

2,5-Cyclohexedienones. 4. Reactions of 4-Bromo-2, 4, 6-tri-tert-butyl-2, 5-cyclohexadien-1-one with Glycols

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2,5-Cyclohexedienones. 4. Reactions of 4-Bromo-2,4,6-tri-*tert*-butyl-2,5-cyclohexadien-1-one with Glycols

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Reactions of 4-bromo-2, 4, 6-tri-*t*-butyl-2, 5-cyclohexadien-1-one (**1**) with ethylene glycol (**2a**), and di-(**2b**) and triethylene glycol (**2c**) were carried out under various conditions. Pyridine can act as a good catalyst for the preparation of the corresponding dienoxo alcohols (**3a-c**). However, ω , ω' -bis (4-oxo-2, 5-cyclohexadien-1-yl) ethers (**4a-c**) were obtained in considerable yields only when α -picoline was used as a catalyst.

In a series of papers, we have shown, as illustrated in Scheme 1 below, a new and convenient method for the selective preparation of *o*- and *p*-substituted phenols by utilizing a reaction of 4-bromo-2, 4, 6-tri-*tert*-butyl-2, 5-cyclohexadien-1-one (**1**)¹⁾, which can be easily prepared by a bromination of 2, 4, 6-tri-*t*-butylphenol (**5**), with nucleophilic reagents such as sodium phenolate²⁾, amines³⁾, alcohols⁴⁾, and pyridines⁵⁾.

In this paper is reported the reaction of **1** with ethylene glycol (**2a**) and di-(**2b**)-and triethylene glycol (**2c**). The results are summarized in Scheme 2 and the Table 1.

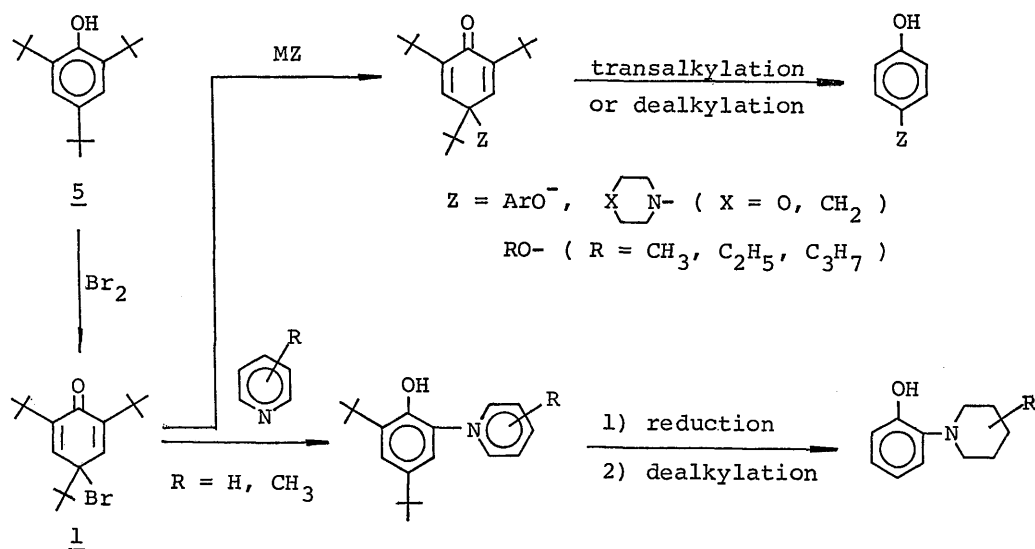
When dienone (**1**) was heated in a large excess amount of glycol (**2**) under a stream of nitrogen with stirring at 110°C (bath temperature) in the presence of pyridine (in the molar ratio of 2 : 1 to **1**), the corresponding dienoxo alcohol (**3**) was obtained in ca. 70 % yield. It was also found that ω , ω' -bis (4-oxo-2, 5-cyclohexadien-1-yl) ethers **4a** and **4b** were obtained in poor yields as minor products in the cases of **2a** and **2b**, respectively, but not from **2c**, even though

these reactions were carried out in a large excesses of glycols⁶⁾. Furthermore, an interesting phenomenon was observed when the reactions were carried out without stirring, namely, the yields of **4a** and **4b** increased from 0.4 % to 19 % and from 0.1 % to 6 %, respectively. In the case of **2c**, however, there was identified scarcely any corresponding compound **4**, even without stirring. It is not yet completely clear why such different results are obtained, but we might say that the difference may be due to the solubility of **1** in glycols used, since **1** is only slightly soluble in **2a**, somewhat soluble in **2b**, but easily soluble in **2c** under the reaction conditions.

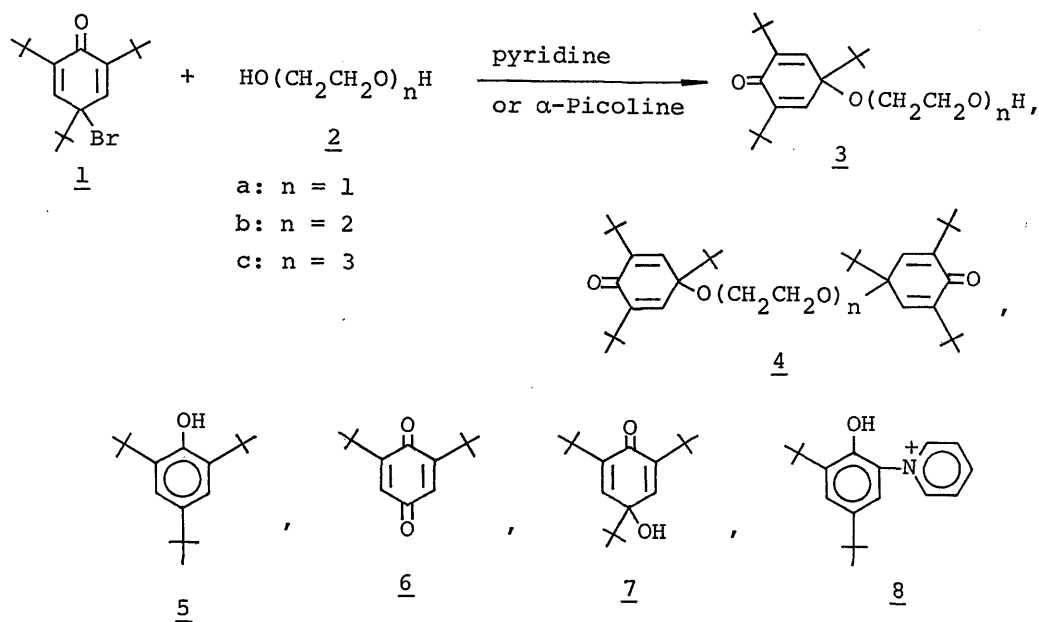
The structures of the products **3a-3c**, **4a** and **4b** are fully supported by their elemental analysis, ¹H-nmr, ir- and mass spectra.

It has already been reported⁴⁾ that the reaction of **1**, **2a** and pyridine in molar ratio 1 : 1-2 : 2, where the possibility for the formation of **4a** seemed to be preferred judged by the molar ratio, afforded the unexpected product, 1-(3, 5-di-*t*-butyl-2-hydroxyphenyl)pyridinium bromide (**8**) in yield of 43 % together with **5**, 2, 6-di-*tert*-butylbenzoquinone

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Scheme 1



Scheme 2

(6) and 2, 4, 6-tri-*t*-butyl-4-hydroxy-2, 5-cyclohexadien-1-one (7) as minor products, but not 4a. It was now, however, found that in this reaction when α -picoline was used instead of pyridine, the expected product 4a could be obtained

in yield of 38% besides 3a, 5, 6 and 7 in 38, 0.1, 2 and 2% yields, respectively. And it was observed in the case of 2b that on the formation of 4b, the yield increased from 6% to 10% (see run 5 and 6). Furthermore, it was observed

Table 1. Reaction of 4-Bromo-2, 4, 6-tri-*t*-butyl-2, 5-cyclohexadien-1-one (**1**) with Glycols in the Presence of Pyridine^{a)}.

Run	2	Products (Yield, %) ^{b)}
1	a	3a (70), 4a (0.4), 5 (0.1)
2 ^{c)}	a	3a (50), 4a (19), 5 (4)
3 ^{d)}	a	3a (34), 4a (38), 5 (0.1), 6 (2), 7 (2)
4	b	3b (68), 4b (0.1), 5 (7)
5 ^{c)}	b	3b (64), 4b (6), 5 (7)
6 ^{d)}	b	3b (44), 4b (10), 5 (19), 6 (0.9), 7 (13)
7	c	3c (73), 5 (4)
8 ^{c)}	c	3c (72), 5 (5)
9 ^{d)}	c	3c (51), 4c (7), 5 (20), 6 (1.4), 7 (5.4)
10 ^{e)}	a	3a (23), 5 (17), 6 (0.9), 7 (5), 8 (45)

a) All reactions were carried out in the conditions where a mixture of **1** (6.8 g, 20 mmoles), glycol (**2**) (50 ml) and pyridine (3.4 ml, 40 mmoles) were heated in an oil bath at ca. 110°C for 6hr under nitrogen atmosphere with stirring magnetically, unless otherwise indicated.

b) The yields, based on **1**, isolated were shown.

c) Without stirring.

d) α -Picoline instead of pyridine was used in this case, the molar of **1**, **2** and α -picoline = 1 : 2 : 2.

e) From M. Tashiro and G. Fukata, *Heterocycles*, **12**, 1551 (1979).

in the case of **2c** that **4c**, which had not been formed under any other conditions where pyridine was used, could be obtained in yield of 7 % besides the other products. Such interesting difference between pyridine and α -picoline on the formation of **4** might reflect steric factors around the nitrogen atoms on their rings.

EXPERIMENTAL

All melting points are uncorrected. IR spectra were measured on a Nippon Bunko IR-A spectrophotometer as KBr pellets or as liquid films on NaCl pellets. ¹H-NMR spectra were determined at 60 MHz on a Hitachi R-20 spectrometer with TMS as an internal reference. Mass spectra were recorded on a Hitachi R-4 mass spectrometer at 70 eV using a direct inlet system.

General Procedure for the reaction of 1 with Glycol.-A (Run 1, 2, 4, 5, 7 and 8): A mixture of **1** (6.8 g, 20 mmoles), glycol (**2**) (50 ml) and pyridine (3.4 ml, 40 mmo-

les) were heated in an oil bath at ca. 110°C for 6hr under nitrogen atmosphere with stirring (or without stirring). After the reaction mixture was cooled down to room temperature, it was extracted with benzene (3×100 ml). The benzene layer was washed with water and after dried it with sodium sulfate, it was evaporated in vacuo to leave a residue. The residue was washed with cold methanol to give compound **4** as crystals. The residue, which was leaved by evaporation of the methanol, was subject to column chromatography on silica-gel (Wako gel C-300) using at first hexane (A) and then benzene (B) and finally ethyl acetate (C) as eluents. Compounds **5** and **6** were obtained from fraction A, **7** and **4** were isolated from fraction B and all of **3** was eluted from fraction C. **B (Run 3, 6 and 9):** A mixture of **1** (3.4 g, 10 mmole), glycol (**2**) (20 mmole) and α -picoline (1.86 g, 20 mmole) was treated and worked up as described above.

Physical and spectral data of the pro-

ducts are as the following. The yields of the products are shown in Table.

2-(1, 3, 5-tri-*t*-Butyl-4-oxo-2, 5-cyclohexadien-1-oxy) ethanol (3a): viscous colorless oil, IR (NaCl): 3450, 1665, 1645, 1635 (sh) cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 0.95 (s, 9H), 1.26 (s, 18H), 2.0 (b, 1H; disappeared with D_2O), 3.35, 3.70 (each t, 2H, $J=6\text{ Hz}$), 6.55 (s, 2H). Mass spectrum m/e : 322 (M^+).

Anal. Calcd for $\text{C}_{20}\text{H}_{34}\text{O}_2 \cdot 1/3\text{H}_2\text{O}$: C, 73.13; H, 10.64.

Found: C,

73.27; H, 10.48.

3-Oxa-5-(1, 3, 5-tri-*t*-butyl-4-oxo-2, 5-cyclohexadien-1-oxy) pentanol (3b): viscous colorless oil, IR (NaCl): 3450, 1665, 1645 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 0.95 (s, 9H), 1.25 (s, 18H), 2.16 (b, 1H; disappeared with D_2O), 3.36–3.76 (m, 8H), 6.56 (s, 2H). Mass spectrum m/e : 366 (M^+). Anal. Calcd for $\text{C}_{22}\text{H}_{38}\text{O}_4 \cdot 1/3\text{H}_2\text{O}$: C, 70.93; H, 10.46.

Found: C,

71.02; H, 10.30.

3, 6-Dioxa-8-(1, 3, 5-tri-*t*-butyl-4-oxo-2, 5-cyclohexadien-1-oxy) octanol (3c): viscous colorless oil, IR (NaCl): 3450, 1665, 1645 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 0.93 (s, 9H), 1.22 (s, 18H), 2.50 (b, 1H; disappeared with D_2O), 3.30–3.80 (m, 12H), 6.56 (s, 2H). Mass spectrum m/e : 410 (M^+). Anal. Calcd for $\text{C}_{24}\text{H}_{42}\text{O}_5 \cdot 1/3\text{H}_2\text{O}$: C, 69.19; H, 10.32.

Found: C, 69.39; H, 10.10.

1, 2-Bis (1, 3, 5-tri-*t*-butyl-4-oxo-2, 5-cyclohexadien-1-oxy) ethylene (4a): mp 168.5–170 °C, colorless prisms (MeOH). IR (KBr): 1665, 1645 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 0.95 (s, 18H), 1.24 (s, 36H), 3.32 (s, 4H), 6.50 (s, 4H). Mass spectrum m/e : 582 (M^+).

Anal. Calcd for $\text{C}_{38}\text{H}_{62}\text{O}_4$: C, 78.30; H, 10.72.

Found: C, 78.16; H,

10.80.

1, 5-Bis (1, 3, 5-tri-*t*-butyl-4-oxo-2, 5-cyclohexadien-1-oxy)-3-oxa-pentane (4b): mp 84.5–85.0 °C, colorless plates (MeOH- H_2O). IR (KBr): 1665, 1645 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 0.96 (s, 18H), 1.26 (s, 36H), 3.43, 3.67 (each m, 4H), 6.62 (s, 4H). Mass spectrum m/e : 626 (M^+). Anal. Calcd for $\text{C}_{40}\text{H}_{66}\text{O}_5$: C, 76.63; H, 10.61.

Found: C, 76.54; H, 10.64.

1, 8-Bis (1, 3, 5-tri-*t*-butyl-4-oxo-2, 6-cyclohexadien-1-oxy)-3, 6-dioxaoctane (4c): mp 77–78 °C, colorless prisms (MeOH- H_2O). IR (KBr): 1665, 1645 cm^{-1} . $^1\text{H-NMR}$ (CDCl_3): δ 0.92 (s, 18H), 1.22 (s, 36H), 3.38, 3.60 (each t, 4H, $J=5\text{ Hz}$), 3.66 (s, 4H), 6.52 (s, 4H). Mass spectrum m/e : 670 (M^+).

Anal. Calcd for $\text{C}_{42}\text{H}_{70}\text{O}_6$: C, 75.18; H, 10.52.

Found: C, 75.27; H,

10.64.

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- 5) M. Tashiro and G. Fukata, *Heterocycles*, **12**, 1551 (1979).
- 6) When equimolecular amount of ethylene glycol to one mole of **1** was used in the presence of pyridine, the unidentified compound was obtained but not **4a**.