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Rotational Isomerism Involving an Acetylenic Carbon VII. Restricted Rotation about Acetylenic Axis in a Diphenylethyne Derivative with Sterically Crowded *m*-Terphenyl Moieties#

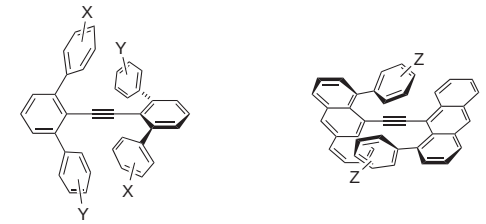
Shinji Toyota,* Takashi Yanagihara, Yukihiro Yoshida, and Michio Goichi

Department of Chemistry, Faculty of Science, Okayama University of Science, 1-1 Ridaicho, Okayama 700-0005

Received February 14, 2005; E-mail: stoyo@chem.ous.ac.jp

Bis(2,4,4″,6-tetramethyl-1,1′:3′,1″-terphenyl-2′-yl)-ethyne was prepared by the Hart reaction and the Stille coupling as a sterically crowded diphenylethyne derivative. The barrier to rotation about the acetylenic axis was determined by the dynamic NMR method to be 51 kJ mol^{-1}. The restricted rotation is attributed to the steric hindrance of the two mesityl groups in the *m*-terphenyl moieties.

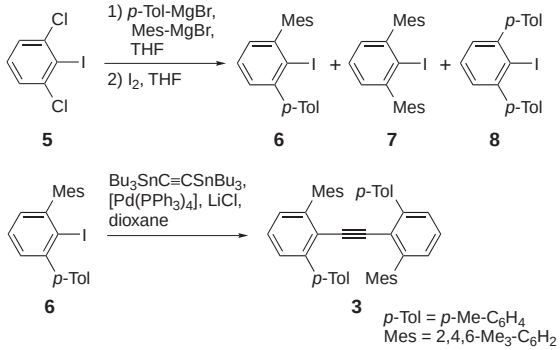
Recently, we have demonstrated that the rotation about the acetylenic axis could be retarded on the NMR timescale when sterically bulky groups were introduced at both ends of an ethyne moiety.[1–4] The rotational barrier was enhanced up to 79 kJ mol^{-1} for the di(9-triptycyl)ethyne system, a dialkylethyne analogue, by introducing a mesityl group at the 1-position in one of the 9-triptycyl groups.[3] As for diarylethynes, we first designed the *m*-terphenyl based system **1**, in which four *p*-tolyl groups were substituted at all the ortho positions in the diphenylethyne core (Chart 1). The variable temperature NMR measurements revealed that its derivative **2** underwent the rotation about the acetylenic axis still very quickly at −100 °C (barrier < 35 kJ mol^{-1}).[4] On the other hand, the use of rigid 1-(substituted phenyl)-9-anthryl groups efficiently enhanced the rotational barrier: the observed value of **4** (ca. 50 kJ mol^{-1}) was the highest for acyclic diarylethynes.[1] This result indicates that additional steric hindrance should achieve the restricted rotation in the *m*-terphenyl system. Therefore, we synthesized compound **3**, in which one of the wing *p*-tolyl groups in each *m*-terphenyl moiety was replaced by a mesityl group.[5] The structure and dynamic stereochemistry of the sterically crowded diphenylethyne **3** are herein reported.



1 (X = Y = 4-Me)
2 (X = 4-Me, Y = 4-CH_2OMe)
3 (X = 4-Me, Y = 2,4,6-Me_3)

4

Chart 1.



Scheme 1. Synthesis of **3**.

Compound **3** was prepared according to the reactions shown in Scheme 1. The *m*-terphenyl moiety was constructed by the Hart reaction[6] of **5** with a mixture of two kinds of Grignard reagents. The reaction mixture was treated with a solution of iodine in THF[7] to afford a mixture of three kinds of terphenyl compounds, from which the asymmetrically substituted product **6** was separated from the other symmetric compounds **7** and **8** by chromatography in 29% yield. The Stille coupling of the iodide with bis(tributylstannyl)ethyne gave the desired diarylalkyne **3** in 26% yield after repeated chromatographic separations.[8] The poor yield results from the steric crowdedness around the reaction sites in the *m*-terphenyl moiety. Compound **3** was reasonably characterized by spectroscopic and analytical data.

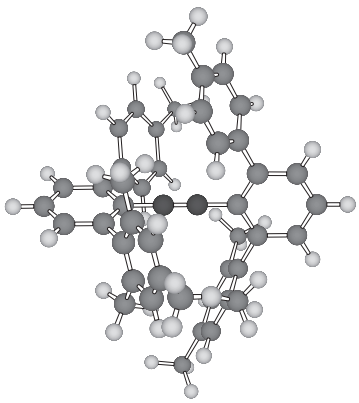


Fig. 1. Optimized structure of **3** by PM3 calculation. Alkynic carbons are indicated in a dark color.

Because we failed to obtain a crystal suitable for the X-ray analysis, the molecular structure was examined by the PM3 calculation. The optimized structure is shown in Fig. 1. In the diphenylethyne moiety, the two phenyl groups are nearly bisected along the acetylenic axis (dihedral angle 84°). The mesityl group is bisected relative to the attaching phenyl group in each *m*-terphenyl unit (dihedral angle 89°) to minimize the steric interactions of the *o*-methyl groups. Accordingly, a molecule takes an approximately C_2 conformation with a chiral axis along the acetylenic moiety.

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In the ^{1}H NMR spectrum of **3**, the signal due to the 2,6-Me protons was observed as a broad singlet at $\delta = 1.60$ at room temperature (Fig. 2). As the temperature was lowered, this signal further broadened, decoalesced at -25 °C, and finally became two separate signals at -59 °C. During the temperature change, the aromatic signal due to the 3,5-H also showed a similar lineshape change, but the other signals remained unchanged. The rates of site exchange were determined by the total lineshape analysis of the 2,6-Me signals (Fig. 2). The Eyring plot afforded the following kinetic parameters: $\Delta H^{\ddagger}$ 40.7 $\pm$ 1.5 kJ mol^{-1}, $\Delta S^{\ddagger}$ -40 ± 7 J mol^{-1} K^{-1}, $\Delta G^{\ddagger}_{250}$ 50.8 kJ mol^{-1}.

In the staggered conformation, the 2,6-Me groups (or the 3,5-H atoms) lie in different environments: one is close to the tolyl group in the other *m*-terphenyl moiety, and the other is close to the mesityl group (Scheme 2). The site exchange between the diastereotopic Me groups takes place either by the rotation of the mesityl group (topomerization) or by the rotation about the acetylenic axis (enantiomerization). Generally, tri-ortho substituted biphenyls have rotational barriers high enough to isolate enantiomers at room temperatures, >100 kJ mol^{-1}.[9] The structural analogy ensures that the rotation of the mesityl group relative to the central phenyl group in **3** should be negligibly slow under the conditions of the NMR measurements. Therefore, it is reasonable to conclude that the rotation about the acetylenic axis is the rate-determining step of the site exchange.

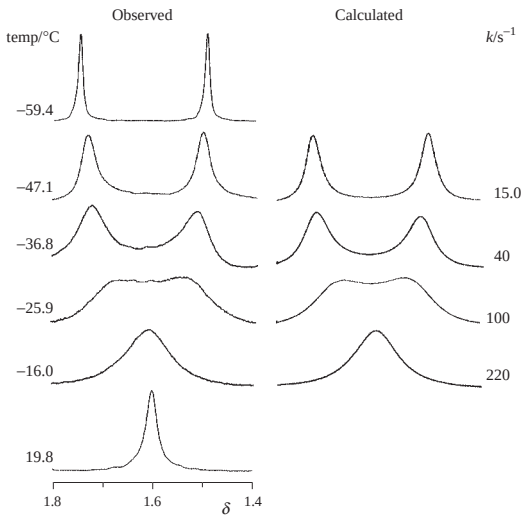
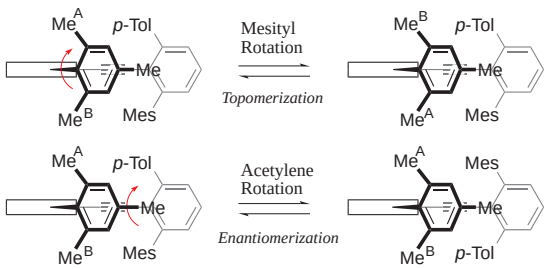


Fig. 2. Observed (solvent: $CDCl_3$) and calculated spectra of 2,6-Me proton signals of **3**.



Scheme 2. Possible routes of site exchange of 2,6-Me groups in **3**. One of the *p*-tolyl groups is not shown in each structure for clarity.

The observed rotational barrier of **3** is higher by >15 kJ mol^{-1} than that of **2**. This enhancement is attributed to the steric effect of the *ortho*-methyl groups in the mesityl groups, which destabilize the transition state of the axial rotation more than the initial state. This rotational barrier is comparable to that observed for **4** (Z = 3,5-^{i}Pr$_2$),[4] being one of the highest values for the rotation of acetylenic axis in acyclic ethynes. These substituent effects give us clues to molecular design toward isolation of rotational isomers with a conformationally locked acetylenic axis.

Experimental

General. Melting points are uncorrected. ^{1}H and ^{13}C NMR spectra were measured on a Varian Gemini-300 spectrometer at 300 and 75 MHz, respectively. Elemental analyses were performed by a Perkin-Elmer 2400-type analyzer. High-resolution mass spectra were measured on a JEOL JMS-700 MStation spectrometer. HPLC was performed with a 20 mm $\phi \times 250$ mm Develosil 60-7 column.

2′-Iodo-2,4,4″,6-tetramethyl-1,1′:3′,1″-terphenyl (6). A solution of 199 mg (1.00 mmol) of 1-bromo-2,4,6-trimethylbenzene and 171 mg (1.00 mmol) of 4-bromotoluene in 10 mL of dry THF was added to a flask charged with 53 mg (2.2 mmol) of magnesium powder and 5 mL of dry THF over 10 min under Ar atmosphere. The whole was stirred for 2 h. To the solution of the mixed Grignard reagent, a solution of 136 mg (0.500 mmol) of 1,3-dichloro-2-iodobenzene **5** in 5 mL of dry THF was added over 10 min. The reaction mixture was refluxed for 3 h. After cooling, a solution of 558 mg (2.20 mmol) of iodine in 5 mL of THF was added over 1 h, and the whole was stirred overnight at room temperature. The reaction mixture was quenched with 50 mL of aq $Na_2S_2O_3$, and extracted with 50 mL of ether. The organic solution was dried over $MgSO_4$ and evaporated. The crude products were separated by chromatography on silica gel with hexane as eluent to afford 60 mg (29%) of the desired product as colorless oil (R_f 0.15, hexane) together with other Hart reaction products. ^{1}H NMR ($CDCl_3$) δ 1.99 (6H, s), 2.35 (3H, s), 2.41 (3H, s), 6.96 (2H, s), 7.07 (1H, dd, $J = 7.5$, 1.7 Hz), 7.21–7.30 (5H, m), 7.41 (1H, t, $J = 7.5$ Hz). ^{13}C NMR ($CDCl_3$) δ 20.4, 21.2, 21.3, 105.5, 128.06, 128.11, 128.2, 128.5, 129.3, 135.4, 137.16, 137.21, 142.37, 142.41, 147.0, 148.0. HRMS (FAB) Found: m/z 413.0746. Calcd for $C_{22}H_{21}I$: $[M + H]^+$, 413.0766. The other two products are known compounds. 2′-Iodo-2,2″,4,4″,6,6″-hexamethyl-1,1′:3′,1″-terphenyl (**7**):[10] yield 21%, mp 212–214 °C, R_f 0.23 (hexane). 2′-Iodo-4,4″-dimethyl-1,1′:3′,1″-terphenyl (**8**):[11] yield 11%, mp 138–140 °C (lit. 139–140 °C), R_f 0.12 (hexane).

Bis(2,4,4″,6-tetramethyl-1,1′:3′,1″-terphenyl-2′-yl)ethyne (3). To a degassed solution of 250 mg (0.606 mmol) of **6** in 10 mL of acetonitrile were added 77 mg (1.8 mmol) of LiCl, 35 mg (0.030 mmol) of [Pd(PPh$_3$)$_4$], and 0.21 mL (0.39 mmol) of bis(tributylstannyl)ethyne. The mixture was refluxed at 80 °C for 48 h. After the solvent was removed by evaporation, the residue was extracted with ether. This organic solution was washed with aq NaCl, dried over $MgSO_4$, and evaporated. The crude product was purified by chromatography on silica gel with hexane–ethyl acetate (20:1) as eluent, and then by HPLC with hexane as eluent. Recrystallization from hexane afforded 47 mg (26%) of the desired compound as a white solid. mp 169–170 °C. ^{1}H NMR

($CDCl_3$) δ 1.60 (12H, s), 2.28 (6H, s), 2.33 (6H, s), 6.77 (4H, s), 6.86–7.28 (14H, m). ^{13}C NMR ($CDCl_3$) δ 20.0, 21.1, 21.2, 92.2, 121.5, 127.5, 127.6, 128.2, 129.0, 135.8, 136.0, 136.5, 137.9, 138.0, 144.1, 144.5. HRMS (FAB) Found: m/z 594.3248. Calcd for $C_{46}H_{42}$: $[M]^+$, 594.3287. Anal. Found: C, 92.55; H, 7.06%. Calcd for $C_{46}H_{42}$: C, 92.88; H, 7.12%.

Dynamic NMR Measurement. VT ^1H NMR spectra of **3** were measured on a JEOL Lambda-300 spectrometer at 300 MHz. The sample temperature was calibrated with the chemical shift differences of methanol signals. About 5 mg of sample was dissolved in ca. 0.7 mL of $CDCl_3$. The total lineshape analyses were performed by the DNMR3K program, a modified version of the DNMR3 program.[12] The lineshape changes were analyzed as 2-site mutual exchanges (A $\rightleftarrows$ X). The chemical shift difference ($\Delta\nu$/Hz) was assumed to be a linear function of the temperature (t/°C) as $\Delta\nu = -0.361t + 49.0$, and the spin–spin relaxation time (T_2) was fixed at 0.08 s. Rate constants are as follows: k/s^{-1} (t/°C) = 8.0 (−52.3), 15.0 (−47.1), 23 (−42.0), 40 (−36.8), 65 (−31.6), 100 (−25.9), 130 (−24.3), 140 (−21.2), 220 (−16.0).

Calculation of Molecular Structures. The structure of **3** was optimized by the PM3 method with Gaussian 98 program[13] on a Tempest 3 workstation. The calculations were started from several conformers, and the structure in Fig. 1 was obtained as a global minimum.

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Part 6 of the series. See Ref. 1a.

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