Novel Synthesis of [2.2.2](1,2,4)Cyclophane

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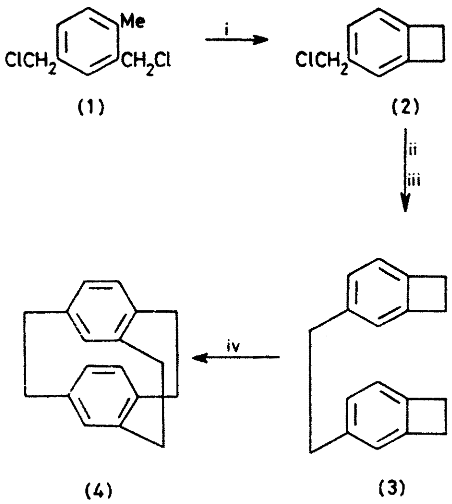
Summary The synthesis of multibridged cyclophanes, a novel application of benzocyclobutenes as intermediates, is illustrated by the thermal bond reorganization of 1,2-bis(1,2-dihydrobenzocyclobuten-4-yl)ethane (**3**) to give [2.2.2](1,2,4)cyclophane (**4**).

RECENTLY, we discovered that the pyrolysis of 2-chloromethyltoluenes is a convenient and easy method for synthesizing benzocyclobutenes.[1,2] Although benzocyclobutenes have received much attention as intermediates in the synthesis of natural products,[3] our interest in them stemmed from the observation of Cava that 5,6-dimethylenecyclohexa-1,3-diene undergoes thermal dimerization in solution to give dibenzo-cyclo-octadiene in 48% yield.[4] If this type of dimerization were in fact general, then appropriate molecules having two benzocyclobutene groups could readily yield multi-bridged cyclophanes. To test this hypothesis we have prepared 1,2-bis(1,2-dihydrobenzocyclobuten-4-yl)ethane (**3**) and studied its gas phase pyrolysis.

Although (**3**) has previously been prepared by trimerization of hexa-1,5-diyne,[5,6] we synthesized it using our pyrolytic method for making benzocyclobutenes. Pyrolysis of 2,4-bis(chloromethyl)toluene[7] (**1**) in the gas phase at 700 °C gave 4-chloromethylbenzocyclobutene (**2**) in 48% yield as a pale yellow oil: ^{1}H n.m.r., δ 3·13 (4H, s, ArCH_2), 4·52 (2H, s, –CH_2Cl), and 6·85—7·50 (3H, m, ArH); mass spectrum, M^+ m/e 152·040 (calc. 152·039). Treatment of (**2**) with magnesium in diethyl ether followed by a catalytic amount of iron(III) chloride readily gave (**3**) whose properties agreed with those previously recorded.[5] Pyrolysis of (**3**) in the gas phase in a flow system at 600 °C and 10^{-3} Torr followed by collection of the exit gases at −30 °C gave a white solid which, after purification by t.l.c. over silica gel with pentane as eluant, gave (**4**) in 12% yield as white crystals whose properties were identical with those reported for [2.2.2](1,2,4)cyclophane.[8]



i, 700 °C; ii, Mg, Et$_2$O; iii, FeCl$_3$; iv, 600 °C.

Thus, the dimerization of benzocyclobutenes appears to be a general reaction providing a novel method for constructing multibridged cyclophanes. Although it should be noted that the rules for conservation of orbital symmetry forbid a concerted 4 + 4 cycloaddition,[9] it is not obvious whether, in fact, the thermal bond reorganization of (**3**) to give (**4**) is a concerted or a stepwise process.

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[1] R. Gray, L. G. Harruff, J. Krymowski, J. Peterson, and V. Boekelheide, *J. Amer. Chem. Soc.*, 1978, **100**, 2892.

[2] By personal communication, Prof. P. Schiess has informed us that he also has explored the pyrolysis of 2-chloromethyltoluenes as a method of synthesis of benzocyclobutenes.

[3] W. Oppolzer, *Angew. Chem.*, 1978, **89**, 10; *Angew Chem. Internat. Edn.*, 1978, **16** 10; R. L. Funk and K. P. C. Vollhardt, *J. Amer. Chem. Soc.*, 1977, **99**, 5483; W. Oppolzer, M. Petrzilka, and K. Bättig, *Helv. Chim. Acta*, 1977, **60**, 2964; T. Kametani, H. Matsumoto, H. Nemoto, and K. Fukumoto, *J. Amer. Chem. Soc.*, 1978, **100**, 6218.

[4] M. P. Cava and A. A. Deana, *J. Amer. Chem. Soc.*, 1959, **81**, 4266.

[5] A. J. Hubert and J. Dale, *J. Chem. Soc.*, 1965, 3160.

[6] P. Perkins and K. P. C. Vollhardt, *Angew. Chem.*, 1978, **90**, 648; *Angew. Chem., Internat. Edn.* 1978, **17**, 615.

[7] G. Blanc, *Bull. Soc. chim. (France)*, 1923, **33** (4), 313.

[8] E. A. Truesdale and D. J. Cram, *J. Amer. Chem. Soc.*, 1973, **95**, 5825; S. Trampe, H. Hopf, and K. Menke, *Chem. Ber.*, 1977, **110**, 371. We thank Prof. Cram for providing the ^{1}H n.m.r. spectrum of an authentic specimen of [2.2.2](1,2,4)cyclophane, which our spectrum reproduced quite precisely, including the complicated fine structure in the region of δ 2·5—3·5.

[9] R. B. Woodward and R. Hoffmann, 'The Conservation of Orbital Symmetry,' Verlag Chemie, GmbH, Weinheim, Bergstr., West Germany, 1971.