Fulvenes

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A Mild, Thermal Pentafulvene-to-Benzene Rearrangement**

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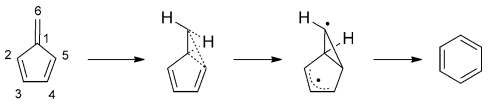
Dedicated to Professor Jack D. Dunitz on the occasion of his 90th birthday

Pentafulvene (C_6H_6)[1] is a nonvalence isomer of benzene that consists of a cyclopentadiene ring with one exocyclic double bond. Similar to the cyclic $(CH)_6$ valence isomers (except for benzene), it is highly reactive and can only be prepared in dilute solution so as to avoid dimerization. Isomerization of pentafulvene to benzene occurs on irradiation[2] or gas-phase pyrolysis at high temperatures (> 500 °C).[3] The thermal automerization of benzene has been proposed to occur via a pentafulvene or fulvenoid intermediate.[4] The thermal isomerization of fulvene, first observed by Henry and Bergman in 1972, is thought to proceed via a biradical "prefulvene" intermediate[3c,5] (Scheme 1). To date, pentafulvene-to-benzene rearrangements have only been performed by the above two methods, thus demonstrating the difficulty of what is, at least on paper, a simple rearrangement. As part of our continuing studies on 6,6-dicyanopentafulvenes (DCFs),[6] a class of molecules with interesting optoelectronic properties, we serendipitously discovered that not all pentafulvenes require such forcing conditions to undergo the thermal rearrangement to benzene. Herein, we report that substituted DCFs undergo quantitative thermal rearrangement to dicyanobenzene isomers in dipolar aprotic solvents under conditions far milder than those required to rearrange unsubstituted pentafulvene.



Scheme 1. Radical-based rearrangement of fulvene.

Recently, we found that a push-pull-substituted DCF rearranges to a benzene isomer at room temperature in the presence of hydrated acidic SiO_2 in acetonitrile.[6j] No other DCF we studied underwent rearrangement under these conditions. However, when tetrakis(4-bromophenyl)-6,6-dicyanopentafulvene **1a** was heated to 160 °C for one hour in *N*,*N*-dimethylformamide (DMF), it quantitatively rearranged to the 1,3-dicyanobenzene derivative **1b** along with trace amounts of 1,4-dicyanobenzene isomer **1c**. The structure of **1b** was confirmed by X-ray crystallography (Figure 1). Highly surprised by this result, we decided to study the scope and properties of this reaction in more detail.

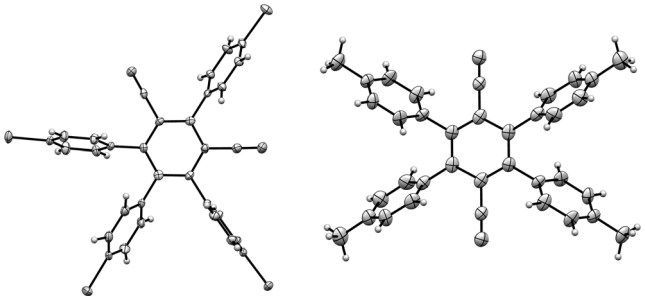
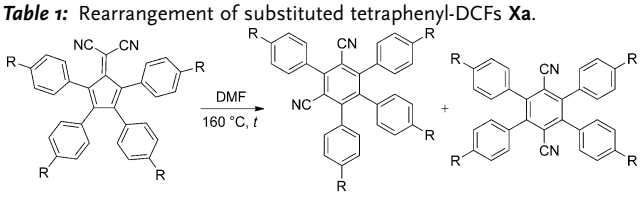


Figure 1. Left: Crystal structure of **1b**. Right: crystal structure of **3c**. $T = 100$ K. Thermal ellipsoids at 50% probability.

First, we set out to understand the importance of electron-donating and -accepting groups on the rate of the rearrangement. Tetraphenyl-substituted DCFs are easily obtained by Knoevenagel condensation of malononitrile with the corresponding cyclopentadienones, provided the latter are sufficiently stable.[6d,e,g,h] We thus prepared substituted DCFs **2a**–**5a** with a broad range of electron-donating and -accepting functionalities (Table 1; see the Supporting Information for details). In all cases, heating the DCF **Xa** to 160 °C led to quantitative conversion into 1,3-dicyanobenzene **Xb** and 1,4-dicyanobenzene **Xc** in various ratios of **Xb/Xc**. Under no circumstances did we observe formation of the 1,2-dicyanobenzene isomer during the course of this study. The structures

Table 1: Rearrangement of substituted tetraphenyl-DCFs **Xa**.



X	R	*t*	Conversion	Xb/Xc
1	Br	1 h	quant.	99.1:0.9
2	H	6 h	quant.	90:10
3	Me	8 h	quant.	95:5
4	OMe	21 h	quant.	75:25
5	CN	10 min	quant.	82:18

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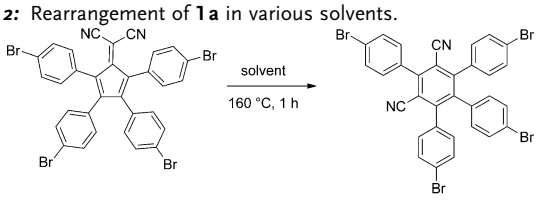
of **1b**–**5b** and **3c** were confirmed by X-ray crystallography (Figure 1 and see the Supporting Information). Electronic substituent effects have a strong impact on the reaction rate, with electron-donating groups slowing the reaction down and electron-accepting groups enhancing it. As an extreme example of the latter case, tetrakis(4-cyanophenyl)-DCF **5a** even undergoes rearrangement at room temperature (299–301 K), and leads to quantitative conversion into **5b**/**c** after 4 days in DMF. To our knowledge, this is the only example of a thermal pentafulvene-to-benzene rearrangement that is possible under ambient conditions. Interestingly, the **Xb**/**Xc** selectivity is independent of temperature. Heating **5a** in DMF to 160 °C for 10 min or letting it sit for 4 days at room temperature leads to the same ratio of **5b**/**5c**, thus suggesting that the isomer selection step is not rate-limiting. There appears to be little correlation between 1,3-/1,4-dicyanobenzene selectivity and the electronic character of the pendant group, as both electron-rich **4a** and electron-poor **5a** led to the formation of significant quantities of the 1,4-dicyanobenzene isomer.

To test the importance of solvent polarity, we heated DCF **1a** at 160 °C in a number of solvents (Table 2). The high-yielding transformation to the benzene derivatives only occurred in dipolar aprotic solvents such as DMF, *N*,*N*-dimethylacetamide (DMA), Me_2SO, and *N*-methylpyrrolidone (NMP). Reactions in MeCN and AcOH gave only trace amounts of product, while 1,2-dichloroethane, EtOH, and pyridine were completely ineffective. In all cases, the only analytes observed were either DCF starting material or the rearrangement products.

Table 2: Rearrangement of **1a** in various solvents.



1a **1b**

Entry	Solvent	Conversion of **1a**
1	DMF	quant.
2	DMA	quant.
3	NMP	quant.
4	Me_2SO	78%
5	MeCN	<1%
6	1,2-dichloroethane	0%
7	EtOH	0%[a]
8	AcOH	<1%
9	pyridine	0%

[a] Low solubility.

At this point, we began to consider the mechanism of the reaction. In the case of the thermal rearrangement of pentafulvene, the proposed biradical "prefulvene" intermediate is formed by a concerted 1,2-H shift from C6 to C1.[3e] To check for the possibility of radical intermediates, the rearrangement of **2a** was performed in the presence of one equivalent of the radical trap galvinoxyl.[7] The formation of **2b**/**c** proceeded as usual with no change in rate, and the galvinoxyl was recovered. While this does not fully preclude a radical-based mechanism, we conclude from this and other experiments that such a pathway is unlikely.

Kinetic data for the rearrangement of **1a** to **1b** was collected by monitoring the reaction in [D_7]DMF by ^{1}H NMR spectroscopy (500 MHz) at 100 °C over the course of 48 h, with 1,3,5-trimethoxybenzene used as an internal standard (see Section SI4 in the Supporting Information). Upon heating the mixture to 100 °C, the signals corresponding to the aromatic protons of **1a** immediately broadened and subsequently sharpened slightly over the course of the first 5.5 h. During this time, the rates of consumption of **1a** and formation of **1b** are nonlinear and could not be fitted to simple zero-, first-, or second-order kinetics. After this time, however, the rates of consumption of **1a** and formation of **1b** follow zero-order kinetics with a rate constant $k = 4.13 \pm 0.013 \times 10^{-9}$ M s^{-1}. The broadening of the signals of **1a** during the "induction period" indicates the formation of a transient intermediate species. The broad signals were retained when **1a** was heated to 160 °C in [D_7]DMF for 10 min, then cooled and analyzed by NMR spectroscopy at room temperature. However, heating **1a** in DMF to 100 °C for 10 min followed by immediate removal of the solvent and ^{1}H NMR spectroscopy in $CDCl_3$ gave sharp signals identical to pristine **1a**, thus indicating that formation of the intermediate is reversible and possibly involves solvent as a reactant.

The strong dependence of the rearrangement rate on the electronic properties of the substituents on the tetraarylated DCFs, along with the necessity for dipolar aprotic solvents to promote the reaction, suggest a polar mechanism for the rearrangement rather than a radical-based one. We propose a "ring-walk" mechanism (Scheme 2). Attack of a nucleophile (in this case, solvent) leads to 1,2-cyano migration and formation of intermediate **2e**[8] by either cyanide release and reattack (pathway a) or formation of a spirocyclic iminocyclopropyl anion (pathway b). The anion attacks at the 2-position of the fulvene ring, thereby leading to bicyclo-[3.1.0]hex-1-ene **2f**, with C6 capable of quickly migrating around the five-membered ring to form intermediate **2g**. This intermediate can either release the nucleophile to form **2b**, or undergo another "ring-walk" to form intermediate **2h**, which forms **2c** upon release of the nucleophile. Based on the kinetic data, the rate-determining step is probably the formation of **2f**, with electron-withdrawing groups on the phenyl ring promoting the nucleophilic attack. We confirmed by ^{13}C labeling studies that C6 of **2a** retains one cyano group in **2b** (see Section SI7 in the Supporting Information).

In this polar mechanism, it is likely that, if solvent attack is reversible as we propose, reversible release of cyanide will occur. To test this, we prepared [$^{15}N_2$]-**2a** and subjected it to rearrangement conditions in [D_7]DMF in the presence of one equivalent of unlabeled **3a**, chosen for its similar rate of rearrangement (see Section SI6 in the Supporting Information). The rearrangement of [$^{15}N_2$]-**2a** alone gives one signal in the ^{15}N NMR spectrum (50.7 MHz, 298 K) at $\delta = 269.7$ ppm. However, when the rearrangement of [$^{15}N_2$]-**2a** takes place in the presence of one equivalent of **3a**, a second signal appears at $\delta = 268.3$ ppm (see Figure SI14 in the Supporting Information). This clearly indicates intermolecular migration of the

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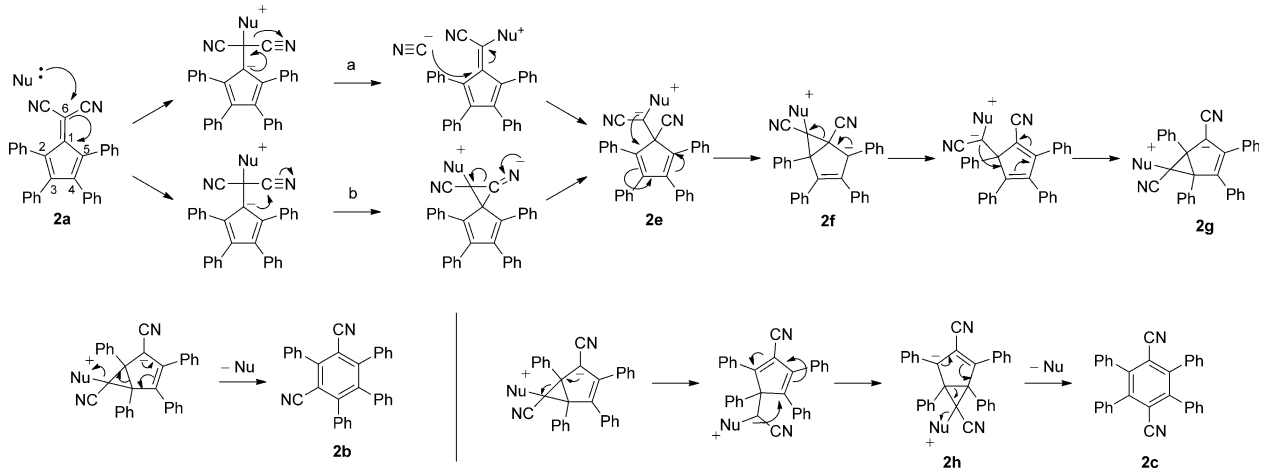
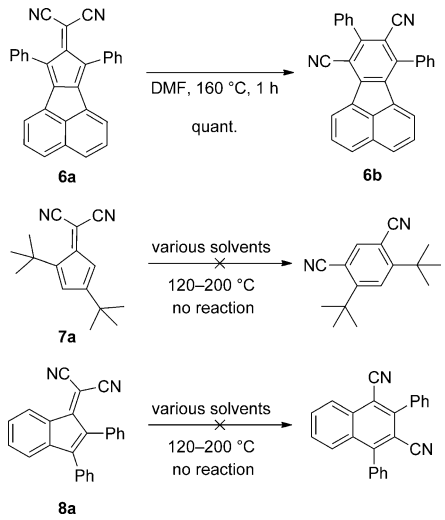


Scheme 2. "Ring-walk" mechanism for the DCF-to-dicyanobenzene rearrangement.

labeled cyano groups, thus confirming our hypothesis that the initial attack of solvent can lead to the release of cyanide. The addition of free cyanide also appears to promote the rearrangement. Addition of one equivalent of $K^{13}CN$/[18]crown-6 (1:1) to a solution of **2a** in [D_7]DMF at room temperature leads to complete consumption of **2a** within seconds. Heating the solution to 160 °C led to quantitative formation of **2b**/**c** in one minute, with incorporation of ^{13}CN into **2b**/**c** as shown by ^{13}C NMR spectroscopy (see Figure SI13 in the Supporting Information).[9]

This simple and quantitative reaction has the potential to generate complex hexasubstituted benzenoid scaffolds that would be difficult to synthesize in other ways. We tested the scope of this reaction with DCFs **6a**,[6e] **7a**, and **8a**[10] (Scheme 3). Acenaphthylene-fused DCF **6a** undergoes rearrangement to **6b** smoothly in 1 h at 160 °C in DMF, and the product structure was confirmed by X-ray crystallography (see Figure SI8 in the Supporting Information). In contrast to **1a**–**5a**, the rearrangement of **6a** led exclusively to the 1,3 isomer **6b**, and no 1,4 isomer was detected. DCFs **7a** and **8a** did not undergo rearrangement in DMF, DMA, or sulfolane at temperatures up to 200 °C, at which the DCFs decompose beyond identification.

In conclusion, we demonstrated the first example of a thermal rearrangement of tetraarylated DCFs to hexasubstituted benzene derivatives that takes place under mild conditions. We postulate a polar mechanism that leads to release of cyanide from the DCF, and which also supports the formation of both the 1,3- and 1,4-dicyanobenzene isomers. Currently, we are undertaking a more detailed mechanistic study of this remarkable rearrangement.



Scheme 3. Other DCFs tested for rearrangement.

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[9] Other strong nucleophiles also promote the rearrangement. Addition of 2 equiv KSCN led to complete rearrangement of **2a** to **2b** after only 1 h in DMF at 160 °C. Thiocyanate did not appear to be incorporated into the product by HPLC and ^{13}C NMR spectroscopy. However, the addition of KSCN does not lead to rate enhancement in MeCN. Addition of 5 equiv Bu_4NI to **2a** in DMF led to neither rate enhancement nor incorporation of iodide.

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