Study on a New Synthesis Approach of Glyphosate

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ABSTRACT: On the basis of glycine-dimethyl phosphite synthesis of glyphosate, a new synthesis approach of glyphosate, without using triethylamine and the establishment of triethylamine recovery equipment, was designed in the laboratory. The environmental pollutants were reduced. The influences of reactant amount (mol), reaction temperature (°C), and reaction time (min) on the glyphosate yield and purity were investigated. The results showed that the glyphosate yield and purity could be 80.12 and 86.31 wt %, respectively, under the optimum scheme for glyphosate yield (glycine consumption, 0.1 mol; dimethyl phosphite consumption, 0.12 mol; condensation reaction temperature, 50 °C; hydrochloric acid consumption in hydrolysis reaction, 0.35 mol; temperature of acidification with hydrochloric acid, 10 °C; adjusting hydrolysis product pH value, 1.0; time of dropping esterifying liquid into hydrochloric acid in hydrolysis reaction, 80 min; hydrolysis reaction temperature, 120 °C; and vacuum distillation time, 90 min), and the glyphosate yield and purity could be 77.92 and 94.94 wt %, respectively, under the optimum scheme for glyphosate purity (glycine consumption, 0.1 mol; dimethyl phosphite consumption, 0.1 mol; condensation reaction temperature, 50 °C; hydrochloric acid consumption in hydrolysis reaction, 0.35 mol; temperature of acidification with hydrochloric acid, 10 °C; adjusting hydrolysis product pH value, 1.5; time of dropping esterifying liquid into hydrochloric acid in hydrolysis reaction, 60 min; hydrolysis reaction temperature, 110 °C; and vacuum distillation time, 90 min). The product structures under the two schemes were confirmed by means of FTIR (Fourier transform infrared spectroscopy) and ^{1}H NMR (^{1}H nuclear magnetic resonance spectroscopy).

KEYWORDS: glyphosate, glycine, dimethyl phosphite, triethylamine, synthesis approach

■ INTRODUCTION

The chemical name of glyphosate is phosphonomethyl imino acetic acid. As a kind of organic phosphine herbicide, glyphosate, which was developed and commercialized in the 1970s by Monsanto Company, has high efficiency, low toxicity, low residue, and broad spectrum characteristics.[1,2] In recent years, the market demand for glyphosate, which is mainly used for weeding of rubber plantation forests, farmland, orchards, mulberry fields, tea gardens, sugar cane fields, railways, airports, warehouses, power plants, oil depots, and fireproof isolation belts,[3] has increased rapidly.[4]

There are a lot of synthesis methods of glyphosate,[4] such as chloromethyl phosphonic, iminodiacetic (IDA), iminodiaceto-nitrile, ethyl bromoacetate, benzyl chloride, chloroacetic acid, oxidazing N-(phosphonomethyl) iminodiacetic acid (PMIDA), etc. All of these methods have their disadvantages. The source of raw materials in the iminodiacetic or iminodiacetonitrile process is difficult; the ethyl bromoacetate or benzyl chloride process has a high cost of raw materials; the chloroacetic acid process is complex; PMIDA oxidation including an iminodi-acetic acid−charcoal-activated process, in which glyphosate and activated carbon are mixed together, leads to postprocessing operation trouble and a large amount of waste liquid;[5] the concentrated sulfuric acid oxidation process has an easily carbonized product; the hydrogen peroxide oxidation process, in which the glyphosate yield is not high, has a lot of industrial wastewater, waste gases, and residues; the air/oxygen continuous oxidation process has advantages of good quality product, high yield, and less environmental pollution but has defects of the presence of precious metal leaching,[6] high energy

consumption, and advanced investment with precious metals[7−10] (palladium, rhodium, osmium, and others) and activated carbon[11] as catalysts; and the intermittent air oxidation process has the disadvantages of low reaction efficiency and high investment.[2]

The process of glycine-dimethyl phosphite synthesis of glyphosate is mainly used in China.[12,13] It has the characteristics of a stable technique and high yield, but there are disadvantages in the process, such as generating a large amount of environmental pollution and waste liquid, waste processing difficulty, high investment, etc. Triethylamine, for instance, as a catalyst needed in the process, which is one of the harmful environmental pollutants that are harmful to human health, is one of 189 hazardous air pollutants included in the new Clean Air Act by the U.S. Congress.[14] Therefore, it is necessary to invest in the establishment of recovery equipment for triethylamine and consume a large amount of sodium hydroxide.[15] A large amount of sodium chloride waste liquid that still contains a small amount of glyphosate can be produced in the production process of 1 ton of glyphosate and is not allowed for the direct emissions.[16] After the liquid waste is processed by conforming with the GB 8978-1996 "Integrated Wastewater Discharge Standard", the production cost will be increased substantially. In light of the malpractice of existence

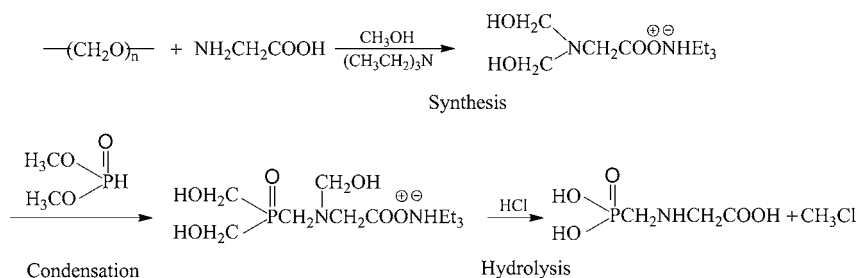**Scheme 1. Original Synthesis Process of Glyphosate**

Synthesis

Condensation   Hydrolysis

in the process, a new laboratory synthesis approach of glyphosate without using triethylamine is designed.

■ DESIGN IDEAS

Analysis of the Original Process. The original process is a three-step reaction (synthesis, condensation, and hydrolysis)

Scheme 2. Formaldehyde Reacts with Glycine To form N-Hydroxymethyl Glycinate or N,N-Dihydroxy Methyl Glycine
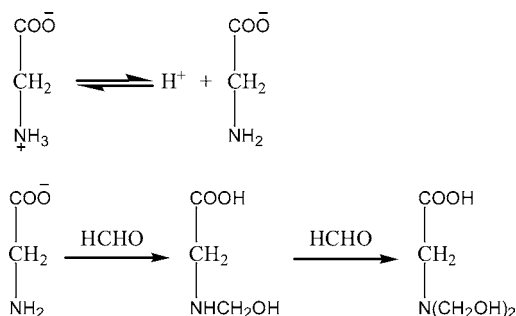
(Scheme 1).[4] The synthesis and condensation reactions proceed in anhydrous methanol and paraformaldehyde, which will be depolymerized to hemiacetal in triethylamine−methanol

solution under the catalytic action of triethylamine, and then react with glycine, dimethyl phosphite, and hydrochloric acid to form glyphosate and glycine are not soluble in. So, the triethylamine is needed to the depolymerization of paraformaldehyde in the original process. The recovery of the triethylamine must be accompanied by a large amount of waste brine production.

New Process Design. According to the principle shown in Scheme 2,[17,18] the molar ratio of formaldehyde and glycine in the reaction is determined to be 1:1. The new process is also a three-step reaction (synthesis, condensation, and hydrolysis). The new synthesis reaction in which the formaldehyde solution participates is carried out instead of the original reaction in which paraformaldehyde and anhydrous methanol participate. The generated intermediate in the new synthesis reaction may be N-hydroxymethyl glycinate hydrochloride, and the product of condensation reaction, in which N-hydroxymethyl glycinate hydrochloride and dimethyl phosphite participate, is hydrolyzed with hydrochloric acid. The reaction is shown in Scheme 3.

■ EXPERIMENTAL PROCEDURES

Synthesis of Glyphosate. *Materials and Equipment.* The materials and equipment are as follows: glycine (Tianjin Guangfu

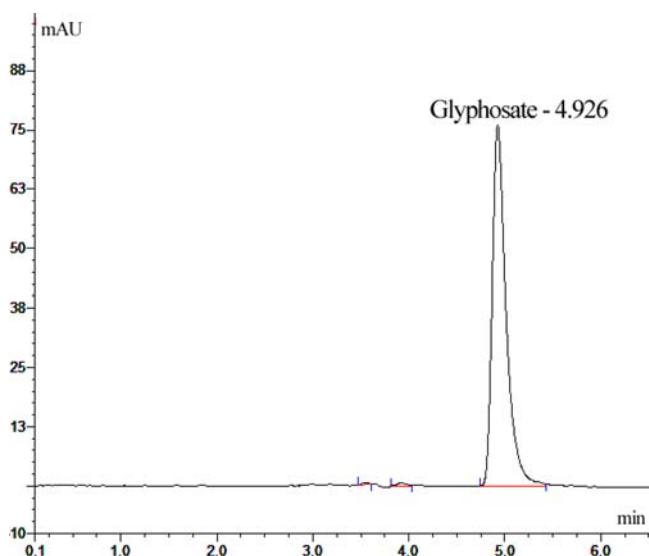**Scheme 3. Synthesis, Condensation, and Hydrolysis of the Three-Step Reaction of the New Process**

Synthesis

Condensation

Hydrolysis
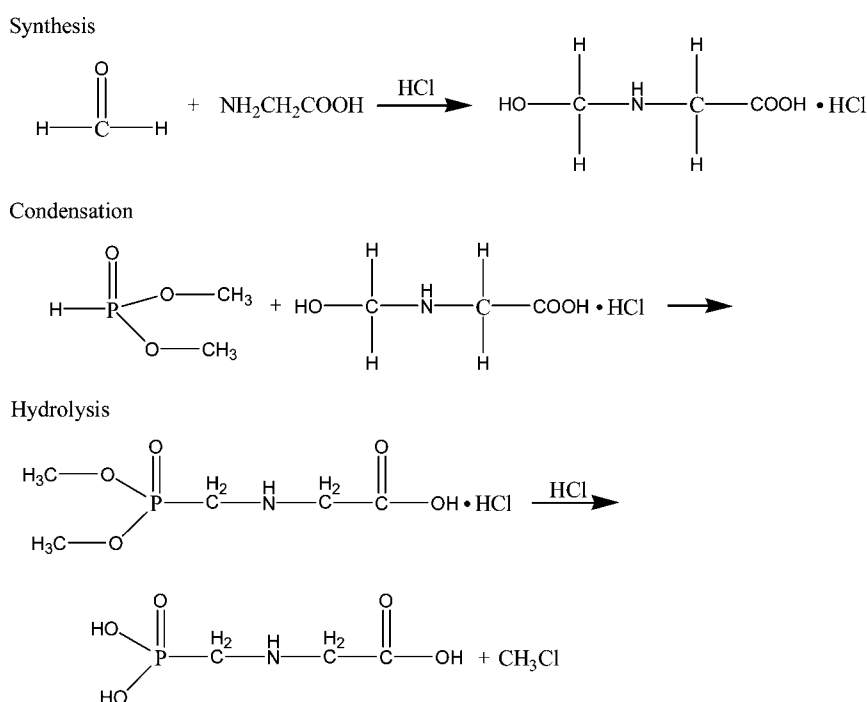
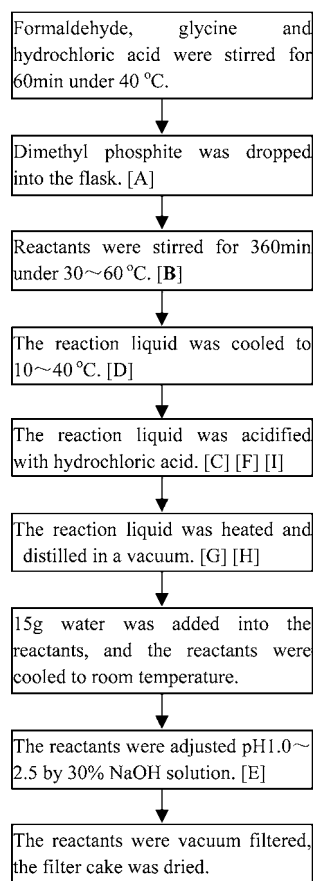**Figure 1.** HPLC chromatogram of glyphosate standard.

Figure 2. Processing procedure flowchart.

Fine Chemical Research Institute, 98 wt %), formaldehyde (Shenyang Tiangang Chemical Reagent Factory, 37 wt %), hydrochloric acid (Sinopharm Chemical Reagent Co., Ltd., 36 wt %), dimethyl phosphite (Xuzhou Guineng Chemical industry Co., Ltd., 98 wt %), stepless speed stirrer (Gongyi Yuhua Instrument Co., Ltd., DW-1-60W), circulating water pump (Gongyi Yuhua Instrument Co., Ltd., SHZ-DIII), and pH meter [Mettler Toledo Instrument (Shanghai) Co., Ltd., FE20K].

Processing Procedure. Gradually added were 0.1 mol each of formaldehyde, glycine, and hydrochloric acid in a four-neck flask

Table 1. Factor Levels of the Orthogonal Experiment

level	factors[a]								
	A	B	C	D	E	F	G	H	I[b]
1	0.08	30	0.20	10	1.0	20	100	60	1
2	0.10	40	0.25	20	1.5	40	110	90	2
3	0.12	50	0.30	30	2.0	60	120	120	
4	0.14	60	0.35	40	2.5	80	130	150	

[a]A, dimethyl phosphite consumption (mol); B, condensation reaction temperature (°C); C, hydrochloric acid consumption in hydrolysis reaction (mol); D, temperature of acidification with hydrochloric acid (°C); E, adjusting hydrolysis product pH value; F, dropping time of the esterifying liquid or hydrochloric acid in hydrolysis reaction (min); G, hydrolysis reaction temperature (°C); H, vacuum distillation time (min); and I, dropping sequence of the esterifying liquid and hydrochloric acid in hydrolysis reaction. [b]1, dropping the hydrochloric acid into the esterifying liquid; and 2, dropping the esterifying liquid into the hydrochloric acid.

equipped with stirrer, reflux condenser, thermometer, and dropping funnel. After it was stirred for 60 min under 40 °C, dimethyl phosphite (about 0.8−1.4 mol) was dropped into the flask. After it was stirred for 360 min under 30−60 °C, the reaction liquid was cooled to 10−40 °C and participated in acidification with hydrochloric acid (about 0.2−0.35 mol) in 20−80 min. Then, the reaction liquid was heated up to 100−130 °C and distilled for 60−150 min in 0.09 MPa vacuum degree with a recovery condenser instead of a reflux condenser. Then, the reactants, into which 15 g of water was added, were cooled to room temperature and adjusted to pH 1.0−2.5 by 30% NaOH solution and then were vacuum filtered. The filter cake was dried at 100 °C in an air oven overnight. The product was thus obtained and reserved. Through weighing the product, measuring the content, and confirming the structure, the purity and yield of the glyphosate in the product could be calculated.

Analysis of Glyphosate by High-Performance Liquid Chromatography (HPLC). According to GB12686-2004 standard[19] for reference, the product was measured by HPLC for qualitative and quantitative analyses.

Materials and Equipment. The materials and equipment were as follows: potassium dihydrogen phosphate (Sinopharm Chemical Reagent Co., Ltd., 99.5 wt %), purified water (Hangzhou Wahaha Group Co., Ltd.), methanol (Sinopharm Chemical Reagent Co., Ltd., HPLC), phosphoric acid (Tianjin Dongli District Tianda Chemical Reagent Factory, 85 wt %), glyphosate standard (Shenzhen Star Care Technology Co., Ltd., 99.9 wt %), HPLC system (DIONEX P680 HPLC Pump, Solvent Rack SOR-100, DIONEX UVD170U), column (Agilent ZORBAX SAX, 5 μm, 4.6 mm × 250 mm), solvent filter (Tianjin Dongkang Science and Technology Co., Ltd. DP-01), ultrasonic cleaner (Kunshan Ultrasonic Instrument Co., Ltd. KQ5200DB), and analytical balance [Mettler Toledo Instrument (Shanghai) Co., Ltd. AL204].

Chromatographic Conditions. The mobile phase was prepared by adding 150 mL of methanol to the solution, which was made by dissolving 13.6 g of potassium dihydrogen phosphate in 850 mL of water, and then, the solution was ultrasonicly oscillated for 10 min after the solution was adjusted to pH 2.0 by phosphoric acid. The flow rate was 1 mL/min. The volume of injection was 20 μL. UV detection was 200 nm. The column temperature was room temperature.

Preparation and determination of standard or sample solution were the same as GB12686-2004 standard. The glyphosate standard chromatographic diagram is shown in Figure 1. The data were processed with Chromeleon Chromatography Software. The external standard method was employed for quantitative analysis after qualitative analysis according to the standard retention time. So, the glyphosate purity and yield could be calculated.

Optimization of Process Conditions. The procedure in the synthesis process of glyphosate is shown in Figure 2. According to Figure 2, the influences of related factors, in the processes of condensation, hydrolysis, and adjustment of the hydrolysis product pH

Table 2. Results and Data of Orthogonal Experiment Design

no.	A^a	B^a	C^a	D^a	E^a	F^a	G^a	H^a	I^a	glyphosate results (wt %) yield	purity
1	0.08	30	0.20	10	1.0	20	100	60	1	0	0
2	0.08	30	0.25	20	2.5	80	120	120	2	12.91	16.20
3	0.08	40	0.30	40	1.0	40	120	150	1	0	0
4	0.08	40	0.35	30	2.5	60	100	90	2	34.72	65.19
5	0.08	50	0.20	30	1.5	80	110	150	1	0	0
6	0.08	50	0.25	40	2.0	20	130	90	2	23.55	31.34
7	0.08	60	0.30	20	1.5	60	130	60	1	39.19	39.83
8	0.08	60	0.35	10	2.0	40	110	120	2	13.64	19.01
9	0.10	30	0.30	40	2.0	80	110	60	1	24.67	30.85
10	0.10	30	0.35	30	1.5	20	130	120	2	19.25	19.76
11	0.10	40	0.20	10	2.0	60	130	150	1	0	0
12	0.10	40	0.25	20	1.5	40	110	90	2	5.29	93.38
13	0.10	50	0.30	20	2.5	20	100	150	1	0	0
14	0.10	50	0.35	10	1.0	80	120	90	2	80.09	81.02
15	0.10	60	0.20	30	2.5	40	120	60	1	0	0
16	0.10	60	0.25	40	1.0	60	100	120	2	9.33	9.64
17	0.12	30	0.30	10	2.5	40	130	90	1	39.69	22.04
18	0.12	30	0.35	20	1.0	60	110	150	2	0	0
19	0.12	40	0.20	40	2.5	20	110	120	1	0	0
20	0.12	40	0.25	30	1.0	80	130	60	2	24.32	23.24
21	0.12	50	0.30	30	2.0	60	120	120	1	27.89	45.55
22	0.12	50	0.35	40	1.5	40	100	60	2	49.18	75.13
23	0.12	60	0.20	20	2.0	80	100	90	1	0	0
24	0.12	60	0.25	10	1.5	20	120	150	2	0	0
25	0.14	30	0.20	40	1.5	60	120	90	1	0	0
26	0.14	30	0.25	30	2.0	40	100	150	2	0	0
27	0.14	40	0.30	10	1.5	80	100	120	1	21.35	36.01
28	0.14	40	0.35	20	2.0	20	120	60	2	42.01	57.18
29	0.14	50	0.20	20	1.0	40	130	120	1	0	0
30	0.14	50	0.25	10	2.5	60	110	60	2	23.84	77.81
31	0.14	60	0.30	30	1.0	20	110	90	1	46.13	55.91
32	0.14	60	0.35	40	2.5	80	130	150	2	0	0
glyphosate yield											
mean1	15.501	12.065	0	22.326	19.984	16.368	14.323	25.401	12.433		
mean 2	17.329	15.961	12.405	12.425	16.783	13.475	14.196	28.684	21.133		
mean 3	17.635	25.569	24.865	19.039	16.470	16.871	20.363	13.046			
mean 4	16.666	13.536	29.861	13.341	13.895	20.418	18.250	0			
glyphosate purity											
mean 1	21.446	11.106	0	29.486	21.226	20.524	23.246	38.005	14.387		
mean 2	29.331	34.375	31.451	25.824	33.014	26.195	34.620	43.610	35.556		
mean 3	20.745	38.856	28.774	26.206	22.991	29.753	24.994	18.271			
mean 4	28.364	15.549	39.661	18.370	22.655	23.415	17.026	0			

^{a}The same as Table 1.

value by alkali, on the yield and the purity of glyphosate were inferred and investigated.

(A) Dimethyl phosphite consumption might have an influence on results (yield and purity). Lower consumption would result in an incomplete condensation product; higher consumption would result in phosphorous acid and methyl chloride that would be formed during the hydrolysis reaction.

(B) The condensation reaction belonged to exothermic reaction, so the temperature needed to be controlled strictly. A higher temperature would result in side reactions, and a lower temperature would result in incomplete reaction.

(C) Hydrochloric acid consumption in hydrolysis reaction. Lower consumption would result in the reaction liquid in low concentration acid environment that was not favorable for a hydrolysis reaction; higher consumption would result in more vacuum distillation time and more 30% NaOH solution consumption.

(D) According to the literature,[20,21] the acidification temperature below 40 °C is appropriate. A higher temperature might result in side reactions, which would affect the results.

(E) The hydrolysis product pH value was adjusted with 30% NaOH solution. One alkaline group (−NHR) and two acidic groups (−COOH, −PO$_3$H$_2$) were in the glyphosate structure. The pH value would directly affect product solubility in water.

(F and I) The dropping time of the esterifying liquid or hydrochloric acid and the dropping sequence of the esterifying liquid and hydrochloric acid in hydrolysis reaction. There was a chemical exothermic reaction of the esterifying liquid mixed with hydrochloric acid. If the dropping speed was too fast, the reaction liquid would heat too fast, and the side reactions might occur. The dropping esterifying liquid into hydrochloric acid might be superior to the dropping hydrochloric acid into esterifying liquid. If the latter was picked, the low concentration acid environment, which was not favorable for the

Table 3. Variance Analysis for Table 2 (Glyphosate Yield)

source	type III sum of squares	df	mean square	F	P
corrected model	10395.647	24	433.152	1.495	0.304
intercept	9013.209	1	9013.209	31.100	0.001
A[a]	21.442	3	7.147	0.025	0.994
B[a]	885.325	3	295.108	1.018	0.440
C[a]	3691.956	2	1845.978	6.370	0.027
D[a]	533.231	3	177.744	0.613	0.628
E[a]	149.467	3	49.822	0.172	0.912
F[a]	194.663	3	64.888	0.224	0.877
G[a]	221.682	3	73.894	0.255	0.856
H[a]	4092.276	3	1364.092	4.707	0.042
I[a]	0.000	0			
error	2028.679	7	289.811		
total	21437.535	32			
corrected total	12424.326	31			

[a]The same as Table 1.

Table 4. Variance Analysis for Table 2 (Glyphosate Purity)

source	type III sum of squares	df	mean square	F	P
corrected model	24516.466	24	1021.519	3.277	0.055
intercept	19954.526	1	19954.526	64.011	0.000
A[a]	486.444	3	162.148	0.520	0.682
B[a]	4497.964	3	1499.321	4.810	0.040
C[a]	3581.331	2	1790.666	5.744	0.033
D[a]	529.710	3	176.570	0.566	0.654
E[a]	703.938	3	234.646	0.753	0.555
F[a]	372.481	3	124.160	0.398	0.759
G[a]	1273.580	3	424.527	1.362	0.330
H[a]	9485.880	3	3161.960	10.143	0.006
I[a]	0.000	0			
error	2182.138	7	311.734		
total	46653.130	32			
corrected total	26698.605	31			

[a]The same as Table 1.

Table 5. Variance Analysis for Glyphosate Yield

source	type III sum of squares	df	mean square	F	P
corrected model	10395.647	24	433.152	1.495	0.304
intercept	9013.209	1	9013.209	31.100	0.001
A[a]	21.442	3	7.147	0.025	0.994
B[a]	885.325	3	295.108	1.018	0.440
C[a]	4297.563	3	1432.521	4.943	0.038
D[a]	533.231	3	177.744	0.613	0.628
E[a]	149.467	3	49.822	0.172	0.912
F[a]	194.663	3	64.888	0.224	0.877
G[a]	221.682	3	73.894	0.255	0.856
H[a]	4092.276	3	1364.092	4.707	0.042
error	2028.679	7	289.811		
total	21437.535	32			
corrected total	12424.326	31			

[a]The same as Table 1.

Table 6. Variance Analysis for Glyphosate Purity

source	type III sum of squares	df	mean square	F	P
corrected model	24516.466	24	1021.519	3.277	0.055
intercept	19954.526	1	19954.526	64.011	0.000
A[a]	486.444	3	162.148	0.520	0.682
B[a]	4497.964	3	1499.321	4.810	0.040
C[a]	7166.471	3	2388.824	7.663	0.013
D[a]	529.710	3	176.570	0.566	0.654
E[a]	703.938	3	234.646	0.753	0.555
F[a]	372.481	3	124.160	0.398	0.759
G[a]	1273.580	3	424.527	1.362	0.330
H[a]	9485.880	3	3161.960	10.143	0.006
error	2182.138	7	311.734		
total	46653.130	32			
corrected total	26698.605	31			

[a]The same as Table 1.

Table 7. Results of Validation Experiment

scheme[a]	trial no.	glyphosate (wt %) yield	purity
$A_3B_3C_4D_1E_1F_4G_3H_2I_2$	1	80.97	85.85
	2	78.81	84.47
	3	80.58	88.62
	average value	80.12	86.31
$A_2B_3C_4D_1E_2F_3G_2H_2I_2$	1	78.58	95.83
	2	76.33	95.61
	3	78.84	93.39
	average value	77.92	94.94

[a]The same as Table 1.

hydrolysis reaction, would last for some time, and the reaction time would be prolonged. If the former was picked, the relatively high concentration acid environment would be favorable for the hydrolysis reaction.

(G) The hydrolysis reaction temperature might affect the results. The lower temperature would result in an incomplete hydrolysis reaction. As the temperature increased, chlorine methane and some water in the hydrolysis reaction would evaporate, which would be favorable for a hydrolysis reaction. However, if the temperature is too high, the side reactions would occur.

(H) The vacuum distillation time might affect the results. A too short time would result in an incomplete hydrolysis reaction; a too long time would result in partial decomposition of the product.

The orthogonal experiment design was carried out with glyphosate yield and glyphosate purity as evaluation indexes, and the above nine factors were investigated by the method of $L_{32}(4^8, 2^1)$ orthogonal design. The experimental design and data processing were dealt with SPSS 19 (Statistical Product and Service Solutions) software. The factors and levels are shown in Table 1, the results and data are shown in Table 2, and the variance analysis is shown in Tables 3 and 4.

■ RESULTS AND DISCUSSION

According to Tables 3 and 4, the sum of squares of deviations of factor I was minimum. The minimum sum of squares of deviations in non-nullable column orthogonal design could be taken as an error estimation.[22] On that basis, the data processing was dealt with SPSS 19 again. The results of data processing and analysis are shown in Tables 2, 5, and 6.

For the results from Tables 2 and 5, the effect factors sequence of glyphosate yield was C > H > B > D > G > F > E >
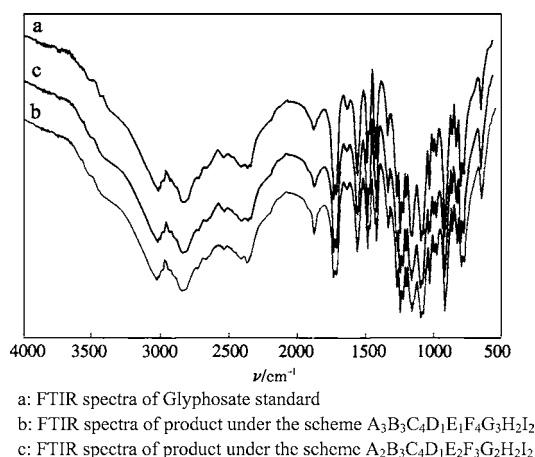
a: FTIR spectra of Glyphosate standard
b: FTIR spectra of product under the scheme $A_3B_3C_4D_1E_1F_4G_3H_2I_2$
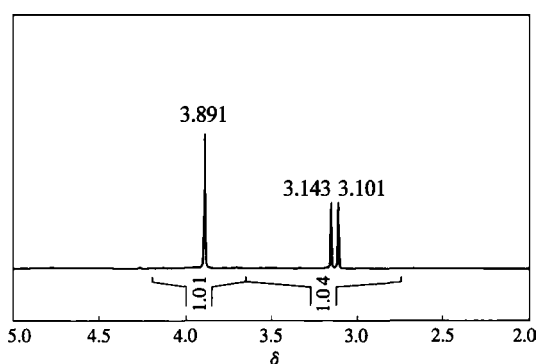c: FTIR spectra of product under the scheme $A_2B_3C_4D_1E_2F_3G_2H_2I_2$

Figure 3. FTIR spectra of glyphosate standard and validation experimental products. (a) FTIR spectra of glyphosate standard, (b) FTIR spectra of product under the scheme $A_3B_3C_4D_1E_1F_4G_3H_2I_2$, and (c) FTIR spectra of product under the scheme $A_2B_3C_4D_1E_2F_3G_2H_2I_2$.

Figure 4. ^{1}H NMR spectra of product under the scheme $A_3B_3C_4D_1E_1F_4G_3H_2I_2$.
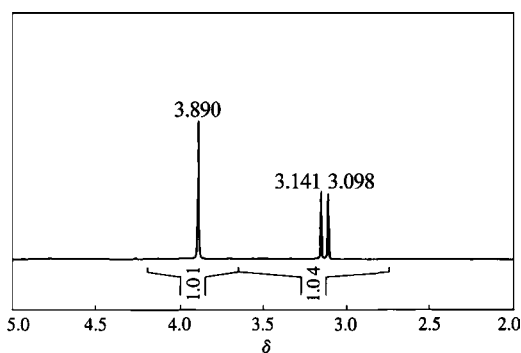

Figure 5. ^{1}H NMR spectra of product under the scheme $A_2B_3C_4D_1E_2F_3G_2H_2I_2$.

A, the optimum scheme was $A_3B_3C_4D_1E_1F_4G_3H_2I_2$, and hydrochloric acid consumption in the hydrolysis reaction and vacuum distillation time gave notable effects on glyphosate yield ($P < 0.05$). For the results from Tables 2 and 6, the effect factors sequence of glyphosate purity was H > C > B > G > E > D > A > F, the optimum scheme was $A_2B_3C_4D_1E_2F_3G_2H_2I_2$, the condensation reaction temperature and hydrochloric acid consumption in hydrolysis reaction gave notable effects on glyphosate purity ($P < 0.05$), and the vacuum distillation time gave a very notable effect on glyphosate purity ($P < 0.01$).

Validation Experiments. The optimum scheme for glyphosate yield was $A_3B_3C_4D_1E_1F_4G_3H_2I_2$ as follows: glycine consumption, 0.1 mol; dimethyl phosphite consumption, 0.12 mol; condensation reaction temperature, 50 °C; hydrochloric acid consumption in hydrolysis reaction, 0.35 mol; temperature of acidification with hydrochloric acid, 10 °C; adjusting hydrolysis product pH value, 1.0; time of dropping esterifying liquid into the hydrochloric acid in hydrolysis reaction, 80 min; hydrolysis reaction temperature, 120 °C; and vacuum distillation time, 90 min. The optimum scheme for glyphosate purity was $A_2B_3C_4D_1E_2F_3G_2H_2I_2$ as follows: glycine consumption, 0.1 mol; dimethyl phosphite consumption, 0.10 mol; condensation reaction temperature, 50 °C; hydrochloric acid consumption in hydrolysis reaction, 0.35 mol; temperature of acidification with hydrochloric acid, 10 °C; adjusting hydrolysis product pH value, 1.5; time of dropping esterifying liquid into the hydrochloric acid in hydrolysis reaction, 60 min; hydrolysis reaction temperature, 110 °C; and vacuum distillation time, 90 min.

We repeated the experiment three times, respectively, according to the optimum schemes of $A_3B_3C_4D_1E_1F_4G_3H_2I_2$ and $A_2B_3C_4D_1E_2F_3G_2H_2I_2$ and then calculated the purity and yield of glyphosate. The results of validation experiments are shown in Table 7.

Verifying the Product Identity. The structures of validation experimental products were characterized by FTIR (Fourier transform infrared spectroscopy) and ^{1}H NMR (^{1}H nuclear magnetic resonance spectroscopy).

Equipment. The equipement used was a Fourier transform infrared spectrometer (Bruker Optics, TENSOR 27), Bruker-400 MHz NMR (Bruker BioSpin, ARX400). The FTIR spectra are shown in Figure 3; the ^{1}HNMR spectra are shown in Figures 4 and 5.

We used a previously reported infrared spectrum[2,23] as a reference to analyze the FTIR spectra of glyphosate standard and validation experimental products. According to Figure 3, absorption bands and the strength of glyphosate standard and validation experimental products in the FTIR spectra were compared, respectively, and they were approximately equal. Band assignments are shown in Table 8.

Following are the results from Figure 4: ^{1}H NMR (D_2O, 500 MHz), δ: 3.891 (s, 2H, CH_2CO), 3.143, 3.101 (d, 2H, CH_2PO). Following are the results from Figure 5: ^{1}H NMR (D_2O, 500 MHz), δ: 3.890 (s, 2H, CH_2CO), 3.141, 3.098 (d, 2H, CH_2PO). The ^{1}H NMR spectra of validation experimental products are in close agreement with the reported magnetic resonance imaging of glyphosate.[24]

Through the optimization of the glyphosate synthesis process conditions, the results showed that the glyphosate yield and purity could be as high as 80.12 and 86.31 wt %, respectively, in the selection of the optimal process conditions for glyphosate yield, and the glyphosate yield and purity could be as high as 77.92 and 94.94 wt %, respectively, in the selection of the optimal process conditions for glyphosate purity. The validation experimental results showed good reproducibility.

As compared to glycine-dimethyl phosphite synthesis of glyphosate, the new synthesis technology of glyphosate, without using triethylamine and methanol, does not require establishment of triethylamine recovery equipment. It can reduce methyl chloride yield and relative investment. The reduction of pollutants formation is conducive to realization of chemical substances in environment friendly emissions. The new synthesis approach of glyphosate is still studied in

Table 8. FTIR Band Assignments for Glyphosate

band assignment	IR (KBr) v (cm^{-1})		
	glyphosate standard	product under the scheme $A_3B_3C_4D_1E_1F_4G_3H_2I_2$	product under the scheme $A_2B_3C_4D_1E_2F_3G_2H_2I_2$
O−H stretching vibration of −COOH and −OP(OH)$_2$ groups	3014.2	3016.7	3014.8
	2806.6	2808.9	2807.7
C=O strong stretching vibration of −COOH groups	1731.3	1732.4	1730.6
	1710.8	1712.1	1711.4
P=O stretching vibration of −OP(OH)$_2$ groups	1160.1	1163.8	1161.5
O−H bending vibration of −COOH and −OP(OH)$_2$ groups	1422.1	1421.7	1421.3
	920.4	923.3	921.2

laboratory, and the intermediate, impurities, side reaction mechanisms, and byproducts in the new synthesis approach remain for further research.

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Notes
The authors declare no competing financial interest.

■ REFERENCES

(1) Murtaza, F. A.; William, C. S. Closing down on glyphosate inhibition-with a new structure for drug discovery. *Proc. Natl. Acad. Sci.* **2001**, *6* (98), 2944−2946.

(2) Zhou, S.; Chen, J.; Wang, S.; Yang, X.; Zhang, H.; Wu, J.; Yu, J. Improved Synthesis of Glyphosate. *Fine Chem.* **2009**, *26* (6), 605−608.

(3) Xu, B. Study on the Catalytic synthesis process of glyphosate with high level vanadyl sulfate. *Sichan Chem. Ind. Corros. Control* **1999**, *2* (2), 16.

(4) Lu, Y.; Tao, J.; Zhou, Z. The Research of Glyphosate Synthetic Technology. *Chem. Intermed.* **2009**, *5* (8), 47−50.

(5) Liu, G. The Cleaner Production of Glyphosate. *Chin. J. Pestic.* **2005**, *44* (12), 549.

(6) Leiber, M. A.; Ebner, J. R. Use of a supplemental promoter in conjunction with a carbon-supported, noble-metal-containing catalyst in liquid phase oxidation reactions. U.S. Patent No. 7,193,107, 2007.

(7) Franz, J. E. Process for producing N-phosphonomethylglycine. U.S. Patent No. 3,950,402, 1976.

(8) Felthouse, T. R. Oxidation with encapsulated co-catalyst. U.S. Patent No. 4,582,650, 1986.

(9) Leiber, M. A.; Ebner, J. R.; Wan, K.-T.; Woods, A.; Rogers, P. Use of a supplemental promoter in conjunction with a carbon-supported, noble-metal containing catalyst in liquid phase oxidation reactions. U.S. Patent No. 6,586,621, 2003.

(10) Hitzler, M.; Thalhammer, F.; Hammer, B. Method for producing n-(phosphonomethyl) glycine. U.S. Patent No. 6,730,813, 2004.

(11) Hayden, R. A.; Matviya, T. M. Method for the manufacture of N-phosphonomethylglycine from N-phosphonomethyliminodiacetic acid using a catalytic carbon. U.S. Patent No. 5,962,729, 1999.

(12) Gao, L.; Hu, J.; Li, F. Glycine-dimethtl phosphite synthesis of glyphosate. *Shanxi Chem. Ind.* **2011**, *31* (3), 15.

(13) Dai, B.; Zhang, H. The latest development in the technique of glyphosate production. *China Agrochemicals* **2006**, *2* (4), 22.

(14) The United States Congress. *United States Code-2008-title42-Chapter85*; 2008; p 5714.

(15) Chen, X. A Continuous Recovery Process of Triethyl Amine in Producing Glyphosate. *Mod. Chem. Ind.* **2004**, *24* (3), 49.

(16) Ministry of Environmental Protection of the People's Republic of China; General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China. *China National Standard* GB 8978-1996 Integrated wastewater discharge standard, 1996; p 10.

(17) Dong, W. B. *Biological Engineering Analysis*; Chemical Industry Press: Beijing, 2006; p 89.

(18) Yao, Y.; Cui, C.; Qiu, L.; Chen, L. Determination of hydrolysis degree of soy protein: A comparison between methods of pH-stat and formol-titration. *Sci. Technol. Food Ind.* **2008**, *29* (9), 269.

(19) General Administration of Quality Supervision, Inspection and Quarantine of the People's Republic of China; Standardization Administration of the People's Republic of China. *China National Standard* GB 12686-2004 Glyphosate technical, 2004; pp 3−5.

(20) Lu, Y.; Tao, J. Z.; Zhou, Z. L. Research on Synthesis Technology of Glyphosate. *Technol. Dev. Chem. Ind.* **2009**, *38* (9), 6.

(21) Zha, Z. J.; Yin, Y. W.; Xie, Z. Y.; Yuan, K. The Technology Improvement of the Synthesis of Glyphosate by Glycine. *Chin. J. Pestic. Sci.* **2008**, *10* (1), 106.

(22) Sun, Y. SPSS13.0 Software Applied to Chemical Orthogonal Design Experiments. *Chin. J. Chem. Educ.* **2006**, *27* (8), 48−49.

(23) Undabeytia, T.; Morillo, E.; Maqueda, C. FTIR Study of Glyphosate-Copper Complexes. *J. Agric. Food Chem.* **2002**, *50* (7), 1918−1921.

(24) Glyphosate MRI (^{1}H NMR); http://www.basechem.org/chemical/image/60995.