

Report

Preparation and Optimization of Iridium Complexes with Quinazolinone Ligands on Solid Supports

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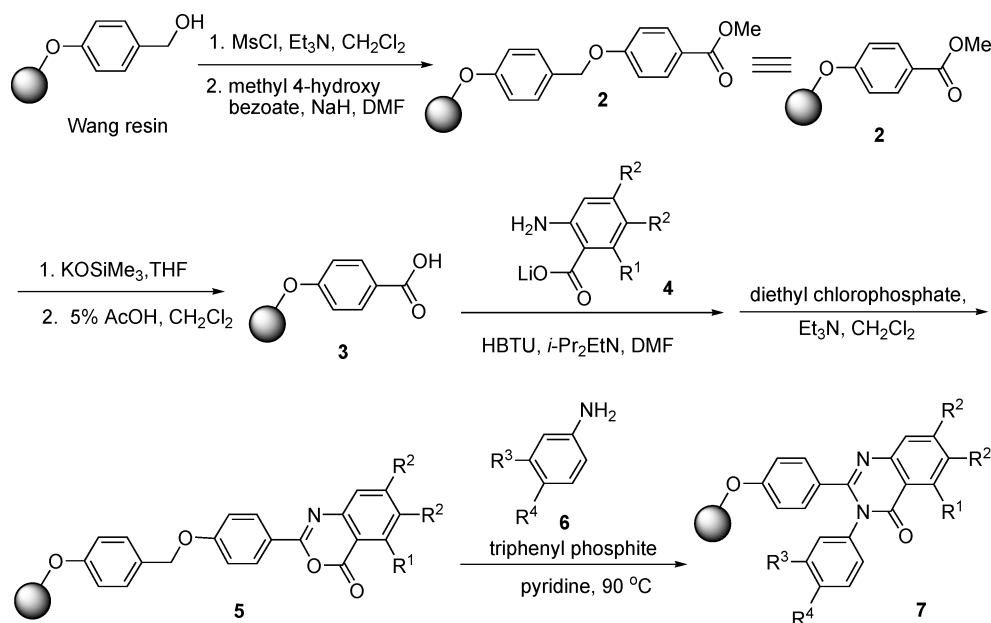
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Solid-phase combinatorial techniques are tremendously useful in the search for new drugs for the treatment of a wide variety of ailments.^{1–4} Materials discovery, however, has yet to benefit significantly from combinatorial methodology. Indeed, only a few exceptional attempts have been made to apply combinatorial approaches to the discovery of materials possessing novel photophysical properties.^{5–8} Moreover, even among these few reports, most of the materials prepared have been organic compounds. Several researchers have reported the immobilization of organometallic complexes onto functionalized polymer supports.^{9–16} Leadbeater attached ruthenium complexes to polymer supports to improve their catalytic efficiencies; Reedijk and co-workers developed methodologies to prepare platinum complexes on solid supports.^{17,18} Nevertheless, it remains rare for solid-phase combinatorial methods to be used for the synthesis of organometallic materials. In this paper, we describe a rapid and efficient parallel solid phase method for the synthesis of iridium complexes. This methodology allows the modification of three different functionalities on the template of the iridium complexes to optimize and fine-tune their photophysical properties for application in organic light-emitting diodes (OLEDs).

OLEDs are advanced alternatives to inorganic light-emitting diodes and liquid-crystal displays. Because of their excellent properties (flexibility, self-luminescence, rapid response, good contrast, low energy consumption), they hold great potential for application in flat-panel displays. In recent decades, much attention has been focused on organometallic complexes of various heavy metals, including Ir,^{19–26} Os,²⁷ Ru,^{28,29} and Pt,³⁰ for their potential use as phosphorescent dopants in OLEDs. Iridium complexes, in particular, are excellent emitters for OLED applications.^{19–26} In 2006, we used a combinatorial organometallic solid phase synthesis and high throughput screening methodology to identify a novel iridium complex having two cyclometallating ligands and a single monoanionic, bidentate ancillary ligand.³¹ The optimization of lead organometallic materials using this library approach, however, remains in its nascent stages.^{32–34} As part of a continuing effort toward the development of organometallic materials exhibiting desired properties, we are aiming to optimize the properties of organometallic complexes through structural modifications using solid phase synthesis. So far, the key ligands we have used have been limited mostly to derivatives of *o*-pyridylarenes and *o*-pyridylheterocycles.^{19–26} Therefore, to extend our optimization studies, for this present study we selected iridium complexes featuring quinazolinone-based cyclometallating ligands. In this Report, we demonstrate the versatility of using a combinatorial parallel approach, applying solid phase synthesis, for the preparation and optimization of iridium complexes incorporating quinazolinone ligands as luminescent emitters.

The parallel solid-phase syntheses of the iridium complexes **1** were carried out using Wang resin (1% DVB, 1.0 mmol/g, Scheme 1). Initially, Mitsunobu alkylation was tested to obtain resin **2** by reacting methyl 4-hydroxybenzoate with Wang resin under standard conditions.^{35,36} In these cases, the reactions afforded poor yields and resulted in several side products. Instead, we first activated the Wang resin as a mesylate and then alkylated it with methyl 4-hydroxybenzoate in DMF using NaH to afford the resin **2**

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Scheme 1. Synthesis of Resin-Bound Quinazolinones **7**

in good yield.³⁷ At the completion of each reaction, we monitored the purities of the products either using 500 MHz NMR spectroscopy, after subjecting a small portion of the resin to cleavage, or magic-angle-spinning gel phase NMR spectroscopy. Hydrolyses of the ester **2** using several common reagents (e.g., EtONa, KOH) in aqueous solvents (H₂O/EtOH/DMF, H₂O/EtOH/THF)^{38–41} were not reproducible because, in several instances, partial hydrolysis occurred leaving significant amounts of the starting materials unreacted. Instead, we reacted the resin **2** with potassium trimethylsilylanolate in THF, followed by treatment of 5% AcOH in CH₂Cl₂, to furnish the acid **3**.^{42–46} To obtain the cyclized oxazinone derivatives **5** in an efficient manner from the resin-bound acid **3**, we attempted several one-pot reactions. Initially, we treated the acid **3** with diethyl chlorophosphate and then reacted the resulting mixed anhydride with various aminobenzoic acids in the presence of Et₃N in CH₂Cl₂. The *N*-acylated products were further treated with additional diethyl chlorophosphate to yield *o*-phosphorylated derivatives, which afforded the oxazinones **5** through in situ cyclization. Unfortunately, this method gave poor yields and several side-products. To improve the yields, we prepared the temporarily protected aminobenzoic acid lithium salts **4** using LiOH in MeOH/H₂O^{47–49} and used them in place of the aminobenzoic acids. The resin-bound acid **3** was reacted in one-pot with the lithium salts **4** in the presence of *O*-benzo-triazole-*N,N,N',N'*-tetramethyl-uroniumhexafluorophosphate (HBTU) and diisopropylethylamine (DIPEA) in DMF to afford *N*-acylated products that we further treated with diethyl chlorophosphate to furnish the resins **5**. These reactions were clean and afforded their products in excellent yields. The oxazinone derivatives **5** were treated with various aromatic amines **6** at 90 °C in the presence of triphenyl phosphite in pyridine to obtain the resin-bound quinazolinones **7**.⁵⁰ Even though the use of excess reagents is generally permissible in solid phase syntheses, in this step the ratio of triphenyl phosphite to the amines had a dramatic effect on the success of this reaction:

a ratio of 1:1 led to incomplete reactions and a 3:1 ratio resulted in very slow reaction rates. A ratio of 1:3 was optimal. We monitored these reactions using magic-angle-spinning gel-phase NMR spectroscopy. The resin-bound quinazolinones **7** were then cleaved from the Wang resin to afford the corresponding ligands in overall yields of 70–80%.

To obtain the resin-bound dimers **8**, we treated the resin-bound quinazolinones **7** in ethoxyethanol with iridium trichloride hydrate in the presence of NaHCO₃ at 100 °C (Scheme 2).^{19–26,51} In these reactions, NaHCO₃ was added to maintain the pH at 7 because the resins **8** are sensitive to acidic conditions at elevated temperatures. The resulting Ir (III)- μ -chloro-bridged dimers **8** are new and unique with respect to their structures and formation of a polymer-bound complex within the same resin. Polarized optical microscopy images of the chloro-bridged complexes **8** revealed that the polymer-bound dimers had formed within single resin beads and that their four ligands were all attached to the same resin. The resin-bound dimers **8** were then reacted with acetyl acetone at 100 °C in the presence of NaHCO₃ to afford the resin-bound complexes **9**,^{52,53} which we cleaved through treatment with 10% TFA in 1,3-dimethoxybenzene/CH₂Cl₂ yield the hydroxyl derivatives. In this reaction, 1,3-dimethoxybenzene behaved as a scavenger to avoid rearrangement during cleavage.⁵⁴ Treatment of the hydroxyl derivatives with acetic anhydride (or BzCl) in the presence of Et₃N and DMAP in CH₂Cl₂, or with MeI and K₂CO₃ at 60 °C in acetone, provided the desired acetyl (or benzoyl), or methyl, derivatives of the iridium complexes **1** (Table 1). Formation of iridium complexes with a facial arrangement of ligands was favored in this present study, consistent with results reported previously.^{52,53} The yields of the final products, starting from the Wang resin, ranged from 25 to 42%, corresponding to ~90% yields in each step of this 11-step solid phase synthesis. Structural characterization of all of the synthesized compounds was performed using ¹H and ¹³C NMR spectroscopy and mass spectrometry.

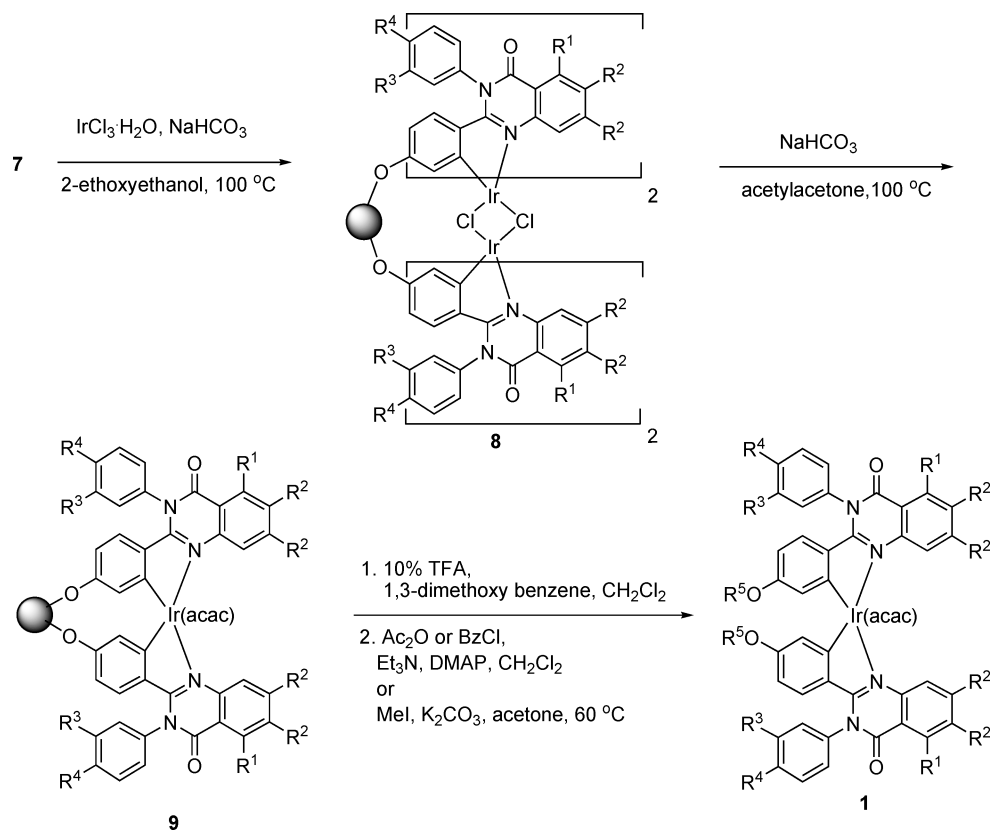
Scheme 2. Synthesis and Cleavage of the Iridium Complexes **1**

Table 1. Representative Iridium Complexes **1** Generated on Solid Supports

entry	R ¹	R ²	R ³	R ⁴	R ⁵	yield ^a	λ_{em} (nm)	Φ_{PL}
1	Me	H	H	H	Me	30	623	0.23
2	Me	H	H	H	Ac	31	625	0.26
3	Me	H	H	H	Bz	33	622	0.32
4	Me	H	OMe	H	Me	27	627	0.30
5	Me	H	H	OMe	Ac	37	629	0.24
6	Me	H	H	OMe	Bz	31	620	0.22
7	Me	H	H	OMe	Me	33	616	0.31
8	H	H	H	H	Me	32	619	0.34
9	H	H	OMe	H	Ac	34	620	0.44
10	H	H	OMe	H	Me	36	619	0.38
11	H	H	H	OMe	Me	32	615	0.32
12	H	H	H	OMe	Ac	42	619	0.62
13	H	H	H	OMe	Bz	40	619	0.73
14	H	OMe	H	H	Ac	25	633	0.16
15	H	OMe	H	H	Bz	27	634	0.18

^a Isolated overall yields (based on the initial loading of the Wang resin) after 11-step syntheses and flash chromatography.

To determine the electroluminescence properties of the synthesized complexes and the effects of structural modifications, we measured their emission wavelengths (λ_{em}) and quantum yields (Φ_{PL}) under UV excitation ($\lambda_{\text{exc}} = 365\text{ nm}$) in CH_2Cl_2 .⁵⁵ Analyses of photoluminescence of these complexes revealed values of λ_{em} located between 615 and 635 nm. This range includes colors from orange to red, reconfirming that the substituents on the ligands play important roles in affecting the color purity. Compounds **14** and **15** exhibited emission wavelengths at 633 and 634 nm, respectively, suggesting that enhanced photophysical properties of iridium complexes occurred when electron donating groups were present in para positions relative to the nitrogen atom and carbonyl group of the quinazolinone ligand. The quantum yields extended over a broad range, from 0.15 to

0.73. Thus, these 3-fold functional modifications led to dramatic changes in quantum yields.

In conclusion, we have developed a method for the optimization of the properties of organometallic iridium complexes through parallel solid phase synthesis. This strategy employs inexpensive and common organic reagents to effect the transformations, which afford pure compounds without the need for HPLC purification. In addition, it also permits the rapid introduction of 3-fold functional diversity into the iridium complexes, thereby accelerating optimization and fine-tuning of the resulting properties. The best photoluminescence emission wavelength was obtained when electron donating groups were present at para positions relative to the nitrogen atom and carbonyl group of the quinazolinone ligand. The synthetic reaction conditions involved in this process are compatible with automation and could be used to prepare suitable quantities of the various emitters to evaluate their photophysical properties. Such data would reveal the relationships between the structures and properties of the complexes. Combining our previous methodology³¹ of lead generation with this present optimization technique allows parallel solid phase synthesis to expedite the discovery and fine-tuning of OLED materials, analogous to the procedures used in drug discovery. The scope of this strategy may be expanded beyond OLED materials to other organometallic drugs or materials exhibiting valuable properties.

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Supporting Information Available. Representative experimental procedures and ^1H and ^{13}C NMR spectra of the compounds in Table 1. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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