

# Reaction of Arylethanals with Boron Tribromide

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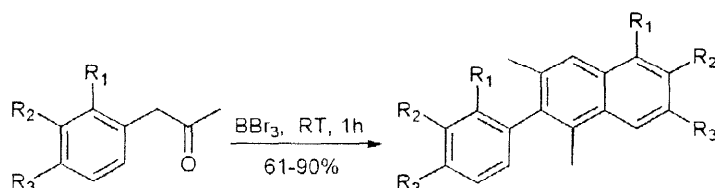
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## Abstract

Treatment of arylethanals **1** with boron tribromide give 2-phenylnaphthalenes **2** or 1,2,9,10-tetrahydro-1,9-epoxydibenzo[a,e]cyclooctenes **3** by a tandem aldol condensation-intramolecular Friedel-Crafts cyclization or a condensation at the O-position followed by a double Friedel-Crafts alkylation respectively. In all cases, a total demethylation of the methoxy groups occurs. © 1998 Elsevier Science Ltd. All rights reserved.

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Natural products containing a naphthalene unit often exhibit biological activity[1-5]. As a result, investigation of new methods for the regioselective synthesis of highly substituted naphthalenes have received significant attention in recent years[6-11]. As a part of our studies on the synthesis of new biologically active polyhydroxylated compounds, we have developed a new convenient synthesis of polyhydroxylated 2-phenylnaphthalenes in a one pot procedure from mono- or dimethoxyphenylacetones[12] (Scheme 1).



Scheme 1

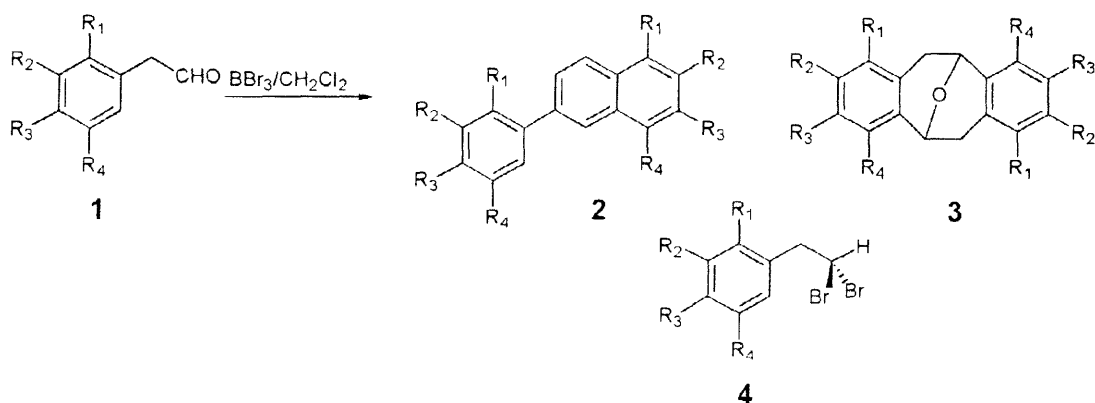
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In order to determine the scope and the limitation of this reaction and to synthesize a natural 2-phenylnaphthalene derivative (from the Marine sponge *Jaspis sp.*)[13], we have prepared phenylethanals[14].

In the present paper, we report the reaction of aryloethanals **1** with boron tribromide. Due to some deceptive results, we also treated 3,4-dimethoxyphenylethanal **1c** and 3,4,5-trimethoxyphenylethanal **1f** with concentrated hydrochloric acid in dioxane.

Whereas arylacetones gave 1,3-dimethyl-2-phenylnaphthalenes in high yields in the presence of boron tribromide, phenylethanals presented a very dissimilar reactivity (Table 1, Scheme 2).

Phenylethanal **1a** gave the expected 2-phenylnaphthalene **2a** with  $\text{BBr}_3$  in low yield whereas methoxyphenylethanals **1b-d** gave a large amount of polymers (All attempts to isolate organic material were unsuccessful).



Scheme 2

Table 1  
Reaction of aryloethanals **1** with  $\text{BBr}_3$  in  $\text{CH}_2\text{Cl}_2$

Starting material	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	Product	R <sub>1</sub>	R <sub>2</sub>	R <sub>3</sub>	R <sub>4</sub>	Yield <sup>a</sup>
<b>1a</b>	H	H	H	H	<b>2a</b>	H	H	H	H	15%
<b>1b</b>	OCH <sub>3</sub>	H	H	H	-	-	-	-	-	0%
<b>1c</b>	H	OCH <sub>3</sub>	H	H	-	-	-	-	-	0%
<b>1d</b>	H	H	OCH <sub>3</sub>	H	-	-	-	-	-	0%
<b>1e</b>	H	OCH <sub>3</sub>	OCH <sub>3</sub>	H	<b>3e</b>	H	OH	OH	H	82% <sup>b</sup>
<b>1f</b>	H	OCH <sub>3</sub>	OCH <sub>3</sub>	OCH <sub>3</sub>	<b>3f</b>	H	OH	OH	OH	Traces
<b>1g</b>	CH=CH-CH=CH		H	H	<b>3g</b>	CH=CH-CH=CH		H	H	33%

a. To a solution of **1** in  $\text{CH}_2\text{Cl}_2$  (25ml) was added at room temperature  $\text{BBr}_3$  (1M in  $\text{CH}_2\text{Cl}_2$ , 1 equiv. and 1 additional equiv. for each methoxy group).

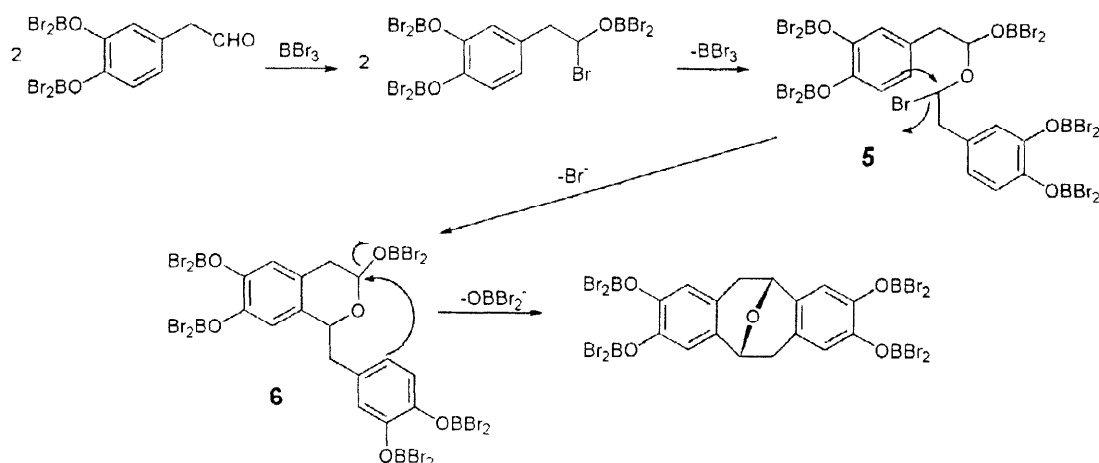
b. Yield of purified compounds[15].

b. **4e** was also formed in 13% yield.

Conversely, 3,4-dimethoxyphenylethanal **1e** led to **3e** and **4e** in 82 and 13% yield respectively. The structure of **3e** has been established on the basis of elemental analysis, mass spectroscopic

and nmr data and comparison with literature spectroscopic data[16,17]. Similarly, 1-naphthylethanal **1g** gave **3g** in 33% yield. Finally, the reaction of 3,4,5-methoxyphenylethanal **1f** with  $\text{BBr}_3$  gave the same disappointing result than for **1b-d** giving **3f** only as traces.

We speculated that the formation of **3e** started by a condensation at the O-position of the enol form and the keto form. The resulting hemiacetal **5** cyclized to give the benzisopyran **6**, which led to **3e** by an intramolecular Friedel-Crafts reaction as previously suggested by Jung[16-17] (Scheme 3).



Scheme 3

Acid treatment of aryloethanals may lead to 2-phenylnaphthalenes [16,18] or 1,2,9,10-tetrahydro-1,9-epoxydibenzo[a,e]cyclooctenes [16,17,19]. The balance between the condensation at O- or C-position depends on the nature of the acid and the substitution on the aryl ring. However with boron tribromide the situation was strongly contrasted. The presence of the methyl group in arylacetones increased the electronic density on the C atom and therefore favored the condensation at the C-position. On the other hand, aryloethanals gave poor yields in 2-arylnaphthalenes due to the occurrence of the condensation at the O-position. However, the Friedel-Crafts cyclization was only possible when the aromatic ring is sufficiently electronically rich. This is the case with **1e** and **1g**. In the case of **1f**, we speculated that **3f** was formed but was rapidly destroyed under the reaction conditions as previously observed[20] with 3,4,5-trihydroxyphenyl derivative. In contrast to **1e** (see below), **1f** when treated with concentrated HCl in dioxane, gave the product of condensation at the O-position, i.e., 5,6,7,13,14,15-hexamethoxy-1,2,9,10-tetrahydro-1,9-epoxydibenzo[a,e]cyclooctene in 51% yield. As expected, this compound treated with boron tribromide was almost totally destroyed and **3f** can be isolated as traces (<1%).

Since one of our goal was to prepare 2-(3,4-dihydroxyphenyl)naphthalene-6,7-diol **2e**, we treated **1e** with concentrated HCl in dioxane. The expected 6,7-dimethoxy-2-(3,4-dimethoxyphenyl)naphthalene, obtained in 20% yield, was easily converted to **2e** with BBr<sub>3</sub> in 78% yield.

In this paper, we have presented remarkable aspects of product differentiation in the reaction of aryloxyacetals with boron tribromide compared to the naphthalene synthesis from aryloxyacetones. Influence of solvent polarity, acidity of the reaction medium, substituent effects at the substrate should be examined in order to define the conditions which favored the condensation at the O- or C-position.

### Acknowledgements

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