

Note

Intramolecular Büchner Reaction and Oxidative Aromatization with SeO₂ or O₂

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Intramolecular Büchner reaction of 1-diazo-5-phenylpentan-2-ones followed by oxidation with SeO₂ or O₂ in the presence of silica gel regioselectively gave 8-formyl-1-tetralones or one-carbon-lacking 1-tetralones, respectively.

Key words Büchner reaction; cycloheptatriene; oxidative aromatization; selenium dioxide; dioxygen

Introduction

Intra- or intermolecular addition of diazo compounds with aromatic compounds gave cycloheptatrienes (CHTs) and norcaradienes by cyclopropanation and reversible electrocyclic ring opening (Büchner reaction).^{1,2)} Recently, CHTs have been utilized in organic synthesis as a source of carbene species by Au-catalyzed retro-Büchner reaction.^{3–9)} For broadening the synthetic utility of CHTs, we envisioned that the combination of Büchner reaction of **1** and aromatization of CHT **2** or an isomerized CHT **3** would provide a new methodology for synthesis of substituted arenes **4** (Chart 1). Besides retro-Büchner reaction, oxidative aromatization of CHTs has been reported to date.¹⁰⁾ For example, sensitized photooxidation of CHT with O₂^{11,12)} gave benzaldehyde in a trace amount.^{13,14)} Oxidation of excess CHT with chromium trioxide in acetic acid gave benzaldehyde in 19.5% yield.¹⁵⁾ Ceric ammonium nitrate (CAN) oxidized CHT to afford benzaldehyde (80%), benzene (18%), and carbon monoxide.¹⁶⁾ Also, treatment of CHT with phenyliodine(III) bis(trifluoroacetate) (PIFA) afforded benzaldehyde quantitatively.¹⁷⁾ In addition, a few examples of oxidation of substituted CHTs to aromatic compounds have been reported. Yagihara and colleagues reported that *o*-substituted benzaldehydes **5** were formed in up to 14% yields by photooxygenation of 7-substituted CHTs¹⁸⁾ (Chart 2a). Celik and Balci reported that a reaction of substituted CHTs with singlet oxygen gave an aromatic compound **7** in addition to a [4 + 2] adduct **6**¹⁹⁾ (Chart 2b). We report here oxidative aromatization of intramolecular Büchner adducts, with selenium dioxide or O₂ in the presence of silica gel.

Results and Discussion

Cycloheptatriene **2a** was prepared by intramolecular Büchner reaction of 1-diazo-5-phenylpentan-2-one (**1a**) with a catalytic amount of Rh₂(OAc)₄ in refluxing dichloromethane. Since many products were formed during purification of **2a** with column chromatography on silica gel, a crude product of **2a** was oxidized by using various oxidizing agents (Table 1). Two-step yields of aromatic compounds based on **1a** are shown in Table 1 when oxidation of **2a** was carried out. Enone **2a'** was isolated in 54% yield for two steps from **1a** as a stable compound by treatment of **2a** with alumina. In the case of oxidation of **2a'**, one-step yields of aromatic compounds based

on **2a'** are shown in Table 1.

Oxidation of CHT **2a** and a conjugated CHT **2a'** with CAN did not provide either **8a** or **9a** and gave a complex mixture (entries 1 and 2). Aromatic compounds **8a** and **9a** were not detected in a crude product by oxidation of **2a** with PIFA¹⁷⁾ (entry 3), while oxidation of **2a'** with PIFA gave **8a** (4%), **9a** (4%), and 6-formyl-1-tetralone (18%) (entry 4).²⁰⁾

Treatment of a crude **2a** with three equivalents of SeO₂²¹⁾ at room temperature (r.t.) for 1 d gave an aldehyde **8a** in 60% yield along with a trace amount of **9a** (entry 5). Oxidation of the crude **2a** with 1.1 eq of SeO₂ at r.t. for 1.5 d gave **8a** in a lower (32%) yield. When the same oxidation was carried out in refluxing CH₂Cl₂ by using 1.1 eq of SeO₂ for 1 d, **8a** was obtained in 38% yield. Thus, three equivalents of SeO₂ were

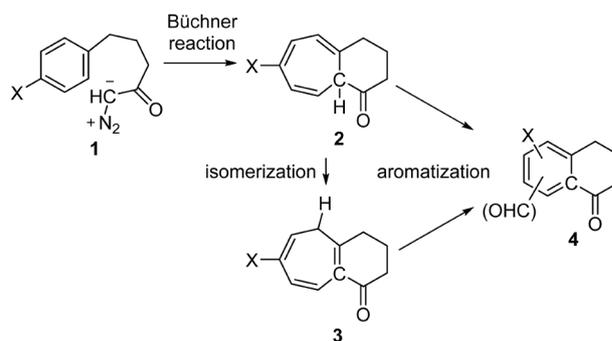


Chart 1. Synthesis of Substituted Arenes by Intramolecular Büchner Reaction, Isomerization, and Aromatization

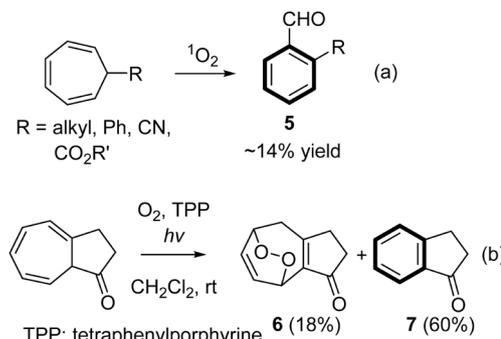
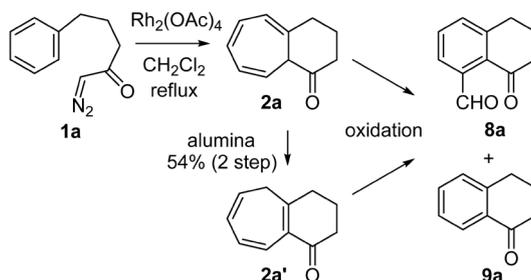


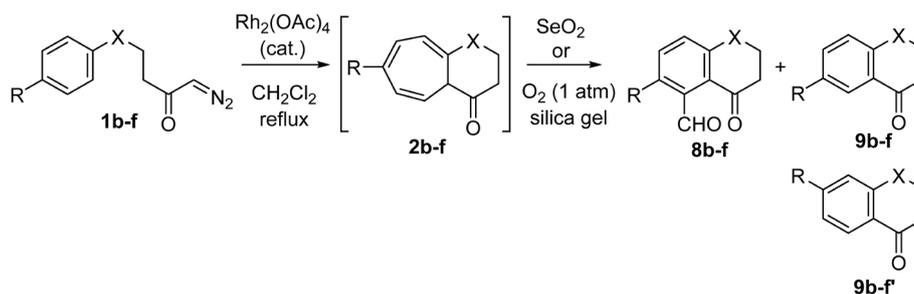
Chart 2. Reported Examples for Oxidative Aromatization of CHTs

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Table 1. Oxidation of **2a** and **2a'**

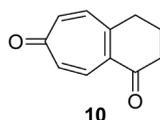
Entry	Substrate	Oxidation	8a (%) ^{d)}	9a (%) ^{d)}
1	2a (71) ^{b)}	CAN (4 equiv), MeCN, reflux, 2 h	0	0
2	2a'	CAN (4 equiv), MeCN, reflux, 5 h	0	0
3	2a (67) ^{b)}	PIFA (1.3 equiv), CH ₂ Cl ₂ , reflux, 18 h	0	0
4	2a'	PIFA (1.3 equiv), CH ₂ Cl ₂ , reflux, 18 h	4 ^{c)}	4
5	2a (93) ^{b)}	SeO ₂ (3 equiv), CH ₂ Cl ₂ , r.t., 1 d	60 ^{d)}	trace
6	2a'	SeO ₂ (3 equiv), CH ₂ Cl ₂ , r.t., 1 d	NR ^{e)}	NR ^{e)}
7	2a (76) ^{b)}	O ₂ , silica gel, CH ₂ Cl ₂ , r.t., 2 d	trace	39 ^{f)}
8	2a'	O ₂ , silica gel, CH ₂ Cl ₂ , r.t., 2 d	NR ^{e)}	NR ^{e)}

a) Isolated yields. b) Yield of **2a** by determination with ¹H-NMR using 1,3,5-trimethoxybenzene or 4,4'-di-*t*-butyldiphenyl as an internal standard. c) 6-Formyl-1-tetralone was also obtained in 18% yield. d) 5-Formyl-1-tetralone (<7%) and 6-formyl-1-tetralone (1%) were also obtained. e) No reaction. f) Yield for two steps from **1a**.

Table 2. Oxidation of Büchner Products **2** with SeO₂ or O₂

Entry	R	X	1	2 (% yield ^{a)})	Oxidation ^{b)}	8 (% yield ^{c)})	9 + 9' (% yield ^{c)})	9/9'
1	Ph	CH ₂	1b	68 (70) ^{e)}	SeO ₂	48 (22) ^{e)}	7 (12) ^{e)}	>10:1 (8:4) ^{e)}
2			1b	74	O ₂ , silica gel	2	20	14:6
3	Me	CH ₂	1c	72	SeO ₂	38	trace	—
4			1c	78	O ₂ , silica gel	3	25	19:6
5	MeO	CH ₂	1d	63	SeO ₂	<7 ^{f)}	0	—
6			1d	77	O ₂ , silica gel	trace	8	5:3
7	AcO	CH ₂	1e	58	SeO ₂	33	1	9e only
8			1e	56	O ₂ , silica gel	<13	20	16:4
9	H	NCbz	1f	87	SeO ₂	36	4	—
10			1f	83	O ₂ , silica gel	4	31	—

a) Determined by ¹H-NMR using 1,3,5-trimethoxybenzene or 4,4'-di-*t*-butyldiphenyl as an internal standard. b) Reaction conditions of oxidation with SeO₂: SeO₂ (3 equiv), CH₂Cl₂, 1 d. Reaction conditions of oxidation with O₂: O₂, silica gel, CH₂Cl₂, r.t., 2 d. c) Isolated yield for two steps from **1**. d) Oxidation was carried out by using O₂ in the absence of silica gel (CH₂Cl₂, r.t., 2 d). e) A catalytic oxidation using SeO₂ (0.1 equiv) and TBHP (1.1 equiv) was performed instead of a stoichiometric oxidation with SeO₂. f) Compound **10** was isolated in 40% yield.



required for effective conversion of **2a** to **8a**. On the other hand, oxidation of the isomer **2a'** with SeO₂ did not proceed (entry 6). Oxidation of **2a** with O₂ (1 atm) in the presence of silica gel in dichloromethane at r.t. for 2 d gave 1-tetralone (**9a**) in 39% yield along with a trace amount of aldehyde **8a** (entry 7). In this case, photoirradiation was not conducted. In the absence of silica gel, conversion of **2a** to **9a** with O₂ did not

proceed. Use of acetic acid (3 equiv) instead of silica gel also promoted oxidation of **2a** with O₂ to **9a**, but **9a** was obtained less efficiently. In the absence of O₂, **9a** was not formed by treatment with silica gel. Therefore, both silica gel and O₂ were necessary for conversion of **2a** to **9a**. We have screened other reaction conditions such as solvents, reaction temperatures, and reaction times, but it was difficult to improve the

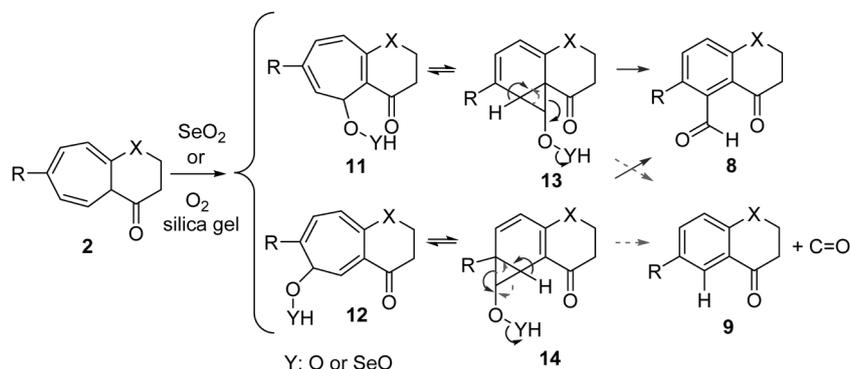


Chart 3. A Proposed Mechanism

yield of **9a**. Oxidation of the conjugated isomer **2a'** with O_2 in the presence of silica gel did not proceed (entry 8).

Regioselective formation of a formyl derivative **8** and a one-carbon-lacking 1-tetralone **9** prompted us to investigate more examples of oxidation of unconjugated CHTs **2** (Table 2). Oxidation of phenyl-substituted CHT **2b** with SeO_2 gave aldehyde **8b** in 48% yield along with 7-phenyl-1-tetralone (**9b**) and 6-phenyl-1-tetralone (**9b'**) in 7% combined yield (**9b/9b'** = > 10:1) (entry 1). The structure of **9b** and **9b'** was confirmed by 1H -NMR analysis. Catalytic oxidation of **2b** using SeO_2 (10 mol%) and *tert*-butyl hydroperoxide (1.1 equiv) gave **8b** (22%), **9b** (8%), and **9b'** (4%). Oxidation of **2b** with O_2 in the presence of silica gel gave **9b** and **9b'** in 14% and 6% yields, respectively (entry 2). Similarly, oxidation of methyl-, methoxy-, or acetoxy-substituted CHTs (**2c–e**) revealed that oxidation with SeO_2 gave aldehydes **8c–e** mainly, while oxidation with O_2 and silica gel gave 7-substituted 1-tetralones **9c–e** as the major isomers (entries 3–8). Oxidation of substituted CHTs **2b–e** with O_2 gave two regioisomers of 1-tetralone derivatives, **9b–e** and **9b'–e'**. In the oxidation of methoxy-substituted CHT **2d** with SeO_2 , the desired aldehyde **8d** was obtained in < 7% yield and compound **10** was isolated in 40% yield (entry 5). Oxidation of **2d** with O_2 in the presence of silica gel afforded **9d** and **9d'** in 8% combined yield along with many unidentified byproducts (entry 6). Interestingly, the formation of 6-substituted 1-tetralones **9b–e'** suggested that a substitution pattern between R- and $-XCH_2CH_2-$ on the phenyl ring of **1b–e** changed by the one-carbon contraction. Büchner reaction of *N*-benzyloxycarbonyl (Cbz)-*N*-(4-diazo-3-oxobutyl)aniline (**1f**) proceeded smoothly to afford the corresponding CHT **2f** in good yields. Oxidation of **2f** with SeO_2 gave a formyl ketone **8f** in 36% yield, while oxidation of **2f** with O_2 in the presence of silica gel gave a ketone **9f** in 31% yield (entries 9 and 10).

A proposed mechanism for oxidation of **2** to **8** or **9** is shown in Chart 3. Treatment of **2** with SeO_2 or O_2 in the presence of silica gel gives peroxide or selenium(II) ester **11** or **12** regioselectively. Rational reasons for regioselective formation of **11** or **12** are not clear. The role of silica gel was not clarified, but we believe silica gel promoted the formation of **11** or **12**. Isomerization to the corresponding norcaradiene **13** or **14** followed by C–H bond scission and cyclopropane ring cleavage affords aldehyde **8**,²² while that followed by C–C bond scission and cyclopropane ring cleavage gives one-carbon-lacking 1-tetralones **9** and CO .^{16,23}

In conclusion, we have developed two reactions for oxida-

tive aromatization of substituted CHTs. Oxidation of intramolecular Büchner adducts of 1-diazo-5-phenylpentan-2-ones with SeO_2 gave 8-formyl-1-tetralones regioselectively, while that with O_2 in the presence of silica gel gave one-carbon-lacking 1-tetralones. These new chemical reactivities of CHTs would contribute to further development of the synthetic application of CHTs.

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Conflict of Interest The authors declare no conflict of interest.

Supplementary Materials The online version of this article contains supplementary materials.

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23) Formation of isomer **11'** or **12'** would lead **9'**.

