Tandem 1,3-dipolar cycloadditions of münchnones. Syntheses and molecular structures of 10-azatetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecanes and azahomopentaprismane

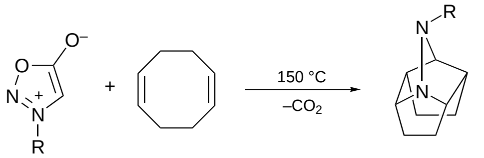
Gordon W. Gribble,*[a] William R. Sponholtz III,[a] Frank L. Switzer,[a] Ferdinando J. D'Amato[a] and Marianne P. Byrn[b]

[a] *Department of Chemistry, Dartmouth College, Hanover, NH 03755-3564, USA*
[b] *Department of Chemistry and Biochemistry, The J. D. McCullough X-ray Crystallography Laboratory, University of California, Los Angeles, CA 90095-1569, USA*

Photocyclization of 10-benzyl-9,11-diphenyl-10-azatetracyclo[6.3.0.0^{4,11}.0^{5,9}]undeca-2,6-diene 11, prepared in one step from münchnone 7 and cycloocta-1,3,5,7-tetraene 10, gives azahomopentaprismane 12.

Although the prismanes and other polycyclic cage compounds are well known and continue to be of great interest,[1] only a few examples of azapolycyclic cage hydrocarbons have been prepared.[2] In continuation of our interest in azapolycyclic compounds[3] we report the first synthesis of an azahomopentaprismane, namely 4-benzyl-3,5-diphenyl-4-azahexacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]undecane **12**.

Our approach to this ring system for a projected conversion to pentaprismane[4] was inspired by the remarkable reaction that Weintraub reported in 1970.[5] Thus, mesoionic sydnones **1** undergo a tandem 1,3-dipolar cycloaddition reaction with cycloocta-1,5-diene **2** to give the novel 9,10-diazatetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecanes **3**.[5,6]



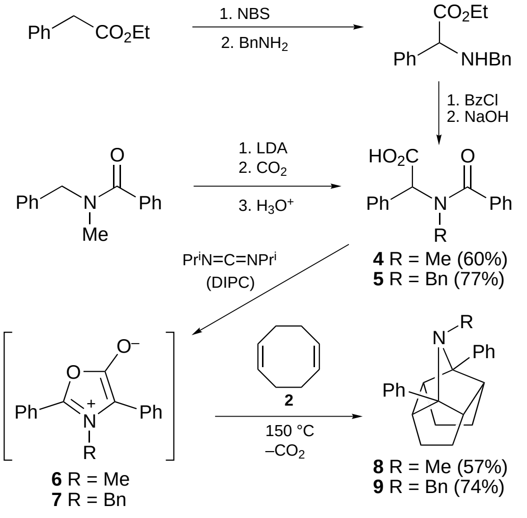
1 **2**

R = Bn, Ph, Me, 4-MeOC$_6$H$_4$, Bu^t

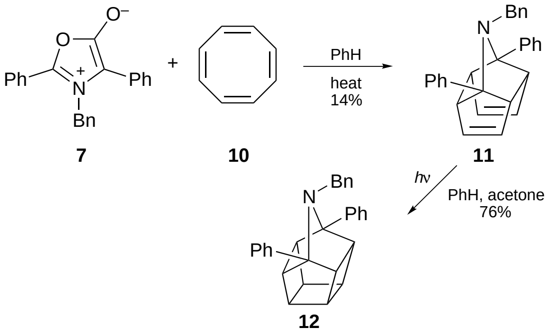
We have now found that the mesoionic münchnones (1,3-oxazolium-5-olates) react similarly with **2** to afford 9,11-diphenyl-10-azatetracyclo[6.3.0.0^{4,11}.0^{5,9}]undecanes **8**–**9** as shown in Scheme 1. The münchnone precursor amino acids **4** and **5** were synthesized according to classical methods[6,7] and the münchnones **6** and **7** (3-methyl- and 3-benzyl-2,4-diphenyloxazolium-5-olate, respectively) were generated using the original method of Huisgen[8] as modified by Anderson,[9] but using diisopropylcarbodiimide to effect cyclodehydration. Although münchnones **6** and **7** could be isolated as yellow solids, it was found that the yields of **8** and **9** were higher if **6** and **7** were generated and trapped with cycloocta-1,5-diene (COD) **2** *in situ*. The resulting azatetracycles **8**† (oil) and **9**† (mp 167–168 °C) have been fully characterized including an X-ray crystal structure for **9**.[10] As we have recently reported, **8** and **9** exhibit not only the expected restricted nitrogen inversion ($\Delta G^\ddagger$ = 12.2 and 10.6 kcal mol^{-1}, respectively, 1 cal = 4.184 J), but they also display remarkably slow bridgehead phenyl rotation ($\Delta G^\ddagger$ = 9.8 kcal mol^{-1}).[10]

In an obvious extension of this tandem 1,3-dipolar cycloaddition reaction, we now report that münchnone **7** reacts with cycloocta-1,3,5,7-tetraene (cot) **10** to afford cycloadduct **11** (10-benzyl-9,11-diphenyl-10-azatetracyclo[6.3.0.0^{4,11}.0^{5,9}]-undeca-2,6-diene) in low yield (Scheme 2). The X-ray crystallographic molecular structure of **11**‡ is shown in Fig. 1. This product represents one of the very few bis-cycloadducts of cot.[11]

Photolysis of **11** (350 W Hanovia medium pressure lamp, pyrex filter, benzene–acetone, 5 : 1, 4 h, room temperature) was followed by NMR spectroscopy and yielded the desired azahomopentaprismane **12**† (4-benzyl-3,5-diphenyl-4-azahexacyclo[5.4.0.0^{2,6}.0^{3,10}.0^{5,9}.0^{8,11}]undecane) in good yield. It is interesting to note that a similar photolysis of the oxygen analogue of **11** failed to yield oxahomopentaprismane.[12] The X-ray crystallographic molecular structure of **12** is shown in Fig. 2. This compound represents the first example of this ring system and attempts to convert **12** to the corresponding diphenylpentaprismane are in progress.



Scheme 1



Scheme 2

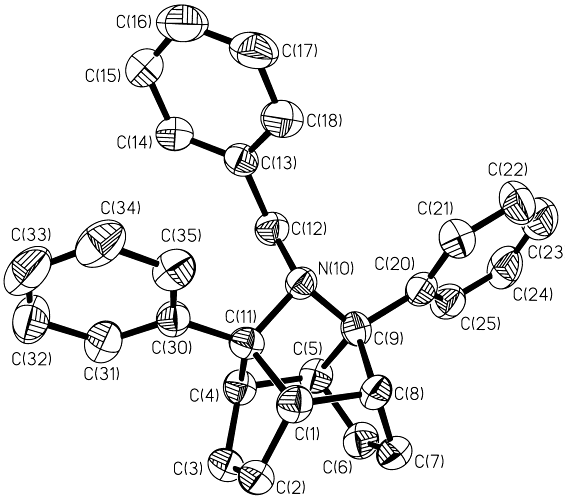


Fig. 1 ORTEP view of the molecular structure of **11**. The hydrogens have been omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level. Selected bond distances (Å) and angles (°) for **11**: C(1)–C(8) 1.607(7), C(4)–C(5) 1.595(7), C(1)–C(2) 1.505(7), C(3)–C(4) 1.520(7), C(1)–C(11) 1.564(6), C(4)–C(11) 1.578(7), C(2)–C(3) 1.323(8), C(6)–C(7) 1.320(8), C(9)–N(10) 1.459(6), C(12)–N(10) 1.464(6), C(9)–C(20) 1.507(6), C(9)–N(10)–C(11) 97.2(3).

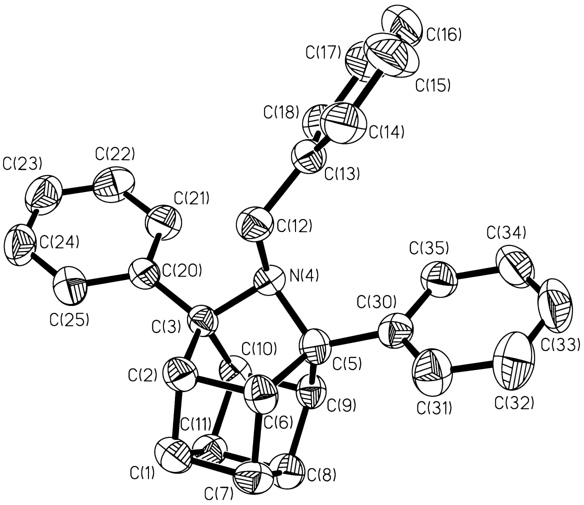


Fig. 2 ORTEP view of the molecular structure of **12**. The hydrogens have been omitted for clarity. Thermal ellipsoids are drawn at the 50% probability level. Selected bond distances (Å) and angles (°) for **12**: C(2)–C(6) 1.547(7), C(9)–C(10) 1.555(7), C(6)–C(7) 1.555(7), C(8)–C(9) 1.550(7), C(6)–C(7) 1.567(8), C(5)–C(9) 1.550(7), C(7)–C(8) 1.562(9), C(1)–C(11) 1.560(9), C(1)–C(7) 1.560(8), C(8)–C(11) 1.568(7), C(3)–N(4) 1.485(6), C(12)–N(4) 1.470(7), C(3)–C(20) 1.512(7), C(3)–N(4)–C(5) 97.0(4).

We thank the donors of the Petroleum Research Fund administered by the American Chemical Society for support of this project and for a summer faculty fellowship to F. L. S., and the National Science Foundation Research Experiences for Undergraduates Program for a fellowship to F. J. D. We also thank Professors David Lemal and David Glueck of this department for their assistance with the photolysis experiments and useful discussions, and Professor Michael Walters for the use of his laboratory.

Footnotes

* E-mail: grib@dartmouth.edu

† *Selected physical and spectroscopic data* for **8**: oil; δ_H (300 MHz, CDCl$_3$) 7.56 (m, 4 H), 7.38 (m, 4 H), 7.28 (m, 2 H), 2.71 (s, 4 H), 1.80 (m, 4 H), 1.69 (s, 3 H) and 1.62 (m, 4 H); δ_C (CDCl$_3$) 140.0, 128.1, 128.0, 126.9, 83.5, 33.3 and 23.0; *m/z* 315, 286, 246 and 172; HRMS calc. for M$^+$ 315.1987, found 315.1989. For **9**: mp 167–168 °C; δ_H (300 MHz, CDCl$_3$) 7.50 (m, 4 H), 7.15 (m, 7 H), 6.84 (m, 2 H), 6.57 (m, 2 H), 3.20 (s, 2 H), 2.74 (s, 4 H) and 1.64 (m, 4 H); δ_C (CDCl$_3$) 141.8, 139.9, 128.6, 128.2, 127.7, 126.9, 126.8, 125.0, 83.9, 50.5, 47.3 and 23.1; *m/z* 391, 301 and 91; anal. calc. for $C_{29}H_{29}N$: C, 88.96; H, 7.47; N, 3.58. Found: C, 88.84; H, 7.44; N, 3.54%. For **11**: mp 190 °C; δ_H (300 MHz, CDCl$_3$) 7.4 (dd, 4 H, *J* 6.6 and 1 Hz), 7.1 (m, 6 H), 6.9 (m, 3 H), 6.7 (m, 2 H), 5.9 (s, 4 H), 3.2 (s, 2 H) and 3.1 (s, 4 H); δ_C (CDCl$_3$) 141.2 (2), 134.6. 129.1, 128.7, 127.7, 127.2, 126.9, 125.6, 97.3, 54.7 and 49.7; HRMS calc. for M$^+$ 387.1987, found 387.1990. For **12**: mp 201 °C; δ_H (300 MHz, CDCl$_3$) 7.3 (dd, 4 H, *J* 7.0 and 1 Hz), 7.15 (m, 6 H), 6.95 (m, 3 H), 6.9 (m, 2 H), 3.55 (s, 4 H), 3.36 (s, 2 H) and 3.3 (s, 4 H); δ_C (CDCl$_3$) 141.7, 141.0, 128.9, 128.1, 128.0, 127.4, 126.6, 125.6, 90.8, 77.4, 53.3 and 41.7; *m/z* 388, 322, 309, 246, 233, 218 and 91; HRMS calc. for M$^+$ 387.1987, found 387.1992.

‡ *Crystal data* for **11**: The compound crystallized from acetone as colourless needles in the tetragonal system $P\bar{4}$. Unit cell dimensions are as follows: $a = b = 18.44(4)$, $c = 6.13(1)$ Å, $V = 2086(7)$ Å^3, $Z = 4$. The crystal was examined on a Syntex (Crystal Logic) diffractometer, Cu-Kα radiation, at 298 K. Total data collected = 1715 and 1326 with $I > 3\sigma(I)$. Full-matrix least-squares refinement based on F of 275 parameters has an agreement value, R, of 0.046 and a weighted R of 0.054. The error of fit is 1.715 and the maximum residual density is 0.69 e Å^{-3}. For **12**: The compound crystallized from acetone as colourless needles in the tetragonal system $P\bar{4}$. Unit cell dimensions are as follows: $a = b = 18.399(8)$, $c = 6.038(3)$ Å, $V = 2044(2)$ Å^3, $Z = 4$. The crystal was examined on a Syntex (Crystal Logic) diffractometer, Cu-Kα radiation, at 298 K. Total data collected = 1678 and 1104 with $I > 3\sigma(I)$. Full-matrix least-squares refinement based on F of 271 parameters has an agreement value, R, of 0.044 and a weighted R of 0.048. The error of fit is 1.405 and the maximum residual density is 0.32 e Å^{-3}. Atomic coordinates, bond lengths and angles, and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). See Information for Authors, Issue No. 1. Any request to the CCDC for this material should quote the full literature citation and the reference number 182/444.

References

1 A. P. Marchand, *Chem. Rev.*, 1989, **89**, 1011; T.-C. Chou, Y.-L. Yeh and G.-H. Lin, *Tetrahedron Lett.*, 1996, **37**, 8779; T. D. Golobish and W. P. Dailey, *Tetrahedron Lett.*, 1996, **37**, 3239.
2 S. L. Sacks, J. R. Scheffer, C.-Z. Teh and A. Tse, *J. Med. Chem.*, 1985, **28**, 819; D. P. Becker, R. Nosal, D. L. Zabrowski and D. L. Flynn, *Tetrahedron*, 1997, **53**, 1.
3 G. W. Gribble and B. H. Hirth, *J. Heterocycl. Chem.*, 1996, **33**, 719; G. W. Gribble, F. L. Switzer, J. H. Bushweller, J. G. Jewett, J. H. Brown, J. L. Dion, C. H. Bushweller, M. P. Byrn and C. E. Strouse, *J. Org. Chem.*, 1996, **61**, 4319; C. H. Bushweller, J. H. Brown, C. M. DiMeglio, G. W. Gribble, J. T. Eaton, C. S. LeHoullier and E. R. Olson, *J. Org. Chem.*, 1995, **60**, 268; G. W. Gribble, N. R. Easton, Jr. and J. T. Eaton, *Tetrahedron Lett.*, 1970, 1075.
4 For the synthesis of pentaprismane, see P. E. Eaton, Y. S. Or and S. J. Branca, *J. Am. Chem. Soc.*, 1981, **103**, 2134; P. E. Eaton, Y. S. Or, S. J. Branca and B. K. R. Shankar, *Tetrahedron*, 1986, **42**, 1621; W. G. Dauben and A. F. Cunningham, Jr., *J. Org. Chem.*, 1983, **48**, 2842.
5 P. M. Weintraub, *J. Chem. Soc., Chem. Commun.*, 1970, 760.
6 For a recent study of this reaction, see G. W. Gribble and B. H. Hirth, *J. Heterocycl. Chem.*, 1996, **33**, 719.
7 R. R. Fraser, G. Boussard, I. D. Postescu, J. J. Whiting and Y. Y. Wigfield, *Can. J. Chem.*, 1973, **51**, 1109.
8 R. Huisgen, H. Gotthardt, H. O. Bayer and F. C. Schaefer, *Chem. Ber.*, 1970, **103**, 2611.
9 W. K. Anderson and A. R. Heider, *Synth. Commun.*, 1986, **16**, 357.
10 G. W. Gribble, F. L. Switzer, J. H. Bushweller, J. G. Jewett, J. H. Brown, J. L. Dion, C. H. Bushweller, M. P. Byrn and C. E. Strouse, *J. Org. Chem.*, 1996, **61**, 4319.
11 K. Saito, Y. Omura, E. Maekawa and P. G. Gassman, *Bull. Chem. Soc. Jpn.*, 1990, **63**, 395.
12 A. P. Marchand, T.-C. Chou, J. D. Ekstrand and D. van der Helm, *J. Org. Chem.*, 1976, **41**, 1438.

Received in Corvallis, OR, USA, 5th February 1997; Com. 7/00857K