Selective Synthesis of Novel Cyclic Phenylazomethine Trimers

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Novel cyclic phenylazomethine trimers (CPAs) were synthesized in a one-step dehydration of the 4-aminobenzophenone derivatives in the presence of $TiCl_4$ or *p*-toluenesulfonic acid (PTS). The CPAs were isolated in over 90% yield under nondilute conditions. When using $TiCl_4$ as the dehydration agent, the induction of bulky substituents at the α-position of the substrate enhanced the yields of the CPAs. On the other hand, PTS served as an effective catalyst for the synthesis of the phenyl-substituted CPA. This different reactivity between $TiCl_4$ and PTS depends on the dehydration mechanism being dominated by a kinetic process or thermodynamic one. The obtained CPAs were confirmed by NMR, UV−vis spectra, and MM2 calculation to have only a *Z* conformation and a nonconjugated structure compared to the linear oligophenylazomethines (OPAs) and the aniline-capped OPAs (OPA's).

Introduction

There has been considerable interest in aromatic macrocyclic oligomers that can be utilized as reactive monomers in the ring-opening polymerization to give linear polyaromatics with high molecular weight and high purity, which are used as thermostable engineering plastics. The thermal polymerization of cyclic thiophenylene oligomers,[1] the metathesis polymerization of cyclic olefins,[2] and the anionic polymerization of cyclic polycarbonates are examples of such.[3] Most of the preparative methods for these cyclic aromatic compounds result in not only low yields but also in the formation of a mixture of cyclic oligomers with different numbers of repeating units along with linear oligomers.[4] Until now, cyclic compounds were synthesized under hyperdiluted conditions, and there have been few reports about the highly selective preparation of a discrete cyclic aromatic in a one-step reaction.[5] The convenient and efficient preparation of a cyclic oligomer potentially leads to a new reactive monomer as a raw material for high performance polymers.

Herein, we report the synthesis of novel cyclic molecules with phenylazomethine backbones, cyclic phenylazomethines (CPAs),[6] which have an alternate structure of phenylene and a C=N bond as compared to the structure of the linear oligophenylazomethines (OPAs) and the aniline-capped OPAs (OPA's). A polyphenylazomethine chain with the alternating structure of a phenylene ring and a C=N bond should be a thermostable aromatic polymer and have electronic functionality because the structure is analogous to poly(phenylene vinylene), which is an important conductive polymer.[7] We have succeeded in the selective synthesis of CPAs with a high yield using $TiCl_4$ or PTS.

Results and Discussion

Synthesis of Cyclic Phenylazomethines (CPAs). In general, the dehydration of amines with aldehydes efficiently takes place in the presence of *p*-toluenesulfonic acid (PTS) as the catalyst, whereas the dehydration of aromatic amines with aromatic ketones proceeded very slowly (Scheme 1, Table 1, Run 1).[8] Instead of PTS, $TiCl_4$ is effective as a Lewis acid and as a dehydration agent (Run 2). In the presence of $TiCl_4$, the dehydration of 4′-aminoacetophenone gave the corresponding polymer and no cyclic trimer (Scheme 2, Table 2, Run 1). However, the novel cyclic (α-phenyl)phenylazomethine trimer (CPA-a) was obtained in a 20% yield under nondilute conditions ([monomer] = 0.1 M) by the dehydration of 4-aminoben-

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Scheme 1. Synthesis of a Model Compound 3

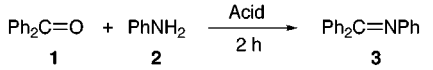


Table 1. Synthesis of a Model Compound 3

Run	Acid (equiv)	Solvent	*T* °C	Yield, %
1	PTS (0.10)	*p*-Xylene	140	19
2	$TiCl_4$ (0.75)	Chlorobenzene	125	91

Scheme 2. Synthesis of CPAs

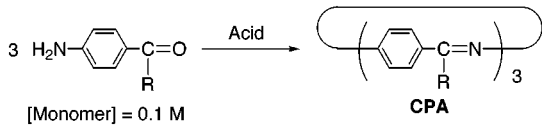


Table 2. Synthesis of CPA

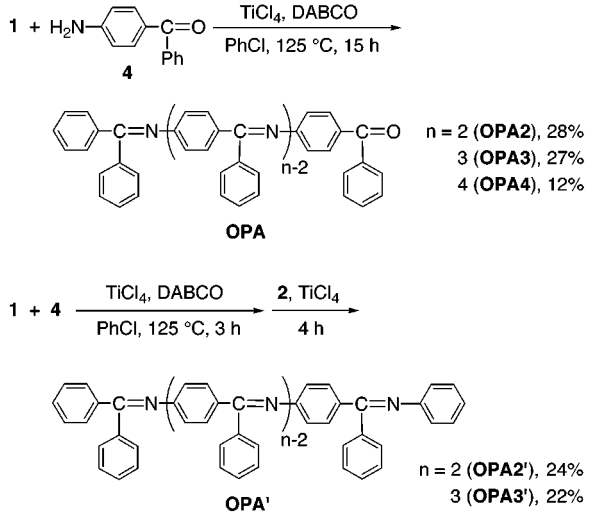
Run	R	Acid (equiv.)	Yield, %
1	Me	$TiCl_4$ (0.75)[a]	0[c]
2	Ph	$TiCl_4$ (0.75)[a]	20[c]
3	NH(*n*-octyl)	$TiCl_4$ (0.75)[a]	49
4	N(*n*-octyl)$_2$	$TiCl_4$ (0.75)[a]	92
5	Me	PTS (0.05)[b]	0[c]
6	Ph	PTS (0.05)[b]	90
7	NH(*n*-octyl)	PTS (0.05)[b]	32
8	N(*n*-octyl)$_2$	PTS (0.05)[b]	trace[d]

[a] Solv.: chlorobenzene, 125 °C, 15 h. [b] Solv.: *p*-xylene, 140 °C, 16 h. [c] The other products were the polymeric compounds. [d] The other products were the oligomers up to pentamer.

zophenone (Run 2). The yield is considerably higher than those of previously reported cyclizations, such as those of carbonate and thiophenylene compounds.[4] As a side-product, poly(α-phenyl)phenylazomethine (PPA) was obtained in this reaction. In the case of using $TiCl_4$, the high yield and the selectivity of the CPA were caused by the bulky substituents at the α-position of the substrate. The dehydration of 4-amino-4′-octylaminobenzophenone resulted in the formation of the corresponding cyclic trimer (CPA-b) in a 49% yield (Run 3). The dehydration of 4-amino-4′-dioctylaminobenzophenone gave the corresponding trimer (CPA-c) with a 92% isolated yield (Run 4).[9] On the other hand, a different reaction behavior was observed in the presence of PTS. The dehydration of 4′-aminoacetophenone by PTS gave the corresponding polymer, similar to the dehydration by $TiCl_4$ (Run 5), but CPA-a was obtained with a 90% yield by the dehydration of 4-aminobenzophenone (Run 6). Contrary to the case of $TiCl_4$, a bulky substituent produced a lower

(9) FAB-MS spectra of CPAs show no contamination of the other cyclic oligomers.

Scheme 3. Synthesis of OPAs and OPA's



yield of CPA (Run 7, 8). The other products were confirmed by GPC to be the oligomers up to pentamer. These different results between $TiCl_4$ and PTS depend on each specific dehydration mechanism as will be described later.

Spectroscopic Analysis of the Azomethine Structure. The linear oligophenylazomethines (OPAs) and the aniline-capped OPAs (OPA's) were synthesized as comparative compounds of CPAs (Schemes 3). The ^{13}C NMR spectra revealed that OPA3 and OPA2′ have 2 isomers and OPA4 and OPA3′ have 4 isomers, respectively (Figure 1). These isomers were caused by the *E*/*Z* conformation of the azomethine moiety. OPA3 has one carbonyl and two azomethines, but two peaks attributed to the carbonyl carbon at 203.04 and 202.85 ppm, and four peaks attributed to the azomethine carbon at 187.20, 187.00, 183.83, and 183.80 ppm were observed in the ^{13}C NMR spectrum (Figure 1b). The formation ratio of the *E* isomer with the *Z* one in the OPA3 was estimated to be 1:1, based on the area ratio of the two peaks attributed to the carbonyl carbon. OPA4 has one carbonyl and three azomethines, but the ^{13}C NMR spectrum (Figure 1c) shows four peaks attributed to the carbonyl carbon at 203.29, 203.11, 202.89, and 202.65 ppm and multiple peaks attributed to the azomethine carbon. On the basis of the integration ratio of each peak in the spectrum of OPA4 (the pulse sequence is NNE), the formation ratio of the four isomers was approximately estimated to be 9:6:3:1. Similar to OPA3 and OPA4, OPA2′ and OPA3′ showed multiple peaks corresponding to the isomeric structures. In OPA2′ with two azomethines, four peaks attributed to the azomethine carbon were observed at 168.96, 168.51, 168.21, and 167.86 ppm (Figure 1e), and the spectrum of OPA3′ with three azomethines shows 12 peaks (Figure 1f). OPA2 and a model compound **3** had simple spectra due to no *E*/*Z* isomers (Figures 1a, d). In the case of the cyclic compounds, the spectrum of CPA that has three azomethines shows only one peak attributed to the azomethine carbon, because CPA has only one conformation with a symmetrical structure (Figure 1g).

UV−vis spectroscopy often provides useful information about the conformation of molecules. The UV−vis spectrum of CPA-a shows the shortest λ_{max} absorbed $\pi-\pi^*$ transition of the azomethine moiety at 318 nm (Figure 2). For the OPAs, the absorption based on the $\pi-\pi^*$

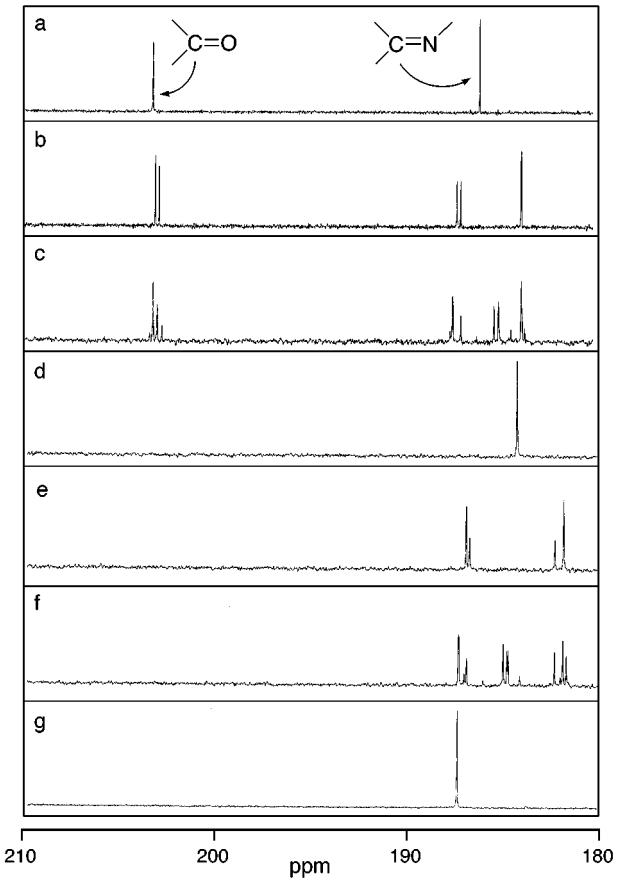


Figure 1. The ^{13}C NMR spectra of a) OPA2, b) OPA3, c) OPA4, d) a model compound **3**, e) OPA2′, f) OPA3′, and g) CPA-a in CF_3COOD.

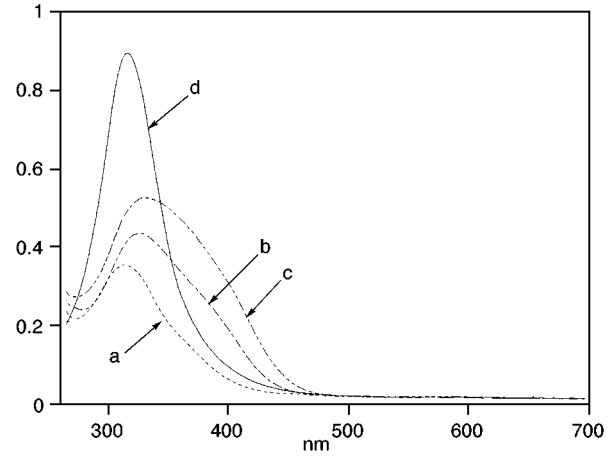


Figure 2. The UV−vis spectra of a) OPA2, b) OPA3, c) OPA4, and d) CPA-a.

transition of azomethine shifts to the longer wavelength according to the conformation. The *E* and *Z* isomers possess different electronic structures, of which the absorption band of the *E* isomer is shifted by about 20−50 nm to a longer wavelength than that of the *Z* isomer due to elongation of the π-conjugation. A MM2 calculation of CPA-a with only the *Z* conformation indicated that the three phenyl rings in the cyclic trimer do not have a coplanar structure (Figure 3). The structure of the *E* isomer possesses a distortion that is too large, as indicated by the large formation energy calculated by molecular modeling. Besides, the single conformation

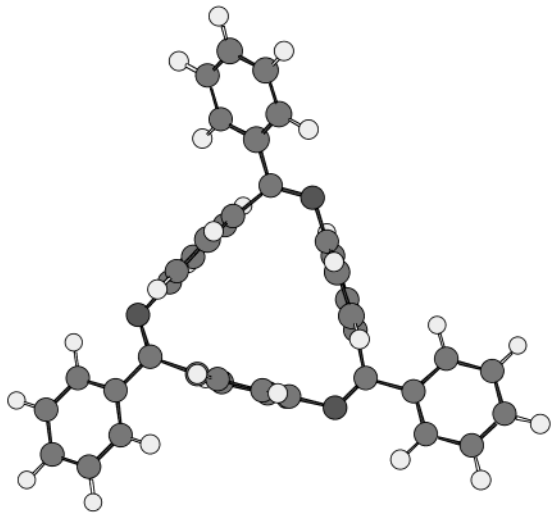
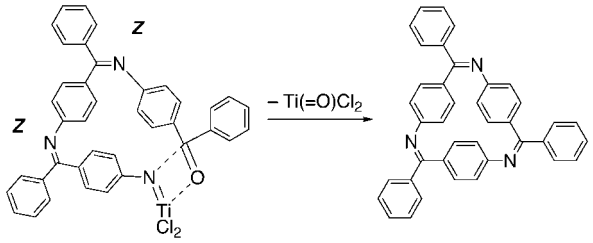


Figure 3. The result of the MM2 calculation of CPA-a.

Scheme 4. Intramolecular Dehydration of the Linear Trimer with *Z,Z* Conformation



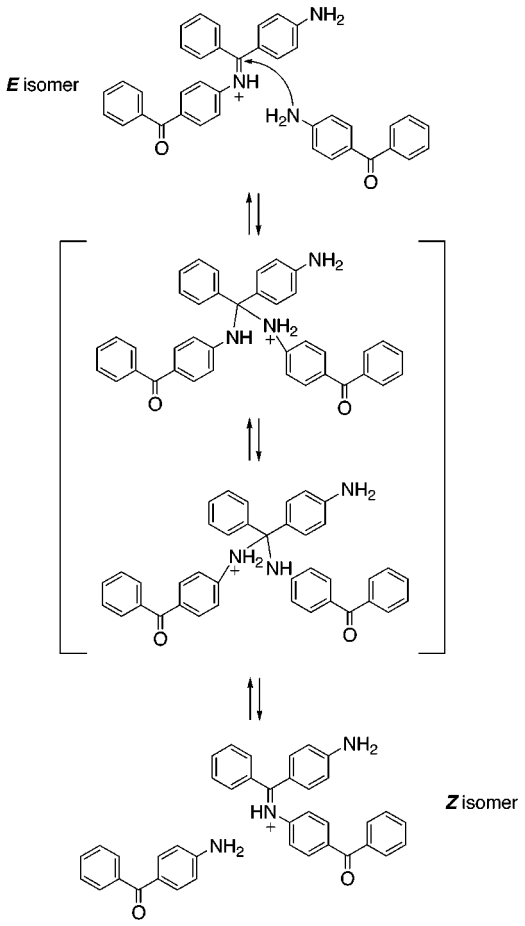
of CPA is also supported by the NMR data. These results support the idea that CPA has only the *Z* conformation.

Thermostability of CPA-a, OPAs, OPA's, PPA. The obtained phenylazomethine compounds have a high thermostability due to the imine bond, which has a large bond energy (615 kJ/mol). The temperatures for a 5% weight loss ($Td_{5\%}$) of OPA2, 3, 4, 2′, 3′, and PPA were determined to be 301, 368, 438, 326, 397, and 508, respectively, based on the thermogravimetric analysis. The $Td_{5\%}$ increased with an increase in the degree of polymerization and capping with aniline. CPA-a shows a good $Td_{5\%}$ at 404 °C, which was close to that of OPA3′, due to no end group in the chain.

The Coupling Mechanism. Dehydration agents drastically influenced the synthesis of the CPAs (Scheme 2). The CPAs are formed through the intramolecular coupling of the linear trimer with the *Z,Z* conformation (Scheme 4). Because the dehydration using $TiCl_4$ is an irreversible reaction, the formation of CPAs is simply dominated by the conformation, that is, the formation ratio of the *E*/*Z* isomers. The *Z* isomer of OPA3 is formed with about a 50% yield, which was confirmed by the NMR spectrum.[10] Therefore, CPA-a is theoretically formed in 25% (0.5^2) yield, which agrees with the experimental one of 20%. The higher yields of CPA-b and -c are based on the preferential formation of the *Z* isomer due to steric effects of the bulky substituents. On the other hand, the dehydration using PTS is an equilibrium reaction, in which the ratio of the isomers is controlled by the thermodynamic process. Therefore, the exchange reaction

(10) No thermal isomerization of OPA3 was confirmed up to 130 °C in the NMR measurement.

Scheme 5. Exchange between the *E* and *Z* Isomers via Transamination



between the *E*/*Z* isomers occurs through the transamination (Scheme 5). In addition, the resulting CPA-a is insoluble in the reaction solvent, so the formation of CPA-a has a possibility to be accelerated in the equilibrium reaction. However, PTS was not useful for the dehydration of the monomers substituted with alkylaminophenyl groups at the α-position because the π-conjugation of the monomers to the aminophenyl group at the α-position lowers the electrophilicity of the carbonyl carbon.

Conclusion

Novel cyclic phenylazomethine trimers were synthesized with high yields via the dehydration of the 4-aminobenzophenone derivatives in the presence of $TiCl_4$ or PTS. In the case using $TiCl_4$ as a dehydration agent, the introduction of bulky substituents at the α-position of the substrate enhanced the yields of the cyclic trimers. On the other hand, PTS was specifically useful in the synthesis of the phenyl-substituted cyclic trimer. This different reactivity between $TiCl_4$ and PTS depends on each dehydration mechanism. The cyclic trimers were confirmed by NMR, UV−vis spectra, and the result of the MM2 calculation to have only the *Z* conformation and a nonconjugated structure compared to the linear oligophenylazomethines. This method is expected to provide an efficient synthesis of the cyclic trimers as a monomer of the polyphenylazomethine with high molecular weight and high thermostability.

Experimental Section

Synthesis of CPA-a using $TiCl_4$ as a Dehydration Agent. To a mixture of 4-aminobenzophenone (4.93 g, 25.0 mmol) and 1,4-diazabicyclo[2,2,2]-octane (DABCO) (8.41 g, 75.0 mmol) in chlorobenzene (150 mL) was added $TiCl_4$ (3.56 g, 18.8 mmol), dropwise. The addition funnel was rinsed with chlorobenzene (5 mL). The reaction mixture was heated in an oil bath at 125 °C for 15 h. The precipitate, including CPA-a, was isolated by filtration. To α-chloronaphthalene (200 mL) was added the filter cake; the heterogeneous solution was stirred at 190 °C for 3 h. The α-chloronaphthalene solution was separated by hot filtration. CPA-a (0.890 g, 4.96 mmol, 20% yield) was isolated by precipitation from methanol.

Synthesis of CPA-a using PTS as a Dehydration Agent. A mixture of 4-aminobenzophenone (5.92 g, 30.0 mmol) and PTS monohydrate (286 mg, 1.50 mmol) in *p*-xylene (300 mL) was refluxed with stirring for 16 h. The condenser was fitted with a Dean−Stark water trap. After the mixture was cooled and concentrated, CPA-a (4.82 g, 8.96 mmol, 90%) was isolated by precipitation with methanol.

Synthesis of CPA-b using $TiCl_4$ as a Dehydration Agent. To a mixture of 4-amino-4′-octylaminobenzophenone (0.195 g, 0.60 mmol) and DABCO (0.202 g, 1.80 mmol) in chlorobenzene (6 mL) was added $TiCl_4$ (0.085 g, 0.45 mmol), dropwise. The addition funnel was rinsed with chlorobenzene (1 mL). The reaction mixture was heated in an oil bath at 125 °C for 15 h. The precipitate was removed by filtration. The filtrate was concentrated, and CPA-b (0.090 g, 49%) was isolated by silica gel column chromatography (ethyl acetate: hexane = 1:10, including 2% Et_3N, $R_f = 0.1$).

Synthesis of CPA-b using PTS as a Dehydration Agent. A mixture of 4-amino-4′-octylaminobenzophenone (0.649 g, 2.00 mmol) and PTS monohydrate (19.1 mg, 0.100 mmol) in *p*-xylene (20 mL) was refluxed with stirring for 16 h. The condenser was fitted with a Dean−Stark water trap. After the mixture was cooled and concentrated, CPA-b (0.194 g, 0.211 mmol, 32%) was isolated by silica gel column chromatography (ethyl acetate/hexane = 1:10, including 2% Et_3N, $R_f = 0.1$).

Synthesis of CPA-c. To a mixture of 4-amino-4′-dioctylaminobenzophenone (0.10 g, 0.23 mmol) and DABCO (0.077 g, 0.69 mmol) in chlorobenzene (5 mL) was added $TiCl_4$ (0.033 g, 0.17 mmol), dropwise. The additional funnel was rinsed with chlorobenzene (1 mL). The reaction mixture was heated in an oil bath at 125 °C for 15 h. The precipitate was removed by filtration. The filtrate was concentrated, CPA-c (0.089 g, 92%) was isolated by silica gel column chromatography (ethyl acetate/hexane = 1:10, including 2% Et_3N, $R_f = 0.2$).

Synthesis of Linear Oligophenylazomethines (OPAs). To a mixture of 4-aminobenzophenone (0.986 g, 5.00 mmol), benzophenone (4.56 g, 25.0 mmol), and DABCO (1.68 g, 15.0 mmol) in chlorobenzene (40 mL) was added $TiCl_4$ (0.711 g, 3.75 mmol), dropwise. The addition funnel was rinsed with chlorobenzene (5 mL). The reaction mixture was heated in an oil bath at 125 °C for 15 h. The precipitate was removed by filtration. The filtrate was concentrated, OPA2 (0.946 g, 52%), OPA3 (0.713 g, 29%), and OPA4 (0.121 g, 10%) were isolated by silica gel column chromatography (ethyl acetate/hexane = 1:10, including 2% Et_3N, $R_f = 0.2$, 0.15, and 0.1, respectively).

Synthesis of a Model Compound 3. To a mixture of aniline (511 mg, 5.49 mmol), benzophenone (984 mg, 5.40 mmol), and DABCO (1.85 g, 16.5 mmol) in chlorobenzene (50 mL) was added $TiCl_4$ (782 mg, 4.12 mmol), dropwise. The addition funnel was rinsed with chlorobenzene (2 mL). The reaction mixture was heated in an oil bath at 125 °C for 2 h. The precipitate was removed by filtration. The filtrate was concentrated, and **3** (1.27 g, 4.93 mmol, 91%) was isolated by silica gel column chromatography (ethyl acetate/hexane = 1:5, $R_f = 0.6$).

Synthesis of Aniline-Capped OPAs (OPA's). To a mixture of 4-aminobenzophenone (3.94 g, 20.0 mmol), benzophenone (7.29 g, 40.0 mmol), and DABCO (20.19 g, 180.0 mmol) in chlorobenzene (200 mL) was added $TiCl_4$ (2.85 g, 15.0 mmol), dropwise. The addition funnel was rinsed with chlorobenzene (5 mL). The reaction mixture was heated in an oil bath at 125

°C for 3 h. After the reaction mixture cooled, aniline (4.66 g, 50.0 mmol) and $TiCl_4$ (5.70 g, 30.0 mmol) were added. The reaction mixture was further heated in an oil bath at 125 °C for 4 h. The precipitate was removed by filtration. The filtrate was concentrated; OPA2′ (2.06 g, 4.71 mmol, 24%) and OPA3′ (1.33 g, 2.16 mmol, 22%) were isolated by silica gel column chromatography (ethyl acetate/hexane = 1:5, including 1.5% Et_3N, R_f = 0.5 and 0.45, respectively).

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Supporting Information Available: All characterization data (^{1}H-, ^{13}C NMR, IR, MS, elemental analysis) of CPAs, OPAs, a model compound **3**, and OPA's. This material is available free of charge via the Internet at http://pubs.acs.org.

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