

# Synthesis of 2,3,4-triphenyl-3-azabicyclo[3.2.0]hepta-1,4-diene and its novel reaction with dimethyl acetylenedicarboxylate

Kiyoshi Matsumoto,<sup>\*,a</sup> Sadahito Goto,<sup>a</sup> Naoto Hayashi,<sup>a</sup> Takane Uchida<sup>b</sup> and Akikazu Kakehi,<sup>\*,c</sup>

<sup>a</sup> Graduate School of Human and Environmental Studies, Kyoto University, Kyoto 606-01, Japan

<sup>b</sup> Faculty of Education, Fukui University, Fukui 910, Japan

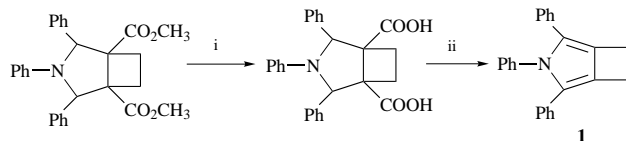
<sup>c</sup> Faculty of Engineering, Shinshu University, Nagano 380, Japan

A 3-azabicyclo[3.2.0]hepta-1,4-diene that is unsubstituted in the cyclobutene moiety has been prepared for the first time and undergoes a novel reaction with dimethyl acetylenedicarboxylate to give azepine **6**.

Benzocyclobutene and related compounds, including hetero-analogues, represent a unique compromise between the thermodynamic stability associated with an aromatic system and the kinetic reactivity of a strained cyclobutene.<sup>1</sup> Although 3-thiabicyclo[3.2.0]hepta-1,4-diene and its derivatives are relatively well known,<sup>2,3</sup> the only example of the corresponding aza-analogue has been reported by Garratt and Neoh who have synthesized 6,7-di-*tert*-butyl-3-thiabicyclo[3.2.0]hepta-1,4-diene and its pyrrole and furan analogues by the base-catalyzed rearrangement of the corresponding 4-heterohepta-1,6-dienes.<sup>4</sup>

We now report the first synthesis of the title compound that has no substituent in the cyclobutene moiety along with its novel reaction with dimethyl acetylenedicarboxylate (DMAD).

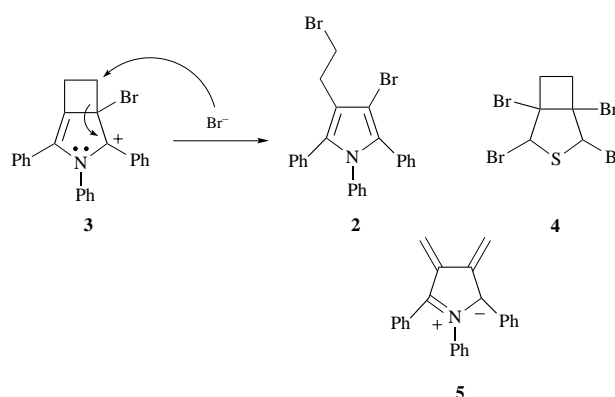
The title compound **1** was prepared by 1,3-dipolar cycloaddition of 1,2,3-triphenylaziridine with dimethyl cyclobutene-1,2-dicarboxylate,<sup>5</sup> followed by hydrolysis<sup>6</sup> and oxidative decarboxylation with lead tetraacetate<sup>7</sup> (Scheme 1). The



**Scheme 1** Reagents and conditions: i, DMSO-H<sub>2</sub>O, KOH, 80 °C, 95%; ii, Pb(OAc)<sub>4</sub>, pyridine, 70 °C, 40–55%

method is well documented for the synthesis of benzocyclobutene and related compounds.<sup>1</sup> However, this method was not, in our hands, amenable to similar adducts<sup>5</sup> from aziridines such as 1-benzyl-2,3-diphenylaziridine and 1-cyclohexyl-2-arylaziridines.

The  $J_{C-H}$  coupling constant in the cyclobutene moiety was 140 Hz. This value is comparable to those of the parent cyclobutene (140 Hz),<sup>8</sup> benzocyclobutene (138 Hz)<sup>9</sup> and the heteroanalogues (137–140 Hz).<sup>2c</sup> The bicycloheptadiene **1** readily reacted with bromine to produce the ring opened product **2** in quantitative yield, probably *via* the carbocation **3** stabilized by the nitrogen atom and phenyl group. In contrast, 3-thiabicyclo[3.2.0]hepta-1,4-diene is reported to add to bromine to give the tetrabromide **4**<sup>2b</sup> (Scheme 2). Next the reaction with DMAD was performed since we hoped that compound **1** would serve either as a diene or as an azomethine ylide as shown in structure **5**. Thus, reaction of **1** with 1 equiv. of DMAD in refluxing 1,2-dichlorobenzene for 3 h afforded the 1:1 adduct as orange needles in 54% yield. An inspection of the <sup>1</sup>H and <sup>13</sup>C NMR spectra confirmed the product retained the cyclobutene



**Scheme 2**

ring which, however, was now unsymmetrically substituted. A preliminary X-ray analysis of this compound established that it had structure **6** which is consistent with the NMR data (Fig. 1). Photochemical<sup>10a</sup> and thermal<sup>10b</sup> formation of analogous but isomeric diester azepines have been reported from pyrrole and DMAD, and from the 3-azaquadricyclane system, respectively. No thermal formation of an azepine from pyrroles has been reported,<sup>11,12</sup> although 1-methylindole with DMAD does give an azepine.<sup>13</sup> A possible mechanism for the formation of **6** is shown in Scheme 3. Either an intramolecular 1,3-shift of **7** to the bicyclic aziridine **8** or a 1,2-shift of **7** to the dihydroazete **9** is thermally symmetry-disallowed.<sup>14</sup>

Further studies on the synthesis and properties of similar 3-azabicyclo[3.2.0]hepta-1,4-dienes are in progress using non-stabilized azomethine ylides.<sup>15</sup>

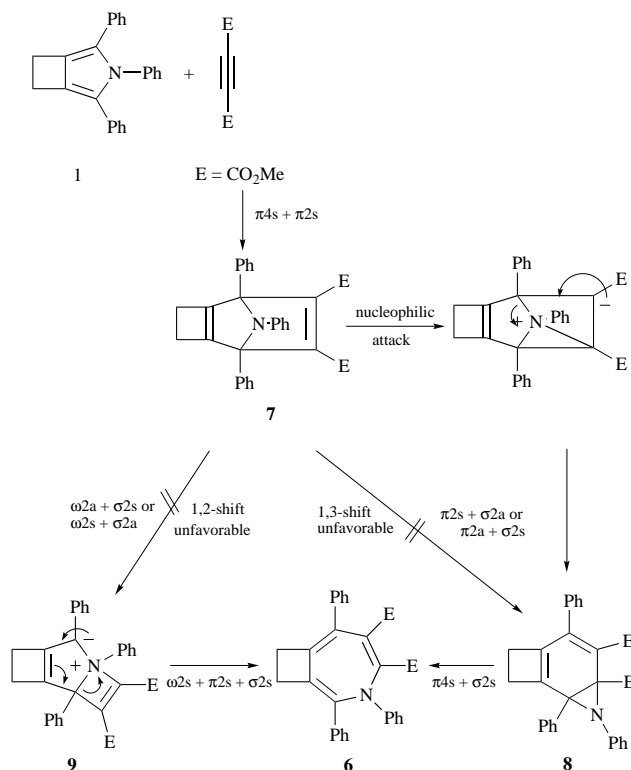
## Experimental

### Preparation of 2,3,4-triphenyl-3-azabicyclo[3.2.0]hepta-1,4-diene **1**

To a solution of *trans*-2,3,4-triphenyl-3-azabicyclo[3.2.0]heptane-1,5-dicarboxylic acid (0.12 mmol) in dry pyridine (2 cm<sup>3</sup>) under argon, lead tetraacetate (0.25 mmol) was added portionwise with stirring. The mixture was heated to 70 °C for 3 h. After evaporation of the solvent under vacuum, the residue was chromatographed on alumina eluting with benzene, giving **1** as a white powder in 55% yield; mp 218.0–219.0 °C;  $\delta_H$  (270 MHz, CDCl<sub>3</sub>) 3.41 (s, 4H), 6.92–7.32 (m, 15H);  $\delta_C$  (67.8 MHz, CDCl<sub>3</sub>) 27.50, 125.45, 126.42, 127.41, 127.78, 127.92, 128.92, 129.55, 132.54, 140.22 (Found: C, 89.7; H, 5.9; N, 4.3. C<sub>24</sub>H<sub>19</sub>N requires C, 89.7; H, 6.0; N, 4.4%).

### Reaction of **1** with bromine

To a stirred solution of **1** (0.1 mmol) in chloroform (2.5 cm<sup>3</sup>) was added dropwise a solution of bromine (0.1 cm<sup>3</sup>) in



Scheme 3

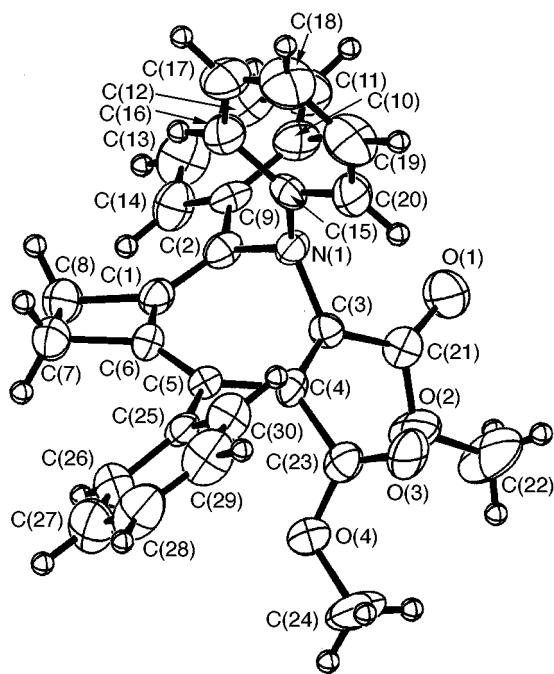


Fig. 1 ORTEP Drawing of **6**

chloroform (1 cm<sup>3</sup>). Evaporation of the solvent gave 3-(2-bromoethyl)-4-bromo-1,2,5-triphenylpyrrole **2** as a white powder in quantitative yield; mp 196.0–197.0 °C (decomp.);  $\delta_{\text{H}}$  (270 MHz, CDCl<sub>3</sub>)  $\dagger$  3.11 (t, *J* 7.8, 2H, ArCH<sub>2</sub>), 3.54 (t, *J* 7.8, 2H, BrCH<sub>2</sub>), 6.84–7.25 (m, 15H, aromatic);  $\delta_{\text{C}}$  (67.8 MHz, CDCl<sub>3</sub>) 30.01 (CH<sub>2</sub>), 31.57 (CH<sub>2</sub>), 99.66, 118.99, 127.04, 127.30, 127.53, 127.75, 128.07, 128.41, 128.61, 130.64, 130.89, 131.41, 132.74, 138.20 (Found: C, 60.0; H, 4.0; N, 2.9. C<sub>24</sub>H<sub>19</sub>NBr<sub>2</sub> requires C, 59.6; H, 4.1; N, 2.8%)

#### Reaction of **1** with DMAD

A solution of **1** (0.11 mmol, 0.034 g) and DMAD (1 mmol, 0.12

$\dagger$  *J* values are given in Hz.

cm<sup>3</sup>) in 1,2-dichlorobenzene (3 cm<sup>3</sup>) was refluxed under argon for 3 h. After evaporation of solvent, the residue was chromatographed on silica gel using hexane–ethyl acetate as eluent to give the product which was recrystallized from ethanol giving pure **6** (0.027 g, 54%); mp 258.3–263.0 °C (decomp.);  $\delta_{\text{H}}$  (270 MHz, CDCl<sub>3</sub>) 2.97–3.41 (m, 4H), 3.55 (s, CH<sub>3</sub>), 3.71 (s, CH<sub>3</sub>), 6.75–7.87 (m, 15H);  $\delta_{\text{C}}$  (67.8 MHz, CDCl<sub>3</sub>) 29.22 (CH<sub>2</sub>), 29.47 (CH<sub>2</sub>), 52.31 (OCH<sub>3</sub>), 52.42 (OCH<sub>3</sub>), 112.71, 119.01, 119.68, 127.64, 128.05, 128.27, 128.39, 128.63, 128.68, 129.18, 132.29, 134.20, 134.63, 135.98, 142.05, 145.23, 146.51, 151.11, 165.25 (C=O), 167.30 (C=O) (Found: C, 69.9; H, 7.2; N, 4.0. C<sub>30</sub>H<sub>25</sub>NO<sub>4</sub> requires C, 70.0; H, 7.3; N, 4.1%).

#### Crystal structure determination for compound **6**

Unfortunately, we could not obtain a good quality crystal that allowed us to determine the unit cell precisely.

Data were collected at *T* = 21 °C on a Rigaku AFC5S diffractometer; C<sub>30</sub>H<sub>25</sub>NO<sub>4</sub>, *M* = 463.53, red needles, dimensions 0.08 × 0.18 × 0.66 mm, monoclinic, space group = *P*2<sub>1</sub>/*a*, *a* = 8.82(7), *b* = 36.41(1), *c* = 8.44(3) Å,  $\beta$  = 114.5(3)°, *U* = 2464(20) Å<sup>3</sup>, *Z* = 4, *D*<sub>c</sub> = 1.249 g cm<sup>-3</sup>, *F*(000) = 976. Mo-K $\alpha$  radiation ( $\lambda$  = 0.710 69 Å)  $\mu$  = 0.077 mm<sup>-1</sup>,  $\omega$  scan mode with  $\omega$  scan width = 0.92 + 0.30 tan  $\theta$ ,  $\omega$  scan speed 32.0 deg min<sup>-1</sup>, 6115 reflections were collected in the range 6.0 < 2 $\theta$  < 55.0 and 5767 unique reflections (*R*<sub>int</sub> = 0.060) were used in the refinement. Twenty-four reflections were used for unit cell determination. The structure was solved by direct methods<sup>16</sup> using full-matrix least squares on *F* for all non-hydrogen atoms using Lorentz polarization and absorption corrections to give *R* = 0.075, and *R*<sub>w</sub> = 0.079 for 1789 independent observed reflections with *I* > 2.00 $\sigma$ (*I*) and 316 variables for 2 $\theta$ <sub>max</sub> = 55.0°. The final difference map maxima and minima were 0.28 and -0.29 e Å<sup>-3</sup>, respectively. The atomic scattering factors for all atoms and the anomalous dispersion correction factors for atoms other than hydrogen were taken from the literature.<sup>17–19</sup> All calculations were performed using TEXSAN<sup>20</sup> crystallographic software package of the Molecular Structure Corporation. Atomic coordinates, bond lengths, bond angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Instructions for Authors, *J. Chem. Soc., Perkin Trans. 1*, 1997, Issue 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 207/142.

#### Acknowledgements

This work was supported in part by a Grant-in-Aid for Scientific Research (No. 08221214) from the Ministry of Education, Science, Sports and Culture, Japan.

#### References

- R. P. Thummel, *Acc. Chem. Res.*, 1980, **13**, 70; B. Halton, *Chem. Rev.*, 1973, **73**, 113.
- (a) P. J. Garratt and K. P. C. Vollhardt, *J. Am. Chem. Soc.*, 1972, **94**, 1022; 7087; (b) P. J. Garratt and D. N. Nicolaidis, *J. Org. Chem.*, 1974, **39**, 2222; (c) P. J. Garratt and S. B. Neoh, *J. Org. Chem.*, 1975, **40**, 970.
- B. E. Ayres, S. W. Longworth and J. F. W. McOmie, *Tetrahedron*, 1975, **31**, 1755; K. P. C. Vollhardt and R. G. Bergman, *J. Am. Chem. Soc.*, 1972, **94**, 8950; 1973, **95**, 7538; R. G. Bergman and K. P. C. Vollhardt, *J. Chem. Soc., Chem. Commun.*, 1973, 214; H. Hauptmann, *Tetrahedron Lett.*, 1974, 3589; M. P. Cava, M. V. Lakshminathan and M. Behforouz, *J. Org. Chem.*, 1974, **39**, 206; P. Vogel and M. Hardy, *Helv. Chim. Acta*, 1974, **57**, 196.
- P. J. Garratt and S. B. Neoh, *J. Am. Chem. Soc.*, 1975, **97**, 3255; *J. Org. Chem.*, 1979, **44**, 2667.
- K. Matsumoto, H. Iida, T. Uchida, Y. Yabe, A. Kakehi and J. W. Lown, *Can. J. Chem.*, 1994, **72**, 2108.
- K. Matsumoto, Y. Kono and T. Uchida, *J. Org. Chem.*, 1977, **42**, 1103.
- R. P. Thummel, *J. Chem. Soc., Chem. Commun.*, 1974, 899.

- 8 S. Borcic and J. D. Roberts, *J. Am. Chem. Soc.*, 1965, **87**, 1056; E. A. Hill and J. D. Roberts, *J. Am. Chem. Soc.*, 1967, **89**, 2047.
- 9 G. Freankel, Y. Asahi, M. J. Mitchel and M. P. Cava, *Tetrahedron*, 1964, **20**, 1179; H. Hart, J. A. Hartlarger, R. W. Fish and R. R. Rafos, *J. Org. Chem.*, 1966, **31**, 2244.
- 10 (a) R. P. Gandhi and V. K. Chadha, *Indian J. Chem.*, 1971, **9**, 305; (b) H. Prinzbach, R. Fuchs and R. Kitzing, *Angew. Chem., Int. Ed. Engl.*, 1968, **7**, 67.
- 11 R. A. Jones and G. P. Bean, *The Chemistry of Pyrroles*, Academic, London, 1977, ch. 6.
- 12 R. M. Acheson, *Adv. Heterocycl. Chem.*, 1965, **1**, 125; R. M. Acheson and N. F. Elmore, *Adv. Heterocycl. Chem.*, 1978, **23**, 263.
- 13 R. M. Acheson, J. Bridson and T. S. Cameron, *J. Chem. Soc., Perkin Trans. 1*, 1972, 968.
- 14 R. B. Woodward and R. Hoffmann, *The Conservation of Orbital Symmetry*, Academic, New York, 1969.
- 15 O. Tsuge and S. Kanemasa, *Adv. Heterocycl. Chem.*, 1989, **45**, 231.
- 16 MITHRIL: C. J. Gilmore, *J. Appl. Cryst.*, 1984, **17**, 42; DIRDIF: P. T. Beurskens, Technical Report 1984/1, Crystallography Laboratory, Toernooiveld, 6525 Ed Nijmegen, Netherlands.
- 17 D. T. Cromer and J. T. Weber, *International Tables for X-ray Crystallography*, vol. IV, The Kynoch Press, Birmingham, UK, 1974, Table 2.2A.
- 18 J. A. Ibers and W. C. Hamilton, *Acta Crystallogr.*, 1964, **17**, 781.
- 19 D. T. Cromer, *International Tables for X-ray Crystallography*, vol. IV, The Kynoch Press, Birmingham, UK, 1974, Table 2.3.1.
- 20 TEXRAY Structure Analysis Package, Molecular Structure Corporation, 1985.

*Paper 7/04090C*  
*Received 11th June 1997*  
*Accepted 17th July 1997*