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Oxidative Substitution Reaction of 1-Amino-3,6-di-*tert*-butyl-9*H*-carbazole at 4 Position

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ABSTRACT

4 position of 1-amino-3,6-di-tert-butyl-9H-carbazole, which was derived from carbazole through three steps, was oxidatively substituted and a carbazole-1,4-diimine type compound was obtained. The sterically crowded molecular structure of the substituted product was revealed by X-ray crystal structural analysis.

Keywords: Carbazole-1,4-diimine, 1-Amino-3,6-di-tert-butyl-9H-carbazole, Oxidative substitution reaction.

Carbazole has much attracted because many organic functional materials such as emitter, semiconductors, electrical materials and drugs are derived from it [1-5]. Because of its applications, many synthetic methods to obtain carbazole derivatives have been studied. In many cases, the 9 position of carbazole is substituted by aromatic rings by Buchwald-Hartwig coupling reaction or Ullmann coupling reaction [6,7]. The electrophilic substitution reaction usually affords 3-substituted or 3,6-disubstituted carbazole derivatives [7,8] because the highest occupied molecular orbital (HOMO) of carbazole is distributed over 1, 3, 6 and 8 position of the heteroaromatic ring. Sometimes 1-substituted carbazole is obtained by halogenation [9,10]. There are many reports for substitution reaction of carbazole and its derivatives, whereas substitution reaction at 4 position of carbazole is rare because of its low reactivity caused by the low distribution of HOMO and the steric hindrance of the hydrogen atom on 5 position of the ring. In this study, the oxidative substitution reaction at 4 position of 1-amino-3,6-di-*tert*-butyl-9*H*-carbazole **(1)** was observed. This reaction affords a carbazole-1,4-diimine type compound (Figure 1), 3,6-di-tert-butyl-N^4-(4-nitrophenyl)-9*H*-carbazole-1,4-diimine **(2).** In this communication report, the substitution reaction of **1** and X-ray crystal structural analysis of **2** are described.

The aminated carbazole **1** was derived from 3,6-di-*tert*-butyl-1-nitro-9*H*-carbazole, which was synthesized by nitration of 3,6-di-*tert*-butyl-9*H*-carbazole (Figure 2). The dialkylcarbazole was synthesized by Friedel-Crafts reaction of 9*H*-carbazole and *tert*-butyl chloride catalysed by zinc (II) chloride [7]. For introduction of a nitro group on the heterocyclic compounds, $AgNO_3$ is sometimes useful as a nitration reagent and the alkylated carbazole was converted to the nitro compound. The nitro group was easily reduced to the amino group by simple catalytic reduction.

As an oxidative substitution reactant, *N,N*-diiodo-4-nitroaniline was used. Minakata and co-workers reported that the *N,N*-diiodo aniline derivatives can be obtained by treatment of aniline derivatives with sodium iodide and *tert*-butyl hypo chloride in THF, and the prepared iodinated compounds were used *in situ* [11-13].

When *N,N*-diiodo-4-nitroaniline was prepared from 4-nitroaniline and reacted with **1** at 0°C, the 1,4-diimine compound **2** was obtained (Figure 1). Recrystallization of **2** with CH_2Cl_2 and *n*-hexane afforded CH_2Cl_2-inclusion crystals. Sometimes the bulky group such as butyl group makes a cavity in the crystal lattice and a small molecule would be included there [14,15]. X-ray crystal structural analysis revealed the sterically crowded molecular structure

of **2** and the guest molecule was observed in the lattice. As shown in Figure 3, the nitrogen atom attached to 4 positions is closed to the hydrogen atom on 5 position and the *tert*-butyl group on 3 position. The mesomeric effect of an amino group on 1 position and the inductive effect of a *tert*-butyl group on 3 position would enhance the distribution of HOMO on 4 position. Low reaction temperature inhibits a C-H stretching vibration of 5 position and a rotation of the *tert*-butyl groups. These electric and thermodynamic effects could allow the nitrogen atom of *N*,*N*-diiodo- 4-nitroaniline to attack at crowded 4 position of **1** (Figure 3).

In conclusion, 4 position of **1** was reacted with *N*,*N*-diiodo-4-nitroaniline and the oxidative substitution reaction afforded **2** as a carbazole-1,4-diimine compound. The sterically crowded molecular structure of **2** was revealed by X-ray crystal structural analysis. The effects of substituents of **1** and low reaction temperature could allow the reaction. The carbazole-1,4-diimine is rare structure and it would contribute the progress of studies on carbazole derivatives.

MEASUREMENTS

^{1}H NMR spectra were determined on a Bruker Advance III NMR spectrometer with $CDCl_3$ and CD_3COCD_3 as solvents and TMS as internal standard (δ=0 ppm). The high resolution ESI-MS spectra were obtained using a Bruker micrOTOF-Q III.

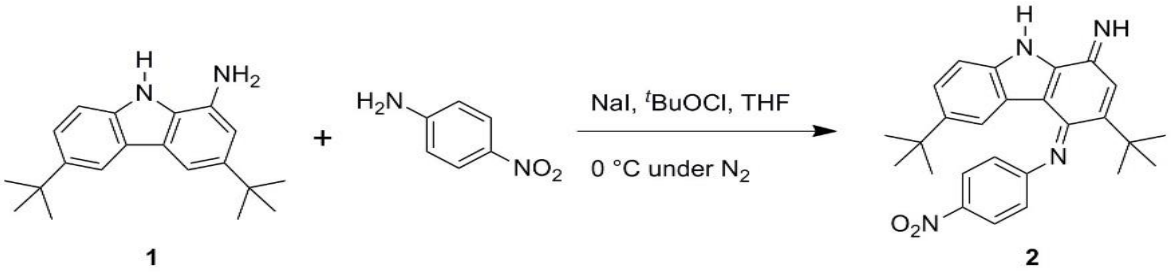

Figure 1: Oxidative substitution reaction of 1-amino-3,6-di-*tert*-butyl-9*H*-carbazole.

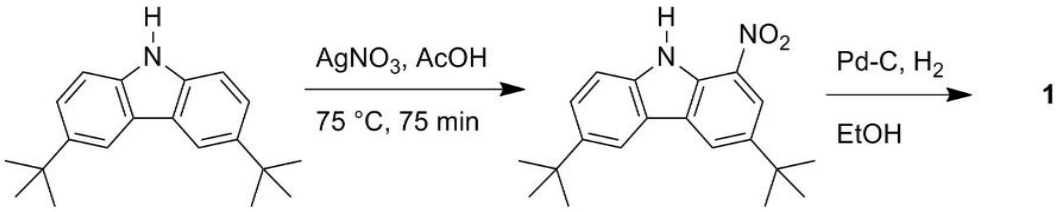

Figure 2: Synthesis of 1-amino-3,6-di-*tert*-butyl-9*H*-carbazole.

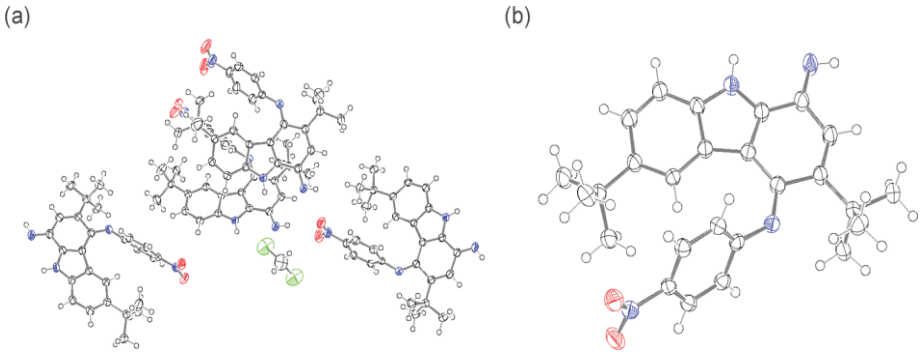

Figure 3: Asymmetric unit of the unit cell (a) and one of the molecular structures of **2** (b) described by ORTEP-3 for Windows [16]. Thermal ellipsoids are drawn at the 50% probability level.

SYNTHESIS

Di-*tert*-butyl-1-nitro-9*H*-carbazole

3,6-Di-*tert*-butyl-9*H*-carbazole (2.00 g, 7.16 mmol) was reacted with $AgNO_3$ (1.16 g, 6.83 mmol) in CH_3COOH (150 mL) at 75°C for 60 min. After the solution was cooled to room temperature, the solution was poured into the water (600 mL) and then precipitated yellowish powder was filtered followed by washing with water. The obtained powder was dissolved into CH_2Cl_2 (200 mL), washed with water (100 mL) and brine (100 mL). The organic layer was dried over $MgSO_4$, concentrated, and the residue was purified by column chromatography on a silica gel by eluting with a 1:2 mixture (v/v) of CH_2Cl_2 and *n*-hexane. Evaporation of the solvent afforded 3,6-di-*tert*-butyl-1-nitro-9*H*-carbazole (1.32 g, 4.07 mmol, 56.8%) as an orange solid.

^{1}H NMR ($CDCl_3$, 298K, 400MHz): δ 1.42 (s, 9H; C<u>H</u>$_3$), 1.44 (s, 9H; C<u>H</u>$_3$), 3.63 (br, 2H; N<u>H</u>$_2$), 6.89 (d, J_{meta} = 1.6 Hz, 1H; Ar<u>H</u>), 7.35 (d, J = 8.4 Hz, 1H; Ar<u>H</u>), 7.45 (dd, J_{ortho} = 8.5 Hz, J_{meta} = 1.9 Hz, 1H; Ar<u>H</u>), 7.60-7.62 (m, 2H; Ar<u>H</u>, N<u>H</u>), 8.03 (d, J_{meta} = 1.8 Hz, 1H; Ar<u>H</u>). ESI-MS: Calcd for $[C_{20}H_{27}N_2]^+$, *m*/z = 295.2174; found, 295.2193.

1-Amino-3,6-di-*tert*-butyl-9*H*-carbazole (1)

3,6-Di-tert-butyl-1-nitro-9H-carbazole (0.968 g, 2.98 mmol) and 5% Pd-C (0.132 g) were placed in a round bottom flask and the flask was purged with nitrogen. Ethanol (75 mL) was added to the flask followed by introduction of hydrogen (1 atom). After the reaction mixture was stirred for 8-hour, acetone (75 mL) was added and filtered. Evaporation of the obtained pale brown solution afforded white solid. Recrystallization of the solid with CH_2Cl_2 and *n*-hexane prepared **1** (764 mg, 2.59 mmol, 86.9%) as a white solid.

^{1}H NMR ($CDCl_3$, 298K, 400MHz): δ 1.42 (s, 9H; CH_3), 1.44 (s, 9H; CH_3), 3.63 (br, 2H; NH_2), 6.89 (d, J_{meta}=1.6 Hz, 1H; ArH), 7.35 (d, J=8.4 Hz, 1H; ArH), 7.45 (dd, J_{ortho}=8.5 Hz, J_{meta}=1.9 Hz, 1H; ArH), 7.60-7.62 (m, 2H; ArH, NH), 8.03 (d, J_{meta}=1.8 Hz, 1H; ArH). ESI-MS: Calcd for $[C_{20}H_{27}N_2]^+$, m/z=295.2174; found, 295.2193.

3,6-Di-*tert*-butyl-N^4-(4-nitrophenyl)-9*H*-carbazole-1,4-diimine (2)

Sodium iodide (300 mg, 2.0 mmol), *p*-nitroaniline (208 mg, 1.5 mmol) and **1** (149 mg, 0.51 mmol) were placed in a three neck round bottom flask. Under flowing of nitrogen gas, dried THF (6 mL) was added and attached an ice bath. Then *tert*-butyl hypochloride (0.23 mL, 2.0 mmol) was added and stirred for 4.5 hours. The reaction mixture was poured into aqueous sodium thiosulfate (1M, 20 mL) and extracted with ethyl acetate. The obtained organic layer was washed with brine, dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by column chromatography on silica gel by eluting with a 1:1 mixture (v/v) of ethyl acetate and *n*-hexane. The collected fraction was evaporated. Recrystallization of the residue with CH_2Cl_2 and *n*-hexane prepared **2** as a CH_2Cl_2-inclusion compound (56 mg, 0.12 mmol, 24%); the guest (CH_2Cl_2)/host **(2)** stoichiometric ratio was 1/4.

^{1}H NMR (400 MHz, CD_3COCD_3): δ = 1.01 (s, 9H; C<u>H</u>$_3$), 1.53 (s, 9H; C<u>H</u>$_3$), 6.38 (b, 1H; Ar<u>H</u>(5)), 5.62 (s, 0.5H, C<u>H</u>$_2$Cl$_2$), 6.83 (b, 1H; Ar<u>H</u>(2)), 7.10 (dt, J_{ortho} = 9.1 Hz, J_{meta} = 2.5 Hz, 2H; Ar<u>H</u>(2', 6')), 7.35 (dd, J_{ortho} = 8.7 Hz, J_{meta} = 1.8 Hz, 1H; Ar<u>H</u>(7)), 7.47 (d, J_{ortho} = 7.0 Hz, 1H; Ar<u>H</u>(8)), 8.20 (dt, J_{ortho} = 9.0 Hz, J_{meta} = 2.1 Hz, 2H; Ar<u>H</u>(3', 5')), 10.70 (br, 1H; N^4<u>H</u>), 11.34 (br, 1H; N<u>H</u>). ESI-MS: Calcd for $[C_{26}H_{29}N_4O_2]^+$, *m*/z = 429.2291; found, 429.2306.

X-ray crystal structural analysis

X-ray diffraction experiments were performed on a Rigaku Saturn 724 diffractometer using multi-layer mirror monochromated Mo-*K*α radiation. Cell constants and an orientation matrix for data collection corresponded to a primitive triclinic cell with dimensions: a=11.3437(14) Å, b=18.379(3) Å, c=25.571(3), α=83.751(10)°, β=80.163(9)°, γ=72.790(6)°, V=5007.9(11) Å^3. For Z=2 and F.W.=1799.06, the calculated density is 1.193 g/cm^3. Based on a statistical analysis of intensity distribution, and the successful solution and refinement of the structure, the space group was determined to be: P(-1). Of the 72482 reflections were collected, where 22787 were unique (R_{int}=0.0621); equivalent reflections were merged. Data were collected and processed using *CrystalClear* (Rigaku) [17]. The linear absorption coefficient, μ, for Mo-*K*α radiation is 1.280 cm^{-1}. An empirical absorption correction was applied which resulted in transmission factors ranging from 0.902 to 0.994. The data were corrected for Lorentz and polarization effects.

Structure solution and refinement were carried out with the *CrystalStructure* [18] crystallographic software package except for refinement, which was performed using *SHELXL* Version 2014/7 [19]. The structure was solved by charge flipping method [20] and expanded using Fourier techniques. The non-hydrogen atoms were refined anisotropically. Hydrogen atoms were refined using the riding model. The contributions of highly disordered dichloromethane molecules to the diffraction data were removed with the SQUEEZE procedure in *PLATON* [21].

The final cycle of full-matrix least-squares refinement on F^2 was based on 22787 observed reflections and 1208 variable parameters and converged (largest parameter shift was 0.00 times its esd) with unweighted and weighted agreement factors of: R_1=0.1047, wR_2=0.2894. The goodness of fit was 1.14. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.96 and -1.13 e /Å^3, respectively.

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