Synthesis of Amino Acid-derived Curing Reagents Containing a Disulfide Bond and Their Application to Anionic UV Curing Materials

Masahiro Furutani*, Kako Maeno, and Arata Tanaka

Department of Chemistry and Biology, National Institute of Technology, Fukui College, Geshi-cho, Sabae, Fukui 916-8507, Japan
*furutani@fukui-nct.ac.jp

Anionic UV curing has been applied for many kinds of industrial resins, because it overcomes technical problems in conventional radical and cationic UV curing. In this study, a cystine-based latent curing reagent was designed, and synthesized from L- and D-cysteine. The reagents showed not only good solubility toward organic media, but also good thermal decomposition behavior in the presence of basic species. Using them with a photo-base generator and an epoxy resin having a disulfide bond, UV-cured films of B-to-3B grade of pencil-hardness were fabricated successfully, after 10 J/cm² of 365 nm-light irradiation and subsequent heating at 120-160°C for 30 min. Furthermore, two glass substrates were adhered by using this anionic UV curing system, and 1.6-3.7 MPa of shear stress was recorded in the photo-adhesion and re-adhesion experiments.

Keywords: Curing reagent, Disulfide bond, Anionic UV curing, Cystine, Photo-adhesion, Re-adhesion

1. Introduction

UV curing is one of powerful tools in various kinds of industries, and it has been applied to manufacturing, printing, maintenance and so on [1-7]. Generally, UV curing materials are consisted of a photo-initiator and reactive resins. Radical, cationic (acidic), or anionic (basic) species are generated from respective photo-initiators. Among the three curing systems, anionic UV curing has been paid much attention, because the curing system circumvents some problems in radical or cationic UV curing systems, such as polymerization inhibition by oxygen and metallic corrosion [5]. Furthermore, base amplifiers (BAs) have been proposed by Arimitsu [8-10]. BAs increase concentration of base through their auto-catalytic decomposition reactions (base proliferation reactions) triggered by photo-generated bases from photo-base generators (PBGs), resulting in improvement of photosensitivity of the photo-reactive materials [8-15].

As one of applications of BAs, a thermal dismantlable photo-adhesive material has been fabricated with a PBG, an epoxy resin, and a BA having a disulfide bond [16]. This anionic UV curing system had a problem that the BA was not miscible toward organic media, probably due to its molecular symmetry [17]. In this study, cystine-based curing reagents have been designed and synthesized by using L- and D-cysteine compounds at once (Fig. 1). It is known that derivatives of several kinds of amino acid including cystine (LL isomer) work as BA where the amino group is protected with 9-fluorenymethoxycarbonyl (Fmoc) group [18]. A disulfide bond is formed by oxidation reactions of two thiol groups of cysteine, obtaining three kinds of cystine derivatives (LL, DD, and LD isomers). It is

---

Received March 30, 2021
Accepted April 30, 2021
expected that both a steric effect of ester moieties and blending three isomers would contribute to improve the solubility and miscibility. Resulting curing reagent was used with PBG and EP (Fig. 2), which was applied to photo-adhesion as well as anionic UV curing.

2. Experimental

Fmoc-L-Cys(Tr)-OH (N-α-(9-fluorenylmethoxy-carbonyl)-S-trityl-L-cysteine, Fmoc-D-Cys(Tr)-OH (D-isomer of Fmoc-L-Cys(Tr)-OH), and WSCI HCl (water soluble carbodiimide hydrochloride, 1-ethyl-3-(3-dimethylaminopropyl) carbodiimide hydrochloride) were purchased from WATANABE CHEMICAL INDUSTRIES, Ltd. (Hiroshima, Japan). Ethanol, iodine, tetrahydrofuran (THF), toluene, dichloromethane, and sodium sulfite were purchased from FUJIFILM Wako Pure Chemical Corporation (Osaka, Japan). DMAP (dimethylaminopyridine), methanol, chloroform, acetone, and ethyl acetate were purchased from NACALAI TESQUE, INC. (Kyoto, Japan). Polystyrene (PSt, Mw: 35000) and thin layer chromatography plate (TLC Silica gel 60 F254) were purchased from Sigma-Aldrich Co. LLC (St. Louis, United States). All reagents were used without further purification.

1H- and 13C-NMR spectra were recorded using a Bruker AVANCE III. APCI-MS measurements were performed using an AB Sciex AP2000. FT-IR spectral measurements were performed using a Perkin Elmer Spectrum 100. Anionic UV curing and photo-adhesion experiments were performed with 3UVTM-36UVLamp (Analytik Jena AG), UIT-250/UV-D365 ultraviolet radiometer (Ushio Inc.), and SA-201 applicator (TESTER SANGYO Co., Ltd.). Glass substrates were washed by ultrasonic treatment in acetone and then chloroform. Pencil-hardness test was carried out with MJ-PHT tester (Sato Shouji Inc.). Shear stress was recorded using MCT-1150 (A&D Co., Ltd., tensile rate: 10 mm/min).

2.1. Synthesis

PBG [19] and EP [16] were synthesized and purified according to the related literatures reported previously.

Synthesis of 1. To a dried flask were added Fmoc-L-Cys(Tr)-OH (0.25 g, 0.43 mmol), Fmoc-D-Cys(Tr)-OH (0.25 g, 0.43 mmol), and WSCI HCl (0.18 g, 0.95 mmol) in dichloromethane (20 mL) under nitrogen atmosphere. The mixture was stirred at 0°C, followed by adding DMAP (8.1 mg, 6.6 µmol) and ethanol (0.60 g, 13 mmol). After stirring at room temperature for 3 days, solvents were evaporated, and the residue was triturated in water. The mixed equal amount of ethyl ester compounds (Fmoc-L-Cys(Tr)-OEt and Fmoc-D-Cys(Tr)-OEt) were obtained quantitatively as a white solid, confirmed by 1H-NMR spectral measurement.

1H-NMR (400 MHz, CDCl3): δ 1.28 (t, 3H, J = 7.0 Hz, -CH3), 2.67 (m, 2H, -CH2S-), 4.2-4.4 (m, 6H, -CH2O-, C*H, >CH-CH2-), 5.30 (d, 0.8H, J = 8.0 Hz, -NH-), 7.2-7.4 (m, 19H, Ar-H), 7.64 (d, 2H, J = 4.8 Hz, Ar-H), 7.79 (t, 2H, J = 4.8 Hz, Ar-H). Product was used for the next reaction without further purification.

The mixture of ethyl ester compounds (0.48 g) in dichloromethane (20 mL) was added to a dried flask, followed by adding iodine (0.20 g, 0.79 mmol). The solution was stirred at room temperature for 66 h, and then quenched by 1% of sodium sulfite aqueous solution. The organic layer was washed twice with brine, and evaporated to be subjected to column chromatography on silica gel (eluent: chloroform to chloroform/methanol = 10/1, v/v). A mixture of LL and DD isomers of cystine derivatives was obtained as a white solid in 73% total yield.

1H-NMR (400 MHz, CDCl3): δ 1.31 (m, 6H, -CH3), 3.23 (m, 4H, -CH2S-), 4.2-4.7 (m, 12H, -CH2O-, C*H, >CH-CH2-), 5.78 (d, 2H, J = 5.2 Hz, -NH-), 7.3-7.4 (m, 8H, Ar-H), 7.63 (br, 4H, Ar-H), 7.78 (t, 4H, J = 7.6 Hz, Ar-H).

13C-NMR (100 MHz, CDCl3): δ 14, 41, 47, 53, 62, 67, 120, 125, 127, 128, 141, 144, 156, 170. APCI-MS: m/z calcd for C40H40O8N2S2: 740.96; found: 741.5.

Compound 2 was also synthesized and purified through the same procedure, obtaining as a white solid in 44% total yield. 1H-NMR (400 MHz, CDCl3): δ 1.31 (m, 6H, -CH3), 3.23 (m, 4H, -CH2S-), 4.2-4.7 (m, 12H, -CH2O-, C*H, >CH-CH2-), 5.78 (d, 2H, J = 5.2 Hz, -NH-), 7.3-7.4 (m, 8H, Ar-H), 7.63 (br, 4H, Ar-H), 7.78 (t, 4H, J = 7.6 Hz, Ar-H).

The mixture of ethyl ester compounds (0.48 g) in dichloromethane (20 mL) was added to a dried flask, followed by adding iodine (0.20 g, 0.79 mmol). The solution was stirred at room temperature for 66 h, and then quenched by 1% of sodium sulfite aqueous solution. The organic layer was washed twice with brine, and evaporated to be subjected to column chromatography on silica gel (eluent: chloroform to chloroform/methanol = 10/1, v/v). A mixture of LL and DD isomers of cystine derivatives was obtained as a white solid in 73% total yield.

1H-NMR (400 MHz, CDCl3): δ 1.31 (m, 6H, -CH3), 3.23 (m, 4H, -CH2S-), 4.2-4.7 (m, 12H, -CH2O-, C*H, >CH-CH2-), 5.78 (d, 2H, J = 5.2 Hz, -NH-), 7.3-7.4 (m, 8H, Ar-H), 7.63 (br, 4H, Ar-H), 7.78 (t, 4H, J = 7.6 Hz, Ar-H).

13C-NMR (100 MHz, CDCl3): δ 14, 41, 47, 53, 62, 67, 120, 125, 127, 128, 141, 144, 156, 170. APCI-MS: m/z calcd for C40H40O8N2S2: 740.96; found: 741.5.
4H, J = 7.6 Hz, Ar-H). APCI-MS: m/z calcd for C_{40}H_{40}O_{3}N_{2}S_{2}: 740.96; found: 741.5.

2.2. Thermal decomposition behavior of I

PSt, I (167 wt% toward PSt), and 1,3-di-4-piperidyl-propane (0 or 5 mol% toward I) were dissolved into THF. Each solution was dropped on a silicon wafer, and dried in air. The samples were heated at 160 or 120°C with FT-IR spectral measurements at 2-10 min intervals.

2.3. Anionic UV curing

EP, 1 (100 mol% toward EP), and PBG (10 mol% toward EP) were dissolved into THF. The solution was bar-coated on a glass substrate with an applicator (4 mil), followed by pre-baking at 80°C for 1 min. The samples were then subjected to 0-10 J/cm² of 365-nm light irradiation (3.9 mW/cm²), followed by post-baking at 120-160°C for 30 min.

2.4. Photo-adhesion and re-adhesion

Glass substrates coated partially with the mixture of EP, 1, and PBG were prepared according to the same method mentioned above. Each coating area was subjected to 10 J/cm² of 365-nm light irradiation (3.9 mW/cm²). Two glass substrates were then stuck with each other through the UV-irradiated area (ca. 50-70 mm²), followed by post-baking at 160°C for 30 min with at least 0.03 kgf of weight-bearing. Shear stress of each sample was recorded at room temperature (22°C). After that, the two fracture surfaces were stuck again with weight-bearing, which was heated at 90°C for few minutes and then cooled to room temperature, to be subjected to shear stress test under the same experimental conditions.

3. Results and discussion

3.1. Synthesis of I

In the oxidation reaction with a mixture of L- and D-isomers of cysteine derivatives, LL, DD, and LD isomers of cystine derivative would be synthesized stochastically. It was confirmed that I consists of LL and DD isomers, from the results on 1H-NMR and thin layer chromatography (TLC, Rf = 0.85, eluent: chloroform/methanol = 30/1, v/v) of I and 2. On the other hand, another fraction (single spot on TLC plate, Rf = 0.60, eluent: chloroform/methanol = 6/1, v/v) was obtained in the purification process. 1H-NMR spectrum of the fraction (CDCl₃) was complicated, and multiple spots were observed in a TLC after the NMR measurement. These results imply the presence of the LD isomer in CDCl₃ that would be unstable.

Cystine derivatives 1 and 2 showed good solubility toward general organic solvents, such as acetone, THF, chloroform, and ethyl acetate. A cystamine analogue reported previously showed poor solubility [7], which indicates that ester moieties in the chemical structure of 1 or 2 would contribute to improvement of the solubility.

3.2. Thermal decomposition behavior of I

In FT-IR spectral measurements, a peak around 1700 cm⁻¹ was assigned to stretching vibration of C=O bonds of I, and decrease of the peak area was monitored. The area decreased dramatically within 2 min by heating at 120°C in the presence of catalytic amount of base (Fig. 3). In contrast, the area did not decrease even after heating at 160°C for 60 min without bases. These results indicated not only auto-catalytic decomposition behavior of I, but also good thermal stability of I. There are three requirements for BAs [10]: 1) thermal stability in the absence of base, 2) auto-catalytic decomposition in the presence of base, and 3) generation of bases to have enough basicity for the following reactions. Cystine derivative I satisfied the first and second requirements.

3.3. Anionic UV curing

To examine whether I also satisfies the third requirement, UV-cured films were fabricated with a homogeneous composition of PBG, I, and EP. In the pencil-hardness tests (JIS K5400), the hardness is arranged as follows: 6B (softest), 5B, ..., B, HB, F, H, 2H, ..., 9H (hardest). In this test, the pencil is moved scratching over the surface of the coating at a 45° angle with a constant pressure (1 kgf). In the case at 120°C, film was
not cured with 0 or 1 J/cm² of UV irradiation, because trigger bases for the following reactions were not generated enough. Increasing irradiation energy, films were cured successfully, which indicates that 1 was converted into its diamine to form cross-linked networks through reactions with epoxy resins. Similar tendency was observed in the cases at 140°C or 160°C, although dark reactions were caused. Nevertheless, B-to-3B grades of UV-cured films were obtained, probably resulting from photo-triggered base proliferation reactions.

3.4. Photo-adhesion and re-adhesion.

Using the anionic UV curing system, two glass substrates were stuck successfully where 1.6 MPa of the maximum shear stress was recorded (Fig. 4). Rough surface of the adhesive layer was remained on each substrate, which became soft even over 50°C. Re-adhesive samples were subjected to shear stress test again, which shear stress became higher up to 3.7 MPa that was comparable with the value required for products in our daily life (ca. 4 MPa). It was probably due to annealing of the adhesive layers in which exchange reactions between disulfide bonds would be caused [16, 20].

4. Conclusion

Oxidation reactions of L- and D-cysteine derivatives gave a mixture of LL and DD isomers of cystine derivatives that dissolved into organic media. The blending reagents worked as a BA, and anionic UV curing of an epoxy resin was performed, which was applied to photo-adhesion and re-adhesion. The UV-cured material containing disulfide bonds would also be dismantled by gentle heating.

Acknowledgement

MF acknowledges Prof. Eiki Matsui at National Institute of Technology, Fukui College for the use of APCI-MS instrument.

References

1. M. Pagac, J. Hajnys, Q. Ma, L. Jancar, J. Jansa, P. Stefek, and J. Mesicek, Polymers, 13 (2021) 598.
2. H. Wang, C. Chen, F. Yang, Y. Shao, and Z. Guo, Mater. Today Commun., 26 (2021) 102037.
3. M. Yuan, S. Wang, G. Li, S. He, W. Liu, H. Liu, M. Huang, and C. Zhu, Mater. Res. Express, 8 (2021) 035134.
4. T. Distler and A. R. Boccaccini, Acta Biomaterialia, 24 (2015) 372.
5. N. Zivic, K. Kuroishi, H. Okamoto, K. Mamada, and K. Maki, J. Photopolym. Sci. Technol., 32 (2019) 209.
6. V. Shukla and M. Bajpai, Pigment and Resin Technol., 33 (2004) 272.
7. K. Arimitsu, M. Miyamoto, and K. Ichimura, J. Photopolym. Sci. Technol., 12 (1999) 317.
8. M. Miyamoto, K. Arimitsu, and K. Ichimura, J. Photopolym. Sci. Technol., 12 (1999) 315.
9. K. Arimitsu, M. Miyamoto, and K. Ichimura, Angew. Chem. Int. Ed., 39 (2000) 3425.
10. Y. Morikawa, K. Arimitsu, T. Gunji, Y. Abe, and K. Ichimura, J. Photopolym. Sci. Technol., 16 (2003) 81.