Syntheses of Long-Chain Quaternary Ammonium Salts from Fatty Alcohols by Microwave Irradiation

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ABSTRACT: The phase-transfer catalysts, long-chain quaternary ammonium salts, were rapidly synthesized from fatty alcohols by the reactions with hydrogen halides in the presence of trialkyl amines under microwave irradiation. The catalysts could be widely applied in a variety of quick and new organic reactions, whether by conventional heating or under microwave irradiation. The reaction efficiencies under microwave irradiation were higher than those obtained with conventional heating.
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KEY WORDS: Fatty alcohols, long-chain quaternary ammonium salts, microwave irradiation, phase-transfer catalysts, rapid organic reactions.

Microwave irradiation is one of the most efficient heating methods in various organic reactions (1,2) and has been used to accelerate reaction rates and yields (3,4). Historically, microwave organic reactions were executed in a household microwave oven (5–7). Self-made atmospheric microwave reactors (8) are now used conveniently in syntheses of phase-transfer catalysts and in applications in rapid organic reactions.

Aliphatic quaternary ammonium salts are important phase-transfer catalysts and bactericides. As catalysts, they could be applied in regioselective addition reactions (9), molecular catalytic organic reactions (10), formation of the Mesienheimer complex of 1,3,5-trinitrobenzene and hydroxide ion (11), and other reactions (12). They also have acted efficiently in microwave organic reactions in our laboratory (2,3,5–7). Here we report a fast procedure for the preparation of long-chain halides and long-chain quaternary ammonium salts in the presence of the quaternary ammonium halide and applications in other phase-transfer catalytic organic reactions. New catalysts, complexes of long-chain quaternary ammonium salts with hydrogen halides, for esterification, transesterification, and transetherification reactions are listed in Table 1.

EXPERIMENTAL PROCEDURES

General procedure 1: preparation of 1-*bromododecane under microwave irradiation (Table 2).* 1-Dodecanol [20 mmol (3.72 g)] [2 mmol (0.65 g)], dodecylpyridinium bromide (DPB), and 48% HBr [100 mmol (16.5 g)] were put in a 100-mL two-neck, round-bottom flask equipped with a mechanical stirrer and an efficient condenser. The flask was placed in the cavity of a self-made atmospheric microwave reactor (60 W) and heated for 1.5 h with continuous stirring. The mixture was then allowed to cool to room temperature and saturated with sodium bromide. The upper organic layer was separated and washed successively with water (1 × 10 mL), 5% $NaHCO_3$ (1 × 10 mL), and water (1 × 10 mL) and dried with anhydrous calcium chloride. The final product, 1-bromododecane, was isolated by distillation in vacuum; yield: 4.5 g (91%); b.p. 138–140°C/12 Torr.

General procedure 2: preparation of dodecyltrimethylammonium bromide under microwave irradiation (Table 2). 1-Bromododecane 1 mmol (0.25 g), dodecyltrimethylammonium bromide (DTAB) 0.05 mmol (0.015 g), and trimethylamine 1.5 mmol (0.089 g) in 1.0 mL anhydrous acetonitrile were put in a 10-mL Pyrex tube and sealed off. The sealed tube was immersed in water in a beaker and put on the carousel (rotating glass plate) of a Philips microwave oven (560 W; Netherland Philips Company, Amsterdam, The Netherlands). Temperature of the water was adjusted automatically by the microwave oven itself. The predetermined reaction temperature was 70°C, and the reaction was carried out for 8 h. The solvent was removed carefully in vacuum, and the product was recrystallized from ethyl acetate; yield: 0.28 g (90%), m.p. 232–235°C.

General procedure 3: N-*Alkylation of* N-*ethylaniline with benzyl chloride in the presence of cetyltrimethylammonium bromide (CTAB) by conventional heating (Table 1).* *N*-Ethylaniline (12.1 g, 0.1 mol), benzyl chloride (13.9 g, 0.11 mol), and CTAB (0.364 g, 0.001 mol) were put in a 100-mL, three-neck, round-bottom flask equipped with a mechanical stirrer, thermometer, and dropping funnel with a pressure equalizer containing a 30% sodium hydroxide solution (NaOH: 10 g; 0.25 mol). The flask was heated in a paraffin-oil bath to 75~80°C. The sodium hydroxide solution was added for 2 h with constant stirring. The reaction temperature was held between 75 and 80°C, and the mixture was stirred for another 14 h. The mixture was cooled, and the upper organic layer was separated, washed with water (3 × 10 mL), dried with anhydrous sodium sulfate, and distilled in vacuum to give *N*-benzyl-*N*-ethylaniline: 19 g (90%); b.p. 164–166°C/10

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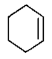
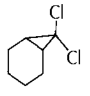
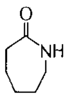
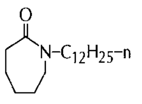
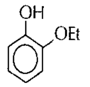
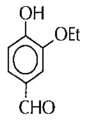
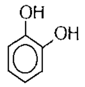
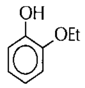
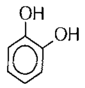
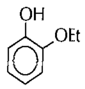
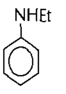
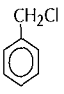
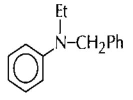
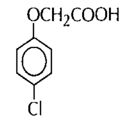
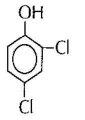
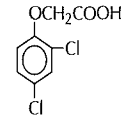
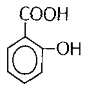
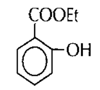
TABLE 1

Reaction in the Presence of Long-Chain Quaternary Ammonium Salt by Classical Heating or Under Microwave Irradiation (560 W)

No.[a]	Substrate 1	Substrate 2	Product	Method	Catalyst 1[b]	Catalyst 2[f]	Temp. (°C)	Time	Yield[g] (%)	m.p. or b.p. Torr (°C)	Lit. data (°C)
16[a]		$CHCl_3$		Classical	OTAB	NaOH (aq)	50–55	1 h	84	79–80/15	108–110/4 (23)
17[a]		$n\text{-}C_{12}H_{25}Br$		Classical	DTAB	NaOH	70–75	9 h	87	210–212/10	
18[a]		$CHCl_3$		Classical	CTAB	NaOH (aq)	60–65	5.5 h	36	76–77	76–78 (24)
19[a]		CH_3CH_2Cl		Classical	CTAB	NaOH (aq)	140–142	8 h	63	94–95/8	93–98/8 (6)
20[a]		CH_3CH_2OH		Classical	CTAB	NaOH	80–82	8 h	42	93–95/8	93–95/8
				Microwave[c]	CTAB	NaOH		2 min	45	93–95/8	93–95/8
21[b]				Classical	CTAB	NaOH (aq)	75–80	16 h	90	164–166/10	185–186/22 (26)
				Microwave[c,d]	CTAB	NaOH (aq)		25 min	90	165–166/10	185–186/22
22[b]	$Me_2C{=}NOH$	$BrCH_2COOH$	$Me_2C{=}NOCH_2COOH$	Classical	ODTA	NaOH (aq)	100	4 h	55	76	76 (26)
				Microwave[e]	ODTA	NaOH (aq)		2 min	68	76	76
23[b]		$ClCH_2COOH$		Classical	DTEAB	NaOH (aq)	100–105	0.5 h	92	150–152	155–156 (27)
				Microwave[e]	DTEAB	NaOH (aq)		5 min	96	151–153	155–156
24[b]		$ClCH_2COOH$		Classical	CPB	NaOH (aq)	105–110	1.5 h	90	138–140	141 (28)
				Microwave[e]	CPB	NaOH (aq)		10 min	95	138–140	141
25[a]		EtOH		Microwave[c]	DTAC	HCl		5 min	84	107–108/12	95–109/15 (29)
26[a]	$n\text{-}C_{12}H_{25}OH$	CH_2COOH	$CH_3COOC_{12}H_{25}\text{-}n$	Microwave[c]	DTAC	HCl		15 min	87	140–142/10	142–144/10 (30)
27[a]	BnOH	$n\text{-}C_4H_9OH$	$BnOC_4H_9\text{-}n$	Microwave[c]	DTAB	HBr		15 min	67	90–92/10	92/10 (31)
28[a]	$BnOCOCH_2$	$n\text{-}C_5H_{11}COOH$	$BnOCOC_5H_{11}\text{-}n$	Microwave[c]	OTAB	HBr		15 min	72	142–144/12	142/10

[aa] Catalyst 1: 0.1 equiv.; [b]catalyst 2: 0.01 equiv.; [c]sealed tube reactions; [d]280 W; [e]atmospheric reactions; [f]catalyst 2, NaOH: 2.5 equiv.; HCl: 0.1 equiv.; [g]product isolated.

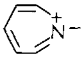
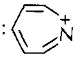
[b] OTAB: $n\text{-}C_8H_{17}\overset{+}{N}(CH_3)_3Br^-$; DTAC: $n\text{-}C_{12}H_{25}\overset{+}{N}(CH_3)_3Cl^-$; DDAC: $n\text{-}C_{12}H_{25}\overset{+}{N}(CH_3)_2(CH_2CH_2OH)Cl^-$; DTAB: $n\text{-}C_{12}H_{25}\overset{+}{N}(CH_3)_3Br^-$; DTEAB: $n\text{-}C_{12}H_{25}\overset{+}{N}(C_2H_5)_3Br^-$; DPB:  $\overset{+}{N}-C_{12}H_{25}\text{-}nBr^-$; CTAB: $n\text{-}C_{16}H_{33}\overset{+}{N}(CH_3)_3Br^-$; CPB:  $\overset{+}{N}-C_{16}H_{33}\text{-}n\ Br^-$; ODTAB: $n\text{-}C_{18}H_{37}\overset{+}{N}(CH_3)_3Br^-$.

TABLE 2
Preparation of Halides from Long-Chain Fatty Alcohol Under Microwave Irradiation (60 W)

No.	Alcohol	HX	Catalyst[a]	Halide	Time (h)	Yield (%)	m.p. or b.p/ Torr (°C)	Lit. data (°C)
1	1-$C_8H_{17}OH$	HBr	OTAB	n-$C_8H_{17}Br$	1.5	92	80–82/10	91–101/22 (13)
2	1-$C_{12}H_{25}OH$	HCl	DTAC	n-$C_{12}H_{25}Cl$	8.0	84	130–132/10	140/15 (14)
3	1-$C_{12}H_{25}OH$	HBr	DPB	n-$C_{12}H_{25}Br$	1.5	91	138–140/12	150–152/18.5 (15)
4	1-$C_{16}H_{33}OH$	HBr	CTAB	n-$C_{16}H_{33}Br$	2.0	88	192–194/10	153–154/1.5 (16)
5	1-$C_{18}H_{37}OH$	HCl	ODTAC	n-$C_{18}H_{37}Cl$	10.0	77	197–201/10	157–158/15 (14)
6	1-$C_{18}H_{37}OH$	HBr	ODTAB	n-$C_{18}H_{37}Br$	2.0	82	17–20	27.4 (17)

[a]For abbreviations, see Table 1 footnote *b*.

Torr. infrared (IR) 3108, 2969, 1601, 1576, 1490, 750, 700. ^1H nuclear magnetic resonance (NMR) d 7.2 (*m*, 5H), 7.1 (*m*, 1H), 6.7 (*d*, 2H), 4.5 (*s*, 2H), 3.4 (*q*, 2H), 1.2 (*t*, 3H). Anal. calcd. for $C_{15}H_{17}N$: C, 85.26; H, 8.11; N, 6.63. Found: C, 85.38; H, 8.24; N, 6.42.

General procedure 4: N*-Alkylation of* N*-ethylaniline with benzyl chloride in the presence of CTAB under microwave irradiation (Table 3).* *N*-ethylaniline [2 mmol (0.23 g)], benzyl chloride [2.2 mmol (0.28 g)], CTAB [0.02 mmol (0.007 g)], and 30% NaOH (NaOH: 0.2 g, 5 mmol) were put in a 10-mL Pyrex tube and sealed off. The sealed tube was protected by a bigger Teflon tube and heated in a household microwave oven (280 W) for 25 min. The mixture was then cooled to room temperature and poured into 10 mL fresh water in a beaker. The mixture was extracted with ether (3 × 10 mL). The organic layer was washed with water (2 × 10 mL) and dried. After the solvent was removed, the residue was chromatographed through a short column of silica gel (70–230 mesh; Beijing Huagong Factory, Beijing, China) with benzene/ethyl acetate as the eluent. The fractions containing *N*-benzyl-*N*-ethylaniline were collected. The eluent was removed in vacuum to give the final product: 0.38 g (90%); b.p. 165–166°C/10 Torr. The product was also verified by IR and ^1H NMR.

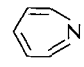
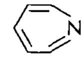
RESULTS AND DISCUSSION

To develop microwave technology in various organic reactions and for practical uses, several devices have been used in our lab, such as single sealed-tube reactions; multiple sealed-tube reactions, which were protected by a bigger Teflon tube; reactions carried out atmospherically with water as a medium; sealed-tube reactions carried out in a water bath at relatively low temperatures; and reactions carried out in a self-made atmospheric microwave reactor. Some methods were selected to synthesize long-chain halides and their quaternary ammonium halides to execute some interesting organic reactions in our laboratory.

In preparation of long-chain halides, a self-made atmospheric microwave reactor and an efficient condenser were used. Hydrohalidation of long-chain alcohols proceeded smoothly and quickly with high yields (Table 2), if quaternary ammonium halide was used as catalyst.

To get a good yield of quaternary ammonium halide, lower reaction temperature and a longer reaction time in a closed reaction vessel would be appropriate (18). To meet the necessary conditions, a microwave oven with a constant-temperature water bath was successful. The results in Table 3 illustrate that not only the reaction time could be shortened, but also that the yield of quaternary ammonium halides could be improved. Because alkyl halide could be alcoholated in the presence of a phase-transfer catalyst and in the absence of any base (3), acetonitrile should be a suitable solvent in the reaction. Although the sealed tube in the water bath was not being protected, an explosion would not be likely because of the low temperature and pressure in the tube. Addition of a catalytic amount of quaternary ammonium halide to the reaction mixture to accelerate the quaternization of tertiary amine

TABLE 3
Preparation of Quaternary Ammonium Halides Under Microwave Irradiation (560 W)

No.	Halide	Amine	Product[a]	Hold temp. (°C)	Time (h)	Yield (%)	m.p. (°C)	
							Found	Reported
7	n-$C_8H_{17}Br$	$N(CH_3)_3$	OTAB	70	8	86	195–198	198–200
8	n-$C_{12}H_{25}Br$	$N(CH_3)_3$	DTAC	70	10	88	245–247	248–249.5 (18)
9	n-$C_{12}H_{25}Cl$	$Me_2NCH_2CH_2OH$	DDAC	80	10	81	188–190	188–190 (19)
10	n-$C_{12}H_{25}Br$	$N(CH_3)_3$	DTAB	70	8	90	232–235	228–230 (18)
11	n-$C_{12}H_{25}Br$	$N(C_2H_5)_3$	DTEAB	80	8	94	113–114	115 (20)
12	n-$C_{12}H_{25}Br$		DPB	70	3	91	72–74	74–75 (21)
13	n-$C_{16}H_{33}Br$	$N(CH_3)_3$	CTAB	70	8	85	233–238	237–243 (18)
14	n-$C_{16}H_{33}Br$		CPB	70	3	92	55–57	56–59 (22)
15	n-$C_{18}H_{37}Br$	$N(CH_3)_3$	ODTAB	70	9	78	232–236	230–240 (18)

[a]For abbreviations, see Table 1 footnote *b*.

under microwave irradiation is the first ever reported on this aspect of the work, even by the conventional heating method.

The phase-transfer catalyst, the household microwave oven, and the self-made atmospheric microwave reactor made possible a variety of organic reactions. The examples given in Table 1 testify to the uncommon effects of phase-transfer catalysts and microwave irradiation. The quaternary ammonium salt is a promoter in catalysis of the reaction as well as in ionization of the reaction medium. The microwave energy can be dissipated efficiently and simultaneously promote molecular collision and friction (32). The probability of a reaction could be increased as the temperature was raised. Thus addition of quaternary ammonium salts, which are efficient phase-transfer catalysts, produces an unexpectedly beneficial effect in microwave reactions.

A new one-pot procedure of the *trans*-Reimer–Tiemann reaction in the presence of a phase-transfer catalyst for synthesizing ethyl vanillin would give a good yield of this fragrant product. Synthesis of *o*-ethoxyphenol, an intermediate of ethyl vanillin, could be achieved by using catechol and ethanol with the quaternary ammonium salt CTAB, and good yields of the product were obtained, whether by classical heating or under microwave irradiation.

The complex of long-chain quaternary ammonium halide with hydrogen halide was formed upon mixing (33) and acted as an efficient catalyst in the esterification of salicylic acid with ethanol, transesterification of benzyl acetate with hexanoic acid, and etherification of benzyl alcohol with 1-butanol under microwave irradiation. The quaternary ammonium salt did promote such reactions as cited. Furthermore, microwave irradiation did accelerate organic reactions, and the long-chain quaternary ammonium salts are the most proper catalysts in these reactions.

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