N-Aryl Acylureas as Intermediates in Sequential Self-Repetitive Reactions To Form Poly(amide−imide)s

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Introduction. Carbodiimides (CDI), easily prepared from isocyanates,[1] have been known to react with carboxylic acids to form a mixture of acid anhydrides (anhydrides), *N*,*N*′-substituted ureas (ureas), and *N*-acyl-*N*,*N*′-disubstituted ureas (or *N*-acylureas). Earlier mechanistic studies by Khorana[2,3] and Silverstein[4,5] showed that two parallel reaction pathways might account for the diversity of products observed. The initial formation of an *O*-acylisourea intermediate that can either rearrange into *N*-acylurea or undergo a further substitution reaction with another acid molecule to produce the corresponding ureas and anhydrides as final products (Scheme 1). The earlier literature indicated that aromatic CDIs seem to favor the formation of *N*-acylureas upon treatment of carboxylic acids, whereas aliphatic CDIs often lead to the formation a mixture of anhydrides and *N*,*N*′-disubstituted ureas.[6] Recent evidence has shown that ferrocenecarboxylic acid was able to selectively add onto an aromatic CDI to yield an *N*-acylurea as the main product.[7] In another report by Lau,[8] the synthesis of di- and trisubstituted *N*-acylureas on a solid support was also achieved in excellent yields.

Although the thermal conversion of an *N*-acylurea into an isocyanate and an amide has been well documented,[9] the overall transformation from isocyanate to CDI and then from CDI to amide through thermolysis of the *N*-acylurea has not been fully exploited either as synthetic intermediates or as latent isocyanate sources. The contamination by urea and anhydride as byproducts may prevent a clean isolation of *N*-acylurea. To the best of our knowledge, high-yield formation of an *N*-acylurea as an isocyanate precursor or as an isolable intermediate for polyamide synthesis has not been developed previously. Herein, we report the preparation of aryl *N*-acylureas in high yield, their consequential thermal reactions, and applications in a stepwise synthesis of aryl amides and polyamides.

Results and Discussion. In our recent selectivity study of CDI reactions, carboxylic acids were allowed to react separately with two CDI model compounds: dicyclohexylcarbodiimide (DCC) as an aliphatic CDI whereas diphenylcarbodiimide (DPCDI) which was prepared from phenyl isocyanate and a catalytic amount of 1,3-dimethyl-3-phospholene oxide (DMPO) as the aromatic CDI (Scheme 1). In doing so, we found two distinctive product types indicating the existence of different pathways in the CDI reaction (Table 1). Using DCC as starting material to react with benzoic acid **2a** or acetic acid **2g,** for example, the reaction yielded anhydrides and ureas as the major product. Low yields (38 and 25%; entry 1 and 2) of *N*-acylurea were observed in the product mixture. Other carboxylic acids also afforded poor yields of *N*-acylureas when treated with DCC.

The selectivity for *N*-acylurea was enhanced dramatically when DPCDI was used instead of DCC. The migration of the acyl group from the O to N atom in the initial isourea seems to be dominant. For example, treatment of DPCDI with acetic acid, **2a**, at room temperature afforded 80% of *N*-acylurea **5c**, with the formation of byproducts, anhydride and diphenylurea**,** in a minute quantity (entry 3). In the case of benzoic acid with DPCDI, the selectivity of *N*-acylurea was found to be even higher (93%). Furthermore, the reaction between DPCDI and aromatic carboxylic acids **2b**−**2f** with electron-withdrawing or electron-donating produced the corresponding *N*-acylureas **5d**−**5h** in high selectivity (95−99%, entry 4−8). These results demonstrate that aryl *N*-acylureas could be prepared in high yields under mild conditions using aryl isocyanates as starting materials.

The *N*-acylurea was stable below 140 °C but decomposed at a higher temperature into fragments consisting of isocyanates and amides. This was confirmed by the trapping of isocyanate by ethylene glycol from heating of **5h** in formation of bisurethane derivative of phenyl isocyanate along with amide−imide both in good yields.[10] Furthermore, when *N*-acylurea **5h** was heated with **2f** in the presence of DMPO catalyst at 140 °C, only amide−imide was isolated in high yield (80%, by isolation). Because of these observations, *N*-acylureas can be regarded both as a blocked isocyanate and reactive intermediate for amides and could be utilized as a stepping stone for further synthetic applications. To further illustrate the synthetic potential of acylureas, *N*-acylurea **5g** was treated with methanol at room temperature to give a new acid-functionalized ester−acylurea **6** (Scheme 2). The ester−acylurea **6** was then heated to 140 °C for 45 min to form the acid−amide derivative **7**. The acid−amide **7** was reacted with DPCDI to give a new acylurea **8** as the intermediate. The reaction temperature was finally raised to 210 °C for 30 min to affect the ring-closure step to yield amide−imide **9**. From this one-pot process, high yield of amide−imide **9** was isolated (93%) and confirmed by analyses to be the sole product.

Thus, we have developed a new and efficient three-step synthesis of amides from aromatic isocyanates and carboxylic acids under the influence of a CDI catalyst such as DMPO. The catalytic conversion of 1 mol of aromatic isocyanate into 0.5 mol of aryl CDI is the first step. The reaction between the CDI and a carboxylic acid to form 0.5 mol of *N*-acylurea as an isolable intermediate is the second. Last, the thermolysis of the *N*-acylurea yielding 0.5 mol of amide as the product but concurrently generating another 0.5 mol of isocyanate is the third. Thus, it points to the fact that 50% of isocyanates were consumed in one full cycle by the sequential self-repetitive reactions (or "SSRR" reactions for abbreviation) to form 50% of amide. Repetitions of the same three sequential reactions will eventually consume all isocyanates, CDIs and *N*-acylureas, when provided with enough carboxylic acid. More significantly, we have demonstrated that highly reactive isocyanate or CDI compounds could be converted into soluble *N*-acylurea intermediate in transient. The *N*-acylurea can be isolated and converted into the high-melting amides directly. Compared to the direct reaction of isocyanate and carboxylic acid, the

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Scheme 1. Synthesis of *N*-Acylurea from Carbodiimide and Carboxylic Acid and the Possible Side Products

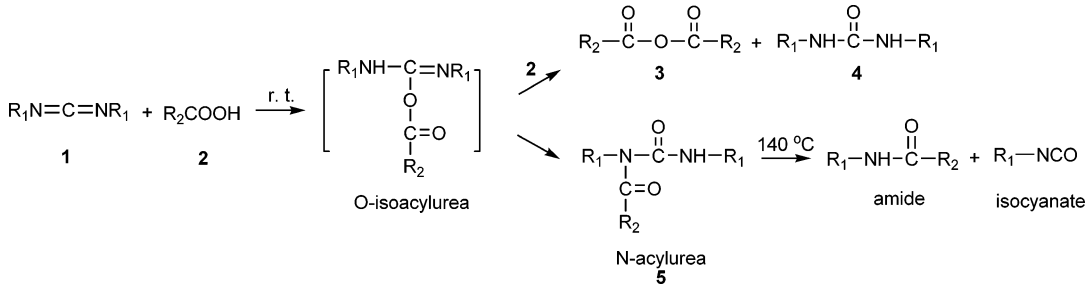
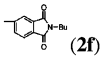
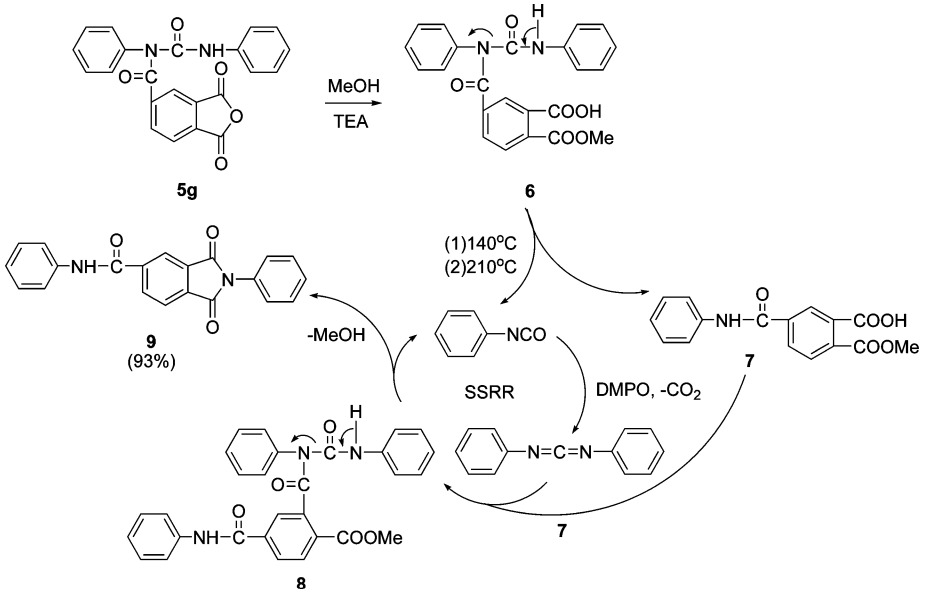


Table 1. Reaction of Carbodiimide and Carboxylic Acid

entry	CDI[a] (R_1 =)	carboxylic acid (R_2 =)	Selectivity (mol %) of N-acylurea[b]	Yield (%)[c]
1	Cy	Ph (**2a**)	38	n.d. (**5a**)
2	Cy	CH_3 (**2g**)	25	n.d. (**5b**)
3	Ph	Ph (**2a**)	93	80 (**5c**)
4	Ph	p-NO_2-Ph (**2b**)	89	85 (**5d**)
5	Ph	p-OMe-Ph (**2c**)	98	88 (**5e**)
6	Ph	o-OMe-Ph (**2d**)	> 99	93 (**5f**)
7	Ph	 (**2e**)	> 99	88 (**5g**)
8	Ph	 (**2f**)	> 99	88 (**5h**)
9	Ph	CH_3 (**2g**)	95	90 (**5i**)
10	Ph	$CH_3(CH_2)_5$ (**2h**)	> 99	88 (**5j**)

[a] Cy = cyclohexyl. [b] Calculated by ^{1}H NMR integration. [c] Isolated by precipitation or recrystallization. [d] n.d. = not determined due to complicated product mixtures (anhydride + urea + *N*-acylurea).

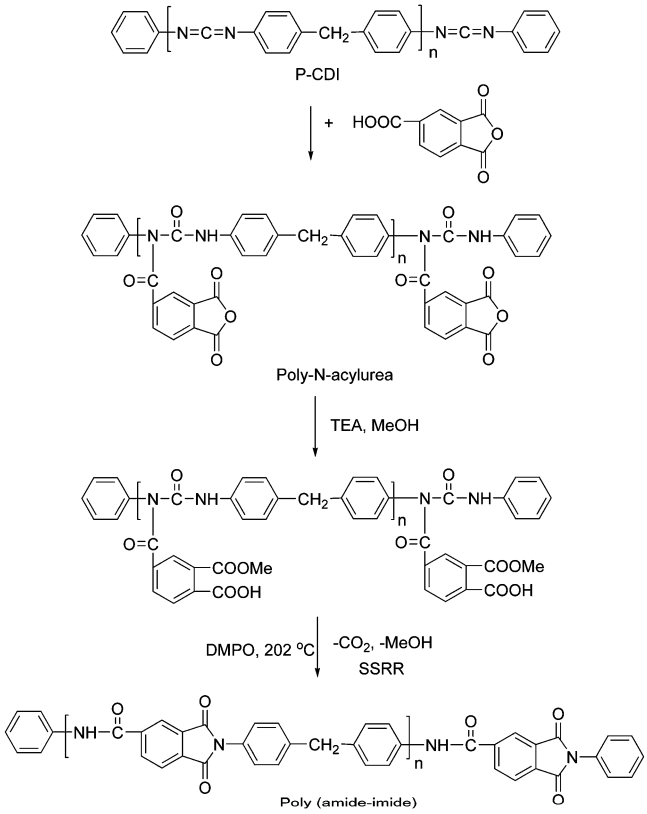
Scheme 2. Reaction Mechanismof Amide−Imide Formation via the SSRR Process from the Anhydride-Functional *N*-Acylurea



sequential reactions appear to offer the advantages of lower temperature conditions and higher selectivity in amide synthesis.

The SSRR reactions also have been successfully applied to the synthesis of polyamides. In this approach, polycarbodiimide (P-CDI) was first prepared from the mixture of methylene diphenylene diisocyanate (MDI) and monofunctional phenyl isocyanate in molar ratio of 16:1.[11] P-CDI was allowed to react with TMA at room temperature in *N*-methyl-2-pyrrolidone (NMP) solution to form the corresponding polyacylurea, as shown in Scheme 3. By following the SSRR procedures used in synthesizing **9**, the anhydride functional groups of poly-*N*-acylurea were opened by the addition of equimolar methanol at room temperature. The final poly(amide−imide) was generated in NMP solution by heating the poly-*N*-acylurea to 202 °C. The final poly(amide−imide) (PAI) was isolated in 92% by precipitation in water and characterized to have a high T_g at 238 °C and T_d at 457 °C. The polymer was further characterized by ^{1}H NMR as shown in the Supporting Information.[12]

Scheme 3. Synthesis of Poly(amide−imide) from Poly-*N*-acylurea via SSRR



In summary, we have demonstrated a high-yield synthesis for aryl *N*-acylureas from aromatic CDI and carboxylic acids by a simple mixing at ambient temperature. The aryl *N*-acylureas are thermally stable up to 140 °C and undergo a rapid transformation into isocyanates and amides at high temperature. With the addition of CDI catalyst and a suitable amount of carboxylic acid, the aryl *N*-acylureas can be further transformed into aryl amides or polyamides in high yields through the SSRR sequence. Further exploration of using this SSRR process for synthesizing PAI elastomers is being pursued.

Supporting Information Available: Experimental procedures and ^{1}H NMR for compound **5c**−**5j**, **9**, and poly(amide−imide) and ^{13}C NMR for **5h** and **9**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(10) Note: 2.2 mmol of **5h** reacted with 1.1 mmol of ethylene glycol and obtained 1.85 mmol of amide−imide and 0.68 mmol of bisurethane (by HPLC). For details see Supporting Information S5.
(11) Alberino, L. M.; Farrissey, W. J. US Pat. 3, 929, 733, 1975.
(12) Note: synthesis of poly(amide−imide) and the ^{1}H NMR characterization for poly(amide−imide) are shown in Supporting Information S3 and S21.

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