Research Paper

Chemical modification of imipramine and desipramine

Hideki Hayashi[1]*, Tadashi Ogawa[2], Hiroshi Seno[2], Yuzo Ishigaki[1], Mitsuo Oda[1]

[1] Nagoya Municipal Industrial Research Institute, 3−4−41 Rokuban, Atsuta-ku, Nagoya, Aichi 456−0058, Japan
[2] Aichi Medical University, 1−1 Yazakokarimata, Nagakute, Aichi 480−1195, Japan

Abstract Chemical modification of imipramine and desipramine, which have pharmaceutical applications such as an antidepressant was carried out. Dibromoimipramine and dibromodesipramine were prepared from imipramine hydrochloride and desipramine hydrochloride, respectively. Dibromodesipramine was reacted with di-*tert*-butyl dicarbonate to prepare *N*-Boc type compound. ESI-MS of the dibromides showed typical MS signals of dibromides. Polymerizations of the dibromides by the nickel-promoted coupling reaction afforded corresponding polymers. These results suggest that chemical modification of imipramine and desipramine expected to develop another functional material.

Key words: imipramine, desipramine, dibromide, polymerization

Introduction

Triclinic compounds have been widely used as medical drugs[1−5]. As a triclinic compound, we focused imipramine (**Imip**, Fig. 1)[6,7]. It is known that metabolization of **Imip** affords desipramine (**Desi**[7,8], Fig. 1)[9−11]. On the other hand, these materials are ethylene unit-bridged diphenylamine derivatives with alkylamine substituent on the N atom of their diphenylamine unit. Diphenylamine with bridged units has been of interest for functional materials. We previously reported the preparation, properties, and applications of sulfur (−S−)[12,13], sulfone (−SO−)[12,13], monosilane ($-SiR_2-$)[14−24], disilane ($-SiMe_2SiMe_2-$)[15,23−25], and disiloxane ($-SiMe_2OSiMe_2-$)[15,24] unit-bridged diphenylamine derivatives.

We also prepared ethylene-bridged diphenylamine-containing polymers[26−30]. Diphenylamine with bridged unit can be expected as materials for bio-conjugation such as DNA[14−17], or biodegradable plastics[18,19,26−30]. Therefore it can also be expected to be functional for medical materials as well. These polymers are prepared from corresponding dibromides as monomers, which seems to be easy to check their structure by MS because their molecular weight is observed as three molecular ion peaks at ±2 at their mother molecular ion peak. Therefore, more detailed analysis of the dibromide with other analysis methods (NMR, IR, etc) will be expected.

In this manuscript, we here report results of MS analysis of dibromoimipramine and dibromodesipramine derivatives. As chemical modification of imipramine and desipramine, we also tried polymerization of the dibromides derivatives as monomers to prepare imipramine or desipramine homopolymers.

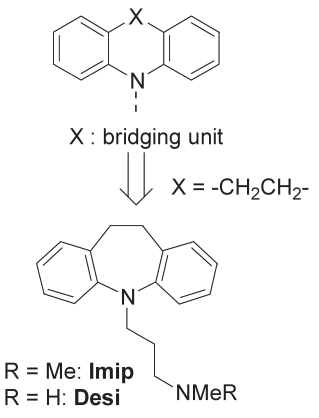

Fig. 1. Diphenylamine with bridging unit.

* **Corresponding author**
Hideki Hayashi
Nagoya Municipal Industrial Research Institute, 3−4−41 Rokuban, Atsuta-ku, Nagoya, Aichi 456−0058, Japan
Tel: +81−52−654−9912, Fax: +81−52−654−6788
E-mail: hayashi.hideki@nmiri.city.nagoya.jp
Received: November 27, 2019. Accepted: March 5, 2020.
Epub April 28, 2020.
DOI: 10.24508/mms.2020.06.002

Materials and Methods

Reagents and measurements

2,8-dibromoimipramine hydrochloride (2,8-dibromo-10,11-dihydro-5-[3,3-di(methylamino)propyl]-5*H*-dibenz[b,f]azepine hydrochloride, **BrImipHCl**)[26] and 2,8-dibromdesipramine hydrochloride (2,8-dibromo-10,11-dihydro-5-[3-(methylamino)propyl]-5*H*-dibenz[b,f]azepine hydrochloride, **BrDesiHCl**)[27] were prepared by the reported procedures. Other chemicals were also used as purchased. NMR spectra were taken by using a Varian INOVA400 spectrometer, and IR spectra were taken by using a JASCO FT/IR-410 spectrometer. UV-visible spectra were measured with a JASCO V-570DS spectrometer.

Shimadzu LCMS-8040 mass spectrometer and Shimadzu NexeraX2 LC system (Shimadzu Co., Kyoto, Japan) were used for ESI-MS analysis.

Preparation of the compounds

Preparation of 2,8-dibromo-10,11-dihydro-5-[3-(dimethylamino)propyl]-5*H*-dibenz[*b*,*f*]azepine (**BrImip**)

NaOH (0.64 g, 16 mmol) was added to **BrImipHCl** (0.51 g, 1.07 mmol) in water and the mixture was stirred for 2 h. Then, the mixture was extracted by ether, and the organic layer was washed in brine and dried over $MgSO_4$. After removal of $MgSO_4$ by filtration, the solvent was removed by evaporation. **BrImip** was obtained as a yellow liquid. Yield was 84%.

^{1}H-NMR ($CDCl_3$): δ 7.2−7.3 (m, 4H), 6.93 (d, 2H, *J*=9.4 Hz), 3.69 (t, 2H, *J*=7.0 Hz), 3.10 (s, 4H), 2.28 (t, 2H, *J*=7.2 Hz), 2.16 (s, 6H), 1.6−1.8 (m, 2H) ppm. ^{13}C-NMR ($CDCl_3$): δ 146.86, 136.00, 132.36, 129.28, 121.77, 115.27, 57.36, 48.93, 45.49, 31.61, 25.92 ppm.

Preparation of 2,8-dibromo-10,11-dihydro-5-[3-(methylamino)propyl]-5*H*-dibenz[*b*,*f*]azepine (**BrDesi**)

Reaction of **BrDesiHCl** (1.38 g, 3.00 mmol) and NaOH (0.53 g, 13.25 mmol) by the same preparation method of **BrImip** resulted **BrDesi** (1.18 g, 2.78 mmol) as a light brown liquid. Yield was 93%.

^{1}H-NMR ($CDCl_3$): δ 7.2−7.3 (m, 4H), 6.92 (d, 2H, *J*=9.4 Hz), 3.70 (t, 2H, *J*=6.8 Hz), 3.09 (s, 4H), 2.56 (t, 2H, *J*=7.0 Hz), 2.36 (s, 3H), 1.6−1.8 (m, 2H) ppm. ^{13}C-NMR ($CDCl_3$): δ 146.71, 135.89, 132.25, 129.16, 121.63, 115.18, 49.49, 48.56, 36.43, 31.47, 27.75 ppm.

Preparation of 2,8-dibromo-10,11-dihydro-5-[3-(*N*-methyl-*N*-*t*-butoxycarbonylamino)propyl]-5*H*-dibenz[*b*,*f*]azepine (**BrDesiBoc**)

BrDesi (0.79 g, 1.86 mmol) and di-*tert*-butyl dicarbonate (Boc_2O, 1.10 g, 5.04 mmol) was dissolved to 20 mL of acetonitrile and *N*,*N*-dimethylaminopyridine (DMAP, 22.4 mg, 0.18 mmol) was added to the mixture. The mixture was stirred overnight, then the solvent was evaporated. The residue was purified by silica gel column chromatography. **BrDesiBoc** (0.78 g, 1.49 mmol) obtained as a light brown liquid. Yield was 80%.

^{1}H-NMR ($CDCl_3$): δ 7.2−7.3 (m, 4H), 6.89 (d, 2H, *J*=9.4 Hz), 3.63 (t, 2H, *J*=6.8 Hz), 3.18 (br, 2H), 3.08 (s, 4H), 2.74 (br, 3H), 1.6−1.8 (m, 2H), 1.38 (s, 9H) ppm. ^{13}C-NMR ($CDCl_3$): δ 146.41, 135.72, 132.11, 128.99, 128.94, 121.25, 115.11, 78.95, 47.84, 33.92, 31.25, 28.02, 25.79 ppm.

Reaction of **BrDesiBoc** and trifluoroacetic acid

BrDesiBoc (305 mg) was dissolved in trifluoroacetic acid (TFA, 3 mL) and the solution was stirred at room temperature for 2 h. The solution was poured into water (5 mL) and NaOH (0.52 g) was added to the solution. The solution was extracted by ether and the organic layer was washed in NaOH aq and brine. Then, the organic layer was dried over $MgSO_4$. After removal of $MgSO_4$ by filtration, the solvent was removed by evaporation. 134 mg of light brown liquid was obtained.

Preparation of polymers

Preparation of poly(10,11-dihydro-5-[3-(dimethylamino)-propyl]-5*H*-dibenz[*b*,*f*]azepine-2,8-diyl) (**PImip**)

Under nitrogen, toluene (5 mL) solution of **BrImip** (370 mg, 0.84 mmol) was added to a mixture of $Ni(cod)_2$ (340 mg, 1.24 mmol, cod=1,5-cyclooctadiene), cod (1 mL) and 2,2′-bipyridyl (bpy, 190 mg, 1.22 mmol) in toluene (5 mL) and the mixture was heated at 60°C for 48 h. A black powder precipitated upon pouring the mixture into methanol was successively washed with water, methanol, and hexane. As colorless powder, 146 mg (0.52 mmol monomer unit) of **PImip** was obtained. Yield was 62%. ^{1}H-NMR ($CDCl_3$): δ 6.8−7.6 (m, 6H), 3.80 (2H), 3.21 (4H), 2.32 (2H), 2.17 (6H), 1.77 (2H). ^{13}C-NMR ($CDCl_3$): δ 147.01, 134.99, 134.13, 128.15, 124.75, 120.18, 57.43, 48.75, 45.05, 32.45, 25.57 ppm.

Preparation of (10,11-dihydro-5-[3-(*N*-methyl-*N*-*t*-butoxycarbonylamino)propyl]-5*H*-dibenz[*b*,*f*]azepine-2,8-diyl) (**PDesiBoc**)

Reaction of 1.17 g (2.23 mmol) of **BrDesiBoc** with 0.74 g of $Ni(cod)_2$ and 0.42 g of bpy afforded 730 mg (2.0 mmol monomer unit) of **PDesiBoc**. Yield was 90%. ^{1}H-NMR ($CDCl_3$): δ 7.0−7.4 (m, 6H), 3.78 (2H), 3.23 (6H), 2.75 (3H), 1.82 (2H), 1.38 (9H). ^{13}C-NMR ($CDCl_3$): δ 155.73, 147.93, 135.01, 134.17, 128.15, 124.81, 120.05, 79.23, 48.20, 46.57, 34.26, 32.41, 28.39, 26.42 ppm.

Preparation of (10,11-dihydro-5-[3-(methylamino)propyl]-5*H*-dibenz[*b*,*f*]azepine-2,8-diyl) (**PDesi**)

PDesiBoc (228 mg) was dissolved in TFA (10 mL) and the solution was stirred at room temperature for two days. The solution was poured into 30 mL of 3M NaOH aqueous solution to obtain precipitation and the precipitation was washed in methanol. Drying under vacuum the precipitation gave 119 mg of **PDesi** as white powder. As **PDesi**, yield was 72%. ^{1}H-NMR ($CDCl_3$): δ 7.0−7.4 (m, 6H), 3.83 (2H), 3.23 (6H), 2.62 (2H), 1.82 (2H), 1.38 (9H).

Results and Discussion

Preparation of dibromides

BrImipHCl[26] and **BrDesiHCl**[27] were prepared as solid from commercially available products imipramine hydrochloride (**ImipHCl**) and desipramine hydrochloride (**DesiHCl**) by the reported method for bromination of *N*-methyldiphenylamine[31]. ESI-MS of **BrImipHCl** and **BrDesiHCl** were shown in Fig. 2(a) and 2(b). As shown in the figures, typical molecular ion peaks assigned as dibromide was observed. When HCl of **BrImipHCl** and **BrDesiHCl** were neutralized by base like NaOH (Fig. 3(a)), HCl in **BrImipHCl** and **BrDesiHCl** was removed and **BrImip** and **BrDesi** were obtained as viscous liquid, respectively. ESI-MS of **BrImip** (Fig. 2(c)) and **BrDesi** (Fig. 2(d)) showed molecular ion peaks as $[M+H]^+$. As shown in Fig. 4, NMR signals based on aminoalkyl unit moved to the high magnetic field by reaction with NaOH. These changes of NMR shift seem to come from the change of electronic state of alkylamine unit by removal of HCl.

The NH unit of **BrDesi** was converted to *N*-butoxycarbonyl (NBoc) by the reported procedure[32] (Fig. 3(b)). As shown in Fig. 5(b), IR spectrum of **BrDesiBoc** showed signal at about 1690 cm^{-1} which is assigned as −N−*CO*−O− unit by reaction of **BrDesi** (Fig. 5(a)) ESI-MS of **BrDesiBoc** is shown in Fig. 2(e). As shown in the figure, the molecular ion peak also observed as typical for dibromide such as **BrImipHCl** and **BrDesiHCl**. These results suggest chemical structure of **BrDesiBoc**.

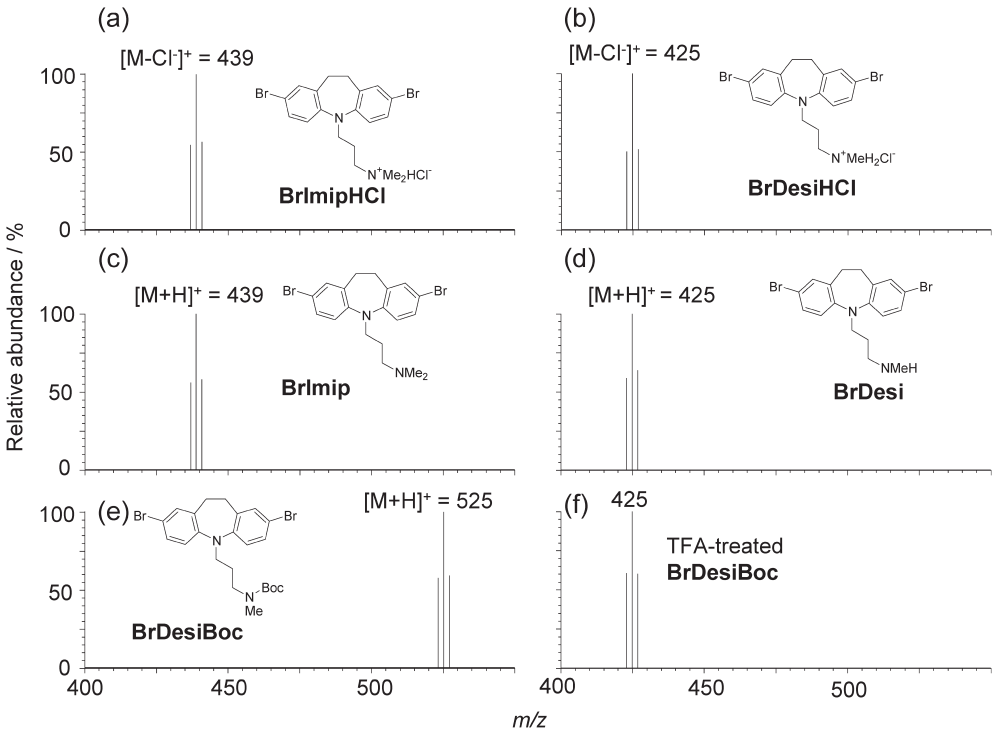

Fig. 2. ESI-MS of the dibromides.

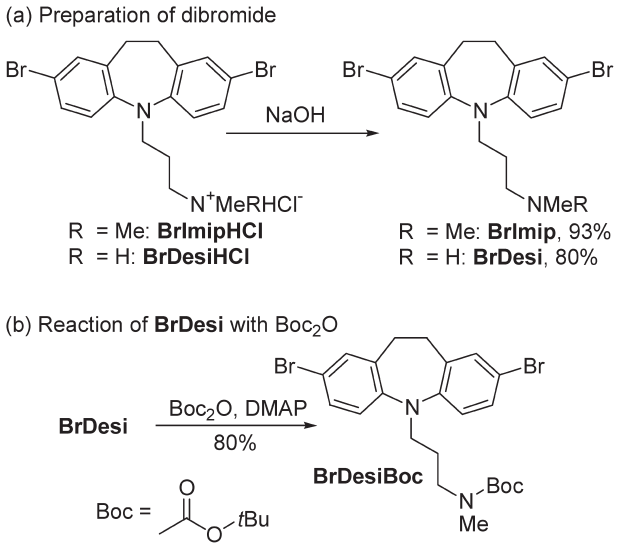

Fig. 3. Preparation scheme of dibromoimipramine and dibromodesipramine derivatives.

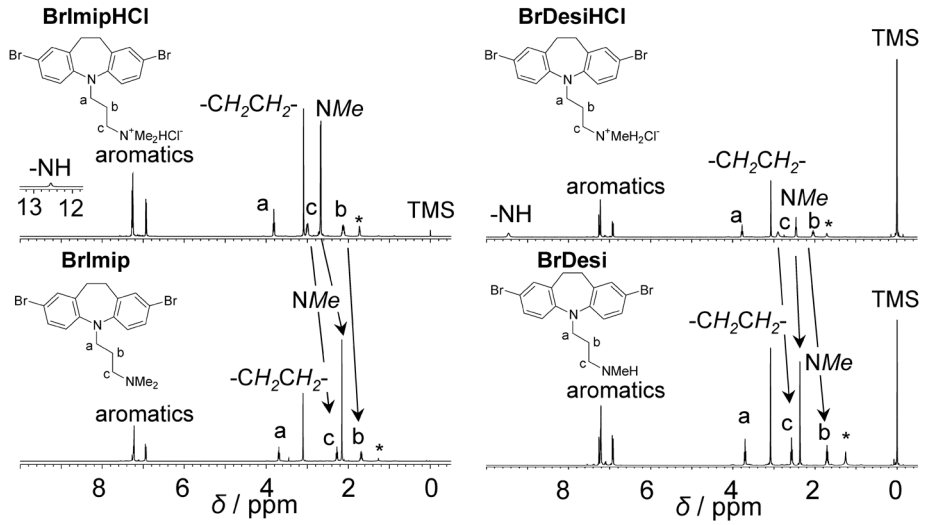

Fig. 4. Change of the ^{1}H NMR spectra of the dibromides by dehydrochlorination.

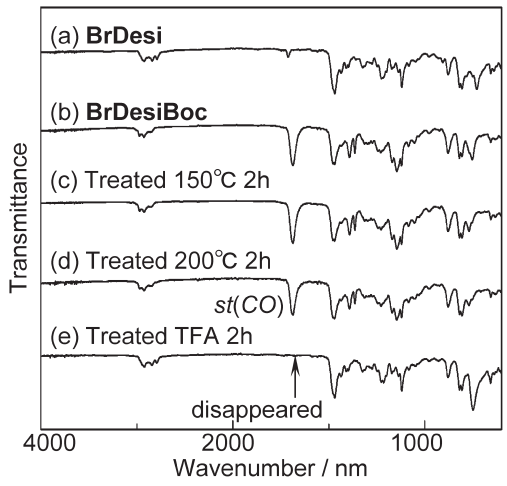

Fig. 5. IR spectra of BrDesi, BrDesiBoc, and reaction product of BrDesiBoc.

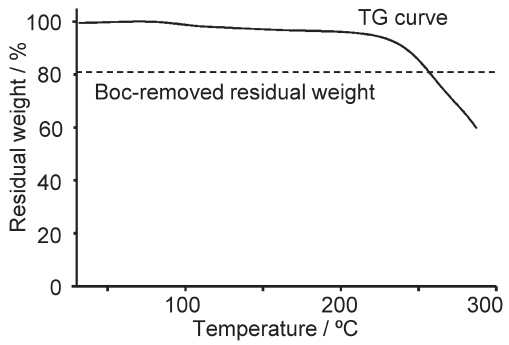

Fig. 6. TG curve of BrDesiBoc. Analyzed under air.

It is known that Boc works as protective group of NH because NBoc is converted to NH unit by heating[33] or treatment of acid[32]. Therefore, **BrDesiBoc** was heated to

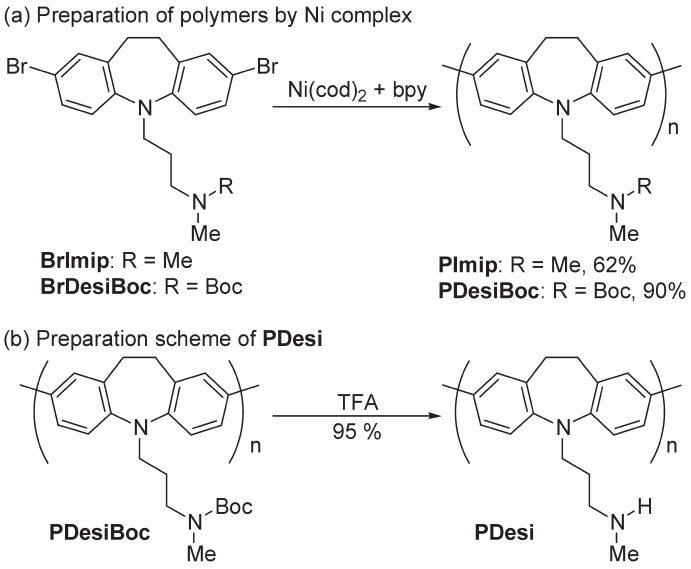

Fig. 7. Polymer preparation scheme.

Table 1. Results of polymerizations

Polymer	yield %	$M_w \times 10^{-3}$ [a]	$M_n \times 10^{-3}$ [a]	M_w/M_n
PImip	62	2.6	2.1	1.2
PDesiBoc	90	10.1	6.5	1.5

[a]Determined by GPC. Eluent was THF. Polystyrene standard.

150°C and 200°C, however, conversion of NBoc to NH was not observed (Fig. 5(c) and Fig. 5(d)). To investigate if NBoc of **BrDesiBoc** can be converted, thermogravimetric (TG) analysis was carried out, however, weight loss by cleavage of Boc was not observed like Boc-substituted diarylamines[32] (Fig. 6). Therefore, **BrDesiBoc** was treated with TFA. As shown in Fig. 2(f) and Fig. 5(e), the MS and the IR spectrum of TFA-treated **BrDesiBoc** was same as **BrDesi**. This result suggests that Boc of **BrDesiBoc** works as protective group of NH of desipramine unit.

Polymerization of dibromides

It is known that coupling reaction of aromatic dihalide by using organometallic compound can afford relative polymers[33–37]. We reported preparation of dibenzazepine-containing copolymers by Suzuki-Miyaura coupling reaction by using **BrImipHCl**[26] and **BrDesiHCl**[27] as corresponding monomers.

On the other hand, our group prepared **PImip** and **PDesi** by oxidative polymerization of **ImipHCl** and **DesiHCl**, respectively[29]. Oxidative polymerization is very convenient method for preparation of poly(arylene) type polymer[20,38,39], however, sometimes the juncture of obtained

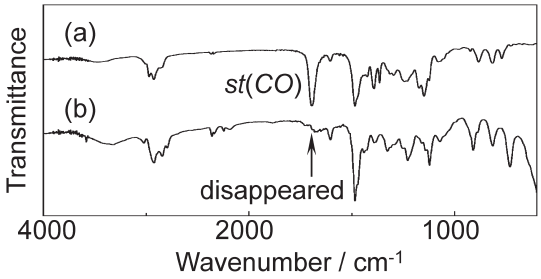

Fig. 8. IR spectra of (a) PDesiBoc and (b) PDesi.

polymer was not completely clear. To prepare poly(arylene) homopolymer with well-defined structure, dehalogenative polycondensations of aromatic dihalide by using organonickel process have been carried out[34]. Therefore, this type polymerizations are carried out as shown in Fig. 7(a). Results of polymerizations were shown in Table 1. **PImip** and **PDesiBoc** were soluble in $CHCl_3$ and THF. Solubility of **PImip** prepared by this method became higher than **PImip** prepared by oxidative polymerization because of forming well-defined structure like poly(phenazasiline)[40].

As described above, the NBoc unit of the products expect to be converted to NH by TFA, therefore, **PDesiBoc** was treated with TFA as shown in Fig. 7(b). The change of IR spectra by the reaction is shown in Fig. 8. As shown in the figure, the signal assigned as originated from urea units at about 1690 cm^{-1} in **PDesiBoc** was disappeared due to the reaction. This suggest that Boc unit of **PDesiBoc** was completely cleaved by TFA and **PDesiBoc** was converted to **PDesi**.

The optical data of the polymers and corresponding

Table 2. Comparison of optical properties of the polymers and corresponding monomeric compounds

R	Polymer[a]	Absorption λ_{max}/nm[b]	Fluorescence λ_{max}/nm[b,c]	Monomeric compound[a]	Absorption λ_{max}/nm[b]
Me	**PImip**	321	410	**Imip**	256
H	**PDesi**	321[d]	406[d]	**Desi**	259
Boc	**PDesiBoc**	321	404	**DesiBoc**	259

[a]Chemical structure of the compounds are shown in Fig. 9(a). [b]$CHCl_3$ solution. [c]Excited at absorption λ_{max}. [d]$CHCl_3$ soluble part.

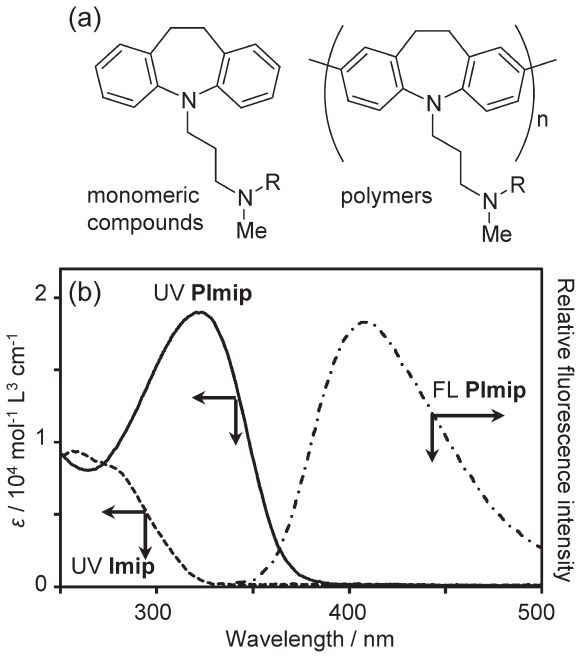

Fig. 9. (a) Chemical structure of the polymers and corresponding monomeric compounds and (b) absorption and fluorescent spectra of PImip and Imip.

monomeric compounds (Fig. 9 (a)) are shown in Table 2. Absorption λ_{max} of the polymers was longer than that of corresponding monomeric compounds, suggesting that π-conjugation system was extended by polymerization such as phenazasiline derivatives[21]. As exemplified in Fig. 9(b), as well as the case of poly(phenazasiline)[22] and poly(diphenylamine)[37], absorption λ_{max} of the polymer was not changed by the substituent on the N atom of alkylamine unit. The polymers showed fluorescence, whereas the corresponding monomeric compounds did not show fluorescence.

Conclusions

Chemical modification of imipramine and desipramine were carried out. ESI-MS of dibrominated imipramine and desipramine derivatives (**BrImipHCl**, **BrDesiHCl** and **BrDesiBoc**) showed molecular ion peak with typical dibromide pattern. Further chemical modifications of the dibromides were carried out by polymerizations. Optical properties of the polymers were changed by polymerizations. The compounds prepared in this manuscript are expected to become medically functional materials such as for detection by fluorometry and for bio-conjugation materials (like DNA or biopolymers).

Conflict of Interest

The authors declare that we have no conflict of interest.

Acknowledgement

The authors thank to Prof. Yukio Onouchi (Aichi Institute of Technology: AIT), Mr. Masanobu Maeda (AIT), Mr. Taiki Naruo (AIT), Mr. Hiroki Hirota (AIT), and Mr. Junpei Kuno (AIT) for their helpful supports.

A part of this work was performed under the Cooperative Research Program of "Network Joint Research Center for Materials and Devices."

References

1) Jeffery BM, Aaron TB: The efficacy of antidepressant drugs: A review of research (1958 to 1972). *Arch Gen Psychiatry* 30: 667−674, 1974.
2) Zhuo C, Xue R, Luo L, Ji F, Tian H, Qu H, Lin X, Jiang R, Tao R: Efficacy of antidepressive medication for depression in Parkinson disease: A network meta-analysis. *Medicine (Baltimore)* 96: e6698, 2017.
3) Rogóż Z, Skuza G, Sowińska H: Effects of antihistaminic drugs in tests for antidepressant action. *Pol J Pharmacol Pharm* 33: 321−335, 1981.
4) Richelson E: Tricyclic antidepressants and histamine H1 receptors. *Mayo Clin Proc* 54, 669−674, 1979.
5) Hazell P, Mirzaie M: Tricyclic drugs for depression in children and adolescentss. *Cochrane Database of Systematic Reviews* Issue 6: Art. No. CD002317, 2013.
6) Hearn L, Moore RA, Derry S, Wiffen PJ, Phillips T: Imipramine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* Issue 5: Art. No. CD010769, 2014.

7) Hattori H, Takashima E, Yamada T, Suzuki O: Detection of tricyclic antidepressants in body fluids by gas chromatography with a surface ionization detector. *J. Chromatogr.* 529: 189−193, 1990.
8) Hearn L, Moore RA, Derry S, Wiffen PJ, Phillips T: Desipramine for neuropathic pain in adults. *Cochrane Database of Systematic Reviews* Issue 9: Art. No.: CD011003. DOI: 10.1002/14651858.CD011003.pub2. 2014
9) Edwards G: Comparison of the effrect of imipramine and desipramine on some symptoms of depressive illness. *Brit J Psychiat* 111: 889−897, 1965.
10) Gram LF: Imipramine: A model substance in pharmacokinetic research. *Acta Psychiatr Scand Suppl* 345: 81−84, 1988.
11) Sutfin TA, DeVane CL, Jusko WJ: The analysis and disposition of imipramine and its active metabolites in man. *Psychopharmacology* 82: 310−317, 1984.
12) Hayashi H, Inoue H, Nakao H, Hattori H, Onouchi Y: Oxidative polymerization behavior of diphenylamine with bridged structure. *Int J Polym Anal Charac.* 17: 189−198, 2012.
13) Hayashi H, Koizumi Ta: Preparation and electrochemical behavior of *N*-substituted phenothiazine oxide. *Heterocycles* 92: 1441−1449, 2016.
14) Nakao H, Hayashi H, Yoshino T, Sugiyama S, Otobe K, Ohtani T: Development of novel polymer-coated substrates for straightening and fixing DNA. *Nano Lett.* 2: 475−479, 2002.
15) Nakao H, Hayashi H, Yoshino T, Sugiyama S, Otobe K, Ohtani T: Useful technique for DNA-stretching and fixation. *Nucleic Acids Research Supplement* 2: 289−290, 2002.
16) Nakao H, Hayashi H, Iwata F, Karasawa H, Hirano K, Sugiyama S, Ohtani T: Fabricating and aligning π-conjugated polymer-functionalized DNA nanowires: Atomic force microscopic and scanning near-field optical microscopic studies. *Langmuir* 21: 7945−7950, 2005.
17) Nakao H, Hayashi H, Shiigi H, Miki K: Highly localized light field on metallic nanoarrays prepared with DNA nanofibers. *Anal Sci* 25: 1177−1179, 2009.
18) Hayashi H, Yamamoto T, Sakamoto M, Iida K. Nakao H, Hirano K, Kawaguchi M, Hibino T, Takenaka S, Hattori T: Preparation of phenazasiline-containing poly(arylene) and their use as functional additives in resins. *Polym J* 37: 52−57, 2005.
19) Hayashi H, Harada M, Maeda M, Onouchi Y: Effect of addition of poly(phenazasiline) to plastic blends for fluorescent properties and impact strength. *J Jpn Soc Colour Mater* 91: 13−16, 2018.
20) Nakao H, Hayashi H, Okita K: Spectroelectrochemical properties of polyphenazilines, *Bunseki Kagaku*, 49: 169−174, 2000.
21) Hayashi H, Murase M, Koizumi Ta, Ohara K, Miyabayashi T, Kojima M: Synthesis of bis(phenazasiline) compounds and their application for TFT as a model of phenazasiline-containing polymers. *Bull Chem Soc Jpn* 83: 1282−1284, 2010.
22) Hayashi H, Nakao H, Miyabayashi T, Murase M: Preparation and properties of poly(phenazasiline) with various substituents. *Jpn J Appl Phys* 52: 05DA13, 2013.
23) Nakao H, Hayashi H, Okita K: Spectroelectrochemical characterization of Si-bridged diphenylamines: Influence of Si-bridging upon electronic structures of diphenylamines. *Anal Sci* 17: 545−550, 2001.
24) Hayashi H, Nakao H, Onozawa Sy, Adachi A, Hayashi T, Okita K: Preparation and properties of disilane and disiloxane unit-fused poly(diphenylamine). *Polym J* 35: 704−710, 2003.
25) Otobe K, Nakao H, Hayashi H, Nihey F, Yudasaka M, Iijima S: Fluorescence visualization of carbon nanotubes by modification with Silicon-based polymer. *Nano Lett.* 2: 1157−1160, 2002.
26) Hayashi H, Maeda M, Naruo T, Onouchi Y,Harada M, Ishigaki Y: Fluorescent additive for estimation of compatibility of polyester blend by imipramine-containing polymer. *Int J Polym Anal Charact* 22: 725−733, 2017.
27) Hayashi H, Ishigaki Y, Kuno J, Naruo T, Hiorota H, Ogawa T, Hattori H, Seno H, Onouchi Y, Oda M: Chemical bond formation of resin and fluorescent additive via multifunctional isocyanates. *J Adhes Soc Jpn* 51: 298−305, 2015.
28) Hayashi H, Maeda M, Kuno J, Naruo T, Hirota H, Harada M, Iida K, Onouchi Y, Hirano K: Estimation of the compatibility of blend composites of resins by measuring the fluorescent spectra. *Anal. Sci.* 32: 1251−1256, 2016.
29) Hayashi H, Murakami K, Inoue H, Hirota H, Harada M, Iida K, Onouchi Y, Hirano K: Preparation of poly(ethylene-bridged diphenylamine)s and their use as functional additives to resins. *Curr Trends Polym Sci* 14: 11−20, 2010.
30) Hayashi H, Murakami K, Onouchi Y, Oda M, Nakao, H: Preparation, properties and use for functional additive of

poly(dibenzazeipne)s. *J Jpn Soc Colour Mater* 92: 2−6, 2019.

31) Wasserman D, Jones RE, Robinson SA, Garber JD: A new synthesis of 5,10-dihydrophenazasilines. *J Org Chem* 30: 3248−3250, 1965.
32) Rawel VH, Jones RJ, Cava MP: Photocyclization strategy for the synthesis of antitumor agent CC-1065: Synthesis of dideoxy PDE-I and PDE-II. Synthesis of thiophene and furan analogs of dideoxy PDE-I and PDE-II. *J Org Chem* 52: 19−28, 1987.
33) Horie M, Yamaguchi I, Yamamoto T: Comparison of optical properties and doping behavior of −[(*p*-C6H4)$_m$NH]$_n$− (m=1−4) type polymers. *Chem Lett* 35: 1110−1111, 2006.
34) Yamamoto T, Koizumi Ta: Synthesis of π-conjugated polymers bearing electronic and optical functionalities by organometallic polycondensations and their chemical properties. *Polymer* 48: 5449−5472, 2007.
35) Ono K, Kobayashi T, Sato Y, Eguchi K, Kato S, Kishi N, Soga T: Synthesis and donor-π-acceptor properties of polyfluorene derivatives containing a phenazasiline moiety and an electron acceptor. *Heterocycles* 83: 1977−1982, 2011.
36) Lu W, Kuwabara J, Iijima T, Higashimura H, Hayashi H, Kanbara T: Synthesis of π-conjugated polymers containing fluorinated arylene units via direct arylation: Efficient synthetic method of materials for OLEDs. *Macromolecules* 45: 4128−4133, 2012.
37) Yamamoto T, Kim SB, Koizumi T: Synthesis and chemical properties of poly(*N*-substituted diphenylamine-4,4′-diyl)s. *Polym J* 41: 810−815, 2009.
38) Hagiwara T, Yamaura M, Iwata, K: Study on polymers prepared by chemical oxidation of aromatic amines. *Nippon Kagaku Kaishi* 1989: 1791−1801.
39) Nomura M, Shibasaki Y, Ueda M, Tsugita K, Ishikawa M, Taniguchi Y: Synthesis and properties of poly[di(1-naphthyl)-4-tolylamine] as a hole transport material. *Macromolecules* 37: 1204−1210, 2004.
40) Hayashi H, Nakao H, Adachi A, Kimura H, Okita K, Hayashi T, Tanaka M: Preparation and properties of π-conjugated polymer with phenazasiline units. *Chem Lett* 29: 688−689, 2000.