Supplementary Materials for

Sustainable production of value-added N-heterocycles from biomass-derived carbohydrates via spontaneous self-engineering

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General information

Materials. Glucose (99%), fructose (99%), mannose (99%), dihydroxyacetone (97%), pyruvaldehyde solution (32 wt% in H_2O), *ortho*-phenylenediamine (*o*-PDA, 98%), 4,5-dimethyl-*o*-phenylenediamine (98%), 4,5-difluoro-*o*-phenylenediamine (97%), 4-methyl-*o*-phenylenediamine (97%), 4-methoxy-*o*-phenylenediamine (97%), 4-chloro-*o*-phenylenediamine (97%) were purchased from Aladdin Chemical Reagent Co. Glyceraldehyde (93%), 4,5-dichloro-*o*-phenylenediamine (98%) were purchased from Alfa Aesar. Potassium carbonate (K_2CO_3), sodium carbonate (Na_2CO_3), potassium hydroxide (KOH), sodium hydroxide (NaOH), lithium hydroxide (LiOH), calcium hydroxide ($Ca(OH)_2$) were purchased from Sinopharm Chemical Reagent Co. Tin(IV) chloride ($SnCl_4$, 99%) was purchased from Sigma Aldrich. Commercial Beta zeolite (Si/Al~12.5) was obtained from Nankai University Catalyst Co., Ltd. All chemicals were used without further purification as received.

Reaction analysis. Reaction samples were analyzed by GC-MS, GC-FID, HPLC, LC-MS, and NMR. Upon the completion of the reaction, the reaction mixture was extracted by organic solvent. The resulted organic extract containing products was analyzed by GC-MS and GC-FID. The aqueous solution was analyzed by HPLC for determining and quantifying sugars and water-soluble sugar fragments. GC-MS analyses were performed with a Shimadzu GC-2010 plus system equipped with a GC-MS-QP2010S detector and DB-5MS column (30 m × 0.25 mm × 0.25 μm). GC-MS system used helium as the carrier. GC-FID analyses were performed with GC-9790 (FuLi) equipped with a FFAP column (30 m × 0.32 mm × 0.25 μm) and FID detector and quantitatively estimated by the combination of using naphthalene as an internal standard. The aqueous solution, after neutralization by diluted HCl solution and subsequent filtration, was analyzed by a Shimadzu HPLC (10AT) equipped with isocratic pump and refractive index (RI) detector on a Bio-Rad Aminex HPX-87H (300 × 6.5 mm), using an aqueous solution of sulfuric acid (5 mM) at a flow rate of 0.5 mL min^{-1} and a column temperature of 60 °C. Quantification of each compound was based on calibration curves obtained by analyzed standard solutions with known concentration.

ESI-MS were recorded with a positive ion mode or a negative mode on Agilent 6460 Triple Quadrupole Liquid Chromatography-Mass Spectrometer (LC-MS), which was equipped with an Agilent ZORBAX Eclipse XDB-C18 column (3.5 μm, 2.1 mm × 150 mm) and a Photo-Diode Array (PDA) detector. The mobile phase consisted of water and methanol with 1:1 volume ratio. The flow rate was 0.3 mL/min and the injection volume was 5 μL. The PDA detector was set 280 nm.

NMR spectra were recorded on a commercial instrument (Bruker Avance 400 MHz) and chemical shifts (δ) were reported in parts per million (ppm) referenced to the internal (NMR) solvent signal. For quantitative

^1H-NMR analysis, DMSO-d_6 was added as the deuterated NMR solvent and 1,4-dioxane (Aladdin, ≥99.9%) was added as the internal standard. For some reactions, the crude reaction mixture was directly submitted for NMR analysis (^1H NMR and ^{13}C NMR) to determine and quantify the products formed during the reaction.

Characterization of Sn-Beta: X-ray diffraction (XRD) data were collected on a Rigaku D/MAX 2550 diffractometer with Cu Kα (λ=1.5418 Å). The step size was 0.02°, and the scanning speed was 20°/min. Si/Al and Si/Sn ratios were determined by inductively coupled plasma (ICP) analysis (Perkin-Elmer 3300DV). Nitrogen sorption isotherms were measured using a Micromeritics ASAP2020 system. Transmission electronmicroscopy (TEM) and energy dispersive spectrometer (EDS) were performed on a JEM-2100F electron microscopy (JEOL, Japan) with an acceleration voltage of 200 kV. In the TEM and EDS characterizations, the sample was loaded on a Cu mesh with carbon film.

Product analysis based on GC

The moles of products *i* were calculated by the following equation

$$n_i = n_s \times \frac{A_i f_i}{A_s f_s}$$

Where n_i is the moles of product *i*, f_i is the response factor of product *i*, n_s is the moles of naphthalene added, A_i is the peak area of product *i*, A_s is the peak area of naphthalene, and f_s denotes the response factor of the internal standard naphthalene that is equal to unity.

The carbon balance for the sugar in the reaction was calculated from the ratio of moles of carbon in the unreacted sugar feedstock and products after the reaction to that of all sugar feedstock loaded.

Preparation of Deal-Beta and Sn-Beta

Deal-Beta and Sn-beta materials were synthesized according to reported procedures[1].

The commercial Al-Beta zeolite (Si/Al = 12.5) was performed by heating in 65% HNO_3 (50 mL/g) at 110 °C overnight for dealumination. The resulted solid residue was filtered and collected after thorough washing with demineralized water until the pH of the washings reached neutral. The collected materials are denoted as Deal-Beta.

Prior to modification with Sn, the dealuminated Beta zeolite was dried in vacuo at 170 °C for 3h in a Schlenk flask. Sn was incorporated by adding an excess of approximately three silanol nest equivalents of anhydrous $SnCl_4$ at 100 °C under an N_2 atmosphere and the mixtures were stirred overnight. To remove unreacted $SnCl_4$ from the zeolite pores, the materials were thoroughly washed with methanol at least six times and dried in air. To remove residual chloride and to complete the condensation of the Sn centers into the framework, the materials were recalcined at 550 °C (ramp rate 1 °C/min, 5h). The final Sn-modified catalysts are denoted as Sn-Beta.

Analysis of products after glucose reaction in the presence of different additives

The glucose degradation (shown in Fig.2A, fig. S6, and table S4) was conducted in H_2O at 180 °C under N_2 (2 MPa) for 5 h. 0.5 mmol glucose was employed in each reaction. In the cases of reactions with amine additive (for both aniline and *o*-PDA), the amount of amine was based on total amino groups of 4 mmol. In the reaction with an alkali, 0.15 mmol of KOH was used. After 5h reaction, the reactor was immediately transferred to ice bath for cooling down.

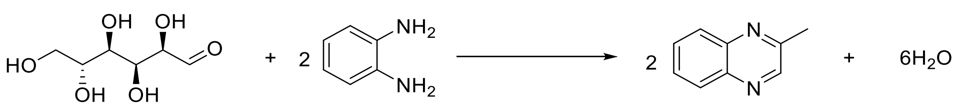
To have a better knowledge of the products formed during the reaction, organic solvent ethyl acetate (EA) was used to extract less polar products into organic layer upon the completion of the reaction. After cooling down the reactor, the resulted aqueous reaction mixture was then extracted by EA (3 × 10 mL). The organic layers were combined, dried and added with an appropriate amount of naphthalene as the internal standard, which was sampled and submitted for analysis by GC-FID. The aqueous layer was sampled, neutralized, syringe filtered with a 0.45 μm PTFE membrane and subjected to HPLC analysis. In the case of glucose reaction with aniline, the quantification estimation of generated product N^1,N^2-diphenylpropane-1,2-diimine (**DPPDI**) was based on using the same response factor of indole.

For the reaction with aniline, products including indole and **DPPDI** with respective 5.6% and 1.5% yields were detected in the extracted organic layer. In the aqueous layer, several common water-soluble products converted from glucose, which include fructose, HMF, GA, DHA and PA, were also detected in a low concentration (table S4). In the presence of aniline, the reaction mixture after reaction seemed muddy and black (fig. S6), implying a low efficiency in glucose carbon utilization. Most of carbons from converted glucose were difficult to be identified. By contrast, the addition of *o*-PDA significantly improved the carbon utilization, affording quinoxalines **1a**, **1b** and **1c**, as the main products, with 22.4%, 49.5% and 10.3% yields respectively. The water-soluble products observed in the above-mentioned reactions can be hardly detected in this aqueous layer, revealing a high carbon utilization for the glucose transformation in the presence of *o*-PDA. An extra addition of KOH to the reaction gave rise to an evident increase in **2b** yield (from 50% to 66%) at the expense of **1a** and **1c** yields.

Calculation of Gibbs free energy (ΔG) and enthalpy change (ΔH) of the reaction

We assessed the thermodynamics of glucose-to-quinoxalines reaction (Eq. 1). Thermodynamic values for converting glucose and *o*-PDA to product 1b in 1 atm N_2, estimated using Benson group contributions for 1b[2], are ΔH_1° = –268.1 kJ/mol and ΔG_1° = –350.2 kJ/mol at standard condition (25 °C). Based on the real reaction temperature (180 °C), the estimated values are ΔH_2 = –62.6 kJ/mol and ΔG_2 = –429.4 kJ/mol (see following calculation details). Thus, the reaction is indeed thermodynamically favored regardless of the reaction temperature employed.

Reaction scheme for the synthesis of 2-methylquinoxaline (**1b**):



Reaction equation:

$C_6H_{12}O_6 + 2C_6H_8N_2 \longrightarrow 2C_9H_8N_2 + 6H_2O$ (Eq.1)

For the reaction at the temperature of 25 °C and 1 atm N_2

$$\Delta H_1{}^{\circ} = \sum \nu \Delta_f\, H^{\circ}(products) - \sum \nu \Delta_f\, H^{\circ}(reactants)$$

$$= 6 \times \Delta_f H^{\circ}(H_2O, l) + 2 \times \Delta_f H^{\circ}(C_9H_8N_2, l) - \Delta_f H^{\circ}(C_6H_{12}O_6, s) - 2 \times \Delta_f H^{\circ}(C_9H_8N_2, s)$$

$$= 6 \times (-285.83) + 2 \times 125.7 - (-1273.7) - 2 \times 39.1$$

$$= -268.08 \text{ (kJ mol}^{-1}\text{)}$$

$$\Delta S_1{}^{\circ} = \sum \nu\, S^{\circ}(products) - \sum \nu\, S^{\circ}(reactants)$$

$$= 6 \times S^{\circ}(H_2O, l) + 2 \times S^{\circ}(C_9H_8N_2, l) - S^{\circ}(C_6H_{12}O_6, s) - 2 \times S^{\circ}(C_9H_8N_2, s)$$

$$= 6 \times 69.95 + 2 \times 224.25 - 288.3 - 2 \times 152.09$$

$$= 275.72 \text{ (J mol}^{-1}\text{K}^{-1}\text{)}$$

Based on the equation: $\Delta G = \Delta H - T\Delta S$

$\Delta G_1{}^{\circ}$ (T_1 = 298 K and 1 atm N_2) of the reaction for converting glucose and *o*-PDA to 2-methylquinoxaline can be calculated by the following equation:

$$\Delta G_1{}^{\circ} = \Delta H_1{}^{\circ} - T_1 \Delta S_1{}^{\circ}$$

$$= -268.08 - 298 \times 275.72 \div 1000$$

$$= -350.24 \text{ (kJ mol}^{-1}\text{)}$$

For the reaction with the temperature of 180 °C and 1 atm N_2

$$\Delta H_2{}^{\circ} = \sum \nu \Delta_f\, H^{\circ}(products) - \sum \nu \Delta_f\, H^{\circ}(reactants)$$

$$= 6 \times \Delta_f H^{\circ}(H_2O, g) + 2 \times \Delta_f H^{\circ}(C_9H_8N_2, l) - \Delta_f H^{\circ}(C_6H_{12}O_6, l) - 2 \times \Delta_f H^{\circ}(C_9H_8N_2, l)$$

$$= 6 \times (-241.83) + 2 \times 125.7 - (-1253.8) - 2 \times 62.2$$

$$= -70.18 \text{ (kJ mol}^{-1}\text{)}$$

$$\Delta S_2{}^{\circ} = \sum \nu\, S^{\circ}(products) - \sum \nu\, S^{\circ}(reactants)$$

$$= 6 \times S^{\circ}(H_2O, g) + 2 \times S^{\circ}(C_9H_8N_2, l) - S^{\circ}(C_6H_{12}O_6, l) - 2 \times S^{\circ}(C_9H_8N_2, l)$$

$$= 6 \times 188.84 + 2 \times 224.25 - 364.2 - 2 \times 214.09$$

$$= 789.16 \text{ (J mol}^{-1}\text{K}^{-1}\text{)}$$

Assume that the heat capacities (C_p) are constant over the temperature range involved.

$$\Delta C_p = \sum \nu\, C_p(products) - \sum \nu\, C_p(reactants)$$

$$= 6 \times C_p(H_2O, g) + 2 \times C_p(C_9H_8N_2, l) - C_p(C_6H_{12}O_6, l) - 2 \times C_p(C_9H_8N_2, l)$$

$$= 6 \times 35.22 + 2 \times 231.2 - 220.9 - 2 \times 201.82$$

$$= 49.18 \text{ (J mol}^{-1}\text{K}^{-1}\text{)}$$

Based on the equation: $\left(\frac{\partial(\Delta H)}{\partial T}\right)_p = \Delta C_p$

The following equations were obtained.

$$\Delta H(T_2) = \Delta H(T_1) + \int_{T_1}^{T_2} \Delta C_p dT$$

$$\downarrow$$

$$\Delta H(T_2) = \Delta H(T_1) + \Delta C_p(T_2 - T_1)$$

$$\downarrow$$

$$\Delta H_2 = \Delta H_2{}^{\circ} + \Delta C_p(T_2 - T_1)$$

$$= -70.18 + 49.18 \times (453 - 298) \div 1000$$

$$= -62.56 \text{ (kJ mol}^{-1}\text{)}$$

$$\Delta S(T_2) = \Delta S(T_1) + \int_{T_1}^{T_2} \frac{\Delta C_p}{T} dT$$

$$\downarrow$$

$$\Delta S_2 = \Delta S_2{}^{\circ} + \Delta C_p(\ln T_2 - \ln T_1)$$

$$= 789.16 + 49.18 \times (6.12 - 5.70)$$

$$= 809.82 \text{ (J mol}^{-1}\text{K}^{-1}\text{)}$$

Hence, ΔG_2 (T_2 = 453 K and 1 atm N_2) of the reaction for converting glucose and *o*-PDA to 2-methylquinoxaline can be calculated by the following equation:

$$\Delta G_2 = \Delta H_2 - T_2 \Delta S_2$$
$$= -62.56 - 453 \times 809.82 \div 1000$$
$$= -429.41 \text{ (kJ mol}^{-1}\text{)}$$

The thermodynamic data of the reactants and products with respect to enthalpy of formation ($\Delta_f H°$), entropy (S°) and constant pressure heat capacity (C_p) at standard conditions can be found in table S5.

Environmental factor (E-factor)

The E-factor of a process is the ratio of the mass of waste per mass of product.[3] For our studied reaction of converting glucose and *o*-PDA to quinoxalines, the calculation of E-factor was based on the following equation. Note that H_2O was not regarded as the waste in the calculation[3].

$$\text{E-Factor} = \frac{mass\ of\ total\ waste}{mass\ of\ product}$$

$$= \frac{mass_{converted\ sugar} + mass_{converted\ diamine} - mass_{all\ quinoxalines} - mass_{water\ produced\ in\ the\ reaction}}{mass_{all\ quinoxalines}}$$

Specifically, the calculation of E-factor was based on the reaction with glucose of 0.4 g scale. The reaction conditions were as follows: Glucose (0.4 g, 2.22 mmol), *o*-PDA (0.96 g, 8.89 mmol), H_2O (89 mL), N_2 (2 MPa), temperature (180 °C), 5 h. After reaction, glucose was found to be completely converted. Products of quinoxalines, including **1a**, **1b** and **1c**, were provided with mass of 172 mg, 329 mg and 59 mg respectively. The generation of H_2O was accompanied with the formation of quinoxalines and the production of one mole of quinoxalines led to the formation of two moles of H_2O according to the reaction Eq. 1. Hence, the amount of H_2O generated during the reaction was evaluated to be 7.7 mmol (139 mg) based on the total amounts of quinoxalines obtained after the reaction. Total 467 mg of *o*-PDA, including 425 mg of *o*-PDA from the organic phase and 42 mg of *o*-PDA from the aqueous phase, was recycled from the reaction mixture after the reaction. The value of mass amount of *o*-PDA (425 mg) in the organic layer was obtained by isolating *o*-PDA from the product mixture by column chromatography on silica gel eluting with methanol–EA (1:1). The value of mass amount of *o*-PDA (42 mg) in the aqueous phase was evaluated by ^{1}H NMR by using 1,4-dioxane as the internal standard, as shown in the fig. S18.

If reactant (*o*-PDA) recycling is not considered for E-factor calculation, an E-factor value of 1.2 for the reaction will be obtained. If the recycling of *o*-PDA is incorporated in the calculation, a much lower value of 0.4 will be obtained.

Even after 5 recycling reactions with KOH additive, the E-factor based on the combined produced quinoxalines and total reactants used in total runs of batch reactions can be still maintained around 0.7. Although the above-mentioned E-factor calculation is based on small lab scale, the encouraging results presented here may hint a great potential of this proposed reaction for the production of quinoxalines in an economic and environmental benign way.

Synthesis of various quinoxalines

<u>The reaction of glucose with *o*-PDA</u>

90 mg (0.5 mmol) of glucose, 216 mg (2 mmol) of *o*-PDA and 20 mL of H_2O were loaded into an autoclave reactor with a magnetic stir bar. The reactor was purged with N_2 for three times to remove the air and charged with 2 MPa of N_2. The autoclave reactor was heated to 180 °C by submerging it in a pre-heated stirred temperature-controlled oil bath. The reaction was conducted at the temperature of 180 °C for 5 h while stirring. After the reaction, the reactor was removed from the heating and rapidly cooled down in an ice bath. The reaction mixture was then extracted by ethyl acetate (3 × 15 mL), the extracted organic layers were combined and dried over Na_2SO_4, filtered, concentrated, and purified by column chromatography on silica gel eluting with petroleum ether – ethyl acetate (from 10:1 to 4:1) to afford 9 mg of 2,3-dimethylquinoxaline **1c** (8%) as a white solid, 66 mg of 2-methylquinoxaline **1b** (46%) as a dark-red liquid and 29 mg of quinoxaline **1a** (15%) as a colorless oil. Analytical NMR data for **1a**: ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 7.84 (m, 2H), 8.08–8.10 (m, 2H), 8.95 (s, 2H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 129.17, 130.23, 142.26, 145.75. For **1b**: ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.69 (s, 3H), 7.74–7.82 (m, 2H), 7.98 (d, J = 8.0 Hz, 1H), 8.03 (d, J = 8.0 Hz, 1H), 8.84 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 22.14, 128.41, 128.86, 129.02, 130.06, 140.33, 141.41, 146.62, 154.27. For **1c**: ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.73 (s, 6H), 7.64–7.67 (m, 2H), 7.96–7.98 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.36, 128.43, 128.98, 141.19, 153.63.

<u>The reaction of glucose with *o*-PDA in the presence of KOH</u>

The procedure for glucose reaction with *o*-PDA in a low concentration of KOH is the same as the above-mentioned reaction procedure except an addition of 9.8 mg of KOH (8.8×10^{-2} mmol). The purification of the product by column chromatography on silica gel eluting with petroleum ether – ethyl acetate (from 10:1 to 4:1) to afford 92 mg of 2-methylquinoxaline **1b** (64%) as the dark-red liquid.

The reaction of glucose with 4,5-dimethyl-*o*-phenylenediamine in the presence of KOH

272 mg (2 mmol) of 4,5-dimethyl-*o*-phenylenediamine, 90 mg (0.5 mmol) of glucose, 9.8 mg of KOH (0.176 mmol) and 20 mL of H_2O were loaded into an autoclave reactor. The reaction procedure follows the same one as described above for "*The reaction of glucose with o-PDA*". The purification of the product by column chromatography on silica gel eluting with petroleum ether – ethyl acetate (from 10:1 to 5:1) to afford 121 mg of 2,6,7-trimethylquinoxaline **2b** (70%) as a brown solid. Analytical NMR data for **2b**: ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.39 (s, 6H), 2.63 (s, 3H), 7.69 (s, 1H), 7.75 (s, 1H), 8.68 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 19.65, 19.80, 21.97, 127.34, 127.75, 138.94, 139.27, 140.08, 140.33, 145.37, 152.97.

The reaction of glucose with 4,5-difluoro-*o*-phenylenediamine in the presence of K_2CO_3

288 mg (2 mmol) of 4,5-difluoro-*o*-phenylenediamine, 90 mg (0.5 mmol) of glucose, 24 mg of K_2CO_3 (0.176 mmol) and 20 mL of H_2O were loaded into an autoclave reactor. The reaction procedure follows the same one as described above for "*The reaction of glucose with o-PDA*". The purification of the product by column chromatography on silica gel eluting with petroleum ether – ethyl acetate (from 10:1 to 2:1) to afford 104 mg of 6,7-difluoro-2-methylquinoxaline **3b** (58%) as a purple brown solid. Analytical NMR data for **3b**: ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.64 (s, 3H), 7.88–8.00 (m, 2H), 8.79 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 21.93, 114.26, 114.28, 114.43, 114.45, 114.71. 114.73, 114.88, 114.90, 137.42, 137.53, 138.69, 138.81, 146.77, 146.80, 149.17, 149.33, 149.84, 150.00, 151.67, 151.83, 152.35, 152.51, 154.68, 154.71.

The reaction of glucose with 4,5-dichloro-*o*-phenylenediamine in the presence of KOH

354 mg (2 mmol) of 4,5-dichloro-*o*-phenylenediamine, 90 mg (0.5 mmol) of glucose, 9.8 mg of KOH (0.176 mmol) and 20 mL of H_2O were loaded into an autoclave reactor. The reaction procedure follows the same one as described above for "*The reaction of glucose with o-PDA*". The purification of the product by column chromatography on silica gel eluting with petroleum ether – ethyl acetate (from 10:1 to 2:1) to afford 100 mg of 6,7-dichloro-2-methylquinoxaline **4b** (47%) as a reddish-brown solid. Analytical NMR

data for **4b**: ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.71 (s, 3H), 8.28 (s, 1H), 8.34 (s, 1H), 8.90 (s, 1H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 22.23, 129.33, 129.77, 131.63, 132.71, 139.24, 140.35, 148.13, 156.06.

<u>The reaction of glucose with 4-methyl-*o*-phenylenediamine in the presence of KOH</u>

244 mg (2 mmol) of 4-methyl-*o*-phenylenediamine, 90 mg (0.5 mmol) of glucose, 9.8 mg of KOH (0.176 mmol) and 20 mL of H_2O were loaded into an autoclave reactor. The reaction procedure follows the same one as described above for "*The reaction of glucose with o-PDA*". The purification of the product by column chromatography on silica gel eluting with petroleum ether – ethyl acetate (from 10:1 to 3:1) to afford 105 mg of the mixture of 2,6-dimethylquinoxaline and 2,7-dimethylquinoxaline (**5b**, 66%) with a ratio of 1:1.2 as a yellow cream[4]. Analytical NMR data for **5b**: ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.50 (s, 3H), 2.65 (s, 3H), 7.54–7.60 (m, 1H), 7.72 (s, 0.55H), 7.78 (s, 0.45H), 7.83–7.90 (m, 1H), 8.73 (s, 0.55H), 8.76 (s, 0.45H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 21.10, 21.25, 21.94, 22.07, 127.19, 127.62, 127.93, 128.37, 130.99, 132.03, 138.79, 138.88, 139.83, 140.02, 140.38, 141.48, 145.52, 146.32, 153.13, 153.98.

<u>The reaction of glucose with 4-methoxy-*o*-phenylenediamine in the presence of KOH</u>

276 mg (2 mmol) of 4-methoxy-*o*-phenylenediamine, 90 mg (0.5 mmol) of glucose, 9.8 mg of KOH (0.176 mmol) and 20 mL of H_2O were loaded into an autoclave reactor. The reaction procedure follows the same one as described above for "*The reaction of glucose with o-PDA*". The purification of the product by column chromatography on silica gel eluting with petroleum ether – ethyl acetate (from 10:1 to 3:1) to afford 124 mg of the mixture of 6-methoxy-2-methylquinoxaline and 7-methoxy-2-methylquinoxaline **6b** (71%) with a ratio of 1:3.5 as a dark brown cream[5]. Analytical NMR data for **6b**: ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.61 (s, 0.61H), 2.63 (s, 2.35H), 3.90 (s, 3H), 7.31–7.41 (m, 2H), 7.84 (d, J = 8.8 Hz, 0.20H), 7.88 (d, J = 8.8 Hz, 0.77H), 8.63 (s, 0.72H), 8.72 (s, 0.20H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 21.68, 21.98, 55.72, 55.74, 106.51, 106.85, 121.42, 122.46, 129.37, 129.83, 136.28, 137.32, 141.83, 143.09, 143.62, 146.23, 151.27, 154.02, 159.38, 160.20.

<u>The reaction of glucose with 4-chloro-*o*-phenylenediamine in the presence of KOH</u>

285 mg (2 mmol) of 4-chloro-*o*-phenylenediamine, 90 mg (0.5 mmol) of glucose, 9.8 mg of KOH (0.176 mmol) and 20 mL of H_2O were loaded into an autoclave reactor. The reaction procedure follows the same one as described above for "*The reaction of glucose with o-PDA*". The purification of the product by column chromatography on silica gel eluting with petroleum ether – ethyl acetate (from 10:1 to 3:1) to

afford 108 mg of the mixture of 6-chloro-2-methylquinoxaline and 7-chloro-2-methylquinoxaline **7b** (60%) with a ratio of 1:1.5 as a earth brown solid[5]. Analytical NMR data for **7b**: ^{1}H NMR (400 MHz, DMSO-d$_6$): δ 2.67–2.68 (3H), 7.72–7.79 (m, 1H), 7.94–8.05 (m, 2H), 8.83 (s, 0.58H), 8.84(s, 0.39H). ^{13}C NMR (100 MHz, DMSO-d$_6$): δ 22.16, 127.12, 127.54, 129.55, 130.21, 130.53, 130.65, 133.20, 134.31, 138.91, 139.99, 140.57, 141.71, 147.01, 147.60, 154.81, 155.48.

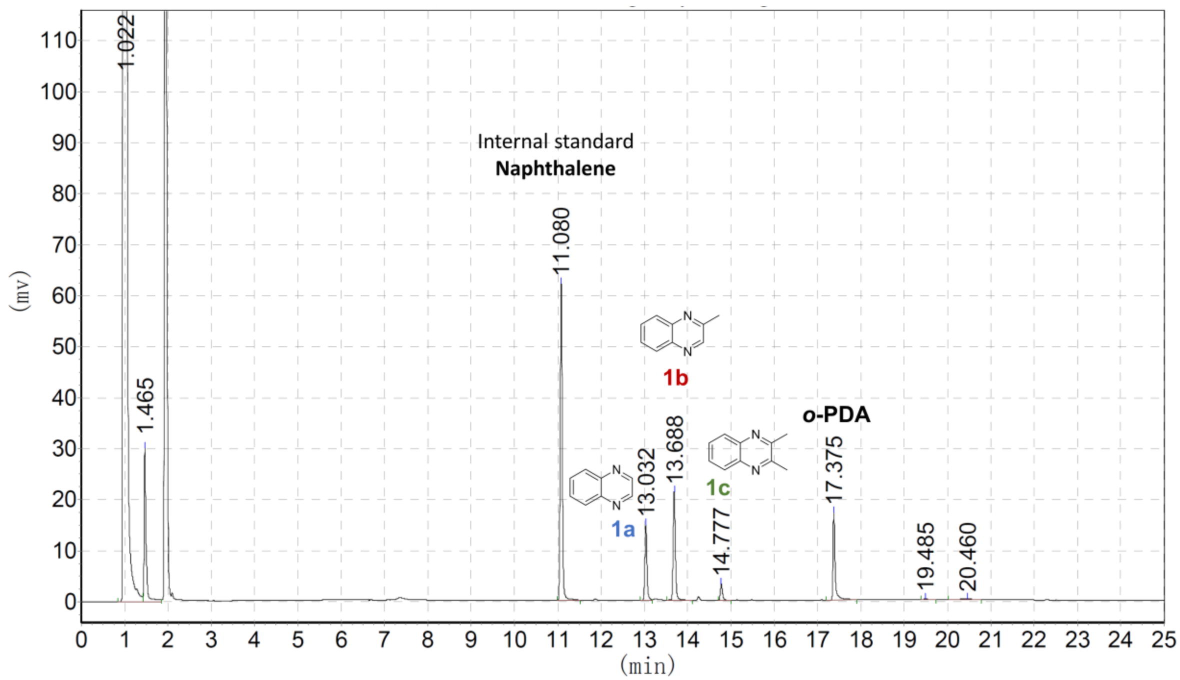


Fig. S1. Representative GC-FID spectrum of the reaction products from the glucose reaction with *o*-PDA in H_2O in the absence of base. Reaction condition: Glucose (0.5 mmol), *o*-PDA (2 mmol), H_2O (20 mL), N_2 (2 MPa), 5 h. After reaction, ethyl acetate (3 $\times$ 10 mL) was added into the aqueous mixture for extracting organic solvent-soluble products, including all produced quinoxalines. Naphthalene (~80 mg) as the GC internal standard was added into the combined organic layers. A portion of the resulted organic solution was taken and submitted for GC-FID analysis.

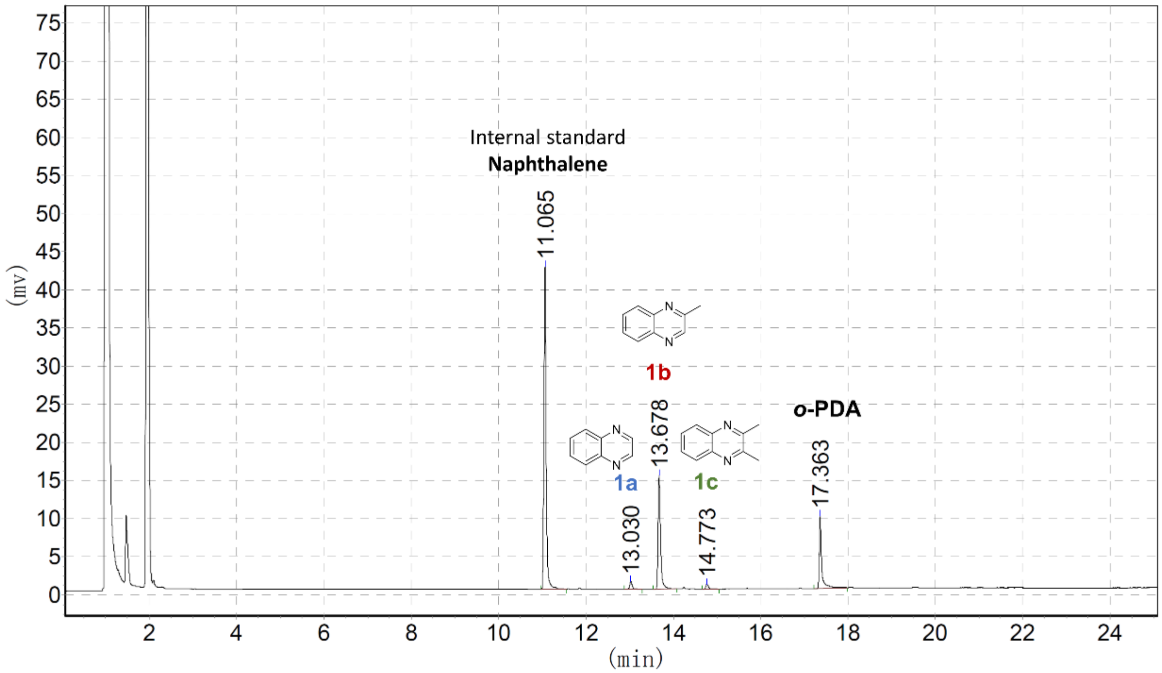


Fig. S2. Representative GC-FID spectrum of the reaction products from the glucose reaction with *o*-PDA in H_2O in the presence of an alkali. Reaction condition: Glucose (0.5 mmol), *o*-PDA (2 mmol), KOH (0.15 mmol), H_2O (20 mL), N_2 (2 MPa), 5 h. After reaction, ethyl acetate (3 × 10 mL) was added into the aqueous mixture for extracting organic solvent-soluble products, including all produced quinoxalines. Naphthalene (~100 mg) as the GC internal standard was added into the combined organic layers. A portion of the resulted organic solution was taken and submitted for GC-FID analysis.

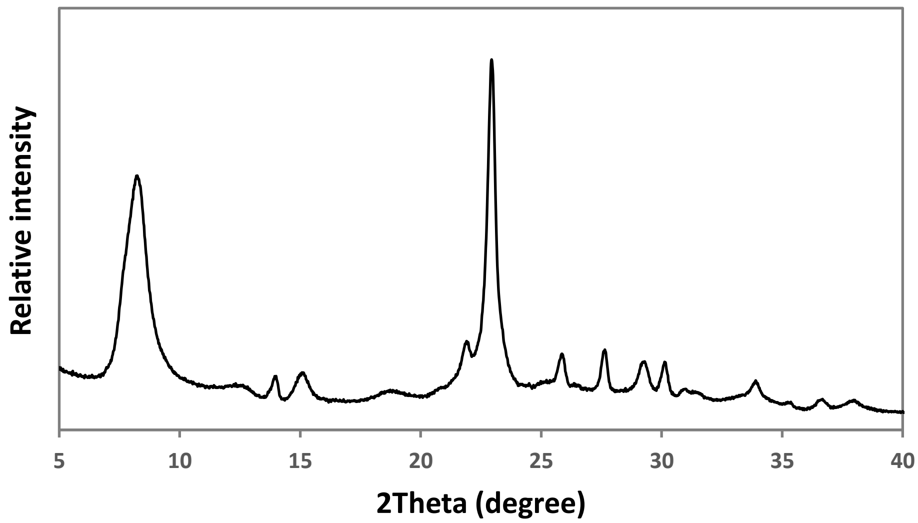


Fig. S3. X-ray diffraction pattern of the prepared Sn-Beta.

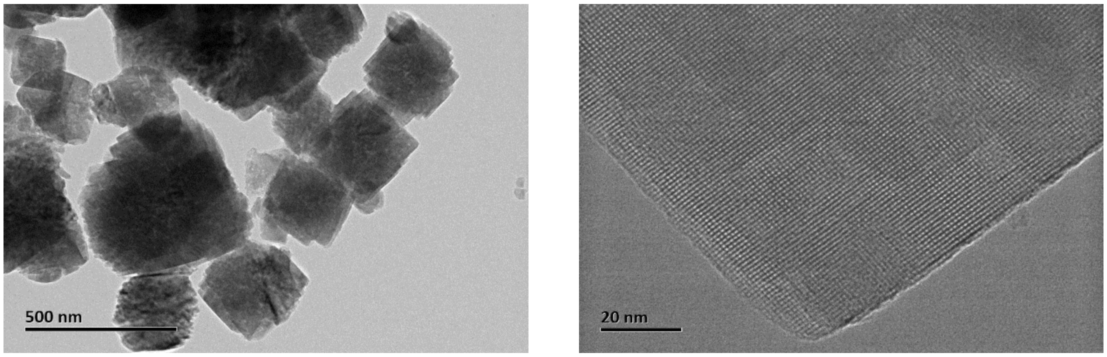


Fig. S4. TEM images of the prepared Sn-Beta in different scale.

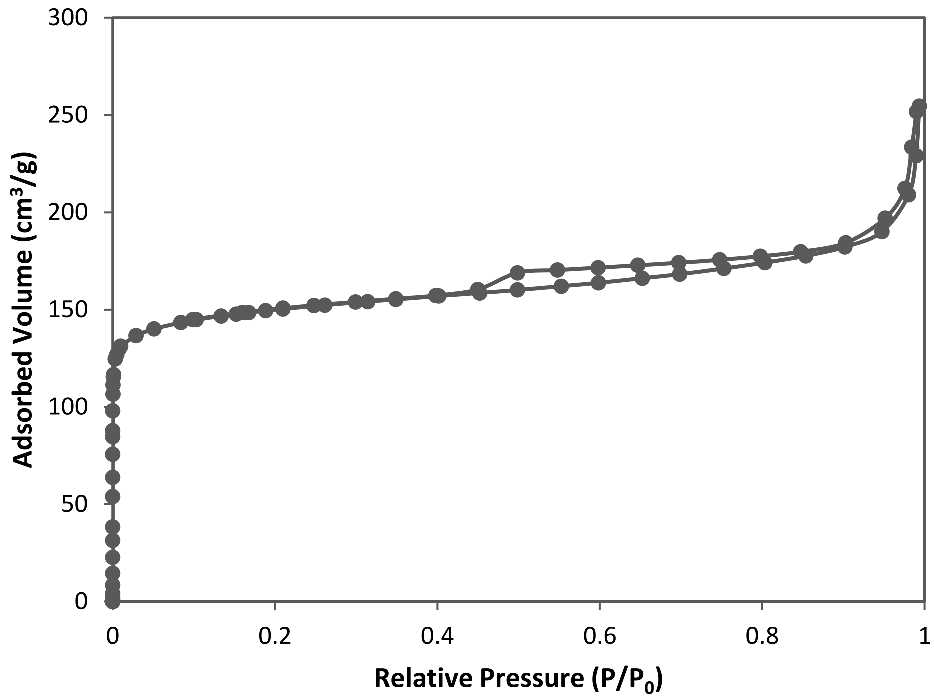


Fig. S5. N_2 sorption isotherms of Sn-Beta. The curve of Sn-Beta presented here is different from the typical I-type N_2-sorption curves due to the presence of mesoporous structures in the microporous Beta zeolite. The formation of additional mesopores in Beta zeolite is resulted from the dealumination operation in concentrated nitric acid, which have been demonstrated in the previous reports[6,7].

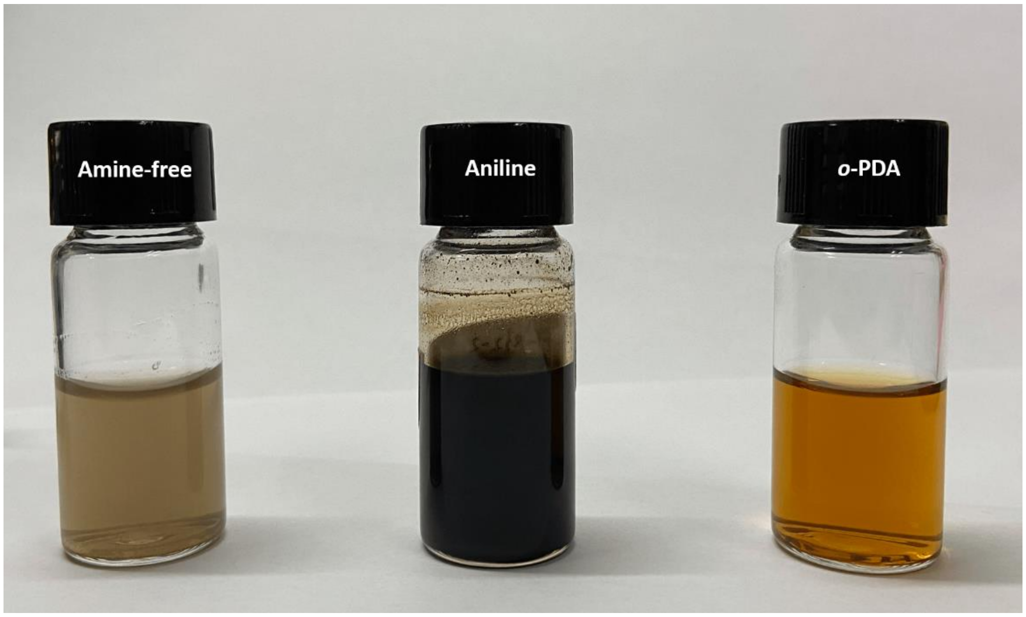


Fig. S6. The comparison of the reaction mixtures after 5 h reaction at 180 °C with different amine additives. The bottle in the left is the resulted mixture from the reaction without amine addition, the bottle in the middle is the resulted mixture from the reaction with the addition of aniline by ethyl acetate extraction, and the bottle in the right is the resulted mixture from the reaction with the addition of *o*-PDA by ethyl acetate extraction.

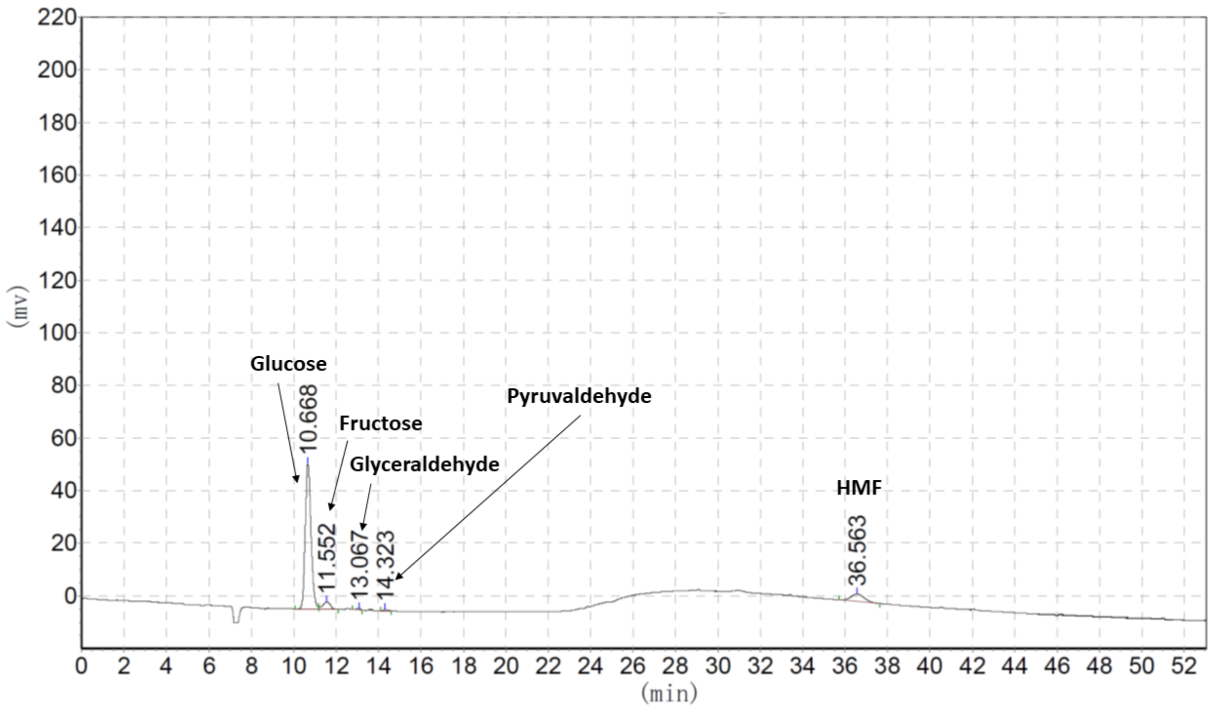


Fig. S7. HPLC spectrum of reaction products from the glucose reaction in H_2O without amine addition. Reaction condition: Glucose (0.5 mmol), H_2O (20 mL), N_2 (2 MPa), temperature (180 °C), 5 h. After 5 h reaction, the reactor was transferred into ice bath for cooling down. The aqueous reaction mixture was first extracted by ethyl acetate (3 × 10 mL) for collecting organic solvent-soluble products into organic phase for GC analysis. The remaining aqueous phase was neutralized, sampled, filtered by a syringe equipped with a 0.45 μm PTFE membrane and then subjected to HPLC analysis. In this spectrum, there were a portion of glucose unconverted and a little amount of fructose. Several other products from glucose degradation, such as GCA, PA, and HMF, were also observed.

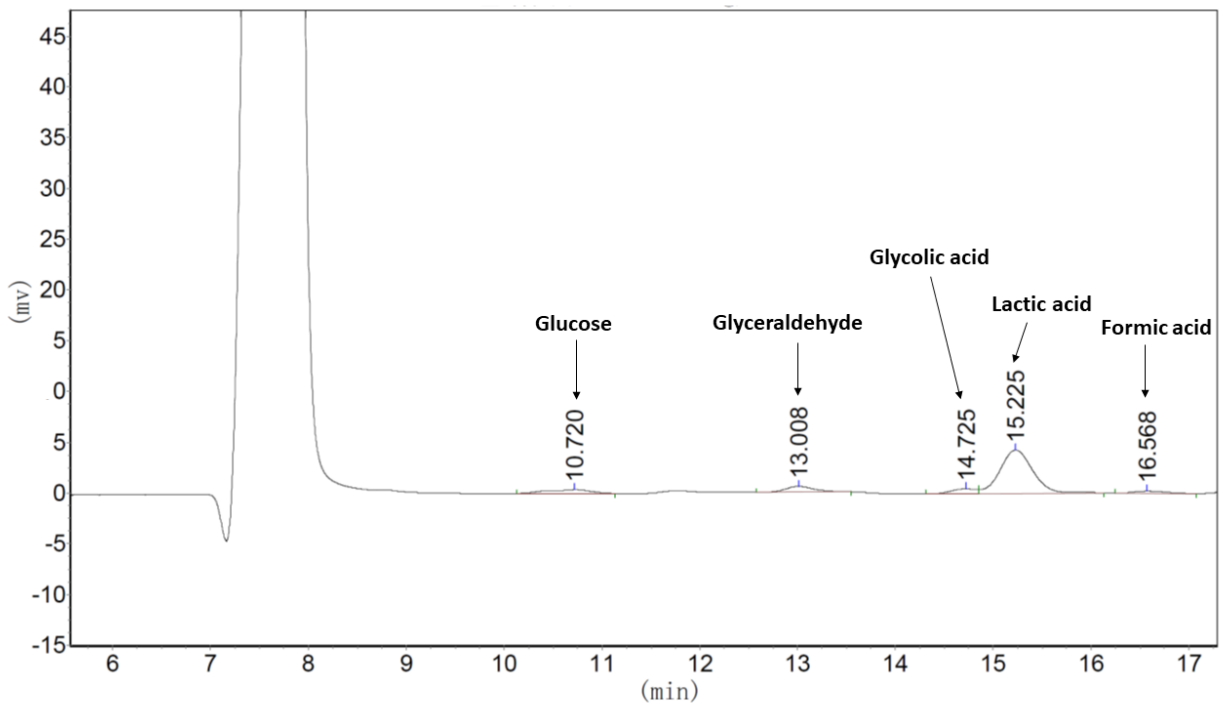


Fig. S8. Representative HPLC spectrum of the reaction products from the glucose reaction with *o*-PDA in H_2O in presence of an alkali. Reaction condition: Glucose (0.5 mmol), *o*-PDA (2 mmol), KOH (0.15 mmol), H_2O (20 mL), N_2 (2 MPa), temperature (180 °C), 5 h. After 5 h reaction, the reactor was transferred into ice bath for cooling down. The aqueous reaction mixture was first extracted by ethyl acetate (3 × 10 mL) for collecting organic solvent-soluble products into organic phase for GC analysis. The remaining aqueous phase was neutralized, sampled, filtered by a syringe equipped with a 0.45 μm PTFE membrane and then subjected to HPLC analysis.

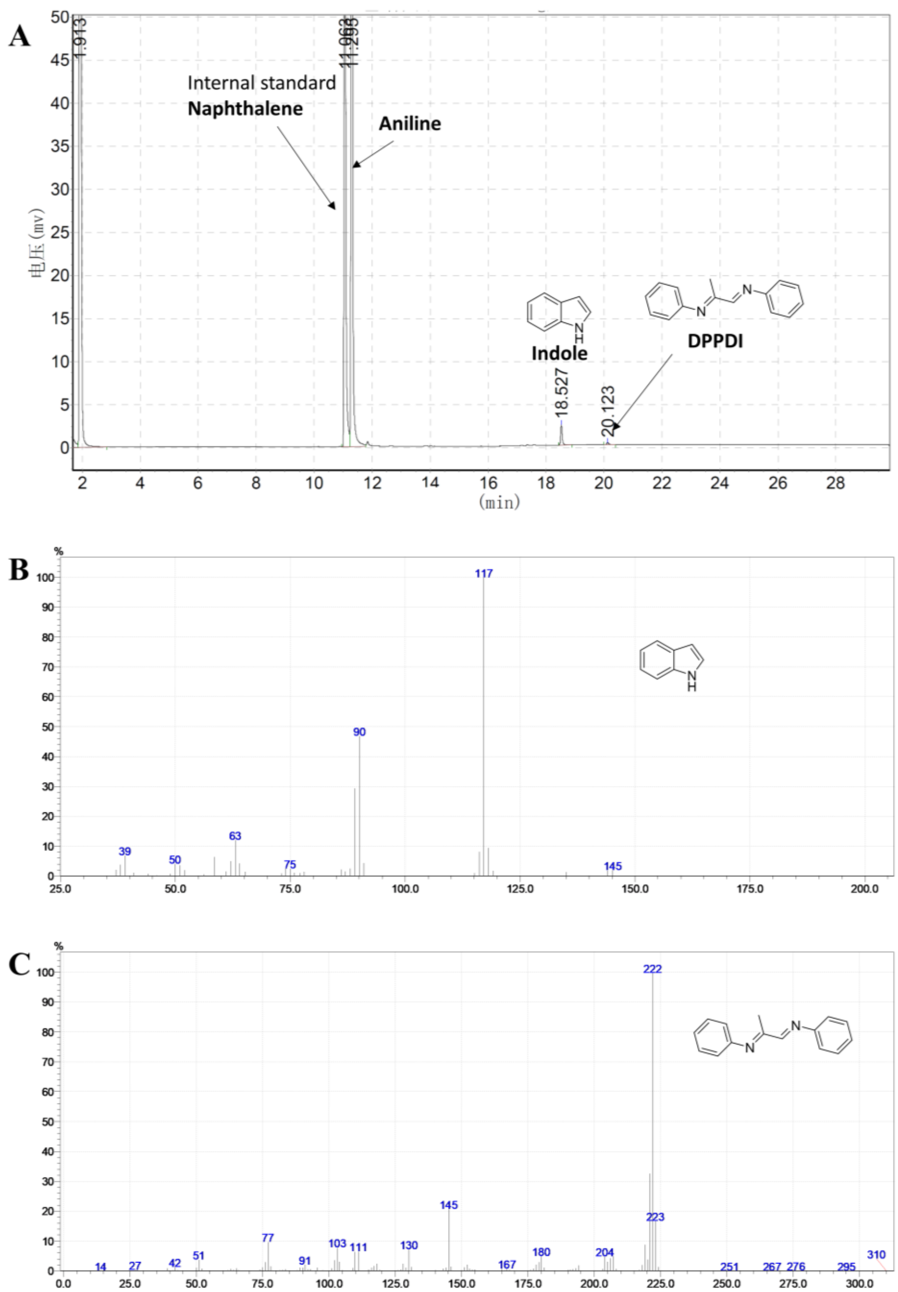


Fig. S9. GC-FID (**A**) and GC-MS analyses (**B** and **C**) of indole and **DPPDI** products in the organic layer for the reaction of glucose with aniline in H_2O. Reaction conditions: Glucose (0.5 mmol), aniline (4 mmol), H_2O (20 mL), 180 °C, N_2 (2 MPa), 5 h. After the reaction, the aqueous reaction mixture was extracted by ethyl acetate (3 × 10 mL). The extracted organic layers were then combined and submitted for GC-FID and GC-MS analyses.

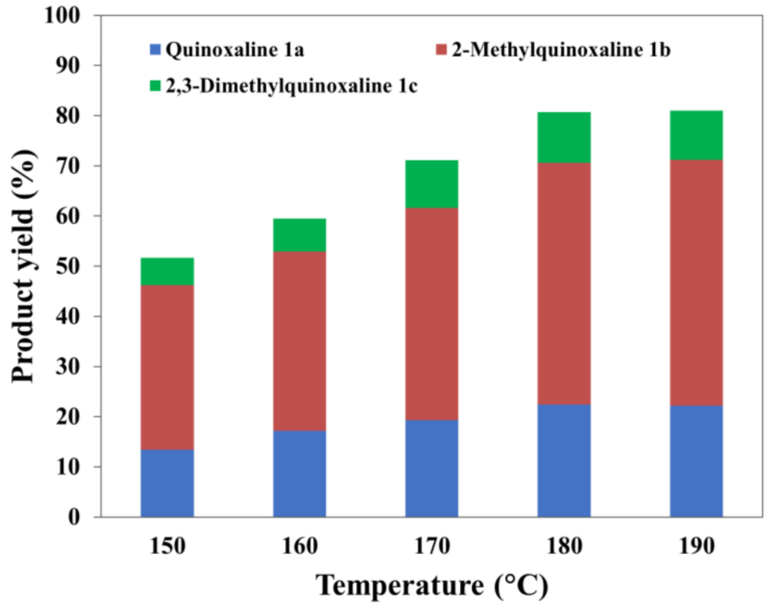


Fig. S10. Temperature effect on the aminolysis of glucose with *o*-PDA for the production of quinoxalines in H_2O under N_2. Reaction condition: Glucose (0.5 mmol), *o*-PDA (2 mmol), H_2O (20 mL), N_2 (2 MPa), and 5 h.

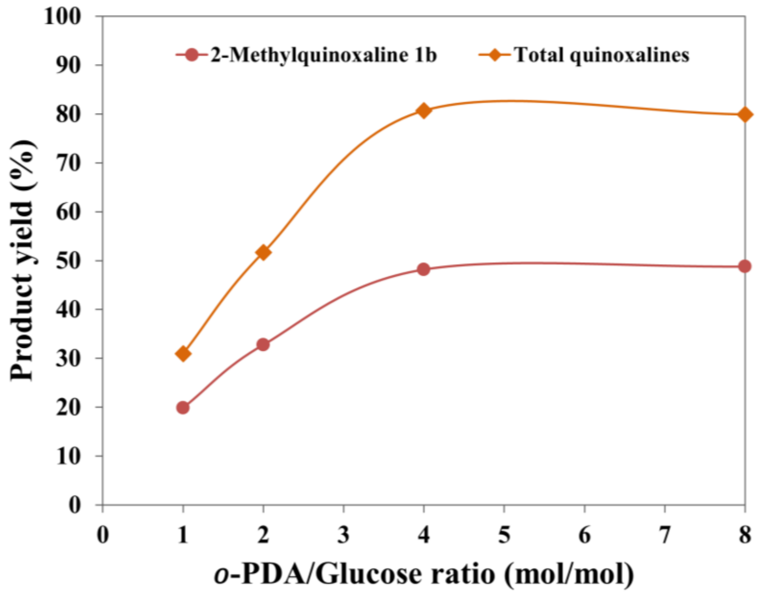


Fig. S11. Study of *o*-PDA/Glucose ratio effect on the aminolysis of glucose with *o*-PDA for the production of 2-methylquinoxaline and total quinoxalines in H_2O at 180 °C under N_2. Reaction condition: Glucose (0.5 mmol), H_2O (20 mL), N_2 (2 MPa), and 5 h.

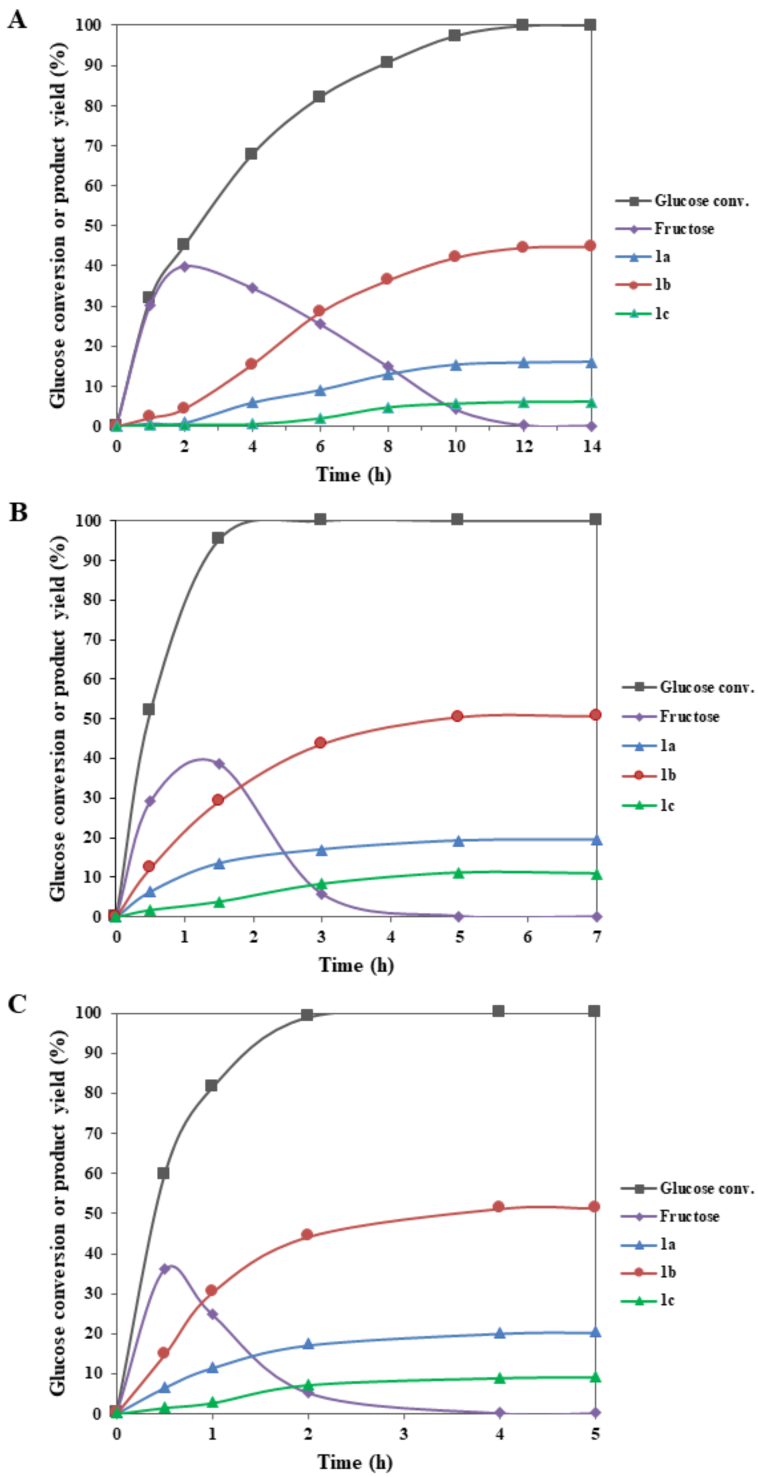


Fig. S12. The progress of the reaction as a function of time in glucose transformation in H_2O in the presence of *o*-PDA at different temperature. (A) 140 °C; (B) 180 °C; (C) 190 °C. Reaction condition: Glucose (0.5 mmol), *o*-PDA (2 mmol), H_2O (20 mL), N_2 (2 MPa).

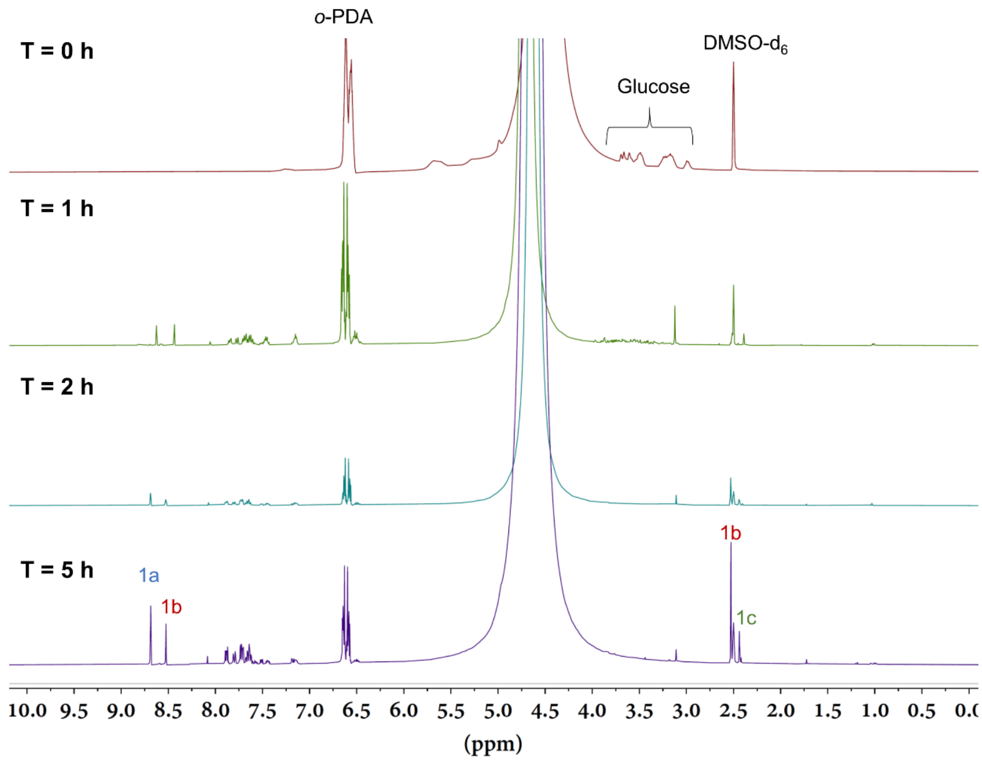


Fig. S13. ^{1}H NMR full spectra of the crude aqueous reaction mixture from the reaction of glucose with *o*-PDA in H_2O at different reaction time. Reaction conditions: Glucose (0.5 mmol), *o*-PDA (2 mmol), H_2O (20 mL), N_2 (2 MPa), 5 h. DMSO-d_6 was used as the deuterated solvent for the NMR measurements.

Note: Before the reaction (T = 0 h), peaks between 2.8 and 3.7 ppm, ascribed to typical C–H groups of glucose, and the characteristic peaks of *o*-PDA at around 6.6 ppm can be observed in the ^{1}H NMR spectrum of the reaction mixture. After 1 h reaction, the peaks at 7.71–7.74, 7.87–7.89, 8.69 ppm and 2.53, 7.62–7.66, 7.79, 7.81, 8.52 ppm, belonging to **1a** and **1b** respectively, started to show up and glucose peaks attenuated substantially. When the reaction time was increased to 2 h, the peaks including at 2.44, 7.49–7.52 and 7.70–7.71 ppm, which are attributed to **1c**, were clearly observed. Further prolonging the reaction time to 5 h, the glucose peaks disappeared while the peaks of all quinoxalines increased significantly in intensity, revealing the full conversion of glucose and quinoxalines **1a-c** are the main products of the reaction. In the reaction with KOH, only characteristic peaks of **1b** were shown as the main product in the ^{1}H NMR spectrum, indicating the high percentage of **1b** in total quinoxalines in presence of an alkali (fig. S16). The same reaction evolution was also observed in the ^{13}C NMR spectra (fig. S14).

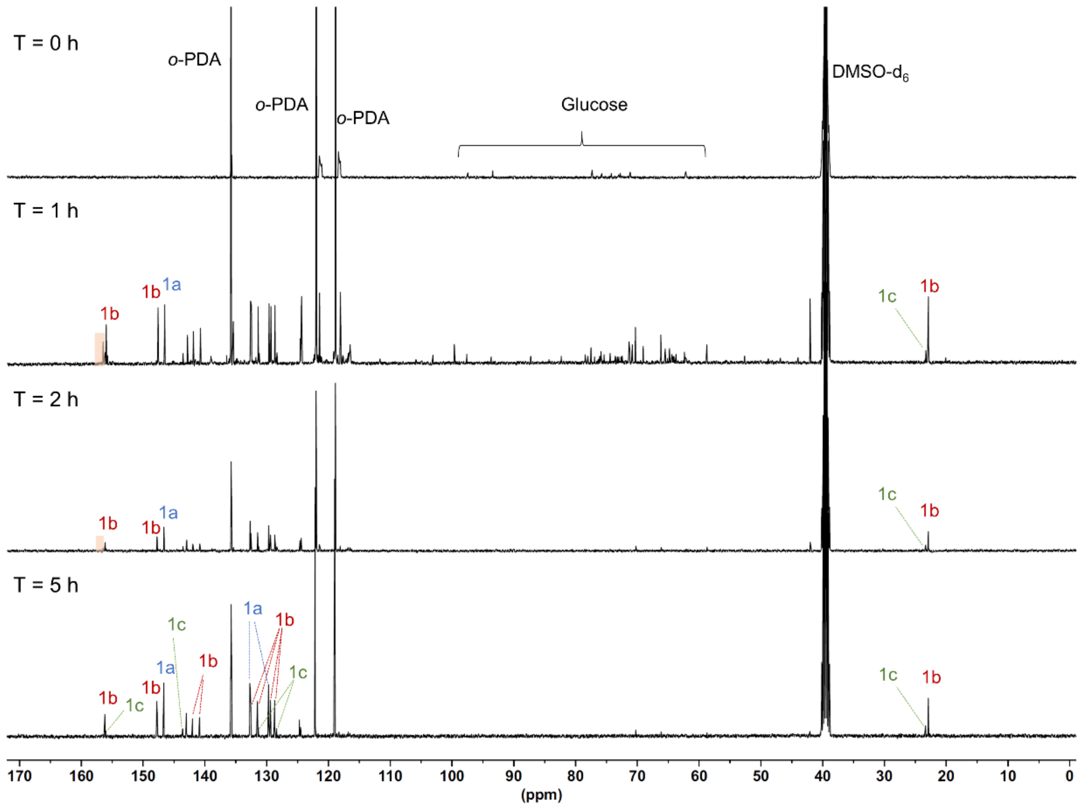
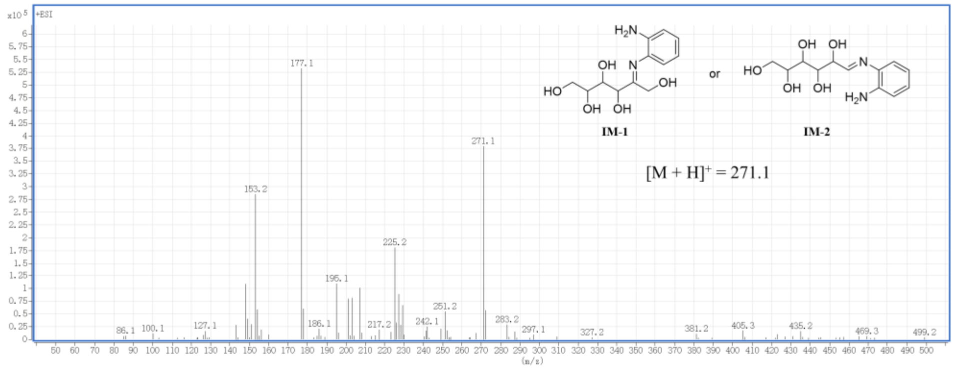
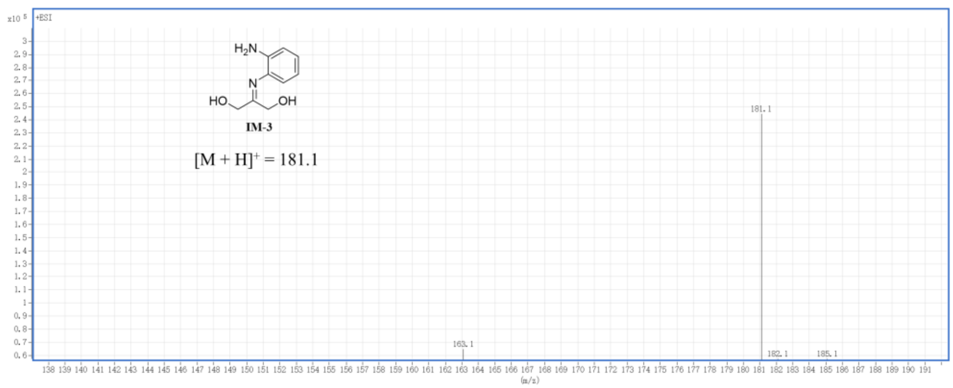
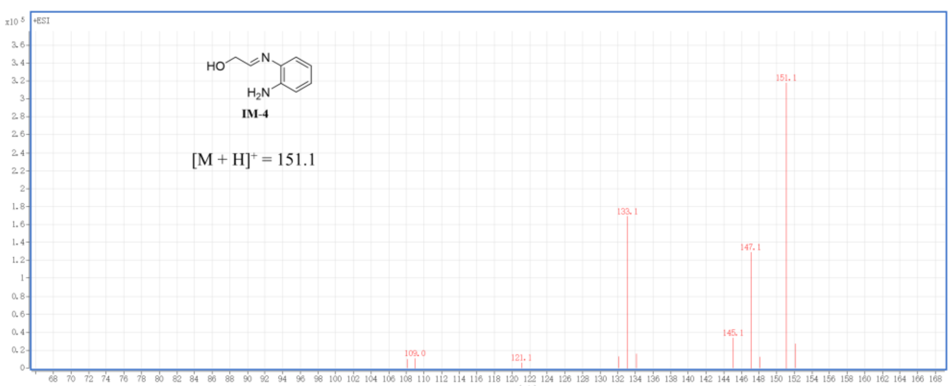


Fig. S14. ^{13}C NMR full spectra of the crude reaction mixture from the reaction of glucose with *o*-PDA in H_2O at different reaction time. Reaction conditions: Glucose (0.5 mmol), *o*-PDA (2 mmol), H_2O (20 mL), N_2 (2 MPa), and 5 h. DMSO-d$_6$ was used as the deuterated solvent for the NMR measurements.







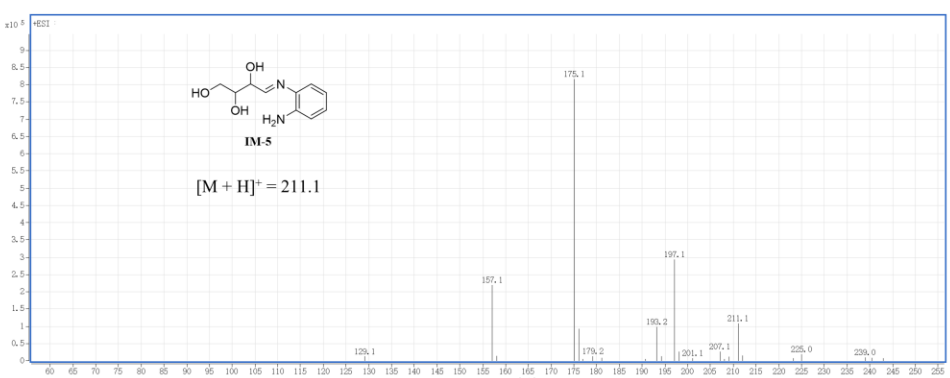


Fig. S15. ESI-MS spectra from LC-MS study for the reaction of glucose with *o*-PDA into quinoxalines. The mass spectra were recorded in a positive mode.

Note: Reaction conditions are as follows: Glucose (0.5 mmol), *o*-PDA (2 mmol), KOH (0.15 mmol), H_2O (20 mL), N_2 (2 MPa), temperature (180 °C). After 1 h's reaction, an aliquot of the aqueous reaction mixture was taken and diluted it by 10 times through adding an appropriate amount of H_2O. After stirring for 5 mins, the resulted diluted solution was sampled, syringe filtered with a 0.45 μm PTFE membrane and subjected to LC-MS analysis.

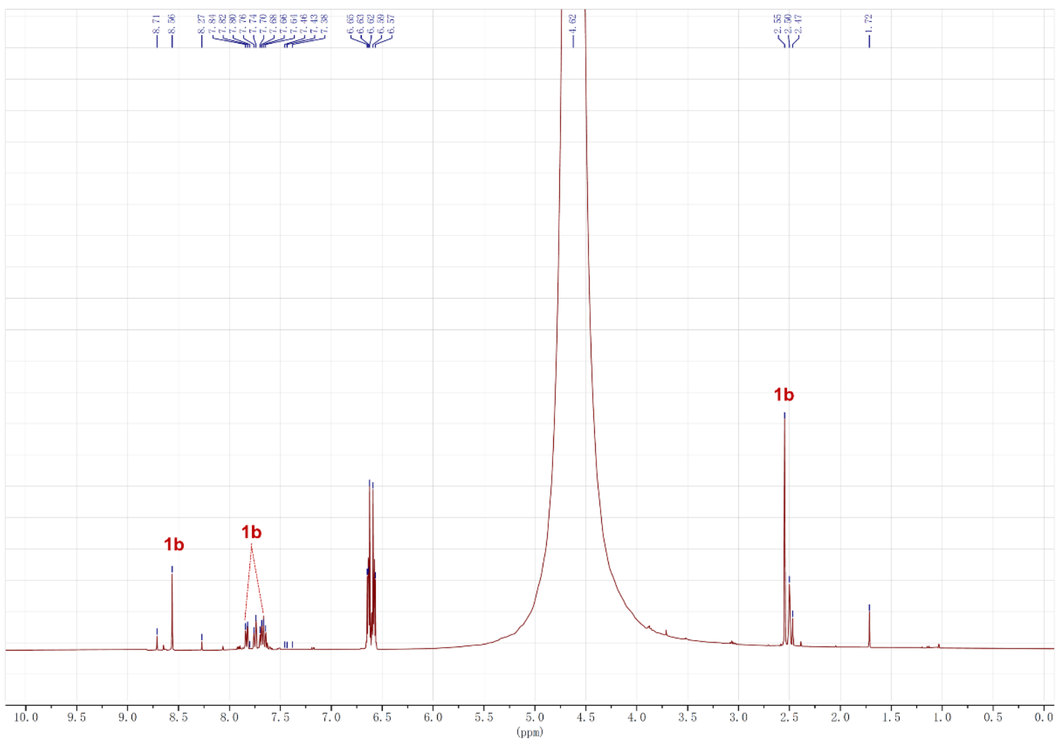


Fig. S16. ^{1}H NMR spectrum of the crude reaction mixture from the glucose transformation in H_2O in the presence of *o*-PDA and KOH. Reaction conditions: Glucose (0.5 mmol), *o*-PDA (2 mmol), KOH (0.15 mmol), H_2O (20 mL), N_2 (2 MPa), temperature (180 °C), 5 h. After reaction, an aliquot of the reaction mixture was taken and dissolved in an appropriate amount of DMSO-d_6, which was submitted for NMR measurement.

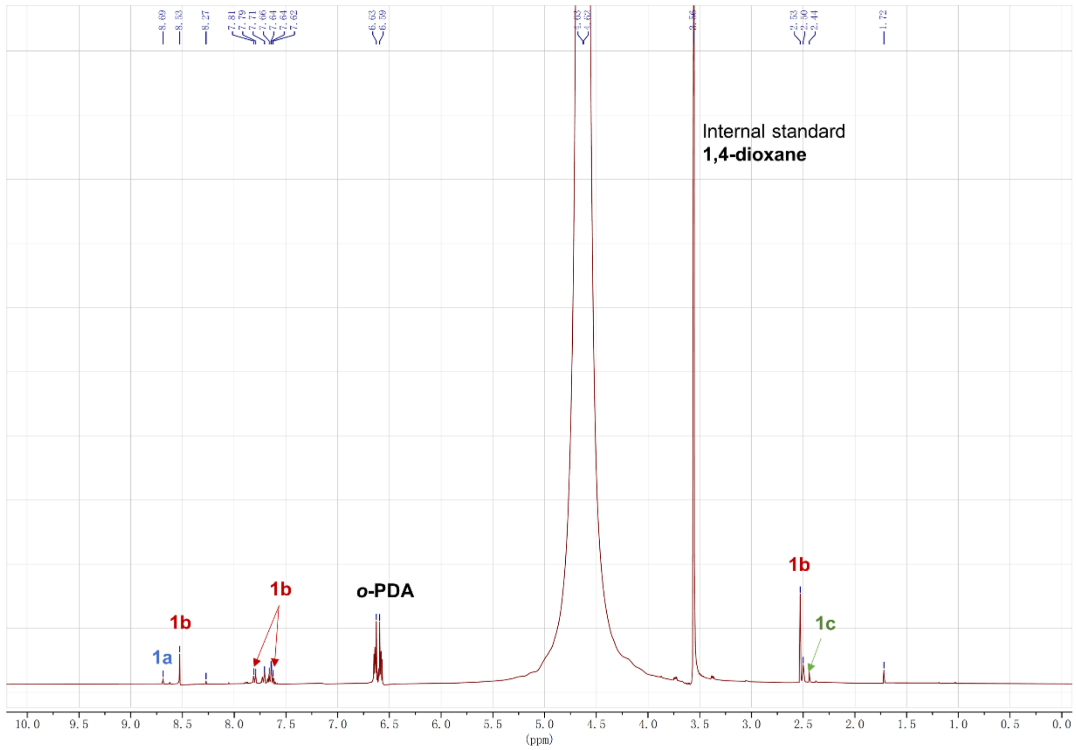


Fig. S17. Representative ^1H NMR spectrum for the quantification of quinoxalines produced from the glucose transformation by using 1,4-dioxane as the internal standard. Reaction conditions: Glucose (0.5 mmol), *o*-PDA (2 mmol), KOH (0.15 mmol), H_2O (20 mL), N_2 (2 MPa), temperature (180 °C), 5 h. After reaction, 1,4-dioxane (~100 mg) was added into the aqueous reaction mixture. The reaction mixture was then vigorously stirred at room temperature for 10 mins. Then an aliquot of the resulted aqueous solution was taken and dissolved in an appropriate amount of DMSO-d_6, which was then submitted for NMR measurement.

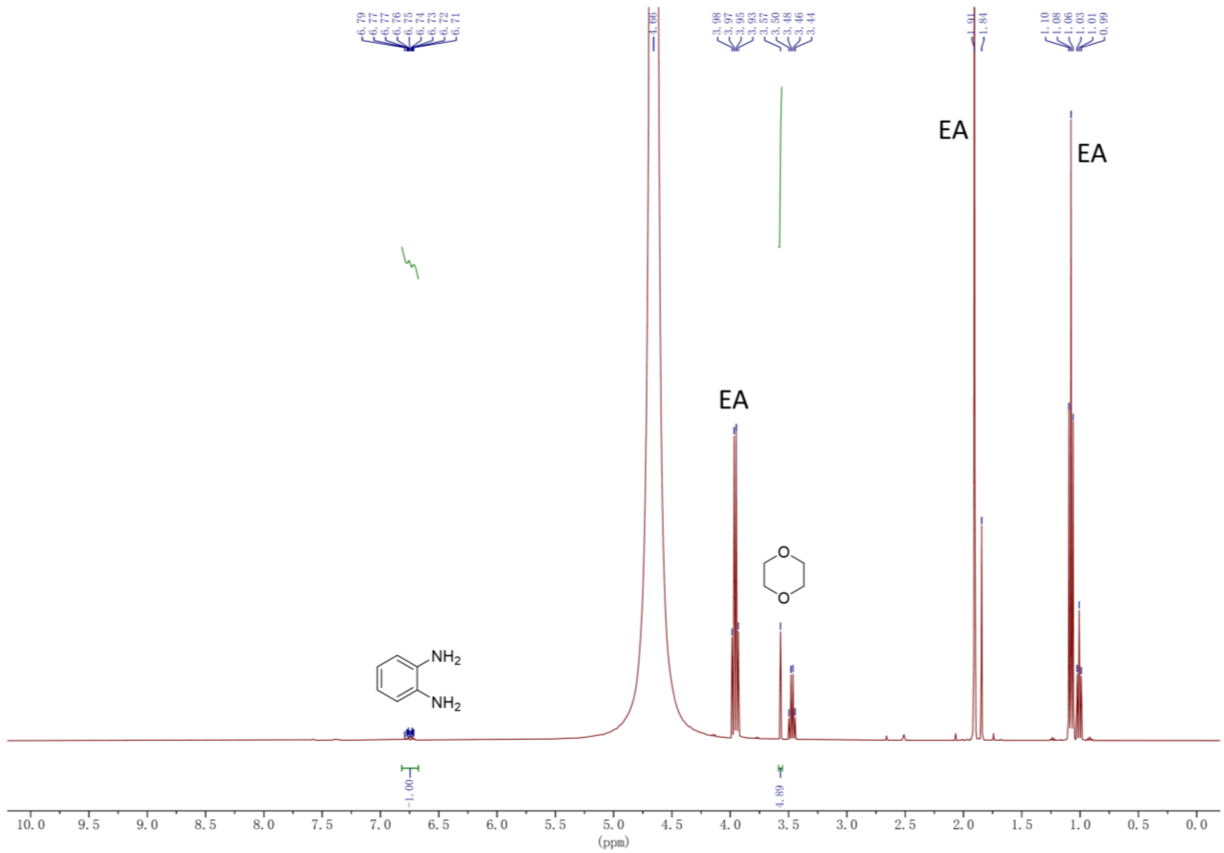


Fig. S18. ^{1}H NMR spectrum of the aqueous solution after ethyl acetate extraction to evaluate the amount of remaining *o*-PDA in the aqueous phase from the glucose transformation in H_2O in the presence of *o*-PDA and KOH. The reaction conditions: Glucose (0.5 mmol), *o*-PDA (2 mmol), KOH (0.15 mmol), H_2O (20 mL), N_2 (2 MPa), temperature (180 °C), 5 h. After reaction, the crude reaction mixture was subjected to the extraction by ethyl acetate (3 × 10 mL). With an addition of proper amount of 1,4-dioxane (internal standard), the resulted aqueous phase was collected and submitted for NMR measurement.

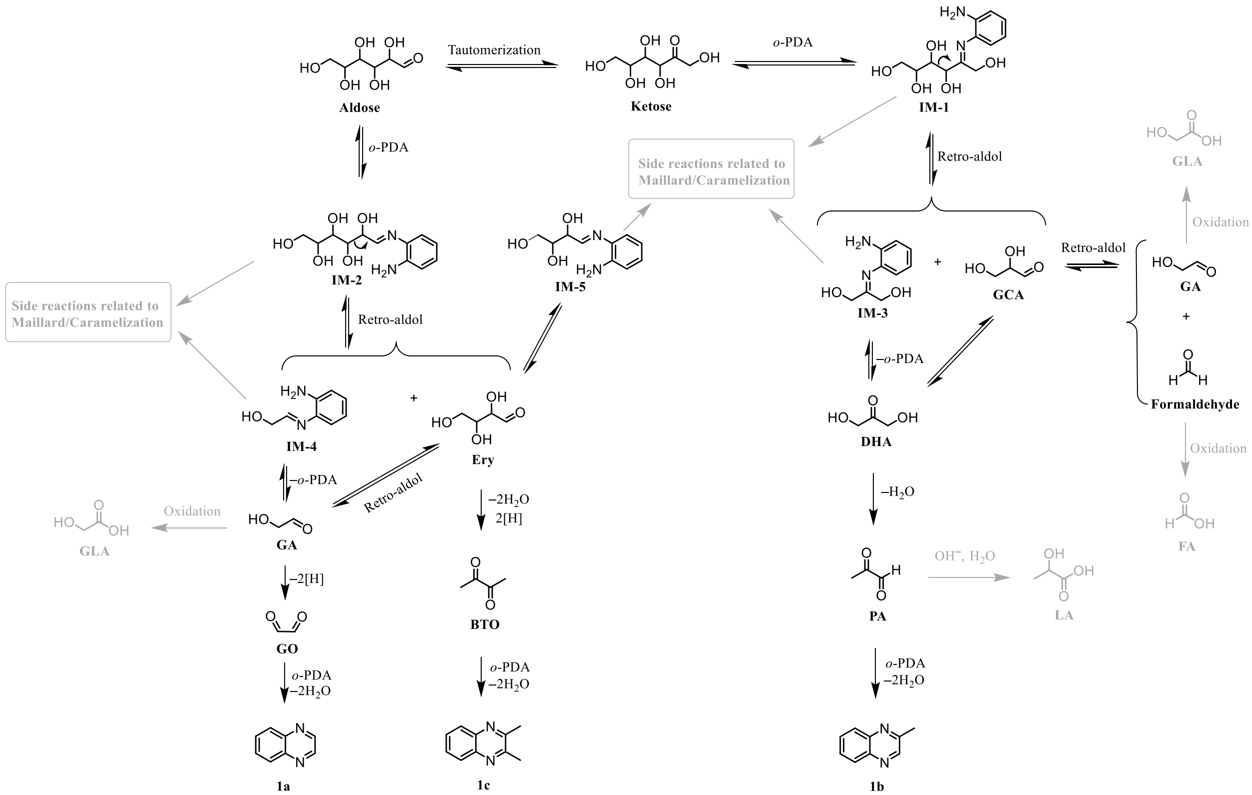


Fig. S19. Plausible reaction pathways for transforming glucose into quinoxalines in the presence of *o*-PDA and a minimal amount of base.

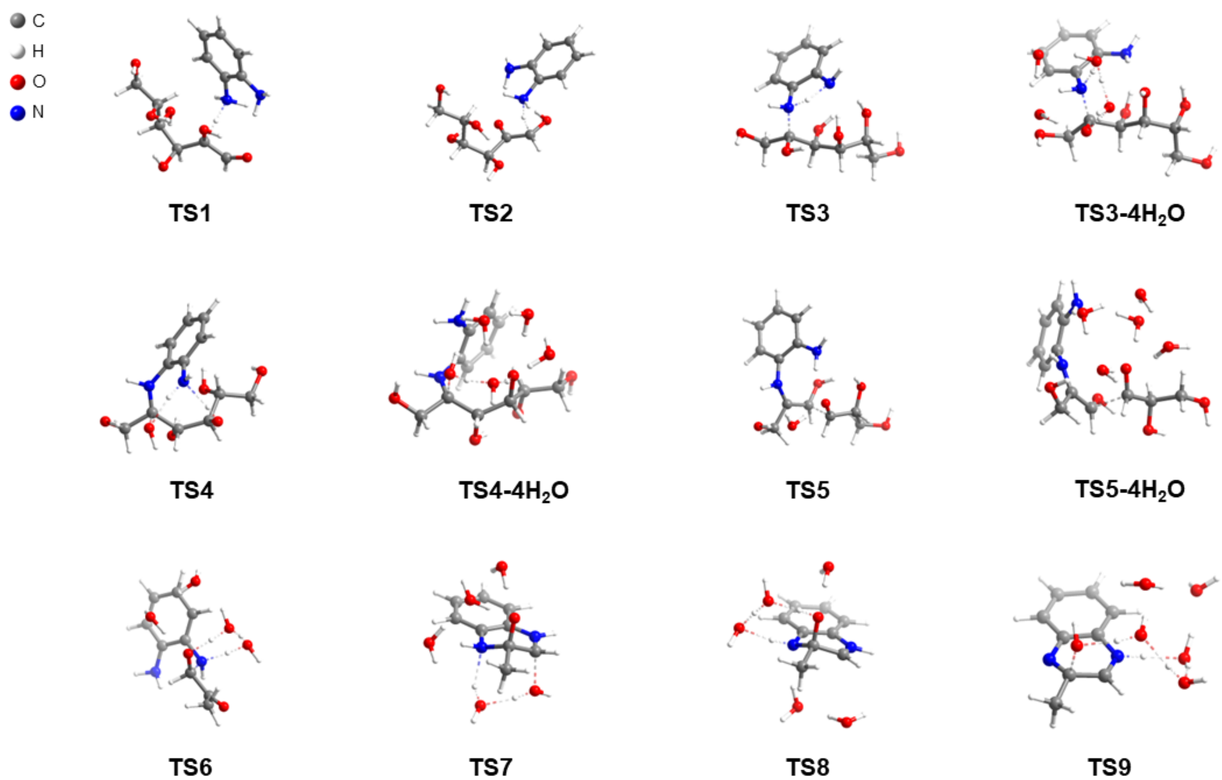


Fig. S20. Structural illustrations of the transition states (**TS1**–**TS8**) from DFT calculations [8–11].

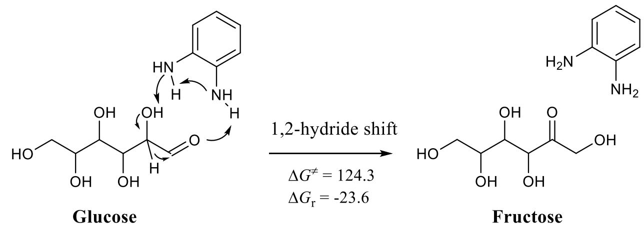


Fig. S21. *o*-PDA facilitated isomerization of glucose to fructose via 1,2-hydride shift mechanism.

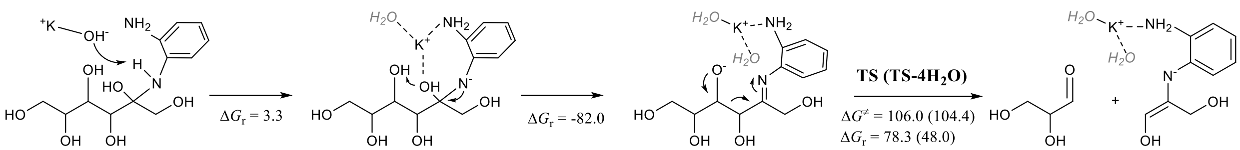


Fig. S22. Effect of KOH on the Retro-Aldol reaction of fructose to C_3 compounds.

Note: The presence of KOH base can promote the deprotonation of NH group of hemiaminal **15** and stabilize the iminium species, and the highest Δ$G^{\neq}$ along the reaction pathways is decreased from 127.7 to 106.0 kJ mol^{-1} (118.5 to 104.4 kJ mol^{-1} when the presence of additional four explicit water molecules was considered) in comparison with KOH-free case, evidencing the promotion effect of KOH on the Retro-Aldol reaction of fructose into C_3 compounds.

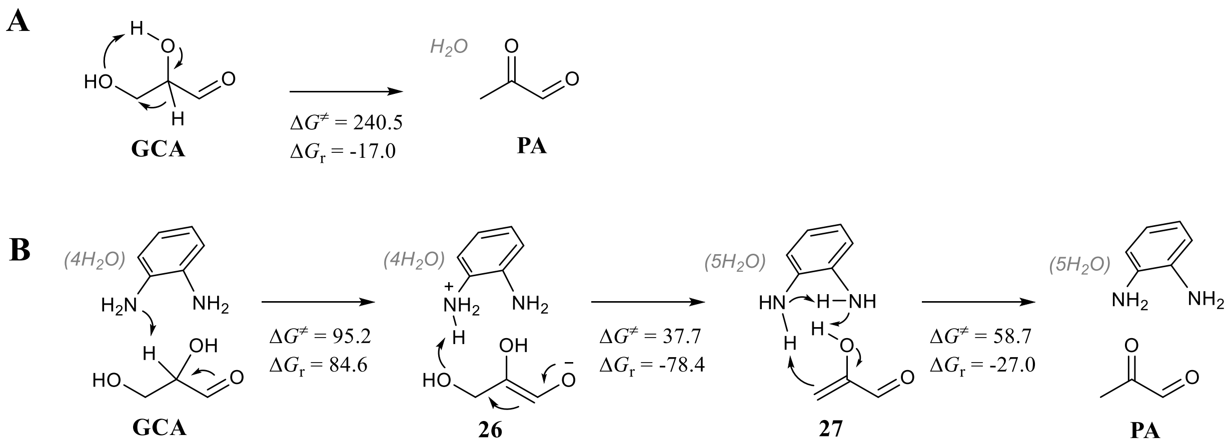


Fig. S23. Formation of PA from GCA: (A) direct dehydration via intramolecular hydride shift; (B) the route promoted by *o*-PDA with explicit water molecules.

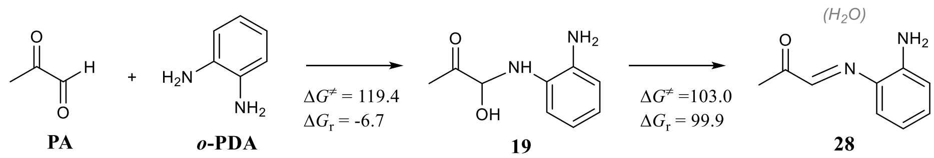


Fig. S24. Reaction of PA with *o*-PDA to form imine **28** via a hemiaminal intermediate **19**.

Recycling experiments

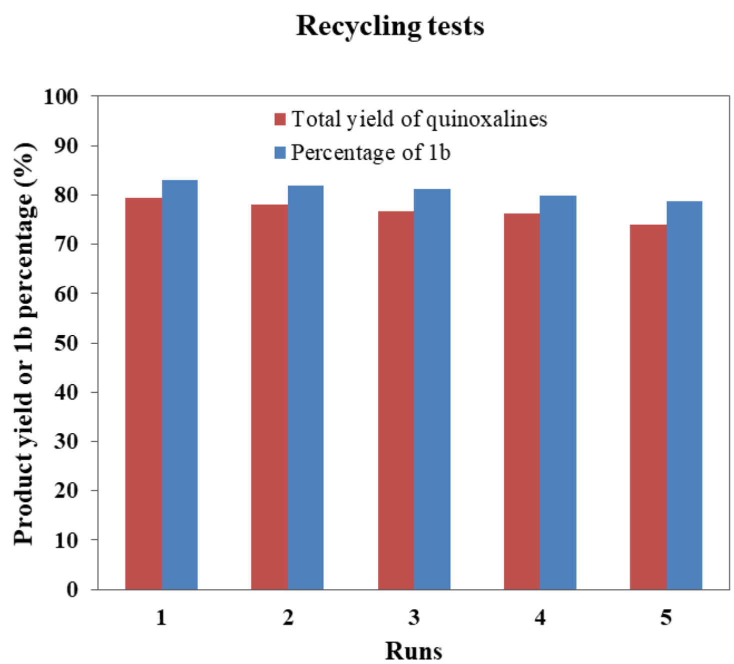


Fig. S25. Experimental results of aqueous solution recycling tests for production of quinoxalines.

Note: The recycling experiments were carried out based on the fresh experiment as shown in Table 1, entry 10. The reaction conditions are as follows: Glucose (0.5 mmol), *o*-PDA (2 mmol), KOH (0.15 mmol), H_2O (20 mL), N_2 (2 MPa), temperature (180 °C), 5 h. For the recycling experiments, the aqueous solution from the previous reaction and fresh glucose as well as fresh *o*-PDA were loaded into the next batch reaction. It should be noted that for each recycling experiment, more KOH, 1.5 times of the amount used in the fresh experiment, was needed to be loaded into the next batch reaction to maintain the high percentage of product 1b in total formed quinoxalines. This may be due to the generation of several acidic byproducts (lactic acid, glycolic acid, formic acid, oligomeric/polymeric acids) during the reaction. For instance, after the completion of the fresh experiment, the resulted reaction mixture was extracted by ethyl acetate (3 × 10 mL) to collect formed quinoxalines products. After extraction, the obtained organic layer contained quinoxalines products and most of remaining *o*-PDA reactant (~91% content). The resulted aqueous solution contained a little amount of remaining *o*-PDA (~9% content) and some water-soluble side product, which were difficult to be identified. The resulted aqueous solution was directly used in the next run batch reaction together with loading additional fresh 0.5 mmol of glucose, 2 mmol of *o*-PDA and 0.23 mmol of KOH.

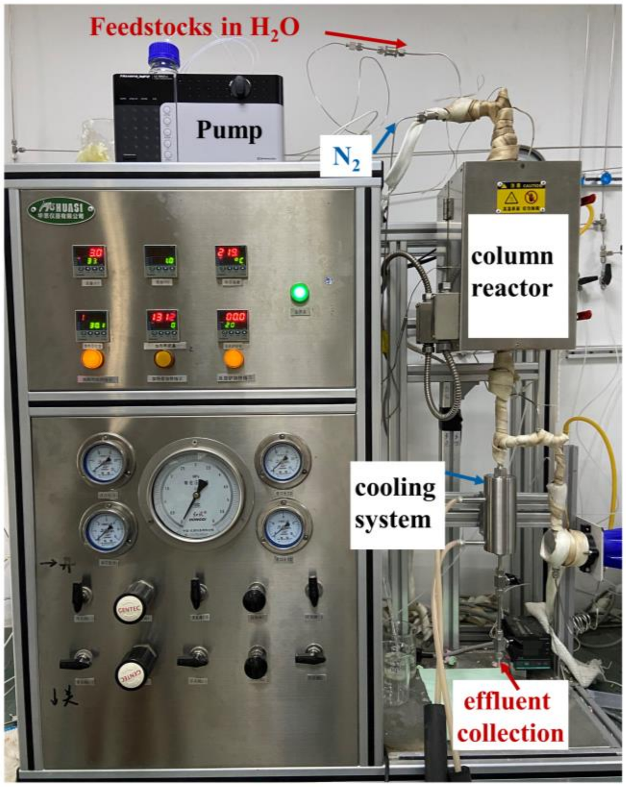


Fig. S26. Photographic image of the continuous-flow reactor tested for production of quinoxalines.

^{1}H NMR and ^{13}C NMR Spectra

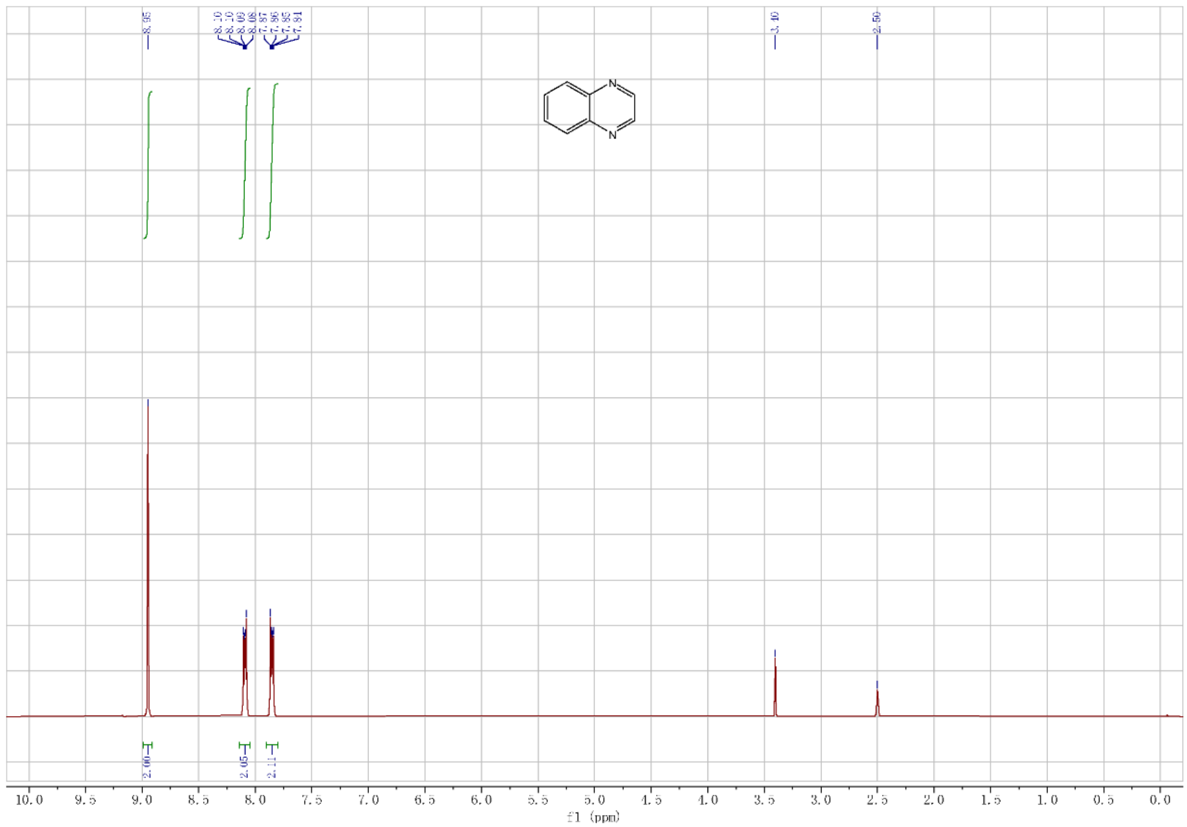


Fig. S27. ^{1}H NMR spectrum of quinoxaline **1a**.

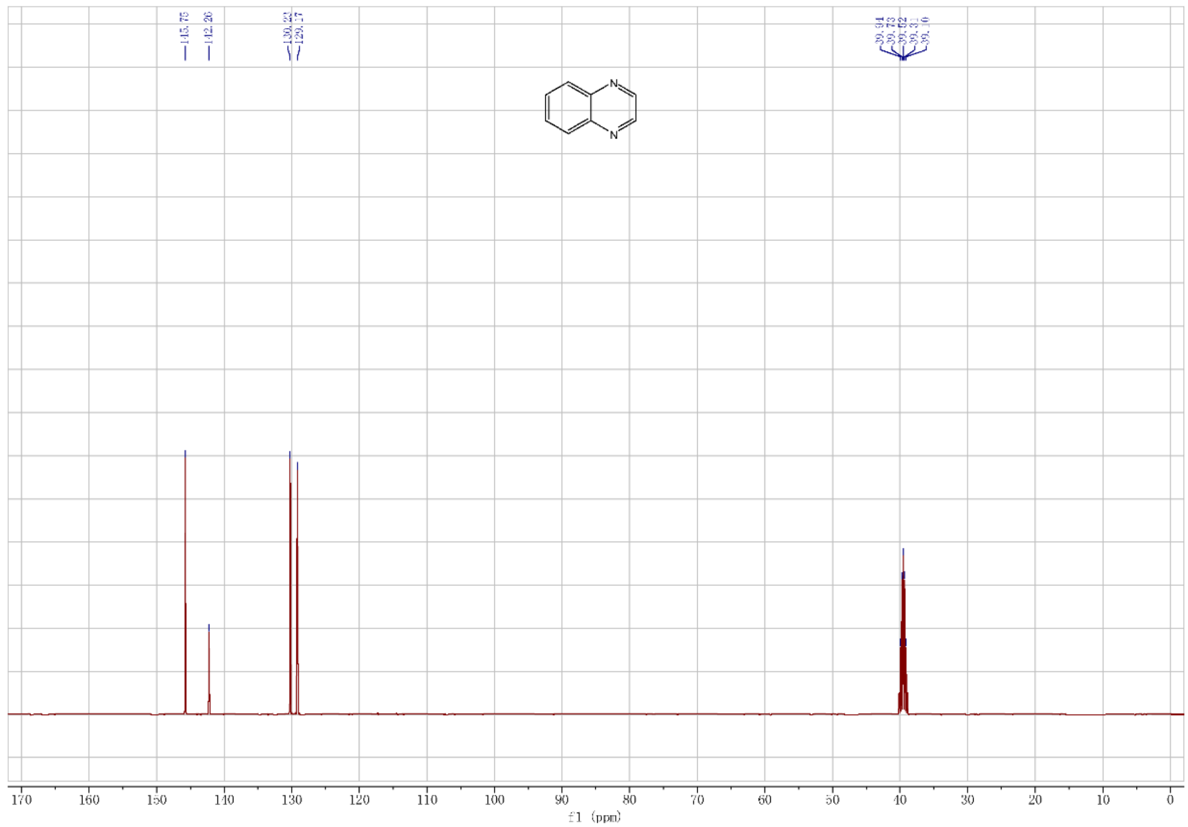


Fig. S28. ^{13}C NMR spectrum of quinoxaline **1a**.

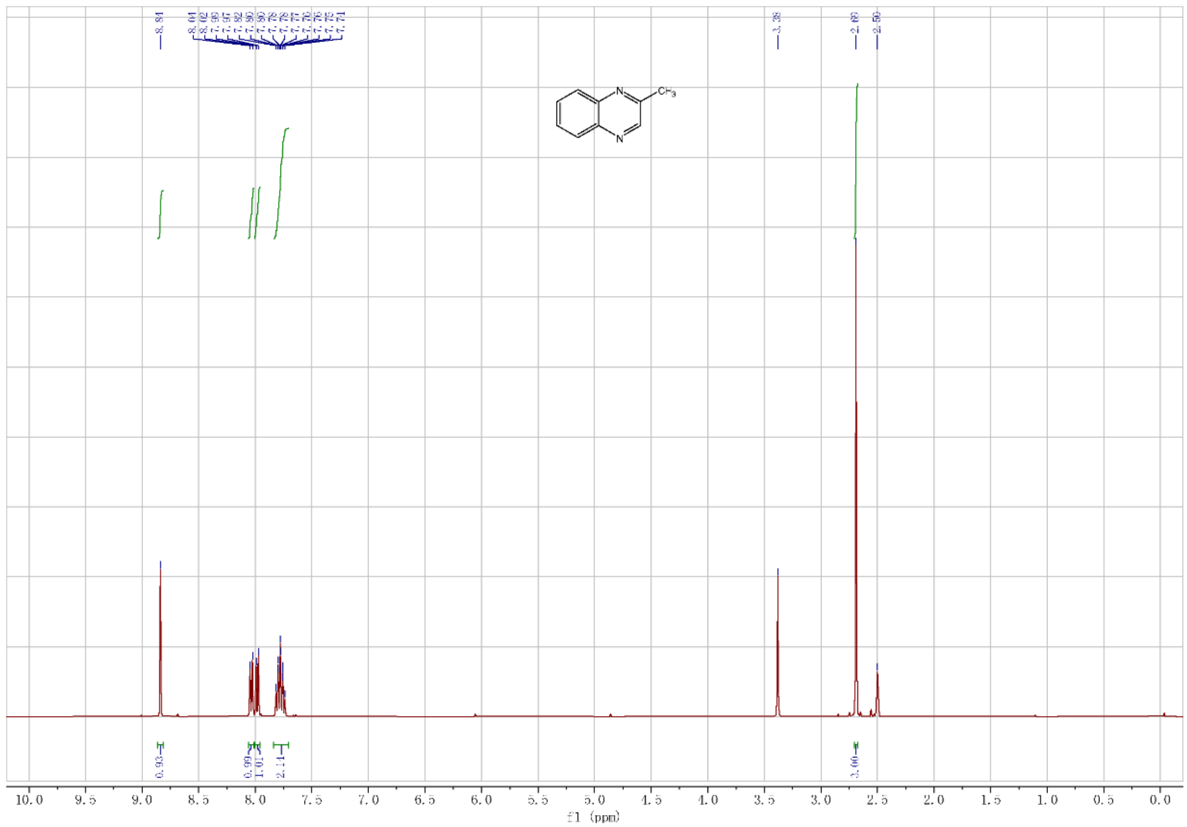


Fig. S29. ^{1}H NMR spectrum of 2-methylquinoxaline **1b**.

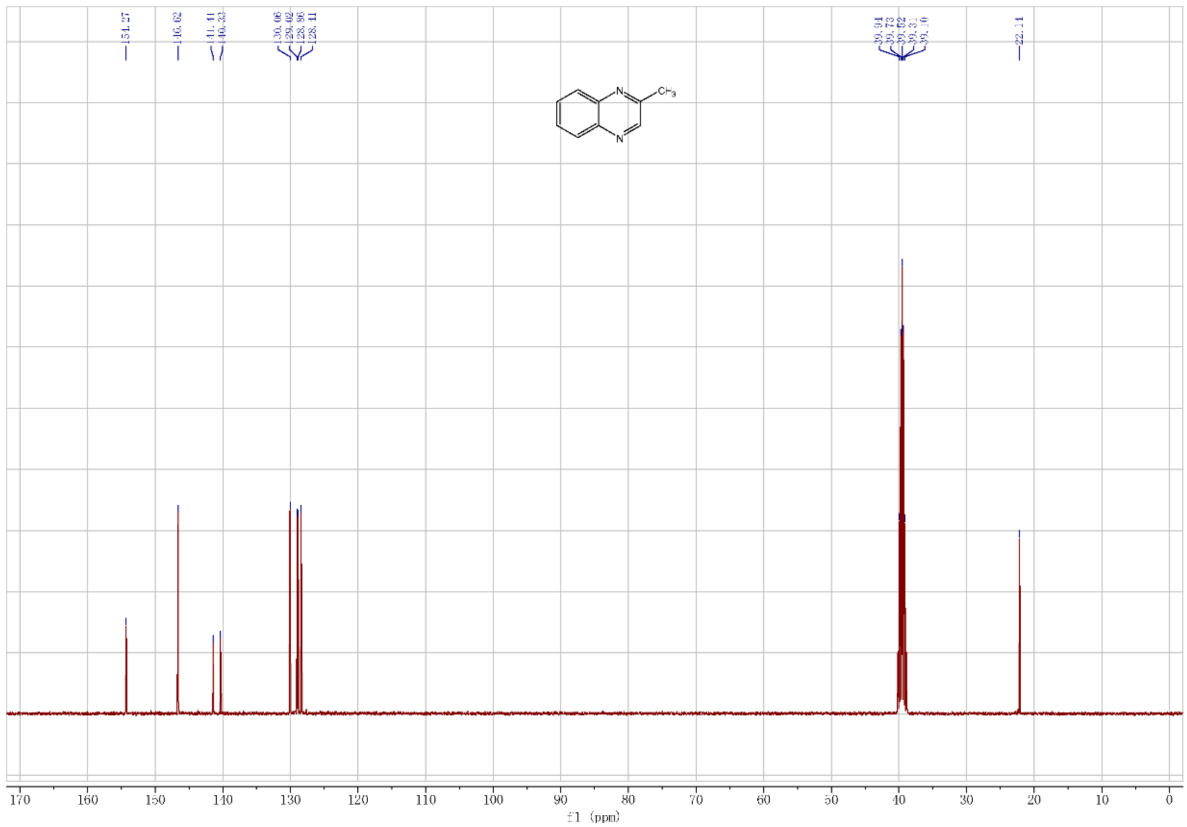


Fig. S30. ^{13}C NMR spectrum of 2-methylquinoxaline **1b**.

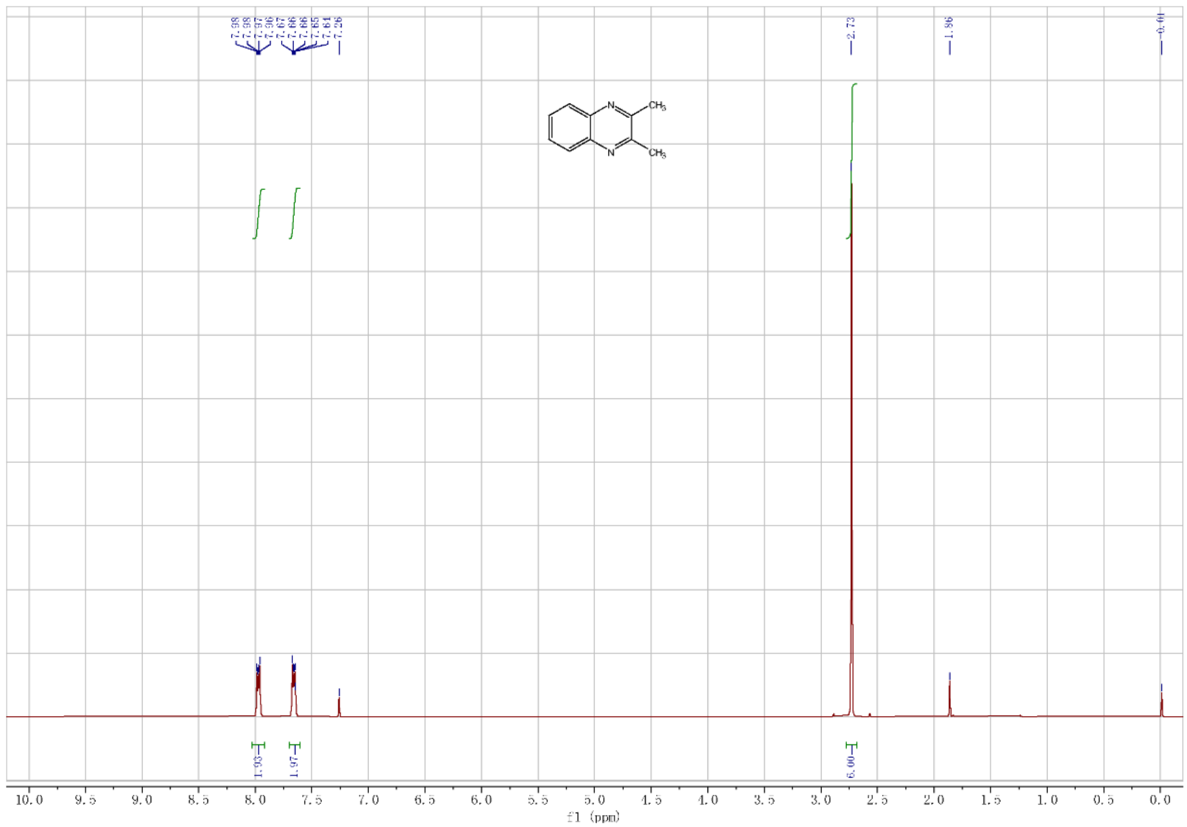


Fig. S31. ^{1}H NMR spectrum of 2,3-dimethylquinoxaline **1c**.

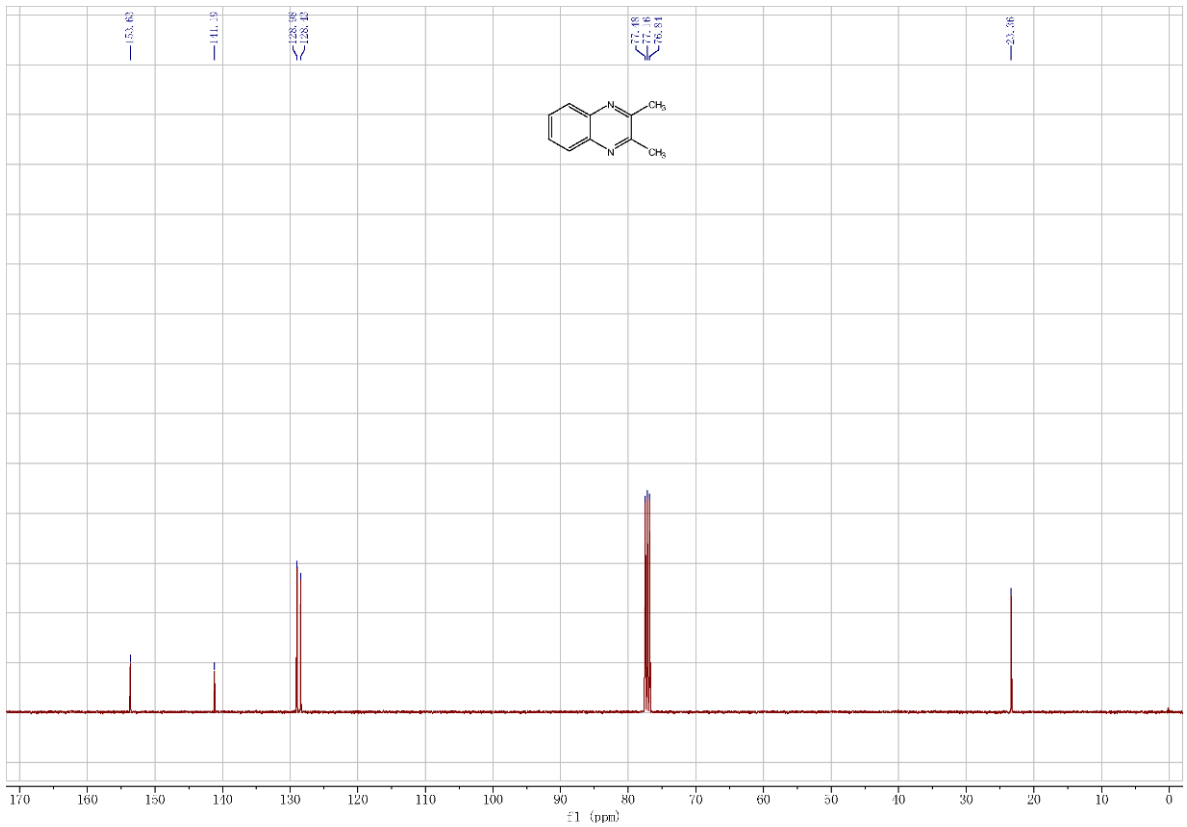


Fig. S32. ^{13}C NMR spectrum of 2,3-dimethylquinoxaline **1c**.

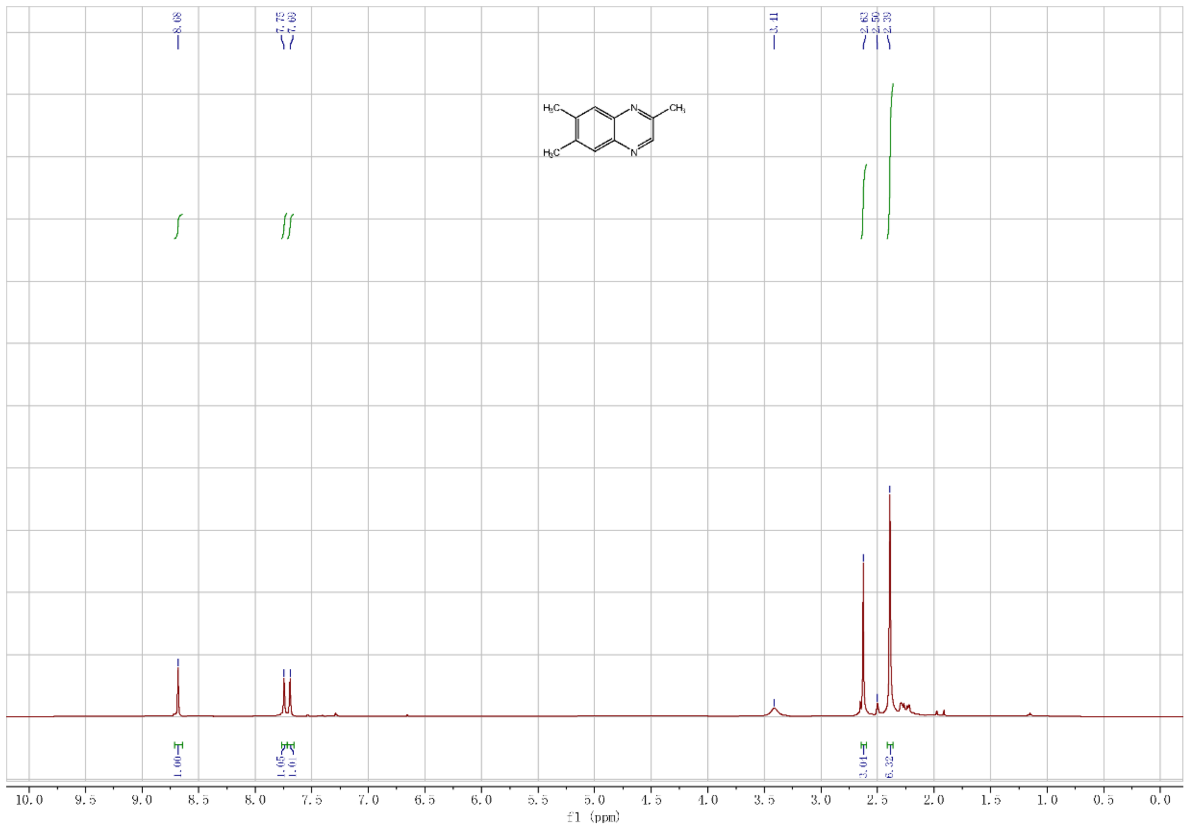


Fig. S33. ^{1}H NMR spectrum of 2,6,7-trimethylquinoxaline **2b**.

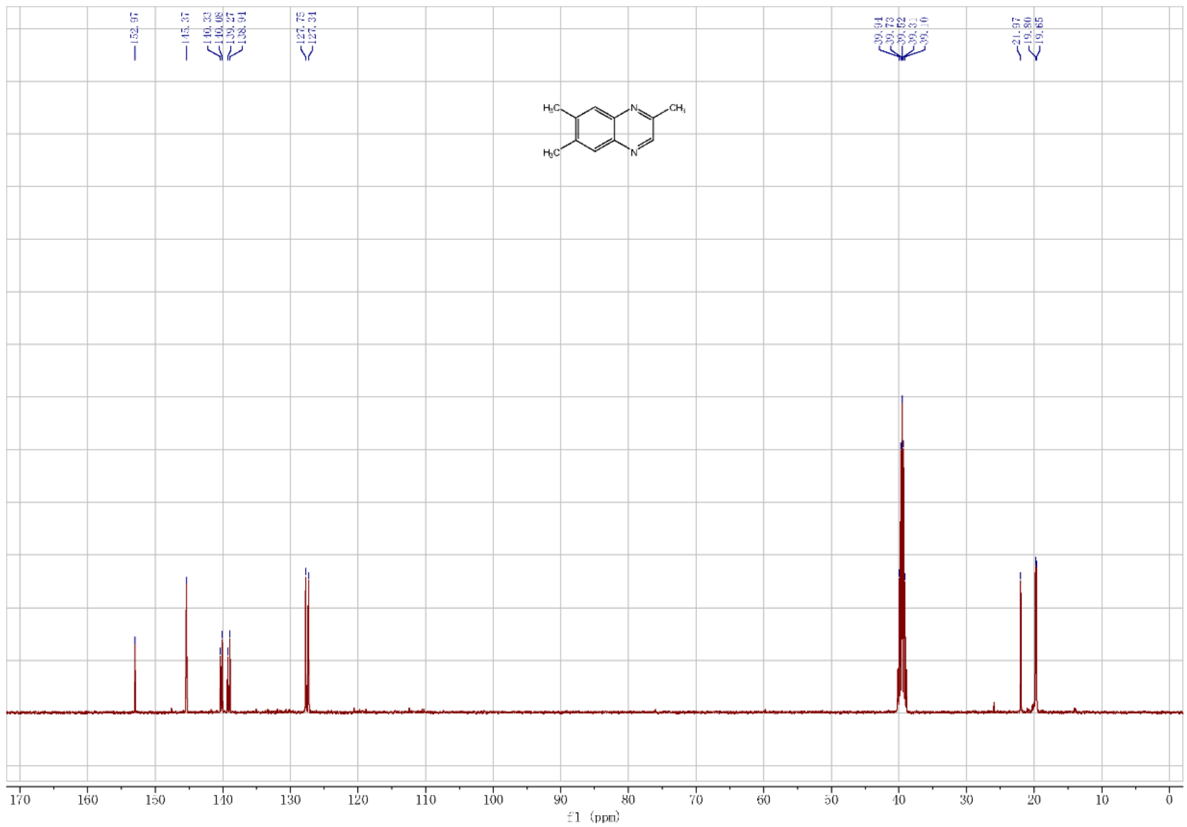


Fig. S34. ^{13}C NMR spectrum of 2,6,7-trimethylquinoxaline **2b**.

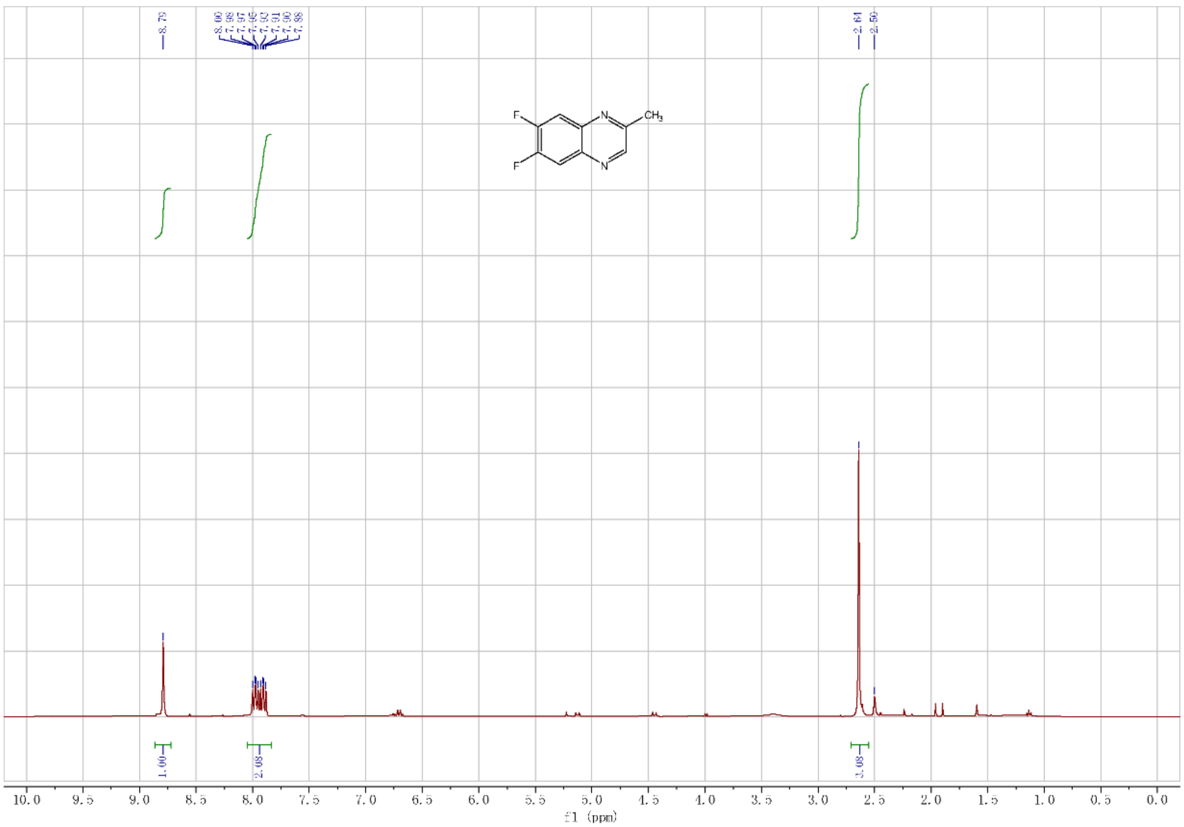


Fig. S35. [1]H NMR spectrum of 6,7-difluoro-2-methylquinoxaline **3b**.

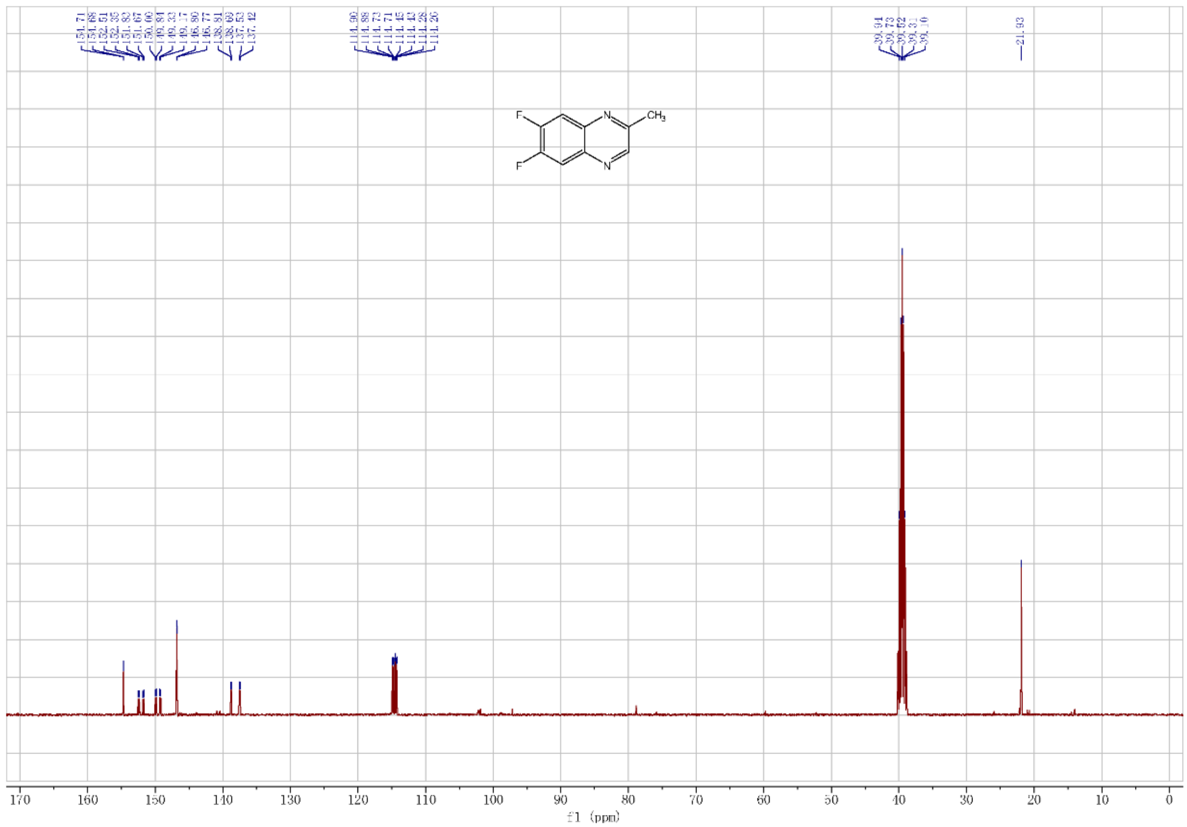


Fig. S36. ^{13}C NMR spectrum of 6,7-difluoro-2-methylquinoxaline **3b**.

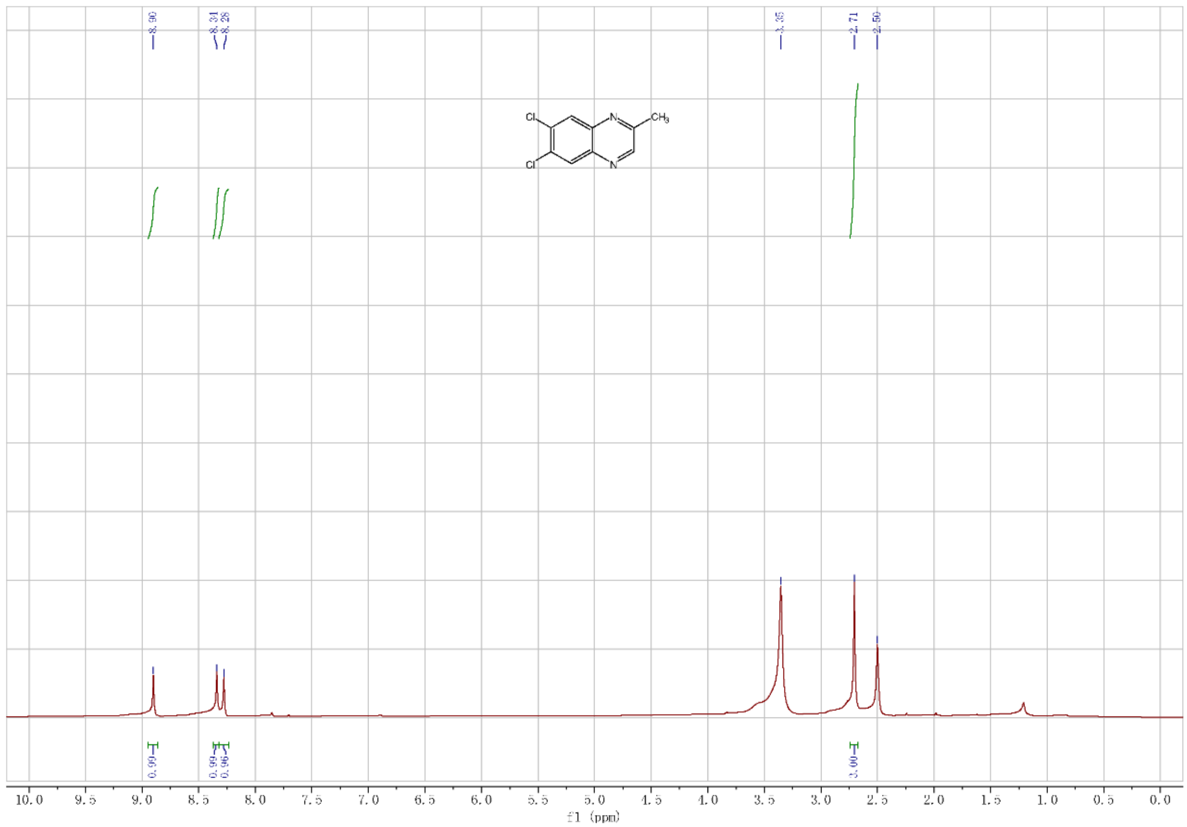


Fig. S37. ^{1}H NMR spectrum of 6,7-dichloro-2-methylquinoxaline **4b**.

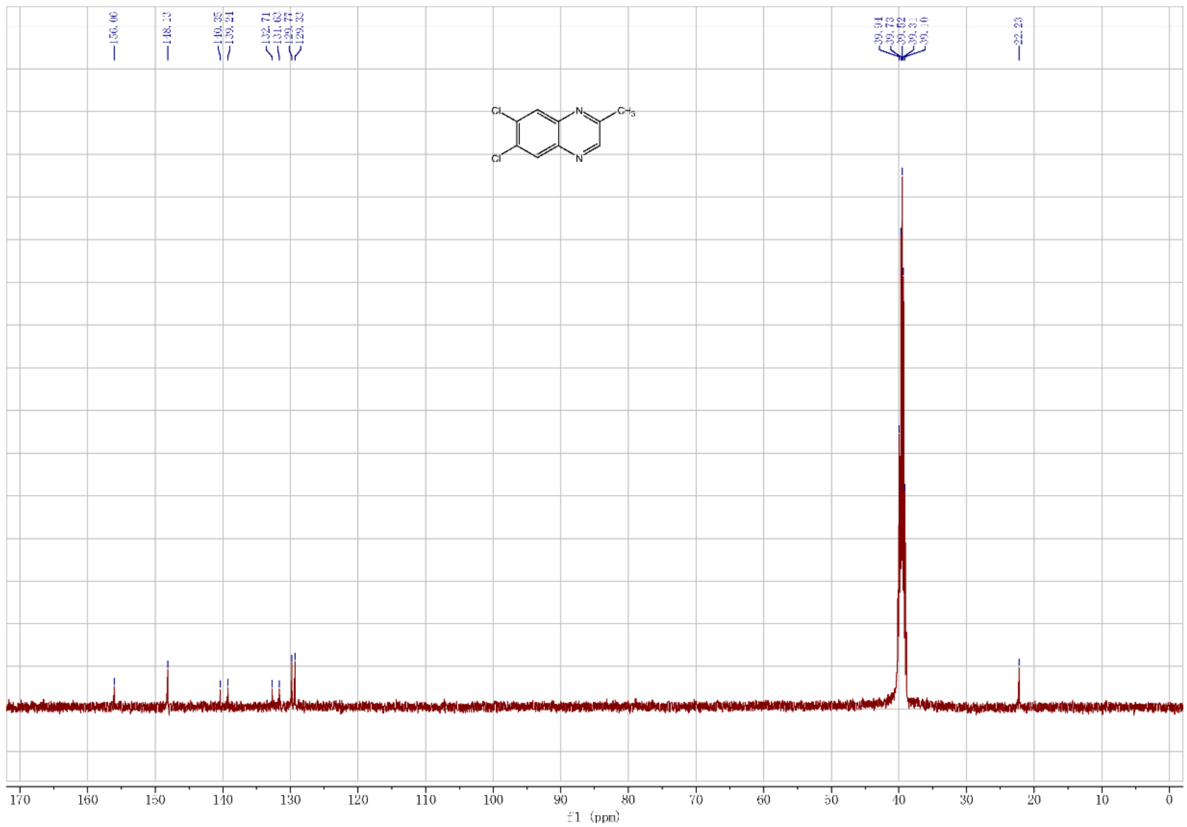


Fig. S38. ^{13}C NMR spectrum of 6,7-dichloro-2-methylquinoxaline **4b**.

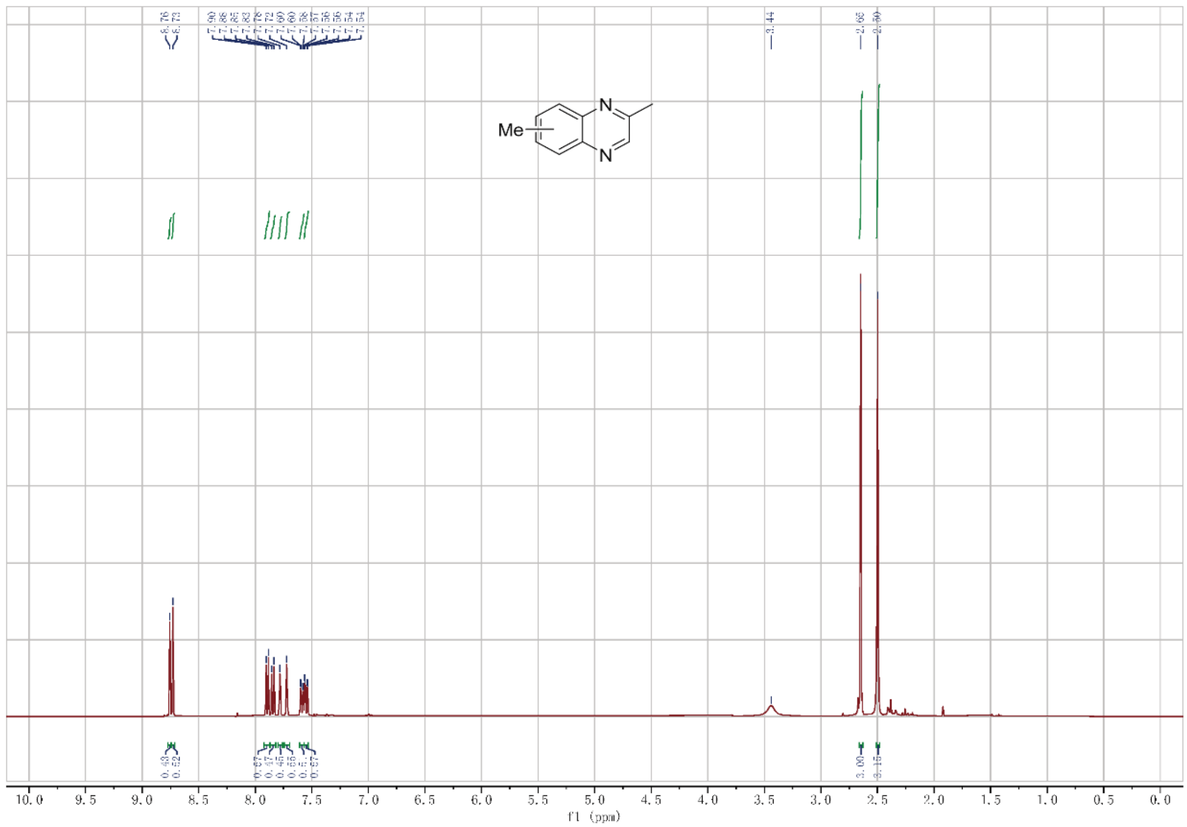


Fig. S39. ^{1}H NMR spectrum of the mixture of 2,6-dimethylquinoxaline and 2,7-dimethylquinoxaline **5b**.

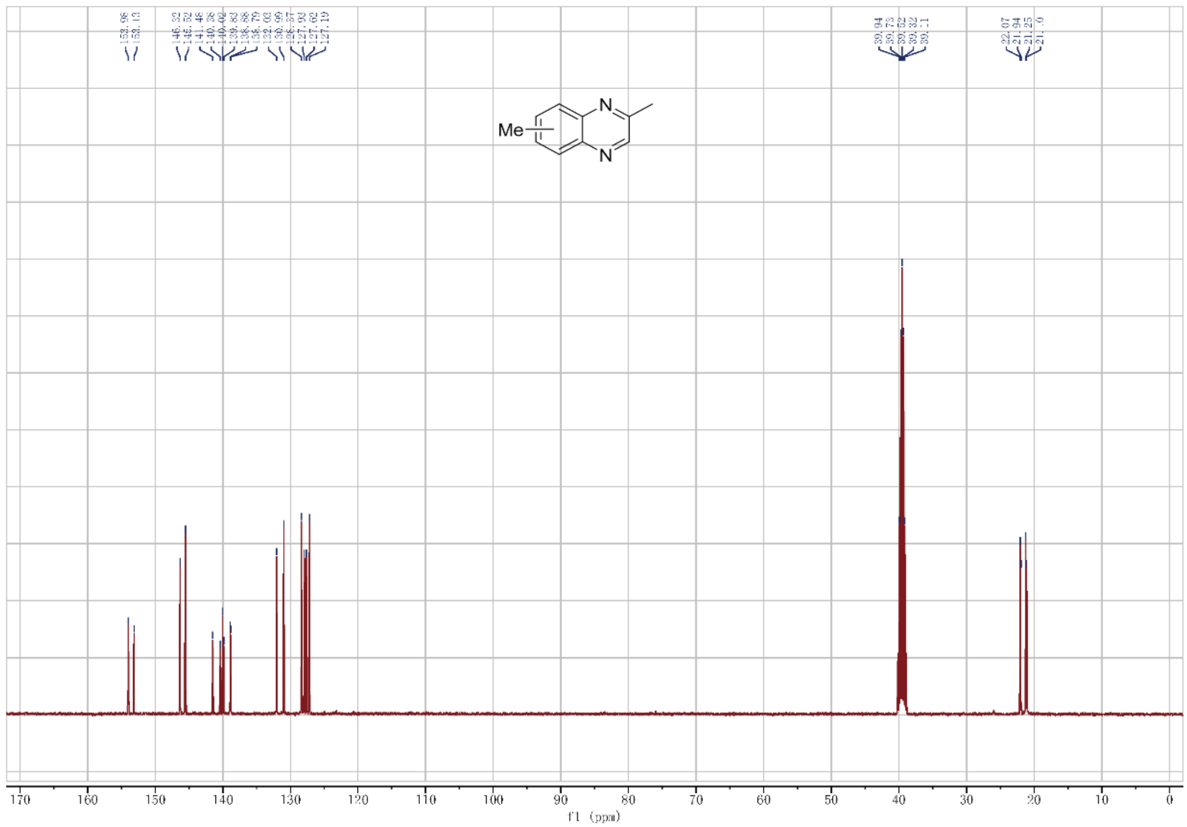


Fig. S40. ^{13}C NMR spectrum of the mixture of 2,6-dimethylquinoxaline and 2,7-dimethylquinoxaline **5b**.

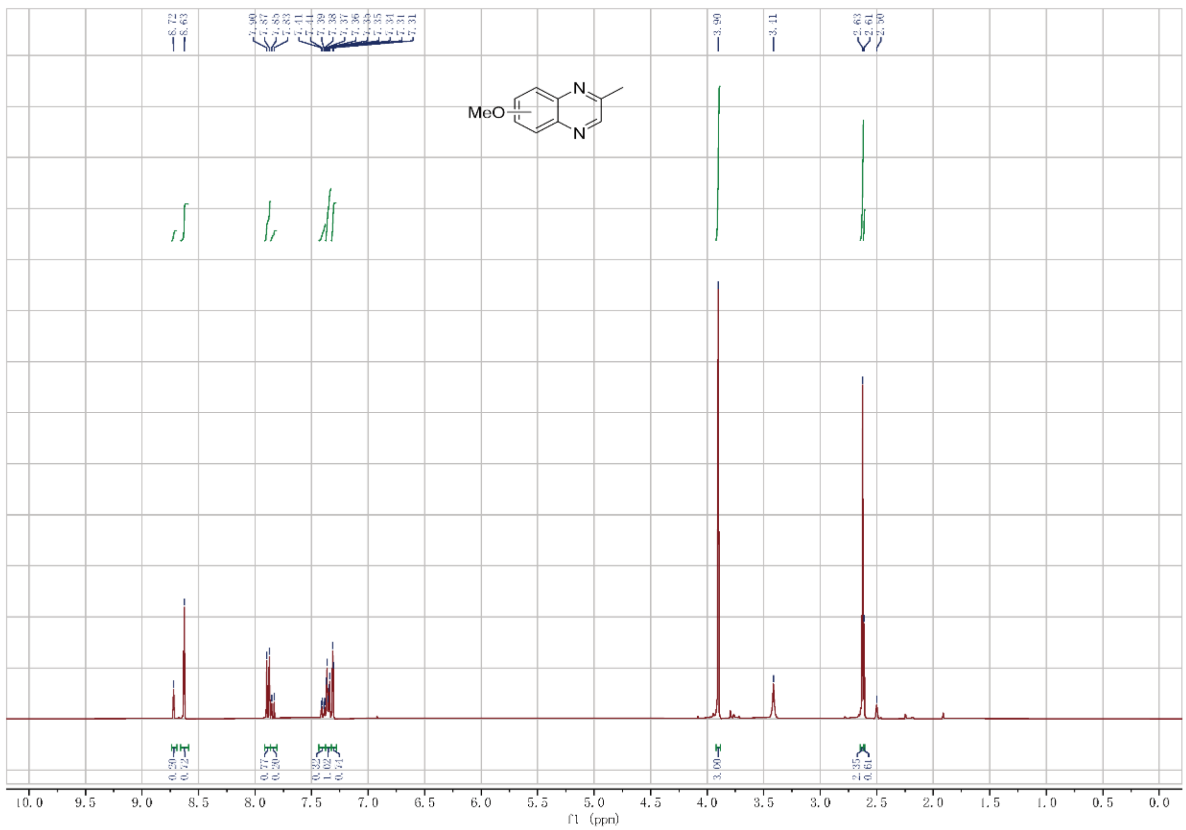


Fig. S41. [1]H NMR spectrum of the mixture of 6-methoxy-2-methylquinoxaline and 7-methoxy-2-methylquinoxaline **6b**.

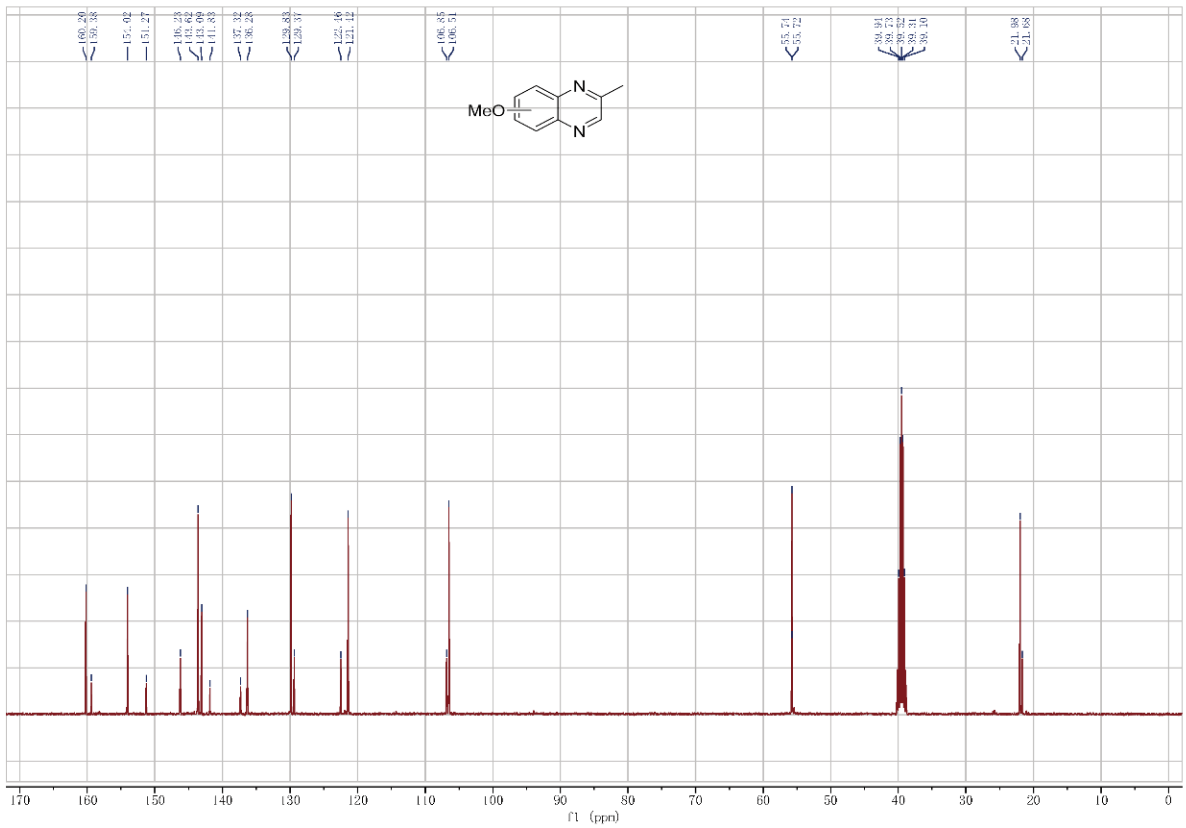


Fig. S42. ^{13}C NMR spectrum of the mixture of 6-methoxy-2-methylquinoxaline and 7-methoxy-2-methylquinoxaline **6b**.

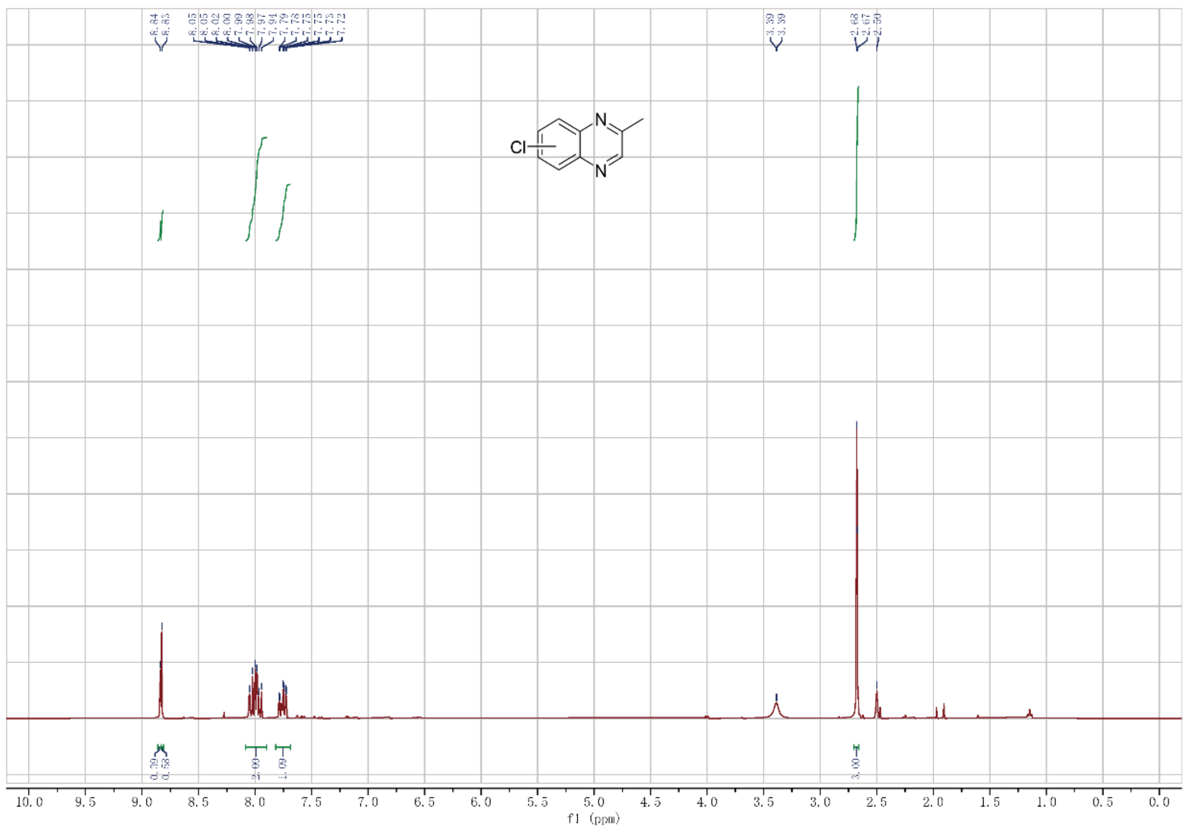


Fig. S43. ^{1}H NMR spectrum of the mixture of 6-chloro-2-methylquinoxaline and 7-chloro-2-methylquinoxaline **7b**.

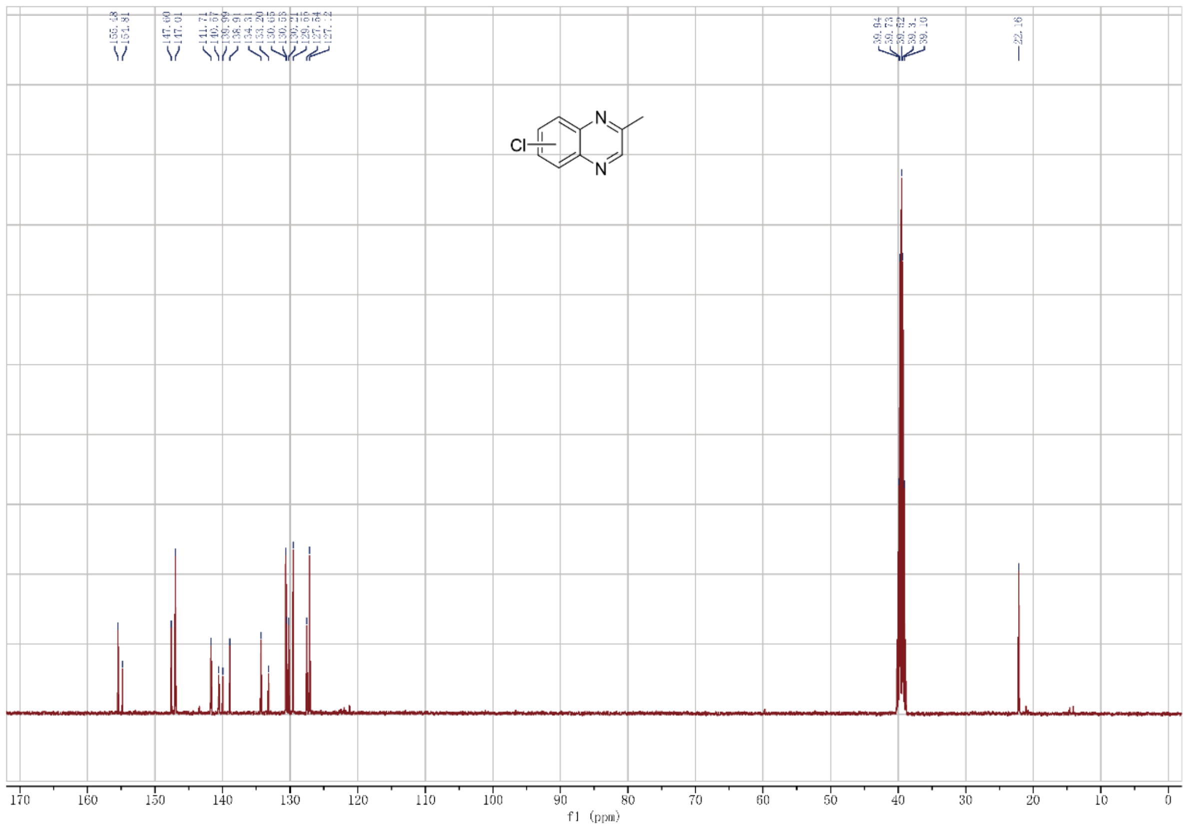


Fig. S44. ^{13}C NMR spectrum of the mixture of 6-chloro-2-methylquinoxaline and 7-chloro-2-methylquinoxaline **7b**.

Table S1. The textural parameters of Sn-Beta prepared via the post-synthesis strategy.

Catalyst	S_{BET} (m^2/g)	V_{Total} (cm^3/g)	V_{micro} (cm^3/g)[a]	Mean Pore Diameter (nm)[b]	Si/Sn[c]
Sn-Beta	516	0.36	0.24	2.78	54

[a]Micropore volume was calculated from *t*-plot. [b]Mean pore diameter was obtained by BET method; [c]The ratio of Si/Sn was determined by ICP analysis.

Table S2. Variations of temperature, concentration of glucose, *o*-PDA and KOH additive for the aqueous aminolysis of glucose to produce quinoxalines.

Entry	Glu. conc. (mmol/L)	*o*-PDA/Glu. (mol/mol)	KOH (mmol)	Temp. (°C)	Yield (%)[a]			
					1a	**1b**	**1c**	Total
1	25	4	—	150	13.4	32.8	5.5	51.7
2	25	4	—	160	17.2	35.7	6.6	59.5
3	25	4	—	170	19.3	42.3	9.5	71.1
4	25	4	—	180	19.2	50.4	11.1	80.7
5	25	4	—	190	22.2	49.0	9.8	81.0
6	50	4	—	180	16.2	41.9	8.9	67.0
7	100	4	—	180	15.0	36.8	7.6	59.3
8	25	8	—	180	19.9	48.8	11.2	79.9
9	25	2	—	180	13.4	32.8	5.5	51.7
10	25	1	—	180	7.5	19.9	3.6	31.0
11	25	4	8.8×10^{-2}	180	7.9	54.5	3.5	65.9
12	25	4	0.18	180	6.3	66.0	7.2	79.5
13	25	4	0.35	180	2.2	66.3	5.5	74.0

Reaction conditions: Glucose (0.5 mmol), N_2 (2 MPa), reaction time (5 h). [a]Yields were determined by GC-FID.

Note: The study of concentration effect on glucose conversion to quinoxalines indicates that the transformation is favored at glucose and alkali concentration of 25 mmol/L and 4.4 mmol/L respectively as well as o-PDA/glucose molar ratio of 4. Under these conditions, the highest overall yield of quinoxalines **1a**–**c** (79.5%), including 66.0% yield of 2-methylquinoxaline **1b**, can be obtained (table S2, entry 12).

Table S3. Production of quinoxalines from carbohydrates.

Entry	Carbohydrate	Time (h)	Yield of Quinoxalines (%)[a]				1b percentage (%)
			1a	1b	1c	Total	
1	Glucose	2	18.8	35.0	6.3	60.1	58.2
2[b]	Glucose	5	19.2	50.8	11.0	81.0	62.7
3[c]	Glucose	5	21.4	47.6	6.8	75.8	62.8
4	Fructose	5	18.8	50.7	12.3	81.8	62.0
5	Mannose	5	20.0	49.2	10.6	79.8	61.7
6	GCA	0.5	5.3	41.4	0	46.7	88.7
7	GCA	4	6.3	67.3	1.3	74.9	89.9
8	DHA	0.5	3.8	74.8	0	78.5	95.3

Reaction conditions: Carbohydrate feedstock (0.5 mmol), *o*-PDA (2 mmol), H_2O (20 mL), N_2 (2 MPa), temperature (180 °C). [a]Yields were determined by GC-FID. [b]N_2 (0.1 MPa) was employed. [c]Air (0.1 MPa) was employed.

Table S4. Carbon distributions of glucose for the experiments of glucose transformation mentioned in Fig. 2A.

Additive	Products in aqueous phase									Products in organic phase					Yield (C%)						Mass balance (%)
	C_6			C_3				C_2	C_1	C_4	C_3		C_2		C_6	C_4	C_3	C_2	C_1	Total	
	Glu	Fru	HMF	GCA	PA	DHA	LA	GA	FA	1c	1b	DPPDI	1a	Indole							
Amine-free	85.7	4.3	6.6	1.2	1.3	0.7	–	–	–	–	–	–	–	–	10.9	–	3.2	–	–	14.1	98.6
Aniline	0.8	3.3	0.5	2.6	2.1	1.0	–	–	–	–	–	1.5	–	5.6	3.8	–	7.2	5.6	–	16.6	17.4
***o*-PDA**	–	0.2	–	–	–	–	–	–	–	11.1	50.4	–	19.2	–	0.2	11.1	50.4	19.2	–	80.9	80.9
***o*-PDA[a]**	–	0.3	–	–	–	–	2.4	0.8	0.9	6.3	66.0	–	7.2	–	0.3	6.3	68.4	8.0	0.9	83.9	83.9

Reaction conditions: Glucose (0.5 mmol), H_2O (20 mL), 180 °C, 5 h, N_2 (2 MPa), the amount of amine additive (aniline and *o*-PDA) was based on total amino groups (4 mmol). [a]KOH (0.15 mmol) was added. Glucose (**Glu**); Fructose (**Fru**); Glyceraldehyde (**GCA**); Pyruvaldehyde (**PA**); Dihydroxyacetone (**DHA**); N^1,N^2-diphenylpropane-1,2-diimine (**DPPDI**); Glycolic acid (**GLA**); Formic acid (**FA**).

Table S5. The compilation of thermodynamic data for the reactants and products with respect to enthalpy of formation ($\Delta_f H°$) and entropy (S°) at standard conditions as well as constant pressure heat capacity (C_p).

Compounds	$\Delta_f H°$ (kJ mol^{-1})	S° (J mol^{-1}K^{-1})	C_p (J mol^{-1}K^{-1})
Glucose	–1273.70 (solid)	288.30 (solid)[12]	219.30 (solid)
	–1253.80 (liquid)	364.20 (liquid)[12]	220.90 (liquid)
o-PDA	39.10 (solid)	152.09 (solid)	150.82 (solid)
	62.20 (liquid)	214.09 (liquid)	201.82 (liquid)[13]
2-Methylquinoxaline	125.70 (liquid)[a]	224.25 (liquid)[a]	231.20 (liquid)[14]
H_2O	–285.83 (liquid)	69.95 (liquid)	75.38 (liquid)
	–241.83 (gas)	188.84 (gas)	35.22 (gas)

Standard thermochemistry data ($\Delta_f H°$, S°, C_p) are according to National Institute of Standards and Technology (NIST) database[15]. [a]Thermodynamic values of $\Delta_f H^{\ominus}$ and S° for 2-methylquinoxaline are estimated by Benson group-contribution method[2,16–18].

Table S6. The effect of flow rate on the continuous-flow production of 2-methylquinoxaline.

Flow rate (mL/h)	**Yield of 1b (%)**	**1b percentage in total formed quinoxalines (%)**
4.8	38.1	95.4
3.0	50.2	91.1
1.8	44.4	93.1
0.6	28.5	89.0

Reaction conditions: The feeding aqueous solution contains glucose (1.80 g/L), *o*-PDA (4.32 g/L) and KOH (0.16 g/L), temperature of flow reactor (180 °C), N_2 flow controlled at 10 mL/min.

Table S7. E-factors evaluated across the chemical industry as references[3,19].

Industry sector	Annual production (t)	E-factor	Waste produced (t)
Oil refining	$10^6 – 10^8$	Ca. 0.1	$10^5 – 10^7$
Bulk chemicals	$10^4 – 10^6$	< 1 – 5	$10^4 – 5\times10^6$
Fine chemicals	$10^2 – 10^4$	5 – 50	$5\times10^2 – 5\times10^5$
Pharmaceuticals	$10 – 10^3$	25 – 100	$2.5\times10^2 – 10^5$

Note: As shown in **table S7**, the E-factors for production of bulk chemicals and fine chemicals are generally in the range of 1–50. With our proposed reaction strategy for the synthesis of quinoxalines, the E-factor of the reaction is evaluated to be as low as 0.4, which is much superior to the currently adopted routes for the production of fine chemicals in industries, exhibiting its huge potential for manufacturing valuable chemicals with heterocyclic quinoxaline skeleton structure in a more environment-friendly and sustainable way in the future.

Table S8. Global warming potential (GWP) for the production of quinoxaline products via our proposed renewable route and conventional fossil oil-based route [20].

Inventory	GWP (in kg CO_2 equivalent)					
	Route with base			Route without base		Fossil oil-based route
	Glucose (WBR)	Glucose (MS)	Glucose (WBR)[a]	Glucose (WBR)	Glucose (MS)	
Reactor	**15.63**	**16.15**	**18.93**	**14.59**	**15.08**	**21.92**
Glucose	0.63	1.15	0.76	0.59	1.08	
1,2-Propanediol						4.44
o-Phenylenediamine	14.78	14.78	17.9	14.00	14.00	13.6
Potassium hydroxide	0.22	0.22	0.27			
Water	0.003	0.003	0.004	0.003	0.003	0.007
Sodium bisulfite						1.64
Sodium carbonate						2.23
Recovery & Separation	**0.783**	**0.783**	**0.950**	**0.933**	**0.933**	
Electricity	0.003	0.003	0.004	0.003	0.003	
Steam	0.78	0.78	0.946	0.93	0.93	
SUM	**16.4**	**16.9**	**19.9**	**15.5**	**16.0**	**21.9**

[a]The value is based on the production of 1 kg 2-methylquinoxaline (1b). If not otherwise indicated, the GWP value provided is based on the production of 1 kg quinoxalines (1a–1c). WBR and MS indicate the biomass resource of glucose, representing woody biomass residue and maize starch respectively. Recovery section includes extractor, recrystallization (recycling *o*-PDA) and rectification (recycling EA).

Table S9. List of economic parameters.

Component	**Price/ \$ kg^{-1}**
Glucose[a]	0.375
o-Phenylenediamine[a]	19.300
Potassium hydroxide[a]	0.440
Ethyl acetate[a]	1.244
Phosphoric acid[b]	1.284
Water[b]	0.0005
Electricity[c]	0.1 \$ kWh^{-1}
2-Methyl quinoxaline[d]	306.3
Quinoxaline[d]	239.9
2,3-Dimethyl quinoxaline[d]	356.2

[a]Estimated based on the average price from Alibaba.

[b]Obtained from chemistry industry

[c]According to the average industrial electricity price in 2022 in China.

[d]Estimated based on the lowest market selling prices from well-known chemical companies in China including Aladdin, J&K Scientific, Energy Chemical and Global Chemical Factory Co., Ltd.

Table S10. Summary of economics for the production of quinoxaline products from glucose.

Inventory	Unit	Route with base	Route without base
Capital Costs	M$	132.23	140.66
Equipment cost	M$	44.08	46.89
Equipment installation	M$	26.45	28.13
Plant construction	M$	22.04	23.44
Indirect cost	M$	39.67	42.20
Operation Cost	M$ $year^{-1}$	7.46	8.38
Raw Materials	M$ $year^{-1}$	2.32	3.07
Labor	M$ $year^{-1}$	2.50	2.50
Maintenance cost	M$ $year^{-1}$	2.64	2.81
Depreciation (8 years)	M$ $year^{-1}$	16.53	17.58
Total revenue	M$ $year^{-1}$	36.70	49.42
Tax on income (50%)	M$ $year^{-1}$	8.01	13.49
Income after tax	M$ $year^{-1}$	21.23	27.55
Internal rate of return	%	11.15	16.53
Payout time	year	8.98	6.40

The production scale is set to be 100 tonnes per year.

DFT-optimized coordinates of transition states

TS1

C	0.77772500	-2.17531100	-0.53438600
O	0.38624300	-1.40542600	-1.65069400
C	-0.20340700	-3.04163800	-0.03150300
H	0.51216500	-1.26089400	0.58332500
O	-1.41536400	-2.96333400	-0.34165300
H	0.12320400	-3.73460800	0.75627100
H	-1.82939200	-0.76550300	-0.12088700
C	-1.13105900	1.16238200	-0.05495600
C	0.00880600	0.96241300	0.73263800
C	-1.25207800	2.37836700	-0.72855300
N	-2.13698400	0.20200700	-0.10223800
C	0.98803100	1.93700700	0.83671200
N	0.17653300	-0.30230600	1.38792500
C	-0.27211000	3.35407300	-0.62565300
C	0.85656800	3.13890400	0.15579400
H	-2.12933900	2.54368800	-1.34174400
H	1.85732800	1.74029200	1.45264800
H	-0.67362000	-0.60429100	1.86500400
H	0.94062200	-0.27006700	2.05914900
H	-0.39161200	4.28509600	-1.16320500
H	1.62511700	3.89439000	0.23749500
H	-2.81252900	0.37290200	-0.83457500
H	-0.52377600	-1.65771100	-1.86297500
O	2.86986300	-0.61283900	-2.58131700
O	3.09087700	-0.89710500	1.02474400
O	2.61113800	-3.32491900	-1.65707200
C	3.20868800	-1.39640700	-0.29800700
C	2.22857800	-2.56392600	-0.51066400
C	2.97382100	-0.20267900	-1.22075300

C	4.10937200	0.79435800	-1.13661900
H	4.21745800	-1.78724400	-0.47020800
H	2.35632900	-3.22672700	0.34889100
H	2.04767500	0.29427800	-0.92240300
H	4.23651900	1.12983100	-0.10933500
H	2.77087300	-2.70791300	-2.38187900
H	1.93303700	-0.78062500	-2.75396700
H	5.03591900	0.31211500	-1.46524900
O	3.84029200	1.94483100	-1.92191000
H	3.65014200	1.64428300	-2.81766400
H	3.33382700	-1.59612000	1.64167400

TS2

C	0.90483500	-2.10045800	-0.38880300
O	0.38161200	-1.27386800	-1.40064900
C	0.03344900	-3.03576900	0.16859100
H	0.92016600	-1.17940200	0.74877400
O	-1.21693000	-2.98197600	-0.02386900
H	-1.48597900	-0.82174800	0.78731400
C	-0.93807500	1.12859000	0.51253500
C	0.42537800	1.04121300	0.81721100
C	-1.38633600	2.26819600	-0.15364100
N	-1.81789500	0.12817900	0.92493300
C	1.30839200	2.03919700	0.44144600
N	0.90133900	-0.13094100	1.49527000
C	-0.50496200	3.27419200	-0.52097900
C	0.84922700	3.16213500	-0.23301500
H	-2.44029800	2.34774200	-0.38975600
H	2.35689000	1.93104100	0.69040500
H	0.32382600	-0.37300200	2.30211500
H	1.85634600	-0.00595000	1.82572700
H	-0.88000000	4.14506600	-1.04144800

H	1.54141000	3.93992300	-0.52249400
H	-2.73989400	0.23034100	0.52226200
H	-0.57850600	-1.39335000	-1.38299100
H	1.95432100	-2.32114000	-0.51962700
O	0.88930300	-2.36256600	3.51296000
O	-1.56730300	-4.69969900	2.08855500
O	1.92754400	-3.84861900	1.40281500
C	-0.27828700	-4.20567700	2.40001100
C	0.56262900	-4.10073200	1.11273700
C	-0.38800000	-2.88318800	3.16011700
C	-1.16061700	-3.04718000	4.45265600
H	0.20869300	-4.94070300	3.04705000
H	0.45552700	-5.05606200	0.58841700
H	-0.92471400	-2.16274100	2.52908900
H	-2.17525000	-3.37711700	4.24487100
H	2.29496200	-4.62599700	1.83861300
H	1.53117700	-2.61391800	2.83328700
H	-0.66339900	-3.79773300	5.07528500
O	-1.25996100	-1.81234500	5.14601500
H	-0.36529100	-1.50303900	5.32495500
H	-1.88035200	-4.16644300	1.33848600

TS3

C	-0.59658200	-1.74450900	0.00792400
C	-1.43910000	-2.28387300	-1.14547700
H	-1.57137000	-1.50946000	-1.89725700
O	-2.72442900	-2.68496500	-0.71694400
H	-0.89258500	-3.11654000	-1.59178900
H	-2.63355000	-3.46521300	-0.15878600
C	-1.79935300	0.52823700	0.22932300
C	-1.16537500	1.55392900	0.96463200
C	-2.70932800	0.77295200	-0.77226800

N	-1.42433500	-0.75887200	0.78964700
C	-1.45700000	2.87440800	0.61114700
N	-0.34287400	1.07517900	1.96005100
C	-2.97951200	2.09728200	-1.11453800
C	-2.34992900	3.12813900	-0.42373600
H	-3.20759600	-0.04352800	-1.27858900
H	-0.99055000	3.68958400	1.14923400
H	-0.84681200	-0.21584100	1.72150400
H	-0.25124900	1.70497000	2.74693300
H	-3.67940000	2.31795900	-1.90775800
H	-2.56497800	4.15491400	-0.69092000
H	-2.25264900	-1.28049300	1.07895100
O	-0.35457900	-2.82566000	0.86694600
H	0.23159900	-2.50988100	1.57382600
O	2.05758100	1.43429200	0.22318900
O	1.43362000	-1.00918500	1.83093900
O	0.47968600	-0.07354200	-1.40101000
C	1.87582200	-1.01112200	0.47983300
C	0.72858400	-1.18831200	-0.56728600
C	2.77849200	0.20135800	0.23848300
C	3.56543000	0.11396700	-1.05400500
H	2.50955600	-1.89361100	0.39675300
H	1.06722600	-1.98322900	-1.23625500
H	3.49348200	0.21578700	1.06695200
H	4.13775500	-0.81255700	-1.05807800
H	0.72435800	0.73905300	-0.93557100
H	1.44446800	1.47369600	0.98027400
H	2.89428900	0.11596700	-1.91457800
O	4.50093700	1.17718200	-1.15415400
H	4.00881300	2.00401000	-1.19413600
H	0.89422000	-0.19944700	1.98548100

TS3'-4H2O

C	0.07502200	-0.65887400	1.01965200
C	0.56928200	-0.31389900	2.43365100
H	0.73339500	0.75693200	2.54388200
O	1.79634800	-0.95813500	2.72666800
H	-0.20001600	-0.62375100	3.14474000
H	1.64157900	-1.90826700	2.67477700
C	1.65876700	1.16581400	0.02999700
C	1.14673100	2.15485400	-0.82198000
C	2.78067100	1.45086300	0.80387400
N	1.12313800	-0.17627300	0.01452000
C	1.75945800	3.41001800	-0.84490200
N	0.00240900	1.92937900	-1.58320300
C	3.38721400	2.69713900	0.77166000
C	2.86499800	3.68172300	-0.05827200
H	3.17883900	0.66807000	1.43709400
H	1.35412100	4.16813600	-1.50371800
H	-0.11437700	2.56952000	-2.35578600
H	4.25724800	2.89292800	1.38243200
H	3.32319700	4.66066500	-0.10168300
H	1.91197200	-0.77178400	0.27181100
O	0.01920300	-2.02907700	0.89944800
H	-1.44866600	-1.41808100	-1.89735700
O	-3.54672400	1.24977400	-1.01990500
O	-1.55767600	-0.52833500	-1.54365500
O	-1.29028600	1.38864500	0.86371100
C	-2.17870500	-0.63321300	-0.26450700
C	-1.32960300	-0.02619200	0.85289400
C	-3.57923800	-0.02698300	-0.39509300
C	-4.30201600	0.12895900	0.92411200
H	-2.31010800	-1.68603400	-0.01250500
H	-1.84963000	-0.30915000	1.77309600

H	-4.16028600	-0.71200600	-1.02238200
H	-4.28871000	-0.81875300	1.46171600
H	-1.07151200	1.70938600	-0.02951700
H	-3.04272100	1.15890800	-1.83722400
H	-3.80526200	0.88631700	1.53532100
O	-5.66611400	0.47329700	0.72868200
H	-5.69560000	1.31440400	0.26053500
H	-0.18557800	0.96659700	-1.83797200
H	1.04484300	-0.78379200	-1.36358100
O	2.33862800	-3.41947600	0.55486700
H	1.50579000	-2.91880200	0.71888600
H	2.06666200	-4.19913500	0.05914500
O	3.67733000	-1.97817800	-1.40953700
H	3.27718800	-2.47050300	-0.66417400
H	3.90884800	-1.11611600	-1.04615600
O	1.15330000	-1.40085100	-2.23631100
H	0.53470500	-2.24386100	-1.92054000
H	2.09800600	-1.67794000	-2.17648300
O	-0.35008600	-3.04994400	-1.27949200
H	-0.23038200	-2.57637600	-0.27565500
H	-0.01925800	-3.95226600	-1.22025200

TS4

C	-1.81668600	-0.27857900	-0.42117400
C	-3.20861200	-0.52001500	-0.98783700
H	-3.10884900	-0.70408600	-2.05857700
O	-4.01178700	0.61499800	-0.78095400
H	-3.62588100	-1.41000000	-0.51594900
H	-3.84815300	0.75442600	0.19996200
C	0.01200800	1.42134100	-0.56061500
C	0.35147000	1.92923600	0.69918900
C	0.86482800	1.54729400	-1.64866700

N	-1.28018300	0.84141300	-0.79398600
C	1.60326100	2.55151400	0.82215400
N	-0.45218300	1.75294500	1.80025600
C	2.10402200	2.14370600	-1.50292600
C	2.46292900	2.64799100	-0.25347800
H	0.54491500	1.15484600	-2.60533500
H	1.88662600	2.94312800	1.79084100
H	-1.41331100	1.40498300	1.69006700
H	-0.27047400	2.35710300	2.58660700
H	2.77389200	2.22467400	-2.34661200
H	3.42455800	3.12526000	-0.11947700
H	-1.92923000	1.45812500	-1.28298900
O	-2.88352900	0.42926200	1.46761500
H	-3.14828700	-0.33175600	1.99174400
O	1.29007200	-1.52512600	-1.30350000
O	0.15307300	-1.09069000	2.12402700
O	-1.22421900	-2.45425900	-0.98060200
C	0.18103700	-1.67732400	0.83990500
C	-1.17242200	-1.55397000	0.11491600
C	1.45829600	-1.27643200	0.08954900
C	2.63734800	-2.06883000	0.62251800
H	0.23429300	-2.75579900	1.01454800
H	-1.89969800	-1.91367000	0.84213300
H	1.66201900	-0.21816100	0.25229500
H	2.71272600	-1.92830300	1.70018600
H	-0.46429700	-2.25393800	-1.54660600
H	1.86873200	-0.93741000	-1.80073900
H	2.48151400	-3.13153800	0.41615600
O	3.86046300	-1.62350200	0.05832400
H	3.87454100	-1.87335400	-0.87148400
H	0.03347500	-0.12608900	2.05884900

TS4'-4H2O

C	-0.56098700	2.00492500	-0.47948600
C	-1.34424100	3.23399000	-0.90350100
H	-0.66135300	3.88706400	-1.44648400
O	-1.82500000	3.95425500	0.20666700
H	-2.14801300	2.92740000	-1.57001900
H	-2.49148400	3.40319000	0.63665700
C	1.11406900	1.29683300	1.19127500
C	0.66369700	0.32103000	2.08714800
C	2.46241800	1.44650400	0.90949000
N	0.17019400	2.19204000	0.59430800
C	1.59602600	-0.58543200	2.59000900
N	-0.69485600	0.24874000	2.42883900
C	3.38550300	0.56000200	1.44476500
C	2.93860100	-0.47273900	2.26167600
H	2.77183800	2.24065400	0.24272400
H	1.25551600	-1.36509100	3.25960500
H	-1.85097800	0.60838900	0.91434900
H	-0.88429600	-0.47939800	3.10624400
H	4.43625100	0.66416400	1.21356200
H	3.64406300	-1.18516100	2.66771700
H	-0.08904400	3.01175300	1.13994300
O	-2.23267100	1.11286400	0.17091100
H	-2.67192600	0.38707300	-0.43688500
O	2.53677000	0.06722700	-1.85414500
O	-0.65886000	-1.14976500	-0.74677900
O	0.63226500	1.82961900	-2.49550500
C	0.17700300	-0.40385700	-1.58910400
C	-0.24642600	1.08872600	-1.66996400
C	1.60353400	-0.78751600	-1.19778900
C	1.87525900	-2.23032600	-1.59479200
H	0.04802700	-0.72150500	-2.63328300

H	-1.20387300	1.04971500	-2.19352100
H	1.71938300	-0.71386200	-0.11937600
H	1.16274800	-2.89026700	-1.10343000
H	1.53541400	1.54431900	-2.28344900
H	3.34385300	0.10876800	-1.32966100
H	1.76968700	-2.33782400	-2.67821800
O	3.16971200	-2.63583700	-1.17673300
H	3.82154700	-2.16724800	-1.70844100
H	-1.06246800	1.13486100	2.76153600
O	-3.52243200	-1.51743500	1.54797300
H	-3.53070900	-1.26481600	0.60386500
O	-1.00318200	-2.85273600	1.45141200
H	-1.83611900	-2.38938500	1.64795500
H	-0.59437400	-2.28781700	0.77627600
O	-2.79779100	-3.56236700	-0.84761300
H	-2.99227000	-2.61719500	-1.01119500
H	-2.17817700	-3.54140700	-0.10553100
O	-3.17206100	-0.81697800	-1.11322800
H	-3.57286100	-0.61489100	-1.96187600
H	-1.62255400	-1.05387400	-1.02138100
H	-3.44591800	-0.68666400	2.02824800

TS5

C	0.06726000	1.16233400	-0.93313000
C	-0.42187800	2.53956600	-1.33153100
H	-0.14157800	2.67719100	-2.37767200
O	0.17459200	3.57810300	-0.59130500
H	-1.51118900	2.57889300	-1.27691700
H	-0.23996400	3.58113900	0.29709900
C	2.17139800	0.08525300	-0.13626800
C	2.10920100	-0.87244900	0.88615300
C	3.23269300	0.09716300	-1.03063400

N	1.20277400	1.14376000	-0.23559500
C	3.15933800	-1.79747900	0.97528600
N	1.04425900	-0.95043900	1.74543600
C	4.25992300	-0.82947000	-0.93635400
C	4.21465500	-1.77549100	0.08267100
H	3.24445300	0.85571500	-1.80325200
H	3.12229200	-2.53851200	1.76417800
H	-0.54152200	3.44848200	2.51750300
H	1.19990100	-1.41761500	2.62417900
H	5.08025300	-0.80877800	-1.63941800
H	5.00791200	-2.50469900	0.18260200
H	1.57051600	2.07160700	-0.05045100
O	-1.13261800	3.27795800	1.77775700
H	-1.20128600	2.29325200	1.71397400
O	-1.95824900	-1.98535900	0.85228500
O	-1.38835200	0.64515500	1.46588000
O	-0.18672200	-1.21254700	-1.18588300
C	-2.02972500	0.39721400	0.40473100
C	-0.72138100	0.07313800	-1.24105500
C	-2.77681200	-0.93138500	0.36999800
C	-3.37463800	-1.33689100	-0.95864500
H	-2.55052900	1.20968700	-0.11430600
H	-1.48055000	0.22917600	-2.00249000
H	-3.61412100	-0.76845600	1.06352200
H	-3.86508900	-0.47143000	-1.40398800
H	-0.57894100	-1.69273000	-0.43969100
H	-1.50144200	-1.66522800	1.64263800
H	-2.60074100	-1.69283300	-1.64006600
O	-4.37003600	-2.33555800	-0.79122800
H	-3.93841900	-3.14569000	-0.50067500
H	0.36169300	-0.20346100	1.74698000

TS5'-4H2O

C	-0.66948900	-0.59344700	1.76244400
C	-0.18461900	-0.09383400	3.10775700
H	-0.78577400	-0.60319900	3.86371700
O	-0.36889300	1.29215700	3.28037000
H	0.85576800	-0.38316500	3.26464800
H	0.41331300	1.74078200	2.91084600
C	-2.51547300	-0.14515000	0.18647100
C	-2.77784600	0.67089700	-0.92036300
C	-3.29912500	-1.26698300	0.43269000
N	-1.49537800	0.22655600	1.10615700
C	-3.82426800	0.31288000	-1.77422800
N	-1.98116900	1.77370400	-1.21776500
C	-4.32489800	-1.61816900	-0.42805800
C	-4.58432200	-0.81836400	-1.53652900
H	-3.09097000	-1.85807100	1.31503900
H	-4.02553000	0.94039800	-2.63350900
H	1.74589000	1.49781900	1.27660000
H	-2.43705500	2.45962600	-1.80393400
H	-4.92282100	-2.49602200	-0.22822300
H	-5.38763300	-1.07222500	-2.21497500
H	-1.56582000	1.15477900	1.51518300
O	1.84564300	2.19365500	1.96779400
H	2.77534300	2.21760800	2.21300700
O	2.05788700	-3.15622000	0.29965200
O	1.40797200	0.32970900	0.08721400
O	-0.71074000	-2.44347500	0.22844700
C	1.60379700	-0.82601300	0.58440800
C	-0.15415600	-1.78623600	1.30438800
C	1.99117000	-1.91988500	-0.38578800
C	3.34946400	-1.55057600	-0.98468400
H	2.08212100	-0.90357500	1.56842400

H	0.35477500	-2.40909500	2.03018800
H	1.25873900	-1.96371000	-1.19742200
H	3.23343600	-0.64938200	-1.58524500
H	-0.12865100	-3.18678400	0.02315000
H	2.30225700	-3.84065300	-0.33381800
H	4.07174600	-1.35876000	-0.18726400
O	3.81365100	-2.57658500	-1.84488300
H	4.27881500	-3.23519300	-1.32023200
H	-1.48025300	2.20746000	-0.44968800
O	-0.11688200	3.53248500	0.39069300
H	0.37048200	3.44800300	-0.44894900
O	0.32946000	0.55089100	-2.46650900
H	-0.52229300	0.92916500	-2.17818500
H	0.77723000	0.36602300	-1.61863900
O	1.35638400	3.20114100	-2.01207800
H	2.20051700	2.95054400	-1.60127800
H	0.99185000	2.35185900	-2.31210900
O	3.60044200	1.99522900	-0.72292600
H	4.12252400	1.58749900	-1.42182500
H	2.94660300	1.32155900	-0.47550400
H	0.52043200	3.24227100	1.05801900

TS6

C	0.73626100	-2.38624200	2.15489800
C	0.86177000	-1.24018200	1.14135200
H	0.79687800	-0.31646900	1.74013900
C	1.99466000	-2.79209300	2.84774300
C	-0.41147600	-0.25706500	-0.72389400
C	-0.90744800	1.01219800	-0.38894400
C	0.05609800	-0.50911800	-2.00572100
N	-0.35513400	-1.31387100	0.25292400
C	-0.89449800	2.00599800	-1.37233500

N	-1.46709100	1.26983700	0.85503700
C	0.06135100	0.48358000	-2.97526000
C	-0.41414000	1.74750000	-2.64550200
H	0.43318700	-1.49713900	-2.23819300
H	-1.26936900	2.98945100	-1.11689400
H	-1.18161000	-1.30871800	0.84900800
H	-1.55295700	2.25238600	1.07193700
H	0.43561700	0.27312100	-3.96778300
H	-0.41344400	2.53929000	-3.38278900
H	-0.29573500	-2.57555100	-0.34533200
O	-0.33721100	-2.90886300	2.37470700
H	-1.10019900	0.74651900	1.63601900
H	2.54915200	-1.91040700	3.16865600
O	2.02362500	-1.27545300	0.43582800
H	1.76889500	-3.43868400	3.69070500
H	2.62622000	-3.32198200	2.13159600
O	2.82152100	0.77785400	-0.99355400
H	2.45438600	0.05104900	-0.41781700
H	2.04955300	1.22185600	-1.36200600
O	3.13321600	-1.26513600	-3.01262800
H	3.02712400	-0.54386700	-2.36628100
H	2.44275500	-1.11079700	-3.66522500
O	-0.10032300	-3.57273800	-0.84094500
H	1.01267100	-3.49444800	-1.01806500
H	-0.26365000	-4.26497000	-0.18751900
O	2.27112700	-3.19499400	-1.06410500
H	2.20355100	-2.36405700	-0.37183600
H	2.49710100	-2.76010700	-1.90399700

TS7

C	1.19867000	-0.37844500	-0.67595200
C	0.41080100	-1.51215200	-1.33558600

H	0.82470500	-1.87708000	-2.26429900
C	2.64800700	-0.74994400	-0.39357200
C	-1.59029000	-0.59041800	-0.36656100
C	-0.83649700	0.10462100	0.58362400
C	-2.96992900	-0.45686200	-0.41216500
N	-0.91812000	-1.38836000	-1.30857400
C	-1.49527800	0.93734900	1.48348900
N	0.54749700	-0.09291200	0.62177000
C	-3.61644100	0.37537200	0.49018200
C	-2.87515700	1.07246800	1.43822300
H	-3.52457300	-1.00102800	-1.16654300
H	-0.90784100	1.48147400	2.21296900
H	-1.47811900	-1.88767200	-1.98612200
H	-4.69138300	0.48039800	0.44930100
H	-3.37053600	1.72708400	2.14208100
O	1.10289700	0.65529500	-1.57365000
H	2.74392300	-1.51309200	0.37696900
O	0.90927500	-2.99857400	-0.44234600
H	3.12083700	-1.10141600	-1.30988200
H	3.16417300	0.15224600	-0.06126300
H	1.04085100	0.64668600	1.11830200
O	-0.99883900	2.32153000	-1.79473200
H	-0.28461900	1.64817500	-1.66911600
H	-1.69105600	2.07587200	-1.17259000
O	0.73096100	-2.49659400	2.11507000
H	1.59108600	-2.65766100	2.51838700
H	0.81253800	-2.89717500	0.55208300
O	2.43127600	2.00644400	2.00317400
H	2.36957600	2.33145800	1.08109200
O	2.11326400	2.81288300	-0.60931400
H	1.72775500	1.95445000	-0.99135700
H	0.73692900	-1.55405300	1.84756400

H	3.17784200	1.39972000	2.00151300
H	1.38065600	3.43683300	-0.60980500
H	0.29762200	-3.69612700	-0.71736400

TS8

C	1.45196100	-0.20358300	0.62559100
C	2.06720800	0.49682800	-0.55875200
H	3.11175100	0.77658900	-0.56807500
C	2.45980700	-1.10309500	1.31766100
C	-0.04288300	0.53985900	-1.63895600
C	-0.53796300	-0.40409600	-0.73598000
C	-0.84055200	1.14630500	-2.59953800
N	1.32791000	0.85049800	-1.54254800
C	-1.89047400	-0.74353900	-0.82401300
N	0.33293700	-0.99530100	0.15670300
C	-2.17854500	0.81192800	-2.66068900
C	-2.69274700	-0.13544900	-1.77127700
H	-0.40207800	1.87131800	-3.27320200
H	-2.29294700	-1.47544900	-0.13654300
H	1.74241600	1.38337500	-2.30784600
H	-2.82082300	1.27821500	-3.39323400
H	-3.74071200	-0.39849600	-1.82015700
O	1.05448100	0.86519100	1.45927100
H	2.82090900	-1.87105300	0.63517000
O	4.13501700	-1.41904800	-1.88692200
H	3.29983100	-0.50741300	1.66968700
H	1.97757400	-1.58211200	2.16967500
H	-0.10948400	-1.55258200	0.92518500
O	-1.20971600	2.53455200	0.80274700
H	-0.45680400	1.94167000	0.95963900
H	-1.74409800	2.09000200	0.13627200
O	1.66863100	-2.79601500	-1.83299300

H	1.93866400	-3.64012900	-1.45630000
H	3.26770200	-1.86099400	-1.89189100
O	-0.77640000	-2.24132600	2.34791700
H	-0.34230800	-1.17141500	3.02884600
O	0.03741500	-0.26460300	3.52704700
H	0.67003800	0.46449600	2.31381000
H	1.20644100	-2.33693500	-1.11319400
H	-0.22566100	-2.98651300	2.60246000
H	-0.73180100	0.23241600	3.82063100
H	4.02547700	-0.64570200	-2.44807100

TS9

C	1.16336800	2.08194200	-0.29917400
C	-0.03154100	1.41197100	-0.78908400
H	-0.90527400	1.96439800	-1.11007200
C	1.26234100	3.54992700	-0.57298900
C	1.00584100	-0.65658400	-0.46788400
C	2.19634300	0.02301300	-0.15768600
C	0.90421900	-2.05023000	-0.45733900
N	-0.07391600	0.12433500	-0.84894500
C	3.31660700	-0.77271000	0.15796900
N	2.29090600	1.38717600	-0.18191500
C	2.01055900	-2.79396900	-0.12254100
C	3.21924600	-2.14360600	0.18155300
H	-0.04173500	-2.51336900	-0.71197100
H	4.24871200	-0.27575400	0.39174600
H	-0.96386400	-0.34231200	-1.16546700
H	1.95397300	-3.87281000	-0.09900900
H	4.08845800	-2.73404000	0.43864200
O	0.34583000	2.26102700	1.46384100
H	1.56384800	3.70052800	-1.61094500
O	-2.45954200	-0.89554200	-1.60946200

H	0.30567300	4.04124000	-0.41258500
H	2.01219300	3.99506000	0.07605200
O	-2.18765600	1.44300100	1.55503100
H	-2.02651100	0.48893700	1.64967200
H	-1.27005200	1.82733200	1.50583300
O	-3.58611100	1.48623700	-0.77897800
H	-3.09651100	1.52529100	0.07254700
H	-2.63056700	-1.63406800	-1.00182300
H	0.65482600	1.43773500	1.86005200
H	-4.51803500	1.47480600	-0.54085800
H	-2.99442400	-0.13834400	-1.29985200
H	-1.97138600	-3.84013700	-0.23229000
O	-2.53509900	-3.13326700	0.09985200
H	-1.70249900	-1.93441600	1.25266800
O	-1.41803800	-1.26468000	1.89749900
H	-3.32685000	-3.56664600	0.43575300
H	-0.45587600	-1.25674300	1.85870900

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