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A novel method for the construction of a benzene ring: a facile ring-closing reaction of (1*E*,3*E*,5*E*)-1-chloro-3-(*p*-tolylsulfonyl)-1,3,5-alkatrienes

Katsuyuki Ogura,[a,]* Mineko Takeda,[b] Jian R. Xie,[a] Motohiro Akazome[a] and Shoji Matsumoto[a]

[a]*Department of Materials Technology, Faculty of Engineering, Chiba University, 1-33 Yayoicho, Inageku, Chiba 263-8522, Japan*

[b]*Graduate School of Science and Technology, Chiba University, 1-33 Yayoicho, Inageku, Chiba 263-8522, Japan*

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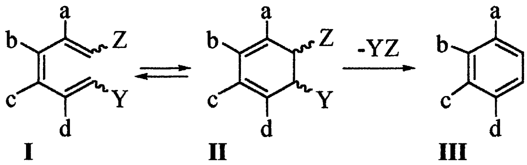
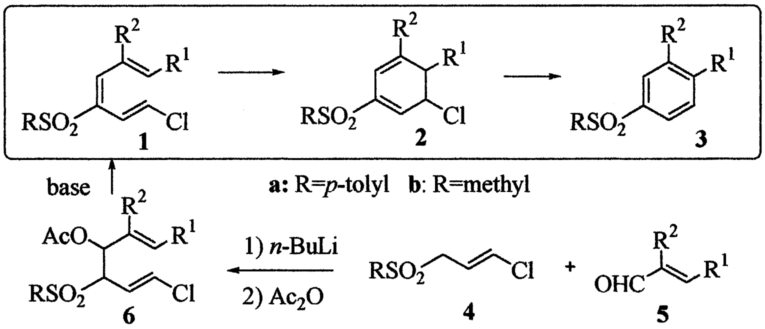
Abstract—(1*E*,3*E*,5*E*)-1-Chloro-3-(*p*-tolylsulfonyl)-1,3,5-alkatrienes (**1**) underwent facile ring-closure followed by spontaneous removal of hydrogen chloride to form a benzene ring. This reaction sequence occurred at relatively low temperature. © 2001 Elsevier Science Ltd. All rights reserved.

Recently, new methods for constructing a benzene ring have been receiving much attention especially in the field of useful functional materials with a π-electron system. Among many precedent methods, we focused on the utilization of electrocyclic interconversion[1] between hexatriene (**I**) and cyclohexadiene (**II**) that can be led to the benzene ring (**III**) by the elimination of an appropriate moiety. This route has been well investigated mainly in terms of the photochemical transformation of stilbene derivatives into the corresponding phenanthrene.[2] In contrast, there are few reports on utilization of this route for preparing simple benzene rings, probably because it works less efficiently. However, it is conceivable that, if a good leaving group (Y) was introduced in the hexatriene, this route would work more efficiently to give the expected **III**.[3]



In order to put this reaction sequence into practice, there were three problems to be solved: (1) a stereoselective synthesis of the starting hexatriene that has the central bond bearing two substituents (**b** and **c**) in *Z* geometry; (2) the development of a method whereby the 1,3,5-alkatriene adopts conformations around the 2,3- and 4,5-



Scheme 1.

Keywords: benzenes; electrocyclic reactions; sulfones; trienes.

* Corresponding author. Fax +81-43-290-3402; e-mail: katsu@galaxy.tc.chiba-u.ac.jp

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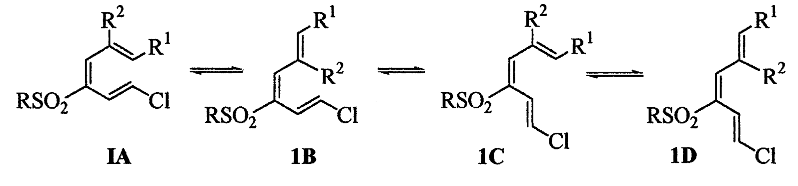
bonds that are favorable for the cyclization; (3) the selection of an appropriate leaving group (Y) that does not disturb the cyclization and can be easily removed after the cyclization. In this letter, we wish to report the facile transformation of a (1*E*,3*E*,5*E*)-1-chloro-3-(*p*-tolyl or methylsulfonyl)-1,3,5-alkatriene (**1**) into a benzene derivative (**3**) which is brought about by thermal electrocyclization followed by spontaneous elimination of the hydrogen chloride moiety. For synthesizing the starting 1,3,5-alkatriene (**1**), the following reaction sequence was devised: lithiation of (*E*)-1-chloro-(*p*-tolyl or methylsulfonyl)propene (**4**)[4] followed by the addition of acetic anhydride gives an adduct (**6**). If this adduct (**6**) is treated with a base, the expected **1** would be obtained.

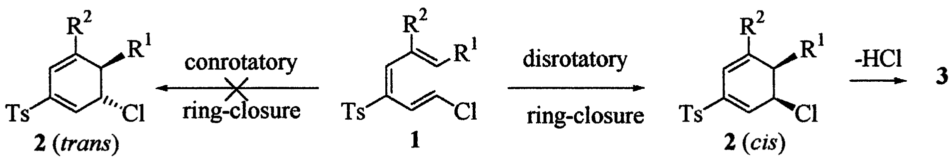
According to Scheme 1, we prepared the adduct (**6**), which consisted of two diastereomers except for **6a** (R^1 = Ph, R^2 = Me).[6,7] In order to form the corresponding **1**, (R^*,R^*)-**6a** (R^1 = Ph, R^2 = Me)[6] was subjected to the reaction with NaH (1.3 equiv) in THF (room temperature/38 h). To our surprise, we did not obtain **1a** (R^1 = Ph, R^2 = Me), but the final product **3** (R^1 = Ph, R^2 = Me) was given in 78% yield. On similar treatment with NaH (room temperature/48 h), both (R^*,R^*)- and (R^*,S^*)-diastereomers of **6b** (R^1 = Ph, R^2 = Me) afforded **3b** (R^1 = Ph, R^2 = Me) in 80 and 54% yields, respectively, along with the starting materials (20 and 40% yields, respectively). These facts implied that, irrespective of the diastereomeric structures of **6**, the present reaction with NaH effects the stereoselective elimination[9] of the acetic acid moiety to give only the desired geometric isomer of **1** (R^1 = Ph, R^2 = Me) that is smoothly derived into **3** (R^1 = Ph, R^2 = Me). When (R^*,R^*)-**6a** (R^1 = Me, R^2 = Me) was treated with NaH at room temperature for a short period of time (24 h), the intermediary **1a** (R^1 = Me, R^2 = Me) was afforded in 23% yield along with **3** (R^1 = Me, R^2 = Me) (41% yield) and the starting material (24%). Transformation of **1** (R^1 = Me, R^2 = Me) into the corresponding **3** in $CDCl_3$ could be pursued by ^1H NMR (300 MHz). It was completed within 65 h at room temperature in the dark and no signal for **2a** was observed, indicating that the release of hydrogen chloride from **2** occurred spontaneously and smoothly. Similarly, (R^*,R^*)-**6a** (R^1 = H, R^2 = Me) gave the corresponding **1a** and **3a** in 5 and 39% yields, respectively.[10] Complete conversion of **1a** (R^1 = H, R^2 = Me) to **3a** (R^1 = H, R^2 = Me) in $CDCl_3$ took place at room temperature.

The reaction of **6a** (R^1 = Ph, or *p*-$MeOC_6H_4$; R^2 = H) with NaH at room temperature did not give **3**, the corresponding **1a** in 57 or 90% yield, respectively. The complete conversion of **1a** (R^1 = Ph, or *p*-$MeOC_6H_4$; R^2 = H) to the corresponding **3a** was accomplished by heating it in toluene at 80°C. This implied that the presence of the R^2 substituent facilitates the electrocyclization of **1**. For the present 1,3,5-alkatriene, many conformations such as **1A**–**D** have to be taken into consideration, though conformation (**1A**) is favorable for the electrocyclization. The presence of the substituent (R^2) and the *p*-tolylsulfonyl group can be considered to increase the population of conformation **1A**. This is due to the repulsive interactions of the R^2 and *p*-tolylsulfonyl groups with the terminal 2-chloroethenyl group (Scheme 2).

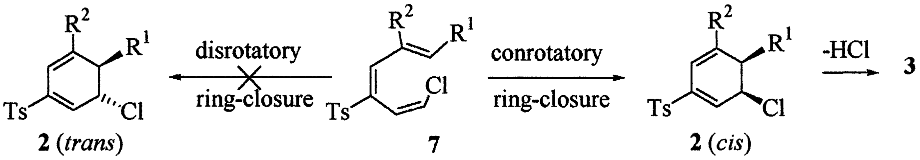
Molecular orbital calculation at the PM3 level[11] revealed that, in the case of **1a** (R^1 = Ph and R^2 = Me), the most stable energy-minimized conformations corresponding to **1A**–**D** are comparable in energy (within 0.34 kcal mol^{-1}). When R^2 is H, the most stable energy-minimized conformation that corresponds to **1B** was calculated to be more stable by 2.3 kcal mol^{-1} than **1A**. Thus, it was shown that (1*E*,3*E*,5*E*)-1-chloro-3-(*p*-tolyl or methylsulfonyl)-1,3,5-alkatriene (**1**) provides an ideal system for construction of a benzene ring via thermal electrocyclization with subsequent elimination of hydrogen chloride. The Woodward–Hoffmann rule predicts that conformation (**1A**) thermally closes a ring in a disrotatory mode. It is noteworthy that the ring-closure of **1** in this direction can avoid the repulsive interaction between R^1 and Cl to be smoothly led to **2**. In contrast, irradiation of **1** (R^1 = Ph, R^2 = H) with ultraviolet light (>290 nm) did not form the benzene derivative (**3**; R^1 = Ph, R^2 = H), and only the isomerization around the C3–C4 double bond was observed. This indicated the ring-closure in a conrotatory mode is disfavored probably because of the repulsive interaction between R^1 and Cl (Scheme 3).



Scheme 2.



Scheme 3.



Scheme 4.

Finally, we would like to comment on the role of the chlorine atom. If this chlorine atom is replaced by hydrogen, the last elimination step to a benzene ring will become slow. In fact, the treatment of 4-acetoxy-5-methyl-3-(*p*-tolylsulfonyl)-1,5-heptadiene with NaH resulted in the formation of stable 5-methyl-3-(*p*-tolylsulfonyl)-1,3,5-heptatriene. We also prepared a geometric isomer (**7**) of **1**. These compounds (**7**) were thermally so stable as to remain unchanged at 80°C. However, the electrocyclization of **7** ($R^1=Ph$, $R^2=H$) was achieved by irradiation with UV light (>290 nm) to form the corresponding **3** in 50% yield along with the starting material (47% yield). These findings are in complete accordance with the Woodward–Hoffmann rule:[1] the thermal ring-closure of **7** in a disrotatory mode undergoes severe steric repulsion between R^1 and Cl (Scheme 4), but the photochemical ring-closure in a conrotatory mode proceeds without such repulsive interaction.

In conclusion, (1*E*,3*E*,5*E*)-1-chloro-3-(*p*-tolylsulfonyl)-1,3,5-alkatrienes (**1**) were shown to be good precursors for the construction of a benzene ring, which was achieved by thermal ring-closure followed by easy removal of the hydrogen chloride moiety. Now we are investigating the application of the present system to other 3-functionalized 1-chloro-1,3,5-alkatrienes.

Acknowledgements

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4. Pure (*Z*)-1-chloro-3-(*p*-tolylsulfonyl)propene was reported, but its (*E*)-isomer (**4**) has been not isolated in a pure form.[5] We prepared a 58:42 mixture of (*E*)- and (*Z*)-chloro-3-(*p*-tolylsulfonyl)propenes from 1,3-dichloropropene and sodium *p*-toluenesulfinate. Preparative HPLC of the mixture gave **4** as colorless crystals: mp 81.2–81.9°C. Anal. calcd for $C_{10}H_{11}ClO_2S$: C, 52.06; H, 4.81%. Found: C, 52.15; H, 4.72%. Its NMR data accorded with those reported in Ref. 5.
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6. Typical procedure: *n*-Butyllithium (1.63 M in hexane, 2.1 mmol) was added to a solution of **4** (0.61 mmol) in THF (3 mL) at −78°C. Then, α-methylcinnamaldehyde (0.63 mmol) was added and the resulting mixture was further stirred at −78°C for 20 min. After the addition of acetic anhydride (0.72 mmol), the stirring was continued at the same temperature for 2 h. The usual workup and column chromatography on silica gel gave **6** ($R^1=Ph$, $R^2=Me$) (83% yield) as one diastereomer. Its stereochemistry was determined by single-crystal X-ray analysis[7] to be (R^*,R^*). In a similar manner, **6** ($R^1=Me$, $R^2=Me$), **6** ($R^1=H$, $R^2=Me$), **6** ($R^1=Me$, $R^2=H$), **6** ($R^1=Ph$, $R^2=H$), and **6** ($R^1=p$-$MeOC_6H_4$, $R^2=H$) were prepared. In these reactions, two diastereomers were formed in the ratios of 89:11, 69:31, 70:30. 75:25, and 69:31, respectively. Their analogy in ^1H NMR suggested that the major isomers, which were isolated by preparative HPLC, have (R^*,R^*)-stereochemistry.
7. The data were collected with Cu Kα ($\lambda=1.54178$ Å) radiation on a Mac Science MXC18 diffractometer. The structure was solved and refined by direct methods (SIR 92[8] on a computer program package: Crystan GM ver. 6.2.1 from MAC Science Co. Ltd.): Orthorhombic, *Pbn*21 (#33), $a=14.076(4)$, $b=26.553(7)$, $c=5.830(2)$ Å, $V=2179(1)$ Å^3, $Z=4$, $R=0.046$, $Rw=0.049$, $T=298$ K.
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9. Since the allylic carbanion of **6** was stabilized by the adjacent sulfonyl group, the E1cb mechanism is likely for the transformation of **6** into **1**.
10. The starting material was also recovered in 24% yield. These low yields of **1** and **3** are probably due to the polymerization on the terminal vinyl part.
11. With MOPAC (ver. 6); Stewart, J. J. P. *QCPE Bull.* **1989**, *10*, 209–220 and 221–264.