

## Oxidation of *N*-benzyl groups

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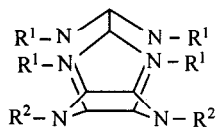
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The oxidative reactivity of 2, 6, 8, 12-tetraacetyl-4, 10-dibenzyl-2, 4, 6, 8, 10, 12-hexaazatetracyclo[5.5.0.0<sup>5,9</sup>. 0<sup>3,11</sup>] dodecane (**3**) in several conditions was studied. It was found that the *N*-benzyl groups in compound **3** could be oxidized to benzoyl groups by Cr(VI) reagents, and could be removed by cerium ammonium nitrate (CAN), meanwhile nitroamine products were given.

**Keywords** Cage compound, oxidation, debenzylation

### Introduction

2, 4, 6, 8, 10, 12-Hexabenzyl-2, 4, 6, 8, 10, 12-hexaazatetracyclo[5.5.0.0<sup>5,9</sup>. 0<sup>3,11</sup>] dodecane (hexabenzyl-hexaazaisowurtzitane, **1**), an interesting cage compound, was synthesized by Nielsen.<sup>1</sup> It was the precursor of hexanitrohexaazaisowurtzitane (**2**).<sup>2</sup> During the past decade, **2** has been at the forefront in the synthesis of high energy density materials. 2, 6, 8, 12-Tetraacetyl-4, 10-dibenzyl-2, 4, 6, 8, 10, 12-hexaazatetracyclo[5.5.0.0<sup>5,9</sup>. 0<sup>3,11</sup>] dodecane (**3**), synthesized by hydrogenolysis of **1** in acetic anhydride, is an important intermediate for synthesis of **2**,<sup>2</sup> meanwhile, **3** could be further reduced to **4**, **5** or **6** in different media. In an effort to find a new debenzylation method, we explored a series of oxidative reactions of **3**.



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|---|--|
| 1 R <sup>1</sup> =R <sup>2</sup> =benzyl          | 5 R <sup>1</sup> =R <sup>2</sup> =acetyl         |
| 2 R <sup>1</sup> =R <sup>2</sup> =NO <sub>2</sub> | 6 R <sup>1</sup> =acetyl, R <sup>2</sup> =formyl |
| 3 R <sup>1</sup> =acetyl, R <sup>2</sup> =benzyl  | 7 R <sup>1</sup> =acetyl, R <sup>2</sup> =benzyl |
| 4 R <sup>1</sup> =acetyl, R <sup>2</sup> =H       |  |

### Results and discussion

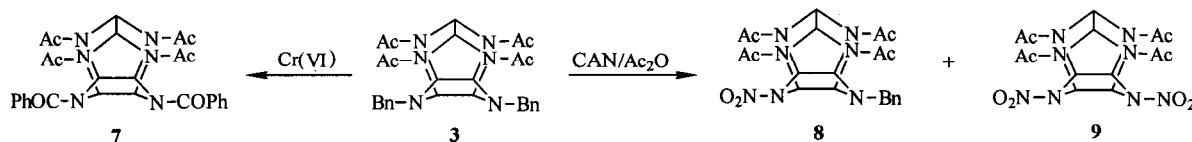
An important feature of amine dealkylation is transition metal-catalyzed oxidation with molecular oxygen. CuCl/Py/Ac<sub>2</sub>O/O<sub>2</sub> is an efficient system for dealkylation of tertiary amine,<sup>3</sup> but under the same condition, compound **3** remains unreacted. Increasing the temperature and the amount of catalyst, we still do not get the expected debenzylated product. Hexacyanoferrate (III) is known to oxidize benzylamine to give benzaldehyde and ammonia in alkaline medium.<sup>4</sup> However upon treating **3** with hexacyanoferrate(III), reactant was recovered after 24 h at 60°C. Treatment of compound **3** with lead tetraacetate,<sup>5</sup> also met with failure. It was reported that photosensitized single electron transfer could conveniently initiate *N*-debenzylolation of tertiary amines.<sup>6</sup> Ammonium peroxydisulfate [(NH<sub>4</sub>)<sub>2</sub>S<sub>2</sub>O<sub>8</sub>], a single electron transfer agent, has removed the *N*-benzyl group in the derivatives of adenosines successfully.<sup>7</sup> Attempt to treat **3** with ammonium peroxydisulfate, made only a retrieval of the reactant.

It is well known that Cr(VI) is an efficient reagent for oxidation of benzylic C—H bonds,<sup>8</sup> but using Cr(VI) to oxidize tertiary amines is rarely reported. Cave<sup>9</sup> used CrO<sub>3</sub>/Py to oxidize tertiary amines and obtained amide products. Yamaura<sup>10</sup> removed *N*-(*p*-methoxy) benzyl by CrO<sub>3</sub>/AcOH. Upon treatment of compound **3** with potassium dichromate in the solution of acetic acid and acetic anhydride at 50°C, an oxidized product, not a debenzylated product, tetraacetyl-dibenzoylhexaazaisowurtzitane (**7**) was obtained.<sup>11</sup> Treating **3** with CrO<sub>3</sub>/AcOH, we obtained the same product. Under both of these two conditions, oxidant is virtually chromate acid. After that, we oxidized the hex-

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abenzylhexaazaisowurtzitane successfully to hexabenzoyl-hexaazaisowurtzitane by  $\text{CrO}_3/\text{Ac}_2\text{O}$ .<sup>12</sup>

The structure of compound **7** was identified by IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, MS(FD) and elemental analyses. At the  $^1\text{H}$  NMR spectra of **7**, the twelve H atoms of



CAN is an efficient reagent to remove the *N*-(*p*-methoxy)benzyl group.<sup>10,13</sup> Imitating the conditions of the literature, when we oxidized **3** with CAN, only reactant was recovered. It may be attributed to the bad solubility of **3**. Instead of  $\text{CH}_3\text{CN}/\text{water}$ , when we used acetic anhydride as solvent, unexpectedly, compound **8** and **9**<sup>a</sup> were obtained in 51% and 9% yield respectively.

Galliani<sup>14</sup> studied the oxidation of CAN in  $\text{CH}_3\text{CN}/\text{water}$ , acetic acid or methanol in detail. He thought that the process had two effects: the oxidation process and nitration reaction, in addition, the oxidative process preceded the nitration process. The above results indicate that the action of CAN on compound **3** also has two effects: the oxidative debenzoylation process and nitration reaction, but its mechanism is not clear yet.

## Experimental

Compound **3** was synthesized by ourselves,<sup>2d</sup> mp 321—323°C. Melting point was uncorrected,  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded by using tetramethylsilane as an internal standard on a Bruker ARX-300 spectrometer for  $\text{CDCl}_3$  solution, and an ARX-400 spectrometer for  $\text{DMSO}-d_6$  solution. IR spectra were taken with a Shimadzu IR-408. MS(FD) spectra were recorded with a Hitach M-80. MS(FAB) spectra were recorded with a VG zabspec VG-ZAB-HS.

2,6,8,12-Tetraacetyl-4,10-dibenzoyl-2,4,6,8,10,12-hexaazatetracyclo[5.5.0.0<sup>5,9</sup>.0<sup>3,11</sup>]dodecane (**7**)

**Procedure A** Compound **3** (206 mg, 0.4 mmol) was dissolved in the solution of acetic acid (10 mL) and acetic anhydride (10 mL), after potassium dichromate (2.8 g) was added, the mixture was stirred at 50°C for 5 h. The cooled solution was poured into

water, extracted three times with chloroform (30 mL × 3), washed with saturated sodium hydrogen carbonate solution (20 mL × 2) and water (20 mL × 2), and dried over anhydrous magnesium sulfate. The solvent was evaporated off under reduced pressure to give white solid (167 mg, yield 76%), and the residue could be purified by recrystallization from  $\text{CHCl}_3/\text{ether}$ . m. p. > 300°C. Anal.  $\text{C}_{28}\text{H}_{28}\text{N}_6\text{O}_6 \cdot 0.5\text{H}_2\text{O}$ , Calcd.: C, 60.75; H, 5.28; N, 15.18. Found: C, 60.12; H, 4.99; N, 15.27.  $\nu_{\text{max}}$ : 1655, 1400, 1315, 1130, 690.  $\delta_{\text{H}}(\text{CDCl}_3, 300 \text{ MHz})$ : 7.71—7.55(m, 10H), 6.95—6.92(m, 2H), 6.58—6.55(m, 2H), 6.50(s, 2H), 2.29(s, 6H), 2.14(s, 6H).  $\delta_{\text{C}}(\text{CDCl}_3, 300 \text{ MHz})$ : 171.65, 168.65, 167.86, 72.50, 69.07, 63.16, 21.96, 21.05.  $m/z(\%)$ : 544 (M, 100).

**Procedure B** The mixture of acetic acid (10 mL) and acetic anhydride (10 mL) was cooled to 0°C, chromium trioxide (120 mg, 1.2 mmol) was added. After 10 min. compound **3** (103 mg, 0.2 mmol) was added and stirred at 0°C for 5 h. The solution was poured into ice water, extracted with chloroform (20 mL × 3), washed with saturated sodium hydrogen carbonate solution (20 mL × 2) and water (20 mL × 2), and dried over anhydrous magnesium sulfate. The solvent was evaporated off under reduced pressure to give white solid (85 mg, yield 78%).

2,6,8,12-Tetraacetyl-4-nitro-10-benzyl-2,4,6,8,10,12-hexaazatetracyclo[5.5.0.0<sup>5,9</sup>.0<sup>3,11</sup>]dodecane (**8**) and 2,6,8,12-tetraacetyl-4,10-dinitro-2,4,6,8,10,12-hexaazatetracyclo[5.5.0.0<sup>5,9</sup>.0<sup>3,11</sup>]dodecane (**9**)

\* <sup>a</sup> Note: Compound **9**:<sup>2e</sup> mp 313—315°C.  $\delta_{\text{H}}(\text{DMSO}-d_6)$ : 7.38(s, 4H), 6.78(s, 2H), 2.1(s, 12H);  $\delta_{\text{C}}$ : 167.35, 78.64, 67.38, 20.98.  $m/z(\text{CI})$ : 427(M+1, 100%).

Compound **3** (206 mg, 0.4 mmol) was dissolved in acetic anhydride (20 mL). After CAN (870 mg, 1.6 mmol) was added, the mixture was stirred at 20–25 °C for 24 h, the mixture was poured into water (50 mL), extracted three times with chloroform (20 mL × 3). The combined chloroform solution was washed with saturated sodium hydrogen carbonate solution (20 mL × 2), and water (20 mL × 2), and dried over anhydrous magnesium sulfate. Evaporated under reduced pressure to give light yellow glutinous solid, which was purified on a flash column of silica gel (CCl<sub>4</sub>/acetone 3:1) to give **8** (96 mg, 51% yield), and **9** (15 mg, 9% yield). Compound **8**: mp 256–257 °C. Anal. C<sub>21</sub>H<sub>25</sub>N<sub>7</sub>O<sub>6</sub>. Calcd.: C, 53.50; H, 5.35; N, 20.80. Found: C, 53.49; H, 5.23; N, 20.59.  $\nu_{\max}$ : 3020, 1655, 1555, 1390, 1285.  $\delta_{\text{H}}$ (DMSO-d<sub>6</sub>, 400 MHz): 7.34–7.25(m, 5H), 7.00–6.56(m, 4H), 5.80–5.59(m, 2H), 4.09–3.97(m, 2H), 2.09(s, 12H).  $m/z$ (%): 472(M+1, 100). Compound **9**: mp > 300 °C;  $\nu_{\max}$ : 3050, 1690, 1565, 1400, 1300.  $\delta_{\text{H}}$ (DMSO-d<sub>6</sub>, 400 MHz): 7.39–7.23(m, 4H), 6.92–6.60(m, 2H), 2.11(s, 12H).

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