

We have previously reported that the reaction of several substituted benzyl alcohols with 1 equiv of BTMA Br₃ in carbon tetrachloride in the presence of water or aqueous sodium hydroxide gave the corresponding benzaldehydes.³⁰ In these cases, the obtained benzaldehydes should have been derived by an elimination of the hydrogen bromide from benzyl

Table 1. Oxidation of Hindered Phenols with BTMA Br₃

Run	Substrate	Molar ratio ^{a)}	Solvent etc.	Reaction conditions		Product ^{b)}	Yield ^{c)}
				Temp/°C	Time		%
1		1.0	CH ₂ Cl ₂ /H ₂ O	R.t.	30 min		97
2 ^{d)}		1.0	CH ₂ Cl ₂ /H ₂ O	R.t.	2 min	 { 2, 3	— ^{e)} — ^{e)}
3		1.0	CH ₃ OH	40	1 h		87
4 ^{d)}		2.0	CH ₂ Cl ₂ /H ₂ O	R.t.	3 h	 { 6, 7	— ^{f)} — ^{f)}
5		2.0	CH ₂ Cl ₂ /H ₂ O/ <i>t</i> -BuOH	R.t.	10 h	6	70
6		4.0	CH ₂ Cl ₂ /H ₂ O	R.t.	3 h	7	98
7 ^{d)}		1.0	CH ₂ Cl ₂ /H ₂ O	R.t.	2 min	 { 6, 7	— ^{g)} — ^{g)}
8		2.0	CH ₂ Cl ₂ /H ₂ O	R.t.	1 h	6	90
9		1.0	CH ₂ Cl ₂ /H ₂ O/NaOH	R.t.	5 h		61

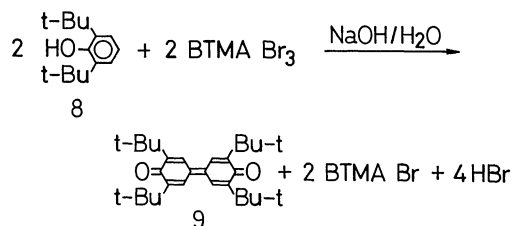
a) BTMA Br₃/substrate. b) Products were characterized by comparing ¹H NMR spectra and mp with those of authentic samples or reported data. c) Yield of isolated product. d) Product was obtained as a mixture, and its ratio was determined by ¹H NMR spectrum. e) 2/3=1/1. f) 6/7=4/5. g) 6/7=2/1.

hypobromites (R-C₆H₄-CH₂OBr), which are produced from benzyl alcohols with Br⁺. However, in the reaction of **2** with BTMA Br₃, it is reasonable to consider that the reaction proceeded via an intermediate, 4-bromo-4-hydroxymethyl-2,6-di-*t*-butyl-2,5-cyclohexadienone, as shown in Scheme 2, since compound **7** is also obtained together with **6** when the reaction is run for a short time (Run 7). That is, compound **2**, a hindered phenolic benzyl alcohol, should first react with Br⁺ at the 1-position, affording the intermediate.

Otherwise, it has already been reported that the reaction of 2,6-di-*t*-butylphenol (**8**) with oxygen in the presence of a base gives 3,5,3',5'-tetra-*t*-butyl-4,4'-

diphenylquinone (**9**).⁵⁾ This compound **9** has also been obtained by the oxidation of **6**, **8**, and 3,5-di-*t*-butyl-4-hydroxybenzoic acid with alkaline hexacyanoferrate (III) or lead dioxide in the absence of molecular oxygen.⁶⁾ We have now found that the reaction of **8** with 1.0 equiv of BTMA Br₃ in dichloromethane in the presence of aqueous sodium hydroxide at room temperature for 5 h gives **9** in satisfactory yield. This reaction may be included a dimerization of the corresponding phenoxyl radical.⁶⁾

We believe that the main active species for oxidation in the presence of water is probably hypobromous acid, which may be produced from a reaction of



Scheme 3.



Scheme 4.

BTMA Br₃ with water. The oxidation of 1,4-benzenediols to 2,5-cyclohexadiene-1,4-diones with BTMA Br₃ in aqueous acetic acid was reported in our previous paper.¹⁾ Similarly, it is almost certain that *t*-butyl hypobromite and sodium hypobromite are the main active oxidizing species for the reaction in *t*-butyl alcohol and in aqueous sodium hydroxide, respectively.

Furthermore, the reaction of phenols, which did not have a bulky *t*-butyl group at both *o*-positions for the hydroxyl group, with BTMA Br₃ gave electrophilic bromo-substituted products. For example, the reaction of 4-hydroxy-3-methoxybenzyl alcohol (vanillyl alcohol) with 1.0 equiv of BTMA Br₃ in dichloromethane in the presence of *t*-butyl alcohol gave 3-bromo-4-hydroxy-5-methoxybenzyl alcohol (60% yield).

We emphasize that the stable solid reagent BTMA Br₃ is a useful oxidizing agent for the hindered phenols, since it can be treated safely and quantitatively in comparison with toxic liquid bromine.

Experimental

Oxidation of 2,6-Di-*t*-butyl-4-methylphenol (1) with 1.0 equiv of BTMA Br₃ and Water (Table 1, Run 1): To a solution of BTMA Br₃ (1.17 g, 3.0 mmol) in dichloromethane (10 ml) was added **1** (0.66 g, 3.0 mmol) and water (10 ml). The mixture was stirred at room temperature for 30 min until the initial orange color faded. The water layer was then filtered through wet filter paper. The separated organic layer was washed with water and dried over MgSO₄, filtered, and evaporated in vacuo to give 3,5-di-*t*-butyl-4-hydroxybenzyl alcohol (**2**) as a yellow solid; yield 0.69 g (97%); mp 133–135 °C (lit.²⁾ mp 137.7–138.1 °C).

Oxidation of 1 with 1.0 equiv of BTMA Br₃ in Methanol (Table 1, Run 3): To a solution of **1** (0.66 g, 3.0 mmol) in methanol (30 ml) was added BTMA Br₃ (2.34 g, 6.0 mmol). The mixture was stirred for 1 h at 40 °C. After the reaction mixture was concentrated in vacuo, a yellow solid obtained was extracted with ether (10 ml×3), and the organic layer was evaporated in vacuo to give 2,6-di-*t*-butyl-4-methoxy-4-methyl-2,5-cyclohexadienone (**5**) as colorless needles; yield 0.29 g (87%); mp 95–97 °C (lit.²⁾ mp 94 °C).

Oxidation of 1 with 2.0 equiv of BTMA Br₃ and *t*-Butyl Alcohol-Water (Table 1, Run 5): To a solution of BTMA Br₃ (2.34 g, 6.0 mmol) in dichloromethane (10 ml) was added **1** (0.66 g, 3.0 mmol), water (10 ml) and *t*-butyl alcohol (10 ml). The mixture was stirred at room temperature for

10 h until the initial orange color faded completely. The mixture was then treated by a similar procedure to that described as Run 1. Thus, 3,5-di-*t*-butyl-4-hydroxybenzaldehyde (**6**) was obtained as colorless crystals; yield 0.49 g (70%); mp 191–193 °C (lit.²⁾ mp 189 °C).

Oxidation of 1 with Large Excess of BTMA Br₃ and Water (Table 1, Run 6): To a solution of BTMA Br₃ (4.68 g, 12 mmol) in dichloromethane (10 ml) was added **1** (0.66 g, 3.0 mmol), and water (20 ml). The mixture was stirred at room temperature for 3 h. The mixture was then treated by a similar procedure to that described as Run 1. Thus, 4-bromo-4-bromomethyl-2,6-di-*t*-butyl-2,5-cyclohexadienone (**7**) was obtained as yellow crystals; yield 1.11 g (98%); mp 132–134 °C (lit.⁵⁾ mp 118 °C). ¹H NMR (CDCl₃) δ=1.27 (18H, s, 2C₄H₉), 3.96 (2H, s, CH₂Br), 6.61 (2H, s, Harom). Found: C, 48.74; H, 5.58%. Calcd for C₁₅H₂₂OBr₂: C, 47.64; H, 5.86%.

Oxidation of 3,5-Di-*t*-butyl-4-hydroxybenzyl Alcohol (2) with 2.0 equiv of BTMA Br₃ and Water (Table 1, Run 8): To a solution of BTMA Br₃ (2.34 g, 6.0 mmol) in dichloromethane (10 ml) was added **2** (0.71 g, 3.0 mmol) and water (10 ml). The mixture was then stirred at room temperature for 1 h. The mixture was treated as Run 1. Thus, compound **6** was obtained as colorless crystals; yield 0.63 g (90%); mp 191–193 °C.

Reaction of 2,6-Di-*t*-butylphenol (8) with 1.0 equiv of BTMA Br₃ and Aqueous Sodium Hydroxide (Table 1, Run 9): To a solution of BTMA Br₃ (1.17 g, 3.0 mmol) in dichloromethane (20 ml) was added **8** (0.62 g, 3.0 mmol) and aqueous sodium hydroxide (NaOH; 0.25 g, 6.3 mmol, H₂O; 14 ml). The mixture was stirred at room temperature for 5 h. The organic layer was then separated, washed with water, dried over MgSO₄, and evaporated in vacuo to give crude 3,5,3',5'-tetra-*t*-butyl-4,4'-diphenylquinone (**9**) as a brown-red solid. The crude product was purified through a column packed with silica gel using hexane as a developing solvent. Thus, **9** was obtained as purple columnar crystals; yield 0.37 g (61%); mp 255–257 °C (lit.⁵⁾ mp 246 °C). IR (KBr) 1598 (C=O); ¹H NMR (CDCl₃) δ=1.35 (36H, s, 4 C₄H₉), 7.64 (4H, s, Harom). Found: C, 81.98; H, 10.21%. Calcd for C₂₈H₄₀O₂: C, 82.28; H, 9.89%.

References

- 1) Part VIII of this series: S. Kajigaeshi, Y. Morikawa, S. Fujisaki, T. Kakinami, and K. Nishihira, *Bull. Chem. Soc. Jpn.*, **64**, 336 (1991).
- 2) G. M. Coppinger and T. W. Campbell, *J. Am. Chem. Soc.*, **75**, 734 (1953).
- 3) a) S. Kajigaeshi, K. Asano, S. Fujisaki, T. Kakinami, and T. Okamoto, *Chem. Lett.*, **1989**, 463; b) S. Kajigaeshi, T. Kakinami, T. Yamaguchi, T. Uesugi, and T. Okamoto, *Chem. Express*, **4**, 177 (1989); c) S. Kajigaeshi, H. Kawamukai, and S. Fujisaki, *Bull. Chem. Soc. Jpn.*, **62**, 2585 (1989); d) S. Kajigaeshi, K. Murakawa, K. Asano, S. Fujisaki, T. Kakinami, and T. Okamoto, *J. Chem. Soc., Perkin Trans., 1*, **1989**, 1702; e) S. Kajigaeshi, K. Murakawa, S. Fujisaki, and T. Kakinami, *Bull. Chem. Soc. Jpn.*, **62**, 3376 (1989); f) T. Okamoto, T. Uesugi, T. Kakinami, T. Utsunomiya, and S. Kajigaeshi, *Bull. Chem. Soc. Jpn.*, **62**, 3748 (1989).
- 4) We previously reported that the reaction of several substituted benzyl alcohols with 2 equiv of BTMA Br₃ in aqueous sodium hydroxide gave sodium benzoates in good yields.³⁾
- 5) M. S. Kharasch and B. S. Joshi, *J. Org. Chem.*, **22**, 1439 (1957).
- 6) C. D. Cook, E. S. English, and B. J. Wilson, *J. Org. Chem.*, **23**, 755 (1958).