Tetrahedron Letters,Vol.27,No.36,pp 4331-4334,1986 0040-4039/86 $3.00 + .00
Printed in Great Britain Pergamon Journals Ltd.

SYNTHESIS OF [3.n.3.n]PARACYCLOPHANE DERIVATIVES BY CATIONIC CYCLIZATION OF STYRENE DERIVATIVES

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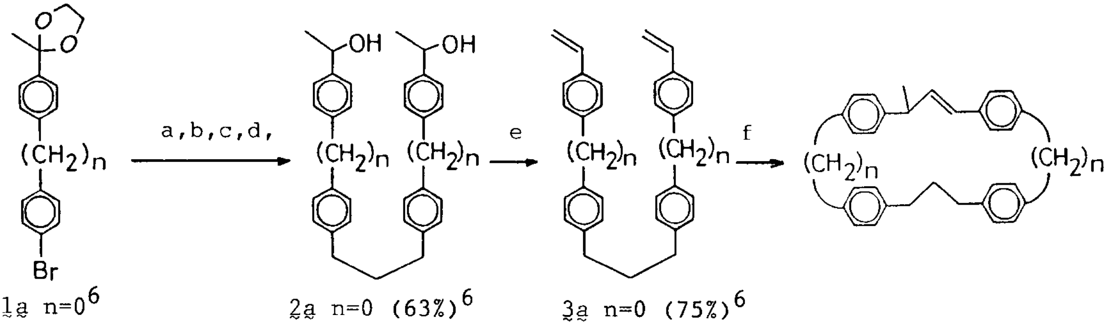
Styrene derivatives (3c and 3d) were treated in dry benzene at 50 °C with a catalytic amount of CF_3SO_3H to afford [3.n.3.n]paracyclophane derivatives (4c and 4d) in 80 and 62% yields, respectively.

Macrocyclic compounds are gathering much attention to their binding of molecules and ions. For instance, recently Tabushi and his coworkers revealed, in an elegant way, the binding of a molecule like methylene chloride in the cavity of a paracyclophane designed.[1] Those macrocyclic compounds were made by many synthetic methods including Wurtz reaction,[2] telomerization of xylylenes,[3] malonate synthesis,[4] and Wittig reaction.[5] Still new methods, however, are sought in order to make a variety of cyclophanes and to improve the relatively low product yields in the previous methods. In this communication, we would like to report a new facile cyclization of styrene derivatives to afford [3.n.3.n]paracyclophane derivatives.

Alcohols (2) were prepared by a Grignard coupling using HMPA-dissolved CuBr as a catalyst.[6] Yields after three steps are listed in eq (1). The alcohols were purified by column chromatography (SiO_2, benzene/cyclohexane) and dehydrated in DMSO by CCl_3COOH-$ZnCl_2$ at 170 °C to afford monomers (3) in reasonable yields.[7]

Monomers (3) depicted in eq (1), expect 3a,[6] did not give cyclocodimers by the usual cyclocodimerization procedure[8] but only linear cooligomers. On the



(1)

1a n=0[6]
1b n=1[6]
1c n=2[6]
1d n=3[6]

2a n=0 (63%)[6]
2b n=1 (21%)[9]
2c n=2 (81%)[6]
2d n=3 (76%)

3a n=0 (75%)[6]
3b n=1 (34%)[9]
3c n=2 (81%)[6]
3d n=3 (60%)

4c n=2 (80%)
4d n=3 (62%)

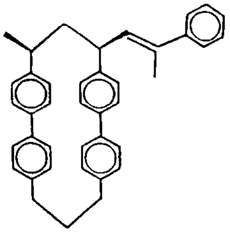
a) Mg, THF. b) Br-$(CH_2)_3$-Br, CuBr-HMPA, THF. c) H^+, DOX/H_2O. d) $LiAlH_4$, ether. e) CCl_3COOH-$ZnCl_2$, DMSO, 170 °C. f) CF_3SO_3H in dry benzene at 50 °C.

other hand, 3a gave cyclocodimers *cis*- and *trans*-1-methyl-3-(α-methylstyryl)-[3.3](4,4')biphenylophane 5 and 6 in 41% yield (5/6 ratio, 1.8) by the cyclocodimerization with 2-phenylpropene.[8,10] This is the first example of the synthesis of [3.3](4,4')biphenylophane skeleton so far as we have searched in literatures. The cis and trans isomers were isolated by a reversed phase HPLC (Cosmosil C-18, MeOH). Since ^{1}H NMR spectra of 5 and 6 showed up-fielded aromatic proton resonances in the range of δ6.6 to δ7.0 and their methyl resonances at δ1.28 and δ1.32, respectively, their structures were unequivocally determined in the same way as reported.[11]

Linear cations generated by the protonation of 3b, c, d and 7 readily reacted intermolecularly with a comonomer before cyclization, so that they were treated with CF_3SO_3H in the absence of comonomers.[12] Among the monomers examined, 3c and 3d gave desired paracyclophanes 4c and 4d in 80 and 62% yields, respectively, whereas others formed only oligomers even under the same cyclization conditions. The coupling constant between olefinic protons (16.3 and 17.0 Hz for 4c and 4d, respectively) and the out-of-plane deformation vibration of olefinic C-H bonds ($\nu_{C=C-H}$, 976 and 969 cm^{-1} for 4c and 4d, respectively) clearly show the *E*-configuration of their double bonds. Other isomers of 4c and 4d were not detected by either chromatographic or spectroscopic analysis.

On the basis of framework examination, two styryl groups in both 3b and 7 can not approach within a distance of ca. 0.3 nm[8] in a face-to-face manner, due to severe steric constraint. This means that intermediate styryl cations are not stabilized sufficiently by the intramolecular complexation[8] with a styrene moiety or electron donor, and this is the reason why both monomers did not afford any desired macrocyclic compounds, since their statistic cyclization seems to be sterically possible.

When 1,6-bis(*m*-vinylphenyl)hexane,[6] which did not undergo the cationic cyclocodimerization with a comonomer either, was treated under the same cationic cyclization conditions as above,[12] cis-cyclic olefin 8 (trace) and two isomeric indane derivatives (9 and 10 in 11 and 16% yields, respectively) were obtained as oily substances. The *Z*-configuration of the double bond incorporated in



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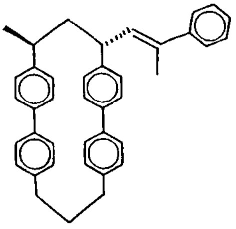

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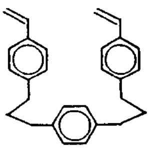
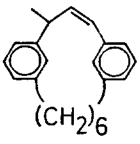


7[13]



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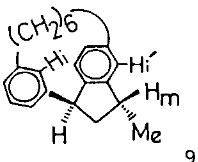
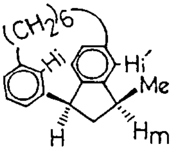


δ5.80(Hi)
7.17(Hi')
3.38(Hm)

9



δ5.88(Hi)
7.11(Hi')
3.42(Hm)

10

Table 1 Physical and Analytical Data

Compd	Mp, °C	MS(M+·, m/z) calcd(found)	^{1}H NMR chem. shift δ$^{a)}$ (integral, multiplicity, *J* in Hz)
3b	57 - 59	428.2506(428.2500)	-
3d	103 - 104	484.3132(484.3129)	-
4c	146 - 148	456.2819(456.2816)	1.41(3H, d, 7.8), 1.74(2H, m), 2.29(2H, m), 2.55(2H, t, 6.8), 2.90(8H, m), 3.53 (1H, quin, 6.4), 5.88(1H, d, 16.5), 6.16 (1H, dd, 16.3 & 6.1), 6.81(4H, AA'BB', 8.1), 6.85(4H, AA'BB', 8.1), 6.90(4H, AA'BB', 8.4), 6.94(4H, AA'BB', 8.4)
4d	124 - 125	484.3132(484.3122)	1.47(3H, d, 7.4), 1.76(6H, m), 2.55(12H, m), 3.55(1H, quin, 7.2), 6.02(1H, dd, 17.0 & 6.0), 6.21(1H, d, 17.0), 6.91(8H, s), 7.01(4H, AA'BB', 9.2), 7.08(4H, AA'BB', 8.8).
5	203 - 205	518.2973(518.2968)	1.28(3H, d, 8.0), 1.94(3H, s), 2.23(4H, m), 2.80(4H, t, 5.2), 2.85(1H, m), 3.65(1H, m), 5.99(1H, d, 10.4), 6.73 - 7.02(16H, m), 7.16 - 7.40(5H, m).
6	190 - 195	518.2973(518.2969)	1.32(3H, d, 8.0), 1.97(3H, s), 2.11(4H, m), 2.70(4H, t, 5.4), 3.09(1H, m), 3.91(1H, m), 6.12(1H, d, 9.4), 6.60 - 6.96(16H, m), 7.08 - 7.46(5H, m).
7	86 - 88	366.2349(366.2353)	-
8	oil	290.2036(290.2033)	1.21(4H, m), 1.36(3H, d, 7.8), 1.59(4H, m), 2.47(4H, m), 3.79(1H, m), 5.89(1H, dd, 11.4 & 11.2), 6.52(1H, d, 11.2), 6.77(1H, t, 1.4), 6.85(1H, t, 1.4), 6.97(1H, dt, 7.5 & 1.4), 7.02(2H, dt, 7.5 & 1.4), 7.12(1H, dt, 7.5 & 1.4), 7.23(2H, t, 7.5).
9	oil	290.2036(290.2032)	0.44(2H, m), 1.25(5H, m), 1.37(3H, d, 7.4), 1.75(1H, m), 2.12(1H, m), 2.35(2H, m), 2.57 (2H, m), 2.79(1H, m), 3.38(1H, m), 4.35(1H, d, 8.4), 5.80(1H, t, 1.2), 6.80(1H, dt, 6.8 & 1.2), 6.98(2H, AB*, 7.7), 7.08(1H, t, 1.2), 7.11(1H, d, 6.8), 7.17(1H, d, 1.2).
10	oil	290.2036(290.2033)	0.43(2H, quin, 8.7), 1.21(4H, m), 1.38(3H, d, 7.4), 1.72(3H, m), 2.57(4H, m), 3.01(1H, m), 3.42(1H, m), 4.37(1H, dd, 10.0 & 3.2), 5.88(1H, t, 1.5), 6.77(1H, d, 7.7), 6.78 (1H, d*, 5.5), 6.97(1H, d*, 7.7), 7.06(1H, d, 1.3), 7.08(1H, dd, 5.5 & 1.3), 7.11(1H, d, 1.4).

a) NMR spectra were taken by a Varian XL-200 NMR spectrometer in chloroform-d_1 with TMS as an internal standard. Asterisked peaks are broadened by fine coupling(s) which are neither measured nor estimated.

8 was assigned by the coupling constant 11.2 Hz. For the indane products **9** and **10**, the observed ^{1}H NMR spectra strongly suggest that their structures are as pictured, because only this pair of regioisomers **9** and **10** can explain the appearance of two isolated protons Hi and Hi' as a triplet and doublet, respectively, with fine coupling constants *J* = 1.4 - 1.5 Hz, and the fact that the Hm proton of **9** was shielded more than that of **10**. This cationic cyclization indicates that such a small membered cyclic cation derived from 1,6-bis(*m*-vinylphenyl)hexane readily attacks intramolecularly an electron-rich substituted benzene ring to afford an indane ring than directly deprotonates to afford a double bond. Obviously eclipsed transition state of E1 elimination for cis olefin is less favorable than anti-staggered transition state for trans one.

The results draw two important aspects of the cationic cyclization of those styrene derivatives. First, the stabilization due to the intramolecular face-to-face complexation between the styrene moiety and the styryl cation is essential. Second, if a desired product like **4c** and **4d** seems to accomodate a trans double bond easily in the three-carbon linkage, then the present cationic cyclization will proceed successfully just as observed in the case of **3c** and **3d**.

Support by a Grant-in-Aid for Special Project Research (No 60035037) from the Ministry of Education, Science and Culture is gratefully acknowledged.

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9 Yields were not optimized.

10 Reaction conditions: [**3a**] = 17 mM, [2-phenylpropene] = 118 mM, [CF_3SO_3H] = 0.17 mM, at 50 °C for 18 min in dry benzene.

11 In general, methyl and allylic protons of *cis*-1-methyl-3-styryl[3.3]paracyclophane resonate at higher fields than those of trans isomers. See ref. 8 for details.

12 Reaction conditions: [monomer **3**] = 3 mM, [CF_3SO_3H] = 0.13 mM, at 50 °C for 4 h in dry benzene.

13 This compound was made from the corresponding Grignard reagent and *p*-dichlorobenzene in the presence of $(dppe)_2NiCl_2$ by the method reported by K. Tamao, K. Sumitani, and M. Kumada, *J. Am. Chem. Soc.*, **94**, 4374 (1972), followed by deprotection, $LiAlH_4$ reduction (yield for 3 steps, 44%), and dehydration (yield, 20%). Yields were not optimized.

(Received in Japan 24 May 1986)