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Heterocycles

Rhenium-Catalyzed Synthesis of 3-Imino-1-isoindolinones by C−H Bond Activation: Application to the Synthesis of Polyimide Derivatives**

*Shunsuke Sueki, Yuanfang Guo, Motomu Kanai, and Yoichiro Kuninobu**

Polyimides, rigid polymers with high strength intensity, heat-resistance properties, and electric nonconductance, are useful and important in the fields of aerospace engineering[1] and electronic materials.[2] Polyimides have low solubility in organic solvents, thus making it difficult to fabricate them into the desired shapes. We considered that the low solubility could be improved by changing the carbonyl group (C=O) of the polyimides into an imino group (C=N) with a long alkyl chain on the nitrogen atom. Polyimides are usually synthesized by polycondensation of pyromellitic dianhydride and diamines,[3] and thus it is difficult to synthesize imino-group-containing polyimides using a standard polyimide synthesis. Because C−H bond transformations are highly efficient and generate only small amounts of waste, we developed a C−H bond transformation which could be applied to the synthesis of such polymers.

Although several studies have reported the synthesis of polymers by C−H bond activation, such as C−H/olefin coupling (Figure 1 a)[4] and C−H/C−X biaryl coupling (Figure 1 b),[5] there are no examples of polymer synthesis by annulation through C−H bond activation. Our group[6] as well as others[7] previously reported transition-metal-catalyzed annulation reactions through C−H bond activation by using an imino group as a directing group. In these reactions, however, the functional groups (directing groups) do not remain in the products. To maintain the functional group, we designed a method to introduce a leaving group to the directing group of a substrate (methoxy groups in Figure 1 c). With this strategy, we expected that the C=N double bonds of the imino groups would be restored by elimination of the leaving groups after intramolecular nucleophilic cyclization. Our retrosynthetic strategy is shown in Figure 2: 1) the final product (3-imino-1-isoindolinone) is produced by the elimination of methanol from the intermediate **A**, 2) **A** is generated from **B** by intramolecular nucleophilic cyclization,

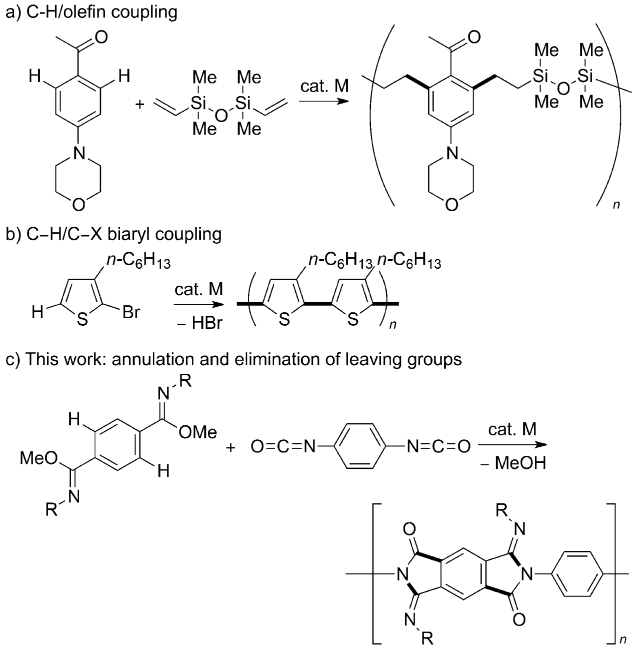

Figure 1. Several types of polymerization by C−H bond activation.

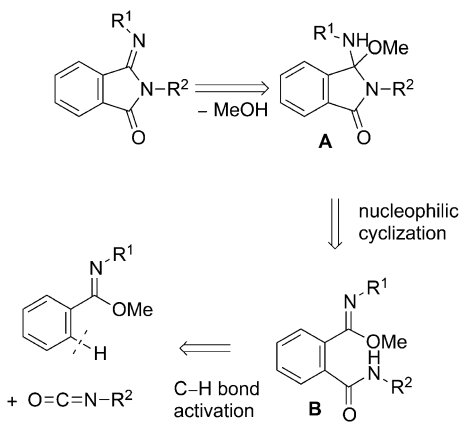

Figure 2. Retrosynthetic scheme for the synthesis of 3-imino-1-isoindolinones.

and 3) **B** is formed by insertion of an isocyanate into an *ortho* C−H bond of an aromatic imidate. Based on this strategy, we successfully synthesized 3-imino-1-isoindolinones by C−H bond activation without loss of the imino functional groups. Herein we report the synthesis of iminoisoindolinones[8] from aromatic imidates and isocyanates under

[*] Dr. S. Sueki, Y. Guo, Prof. Dr. M. Kanai, Prof. Dr. Y. Kuninobu
Graduate School of Pharmaceutical Sciences
The University of Tokyo
7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033 (Japan)
E-mail: kuninobu@mol.f.u-tokyo.ac.jp
Dr. S. Sueki, Prof. Dr. Y. Kuninobu
CREST (Japan) Science and Technology Agency (JST)
7-3-1 Hongo, Bunkyo-ku, Tokyo 113-0033 (Japan)

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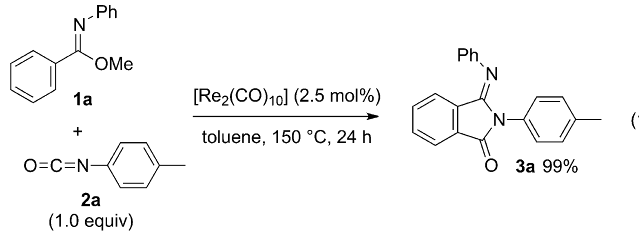
rhenium catalysis and its application to the synthesis of polyimide derivatives.

Through the optimization of the reaction conditions (catalysts, solvents, temperatures, and reaction times), we found that the reaction of (*Z*)-methyl *N*-phenylbenzimidate (**1a**) with *p*-tolyl isocyanate (**2a**) in the presence of the rhenium catalyst [$Re_2(CO)_{10}$] in toluene at 150 °C for 24 hours proceeded smoothly and gave (*E*)-3-(phenylimino)-2-(*p*-tolyl)isoindolin-1-one (**3a**) in 99 % yield [Eq. (1); for details of



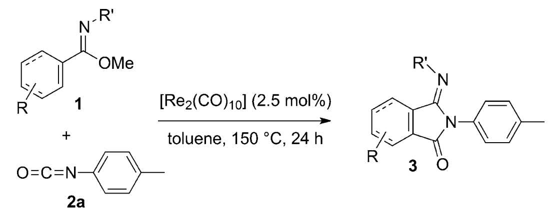
(1)

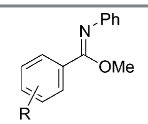
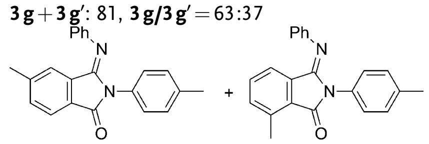
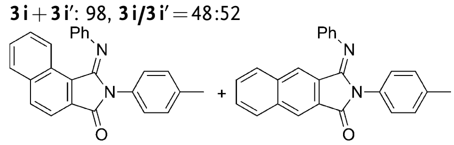
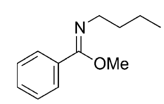
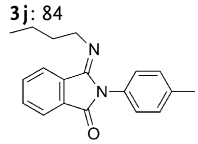
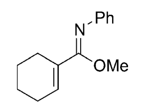
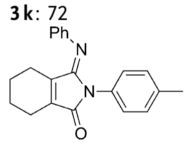
the optimization of the reaction conditions, see Table S1 in the Supporting Information].[9,10] After the reaction, methanol was observed in the ^{1}H NMR spectra as a side product. The structure of **3a** was determined by single-crystal X-ray structure analysis (see the Supporting Information).[11] In this reaction, the imino group (the directing group) remains after the reaction, and this result is quite different from previous reports in which directing groups did not remain after the transformations.[6,7]

The scope of the imidates **1** was investigated (Table 1). The desired 3-imino-1-isoindolinones **3b–f** were obtained in good to excellent yield using the imidates **1b–f** having either an electron-donating or electron-withdrawing group (entries 1–5). In these cases, the functional group remained unchanged during the reaction. An imidate with a substituent at the *meta*-position, **1g**, provided a mixture of two regioisomers, **3g** and **3g′** (entry 6). The reaction was affected by steric hindrance from a substituent at the *ortho*-position (entry 7). Although an imidate with a naphthyl group, **1i**, had high reactivity, a mixture of two regioisomers, **3i** and **3i′**, was generated (entry 8). The reaction of the *N*-alkyl imidate **1j** gave the desired product **3j** in 84 % yield (entry 9). The reaction also proceeded at the olefinic C–H bond and the corresponding cyclic product **3k** was produced in 72 % yield (entry 10).

Next, we investigated the scope of isocyanates (Table 2). The annulation reaction proceeded in excellent yield using aryl isocyanates (**2b–e**) having either an electron-donating or electron-withdrawing group (entries 1–4). In entry 4, the desired product **3o** was obtained quantitatively without loss of the bromine atom, and the reaction was not inhibited by steric hindrance (entry 5). 1-Naphthyl isocyanate (**2g**) also provided the corresponding 3-imino-1-isoindolinone **3q** quantitatively (entry 6). The 3-imino-1-isoindolinones **3r** and **3s** were obtained in 88 % and 87 % yields, respectively, from the corresponding primary and secondary alkyl isocyanates **2h** and **2i**.[12]

Table 1: Reactions between several benzimidates **1** and *p*-tolylisocyanate (**2a**).[a]



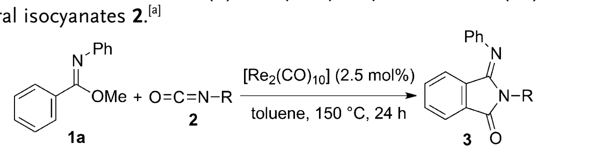
Entry	1	3 Yield [%][b]
		
1	R = 4-MeO: **1b**	**3b**: 80
2	R = 4-CF_3: **1c**	**3c**: 68
3	R = 4-Br: **1d**	**3d**: 90
4	R = 4-CN: **1e**	**3e**: 60
5	R = 4-CO_2Me: **1f**	**3f**: 80
6	R = 3-Me: **1g**	**3g** + **3g′**: 81, **3g/3g′** = 63:37 
7	R = 2-Me: **1h**	**3h**: 36
8	**1i**	**3i** + **3i′**: 98, **3i/3i′** = 48:52 
9	**1j** 	**3j**: 84 
10	**1k** 	**3k**: 72 

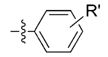
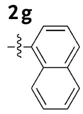
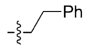
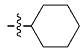
[a] Used 1.0 equiv **2a**. [b] Yield of the isolated product.

The proposed mechanism for the rhenium-catalyzed formation of the 3-imino-1-isoindolinones **3** is as follows (Scheme 1): 1) oxidative addition of methyl benzimidate **1** to the rhenium catalyst (C–H bond activation),[6] 2) insertion of **2** into the formed rhenium–carbon bond,[6b] 3) intramolecular nucleophilic cyclization,[6b] and 4) reductive elimination and elimination of methanol to give **3** and regenerate the rhenium catalyst. In fact, methanol was formed during the reaction as mentioned above. In this reaction, the elimination of methanol is important for retaining the imino group in the products.[13]

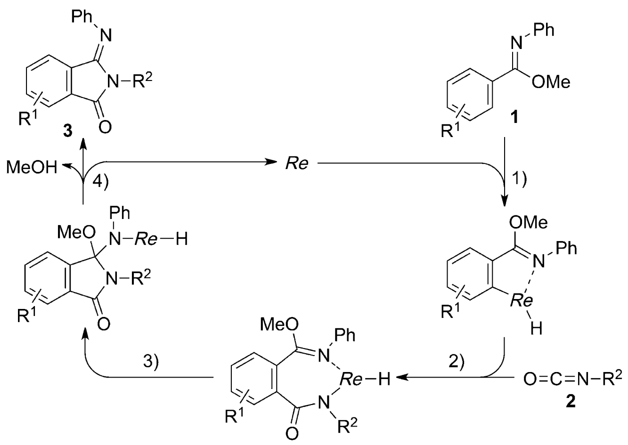
Notably, the yield of **3a** was also high even on gram scale. When 845 mg of **1a** was used as the substrate, the reaction

Table 2: Reactions between (*Z*)-methyl *N*-phenylbenzimidate (**1a**) and several isocyanates **2**.[a]



Entry	R	**3** Yield [%][b]
		
1	R′ = 4-H: **2b**	**3l**: 97
2	R′ = 4-MeO: **2c**	**3m**: 89
3	R′ = 4-CF_3: **2d**	**3n**: 99
4	R′ = 4-Br: **2e**	**3o**: 99
5	R′ = 2-Me: **2f**	**3p**: 99
6	**2g** 	**3q**: 99
7	**2h** 	**3r**: 88
8	**2i** 	**3s**: 87

[a] Used 1.0 equiv **2**. [b] Yield of the isolated product.

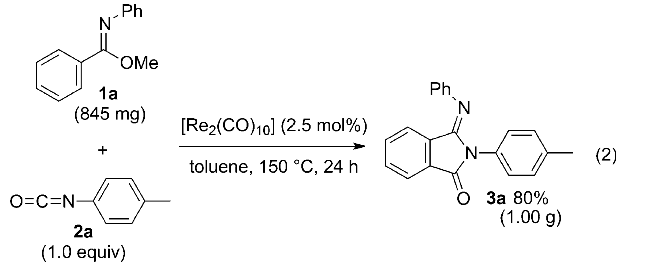


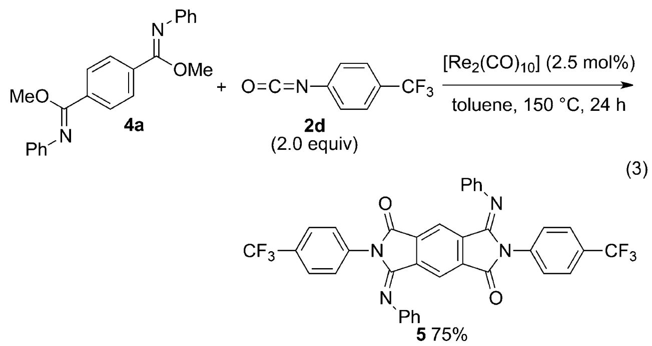
Scheme 1. Proposed mechanism for the formation of the 3-imino-1-isoindolinones **3**.

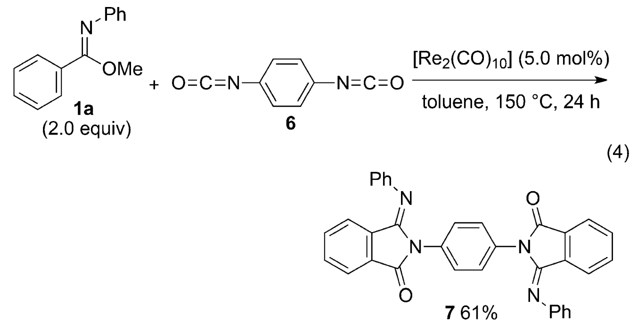
produced 1.00 g of **3a** in 80% yield [Eq. (2); for Eq. (1), **1a**: 52.8 mg].

Double annulation reactions also proceeded by a reaction between the diimidate **4a** and isocyanate **2d** [Eq. (3)], or the imidate **1a** and diisocyanate **6** [Eq. (4)]. In Equation (3), two regioisomeric products are possible, however, only the single product **5** was obtained.

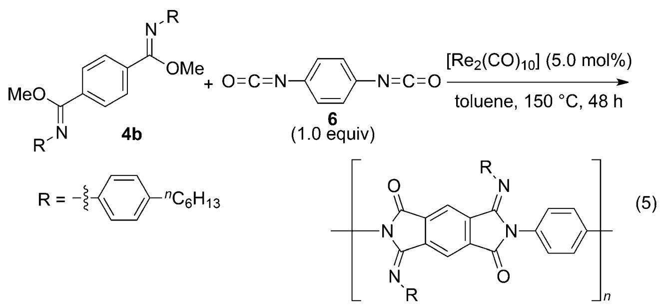
Based on the results of Equations (3) and (4), we thought that polymers (polyimide derivatives) could be synthesized from diimidates and diisocyanates. We expected that the







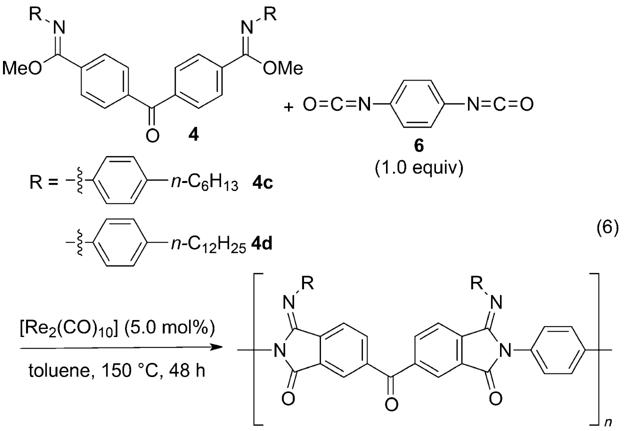
introduction of alkyl chains on the nitrogen atoms of polyimide derivatives would improve the solubility. Treatment of the diimidate **4b** with **6** led to alternating copolymerization and the polyimide derivative **8a** was obtained in 53% yield [Eq. (5)]. This outcome is the first example of the synthesis of a polyimide derivative having imino groups. Interestingly, **8a** is highly soluble in organic solvents such as toluene, THF, dichloromethane, and chloroform. The use of



	Yield [%]	M_n	M_w/M_n	Td_5/N_2 [°C][a]
8a	53	4700	3.12	323

[a] 5%-wt loss temperature, 10 °C/min

the diimidate **4c**, bearing a carbonyl group, increased the decomposition point of the obtained polymer **8b** [Eq. (6)].[14] In the case of the diimidate **4d**, which has a longer alkyl chain, the decomposition point of the polymer **8c** decreased slightly, but the solubility of **8c** increased [Eq. (6)].[15] For the thermal



(6)

	R	Yield [%]	M_n	M_w/M_n	Td_5/N_2 [°C][a]
8b	n-C_6H_{13}	60	4400	2.87	362
8c	n-$C_{12}H_{25}$	68	6200	2.97	328

[a] 5%-wt loss temperature, 10 °C/min

stability of the polyimide analogues **8a–c**, the values of Td_5/N_2 were lower than that of a related polyimide which is synthesized from pyromellitic dianhydride and 1,4-phenylenediamine (Td_5/N_2: 539 °C).[16]

In summary, we succeeded in the rhenium-catalyzed synthesis of 3-imino-1-isoindolinones from aromatic imidates and isocyanates in good to excellent yields. In this reaction, the imino groups of the imidates were retained by eliminating the methoxy unit of the imidates as a leaving group. Examples of such a reaction pattern (insertion of an unsaturated molecule into a C–H bond, intramolecular nucleophilic cyclization, and elimination of a small molecule) are quite rare. A gram-scale reaction proceeded in excellent yield, and double annulation reactions occurred using a diimidate or diisocyanate. These double annulation reactions were applied to the synthesis of polyimide derivatives having high solubility in organic solvents, such as toluene, THF, dichloromethane, and chloroform. This protocol is the first example of the synthesis of polyimide derivatives with imino groups. We hope that this reaction will become a useful method for the synthesis of 3-imino-1-isoindolinones and polyimide derivatives.

Experimental Section

Typical procedure for rhenium-catalyzed synthesis of 3-imino-1-isoindolinone **3a** by a C–H bond activation and successive dealkoxylative annulation: A mixture of (*Z*)-methyl *N*-phenylbenzimidate (**1a**, 52.8 mg, 0.25 mmol), *p*-tolylisocyanate (**2a**, 33.3 mg, 0.25 mmol), [$Re_2(CO)_{10}$] (4.1 mg, 6.3 μmol), and toluene (1.0 mL) was stirred at 150 °C for 24 h in a sealed tube. Then, the solvent was removed in vacuo and the product was isolated by column chromatography on silica gel (*n*-hexane/EtOAc = 10:1) to give (*E*)-3-(phenylimino)-2-*p*-tolyl-1-isoindolinone (**3a**, 77.3 mg, 99% yield).

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Keywords: C–H activation · isocyanate · polymers · rhenium · synthetic methods

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[9] As a first trial, *N*,*N*-dimethylbenzamide was selected as a substrate because dimethylamine might be formed after the desired annulation reaction. Treatment of *N*,*N*-dimethylbenzamide with 2.0 equiv of phenylisocyanate in the presence of $[Re_2(CO)_{10}]$ (2.5 mol%) in toluene at 180°C for 24 h gave 2-phenylisoindoline-1,3-dione in 34% yield by the formation of 1,1-dimethyl-3-phenylurea (27%) from dimethylamine (byproduct) and the isocyanate. The yield of isoindolinedione was low because the reaction was inhibited by the urea.

[10] There have been several reports on C–H bond transformations by insertion of isocyanates into an aromatic C–H bond. For examples, see: a) Y. Kuninobu, Y. Tokunaga, K. Takai, *Chem. Lett.* **2007**, *36*, 872; b) K. D. Hesp, R. G. Bergman, J. A. Ellman, *J. Am. Chem. Soc.* **2011**, *133*, 11430; c) K. Muralirajan, K. Parthasarathy, C.-H. Cheng, *Org. Lett.* **2012**, *14*, 4262; d) B. Zhou, W. Hou, Y. Yang, Y. Li, *Chem. Eur. J.* **2013**, *19*, 4701. See also: ref. [6b].

[11] CCDC 951151 (**3a**) contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

[12] The reaction did not proceed using phenyl isothiocyanate.

[13] Methanol was formed in 32%, as determined by NMR spectroscopy, from the reaction between **1a** and **2a**.

[14] In this reaction, 41.8 mg of an insoluble dark reddish brown solid (**8b′**) was obtained from 154.2 mg of **4c**. Comparison of IR spectra between **8b** and **8b′** indicates that the insoluble solid **8b′** may be a polymer with higher molecular weights compared with **8b**.

[15] Glass transition temperatures (T_g) of **8a**, **8b**, and **8c** were not observed within a measurable temperature range (−50–220°C).

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