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The newly modified McMurry reaction toward the improved synthesis of cyclic paraphenylacetylenes

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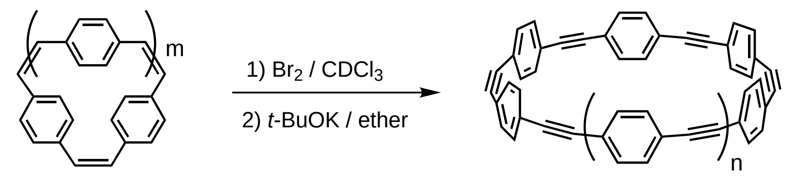
Abstract—Treatment of stilbenedialdehyde derivatives with low-valent titanium generated in a mixed solvent of DME and toluene favored reductive *cyclo*-oligomerization to give macrocyclic cyclophanepolyenes in relatively good yields leading to improved or new synthesis of a series of cyclic paraphenylacetylenes ([6] to [9]CPPAs). © 2001 Elsevier Science Ltd. All rights reserved.

Phenylacetylene macrocycles (PAMs) having well-defined shapes with rigid cavities are intriguing molecules from both physicochemical and supramolecular points of view.[1] In this context, we have recently reported the synthesis of two members of cyclic paraphenylacetylenes, [6]CPPA **1a** and [8]CPPA **1c**[2] (Scheme 1), and more recently found that [6]CPPA **1a** having a smooth belt-shaped structure with a 13.2 Å diameter forms inclusion complexes with fullerenes (C_{60} and C_{70}) and hexamethylbenzene.[3,4] To understand the novel supramolecular properties of CPPAs more deeply, development of practical synthesis of them has become an important problem of the study. We have prepared **1a** and **1c** from the corresponding cyclophanepolyenes **2a** and **2c**, which are usually mixtures of geometric isomers, through bromination–dehydrobromination in good yields.[2] However, the availability of the cyclophanepolyenes has been unsatisfactory, because the synthesis of them using the Wittig or McMurry reaction suffered from low yields and difficulty in purification.[5,6] Therefore, improvement of the synthesis of cyclophanepolyenes **2** was desired. Here we report an effective synthesis of **2a** and related compounds by a newly modified McMurry reaction,[7] which has led to the synthesis of previously unknown [7]- and [9]CPPAs, **1b** and **1d**. The properties of a series of [6]- to [9]CPPA thus obtained are also reported for comparison.

Wennerström and co-workers reported that treatment of 1,4-bis(4-formyl-(*Z*)-styryl)benzene (*Z*,*Z*)-**3** with low-valent titanium, generated from $TiCl_4$ and zinc in THF, afforded [2.2.2]paracyclophanetriene **2e** in 50% yield, but the formation of cyclic oligomers was not mentioned.[8] In order to improve the yield of cyclodimer **2a**, we investigated the McMurry reaction of **3** under several conditions (Scheme 2 and Table 1), and found that the use of a mixed solvent of DME/toluene (1:1) gives an isomeric mixture of **2a** in 53% yield with a small amount of **2e** (entry 5 in Table 1). Notably, the known isomer (*Z*,*Z*,*E*)[2]-**2a** was formed predominantly. Variation of the ratio between toluene and DME (2:1 to 1:9) resulted in little change of the yields (entries



2a (m = 4), **b** (m = 5), **c** (m = 6), **d** (m = 7)

1a (n = 1), **b** (n = 2), **c** (n = 3), **d** (n = 4)

Scheme 1.

Keywords: modified McMurry reaction; cyclodimerization; solvent effects; new cyclic paraphenylacetylenes.

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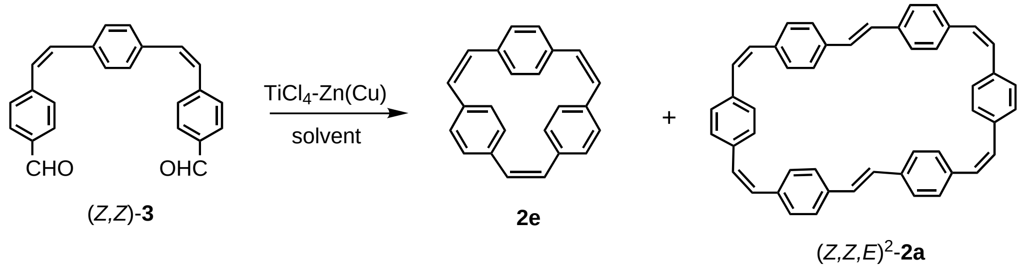


Scheme 2.

Table 1. Yields of **2a** and **2e** in various solvents[a]

Entry	Solvent	Yields (%)	
		2e	**2a**
1[b]	THF	50	–
2	DME	34	12
3	THF–toluene (1:1)	18	16
4	DME–toluene (9:1)	4	40
5	DME–toluene (1:1)	3	53
6	DME–toluene (1:2)	Trace	41

[a] *Conditions*: A suspension of $TiCl_4$–Zn in the solvent system was heated at reflux for 2 h, then a solution of the dialdehyde **3** in the solvent was added dropwise to the suspension over 30 min at rt, and the reaction mixture was stirred at rt for 12 h, then heated at reflux for 5 h.

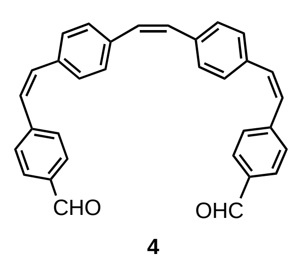
[b] Ref. 8.

4–6). The reaction in DME only or THF/toluene (1:1)[9] gave **2e** as a major product together with a stereoisomeric mixture of **2a** (entries 2 and 3). In toluene only, the reduction of $TiCl_4$ with Zn–Cu did not proceed smoothly. The McMurry couplings in ethereal solvents generally afford a mixture of geometric isomers probably due to isomerization through an electron transfer process.[7] Actually, **2a** was obtained as a messy mixture of the geometric isomers when the coupling was carried out in DME only. Therefore, *E*-selective double bond formation under the present modified McMurry reaction seems to play a key role for the cyclooligomerization. The strong solvent effects suggest that the reactive intermediate generated in DME/toluene would be different from those generated in solvents without toluene. Although the elucidation of the reactive intermediate has been unsatisfactory, the present modified reaction would be promising for the preparation of macrocyclic compounds of physicochemical interest.

A stereoisomeric mixture of **2c**, the precursor for [8]CPPA **1c**, was also obtained from (*Z*,*Z*,*Z*)-4,4′-bis(4-formylstyryl)stilbene **4**[10] under the present conditions in 37% yield together with [2.2.2.2]paracyclophanetetraene (21%), the intramolecular cyclization product. The yields of **2a** and **2c** were thus significantly improved as compared with those in the previous procedures, and the corresponding CPPAs were readily obtained in almost pure forms simply by chromatographic filtration through alumina gel. The present improvement allowed the synthesis of [7]CPPA **1b**[11] by [3+4] coupling approach and [9]CPPA **1d**[11] by cyclotrimerization of **3**: the sequential treatments converted a mixture of **3** and **4** (1:1) into a mixture of **1a**, **1b** and **1c** (ca. 1:2:1), and a mixture of the *Z*,*Z*- and *E*,*Z*-isomer[10] of **3** (ca. 3:1) into a mixture of **1a** and **1d** (ca. 10:1). Gel permeation chromatography of the mixtures afforded **1b** and **1d** in 20 and 4% yield, respectively, as fine yellow needles. The cyclotrimerization of **3** occurred only when a mixture of (*Z*,*Z*)-**3** and (*E*,*Z*)-**3** was used as a substrate.

The selected spectral data of **1a**–**d** together with those of an acyclic oligomer **5**[2] are shown in Table 2. The averaged values of the inner phenylacetylene part of **5** is taken as reference for comparison. The simple NMR spectra of **1b** and **1d** clearly indicate that the molecules have a belt-shaped structure similar to **1a** and **1c**. While the aromatic protons move slightly up-field, the *sp* carbons move appreciably down-field (more sp^2-like due to bending) as the ring-size becomes smaller (higher strain). Thus, the ^1H NMR spectra exhibit no alternate changes associated with a peripheral conjugation. Similar to the case of acyclic oligomers,[12] no significant bathochromic shift of the longest UV–vis absorptions are observed for **1a** to **1d**. The emission spectra, however, exhibit broadening and bathochromic shift with decrease of the ring-size, probably due to the increase of strain and rigidity of the molecules.

In conclusion, the newly modified McMurry reactions allowed the improved or new synthesis of cyclic para-



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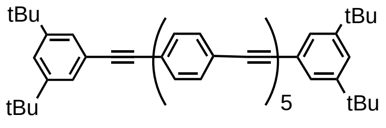

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Table 2. Selected spectral data of **1a**–**1d** and **5**

		1a	**1b**	**1c**	**1d**	**5**
^{1}H NMR[a]		7.35	7.36	7.40	7.43	7.52[c]
^{13}C NMR[a]	*sp* Carbon	97.65	96.14	94.95	94.21	90.7[c]
	ipso	123.93	123.92	123.67	123.56	
	Aromatic	130.87	131.07	131.21	131.33	
Absorption max.	(log ε)[b]	349 (5.40)	355 (5.41)	355 (5.47)	354 (5.51)	358 (5.05)
Emission max.[b]		471	418, 448	416, 447	414, 442	398, 418

[a] δ ppm, in $CDCl_3$.

[b] In cyclohexane.

[c] Averaged values of inner phenylacetylene units of the molecule.

phenylacetylenes composed of six to nine phenylacetylene units. The reaction would be applicable to the preparation of other macrocyclic cyclophanes.[13] CPPAs thus obtained provide no evidence for cyclic conjugation around the curved periphery. Their spectral properties vary mainly with decrease of ring-size of the molecules, which increases the strain of the molecules due to larger bending of the triple bonds and deeper boat-form of the benzene rings. Further studies on CPPAs are in progress from the supramolecular point of view.

Acknowledgements

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10. ^{1}H NMR data of the new dialdehydes; (*E*,*Z*)-**3**: ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 6.65$ (d, $J = 12.2$ Hz, 1H), 6.74 (d, $J = 12.2$ Hz, 1H), 7.13 (d, $J = 16.4$ Hz, 1H), 7.19 (d, $J = 16.4$ Hz, 1H), 7.23–7.25 (m, AA′BB′ pattern, $J_{AB} = 8.1$ Hz, 2H), 7.40–7.43 (m, AA′BB′ pattern, $J_{AB} = 8.5$ Hz, 2H), 7.42–7.44 (m, AA′BB′ pattern, $J_{AB} = 8.1$ Hz, 2H), 7.62–7.64 (m, AA′BB′ pattern, $J_{AB} = 8.2$ Hz, 2H), 7.75–7.77 (m, AA′BB′ pattern, $J_{AB} = 8.2$ Hz, 2H), 7.85–7.87 (m, AA′BB′ pattern, $J_{AB} = 8.2$ Hz, 2H), 9.97 (s, 1H), 9.99 (s, 1H). (*Z*,*Z*,*Z*)-**4**: mp 130–131°C, ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 6.54$ (s, 2H), 6.59 (d, $J = 12.2$ Hz, 1H), 6.70 (d, $J = 12.2$ Hz, 1H), 7.06–7.08 (m, AA′BB′ pattern, $J_{AB} = 8.6$ Hz, 4H), 7.11–7.13 (m, AA′BB′ pattern, $J_{AB} = 8.6$ Hz, 4H), 7.38–7.40 (m, AA′BB′ pattern, $J_{AB} = 8.3$ Hz, 4H), 7.70–7.72 (m, AA′BB′ pattern, $J_{AB} = 8.3$ Hz, 4H), 9.93 (s, 2H). (*E*,*Z*,*Z*)-**4**: ^{1}H NMR (270 MHz, $CDCl_3$): $\delta = 6.58$ (s, 2H), 6.60 (d, $J = 13.2$ Hz, 1H), 6.72 (d, $J = 13.2$ Hz, 1H), 7.08–7.19 (m, 6H), 7.26–7.28 (m, AA′BB′ pattern, $J_{AB} = 8.6$ Hz, 2H), 7.40–7.42 (m, AA′BB′ pattern, $J_{AB} = 8.3$ Hz, 2H), 7.64–7.66 (m, AA′BB′ pattern, $J_{AB} = 8.3$ Hz, 2H), 7.73–7.75 (m, AA′BB′ pattern, $J_{AB} = 8.3$ Hz, 2H), 7.85–7.87 (m, AA′BB′ pattern, $J_{AB} = 8.3$ Hz, 2H), 9.95 (s, 1H), 9.99 (s, 1H).
11. **1b**: Yellow needle, mp >70°C (decomp.), MS(FAB) $m/z = 700$ [M^+]; **1d**: pale yellow powder, mp >190°C (decomp.), MS(FAB) $m/z = 901$ [$(M+H)^+$].
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