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DIBROMIDES OF BOC-PROTECTED 1-AMINOPYRROLE AND 4-AMINO-1,2,4-TRIAZOLE: SYNTHESIS, X-RAY MOLECULAR STRUCTURE, AND NMR BEHAVIOR

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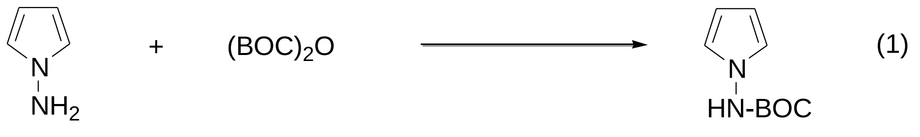
Abstract – α-Dibromides of BOC-protected 1-aminopyrrole and 4-amino-1,2,4-triazole have been prepared and their molecular structures have been confirmed by X-ray crystallography. They can be used for polymer synthesis.

INTRODUCTION

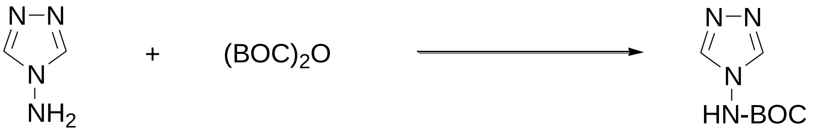
Dibromides of heterocycles have been used for preparation of functional compounds. For example, 3,8-dibromo-1,10-phenanthroline affords 1,10-phenanthroline-based functional molecules[1,2,3,4] and π-conjugated polymers.[5,6,7] Pyrrole is an important building block of π-conjugated oligomers and polymers.[8,9] 1,2,4-Triazole is also an important building block of π-conjugated oligomers and polymers,[10,11,12] besides its importance in pharmacology and biology.[13,14,15] However, their related 1-aminopyrrole and 4-amino-1,2,4-triazole as building blocks of π-conjugated molecules have received less attention. To develop chemistry of 1-aminopyrrole and 4-amino-1,2,4-triazole, we have synthesized α-dibromides of the compounds. To avoid complexity, the $-NH_2$ group of 1-aminopyrrole and 4-amino-1,2,4-triazole was first protected by BOC.

RESULTS AND DISCUSSION

BOC-protected 1-aminopyrrole and 4-amino-1,2,4-triazole were synthesized using $(BOC)_2O$.



1



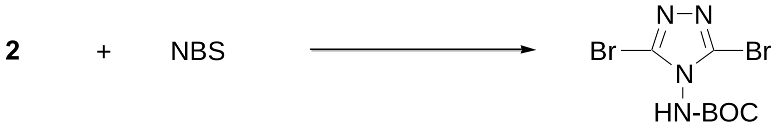
(2)

2

α-Dibromides of the BOC-protected 1-aminopyrrole and 4-amino-1,2,4-triazole were synthesized using NBS.

(3)

3



(4)

4

3 and **4** were characterized by IR, NMR, and elemental analysis, and the position of Br in **3** was confirmed by X-ray crystallography. Molecular structure of **4** was also determined by X-ray crystallography, and X-ray crystal structures of **3** and **4** are presented in Figure 1.

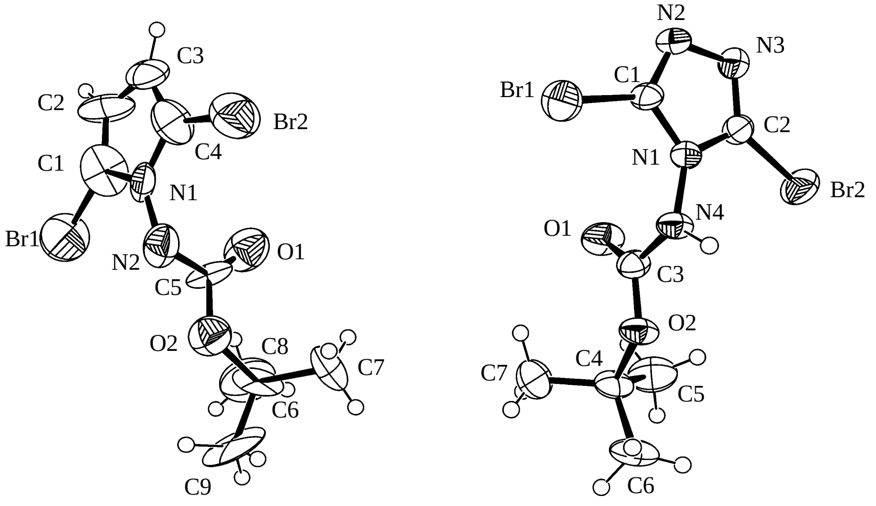


Figure 1. X-Ray crystal structures of **3** (left, one of four independent molecules) and **4** (right). The hydrogen atom on N2 in **3** could not be determined.

^{1}H NMR data of **3** also agreed with the position of Br (*vide infra*).

^{1}H NMR spectra of **3** and **4** showed temperature dependence as shown in Figures 2 and 3.

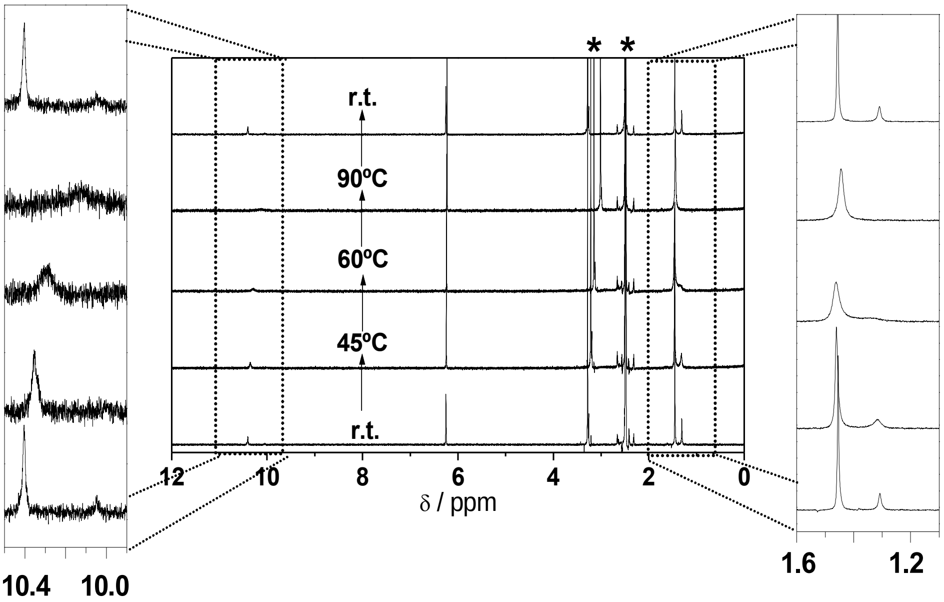


Figure 2. Temperature dependent ^{1}H NMR spectra of **3** in DMSO-d_6. Peaks with * are due to solvent impurities (DMSO-d_6 and H_2O).

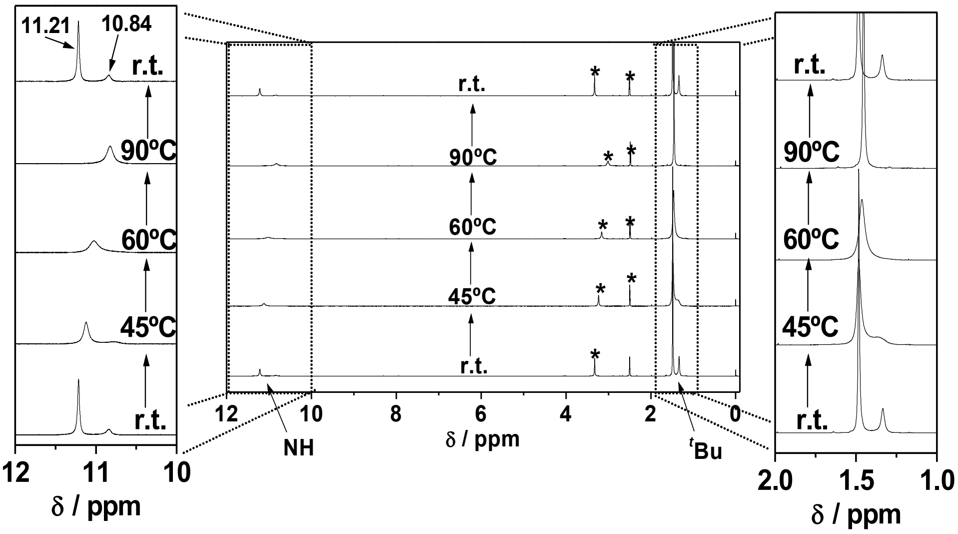
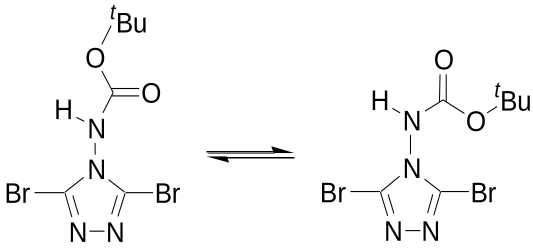


Figure 3. Temperature dependent ^{1}H NMR spectra of **4** in DMSO-d_6. Peaks with * are due to solvent impurities (DMSO-d_6 and H_2O).

The ^{1}H NMR spectrum of **3** at room temperature shows two couples of peaks in regions of δ 1.5-1.3 for the *t*-Bu group and δ 10.4-10.0 for the pyrrole-H, respectively, and the peaks are broadened and coalesce at 60-90 ºC. The ^{1}H NMR spectrum of **4** shows a similar temperature dependence more clearly. The two peaks at room temperature and the temperature dependence are accounted for by the presence of the following rotamers.



s-*cis* rotamer
(X-ray major)

s-*trans* rotamer

The s-*cis* rotamer is considered to be a major species and fractions of the s-*cis* species in **3** and **4** at room temperature are calculated as 86% and 78%, respectively, from the ^{1}H NMR peak intensities. The presenece of similar rotamers in BOC-protected amino acids was reported;[16] a similar s-*cis* rotamer was reported to be a major species. ^{1}H NMR spectra of **1** and **2** showed only single peaks for the *t*-Bu-H and the pyrrole-H, respectively.

^{1}H NMR spectrum of **1** showed two peaks at δ 6.67 (α-CH) and 5.95 (β-CH), whereas ^{1}H NMR spectrum of **3** gave rise to a single peak at δ 6.25 for the pyrrole ring. The position of the ^{1}H NMR peak of **3** agrees with those of reported pyrrole-β-CH signals (at about δ 6.25 (± 0.3)[17,18] of 1-substituted 2,5-dibromo-pyrroles.

Oxidative polymerization of **1** with $FeCl_3$[19,20,21] gave BOC-protected poly(1-aminopyrrole), **5**(Fe). Dehalogenative polycondensation of **3** using a zerovalent complex, Ni(0)L_m,[5,6,8,9,10,11,12,13,14,15] also gave BOC-protected poly(1-aminopyrrole), **5**(Ni). Oxidative polymerization of pyrroles usually occurs at the α-position of the five membered ring,[8,9,19,20,21] and conceivable polymerization at the –NH_2 group to give a polyaniline type product[8,9] does not seem to take place because of the protection of the –NH_2 group by BOC.

5(Fe)

(5)

5(Ni)

(6)

Ni(0)L_m: mixture of bis(1,5-cyclooctadiene)nickel (0), Ni$(cod)_2$, and 2,2'-bipyridyl, bpy.

Gel permeation chromatography indicated that **5**(Fe) and **5**(Ni) had number average molecular weight (M_n, vs. polystyrene standards) of 12800 and 4300 with M_w/M_n (M_w = weight average molecular weight) of 1.38 and 1.28, respectively. As shown in Figure 4, **5**(Fe) and **5**(Ni) showed similar IR spectra, although the IR spectra of **5**(Fe) and **5**(Ni) show some difference at a low frequency region from about 500-700 cm^{-1}.[22]

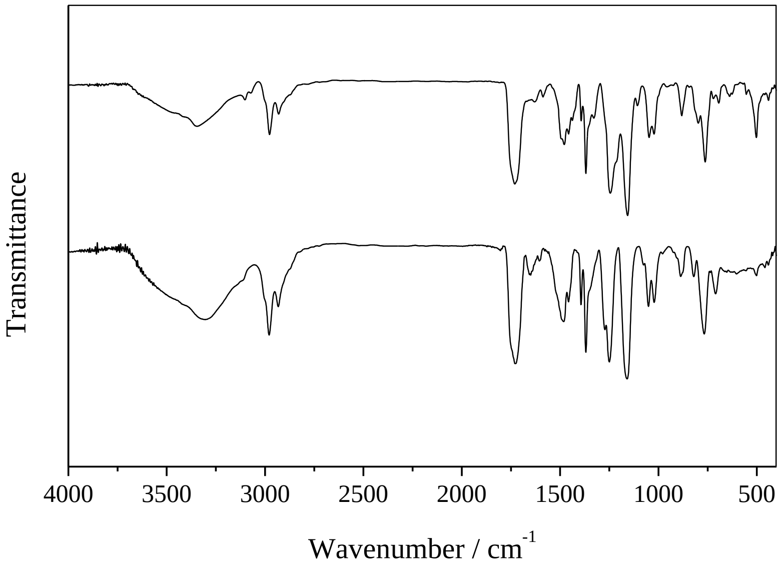


Figure 4. IR spectra of **5**(Fe) (top) and **5**(Ni) (bottom).

Preliminary experiments indicated that thermal treatment of **5**(Ni) at 200 ºC for 1 h caused almost complete deprotection[23,24,25,26] of the –NH_2 group as judged from disappearance of the ν(C=O) IR peak at 1740 cm^{-1}. A similar thermal treatment of **5**(Fe) also caused decrease of the ν(N-H) IR peak. However, the product still showed the ν(C=O) IR peak at 1740 cm^{-1} as a shoulder peak, suggesting that the deprotection reaction of the BOC-polymer with a larger molecular weight did not proceed well. Electrochemical oxidative polymerization of 1-aminopyrrole to give a polymer film has been reported,[27,28] however, enough characterization of the polymer has not been reported. Stille-type copolymerization of **4** with 2,5-bis(trimethylstannyl)thiophene and 5,5'-bis(trimethylstannyl)-2,2'-bithiophene was also carried out to obtain copolymers. Details of polymerization and chemical properties of the obtained polymers will be reported elsewhere.

As described above, new dibromides of BOC-protected 1-aminopyrrole and 4-amino-1,2,4-triazole have been prepared. They are expected to be useful for preparation of functional π-conjugated compounds and polymers.

EXPERIMENTAL

1-Aminopyrrole was purchased from Tokyo Chemical Industry Co. NMR spectra were recorded on a JEOL EX-400 spectrometer. Ni(cod)$_2$[29] was prepared according to the literature. UV-vis spectra and IR spectra were measured with a Shimadzu UV-3100PC spectrometer and a JASCO-IR 460 spectrometer, respectively. Mass spectra were obtained with a JEOL JMS-700. Elemental analysis was carried out with a LECO CHNS-932 analyzer and a Yanaco YS-10 SX-Elements microanalyzer. Gel-permeation chromatography (GPC) was carried out with a Toso HLC-8120GPC liquid chromatograph using DMF as the eluent.

Preparation of 1 (BOC)$_2$O (3.99 g, 18.3 mmol) was added to a mixture of 1-aminopyrrole (1.50 g, 18.3 mmol) and *t*-BuOK (2.05 g, 17.2 mmol) in 10 mL of dry DMF under N_2. The mixture was stirred for 5 h at 85 ºC, and cooled to rt. After addition of water, the product was extracted with $CHCl_3$ and the extract was dried over $MgSO_4$. After drying up the solution, the product **1** was purified by recrystallization from hexane (yield = 59%); mp 110 – 111 ºC. ^{1}H NMR (300 MHz in DMSO-*d*$_6$): δ 10.24 (s, 1H), 6.67 (t, *J* = 4.4 Hz, 2H), 5.95 (t, *J* = 4.4 Hz, 2H), 1.41 (s, 9H). ^{13}C NMR (100 MHz in DMSO-*d*$_6$): δ 154.54, 121.85, 106.16, 80.06, 27.98. Anal. Calcd for $C_9H_{14}N_2O_2$: C, 59.32; H, 7.74; N, 15.37. Found: C, 59.14; H, 7.68; N, 15.50.

Preparation of 2 (BOC)$_2$O (25.9 g, 119 mmol) was added to a mixture of 4-amino-1,2,4-triazole (10.0 g, 119 mmol) and 4-dimethylaminopyridine (4.40 g, 36 mmol) in 30 mL of dry DMF under N_2. The mixture was stirred for 5 h at 85 ºC, and cooled to rt. After drying up the solution, the product was dissolved in $CHCl_3$, and purified by reprecipitation into hexane. After washing with water, the product **2** was dried under vacuum (yield = 52%); mp 143 – 144 ºC.^{1}H NMR (400 MHz in DMSO-*d*$_6$): δ 10.75 (s, 1H), 8.69 (s, 2H), 1.44 (s, 9H). ^{13}C NMR (100 MHz in DMSO-*d*$_6$): δ 153.65, 143.90, 81.52, 27.81. FAB-MS m/z = 342.9 $[M+H]^+$. Anal. Calcd for $C_7H_{12}N_4O_2$: C, 45.64; H, 6.57; N, 30.42. Found: C, 45.43; H, 6.51; N, 30.66.

Preparation of 3 A dry DMF (5 mL) solution of NBS (1.02 g, 5.75 mmol) was slowly added to a dry DMF (5 mL) solution of **1** (0.50 g, 2.74 mmol), and the mixture was stirred for 30 min at 0 ºC and 16 h at rt. After addition of water, the product was extracted with $CHCl_3$ and **3** was purified by column chromatography on SiO_2 ($CHCl_3$) and recrystallization from hexane (yield = 81%); mp 110 – 111 ºC. ^{1}H NMR (300 MHz in DMSO-*d*$_6$, rt): δ 10.41 (s, 0.86H), 10.05 (s, 0.14H) 6.25 (m, 2H), 1.45 (s, 7.73H), 1.30 (s, 1.27H). ^{13}C NMR (100 MHz in DMSO-*d*$_6$): δ 153.81, 109.82, 103.54, 80.90, 27.91. Anal. Calcd for $C_9H_{12}Br_2N_2O_2$: C, 31.79; H, 3.56; Br, 47.00; N, 8.24. Found: C, 32.01; H, 3.53; Br, 46.93; N, 8.33.

Preparation of 4 NBS (2.41 g, 13.5 mmol) was slowly added to a dry DMF (15 mL) solution of **2**, and the mixture was stirred for 2 h at 85 ºC. After cooling to rt, an aqueous solution of $NaHSO_3$ (5%, 100 mL) was added and the mixture was stirred for 1 h. The product was extracted with $CHCl_3$ and **4** was obtained by column chromatography on SiO_2 (eluent = 1:1 mixture of EtOAc and $CHCl_3$) (yield = 36%); mp 149 – 150 ºC. ^{1}H NMR (400 MHz in DMSO-d_6, rt): δ 11.21 (s, 0.78H), 10.84 (s, 0.22H), 1.48 (s, 7H), 1.33 (s, 2H). ^{13}C NMR (100 MHz in DMSO-d_6): δ 152.97, 133.74, 103.54, 82.66, 27.65. FAB-MS m/z = 342.9 $[M+H]^+$. Anal. Calcd for $C_7H_{10}Br_2N_4O_2$: C, 24.58; H, 2.95; Br, 46.73; N, 16.38. Found: C, 24.75; H, 3.15; Br, 47.04; N, 16.24.

Preparation of 5(Fe) A dry chloroform solution of $FeCl_3$ (1.78 g, 11.0 mmol) was slowly added to a dry $CHCl_3$ (5 mL) solution of **1** (0.500 g, 2.74 mmol) at 0 ºC, and the mixture was stirred for 12 h at 0 ºC. The reaction mixture was poured into MeOH. At this stage the obtained polymer was soluble in MeOH. After removal of insoluble particles by filtration, the solution was removed by evaporation. The remaining solid became only partly soluble in MeOH, and was washed with hot water under reflux conditions three times to remove iron compounds. After the water solution became colorless, the brown solid was dried under vacuum to obtain **5**(Fe) (yield = 30%); a considerable part of **5**(Fe) seemed to be lost during repeated washing. Anal. Calcd for $C_9H_{12}N_2O_2$: C, 59.99; H, 6.71; N, 15.55. Found: C, 60.23; H, 6.59; N, 15.37. GPC (eluent = DMF, vs. polystyrene standards): M_n = 12800. M_w = 17600.

Preparation of 5(Ni) A mixture of **3** (0.200 g, 0.59 mmol), $Ni(cod)_2$ (0.399 g, 1.42 mmol), bpy (0.221 g, 1.42 mmol), and 1,5-cyclooctadiene (0.153 g, 1.42 mmol) in dry DMF (5 mL) was stirred for 48 h at 60 ºC under N_2. After cooling to rt, water was added and the mixture was stirred overnight. The precipitate was separated by filtration and washed with an aqueous solution of a disodium salt of EDTA at 100 ºC. The remaining polymer was dissolved in chloroform, recovered by reprecipitation in hexane, and dried under vacuum (yield = 32%).

Data collection of 3 and 4 Crystal data of **3** (CCDC number 687489): $C_9H_{12}Br_2N_2O_2$, M = 340.01, monoclinic, $P2_1/n$ (No. 14), a = 19.234(15), b = 10.995(8), c = 24.969(19) Å, β = 95.221(9) °, V = 5258(7) Å^3, Z = 16, D_{calcd} = 1.718 g cm^{-3}, μ(Mo Kα) = 61.693 cm^{-1}, T = 113 K, F(000) = 2656.00, observed reflections 11554 (all data), variables 585, R_1 = 0.1117 ($I > 2\sigma(I)$), R = 0.3313, R_w = 0.3595. Crystal data of **4** (CCDC number 687490): $C_7H_{10}Br_2N_4O_2$, M = 341.99, orthorhombic, Pbca (No. 61), a = 9.788(3), b = 13.883(5), c = 17.856(6) Å, V = 2426.3(14) Å^3, Z = 8, D_{calcd} = 1.872 g cm^{-3}, μ(Mo Kα) = 66.900 cm^{-1}, T = 113 K, F(000) = 1328.00, observed reflections 2768 (all data), variables 149, R_1 = 0.0357 ($I > 2\sigma(I)$), R = 0.0852, R_w = 0.0315.

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22. The IR spectrum of **5**(Ni) seems to contain a broad IR absorption band in the low frequency region of 500-700 cm^{-1}, and several IR peaks, which are clearly observed with **5**(Fe), seem to be overlapped with the broad absorption band. This broad IR absorption band may be due to the presence of some doped state(s) in **5**(Ni). P- and n-type doping of π-conjugated polymers[8,9] often affords broad IR peak(s).
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