

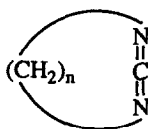
## Medium- and Large-Membered Rings from Bis(iminophosphoranes): An Efficient Preparation of Cyclic Carbodiimides

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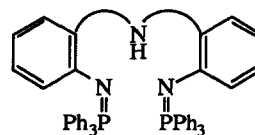
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**Abstract:** The new cyclic carbodiimides **3** are synthesized from bis(iminophosphoranes) **2** and Boc<sub>2</sub>O in the presence of DMAP; similar results can be achieved from the N-Boc-protected bis(iminophosphoranes) and carbon dioxide.

Although an enormous variety of heterocumulenes are known, only a few have been incorporated in strained rings<sup>1</sup>. Carbodiimides are the best known among strained heterocumulenes, and they have been the subject of spectroscopic studies in an attempt to examine the configurational stability of nitrogen in the NCN linkage<sup>2</sup>. The nine-membered cyclic carbodiimides dibenzo[*e,g*][1,3]diazonine and 1,3-diazacyclonona-1,2-diene were prepared by dehydrosulfurization of the corresponding cyclic thiourea, though they had not been isolated in a pure state<sup>3</sup>. Modified Tiemann rearrangement on cyclic amidoxime *O*-methanesulfonates has been used to synthesise cycloalkylene carbodiimides **1** and 4,5,6,7-tetrahydrobenzo[1,3]diazonine<sup>2,4</sup>.



**1** n = 5,6,7,10,11

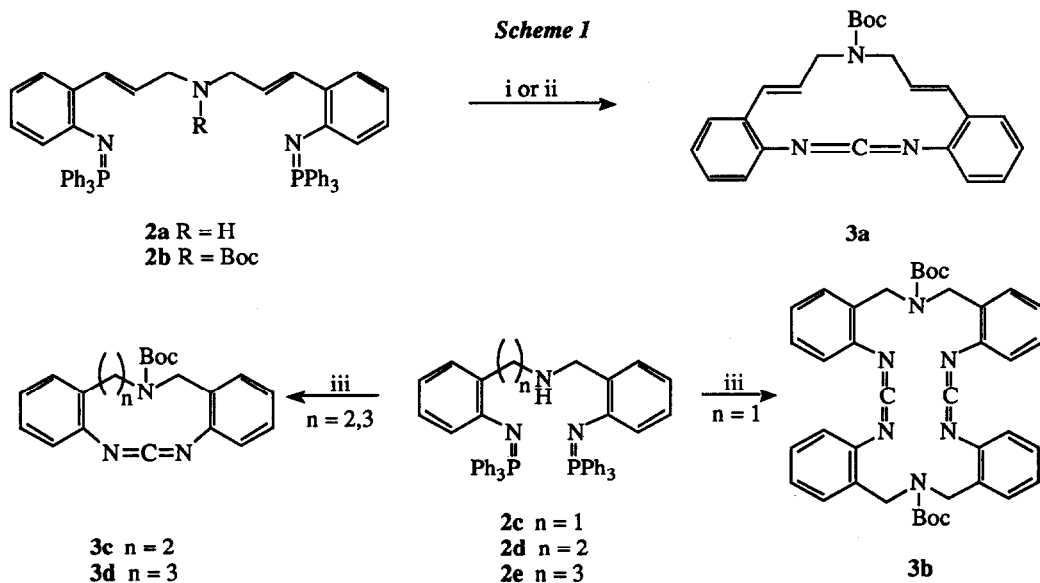


**2**

Continuing our interest on the preparation and synthetic applications of functionalized carbodiimides, we have shown that bis(iminophosphoranes) are valuable building blocks for the preparation of bis(carbodiimides) which undergo a plethora of heterocyclization reactions via multistep processes to give complex nitrogen-containing heterocyclic systems<sup>5</sup>. In this context, we have recently reported that bis(iminophosphoranes) type **2** react with aromatic isocyanates to give directly rigid bicyclic guanidines<sup>6</sup>. We report herein an easy and efficient preparation of cyclic carbodiimides of varying ring size starting from appropriate C,C-bis(iminophosphoranes).<sup>7</sup>

The bis(iminophosphorane) **2a** was easily prepared in 72 % overall yield by the following sequence: (a) condensation of *o*-azidocinnamaldehyde<sup>8</sup> with *o*-azidocinnamylamine<sup>9</sup> (81 %); (b) Staudinger reaction with triphenylphosphine (TPP) (95 %); and (c) reduction with sodium borohydride (94 %). Compound **2a** reacted with two

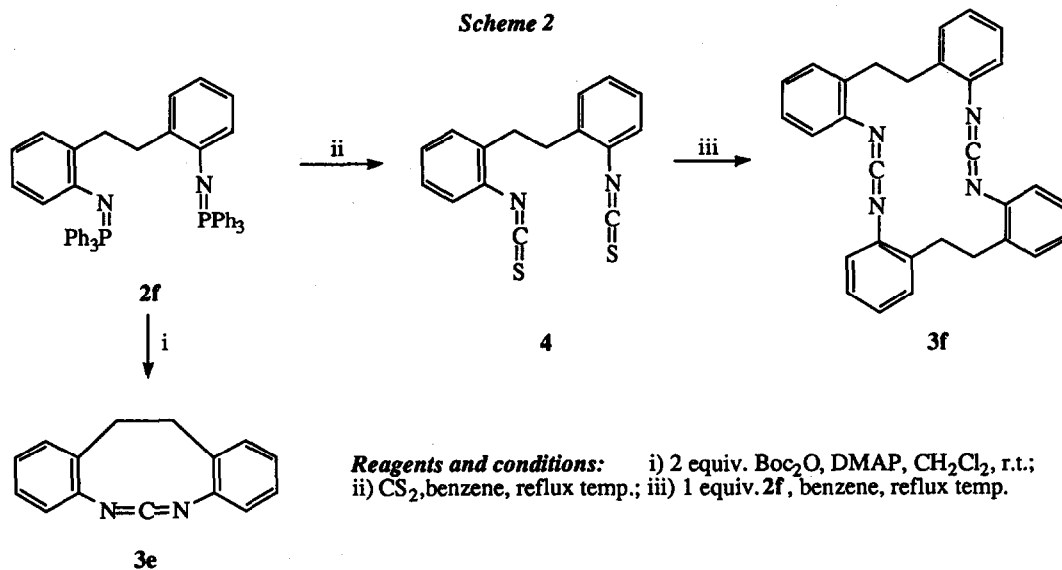
equivalents of  $\text{Boc}_2\text{O}$  in the presence of 4-dimethylaminopyridine (DMAP) in dry dichloromethane at room temperature to give the cyclic carbodiimide **3a** as a viscous oil in 45 % yield. Better results were obtained starting from the bis(iminophosphorane) **2b**, available from **2a** and  $\text{BocN}_3$  in 67 % yield. In this case, the reaction with a slight excess of  $\text{Boc}_2\text{O}$  under the same conditions led to **3a** in almost quantitative yield (98 %). Compound **2b** also reacted with carbon dioxide in dry benzene at 70 °C in a sealed tube to give **3a** in 78 % yield. Similarly, reaction with carbon disulfide in benzene at reflux temperature also led to **3a** albeit in low yield (15 %). It is worth noticing that the reaction of **2a** with carbon dioxide yielded a complex mixture in which the cyclic carbodiimide **3a** could not be detected (Scheme 1).



**Reagents and conditions:** for **2a** i) 2 equiv.  $\text{Boc}_2\text{O}$ , DMAP,  $\text{CH}_2\text{Cl}_2$ , r.t. (45 %); for **2b** ii) excess  $\text{Boc}_2\text{O}$ , DMAP,  $\text{CH}_2\text{Cl}_2$ , r.t. (98%) or  $\text{CO}_2$ , benzene, 70 °C, sealed tube (78 %); iii) excess  $\text{Boc}_2\text{O}$ , DMAP,  $\text{CH}_2\text{Cl}_2$ , r.t.

Bis(iminophosphorane) **2c**<sup>6</sup> reacted with excess of  $\text{Boc}_2\text{O}$  in the presence of DMAP in dry dichloromethane at room temperature to give the twenty-membered bis(carbodiimide) **3b**, as evidenced its HRFAB mass spectrum, in 50 % yield. The N-Boc-protected bis(iminophosphorane) **2c** also reacted either with  $\text{Boc}_2\text{O}$  / DMAP or carbon dioxide to give **3b** in low yields (16-20 %), whereas with carbon disulfide led to the corresponding bis(isothiocyanate). However, bis(iminophosphoranes) **2d** and **2e**<sup>10</sup> under the same conditions afforded the cyclic carbodiimides **3c** and **3d** in 67 % and 55 % yields respectively. The  $^1\text{H}$ - and  $^{13}\text{C}$ -NMR spectra of **3c** and **3d** exhibited signals very similar to those of compounds **3a** and **3b**. Likewise, other analytical and spectral data confirmed the structure shown<sup>11</sup>. On the other hand, bis(iminophosphorane) **2f**, easily prepared in 92 % yield from the corresponding bis(azide) and triphenylphosphine, reacted with two equivalents of  $\text{Boc}_2\text{O}$  in the presence of DMAP at room temperature to give 6,7-dihydrodibenzo[*d,h*]-1,3-diazonine **3e**, isolated as a crystalline solid after chromatographic purification in 77

% yield, accompanied by a minor amount of the bis(carbodiimide) **3f** (less than 10 %). Earlier attempts to prepare **3e** were unsuccessful<sup>4</sup>. Bis(carbodiimide) **3f** was prepared by a two-step route: reaction of bis(iminophosphorane) **2f** with carbon disulfide led to the bis(isothiocyanate) **4** in 93 % yield, which reacted in aza Wittig-type fashion with **2f** to afford the cyclic bis(carbodiimide) **3f** as a crystalline solid in 97 % yield, high-dilution techniques being not mandatory to favour the **3f** formation<sup>12</sup>. The reaction of bis(iminophosphorane) **2f** with carbon dioxide led to a mixture of **3e** (major component), **3f**, and the corresponding bis(isocyanate) (Scheme 2).



It has been reported<sup>13</sup> that  $\text{Boc}_2\text{O}$  slowly decomposes to *t*-butanol, isobutene and two molecules of carbon dioxide, so at first it seemed likely that the formation of carbodiimides **3** could involve an aza-Wittig reaction between one iminophosphorane group of the bis(iminophosphorane) **2** and carbon dioxide resulting from the decomposition of  $\text{Boc}_2\text{O}$ , to give an isocyanate as intermediate which eventually underwent an intramolecular aza-Wittig reaction with the second iminophosphorane group to give the cyclic carbodiimide. However, when the reaction between **2** and  $\text{Boc}_2\text{O}$  was carried out without DMAP, the corresponding *N*-Boc-protected bis(imino-phosphoranes) were isolated as the only reaction products. So the DMAP catalyst must play an unusual role to generate an unstable carbamic carbonic anhydride<sup>14</sup> which on standing at room temperature underwent a four-center rearrangement with loss of carbon dioxide and in this fashion is acting as a controlled-source of carbon dioxide avoiding side reactions. In conclusion, this work shows for the first time that easily available bis(iminophosphoranes) undergo an intramolecular aza-Wittig reaction to afford the otherwise not readily available cyclic carbodiimides. Although aza-Wittig reactions have recently been utilized in the synthesis of five-, six- and even seven-membered nitrogen heterocycles<sup>15</sup>, the present result is the first example of utilization for the synthesis of large-membered heterocycles<sup>16</sup>.

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- We denote as C,C-bis(iminophosphoranes) to those compounds where both iminophosphorane groups are placed on an aromatic, heteroaromatic or unsaturated carbon-carbon side chain.
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- Prepared from the commercially available *o*-nitrocinnamaldehyde by a six-step sequence in 49 % yield: (a) reduction with sodium borohydride (99 %); (b) reduction with sodium borohydride / Pd system (98 %); (c) diazotization followed by azidation (82 %); (d) reaction with N-chlorosuccinimide / dimethylsulfide (96 %); (e) treatment with potassium phthalimide (91 %); (f) hydrazinolysis (70 %).
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- Compound **3a**: <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ 1.51 (s, 9H), 4.10-4.22 (m, 4H), 6.13-6.25 (m, 2H), 6.81 (d, 2H, *J* = 15.7 Hz), 7.07-7.24 (m, 4H), 7.22 (td, 2H, *J* = 7.6, 1.6 Hz), 7.42 (dd, 2H, *J* = 7.6, 1.6 Hz); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ 28.5 (CH<sub>3</sub>), 48.5 (CH<sub>2</sub>), 80.1 (q), 124.4, 125.3, 127.3, 128.5, 128.9, 129.6, 130.9 (q), 132.0 (q), 135.5 (q), 155.2 (q); IR (neat) 2186 (vs) cm<sup>-1</sup>; FAB mass spectrum *m/z* (%) 387 (10).  
Compound **3b**: <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ 1.55 (s, 9H), 4.59-4.65 (m, 4H), 7.07-7.52 (m, 8H); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ 28.7 (CH<sub>3</sub>), 45.4 (CH<sub>2</sub>), 46.0 (CH<sub>2</sub>), 80.2 (q), 125.2 (br), 125.7 (br), 128.4, 129.5 (br), 130.6 (br, q), 132.8 (q), 136.9 (q), 156.4 (q); IR (neat) 2182 (vs) cm<sup>-1</sup>; HRFAB<sup>+</sup> mass spectrum 671.33336 C<sub>40</sub>H<sub>43</sub>N<sub>6</sub>O<sub>4</sub> requires 671.334579.
- Compound **3e**: mp 140-142 °C; <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ 2.94-3.07 (m, 2H), 3.23-3.36 (m, 2H), 6.99-7.25 (m, 8H); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ 32.6 (CH<sub>2</sub>), 123.9, 125.4, 128.2, 130.4, 134.5 (q), 135.5 (q), 138.5 (q); IR (Nujol) 2129 (vs) cm<sup>-1</sup>; EI mass spectrum *m/z* (%) 220 (M<sup>+</sup>, 70).  
Compound **3f**: mp 234-235 °C; <sup>1</sup>H-NMR (300 MHz, CDCl<sub>3</sub>) δ 2.99 (s, 8H), 7.04-7.09 (m, 4H), 7.12-7.21 (m, 12H); <sup>13</sup>C-NMR (75 MHz, CDCl<sub>3</sub>) δ 34.1 (CH<sub>2</sub>), 125.0, 125.2, 127.3, 130.2, 132.3 (q), 135.5 (q), 137.7 (q); IR (Nujol) 2169 (vs) cm<sup>-1</sup>; EI mass spectrum *m/z* (%) 440 (M<sup>+</sup>, 15).
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- Satisfactory <sup>1</sup>H, <sup>13</sup>C-NMR, mass spectra and elemental analyses were obtained for all new compounds.

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