

# REACTION OF MALEIMIDES WITH NEW SILYLOXYDIENES, 2-AMINO-4-(TRIMETHYLSILOXY)-1,3-PENTADIENES

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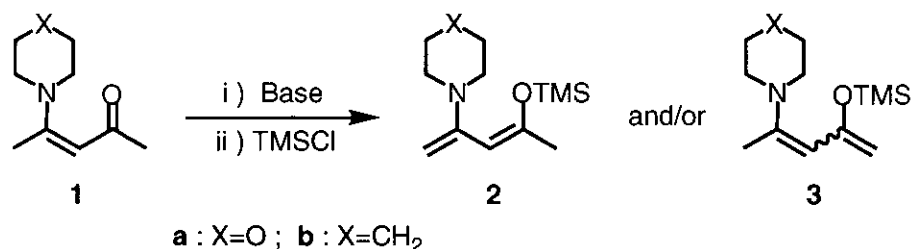
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**Abstract** - New siloxydienes, 2-amino-4-(trimethylsilyloxy)-1,3-pentadienes which were easily obtained *via* enolization of enaminones derived from 2,4-pentane-dione, and immediate silylation, reacted with maleimides to furnish reduced benzo-[c]pyrrole-1,3-diones as major products, derived from initial [4 + 2] cycloadducts.

Since the pioneering studies of Danishefsky and his group,<sup>1</sup> a number of siloxydienes have been prepared and widely applied in synthesis of carbocyclic and heterocyclic compounds. In sharp contrast with versatilely utilized siloxydienes with an electron-donating oxygen-<sup>1,2</sup> or sulfur-substituent<sup>2h,i,3</sup> in the 1,3-pattern, however, dienes bearing siloxy and amino groups in the same pattern are not used so much in organic synthesis: To date there have been only limited studies concerning siloxydienes bearing an amino group.<sup>4,5</sup> Here we wish to report the preparation of new amino-substituted siloxydienes and their reaction with maleimides.

Several attempts were made to prepare enol silyl ethers from enaminones (**1**) derived from 2,4-pentanedione. Enolization with LDA in THF at -78 °C followed by quenching with chlorotrimethylsilane (TMSCl) furnished an inseparable mixture of the corresponding 2-amino-4-(trimethylsilyloxy)- (**2**) and 4-amino-2-(trimethylsilyloxy)-1,3-pentadiene (**3**) in quantitative yield (**2a/3a**=6/5; **2b/3b**=2/3).<sup>6</sup> However, it

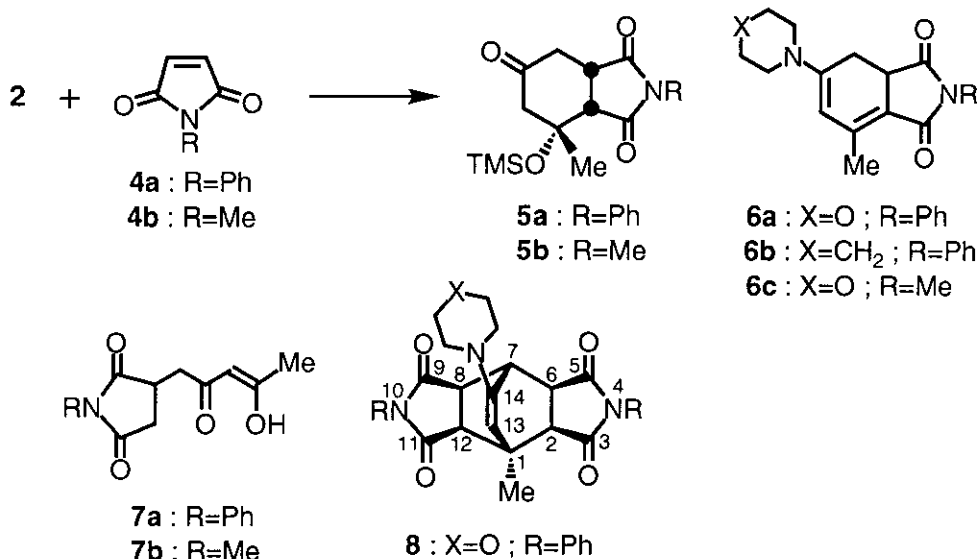


Scheme 1

has been found that enolization with BuLi at 0 °C in THF followed by quenching with chlorotrimethylsilane (TMSCl) furnished **2** quantitatively (Scheme 1).<sup>7</sup> The stereochemistry of **2** was assigned to be *Z* by NOE experiment.

Dienes (**2**) belong to a class of 1-siloxydienes that have not been used so extensively in Diels-Alder reactions. It has been reported that the sole reported 3-amino-1-siloxydiene system, 3-amino-1-methoxy-1-(trimethylsiloxy)-1,3-butadiene<sup>5</sup> generated *in situ*, reacted with carbonyl electrophiles in the presence of TiCl<sub>4</sub> to give  $\gamma$ -adducts, although Diels-Alder adducts formed in the reaction with an acetylenic dienophile. Reactions of **2a** with an equivalent of *N*-phenylmaleimide (**4a**) gave an intractable mixture owing to polymerization of **4a**. In the reaction using two equivalents of **2a** no polymerization of **4a** was observed, but instead the reaction proceeded cleanly. The reaction of **2a** or **2b** with **4a** in benzene or THF at 25 °C for 1 h furnished **5a** and **6a** or **6b** as major products, together with a small amount of **7a**, respectively.<sup>8</sup> Under the similar conditions **2a** reacted with *N*-methylmaleimide (**4b**) to give the corresponding products (**5b**, **6c** and **7b**). On the other hand, the reaction of **2a** with **4a** under reflux gave a new 1:2 adduct (**8**) in place of **7a**, although again **5a** and **6a** were major products. The results are summarized in Table 1.

Table 1. Reaction of Siloxydienes (**2**) with Maleimides (**4**).



Run	Diene	Imide	Solvent	Temp. °C	Product (Yield, %)
1	<b>2a</b>	<b>4a</b>	Benzene	25	<b>5a</b> (55), <b>6a</b> (33), <b>7a</b> (6)
2	<b>2a</b>	<b>4a</b>	Benzene	80	<b>5a</b> (40), <b>6a</b> (28), <b>8</b> (12)
3	<b>2a</b>	<b>4a</b>	THF	25	<b>5a</b> (30), <b>6a</b> (45), <b>7a</b> (13)
4	<b>2a</b>	<b>4a</b>	THF	67	<b>5a</b> (21), <b>6a</b> (48), <b>8</b> (10)
5	<b>2b</b>	<b>4a</b>	Benzene	25	<b>5a</b> (34), <b>6b</b> (52), <b>7a</b> (10)
6	<b>2b</b>	<b>4a</b>	THF	25	<b>5a</b> (42), <b>6b</b> (47), <b>7a</b> (10)
7	<b>2a</b>	<b>4b</b>	Benzene	25	<b>5b</b> (51), <b>6c</b> (26), <b>7b</b> (11)

On the basis of spectral data, major products (**5**) and (**6**) were assigned as reduced isoindolediones derived from initial [4 + 2] cycloadducts (**B**), while **7** was as that came from Michael adducts, respectively.<sup>9</sup> The structure of **5b** arising from hydrolysis of **B** in which has an enamine structure was unambiguously established by its X-Ray crystallographic analysis (Figure 1).<sup>10</sup>

Based on the stereochemistry of **5**, the initial adduct (**B**) might be attributable to *exo* cycloadduct that formed *via* an electronically favorable betaine (**A**) generated by the regioselective addition at the  $\gamma$ -position characteristic of 1-siloxydiene<sup>11</sup> rather than a concerted manner. The pathways for the formation of **6** and **8** are clearly illustrated in Scheme 2.

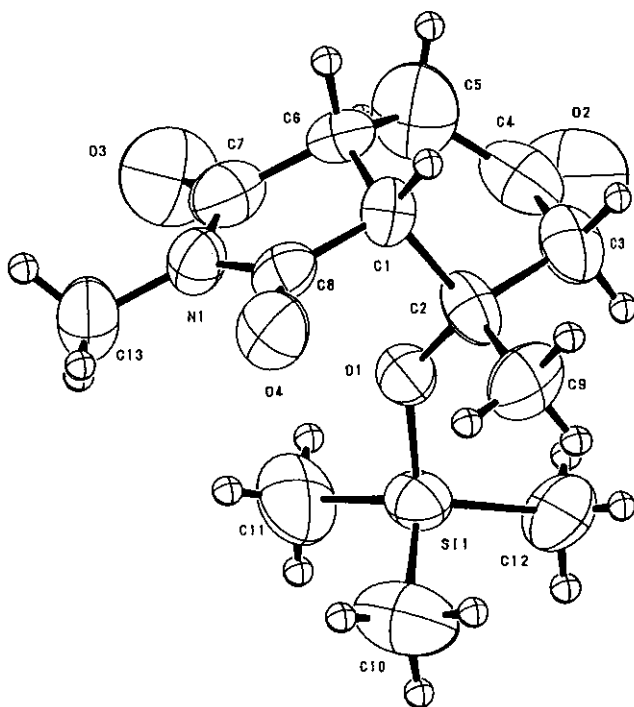
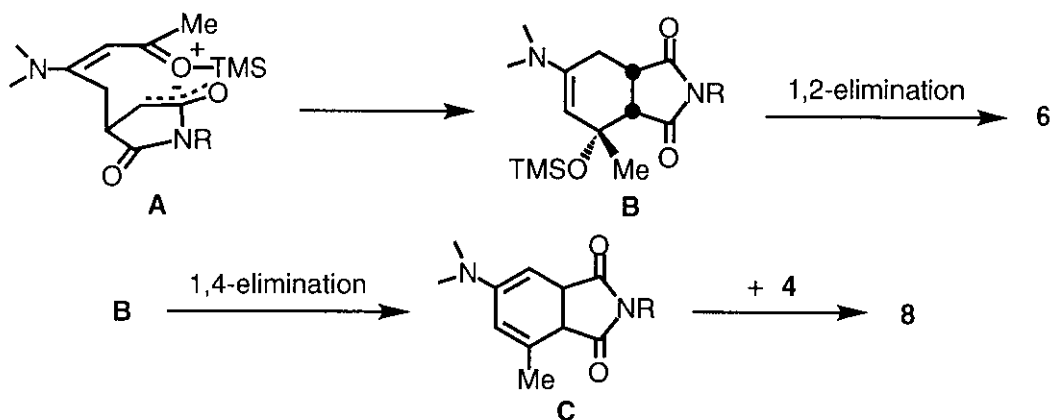


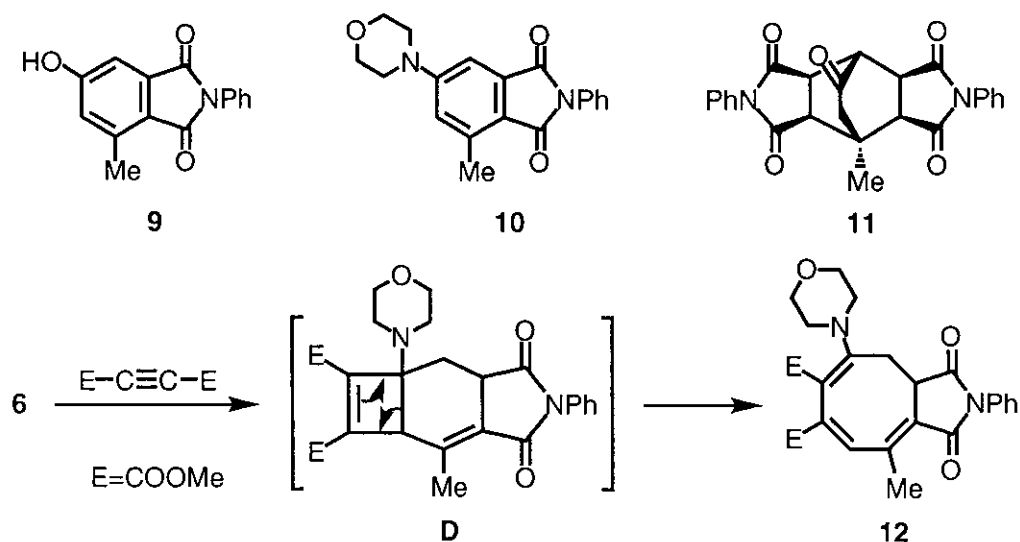
Figure 1. An ORTEP drawing of **5b**.

At room temperature 1,2-elimination of silanol from **B** exclusively occurs to give **6**. On the other hand, at elevated temperature an alternate elimination of silanol *via* 1,4-fashion takes place concomitantly to form **C**, which undergoes Diels-Alder reaction with **4** to furnish **8**.



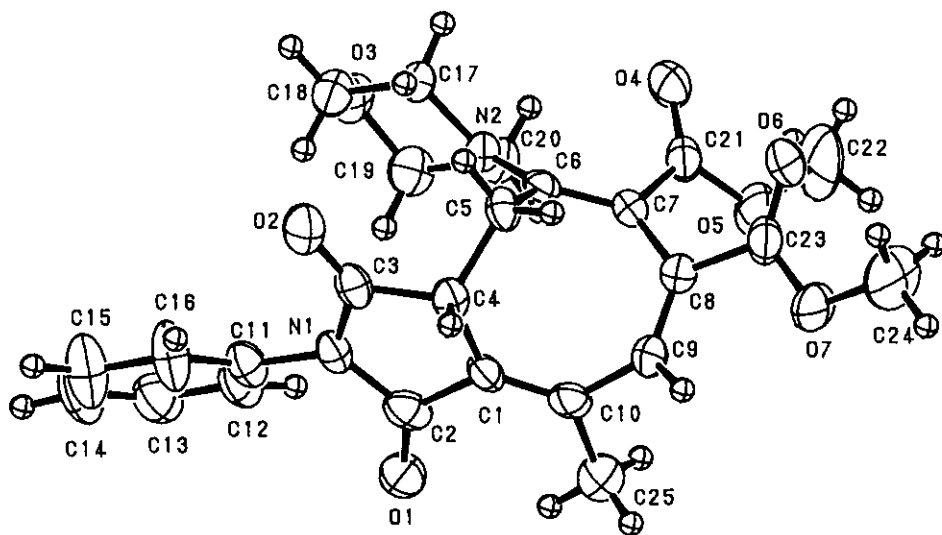
Scheme 2

Desilylation of **5a** with CsF in DME (reflux, 5 h) gave a 46% yield of phenol derivative (**9**) (mp > 300 °C) with concomitant dehydrogenation. Dehydrogenation of **6a** with 5% Pd-C in benzene (reflux, 10 h) furnished isoindoledione (**10**) (mp 231-231.5 °C) quantitatively. The 1:2 adduct (**8**) was readily



Scheme 3

hydrolyzed to the ketone derivative (**11**) (mp > 300 °C) when treated in refluxing 10% ethanolic hydrochloric acid. The stereochemistry of **8** was assumed on the basis of NMR spectral data<sup>12</sup> and inspection of molecular models. It was also found that **6a** reacted with dimethyl acetylenedicarboxylate in benzene (reflux, 45 h) to give a 21% yield of cyclooctatriene (**12**) (mp 183-184 °C) *via* an electrocyclic reaction of [2 + 2] cycloadduct **D** (Scheme 3). The structure of **12** was unambiguously established by its X-Ray crystallographic analysis (Figure 2).<sup>13</sup>

Figure 2. An ORTEP drawing of **12**.

Thus the reaction of **2** with **4** whose major reaction path is [4 + 2] cycloaddition presents a striking contrast to the reaction of 3-amino-1-methoxy-1-silyloxybutadiene.<sup>5</sup>

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6. The ratios were calculated by integral values of methyl proton in  $^1\text{H}$  NMR spectra at  $\delta$  1.85 (**2a**), 1.84 (**2b**), 2.04 (**3a**) and 2.04 (**3b**), respectively.
7. **2a** and **2b**: Both yellow oil, and can be kept in a stoppered container for up to several days in the freezer without obvious decomposition, but are slowly hydrolyzed when exposed to air. **2a**:  $^1\text{H}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.20 (9H, s), 1.85 (3H, d,  $J=0.9$  Hz), 2.78-2.88, 3.68-3.77 (each 4H, m), 4.08, 4.36 (each 1H, s), 4.85 (1H, br s);  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ )  $\delta$  0.86, 23.79, 49.29, 66.83, 89.56, 106.43, 150.37, 150.60. NOE enhancement (15%) was observed between 3-CH= and  $\text{CH}_3$  in **2a**. Brassard's diene<sup>2a</sup> and Chan's diene<sup>3a</sup> whose structures are 1-siloxydienes have been reported as (Z)-stereochemistry.
8. Typical run is as follows (Run 1 in Table 1): After a solution of **2a** (1.2 g, 5 mmol) and **4** (0.43 g, 2.5 mmol) in dry benzene (30 mL) was stirred at 25 °C for 1 h, the reaction mixture was concentrated in vacuo. Flash chromatography ( $\text{SiO}_2$ ) using benzene-AcOEt (1:1) and then benzene-AcOEt (1:2) gave **5** (0.47 g, 55%), **6a** (0.27 g, 33%) and then **8** (43 mg, 6%), respectively.
9. All the new compounds gave satisfactory analytical and spectral data. All the NMR spectra in this paper were measured in  $\text{CDCl}_3$ . Selected data: **5a**: Colorless needles, mp 140-141 °C; IR (KBr) 1715  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  0.11 (9H, s), 1.69 (3H, s), 2.24-3.43 (6H, m), 7.21-7.55 (5H, m);  $^{13}\text{C}$  NMR  $\delta$  1.98, 26.73, 35.80, 37.67, 50.87, 52.53, 75.74, 126.20, 128.56, 129.16, 131.96, 174.76, 177.56, 206.20. MS  $m/z$  345 ( $\text{M}^+$ ). **6a**: Yellow needles, mp 210.5-211.5 °C; IR (KBr) 1709  $\text{cm}^{-1}$ ;  $^1\text{H}$  NMR  $\delta$  2.09-3.60 (7H, m), 2.33 (3H, d,  $J=1.8$  Hz), 3.70-3.85 (4H, m), 5.02 (1H, q,  $J=1.8$  Hz), 7.22-7.58 (5H, m); MS  $m/z$  324 ( $\text{M}^+$ ).
10. X-Ray crystallographic analysis was carried out on a Rigaku AFC5S diffractometer. The diffraction data were collected with the use of  $\text{MoK}\alpha$  radiation and 2121 independent reflections were used for

solving the structure by the TEXSAN program (TEXSAN TEXRAY. Structure Analysis Package, Molecular Structure Corporation). Crystal data for **5b**:  $C_{13}H_{21}NO_4Si$ , F.W.=283.40, tetragonal, space group  $P4_2/c$  (#114),  $a=18.899$  (4) Å,  $c=8.87$  (13) Å,  $V=3168$  (4) Å<sup>3</sup>,  $Z=8$ ,  $D_{cal}=1.188$  g/cm<sup>3</sup>,  $\mu$  (MoK $\alpha$ )=1.51 cm<sup>-1</sup>,  $R=0.057$ ,  $R_w=0.064$ .

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12. **8**: Pale yellow needles, mp 233-234 °C; IR (KBr) 1717 cm<sup>-1</sup>; <sup>1</sup>H NMR  $\delta$  1.88 (3H, s), 2.77 (2H, d,  $J=8.2$  Hz, H-2, H-12), 2.78-2.88 (4H, m), 3.12 (2H, dd,  $J=8.2, 3.2$  Hz, H-6, H-8), 3.59-3.70 (4H, m), 4.00 (1H, dd,  $J=2.0, 3.2$  Hz, H-7), 4.52 (1H, d,  $J=2.0$  Hz, H-13), 7.08-7.52 (10H, m); <sup>13</sup>C NMR  $\delta$  20.35, 34.42, 41.05, 44.29, 47.83, 49.27, 66.38, 99.78, 126.31, 128.83, 129.23, 131.75, 148.06, 174.96, 175.46; MS  $m/z$  497 ( $M^+$ ).
13. Crystal data for **12**:  $C_{25}H_{26}N_2O_7$ , F.W.=466.49, monoclinic, space group  $P2_1/n$ ,  $a=10.777$  (8) Å,  $b=13.504$  (3) Å,  $c=16.148$  (2) Å,  $\beta=95.28$  (3)°,  $V=2340$  (2) Å<sup>3</sup>,  $Z=4$ ,  $D_{cal}=1.324$  g/cm<sup>3</sup>,  $\mu$ (MoK $\alpha$ )=0.91 cm<sup>-1</sup>, Rigaku AFC5S diffractometer, 1642 reflections ( $I>3.00\sigma$  ( $I$ )),  $R=0.058$ ,  $R_w=0.065$ .

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