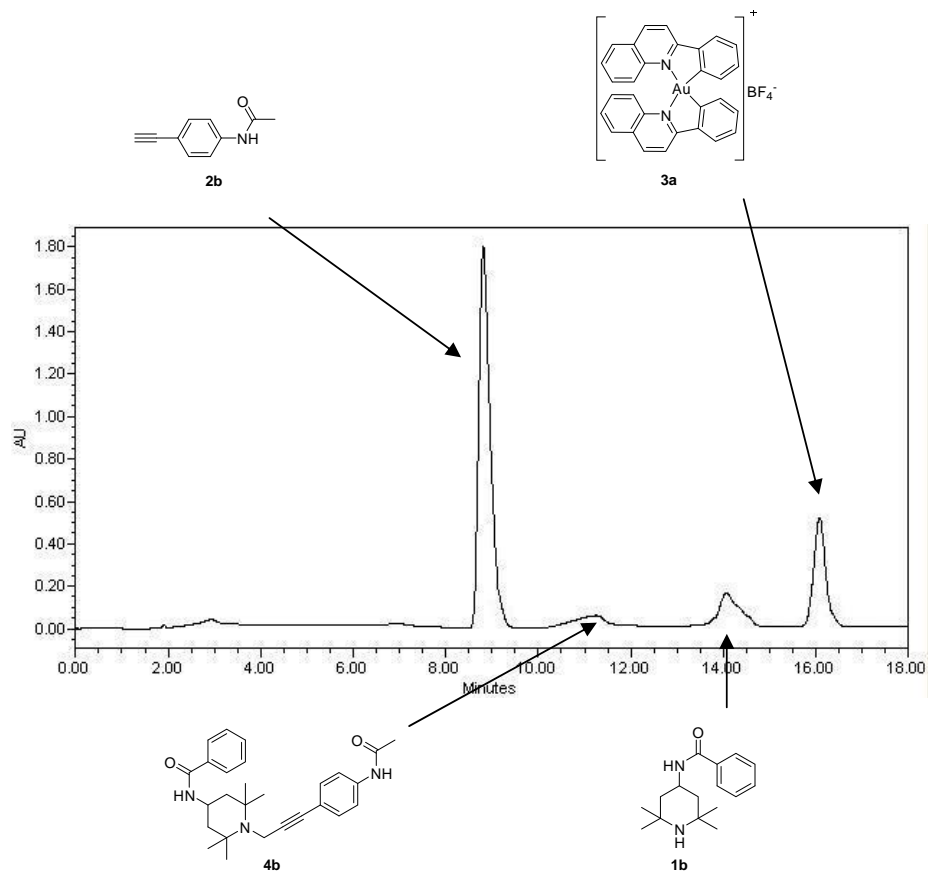


Figure S1. HPLC chromatogram for study of the model reaction.

Table S1. Data for construction of calibration curve for the model reaction

Concentration of 4b	Peak Area (Determined by HPLC)
1	39195
10	324417
50	1797622
100	3481545
200	7222159

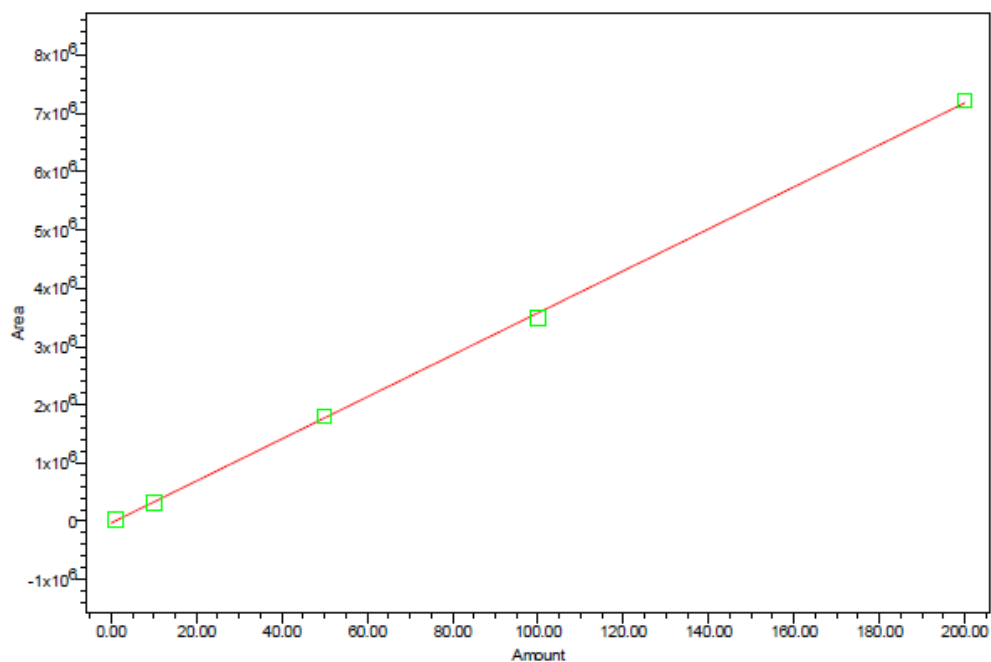
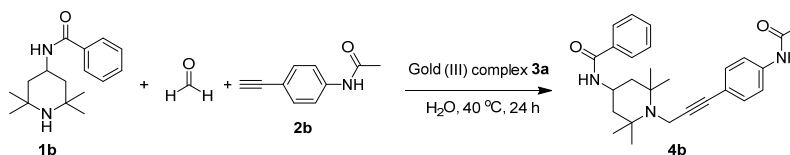


Figure S2. Calibration curve for quantification of propargylamine **4b** formed in the model reaction by HPLC. The x-axis is formaldehyde concentration and y-axis is peak area.

Procedure for the Model Reaction for Optimization of Reaction Conditions



Effect of Cyclometallated Gold(III) Complexes

A mixture of formaldehyde ($20\text{ }\mu\text{mol}$, in form of a $100\text{ }\mu\text{L}$ aqueous solution), amine **1b** ($22\text{ }\mu\text{mol}$), alkyne **2b** ($30\text{ }\mu\text{mol}$) and cyclometallated gold(III) complex **3a** ($4\text{ }\mu\text{mol}$) in water ($600\text{ }\mu\text{L}$) was stirred at $50\text{ }^\circ\text{C}$ for 1 h. After reaction, $20\text{ }\mu\text{L}$ of the reaction mixture was mixed with $980\text{ }\mu\text{L}$ acetonitrile for HPLC analysis. The reactions were repeated with cyclometallated gold(III) complexes **3b** and **3c**, respectively.

Effect of Solvents

A mixture of formaldehyde ($20\text{ }\mu\text{mol}$, in form of an $100\text{ }\mu\text{L}$ aqueous solution), amine **1b** ($22\text{ }\mu\text{mol}$), alkyne **2b** ($30\text{ }\mu\text{mol}$) and bis-cyclometallated gold(III) complex **3a** ($4\text{ }\mu\text{mol}$) in water ($600\text{ }\mu\text{L}$) was stirred at $50\text{ }^\circ\text{C}$ for 1 h. After reaction, $20\text{ }\mu\text{L}$ of the reaction mixture was mixed with $980\text{ }\mu\text{L}$ acetonitrile for HPLC analysis. The reactions were repeated with acetonitrile, dimethylformamide, tetrahydrofuran, 1,4-dioxane, toluene, ethyl acetate and 1,2-dichloroethane as the solvent, respectively.

Effect of Solvent Ratio

Mixtures of formaldehyde ($20\text{ }\mu\text{mol}$, in form of a $50\text{ }\mu\text{L}$ aqueous solution), amine **1b** ($22\text{ }\mu\text{mol}$), alkyne **2b** ($30\text{ }\mu\text{mol}$) and bis-cyclometallated gold(III) complex **3a** ($4\text{ }\mu\text{mol}$) in different volumes of 1,2-dichloroethane and water were stirred at $50\text{ }^\circ\text{C}$ for 1 h. After reaction, 1,2-dichloroethane was added to the reaction mixtures to make up the organic layer to a final volume of $450\text{ }\mu\text{L}$, respectively. Then, the reaction mixtures were mixed by a vortex mixer for 1 min. $20\text{ }\mu\text{L}$ of the organic layer was mixed with $980\text{ }\mu\text{L}$ acetonitrile for HPLC analysis.

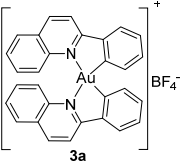
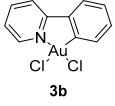
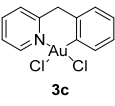
Effect of Temperature

A mixture of formaldehyde ($20\text{ }\mu\text{mol}$, in form of a $50\text{ }\mu\text{L}$ aqueous solution), amine **1b** ($22\text{ }\mu\text{mol}$), alkyne **2b** ($30\text{ }\mu\text{mol}$) and bis-cyclometallated gold(III) complex **3a** ($4\text{ }\mu\text{mol}$) in 1,2-dichloroethane ($450\text{ }\mu\text{L}$) was stirred at room temperature for 1 h. After reaction, $20\text{ }\mu\text{L}$ of the organic layer was mixed with $980\text{ }\mu\text{L}$ acetonitrile for HPLC analysis. The reaction was repeated at $40\text{ }^\circ\text{C}$, $50\text{ }^\circ\text{C}$ and $60\text{ }^\circ\text{C}$, respectively.

Effect of Reagent Ratio

A mixture of formaldehyde (in form of a 50 μL aqueous solution), amine **1b**, alkyne **2b** and bis-cyclometallated gold(III) complex **3a** in different amounts in 1,2-dichloroethane (450 μL) was stirred at 50 $^{\circ}\text{C}$ for 1 h. After reaction, 20 μL of the organic layer was mixed with 980 μL acetonitrile for HPLC analysis.

Table S2. Screening for the effect of different cyclometallated gold (III) complexes on the yield of propargylamine **4b** in the model reaction^a

Entry	Cyclometallated gold(III) complex	Yield of 4b ^b (%)
1		4.0
2		1.1
3		2.2

^a Reactions were carried out with formaldehyde (20 μmol , in form of an aqueous solution), amine **1b** (22 μmol), alkyne **2b** (30 μmol) and cyclometallated gold(III) complexes **3a-c** (4 μmol) in water at 50 $^{\circ}\text{C}$ for 1 h. ^b Determined by HPLC.

Table S3. Screening for the effect of solvents on the yield of product **4b** in the model reaction^a

Entry	Solvent ^b	Yield of 4b ^c (%)
1	Water	3.8
2	Acetonitrile	-
3	Dimethylformamide	-
4	Tetrahydrofuran	1.6
5	1,4-Dioxane	2.2
6	Toluene	1.1
7	Ethyl Acetate	5.4
8	1,2-Dichloroethane	12.1

^a Reactions were carried out with formaldehyde (20 μmol , in form of an aqueous solution), amine **1b** (22 μmol), alkyne **2b** (30 μmol) and bis-cyclometallated gold(III) complex **3a** (4 μmol) at 50 $^{\circ}\text{C}$ for 1 h. ^b 600 μL of solvent was used. ^c Determined by HPLC.

Table S4. Screening for the effect of ratio of 1,2-dichloroethane to water on the yield of product **4b** in the model reaction^a

Entry	1,2-Dichloroethane (μL)	Water (μL)	Ratio	Yield of 4b ^b (%)
1	50	450	1:9	2.2
2	100	400	1:4	3.1
3	150	350	3:7	3.7
4	200	300	2:3	2.5
5	250	250	1:1	3.7
6	300	200	3:2	4.2
7	350	150	7:3	4.5
8	400	100	4:1	8.8
9	450	50	9:1	11.4

^a Reactions were carried out with formaldehyde (20 μmol , in form of an aqueous solution), amine **1b** (22 μmol), alkyne **2b** (30 μmol) and bis-cyclometallated gold(III) complex **3a** (4 μmol) at 50 °C for 1 h. ^b Determined by HPLC.

Table S5. Screening for the effect of temperatures on the yield of product **4b** in the model reaction^a

Entry	Temperature ($^{\circ}\text{C}$)	Yield of 4b ^b (%)
1	25	-
2	40	3.6
3	50	12.1
4	60	4.1

^a Reactions were carried out with formaldehyde (20 μmol , in form of an aqueous solution), amine **1b** (22 μmol), alkyne **2b** (30 μmol) and gold(III) complex **3a** (4 μmol) in 1,2-dichloroethane (450 μL) for 1 h. ^b Determined by HPLC.

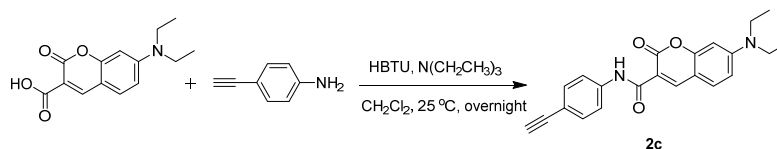
Table S6. Screening for the effect of reagents ratios on the yield of product **4b** in the model reaction^a

Entry	Amine 1b (μmol)	Alkyne 2b (μmol)	Gold(III) complex 3a (μmol)	Yield of 4b ^b (%)
1	10	15	2	-
2	10	50	10	18
3	10	50	30	19
4	10	100	1	5
5	10	100	2	-
6	10	150	2	-
7	10	200	1	1
8	50	10	10	19
9	50	50	30	41

10	50	50	50	8
11	50	100	2	-
12	50	100	50	56
13	50	150	2	-
14	100	50	50	40
15	100	150	2	6
16	100	100	50	53
17 ^c	10	15	1	3
18 ^c	10	100	1	9
19 ^c	10	100	2	16
20 ^d	20	30	2	4
21 ^d	20	200	2	23
22 ^d	20	200	4	46
23 ^e	10	15	1	5
24 ^e	10	100	2	28
25 ^f	20	30	2	12

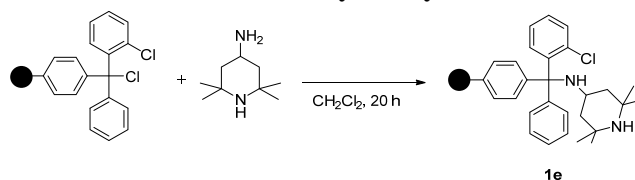
^a Unless otherwise specified, reactions were carried out with formaldehyde (10 μmol , in form of an aqueous solution) in 1,2-dichloroethane (450 μL) at 50 $^{\circ}\text{C}$ for 1 h. ^b Determined by HPLC. ^c 100 μmol of formaldehyde was used. ^d 200 μmol of formaldehyde was used. ^e 300 μmol of formaldehyde was used. ^f 600 μmol of formaldehyde was used.

Procedure for Synthesis of **2c**



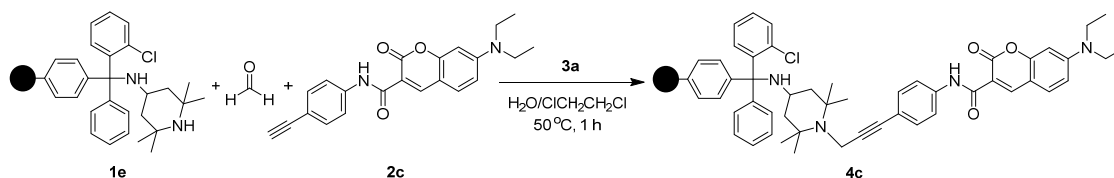
A mixture of 7-(diethylamino)coumarin-3-carboxylic acid (0.5 mmol), 4-ethynylaniline (0.6 mmol), triethylamine (1 mmol) and HBTU (0.6 mmol) in dichloromethane (20 mL) was stirred under nitrogen atmosphere at room temperature for overnight. After reaction, the mixture was washed with water (15 mL \times 3). The organic layer was dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography using dichloromethane/n-hexane as eluent to give **2c** in 79% yield.

Procedure for Synthesis of Resin-linked Sterically Bulky Amine **1e**



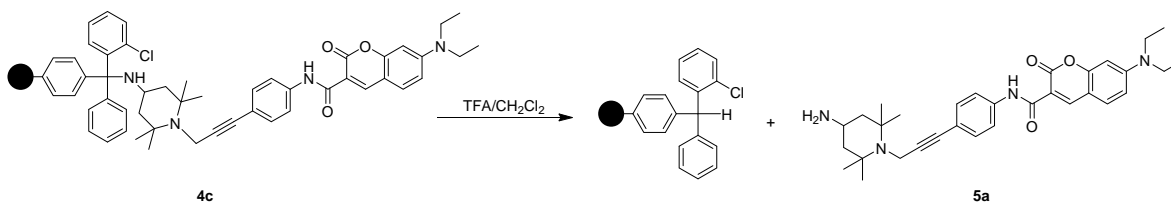
Commercially available polymer-bound 2-chlorotrityl chloride resin (15 mg) was swollen in dichloromethane (250 μ L) for 15 min. 4-Amino-2,2,6,6-tetramethylpiperidine (0.19 mmol) was added and the reaction vessel was gently shaken for 20 h. After reaction, 12 μ L HPLC grade methanol was added and mixed for 15 min to endcap any remaining reactive 2-chlorotrityl groups. The resin was washed three times with 1 mL of dichloromethane, two times with 1 mL of dimethylformamide, and three times with 1 mL of dichloromethane and then dried for future use. Reference: J. J. McNally, M. A. Youngman and S. L. Dax, *Tetrahedron Lett.*, 1998, **39**, 967-970.

Procedure for A3-Coupling of Formaldehyde with Resin-linked Sterically Bulky Amine **1e** and Coumarin-linked Alkyne **2c**



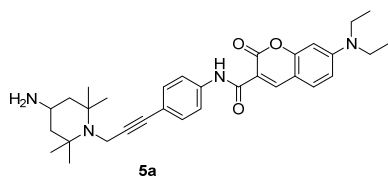
A mixture of solid-supported amine **1e** (15 mg), formaldehyde (0.02 mmol, in form of an 100 μ L aqueous solution), coumarin-linked alkyne **2c** (0.02 mmol), bis-cyclometallated gold(III) complex **3a** (0.01 mmol), and 600 μ L of 1,2-dichloroethane was gently stirred at 50 $^{\circ}$ C for 1 h. After reaction, the resin was washed four times with 1 mL of dichloromethane, two times with 1 mL of dimethylformamide, and three times with 1 mL of dichloromethane.

Procedure for Cleavage from Resin Support **4c** to Give Propargylamine **5a**



Resins **4c** (15 mg) were suspended in 1:1 trifluoroacetic acid and dichloromethane (300 μ L) at room temperature for 1 min for cleavage of propargylamine **5a** from the solid support. The solution was analyzed by ESI-MS, and propargylamine **5a** ($m/z = 529.27$ $[M+H]^+$) was detected. The solution was then neutralized by saturated NaHCO_3 solution (5 mL). The organic layer was dried over anhydrous MgSO_4 , filtered, and concentrated under reduced pressure. The residue was purified by flash column chromatography using methanol/dichloromethane as eluent to give propargylamine **5a** in 4% yield.

Characterization Data of 5a



Yellow powder; analytical TLC (silica gel 60) (10% methanol/dichloromethane), $R_f = 0.42$; ^1H NMR (400 MHz, d_6 -DMSO) δ 8.75 (s, 1H), 7.73 (d, $J = 9.1$ Hz, 1H), 7.68 (d, $J = 8.6$ Hz, 2H), 7.33 (d, $J = 8.6$ Hz, 2H), 6.85 (dd, $J = 4.5$ Hz, 1H), 6.66 (d, $J = 2.1$ Hz, 1H), 3.56 (s, 2H), 3.48-3.53 (m, 4H), 1.78 (dd, $J = 6.1$ Hz, 4H), 1.41 (t, $J = 6.7$ Hz, 3H), 1.23 (s, 6H), 1.15 (t, $J = 6.7$ Hz, 3H), 1.08 (s, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ 163.34, 162.24, 158.15, 153.74, 148.96, 131.79, 131.68, 119.95, 119.83, 114.50, 110.75, 108.98, 108.77, 96.15, 91.35, 81.14, 55.62, 47.37, 45.02, 32.65, 27.53, 21.08, 11.51; ESI-MS m/z 529 $[\text{M}+\text{H}]^+$; HRMS (ESI+) for $\text{C}_{32}\text{H}_{41}\text{N}_4\text{O}_3$, calcd. 529.3173, found 529.3177.

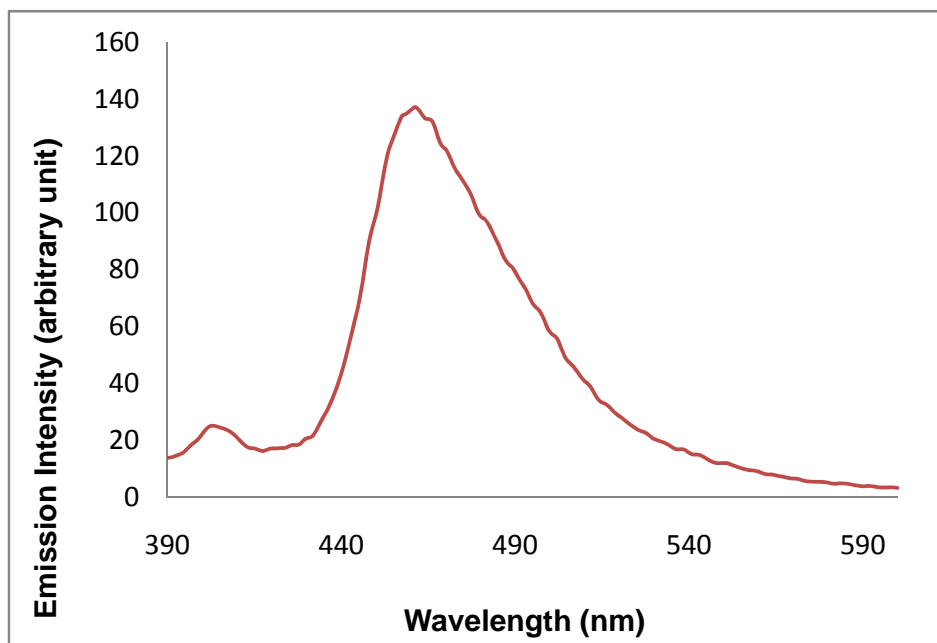


Figure S3. Fluorescent spectrum of propargylamine **5a**.

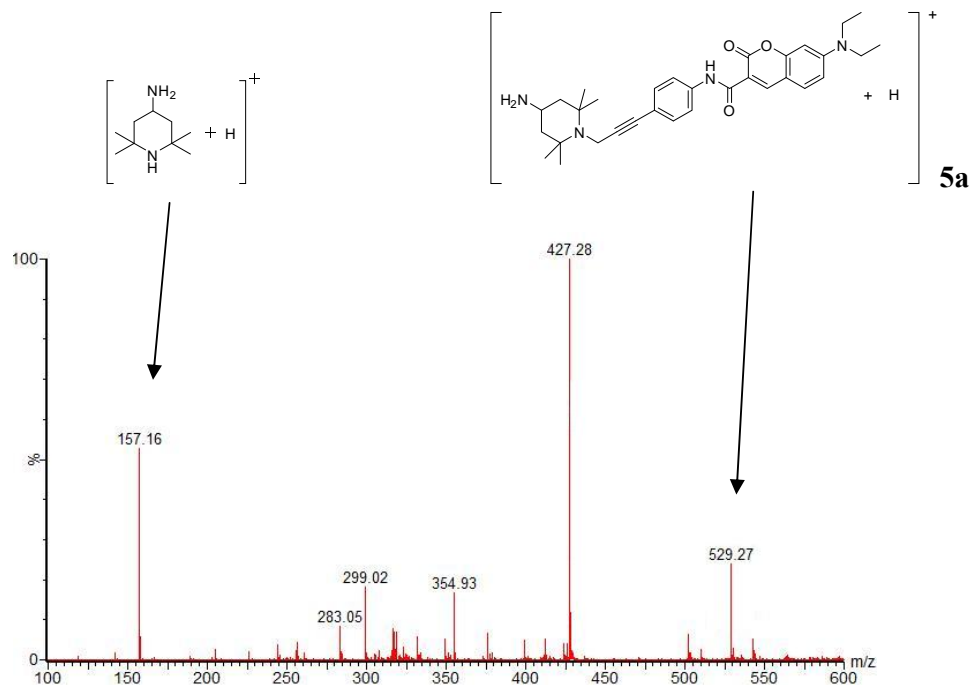


Figure S4. MS spectrum of propargylamine **5a** cleaved from the resin beads.

Determination of Propargylamine **5a** by LC-MS/MS

Resins **4c** (15 mg) from different reaction mixtures (concentration of formaldehyde from 4 to 103 ppm) were suspended in 1:1 trifluoroacetic acid and dichloroethane (300 μ L) at room temperature for 10 min for cleavage of propargylamine **5a** from the solid support. The solution was then neutralized by saturated NaHCO_3 solution (300 μ L). The upper aqueous layer was removed by dropper, and the organic layer and the resins were dried in oven at 75 $^\circ\text{C}$. Then, 1.3 mL of acetonitrile was added into the dried mixtures, and the solution was prepared for LC-MS/MS analysis.

For LC-MS/MS analysis, the m/z of precursor ions were 529.4 ($[\text{M}+\text{H}]^+$) for propargylamine **5a** while the fragment ions (daughter ions) were 373.2.

Table S7. Data for construction of calibration curve for the cleavage propargylamine **5a**.

Formaldehyde concentration	Peak area (arbitrary unit)
4	1.71E+05
10	2.83E+05
51	8.96E+05
103	1.96E+06

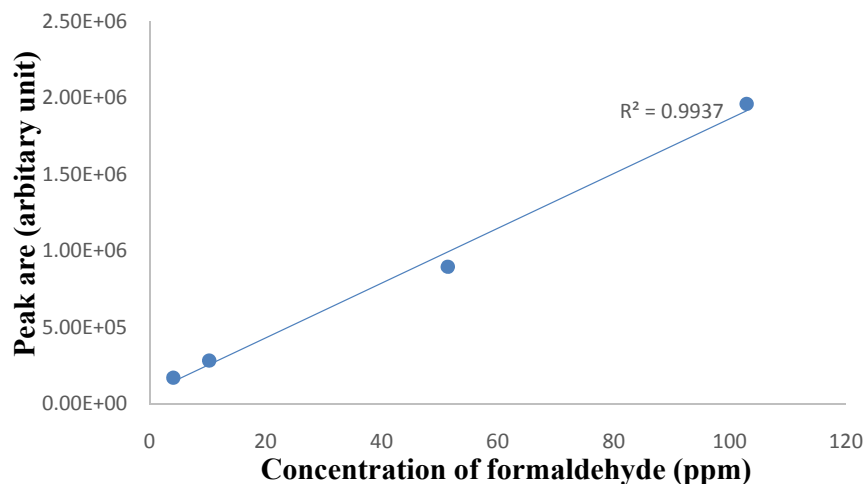


Figure S5. Calibration curve for the cleavage propargylamine **5a**.

Measurement of Fluorescent Intensity by Microplate Reader

Resins **4c** (2.0 mg) from different reaction mixtures (concentration of formaldehyde from 0 to 500 ppm) were accurately weighed and transferred to a microplate for measurement of fluorescent intensity. The fluorescent intensity was measured by a BMG FLUOstar Galaxy Fluorescence Microplate Reader. The number of cycles, number of flash, and cycle time were set as 10. The delay time was set as 0.5 second. The excitation wavelength was 355 nm and emission wavelength was 460 nm.

Table S8. Data for construction of calibration curve for the resin beads

Formaldehyde concentration	Fluorescent intensity (arbitrary unit)
0	1031
50	2187
100	2939
500	7603

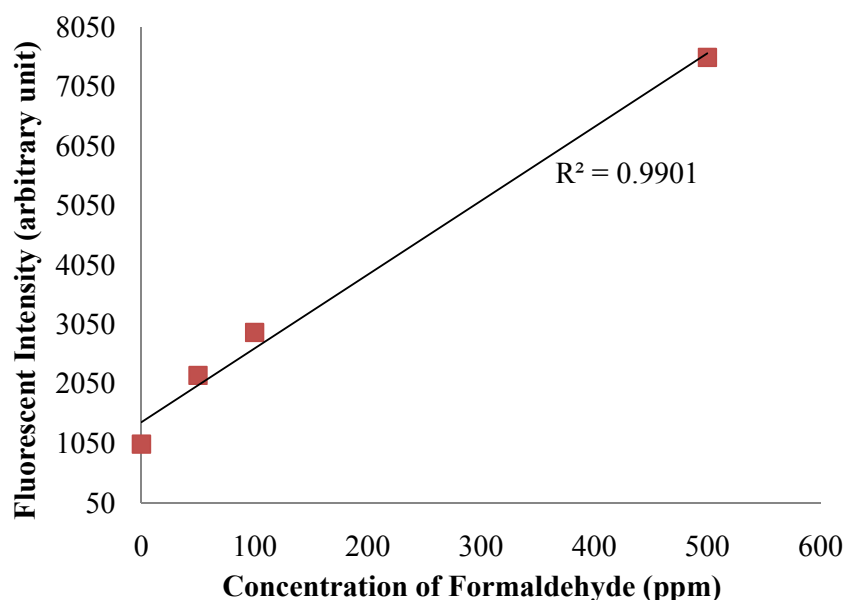


Figure S6. Calibration curve for the resin beads.

Procedure for Using Water Extract of Mushroom as Formaldehyde Source

The purchased dried mushroom sample was sealed in plastic bags at room temperature without direct exposure to light. The mushroom sample with stems removed was homogenized by a blender. About 2 g of the sample was weighed and stored in a centrifuge tube. Milli-Q[®] water (20 mL) was added into the tube and the tube was sealed. The tube was placed into an ultrasonic bath for extraction at 40 °C for 1 hour. After that, the sample was centrifuged at 4000 rpm for 10 mins. The centrifuged sample was filtered with filter paper and funnel. The filtrate was collected by a 50 mL volumetric flask. Milli-Q[®] water (20 mL) was added into the centrifuge tube again and the tube was placed into an ultrasonic bath for extraction at 40 °C for 30 mins. The sample was centrifuged at 4000 rpm for 10 mins. The centrifuged sample was filtered with filter paper and funnel. The filtrate was collected by the 50 mL volumetric flask used previously. The flask was made up with Milli-Q[®] water and was mixed well. This gave the water extract of the mushroom sample.

ESI-MS analysis was used to confirm the cleaved product **5a** when mushroom water extract was used as formaldehyde source. A mixture of solid-supported amine **1e** (15 mg), water extract of mushroom (100 µL), coumarin alkyne **2c** (0.02 mmol), bis-cyclometallated gold(III) complex **3a** (0.01 mmol) and 600 µL of 1,2-dichloroethane was gently stirred at 50 °C for 1 h. After reaction, the resins were washed four times with 1 mL of dichloromethane, two times with 1 mL of dimethylformamide, and three times with 1 mL of dichloromethane. The product was cleaved (by using 1:1 trifluoroacetic acid and dichloromethane (300 µL) at room temperature for 1 min) from the resin support and analyzed by ESI-MS for confirmation of product formation.

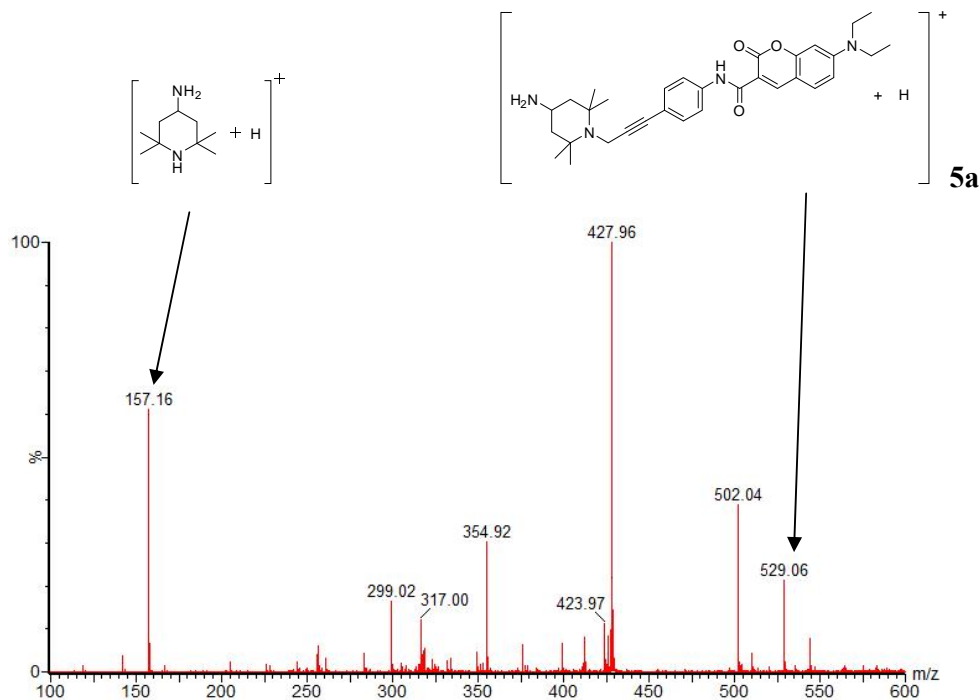


Figure S7. MS spectrum of cleaved product from the resin beads using mushroom sample as the formaldehyde source.

LC-MS/MS analysis was used to quantify the amount of formaldehyde in mushroom water extracts. Another calibration curve was built up for quantitative analysis based on the mentioned procedure and a good linear relationship ($R^2 = 0.9799$) between the formaldehyde concentration and peak area was obtained.

Table S9. Data for construction of calibration curve for the cleavage propargylamine **5a**.

Formaldehyde concentration	Peak area (arbitrary unit)
10	107000
10	98900
51	301000
51	332000
103	429000
103	399000

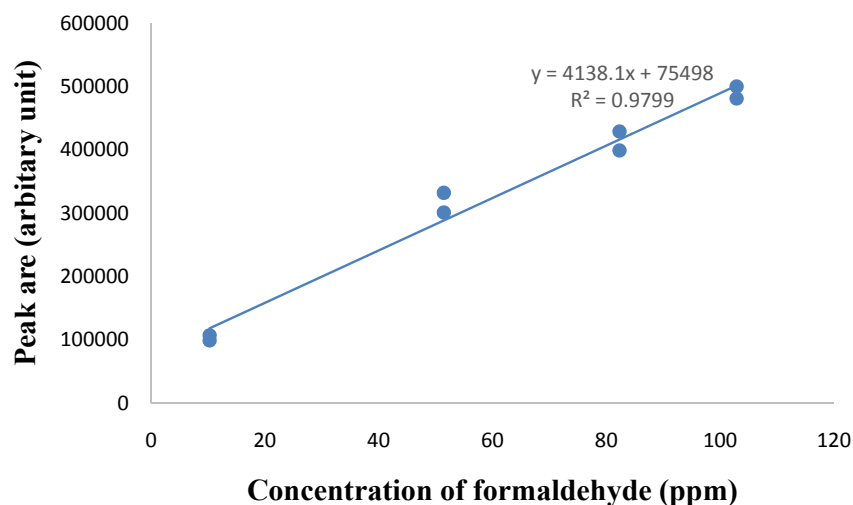


Figure S8. Calibration curve for the cleavage of propargylamine **5a**.

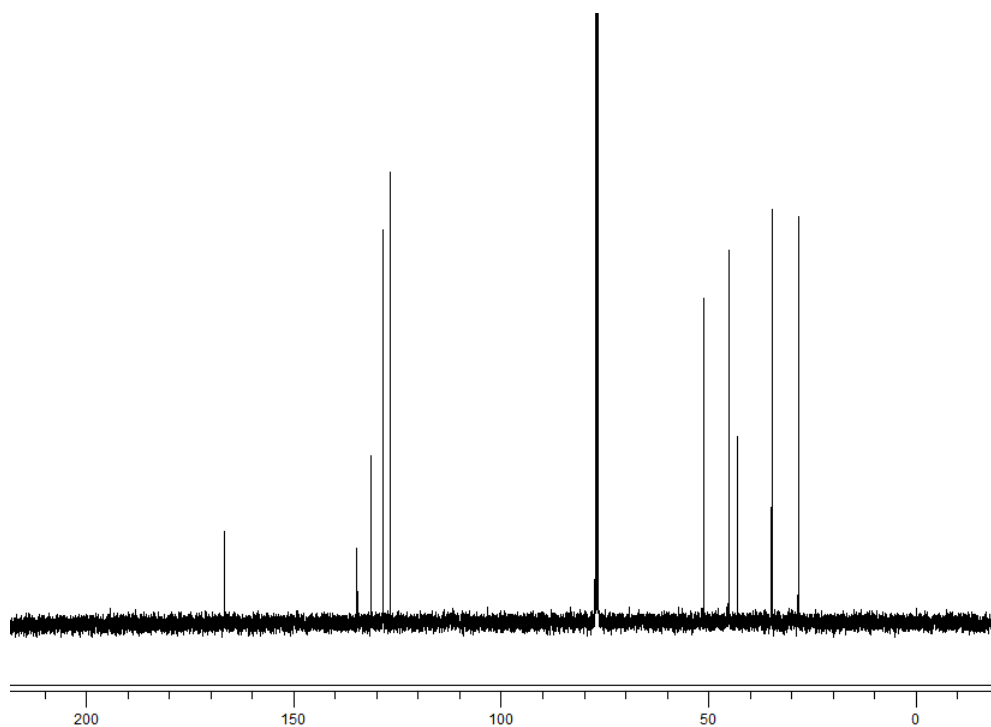
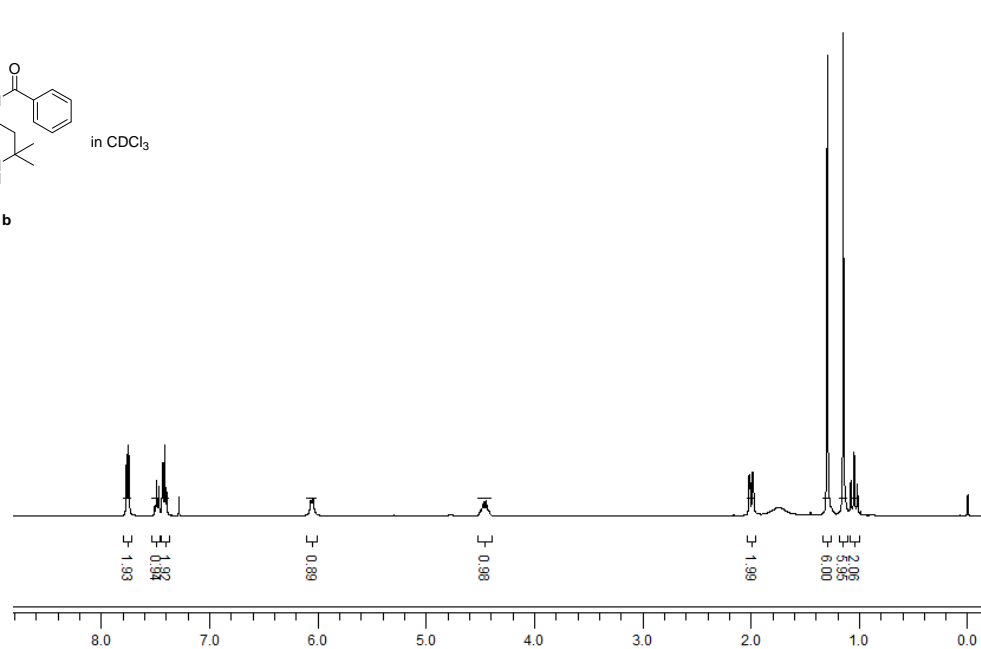
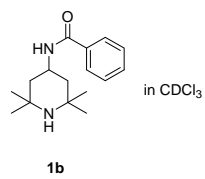
Resins **4c** (15 mg) from reaction mixtures (mushroom water extracts were used as formaldehyde source) were suspended in 1:1 trifluoroacetic acid and dichloroethane (300 μ L) at room temperature for 10 min for cleavage of propargylamine **5a** from the solid support. The solution was then neutralized by saturated NaHCO_3 solution (300 μ L). The upper aqueous layer was removed by dropper, and the remaining organic layer and resins were dried in oven at 75 $^\circ\text{C}$. Then, 1.3 mL of acetonitrile was added into the dried mixtures, and the solution was prepared for LC-MS/MS analysis. For LC-MS/MS analysis, the m/z of precursor ions were 529.4 ($[\text{M}+\text{H}]^+$) for propargylamine **5a** while the fragment ions (daughter ions) were 373.2.

The quantity of formaldehyde in water extract was calculated by correlating the peak area and the calibration curve built up (**Figure S8**).

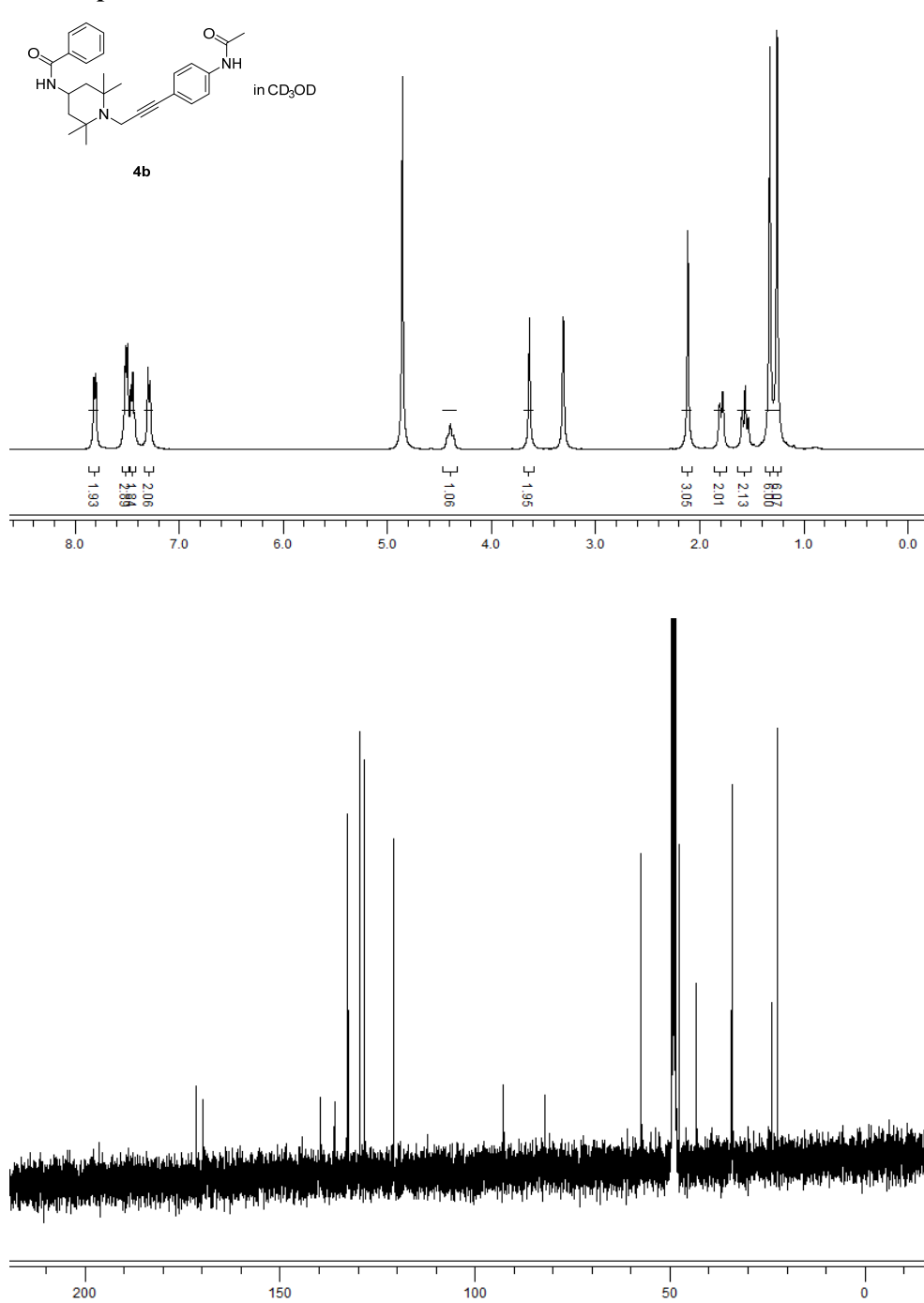
Table S10. Data for quantitative determination of formaldehyde in mushroom water extract

Sample	Peak area (arbitrary unit)	Formaldehyde concentration (ppm)
Mushroom sample 1	234000	36.0
	239000	37.2
Mushroom sample 2	218000	31.8
	219000	32.0

NMR Spectrum of 1b



NMR Spectrum of 4b



NMR Spectrum of 5a

