Pergamon

Tetrahedron Letters 39 (1998) 8457–8460

TETRAHEDRON LETTERS

Reaction of Arylethanals with Boron Tribromide

Romain Dupont and Philippe Cotelle*

Laboratoire de Chimie Organique Physique, associé au CNRS, ENSCL
Université de Lille 1, F-59655 Villeneuve d'Ascq, France

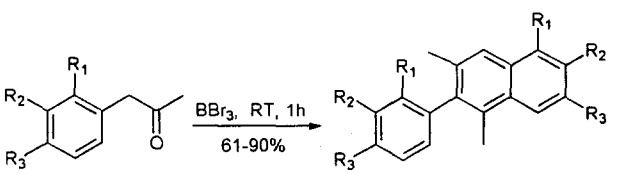
Received 9 July 1998; accepted 10 September 1998

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.

Keywords: Boron and compounds, naphthalenes, polycyclic heterocyclic compounds, Friedel-Crafts reactions.

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

Fax: 33 (0)320336309; E-mail: cotelle@univ-lille1.fr

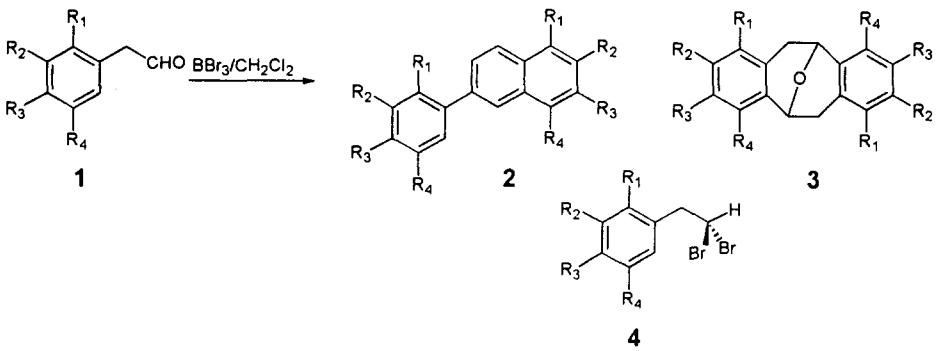
0040-4039/98/$ - see front matter
PII: S0040-4039(98)01895-4

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 arylethanals **1** with boron tribromide. Due to some deceptive results, we also treated 3,4-dimethoxyphenylethanal **1e** 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-phenylnaphtalene **2a** with 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 arylethanals 1 with BBr_3 in CH_2Cl_2

Starting material	R_1	R_2	R_3	R_4	Product	R_1	R_2	R_3	R_4	Yield[a]
1a	H	H	H	H	**2a**	H	H	H	H	15%
1b	OCH_3	H	H	H	-	-	-	-	-	0%
1c	H	OCH_3	H	H	-	-	-	-	-	0%
1d	H	H	OCH_3	H	-	-	-	-	-	0%
1e	H	OCH_3	OCH_3	H	**3e**	H	OH	OH	H	82%[b]
1f	H	OCH_3	OCH_3	OCH_3	**3f**	H	OH	OH	OH	Traces
1g	CH=CH-CH=CH		H	H	**3g**	CH=CH-CH=CH		H	H	33%

a. To a solution of **1** in CH_2Cl_2 (25ml) was added at room temperature BBr_3 (1M in CH_2Cl_2, 1 equiv. and 1 additional equiv. for each methoxy group).

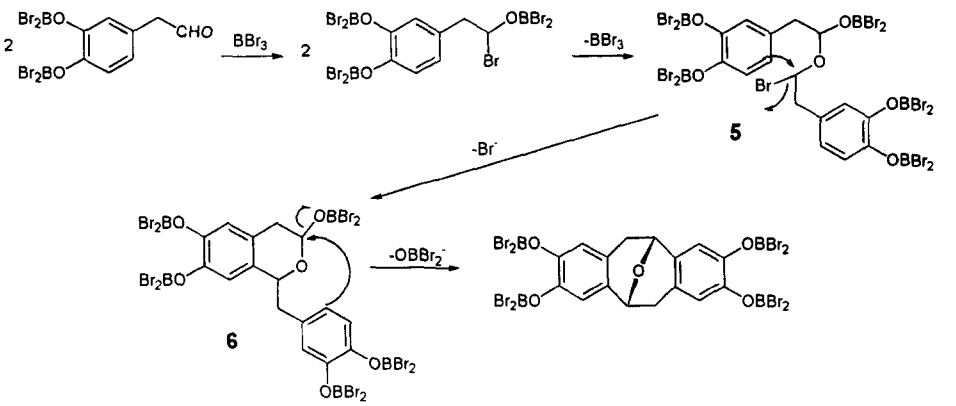
b. Yield of purified compounds[15].

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 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 arylethanals 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, arylethanals 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)naphtalene, obtained in 20% yield, was easily converted to **2e** with BBr_3 in 78% yield.

In this paper, we have presented remarkable aspects of product differentiation in the reaction of arylethanals with boron tribromide compared to the naphthalene synthesis from arylacetones. 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

This work was supported by grants from the Centre National de la Recherche Scientifique (CNRS) and the Région Nord-Pas-de-Calais.

References and notes

[1] Mc Rae WD, Yowers GHN Phytochemistry 1984;23:1207-1220.
[2] Gordaliza M, Del Corral JMM, Castro MA, Lopez-Vasquez ML, Garcia PA. San Feliciano A, Garcia-Gravalos MD Bioorg. Med. Chem. Lett. 1995;5:2465-2468.
[3] Kashiwada Y, Bastow KF, Lee KH Bioorg. Med. Chem. Lett. 1995;5:905-908.
[4] Gnabre J, Huang RCC, Bates RB, Burns JJ, Caldera S, Malcomson ME, Mc Clure KJ Tetrahedron 1995;51:12203-12210.
[5] Eich E, Pertz H, Kaloga M, Schulz J, Fesen MR, Mazumder A, Pommier Y J. Med. Chem. 1996;39:86-95.
[6] Turnbull P, Moore HW J. Org. Chem. 1995;60:644-649.
[7] Yadav KM, Mohanta PK, Ila H, Junjappa H Tetrahedron 1996;52:14049-14056.
[8] a) Tanabe Y, Seko S, Nishii Y, Yoshida T, Utsumi N, Suzukamo G J. Chem. Soc. Perkin Trans. 1 1996;2157-2165. b) Nishii Y, Tanabe Y Tetrahedron Lett. 1995;36:8803-8806.
[9] Karady S, Amato JS, Reamer RA, Weinstock LM Tetrahedron Lett. 1996;37:8277-8280.
[10] Jamie JF, Rickards RW J. Chem. Soc. Perkin Trans. 1 1996;2603-2613.
[11] De Konig CB, Michael JP, Rousseau AL Tetrahedron Lett. 1997;38:893-896.
[12] Cotelle P, Catteau JP Tetrahedron Lett. 1997;38:2969-2972.
[13] Tsukamoto S, Kato H, Hirota H, Fusetani N Tetrahedron 1994;50:13583-13592.
[14] Coote SJ, Davies SG, Middlemiss D, Naylor A Tetrahedron Asymmetry 1990 ;1 :33-56.
[15] All new compounds gave satisfactory spectroscopic and elemental analytical data.
[16] Jung ME, Mossman AB, Lyster MA J. Org. Chem. 1978;43:3698-3701.
[17] Jung ME, Miller SJ J. Amer. Chem. Soc. 1981;103:1984-1992.
[18] Carter HE, Van Loon EJ J. Amer. Chem. Soc. 1938;60:1077-1080.
[19] Kagan J, Chen SY, Agdeppa DA, Watson WH, Zabel V Tetrahedron Lett. 1977:4469-4470.
[20] Unpublished laboratory observations.