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Tandem carbon–carbon bond insertion and intramolecular aldol reaction of benzyne with aroylacetones: novel formation of 4,4′-disubstituted 1,1′-binaphthols†

Kentaro Okuma,* Ryoichi Itoyama, Ayumi Sou, Noriyoshi Nagahora and Kosei Shioj

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An efficient route to 4-aryl-2-naphthols from arynes and aroylacetones was developed by carbon–carbon bond insertion followed by an intramolecular aldol reaction and dehydration. Benzyne derived from 2-(trimethylsilyl)phenyl triflate reacted with benzoylacetones in refluxing acetonitrile to give 4-aryl-2-naphthols and 3-aryl-1-naphthols.

Fluoride-induced aryne formation by using 2-(trimethylsilyl)-phenyl triflate (**1**) has gathered much attention as a valuable synthetic building tool.[1] Naphthalene derivatives are ubiquitously present in natural products, pharmaceuticals, and ligands for transition-metal catalysts.[2] In particular, binaphthyl compounds are very important for enantioselective catalytic reactions.[3] Although the synthesis of 1-naphthols through the reaction of aryne with furans followed by acidic dehydration is a popular method that emerged from the discovery of benzyne chemistry,[4] 2-naphthols are difficult to synthesize *via* benzyne intermediates. 4-Aryl-2-naphthols were previously synthesized by the intramolecular carbocyclization of alkynyl ketones,[5] the Wittig reaction of 2-benzoylphenylacetate,[6] the cyclization of alkynone with I_2,[7] and the Friedel–Crafts reaction of cyclopropanecarbonyl chloride with benzene.[8] All those methods, however, presented some difficulties, such as the unavailability of starting materials and/or the requirement of multi-step reactions. Thus, a more convenient method for the synthesis of 4-substituted 2-naphthols is required. A recently developed carbon–carbon insertion reaction of arynes offers a new method for the synthesis of *ortho*-selective aromatic compounds. For example, the reaction of benzyne derived from triflate **1** with β-diketones, β-diketo esters, or β-keto esters gave carbon–carbon insertion products.[9,10] Other carbon–heteroatom insertion reactions of arynes were reported as well.[11] Whereas the reaction of benzyne with acetylacetone (**2a**) gave 1-(2-acetylphenyl)propane-2-one (**3a**),[9] treatment of benzyne with benzoylacetone (**2b**) in the presence of CuI catalyst resulted in the formation of 1,3,3-triphenylbutane-1,3-dione.[12] We have been interested in the difference in reactivity between those two results. If the carbon–carbon bond insertion reaction of arynes proceeds in β-diketones, the tandem intramolecular aldol reaction followed by dehydration would provide a new route to produce substituted 2-naphthols in a one-pot operation (Fig. 1). Herein, we report the one-pot synthesis of 2-naphthols from benzyne precursor **1** and CsF and its application to 4,4′-biaryl-2,2′-binaphthols.

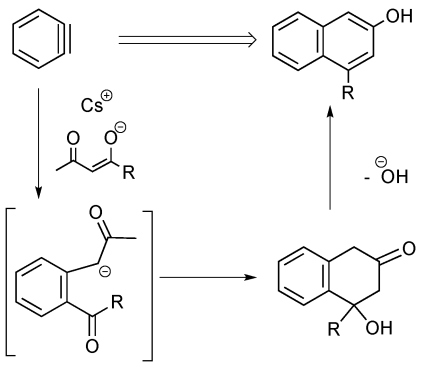


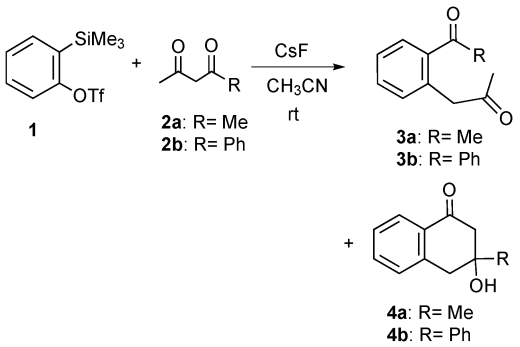
Fig. 1 Proposed synthesis of 4-substituted 2-naphthols from arynes.

We began our study by reacting diketone **2a** or **2b** with benzyne generated from triflate **1** and CsF (Table 1). Treatment of triflate **1** with CsF followed by the addition of acetylacetone **2** at rt for 3 h resulted in the formation of 1-(2-acetylphenyl)propan-2-one **3a** in 52% yield, the result of which was similar to that of Yoshida *et al.* (entry 1).[9] However, 3,4-dihydro-3-hydroxy-3-methylnaphthalen-1(2*H*)-one (**4a**) was also isolated as the side product (12%). Prolonging the reaction time produced a larger amount of cyclized product **4a**; the yield was increased to 25% (entry 2). When excess amounts of **1** and CsF were used, **4a** was obtained in 40% yield (entry 3). Interestingly, when benzoylacetone **2b** was treated with triflate **1**, not 1,2,2-triphenyl-1,3-butanedione, the product reported by Yang *et al.*,[12] but 1-(2-benzoylphenyl)propan-2-one (**3b**) was obtained in 60% yield along with 3,4-dihydro-3-hydroxy-3-phenylnaphthalen-1(2*H*)-one (**4b**) and 1,2-diphenylbutane-1,3-dione (7%). Since the acetyl group attached to the aromatic group is more acidic than a normal aliphatic acetyl group, the intramolecular aldol reaction might proceed to give **4** even at room temperature.[13] Thus, we then performed the reaction under refluxing conditions to determine whether or not the intramolecular aldol reaction

Department of Chemistry, Faculty of Science, Fukuoka University, Jonan-ku, Fukuoka 814-0180, Japan. E-mail: kokuma@fukuoka-u.ac.jp; Fax: +81-92-865-6030; Tel: +81-92-871-6631

† Electronic supplementary information (ESI) available: Detailed experimental procedures and analytical data. CCDC 874289. For ESI and crystallographic data in CIF or other electronic format see DOI: 10.1039/c2cc36128k

Table 1 Reaction of triflate **1** with β-diketones **2** in the presence of CsF



Entry	1 (equiv.)	2	Time/h	Products 3		Yields (%) 4	
1	1.2	**2a**	3.0	**3a**	52	**4a**	12
2	1.2	**2a**	6.0	**3a**	40	**4a**	25
3	2.2	**2a**	14.0	**3a**	30	**4a**	40
4	1.2	**2b**	6.0	**3b**	60	**4b**	15[a]
5	2.2	**2b**	12.0	**3b**	55	**4b**	12[a]

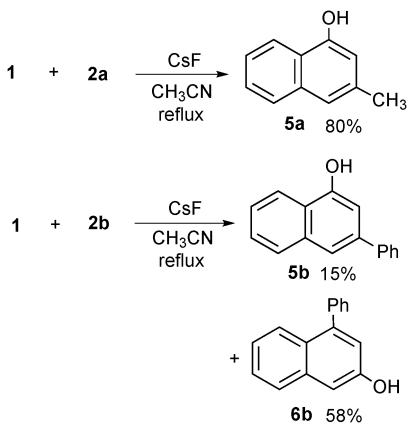
[a] A small amount of 1,2-diphenylbutane-1,3-dione was isolated.

and dehydration would proceed. The reaction of **1** with **2a** and CsF in refluxing acetonitrile proceeded with regioselectivity to give 3-methyl-1-naphthol (**5a**) in 80% yield. Meanwhile, when **1** was treated with **2b** and CsF in refluxing acetonitrile, a mixture of 4-phenyl-2-naphthol (**6b**) and 3-phenyl-1-naphthol (**5b**) was obtained in 58% and 15% yields, respectively (Scheme 1).

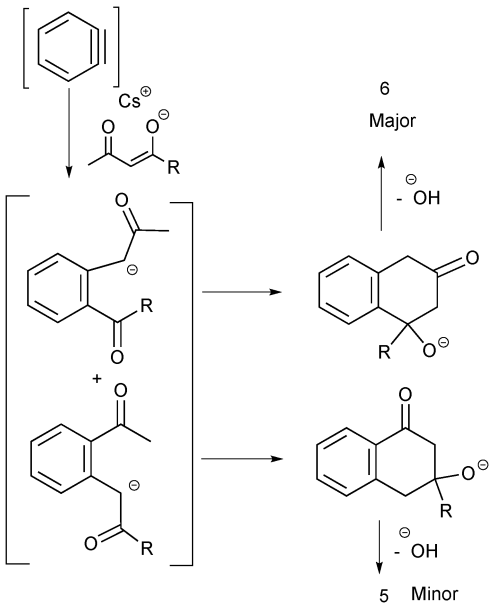
Thus, not only carbon–carbon insertion but also intramolecular aldol cyclization and dehydration proceeded under refluxing conditions (Scheme 2). This reaction has an interesting feature: it proceeded regioselectively (4 : 1) and the intramolecular aldol reaction proceeded even under these conditions.

Other substituted benzoylacetones **2** also reacted with triflate **1** and CsF to give the corresponding 3-substituted 1-naphthols **5** and 4-substituted 2-naphthols **6** in moderate to good yields (Table 2).[14]

When electron-donating groups were substituted, moderate amounts of 1-naphthols **5** were obtained (entries 1 and 2). When electron-withdrawing groups were substituted at the *para* position, 2-naphthols **6** were obtained in better yields (entries 3–5). In particular, the nitro substituent afforded only

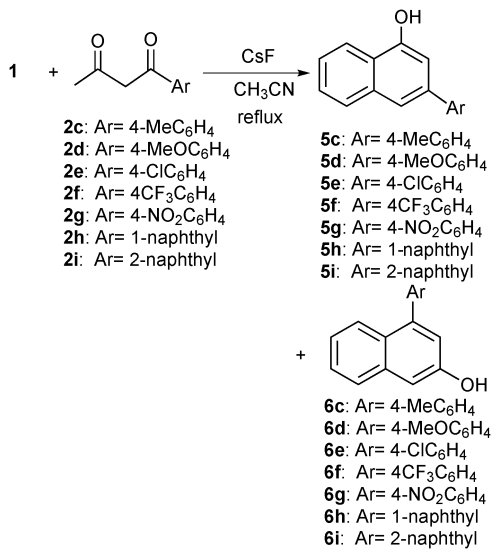


Scheme 1



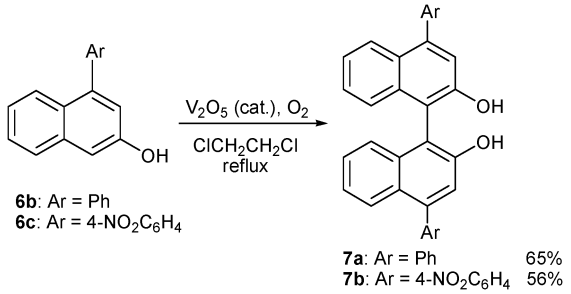
Scheme 2

Table 2 Reaction of triflate **1a** with aroylacetones **2**



Entry	2	Time/h	1-Naphthol Yield (%)		2-Naphthol Yield (%)	
1	**2c**	5	**5c**	39	**6c**	25
2	**2d**	4	**5d**	22	**6d**	35
3	**2e**	6	**5e**	15	**6e**	65
4	**2f**	8	**5f**	15	**6f**	40
5	**2g**	8	**5g**	0	**6g**	67
6	**2h**	8	**5h**	31	**6h**	44
7	**2i**	8	**5i**	39	**6i**	35

2-naphthol **6g** (entry 5). By using 1-(1-naphthyl)butane-1,3-dione (**2h**) and 1-(2-naphthyl)butane-1,3-dione (**2i**) as substrates, the corresponding 3-naphthyl-1-naphthols and 4-naphthyl-2-naphthols were obtained in moderate yields (entries 6 and 7). Thus, naphthols **5** and **6** were synthesized in a one-pot operation starting from easily available substituted benzoylacetones and the benzyne precursor.



Scheme 3

Previously, 4-aryl-2-naphthols **6** were synthesized by the $AuCl_3$/AgOTf-catalyzed intramolecular cyclization of terminal alkynyl benzophenone[5] or the $TiCl_4$ condensation of silyl enol ether of α-diazoacetoacetate and ketones followed by rhodium octanoate catalyzed annelation.[15] However, those methods required multistep synthesis of the starting materials. Although the most straightforward synthesis of 4-phenyl-2-naphthol **6b** would be the Suzuki–Miyaura coupling of 4-bromo-2-naphthol, the synthesis of 4-bromo-2-naphthol is relatively difficult, requiring a three-step reaction from 1-naphthylamine.[16] The present method requires only a one-pot reaction starting from commercially available triflate **1** and benzoylacetone. Thus, a convenient synthesis of 1- and 2-naphthols was accomplished.

Binaphthols are well known for their synthetic ability due to their chiral auxiliary and catalytic activity.[17] Thus, many substituted binaphthols were synthesized. In contrast, very few 4,4′-biaryl-1,1′-binaphthols (**7**) were synthesized due to the difficulty of synthesizing starting 4-aryl-2-naphthols.[18] As the regioselective synthesis of 4-substituted 2-naphthols was achieved, we tried to perform the oxidative coupling of 4,4′-diaryl-1,1′-binaphthols according to the method described by Joseph *et al.*[19] Treatment of 4-phenyl-2-naphthol with V_2O_5 in refluxing dichloroethane resulted in the formation of 4,4′-diphenyl-1,1′-binaphthol (**7a**) in 65% yield (Scheme 3).

The structure of **7a** was determined by ^1H and ^{13}C NMR analysis. In addition, the X-ray crystallographic analysis of **7a** was performed (Fig. S1, ESI†).[20]

In conclusion, the synthesis of 4-aryl-2-naphthols **6** from easily available triflate **1** and aroylacetone **2** was accomplished in a one-pot operation. Oxidation of 4-aryl-2-naphthols afforded the corresponding binols **7** in moderate yields.

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14 Synthesis of **6b**: To a solution of benzoylacetone **2** (73 mg, 0.45 mmol) and CsF (228 mg, 1.5 mmol) in acetonitrile (7 mL) was added triflate **1** (149 mg, 0.50 mmol). After refluxing for 5 h, the reaction mixture was evaporated to give pale yellow oil, which was chromatographed over silica gel by elution with hexane–dichloromethane (1 : 1) to afford a mixture of 3-phenyl-1-naphthol **5b** and 4-phenyl-2-naphthol **6b**. The mixture was subjected to gel permeation chromatography to give 1-naphthol **5b** (15 mg, 0.07 mmol) and 2-naphthol **6b** (57 mg, 0.26 mmol).

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20 Compound **7a**: yellow crystals, mp 145–146 °C; ^1H NMR ($CDCl_3$) δ = 5.21 (br, 2H, OH), 7.35 (m, 6H, Ar), 7.40 (m, 6H, Ar), 7.81 (m, 6H, Ar), 8.45 (d, 4H, J = 8.8 Hz, Ar). ^{13}C NMR ($CDCl_3$), δ = 111.76, 119.13, 124.04, 125.04, 125.14, 126.27, 127.54, 128.23, 131.11, 134.16, 141.70, 146.80, 147.81 (Ar). Anal. calcd for $C_{32}H_{22}O_2$ + 2EtOH; C, 81.48; H, 6.46%. Found, C, 81.34; H, 6.65%.