Efficient Synthesis of 1-Tetralones from 4-Arylbutyric Acids by Combined Use of Solid Acid Catalysts and Microwave Irradiation

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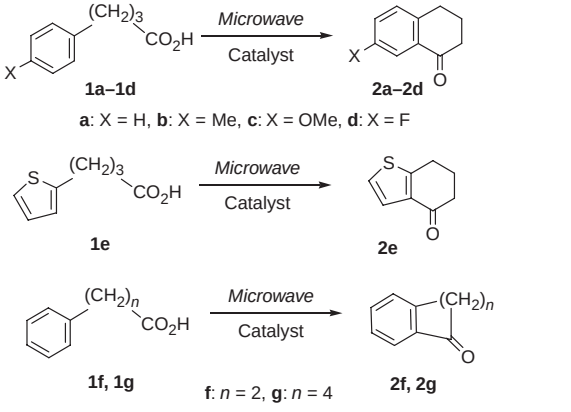
Solid acid catalysts such as H–Beta zeolites effectively promote dehydrative intramolecular cyclization of 4-arylbutyric acids under microwave irradiation to give 1-tetralone derivatives in high yields.

1-Tetralone and its relatives are useful compounds as medicinal chemicals or their synthetic intermediates.[1] For preparation of 1-tetralone derivatives, the Friedel–Crafts type dehydrative cyclization reaction of 4-arylbutyric acids is a convenient synthetic method. The reaction has been reported to proceed in the presence of some acid compounds such as sulfuric acid,[2] methanesulfonic acid,[3] metal trifrates,[4] etc., including solid acid catalysts such as Nafions[5] and metal cation-exchanged or H–Y zeolites.[6] Solid catalysts have a large merit of easy separation of catalysts and are favorable for industrial use. However, the reported reactions seem to require long reaction time of several hours and/or to give 1-tetralone in not so high yield. On the other hand, microwave-assisted chemical processes have been attracted current interest.[7] In the course of our studies on development of efficient chemical reactions using microwave irradiation, we have found combined use of commercially available appropriate solid acids and microwave irradiation is highly effective for the intramolecular cyclization of 4-arylbutyric acids affording 1-tetralone derivatives.

Thus, when a mixture of 4-phenylbutyric acid (**1a**), a H–Beta zeolite, HSZ-940HOA (Tosoh, $SiO_2/Al_2O_3 = 37$), and 1,2-dichlorobenzene was heated in a glass tube (ca. 10 mL, proof pressure 20 atm) with a sealed Teflon-septum cap fixed by a plastic ring under temperature-controlled microwave irradiation (CEM, Discover S-class, 2.45 GHz, 300 W) at 200 °C for 10 min,[8,9] 1-tetralone[10] (**2a**) was formed in 89% yield (Table 1, Entry 1). Microwave irradiation was essential in the reaction. The yields of **2a** in the reactions by microwave irradiation and by conventional oil bath heating using reaction vessels with the same shape (190 °C, 5 min) were 71 and 7%, respectively (Entries 2 and 3),[8,9] indicating microwave irradiation efficiently accelerated the dehydrative cyclization reaction. In the initial 2 min, the yield of **2a** was 20% for the microwave reaction, while the yield was only 2% for the oil bath reaction, showing acceleration effect by microwave was already present in the early stage of the reaction. The change of the appearance of the reaction under microwave irradiation could be monitored by a CCD camera attached to the microwave instrument.[9] In the microwave reaction the color of the suspended solution turned from colorless to yellow immediately after heating at 190 °C. On the contrary, almost no color change was observed in the conventional reaction using an oil bath even after heating at 190 °C for 5 min.

As catalyst, another H–Beta zeolite, HSZ-930HOA whose SiO_2/Al_2O_3 ratio was 27 and had somewhat stronger acidity than HSZ-940HOA, also gave **2a** in the same yield as HSZ-940HOA (Entry 4). However, when H-ZSM-5 zeolites, 840HOA and HSZ-830HOA whose SiO_2/Al_2O_3 ratios (39 and 28, respectively) were similar to those of HSZ-940HOA and

Table 1. Solid acid-catalyzed dehydrative cyclization reactions of **1** under microwave irradiation[a]



Entry	1	Method[b]	Catalyst[c]	Temp /°C	Time /min	Yield[d] /%
1	**1a**	MW	940HOA	200	10	89
2	**1a**	MW	940HOA	190	5	71
3	**1a**	OB	940HOA	190	5	7
4	**1a**	MW	930HOA	190	5	71
5	**1a**	OB	930HOA	190	5	4
6	**1a**	MW	840HOA	190	5	5
7	**1a**	OB	840HOA	190	5	trace
8	**1a**	MW	830HOA	190	5	10
9	**1a**	OB	830HOA	190	5	trace
10	**1a**	MW	SAC-13	190	5	51
11	**1a**	OB	SAC-13	190	5	7
12	**1a**	MW	NR50	190	5	42
13	**1a**	OB	NR50	190	5	9
14	**1b**	MW	940HOA	200	10	93 (85)
15	**1c**	MW	940HOA	200	10	65
16	**1d**	MW	940HOA	220	10	95 (85)
17	**1e**	MW	940HOA	200	10	65
18	**1f**	MW	940HOA	220	10	36
19	**1f**	OB	940HOA	220	10	15
20	**1g**	MW	940HOA	220	10	8
21	**1g**	OB	940HOA	220	10	2

[a]Reaction conditions: **1** 0.80 mmol, catalyst 100 mg, 1,2-dichlorobenzene 1.0 mL. [b]OB: oil bath heating, MW: microwave irradiation. [c]Catalysts were obtained from Tosoh Co., Ltd. (zeolite HSZ series; 940HOA, 930HOA, 840HOA, and 830HOA) and Sigma-Aldrich Co., Ltd. (Nafion series; SAC-13 and NR50). [d]Yields of **2**[10] were estimated by GC. Figures in parentheses were isolated yields.

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HSZ-930HOA (37 and 27, respectively) but had smaller pore ring size were used, the yields of **2a** profoundly decreased to 5 and 10%, respectively (Entries 6 and 8). This suggests suitably large pore size is needed for the cyclization reaction. Other solid acid catalysts such as Nafions SAC-13 and NR50 (Sigma-Aldrich) could be used, although the yields of **2a** (51 and 42%, respectively, Entries 10 and 12) were not as high as that obtained by the H–Beta zeolite HSZ-940HOA. In the reactions of **1a** at 190 °C for 5 min the catalytic efficiency increased in the order of HSZ-840HOA (5% yield) < HSZ-830HOA (10%) < NR50 (42%) < SAC-13 (51%) < HSZ-930HOA (71%) ≈ HSZ-940HOA (71%). Microwave irradiation is also effective in the catalysts other than HSZ-940HOA. When oil bath heating was used in place of microwave irradiation, the yields of **2a** using HSZ-840HOA, HSZ-830HOA, NR50, SAC-13, and HSZ-930HOA significantly decreased from 5, 10, 42, 51, and 71% to trace, trace, 9, 7, and 4%, respectively (Entries 5, 7, 9, 11, and 13).

In the present microwave reaction selection of solvent is also important. For instance, replacement of 1,2-dichlorobenzene by chlorobenzene caused very slow increase in temperature, and maximum temperature was about 170 °C, while 1,2-dichlorobenzene reached 190 °C within 2 min. On the other hand, when 1,3-dichlorobenzene was used as solvent, the temperature could become 190 °C. However, the yield in the reaction at 190 °C for 5 min (56%) was lower than that obtained in 1,2-dichlorobenzene (71%). Measurements of complex permittivities at 2.45 GHz by a perturbation method[11] using a cylindrical cavity and a network analyzer showed the dielectric loss factors of 1,2- and 1,3-dichlorobenzene and chlorobenzene were 2.30, 0.65, and 0.53, respectively. In general, compounds with larger loss factors tend to absorb microwave energy more easily.[12] Accordingly, solvents with appropriately large loss factors seem to be favorable for smooth progress of the microwave reaction.

Derivatives of **1a** also undergo the cyclization reaction. Thus, 4-*p*-tolylbutyric acid (**1b**) reacted at 200 °C for 10 min to give the corresponding 1-tetralone derivative **2b** in 93% yield (Entry 14). In addition, 4-*p*-methoxypenylbutyric acid (**1c**) gave a methoxy group-substituted product **2c** in 65% yield (Entry 15). The reaction of **1d** containing somewhat electron-withdrawing fluorine atom smoothly proceeded as well to give **2d** in 95% yield (Entry 16). Furthermore, 4-thienylbutyric acid (**1e**) could also undergo the cyclization to provide a thiophene ring-containing product **2e** in 65% yield (Entry 17). In these reactions isolation of the products was easily achieved by standard methods. For instance, in the cases of **1b** and **1d**, separation of the zeolite catalyst by centrifugation followed by column chromatography (silica gel, hexane/ethyl acetate = 7/1) gave **2b** and **2d** in both 85% isolated yields. Besides butyric acid derivatives, a propionic or a valeric acid derivative, **1f** or **1g**, reacted in the presence of HSZ-940HOA under microwave irradiation to form a five-membered or a seven-membered product, 1-indanone (**2f**) or 6,7,8,9-tetrahydro-5*H*-benzocycloheptene-5-one (**2g**), respectively (Entries 18 and 20). Although the yields (36% for **2f** and 8% for **2g**) were not high enough, these values were better than those obtained by conventional oil bath heating (15 and 2%, respectively, Entries 19 and 22). For the acceleration effect of microwave in the present reaction, microwave is likely to activate rather polar protic catalytic sites of solid acids more efficiently than conventional heating, although further study is required to confirm such microwave local heating effect in heterogeneous reaction systems.

In summary, combined use of appropriate solid acid catalysts and microwave irradiation can efficiently promote the intramolecular cyclization of 4-arylbutyric acids and related compounds. Further study on development of efficient chemical processes using microwave is under way.

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8 In the microwave reaction the reaction vessel was heated from room temperature, while in the oil bath reaction the vessel was immersed in a preheated oil bath. In both reactions, some time (ca. 1 min) was needed to heat the vessels to appropriately high temperature (≥ca. 150 °C). Therefore, the total heating time adopted in the present reaction was ca. 11 or ca. 6 min for the 10 or 5 min reaction, respectively.
9 Supporting Information is available electronically on the CSJ-Journal Web site, http://www.csj.jp/journals/chem-lett/index.html.
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