

Synthesis and Solid-state Reaction of 1-[3'-(Benzotriazol-2''-yl)-4'-hydroxybenzoyl]-3-methyl-5-pyrazolones

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A new kind of UV stabilizers, 1-(3'-(benzotriazol-2''-yl)-4'-hydroxy-benzoyl)-3-methyl-5-pyrazolones (**1a—d**), was synthesized with the aim to bind them chemically to certain polymers. The reaction of **1d** with substituted benzaldehydes **4** in the molten state at 150°C and in the solid state at room temperature produced the condensation products 1-(3'-(5''-chlorobenzotriazol-2''-yl)-4'-hydroxy-5'-chlorobenzoyl)-3-methyl-4-arylmethylene-5-pyrazolones (**2**) and 4,4'-arylmethylene-bis [1-(3'-(5''-chloro-benzotriazol-2''-yl)-4'-hydroxy-5'-chloro-benzoyl)-3-methyl-5-pyrazolone]s (**3**), respectively, as the major product. On the other hand, the reaction of **1d** with **4** at 50°C in chloroform solution proceeded non-selectively to give a mixture of **2** and **3**.

Keywords Pyrazolones, synthesis, solid-state reaction, photostabilizer

Introduction

There are many kinds of photostabilizers to reduce the undesirable degradation effects of solar irradiation on natural or synthetic polymers, among which 2-hydroxyphenylbenzotriazole derivatives are important UV absorbers in protecting polymers against the UV rays from sun light.¹ However, the stabilizers are often denuded from the surface of the protected polymers. The strong attachment (preferably through a chemical bond) of the stabilizers to the surface is crucial for enhancing the durability of the stabilizers. The stabilizer containing a reactive group can be linked to a polymer through the formation of a chemical bond between the reactive group and an active group at the surface of polymers to be protected.

It is desirable to carry out the binding reaction of such a stabilizer to the surface of a solid polymer under easily accessible conditions. We have approached this binding reaction using the solid-state reaction of the titled compounds. In most natural and synthetic polymers, there are various photosensitive groups such as carbonyl group.² Under the solar irradiation, the carbonyl groups were normally transformed into their excited states which may contribute to the formation of singlet oxygen (¹O₂) and free radicals,³ initiating the photooxidation of the polymer.⁴

Recently we have found that the solid-state reactions between carbonyl compounds and heterocyclic compounds containing acidic C—H bond occurred efficiently at room temperature.⁵⁻⁸ These solid-state reactions may be applied to bind stabilizers to polymers to be protected. Based upon this idea, we synthesized a new series of compounds, 1-(3'-(benzotriazol-2''-yl)-4'-hydroxybenzoyl)-3-methyl-5-pyrazolones (**1a—d**) which contain two functions, the reactive function of 1-substituted-3-methyl-5-pyrazolone and the UV absorbing function of 2-hydroxyphenylbenzotriazole. The solid-state reaction of **1d** with aromatic aldehydes **4** was investigated as a model reaction for the linking of a photostabilizer to polymers, from which two kinds of condensation products were obtained.

Results and discussion

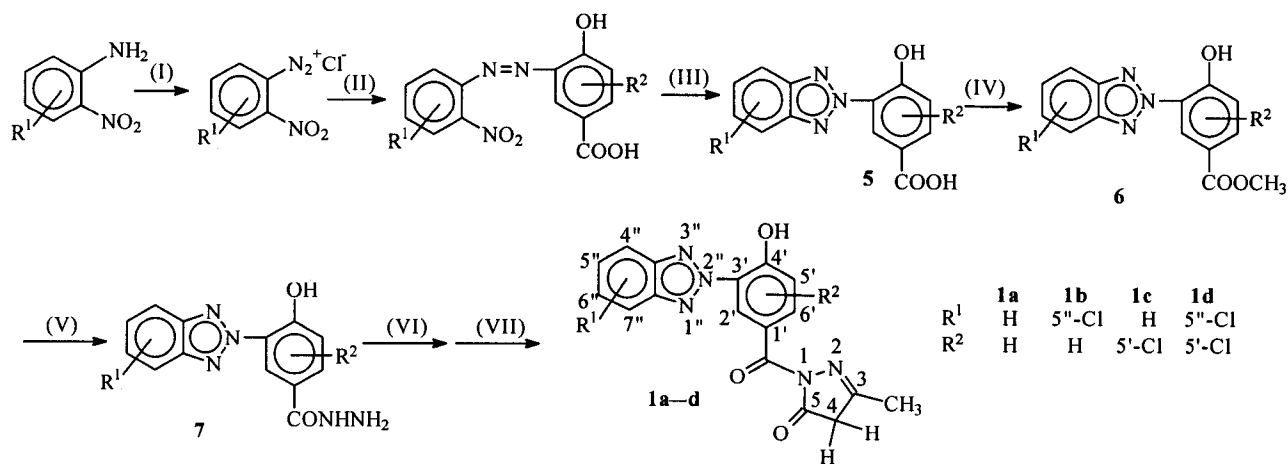
The synthetic route of compounds **1a—d** is shown in Scheme 1.

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Scheme 1



Reagent and conditions: (I) and (II) see ref. 9; (III) Thiourea dioxide, NaOH, ethanol, 78 °C, 3 h, then water; (IV) and (V) see ref. 10; (VI) Acetoacetate, ethanol, refluxed 5 h; (VII) PPA, acetic acid, refluxed 6 h, then water.

The diazotization and coupling reactions (steps I and II) were performed according to the literature procedure.⁹ The intermediates **5**–**7** (steps III–V) were synthesized according to the literature.¹⁰ In step III, the reductive cyclization reaction of 3-(2'-nitrophenylazo)-4-hydroxybenzoic acid, we compared several reducing reagents, i: Zn/NaOH/C₂H₅OH, ii: NH₂NH₂·H₂O/C₂H₅OH, iii: Na₂S/C₂H₅OH/H₂O, and iv: thiourea dioxide/NaOH/C₂H₅OH/H₂O. The results were listed in Table 1. The reducing reagent (i) needed a long reaction time due to the poor solubility of zinc powder and the formation of insoluble ZnO which were difficult to be separated from the reduction product. In the cases of (ii) and (iii), the reduction of the nitro group into the amino group occurred readily, but the cyclization reaction did not proceed effectively. The reductive cyclization reaction occurred effectively using thiourea dioxide as the reducing reagent producing high yield of 3-(benzotriazol-2'-yl)-4'-hydroxybenzoic acid (85%). It has been reported that thiourea dioxide was successfully applied to the reduction and cyclization of dinitro-diarene.¹¹

Table 1 Reductive cyclization reaction (step III in scheme 1) of 3-(2'-nitrophenylazo)-4-hydroxybenzoic acid with various reducing reagents

Reagent	Temp. (°C)	Time (h)	Yield of 5a (%)
zinc powder	78	3	20
hydrazine	78	3	55
sodium sulfide	78	3	58
thiourea dioxide	78	3	85

In the steps IV and V, the methyl esterification of 3-(2'-nitrophenylazo)-4-hydroxybenzoic acid and the subsequent hydrazinolysis reaction were carried out. For the condensation of 3-(benzotriazol-2'-yl)-4'-hydroxybenzoylhydrazines with ethyl acetoacetate to form the corresponding pyrazolone products (steps VI and VII), the use of PPA (Polyphosphoric acid) as a catalyst was necessary due to the low reactivity of the benzoylhydrazines.

Compounds **1** display three strong UV absorption maxima ($\lambda_{\max} = 250$ – 350 nm, $\log \epsilon = 4.4$ – 4.6). All of the compounds have been characterized by elemental analysis, ¹H NMR, MS, IR, and UV-Vis.

Through the reaction of the 1-substituted-3-methyl-5-pyrazolone part with carbonyl groups,¹² the stabilizers **1** could be attached to the surface of the polymers. In order to know the reactivity of the novel stabilizers **1** to carbonyl functions, we carried out the condensation reactions of **1d** with substituted benzaldehydes **4**. It was found that the reaction occurred readily at room temperature by grinding a solid mixture of the substrates or by melting the mixture and produced 4,4'-phenylmethylene-bis(pyrazolone)s (**3**) or 4-phenylmethylene-pyrazolones (**2**), respectively as the major product, and that the reaction at 50 °C in chloroform solution produced a mixture of **2** and **3** (Scheme 2). The reaction of **1d** with **4** proceeded more efficiently and selectively in the solid state and molten state than in solution. The results were listed in Table 2.

Scheme 2

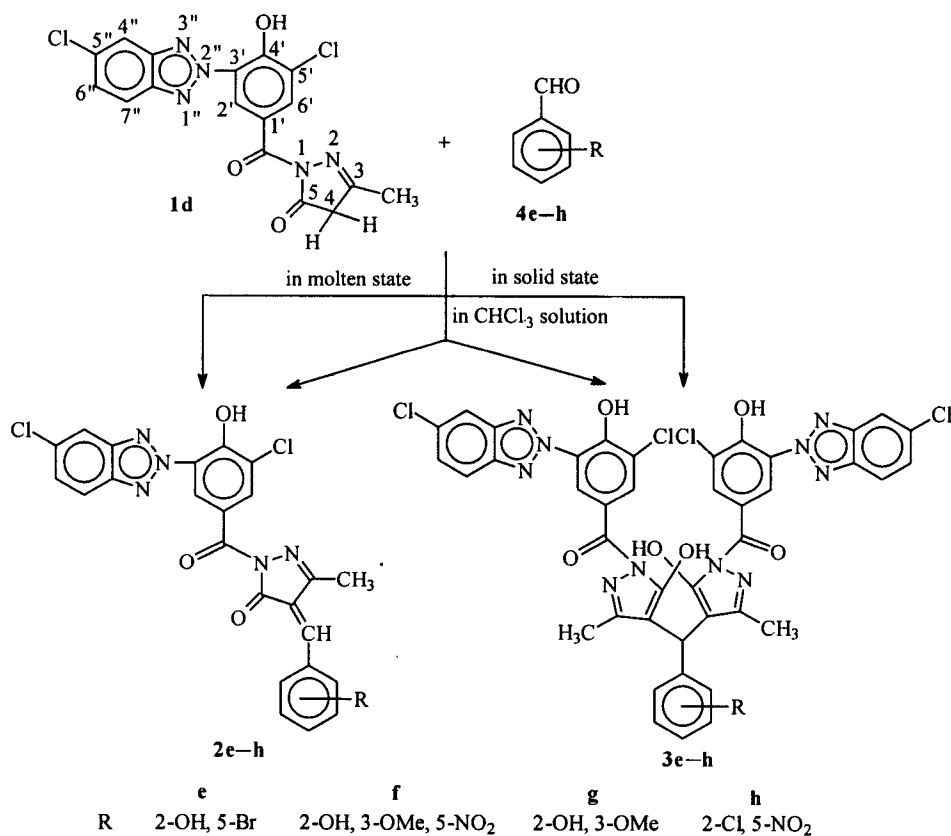


Table 2 Reactions of **1d** and **4** in the solid state, in the molten state and in chloroform solution ^a

Compounds	Solid state at rt ^b		Molten state at 150°C ^c		In CHCl ₃ solution at 50°C ^c	
	2	3	2	3	2	3
e	4	80	94	0	46	33
f	0	87	84	5	32	52
g	3	70	89	0	28	49
h	0	92	79	8	61	21

^aIsolated yield; ^b The molar ratio of **1d** to **4** was 1:2; ^c The molar ratio of **1d** to **4** was 1:1.

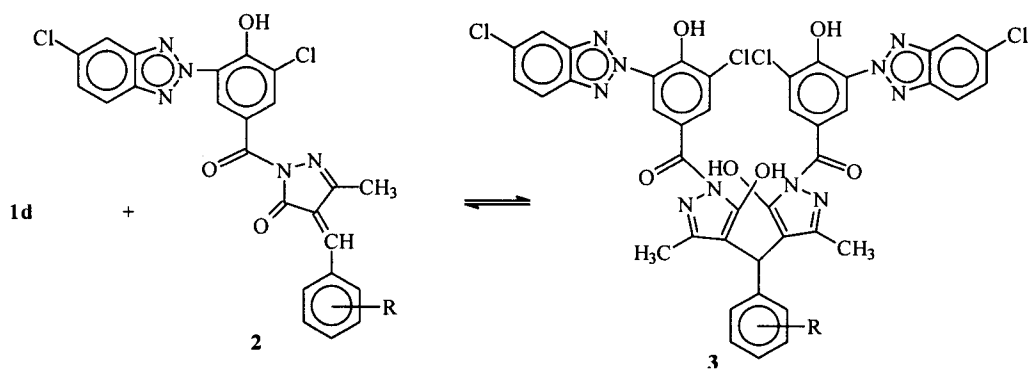
Compounds **3** were not stable to heat. The color of the compounds in the solid state changed gradually from pale yellow to dark red with the temperature going up, due to the decomposition of compounds **3**, which was similar to that reported previously.⁵ Generally, the stability of compound **3** increased with the existence of an electron-withdrawing group such as a nitro group in the phenyl ring of the starting aldehydes **4**.^{5,7} However, in the presence of 2-hydroxyl group in aldehydes **4** (in the cases of **3e**, **3f**, **3g**), the thermal stability of compounds **3** increased, which was attributable to the interactions of the intramolecular H-bonding among the hydroxyl groups.

In the solution of chloroform, the reactions of **1d**

and **4** always produced a mixture of **2** and **3** due to the equilibrium between them under the reaction conditions (Scheme 3).⁷

In compounds **3**, the carbonyl groups of pyrazolones exist in an enolic form, which can be confirmed by IR spectra, an absorption peak (around 1680 cm⁻¹) of carbonyl groups disappeared in pyrazolones **1** and **2** and the appearance of a strong broad absorption around 2500 cm⁻¹ was contributed due to the enolic hydroxy group with hydrogen binding. The carbonyl absorption around 1680 cm⁻¹ and OH absorption around 3450 cm⁻¹ of pyrazolones in compounds **2** remained the same as those in **1**. The compounds **3** and **2** displayed a strong UV absorption ($\lambda = 250 - 350 \text{ nm}$) which sug-

Scheme 3



gested that it could serve as a new type of UV stabilizers. The photochromic and photoprotective properties are under investigation.

Experimental

All melting points (uncorrected) were taken on a microscopic melting point apparatus. The ^1H NMR spectra were recorded on a JEOLX-90Q spectrometer. The MS spectra were determined on a 7070E-HE spectrometer. The IR spectra (cm^{-1}) were measured with a NICOLE 170SX spectrophotometer. Elemental analyses were performed on a PE-240 analyzer. The UV spectra were recorded on a Shimadzu UV-240 spectra photometer.

2-Nitrobenzodiazonium chloride derivatives and 3-(2'-nitrophenylazo)-4-hydroxy-benzoic acids were synthesized according to the literature procedure.⁹

Intermediates **5**–**7** were synthesized according to the literature¹⁰ with slight modifications.

General procedure for the preparation of **1a**–**d**

A solution of **7** (0.007 mol) and ethyl acetoacetate (0.91 g, 0.007 mol) in 30 mL of absolute ethanol was refluxed for 5 h. To this solution was added 10 mL of PPA and 5 mL of acetic acid, then the mixture was refluxed for another 6 h and cooled. To this reaction mixture was added 30 mL of water. The produced solid was collected by filtration, dried and purified with column chromatography (Qingdao silica gel 200–300 mesh) using ethyl acetate/petroleum ether (6:1) as the eluent to give the target product.

1a Pale yellow solid, yield 25%, m. p. 176–177°C; UV-vis (CH_3OH) λ_{max} : 274, 302, 332

nm; ^1H NMR (CDCl_3 , 90 MHz) δ : 2.11 (s, 3H), 3.27 (s, 2H), 6.91–7.30 (m, 4H), 7.40–7.80 (m, 3H); IR (KBr) ν : 3360, 1675, 1610, 1600, 1510, 1314, 990 cm^{-1} ; MS (70 eV) m/z : 335.0 (M^+); Anal. caclcd for $\text{C}_{17}\text{H}_{13}\text{N}_5\text{O}_3$: C 60.90, H 3.88, N 20.90; found C 60.64, H 3.98, N 20.71.

1b Pale yellow solid, yield 20%, m. p. 188–189°C; UV-vis (CH_3OH) λ_{max} : 279, 300, 329 nm; ^1H NMR (CDCl_3 , 90 MHz) δ : 2.00 (s, 3H), 3.50 (s, 2H), 6.99–7.33 (m, 3H), 7.65–7.75 (m, 3H); IR (KBr) ν : 3360, 1660, 1610, 1590, 1515, 1390, 1000 cm^{-1} ; MS (70 eV) m/z : 367.4 (M^+); Anal. caclcd for $\text{C}_{17}\text{H}_{12}\text{ClN}_5\text{O}_3$: C 55.21, H 3.25, N 18.94; found C 55.48, H 3.54, N 18.70.

1c Pale yellow solid, yield 34%, m. p. 183–184°C; UV-vis (CH_3OH) λ_{max} : 273, 304, 340 nm; ^1H NMR (CDCl_3 , 90 MHz) δ : 2.23 (s, 3H), 3.61 (s, 2H), 6.99–7.33 (m, 3H), 7.54–7.78 (m, 3H); IR (KBr) ν : 3400, 1665, 1610, 1600, 1520, 1310, 995 cm^{-1} ; MS (70 eV) m/z : 367.2 (M^+); Anal. caclcd for $\text{C}_{17}\text{H}_{12}\text{ClN}_5\text{O}_3$: C 55.21, H 3.25, N 18.94; found C 55.36, H 3.00, N 18.64.

1d Pale yellow solid, yield 50%, m. p. 193–194°C; UV-vis (CH_3OH) λ_{max} : 266, 305, 342 nm; ^1H NMR (CDCl_3 , 90 MHz) δ : 2.10 (s, 3H), 3.35 (s, 2H), 7.01–7.40 (m, 2H), 7.55–7.80 (m, 3H); IR (KBr) ν : 3350, 1688, 1615, 1590, 1520, 1350, 1000 cm^{-1} ; MS (70 eV) m/z : 403.9 (M^+); Anal. caclcd for $\text{C}_{17}\text{H}_{11}\text{Cl}_2\text{N}_5\text{O}_3$: C 50.50, H 2.72, N 17.33; found C 50.85, H 2.75, N 16.98.

General procedure for the preparation of **2e**–**h** in molten state

Pulverized **4** (2.0 mmol) and **1d** (0.81 g, 2.0

mmol) were mixed thoroughly and heated in the molten state at 150°C on an oil bath for 1 h. After cooled, the reaction mixture was agitated with CHCl₃ and the insoluble solid was removed by filtration. The filtrate was concentrated and the residue was purified by column chromatography on silica gel (Qingdao 200–300 mesh) using dichloromethane as the eluent to give the target product.

2e Red crystals, yield 94%, m. p. 169–170°C; UV-vis (CH₃OH) λ_{max}: 304, 330, 358 nm; ¹H NMR (CDCl₃, 90 MHz) δ: 2.39 (s, 3H), 7.10–7.60 (m, 7H), 7.90–8.10 (m, 2H); IR (KBr) ν: 3360, 1685, 1610, 1595, 1570, 1350, 1010 cm⁻¹; MS (70 eV) *m/z*: 588.6 (M⁺); Anal. caclcd for C₂₄H₁₄BrCl₂N₅O₄: C 49.06, H 2.38, N 11.92; found C 49.30, H 2.23, N 11.68.

2f Red crystals, yield 84%, m. p. 219–220°C; UV-vis (CH₃OH) λ_{max}: 301, 329, 355 nm; ¹H NMR (CDCl₃, 90 MHz) δ: 2.40 (s, 3H), 3.70 (s, 3H), 7.40–7.60 (m, 3H), 7.99–8.10 (m, 5H); IR (KBr) ν: 3250, 1695, 1635, 1620, 1560, 1384, 995 cm⁻¹; MS (70 eV) *m/z*: 584.21 (M⁺); Anal. caclcd for C₂₅H₁₆Cl₂N₆O₇: C 51.44, H 2.74, N 14.40; found C 51.64, H 2.83, N 14.07.

2g Dark red crystals, yield 89%, m. p. 160–161°C; UV-vis (CH₃OH) λ_{max}: 296, 339, 368 nm; ¹H NMR (CDCl₃, 90 MHz) δ: 2.38 (s, 3H), 3.90 (s, 3H), 7.05–7.60 (m, 5H), 7.90–8.15 (m, 2H), 8.40–8.60 (m, 2H); IR (KBr) ν: 3370, 1680, 1631, 1600, 1550, 990 cm⁻¹; MS (70 eV) *m/z*: 540.20 (M⁺); Anal. caclcd for C₂₅H₁₇Cl₂N₅O₅: C 55.75, H 3.16, N 13.00; found C 55.43, H 3.06, N 13.38.

2h Purple crystals, yield 79%, m. p. 172–173°C. UV-vis (CH₃OH) λ_{max}: 298, 330, 358 nm; ¹H NMR (CDCl₃, 90 MHz) δ: 2.37 (s, 3H), 7.40–7.90 (m, 7H), 8.00–8.20 (m, 2H); IR (KBr) ν: 3400, 1680, 1610, 1590, 1540, 1060 cm⁻¹; MS (70 eV) *m/z*: 573.60 (M⁺); Anal. caclcd for C₂₄H₁₃Cl₃N₆O₅: C 50.39, H 2.54, N 14.70; found C 50.10, H 2.54, N 14.36.

General procedure for the preparation of 3e–h in solid state

A mixture of 0.81 g (2.0 mmol) of **1d** and 1.0

mmol of **4** was ground with an agate and a pestle for 20 min and allowed to stand for 24 h at room temperature. The mixture was washed with ethanol one time, then with methanol three times to give the target product.

3e White solid, yield 80%, m. p. 256–257°C; UV-vis (CH₃OH) λ_{max}: 264, 300, 340 nm; ¹H NMR (DMSO-d₆, 90 MHz) δ: 2.39 (s, 6H), 5.21 (s, 1H), 6.84–6.96 (m, 4H), 7.20–7.90 (m, 9H); IR (KBr) ν: 3350, 2525, 1610, 1590, 1010 cm⁻¹; Anal. caclcd for C₄₁H₂₅BrCl₄N₁₀O₇: C 49.64, H 2.52, N 14.13; found C 50.01, H 2.36, N 14.49.

3f Pale yellow solid, yield 70%, m. p. 268–269°C; UV-vis (CH₃OH) λ_{max}: 266, 304, 338 nm; ¹H NMR (DMSO-d₆, 90 MHz) δ: 2.40 (s, 6H), 3.80 (s, 3H), 5.34 (s, 1H), 7.46–7.89 (m, 10H), 8.34–8.50 (d, 2H); IR (KBr) ν: 3400, 2500, 1620, 1600, 1575, 1340, 995 cm⁻¹; Anal. caclcd for C₄₂H₂₇Cl₄N₁₁O₁₀: C 51.06, H 2.74, N 15.60; found C 50.90, H 2.49, N 15.93.

3g Pale yellow solid, yield 92%, m. p. 237–238°C. UV-vis (CH₃OH) λ_{max}: 272, 306, 329 nm; ¹H NMR (DMSO-d₆, 90 MHz) δ: 2.45 (s, 6H), 3.78 (s, 3H), 5.25 (s, 1H), 6.84–6.96 (m, 11H), 7.43–7.90 (m, 2H); IR (KBr) ν: 3300, 2600, 1625, 1600, 1580, 995 cm⁻¹; Anal. caclcd for C₄₂H₂₈Cl₄N₁₀O₈: C 53.50, H 2.97, N 18.86; found C 53.11, H 3.14, N 15.03.

3h Pale yellow solid, yield 87%, m. p. 181–182°C; UV-vis (CH₃OH) λ_{max}: 260, 302, 339 nm; ¹H NMR (DMSO-d₆, 90 MHz) δ: 2.38 (s, 6H), 5.31 (s, 1H), 7.46–7.89 (m, 9H), 8.22–8.50 (m, 2H), 8.80 (d, 2H); IR (KBr) ν: 3450, 2520, 1630, 1590, 1580, 1360, 995 cm⁻¹; Anal. caclcd for C₄₁H₂₄C₁₅N₁₁O₈: C 50.34, H 2.46, N 15.78; found C 50.13, H 2.83, N 15.58.

General procedure for the reaction of 1d and 4 in chloroform solution

A mixture of **1d** (0.81 g, 2.0 mmol) and **4e** (0.20 g, 1.0 mmol) was dissolved in chloroform (10.0 mL) and heated at 50°C for 3 h. The reaction mixture was evaporated to a residue which was submitted to silica gel chromatography as described above to give 0.27 g (46%) of **2e** and 0.32 g (33%) of **3e**. Using the

same procedure, the reactions of **1d** and **4f—h** were carried out, and the results were shown in Table 2.

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