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$[2_6](1,4)_3(1,3,5)_2$BICYCLOPHANEHEXAENE, A NEW CAGE CYCLOPHANE FROM A SIXFOLD WITTIG REACTION

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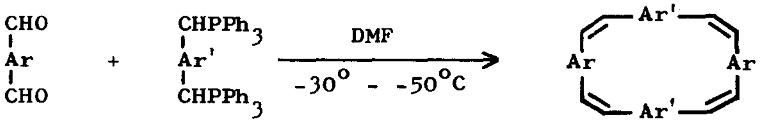
Cage compounds with a cavity large enough to accomodate simple ions or molecules have only recently become accessible. Such cage compounds with a flexible structure of the crown ether type are now available for the trapping of ions[1] and for e.g. the separation of enantiomers of amino acids.[2] In the synthetic approaches to cage compounds it is important to consider entropy factors and steric interactions in the intermediates and products. Both factors usually favour linear polymerizations over cyclizations.

We have recently prepared several $[2_4]$ cyclophanetetraenes containing four cis-double bonds via a one-step Wittig reaction (Scheme 1).[3-7] The yields of more than twenty different cyclophanes ranged from a few up to fifteen per cent. We have found that the stability of the ylid and to some extent the reactivity of the aldehyde influence the yields of the reactions. If suitable reactants are used and only minor steric interactions can be anticipated, it should be possible to prepare cage cyclophanes or bicyclophanes[8] via this method.

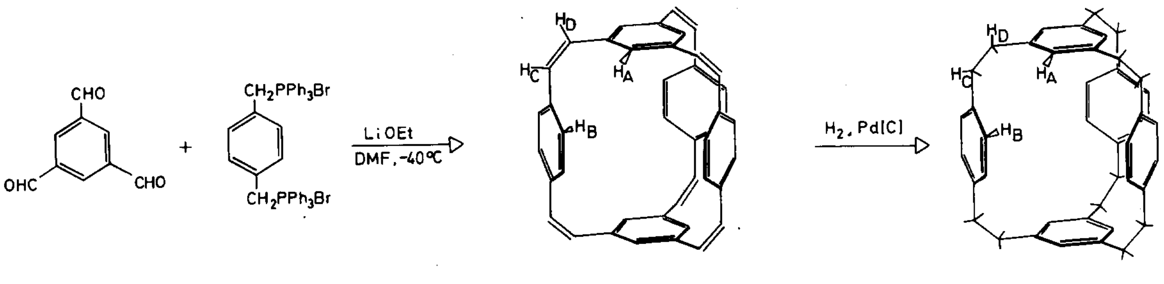


Dialdehyde: 1,2-, 1,3-, 1,4-benzenedicarbaldehyde, 2,5-thiophene-, 2,5-furandicarbaldehyde, 4,4'-biphenyl- or 4,4'-bibenzyldicarbaldehyde
Diphosphorane from the bisphosphonium salts of 1,2-, 1,3-, 1,4-bis-(halomethyl)benzene or 2,5-bis(chloromethyl)thiophene

SCHEME 1

We now report on the synthesis (Scheme 2) of the bicyclophane 1, $[2_6](1,4)_3(1,3,5)_2$bicyclophanehexaene^8 or heptacyclo $[12.12.8^{1,14}.2^{6,9}.2^{19,21}.2^{29,32}.1^{3,25}.1^{12,16}]$dotetraconta-1,3(41),4,6,8,10,12(42),13,15,17,19,21,23,25,27,29,31,33,35,37,39-heneicosaene.

1,3,5-Benzenetricarbaldehyde (16 mmol) and the bistriphenylphosphonium salt of 1,4-bis(bromomethyl)benzene (24 mmol) were stirred in dry dimethylformamide (500 ml) under nitrogen. Lithium ethoxide in abs. ethanol was slowly added at such a rate that the red ylid was consumed between successive additions. The reaction was complete after 3 h, and then the mixture was warmed to room temperature, diluted with water, and filtrated. The residue was triturated with warm ethanol, which dissolved the triphenylphosphineoxide, and chromatographed on silica gel. Tetrachloromethane eluted the bicyclophane 1 (72 mg, 1.7 %). Recrystallization from quinoline or sublimation (10^{-2} mm, 400 °C) gave white prisms which did not melt below 550 °C (under N_2, some dec.). (Found: C 94.1, H 5.7; $M^+ = 534.233 \pm 0.003$. Calc. for $C_{42}H_{30}$: C 94.4, H 5.5; $M^+ = 534.235$). IR(KBr): 570(m), 695(s), 725(w), 738(w), 803(m), 850(s), 910(s),



1 2

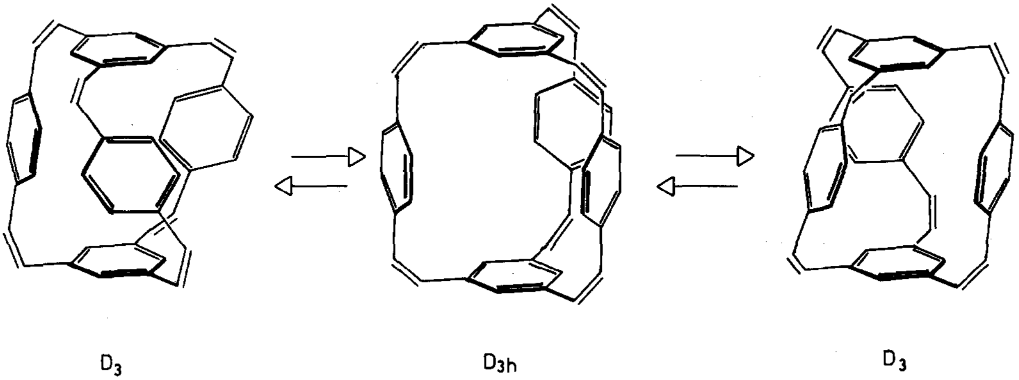
SCHEME 2

1325(w), 1504(w), 1576(w) and 3000(w) cm^{-1}. UV ($CHCl_3$) λ_{max}(log ε) : 257(4.35) sh and 288(4.33). ^{1}H-NMR (270 MHz, $CDCl_3$): δ = 7.08 (12H,s, H_B), 6.98 (6H,s,H_A), 6.65 and 6.42 ppm (6+6H, H_C and H_D, $\underline{J}_{CD}$=12 Hz). MS(70eV) $\underline{m}/\underline{e}$(rel. int.) : 534(100, M^+), 267(6, M^{2+}), 115(4) and 91(4).

The bicyclophane 1 was hydrogenated in dry benzene over palladium on charcoal to give a quantitative yield of $[2_6](1,4)_3(1,3,5)_2$bicyclophane, 2. M.p. 207-208 (acetic acid). (Found: C 91.9; H 7.7; M^+ 546.328 ± 0.003. Calc. for $C_{42}H_{42}$: C 92.2; H 7.8; M^+ 546.329). IR(KBr): 695(m), 708(s), 800(s), 820(s), 845(m), 1025(broad m), 1105(broad m), 1260(m), 1330(w), 1420(w), 1440(m), 1445(m), 1515(m), 1605(m), 2920(w), 2950(w), 2965(w) and 3005(w) cm^{-1}. UV (cyclohexane) λ_{max} (log ε) : 215(end abs), 262(2.02), 266(2.13) and 276(2.08). ^{1}H-NMR($CDCl_3$): δ = 6.65 (6H,s,H_A), 6.48 (12H,s,H_B) and 2.79 ppm

(24 H,s,H_C and H_D). MS (70eV) m/e(rel. int.) : 546(100,M^+), 455(8), 441(7), 233(13), 221(11), 219(22), 207(12), 205(18), 131(9), 119(21), 117(18), 105(28), 91(13) and metastables for m/e 546 → 455 and 546 → 441.

The bicyclophane 1 must be a highly symmetric molecule since the NMR spectrum shows signals due to only four different sets of protons. The singlet observed for the protons (H_B) of the p-substituted rings implies a somewhat flexible molecule. Inspection of models reveals that it should be chiral in the ground state (symmetry point group D_3) with the trisubstituted rings twisted relative to each other. The non-chiral conformation with identically oriented trisubstituted rings (point group D_{3h}) could be slightly higher in energy and then represent the barrier to inversion (Scheme 3) between the two enantiomeric D_3 conformations. Compound 1 is therefore not likely to be resolvable.



SCHEME 3

The saturated bicyclophane 2 is much more flexible than the unsaturated, 1, as judged from its lower melting point and higher solubility. The simple NMR spectrum of compound 2, with only one singlet for the methylene protons indicates that twisting around the single bonds is rapid at normal temperatures. Thus, the size of the cavity in the bicyclophane 2 can change appreciably, whereas it is more defined in compound 1.

A previous attempt to prepare cage cyclophanes of this type by a metal catalyzed cyclotrimerization of para-bis(but-3-ynyl)benzene has been reported. A bicyclophane, probably $[2_6](1,4)_3(1,2,4)_2$bicyclophane was isolated from a mixture containing other cyclophanes as well.[9] Other bicyclophanes with only two benzene rings have been prepared by the same method.[10] A highly strained $[2_3](1,3,5)_2$bicyclophanetriene and the saturated analogue have been prepared via Stevens rearrangements and Hofmann eliminations of an alkylated dithia $[3_3]$-$(1,3,5)_2$bicyclophane.[11] The present method should make it possible to prepare a variety of $[2_6]$ bicyclophanes. Such bicyclophanes may well show interesting properties as host molecules and if properly substituted as multidentate ligands.

Acknowledgement

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References and Notes

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