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Preparation of a Cycloheptane Ring from a 1,2-Diketone with High Stereoselectivity

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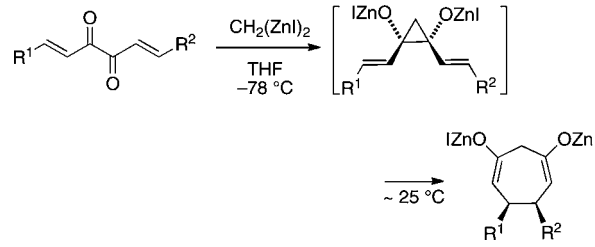
ABSTRACT



Treatment of 1,6-dialkylhexa-1,5-diene-3,4-diones with bis(iodozincio)methane gave zinc alkoxides of *cis*-5,6-dialkylcyclohepta-3,7-diene-1,3-diol in good yields at room temperature. The reaction proceeded with high stereospecificity. Bis(iodozincio)methane converted the diketone into the *cis*-divinylcyclopropane-1,2-diol stereoselectively; this diol transformed into the corresponding cycloheptane derivative stereospecifically via Cope rearrangement.

The Cope rearrangement of *cis*-divinylcyclopropane has been recognized as an efficient route to obtain a cycloheptane skeleton.[1,2] Despite its efficiency, the difficulty of the selective preparation of the *cis*-isomer of the substrate often causes the transformation to be less successful. Although some practical methods for the preparation of the *cis*-isomer have been shown,[3] most methods yielded the *trans*-isomers that require a temperature of over 100 °C to perform the Cope rearrangement.[4] During the course of our research concerning bis(iodozincio)methane (**1**), we found the nucleophilic cyclopropanation of 1,2-diketone, which gave *cis*-cyclopropane-1,2-diol stereoselectively.[5] The selectivity was rationalized by a computational method based on the face-to-face coordination of **1** with the diketone.[6] When the 1,6-dialkylhexa-1,5-diene-3,4-diones **2** were treated with **1**, the products would be zinc alkoxides of *cis*-divinylcyclopropane-1,2-diols **3**. The alkoxides of *cis*-divinylcyclopropane derivatives **3** would undergo Cope rearrangement more rapidly due to acceleration by the alkoxide groups (Scheme 1).[7] These two reactions can be performed sequentially without isolation.

A simple treatment of (1*E*,5*E*)-1,6-diphenylhexa-1,5-diene-3,4-dione (**2a**) at 0 °C with bis(iodozincio)methane (**1**) gave a messy mixture. As the Cope-rearrangement product is a zinc

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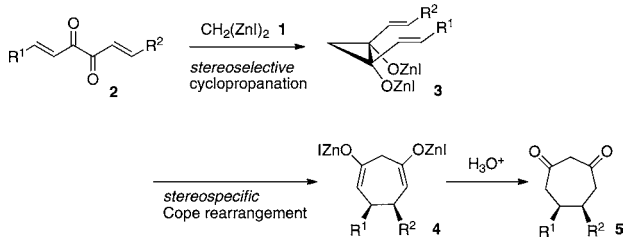
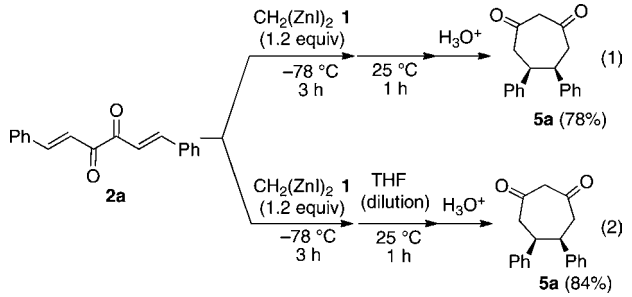
Scheme 1. Syntheses of Cycloheptane Derivatives



enolate **4** which may attack nucleophilically the substrate **2**, the first reaction, that is, the cyclopropanation of **2** with **1**, should complete before the start of the Cope rearrangement to prevent the side reactions. To realize this situation, we treated the diketone **2** with **1** at a low temperature for an appropriate period until the completion of cyclopropanation, and the resulting mixture was warmed to promote the Cope rearrangement. Actually, as shown in Scheme 2 (eq 1), (1*E*,5*E*)-1,6-diphenyl-

Scheme 2. Preparation of (5*R*,6*S*)-5,6-Diphenylcycloheptane-1,3-dione



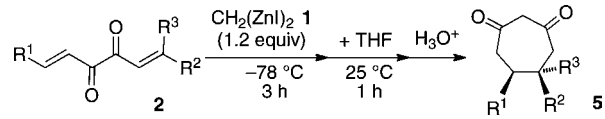
hexa-1,5-diene-3,4-dione (**2a**) was treated with **1** for 3 h at −78 °C, and the resulting mixture was warmed to 25 °C gradually to give the seven-membered ring **5a** in 78% yield.[8] Moreover, a dilution procedure improved the yield of **5a** up to 84% as shown in Scheme 2 (eq 2). As the rearrangement is an intramolecular reaction, the dilution did not affect the reaction rate and would suppress the side reactions which proceed intermolecularly.

Some examples of the preparation of cycloheptane-1,3-diones are shown in Table 1. Various cycloheptane-1,3-diones substituted with two aryl groups in *cis*-manner **5** were prepared and isolated in good yields (Table 1, entries 1−7). As substituents (R^1, R^2, R^3), an alkyl group did not disturb the reaction (Table 1, entries 8−11). These transformations were stereospecific. As shown in entries 8 and 9, the *cis*- and *trans*-isomers were obtained specifically depending on the *E*,*Z*-configuration of the substrate.

The intermediary zinc enolate corresponding to **4** in Scheme 1 was trapped with chlorotrimethylsilane and acetic

(8) The structure of **5a** was determined by a single-crystal X-ray analysis (see Supporting Information). The structure of the other products was detemined by analogy of the structure of **5a**.

Table 1. Various Examples of Preparation of Cycloheptane-1,3-diones[a]

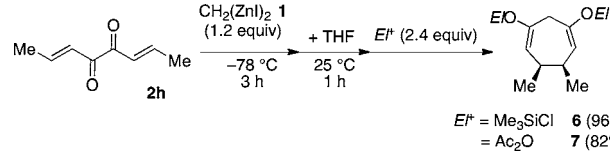


		2			
entry		R^1	R^2	R^3	**5** (yield %)[b,c]
1	**2a**	Ph	Ph	H	**5a** (84%)
2	**2b**	*p*-Tol	*p*-Tol	H	**5b** (93%)
3	**2c**	*p*-Anisyl	*p*-Anisyl	H	**5c** (98%)
4	**2d**	4-F-C_6H_4	4-F-C_6H_4	H	**5d** (47%)
5	**2e**	1-Naphtyl	1-Naphtyl	H	**5e** (41%)
6	**2f**	2-Furyl	2-Furyl	H	**5f** (78%)
7	**2g**	4-*t*-Bu-C_6H_4	4-*t*-Bu-C_6H_4	H	**5g** (96%)
8	**2h**	Me	Me	H	**5h** (99%)
9	**2i**	Me	H	Me	**5i** (65%)
10	**2j**	Me	Ph	H	**5j** (88%)
11	**2k**	Me	Me	Me	**5k** (86%)

[a] The reaction was performed with the following scale: **1** (1.2 mmol, 0.35 M THF solution), **2** (1.0 mmol in 5 mL of THF). After 3 h at −78 °C, 10 mL of THF (25 °C) was added in one portion. [b] Isolated yields. [c] The diastereomer was not detected.

anhydride. As shown in Scheme 3, after treatment of **2h** with bis(iodozincio)methane (**1**) at −78 °C for 3 h and at 25 °C

Scheme 3. Trapping of Intermediary Zinc Enolates with Chlorotrimethylsilane and Acetic Anhydride



for 1 h after an addition of THF, chlorotrimethylsilane was added. The corresponding silyl enol ether **6** was isolated in 96% yield. Acetylation also worked efficiently to give the corresponding enol acetate **7** in 82% yield.

Thus, we can show an efficient and facile route to cyclopropane-1,3-dione derivative **5** starting from **2**. The preparation of 1,2-diketone **2** was accomplished easily by the reported procedures.[9] The further transformations of enol derivatives **6** and **7** would give the more substituted cycloheptane derivatives with high stereoselectivities.

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Supporting Information Available: Experimental procedures including spectroscopic and analytical data. This material is available free of charge via the Internet at http://pubs.acs.org.

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