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Hydride-Induced Novel Cyclization of Dienedinitriles Leading to Multifunctionalized Cyclopentadienes

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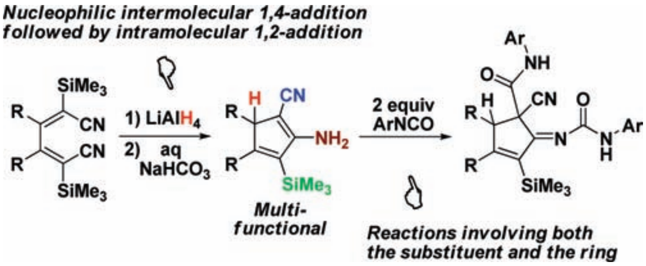
ABSTRACT



By treatment with $LiAlH_4$, 1,4-dicyano-1,4-bis(trimethylsilyl)-1,3-dienes underwent a novel hydride-induced nucleophilic intermolecular 1,4-addition to the α,β-unsaturated nitrile moiety, followed by an immediate nucleophilic intramolecular 1,2-addition to the remaining CN group, to afford multiply functionalized cyclopentadienes in high isolated yields. These multifunctional ($-CN$, $-NH_2$, $-SiMe_3$, $-H$) cyclopentadienes are of a rich and interesting reaction chemistry as preliminarily demonstrated by their reaction with ArNCO involving both the substituent and the ring.

Cyclopentadienes are among the most useful and the most frequently applied organic compounds in many aspects including organic synthesis and organometallic chemistry.[1−3] Therefore, the development of efficient synthetic approaches to cyclopentadienes, especially the functionalized ones,[3,4] has been in great demand. In this paper, we report a convenient and efficient synthesis of novel multiply functionalized cyclopentadienes concomitantly bearing cyano, amino, and

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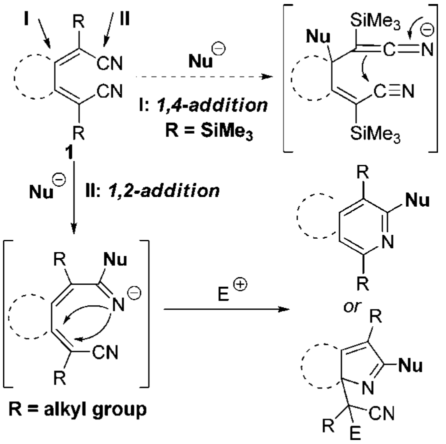
trimethylsilyl groups which are all directly bound to the cyclopentadienyl ring via an unprecedented nucleophilic domino intermolecular 1,4-addition/intramolecular 1,2-addition of dienedinitriles. The unique functionalized structure containing an enaminonitrile moiety is of particular interest as it provides valuable precursors for important heterocyclic systems.[5] Indeed, as preliminarily demonstrated by their reaction with ArNCO, this type of multiply functionalized cyclopentadienes does have interesting and useful properties.

The addition reaction of nucleophiles to α,β-unsaturated nitriles (for examples acrylonitrile and derivatives) is a fundamental reaction in organic chemistry and of great synthetic interest.[6] We have recently developed an efficient synthetic method for 1,4-dicyano-1,3-butadienes **1**,[7] which can be considered as analogues of acrylonitrile derivatives, but they should have much richer reaction chemistry because of their unique conjugated structure. As shown in Scheme 1, when treated with a nuchleophile, 1,4-dicyano-1,3-butadienes **1** should have at least two reaction sites to be attacked by the nucleophile, e.g., 1,4-addition fashion (**I**) and 1,2-addition fashion (**II**), in the first step. When the substituents of **1** are alkyl groups, as we previously noted,[7] the 1,2-addition fashion (**II**) proceeded exclusively to afford pyridine derivatives or pyrroles. Suprisingly, during our continuous investigation into the reaction chemistry of various 1,4-dicyano-1,3-butadienes **1**, we found that a totally new structure of products was generated starting from 1,4-dicyano-1,4-bis(trimethylsilyl)-1,3-butadienes via 1,4-addition fashion (**I**) at the first nucleophilic attack.

Scheme 1. Reaction Patterns of 1,4-Dicyano-1,3-butadienes **1** with Nucleophiles



As shown in Table 1, 1,4-dicyano-1,4-bis(trimethylsilyl)-1,3-butadienes **1a**−**d**, which can be readily prepared,[8] reacted with $LiAlH_4$ affording their corresponding enaminonitrile cyclopentadienes **2a**−**d** in high isolated yields. Starting from **1a**, the enaminonitrile cyclopentadiene **2a** was formed in quantitative yield (entry1, Table 1), and its structure was confirmed by X-ray single-crystal analysis (Figure 1).

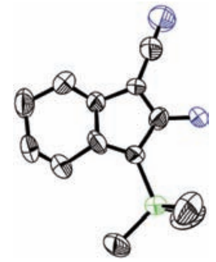


Figure 1. Single-crystal X-ray structure of **2a**. Hydrogen atoms are omitted for clarity.

Although complete conversion of **1b** was also observed, the enaminonitrile cyclopentadiene **2b** was isolated in a lower yield due to the undesired desilylation reaction during workup (entry 2, Table 1). The noncyclic substrates **1c**,**d** required a longer reaction time to afford the enaminonitrile cyclopentadienes in good yields of 71% and 74%, respectively (entries 3−4, Table 1). Of particular interest, similar cyclization forming an indene derivative **2e** in 84% isolated yield also occurred starting from the analogous substrate **1e** featuring an aromatic ring (entry 5, Table 1). A similar cyclopentadiene formation was also obtained from the reaction of **1a** with *n*-BuLi or MeLi (see the Supporting Information).

The formation of **2a**−**e** showed a cleavage of one $SiMe_3$−C bond besides the formation of the cyclopentadienyl ring and the reduction of one nitrile group to NH_2. To further investigate the reaction mechanism, deuterated $LiAlD_4$ was applied, and ***d*-2a** was isolated in 95% yield with D incoporation of more than 98% (Scheme 2).

On the basis of the above results, a plausible mechanism was proposed as outlined in Scheme 3. First, the nucleophile might selectively attack the β-carbon to CN (1,4-addition) to form the intermediate **A**, which underwent a second nucleophilic attack (intramolecular 1,2-addition) to form the intermediates **B** and/or **C**.[9] Then, hydrolysis of **C** completed

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(5) (a) Robinson, J. M.; Brent, L. W.; Chau, C.; Floyd, K. A.; Gillham, S. L.; McMahan, T. L.; Magda, D. J.; Motycka, T. J.; Pack, M. J.; Roberts, A. L.; Seally, L. A.; Simpson, S. L.; Smith, R. R.; Zalesny, K. N. *J. Org. Chem.* **1992**, *57*, 7352–7355. (b) Badia, L.; Baños, J. E.; Camps, P.; Contreras, J.; Görbig, D. M.; Muñoz-Torrero, D.; Simón, M.; Vivas, N. M. *Bioorg. Med. Chem.* **1998**, *6*, 427–440. (c) Booth, B. L.; Dias, A. M.; Proença, M. F.; Zaki, M. E. A. *J. Org. Chem.* **2001**, *66*, 8436–8441. (d) Macho, S.; Miguel, D.; Neo, A. G.; Rodríguez, T.; Torroba, T. E. *Chem. Commun.* **2005**, 334–336. (e) Gómez, T.; Macho, S.; Miguel, D.; Neo, A. G.; Rodríguez, T.; Torroba, T. E. *Eur. J. Org. Chem.* **2005**, 5055–5066.

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(8) The dienedinitriles **1a**−**d** were prepared through the substitution of the iodine atoms of the corresponding 1,4-diiodo-1,4-bis(trimethylsilyl)-1,3-dienes using CuCN (see the Supporting Information).

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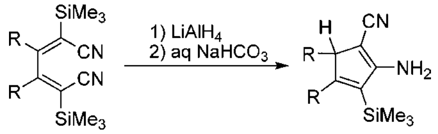
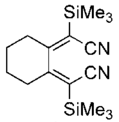
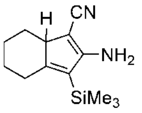
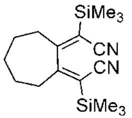
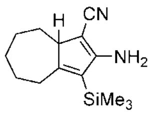
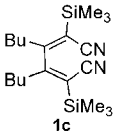
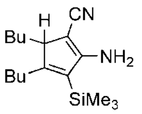
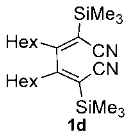
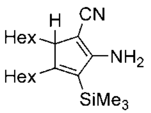
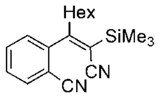
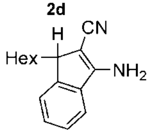
Table 1. Reaction of Different 1,4-Dicyano-1,4-bis(trimethylsilyl)-1,3-butadienes with $LiAlH_4$



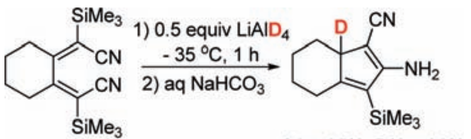
1 **2**

entry[a]	substrate	product	yield (%)[b]
1	 **1a**	 **2a**	97
2	 **1b**	 **2b**	56
3	 **1c**	 **2c**	71[c]
4	 **1d**	 **2d**	74[c]
5	 **1e**	 **2e**	84

[a] Reaction conditions: **1** (0.5 mmol), $LiAlH_4$ (0.25 mL, 0.25 mmol), E_2O (4 mL), -35 °C, 1 h. [b] Isolated yield based on **1**. [c] 4 h.

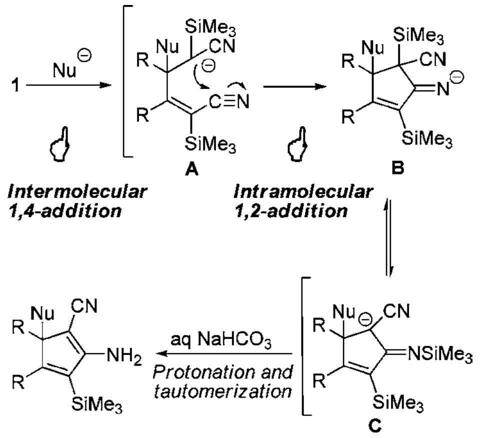
the formation of enaminonitrile cyclopentadienes. Here, a steric effect and the α-anion-stabilizing effect of the trimethylsilyl group[10] is supposed to be essential for the formation of intermediate **A**.

Scheme 2



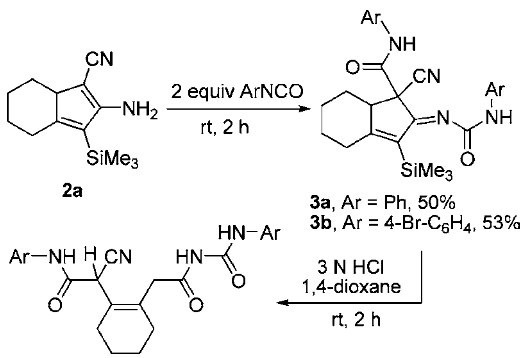
1a ***d*-2a**, 95%, D% > 98%

Scheme 3



Because of the introduction of cyano, amino, and trimethylsilyl groups, the cyclopentadienyl ring of compounds **2** was strongly polarized. The unique reactivity of these new cyclopentadienes is demonstrated by the direct reaction of **2a** with aryl isocyanates[11] (Scheme 4). The attack of two aryl isocyanate molecules on both the amino group and the carbon atom adjacent to CN group led to the formation of bis-addition products **3** with high selectivity. Moreover, the reaction proceeds smoothly without any base or other additives.

Scheme 4



3a, Ar = Ph, 50%
3b, Ar = 4-Br-C_6H_4, 53%

4a, Ar = Ph, 80%
4b, Ar = 4-Br-C_6H_4, 76%

Interestingly, with normal workup of the reaction mixture with aqueous 3 N HCl, C−C bond cleavage was observed. Then starting from **3a**,**b**, optimized hydrolysis condition with aqueous 3 N HCl in 1,4-dioxane at room temperature afforded the unexpected ring-opening products **4** in good yields, with survival of the cyano group. The structures of **3a** and **4b** were identified by single-crystal X-ray structral analysis (Figure 2).

Shown in Scheme 5 is a proposed mechanism for the unexpected reaction of **2** with aryl isocyanates. First, the amino group of **2a** reacted with one aryl isocyanate molecule

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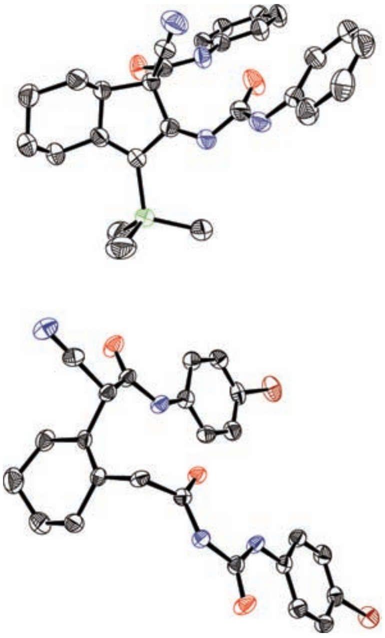
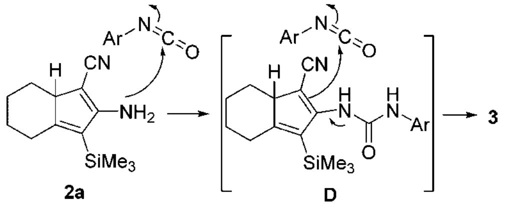


Figure 2. Single-crystal X-ray structures of **3a** (up) and **4b** (down). Hydrogen atoms are omitted for clarity.

to form the corresponding urea derivative **D**. Then the addition of β-carbon of the tautomeric enamine to another aryl isocynate molecule gave rise to **3**.

In conclusion, we have developed an unprecedented efficient method for the preparation of a variety of multifunctionalized cyclopentadienes of unique substituted patterns and interesting reaction chemistry. This new strategy highlights a novel highly selective 1,4-addition of hydride to the conjugated bis(trimethylsilyl) dienedinitriles. Moreover, the resulting new cyclopentadienes also exhibited an unexpected reactivity toward aryl isocyanates.

Scheme 5



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Supporting Information Available: Experimental details, spectroscopic data for synthetic compounds, and X-ray crystallographic data (CIF) for compounds **2a**, **3a**, and **4b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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