

Cyclohexadienones. 2. Silver Perchlorate-Induced Reaction of 4-Halocyclohexadienones Affording Rearrangement Products.

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Cyclohexadienones. 2.

Silver Perchlorate-Induced Reaction of 4-Halocyclohexadienones Affording Rearrangement Products.¹

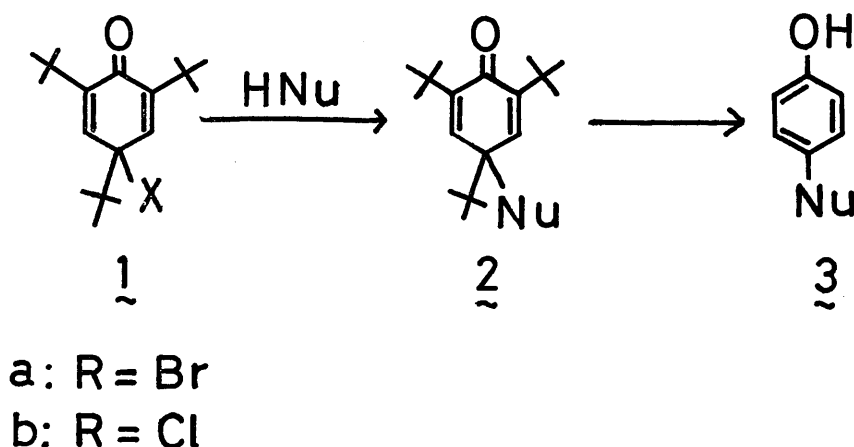
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(received September 29, 1984)

Treatment of 4-bromo-(**1a**), 4-chloro-2, 4, 6-tri-tert-butyl-(**1b**), 2, 4-dibromo-4, 6-di-tert-butyl-(**1c**), and 2-chloro-4-bromo-4, 6-di-tert-butyl-2, 5-cyclohexadien-1-one(**1d**) with silver perchlorate in benzene afforded various phenols produced via rearrangement of atom migration, dehalogenation and/or de-tert-butylation. When **1b** was treated with trifluoroacetic acid or silica gel in benzene, 2-chloro-4, 6-di-tert-butylphenol was obtained in good yield. Similarly, treatment of **1a** with trifluoroacetic acid afforded 2-bromo-4, 6-di-tert-butylphenol. However, when **1a** was column chromatographed on silica gel using benzene as an eluent, 2, 4, 6-tri-tert-butylphenol was formed in good yield.

It has been previously reported that 4-halo-2, 4, 6-tri-tert-butyl 1, 2, 5-cyclohexadien-1-ones (**1**) react with some nucleophiles in the presence or absence of base to give the corresponding 4-substi-

tuted cyclohexadienones (**2**) which are converted to the corresponding 4-substituted phenols (**3**) by Lewis acid-catalyzed trans-tert-, butylation or de-tert-butylation (**Scheme 1**)²⁻⁴.



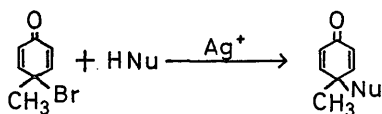
Scheme 1

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Nilson et al., reported that 4-chloro-4-methyl-2,5-cyclohexadien-1-one reacted with nucleophiles in the presence of silver cation to give the corresponding dienones (Scheme 2⁵⁾).



Scheme 2

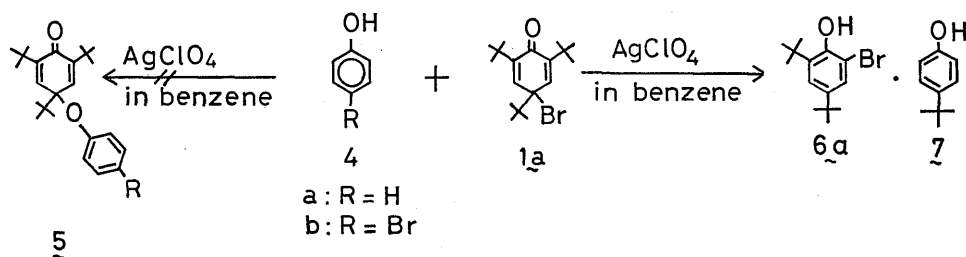
This result suggests that compound 1 may react with nucleophiles in the presence of silver perchlorate to give in good yield the corresponding 4-substituted dienones 2 which are suitable starting materials for the preparation of 4-substituted phenols 3. However, we found that the reaction of 1a with phenols in the presence of silver perchlorate did not give the expected compound but gave products resulting from rearrangement of the bromo substituent and de-tert-butylation. Similar rearrangement and

de-tert-butylation of other halocyclohexadienones having tert-butyl substituents were observed on treatment of them with silver perchlorate, trifluoroacetic acid and silica gel.

Results and Discussion

Treatment of Halocyclohexadienones with Silver Perchlorate

Reaction of 1a with phenol (4a) or 4-bromophenol (4b) in the presence of silver perchlorate was carried out under various conditions. The results are summarized in Table 1 and Schme 3. As shown in the Table, reaction of 1a with 4a or 4b in the presence of silver perchlorate in benzene did not afford the expected 5a or 5b but unexpected 6a was obtained in good yield. Treatment of 1a with silver perchlorate in absence of 4a or 4b in benzene gave 6a. It should be noted that a very small amount (1-10 mole% to 1a) of silver perchlorate could catalyze the conversion

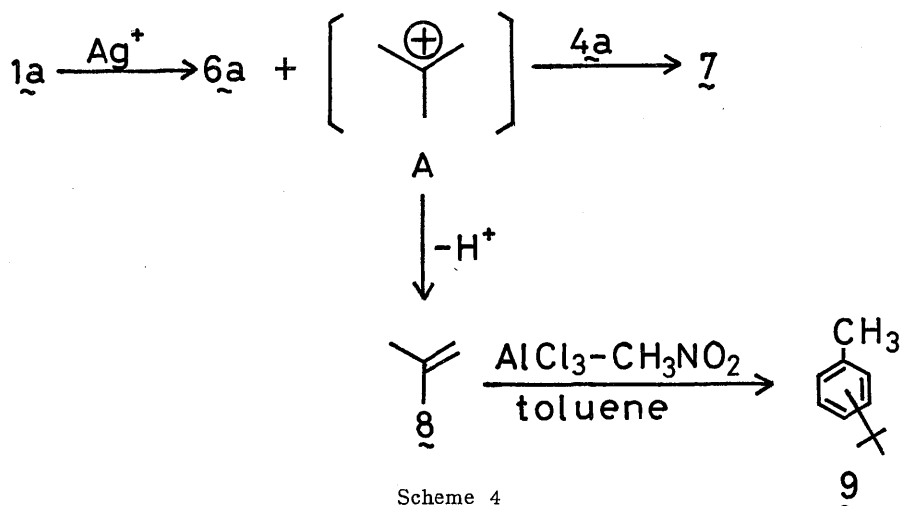


Scheme 3

Table 1 Reaction of 4-bromo-2,4,6-tri-tert-butyl-2,5-cyclohexadien-1-one (1a) with Phenols 4a and 4b in the presence of silver perchlorate in Benzene^{a)}.

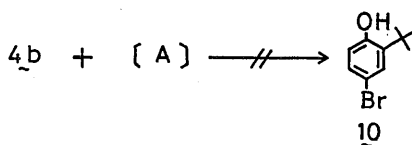
Run	Phenol	AgClO ₄ /1a (mole/mole)	Time, h	Product (%)
1	4b	1	1	6a (42)
2	4b	0.01	5	6a (72)
3	4a	0.1	1.5	6a (82), 7 (13)
4	...	0.1	1.5	6a (60)

a) Reaction was carried out under a stream of nitrogen at room temperature; The molar ratio of 1a: 4=1:1. b) Isolated yields.



of **1a** to **6a**.

When the gaseous component generated during the silver perchlorate-induced reaction of **1a** without **4a** was introduced by a nitrogen stream into toluene containing a small amount of aluminum chloride-nitromethane as a catalyst, the formation of tert-butyltoluenes **9** was detected by a G.C. analysis of the toluene solution after the reaction was finished. This finding suggests that the tert-butyl cation was generated in the silver perchlorate-induced reaction of **1a**, and it reacts with **4a** to afford **7** and is deprotonated to give isobutylene **8**. 2-tert-Butyl-4-bromophenol (**10**) was not formed in the reaction of **1a** with **4b** since **4b** might be less reactive to the cation A than **4a**.

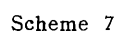
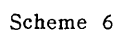


Similar silver perchlorate-induced reaction of 4-chloro-2, 4, 6-tri-tert-butyl-

(**1b**), 2, 4-dibromo-4, 6-di-tert-butyl-(**1c**) and 2-chloro-4-bromo-4, 6-di-tert-butyl-2, 5-cyclohexadien-1-one (**1d**) was carried out in the presence of 10 mole% of the catalyst at room temperature for 1 h. The results are summarized in Scheme 6. This silver perchlorate-induced reaction of **1a** afforded **6b** together with de-tert-butylated compound **11** and de-chlorinated product **12**. Formation of **11** suggests that direct de-tert-butylation occurs without rearrangement of the chloro substituent. In the case of **1c**, **13a** and debrominated compound **6a** were obtained. However, the reaction of **1a** did not give the expected **13b** but only dechlorinated compound **6a** and de-tert-butylated compound **14**. This means that rearrangement of the chloro substituent did not occur.

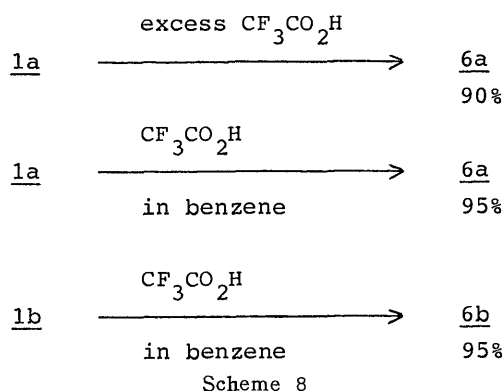
The above results indicate that the chloro substituent is less removable from the position 4 to the position 2 of halocyclohexadienones than a bromo substituent under the conditions used.

Although the detailed reaction pathway is still obscure, the following path



way tentatively proposed (Scheme 7). Compound **1** might convert to the isomeric 2, 4-cyclohexadienone **1'**. The silver cation attacks the carbonyl oxygen atom of **1** and **1'** to afford the intermediates B and F, respectively. From these intermediates, the corresponding phenols are formed by de-tert-butylation. Compounds **12** and **6a** are probably produced from **1b** and **1c**, respectively, through the intermediate E when the reaction mixture was quenched with water after the reaction was finished, although there is no evidence for this.

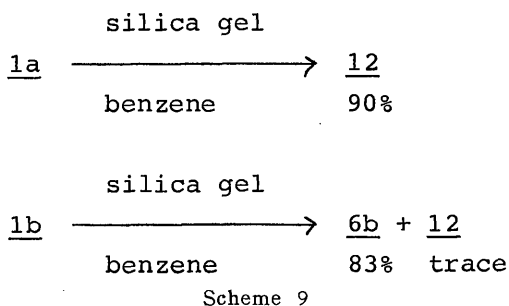
The above results suggested that when **1** was treated with a protic acid, rearrangement of the halogen atom position 4 to position 2 and de-tert-butylation might occur as in the silver cation-induced reaction. Indeed, Rieker and Zeller reported that treatment of **1a** with excess trifluoroacetic acid afforded **6a** in good yield⁶. When **1a** and **1b** were treated with 1/2 equivalent amount of the acid in benzene, **6a** and **6b** were formed in good yield, respectively.



The silver perchlorate- and the acid-induced reaction of **1a** afforded the same product **6a** as shown in Scheme 8. However, the acid-induced reaction of **1b** gave only **6b** in good yield, although the

silver perchlorate-induced reaction of it afforded a mixture of **6b**, **11** and **12** as described above. This results suggest that the chloro substituent of **1b** is more easily rearranged from position 4 to position 2 under the conditions using trifluoroacetic acid rather than with silver perchlorate.

It was also found that column chromatographies of **1a** and **1b** using silica-gel with benzene gave **12** and a mixture of **6b** and small amount of **12**, respectively.



It should be noted that acid catalyzed reaction of **1** with the different catalysts such as silver perchlorate, trifluoroacetic acid, and silica-gel afforded different products.

However, it is still obscure why such different results were obtained by changing the reaction conditions.

Experimental Section

All melting points are uncorrected. IR spectra were measured by a Nippon Bunko IR-A spectrometer as KBr pellets. ¹H-NMR spectra were recorded on a Nihon Denshi JEOL FT-100 spectrometer with Me₄Si as an internal reference. Gas chromatographic analyses were carried out by a Yanagimoto Yanaco G-180 (30 % high-vacuum silicone grease; 2 m; carrier gas, N₂ 1 kg/cm²).

Preparation of Halocyclohexadienones

(1).—The halocyclohexadienones (1) used in the present work were prepared according to Pearson's procedure⁷.

1a: Pale yellow prisms (Hexane), mp 81–82°C; lit⁹. 80°C.

1b: Pale yellow prisms (Hexane), mp 93–94°C; lit⁷. 94–95°C.

1c: Pale yellow prisms, mp 102–103°C; lit⁹. 101–102°C.

1d: Colorless prisms, mp 75–77°C; IR (KBr) 1,660, 1,635 cm⁻¹; ¹H-MNR (CDCl₃) δ 1.12, 1.24 (each 9H, s), 6.82, 7.38 (each aH, d, J=3Hz).

Compound **1d** was so unstable that it could be purified only by washing with cold methanol but could not be recrystallized.

Reaction of Halocyclohexadienones (1).**Catalyzed by Silver perchlorate. Typical**

Procedure: To a solution of **1a** (2.5 g, 7.32 mmol) and **2a** (690 mg, 7.33 mmol) in dry benzene (20 ml) was added silver perchlorate (150 mg, 0.72 mmol) at room temperature under an atmosphere of oxygen-free nitrogen gas. After the reaction mixture was stirred for 1 h (until **1a** was not detectable by T.L.C.), the precipitates formed were filtered off. Then, the filtrate was washed with water, dried over sodium sulfate and evaporated *in vacuo* to leave the residue which was chromatographed on a silica gel column using hexane as an eluent to give **4a** and **5a** in 82% and 13% yields, respectively.

4a: mp 56–57°C, lit¹⁰. 57–58°C.

5: mp 97–98°C, lit¹¹. mp 97°C.

4b: Colorless oil, lit¹². mp 97°C.

11: mp 74–75°C, lit¹³. mp 75–76°C.

12: mp 131–132°C, lit¹⁴. mp 131°C.

13: mp 78–79°C, lit¹⁵. mp 77–79°C.

Formation of tert-butyltoluenes (**9**) was

confirmed by the following experiment.

To a solution of **1a** (2.5 g, 7.32 mmol) in dry benzene (20 ml) was added silver perchlorate (150 mg, 0.72 mmol) at room temperature under an atmosphere of oxygen-free nitrogen gas. The gaseous component generated during the reaction was introduced by nitrogen gas stream into the toluene (30 ml) solution containing aluminum chloride (700 mg, 5.3 mmol) and nitromethane (1.5 ml). After the reaction mixture was stirred for 30 min, it was worked up as described above to give 1.25 g (60%) of **4a**. The toluene solution was poured into a large amount of ice-water and extracted with toluene. The extract was washed with water, dried over sodium sulfate and evaporated *in vacuo* to leave the residue. Compounds **9** were detected by a G.C. analysis of the residue.

Reaction of 1 Catalyzed by CF₃CO₂H.

Typical Procedure: To a solution of **1a** (680 mg, 2 mmol) in benzene (20 ml) was added a solution of CF₃CO₂H (110 mg, 1 mmol) in benzene (5 ml) at room temperature. After the reaction mixture was stirred for 3 h, it was poured into a large amount of ice-water. The organic layer was extracted with benzene, washed with water, dried over sodium sulfate and evaporated *in vacuo* to leave the residue. The residue was column chromatographed on silica-gel using hexane as an eluent to give **4a**: yield 540 mg (95%).

Reaction of 1. Catalyzed by Silica-gel.

Typical Procedure: Compound **1a** (500 mg) was column-chromatographed on silicagel (Wako C-300) using benzene as an eluent to give **2**, **4**, **6**-tri-tert-butylphenol (**12**): yield 345 mg (90%).

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