SHORT PAPER

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A controlled and selective bromination of phenols by benzyltriphenylphosphonium tribromide[†]

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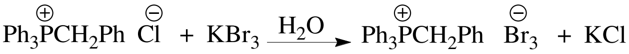
Reactions of phenols with benzyltriphenylphosphonium tribromide in dichloromethane–methanol mixture (2:1) gave mono,di and tri brominated phenols at room temperature with high selectivity and good yields.

Keywords: phenols, bromination, benzyltriphenylphosphonium tribromide

Bromination, especially of aromatic substrates, is usually carried out by bromine[1] solution, but organic ammonium tribromides (OATB) are preferable, since they do not have the hazards that are associated with liquid bromine. Other advantages of OATB are that they are crystalline, easy to handle, and maintain the desired stoichiometry.[2] Therefore several tribromides have been synthesised *i.e.* tetramethylammonium tribromide,[3] tetrabutylammonium tribromide,[4] 1,8-diazabicyclo [5,4,0]undecene hydrobromide perbromide,[5] and benzyltrimethylammonium tribromide.[6] These reagents have been used as brominating agents.

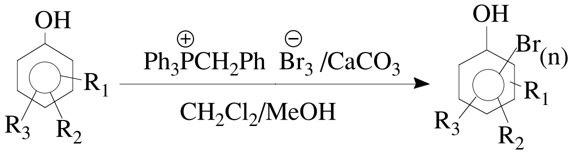
Ammonium tribromides often give polybrominated aromatic compounds.[6] Since phosphonium tribromide have shown milder reactivity in bromination of organic compounds,[7,8] we now wish to report benzyltriphenylphosphonium tribromide as a selective and mild reagent for the bromination of phenolic derivatives. Thus benzyltriphenylphosphonium tribromide (**3**) was synthesised by the reaction of benzyltriphenylphosphonium chloride (**1**) with KBr_3 (**2**) in good yield Scheme 1. Reagent **3** was also prepared by the addition of hydrobromic acid to an aqueous solution of benzyltriphenylphosphonium chloride and sodium bromate.[9] This reagent showed an intense ultraviolet absorption at 267 nm typical of tribromide (Br_3^-) group.[10]



$$\underset{\textbf{(1)}}{Ph_3\overset{\oplus}{P}CH_2Ph\ \overset{\ominus}{Cl}} + \underset{\textbf{(2)}}{KBr_3} \xrightarrow{H_2O} \underset{\textbf{(3)}}{Ph_3\overset{\oplus}{P}CH_2Ph\ \overset{\ominus}{Br_3}} + KCl$$

Scheme 1

Reagent **3** was reacted with several phenol derivatives **4a–o** in presence of $CaCO_3$ in dichloromethane–methanol solution (2:1) at room temperature. The bromination reactions occurred under mild conditions and gave mono, di and tribrominated compounds in good yields, Scheme 3, Table 1. It is important to note that, the bromination reaction can lead to the formation of specific products which could be controlled by the stoichiometry of the reagent **3** to the phenol derivatives. For example phenol can be monobrominated as well as tribrominated (Table 1, entry **4a**, **4a′**). This reagent also showed regioselectivity in the bromination of phenol. Although in phenol there are two positions (*ortho* and *para*) which could be brominated, only the *para* position was brominated (Table 1, entry **4a**), and no *ortho* brominated product was detected by TLC or ^1H NMR. When compound **4m**, was treated with 3 or 4 molar equivalents of reagent **3**, a mixture of brominated products were observed, which were not separated. However, when only 2 molar equivalents of reagent **3** was used only the dibrominated adduct was isolated in high yield. It has been reported that bromine chloride under harsh condition has been employed for the bromination of compound 4l.[11] However, reagent **3** resulted in a monobrominated adduct in high yield under mild conditions.



(4) **(5)**

R_1, R_2, R_3 = H or Cl or CH_3 or NO_2

Scheme 2

The mechanism of bromination by reagent **3** could be explained in terms of formation of MeOBr by the reaction of MeOH with reagent **3**. Subsequently MeOBr will transfer Br^+ to the aromatic phenols and MeOH will be regenerate[6] (Scheme 3).

In conclusion we have developed an easy, highly efficient, regioselective method for the bromination of phenol derivatives by reagent **3**. This reagent is a stable solid crystalline substance, which can be easily handled and kept for months without losing its activity. Furthermore, the bromination reaction can be controlled in many cases by the amount of reagent. From the proposed mechanism, it is clear that the by-product $Ph_3P^+CH_2Ph\ Br^-$ can be reacted with liquid bromine and reagent **3** will be regenerated and used again.

Experimental

General: All yields refer to isolated products after purification. All the products were confirmed by comparison with authentic samples (m.p., TLC and ^1H-NMR). All melting points were taken on a Gallenkamp melting apparatus and are uncorrected. ^1H-NMR spectra were recorded on a Varian EM-390 NMR Spectrometer operating at 90 MHz. The spectra were measured in $CDCl_3$ unless otherwise stated, relative to TMS.

Preparation of benzyltriphenylphosphonium tribromide (**3**)*:* Bromine (16.0 g, 0.1 mol) was addedd dropwise to a solution of KBr

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[†] This is a Short Paper, there is therefore no corresponding material in *J Chem. Research (M).*

$$\mathrm{Ph_3\overset{\oplus}{P}CH_2Ph\ \overset{\ominus}{Br_3}} + \mathrm{MeOH} \longrightarrow \mathrm{Ph_3\overset{\oplus}{P}CH_2Ph\ \overset{\ominus}{Br}} + \mathrm{MeOBr} + \mathrm{HBr}$$

$$\mathbf{(4)} + \mathrm{MeOBr} \longrightarrow \mathbf{(5)} + \mathrm{MeOH}$$

Scheme 3

Table 1 Bromination of phenols (**4**) by reagent (**3**)

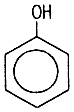
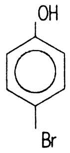
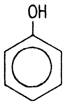
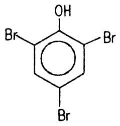
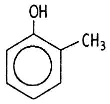
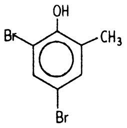
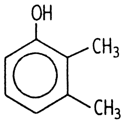
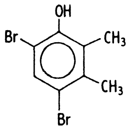
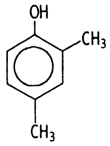
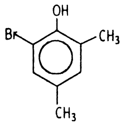
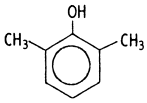
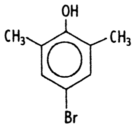
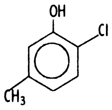
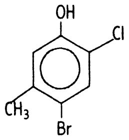
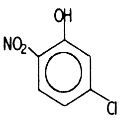
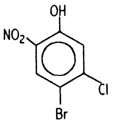
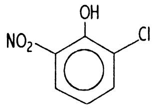
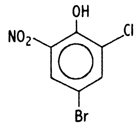
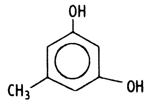
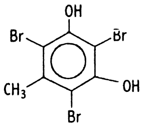
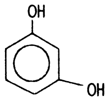
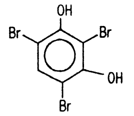
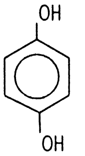
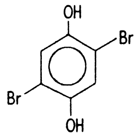
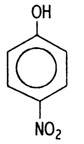
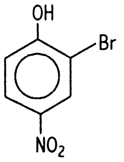
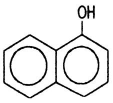
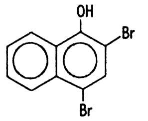
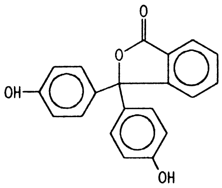
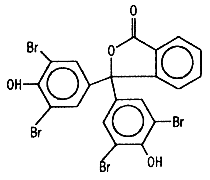
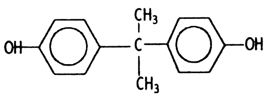
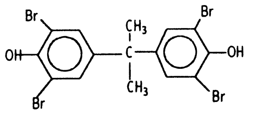
Entry	Starting material (**4**)	Product (**5**)[a]	Molar ratio (3/4)	Time/h	Yield%[b]	m.p./°C or bp °C/torr	
						Found	Reported
4a			1/1	0.5	92	63–65	66[12]
4a′			3/1	0.5	95	90–91	95–96[13]
4b			2/1	0.5	95	54–56	57[14]
4c			2/1	1	70	66–67	67–68[6]
4d			1/1	0.5	94	232/760	231/760[15]
4e			1/1	0.5	93	78–79	79.5[16]
4f			1/1	1	94	55–57	——
4g			1/1	7	85	65–66	68[17]

Table 1 Bromination of phenols (**4**) by reagent (**3**) *(continued)*

Entry	Starting material (**4**)	Product (**5**)[a]	Molar ratio (3/4)	Time/h	Yield%[b]	m.p. °C or bp °C/torr	
						Found	Reported
4h			1/1	7	90	114	114[18]
4l			3/1	0.5	95	95–96	98–99[19]
4j			3/1	0.5	80	110–111	112[20]
4k			2/1	0.5	85	185–186	186[21]
4l			1/1	5	90	111–112	114[22]
4m			2/1	1	95	103–104	105[23]
4n			4/1	1	92	278–279	278–279[24]
4o			4/1	1	92	178–180	179–181[25]

[a]All of isolated products are known and their spectra and physical data have been reported in literature.
[b]Pure product.

(11.9 g, 0.1 mol.) in water (200 ml) with stirring at room temperature. After one hour the bromine layer disappeared and KBr_3 was formed. The KBr_3 solution was added dropwise to a solution of benzyltriphenylphosphonium chloride (38.8 g, 0.1 mol) in water (200 ml) was added until a yellow precipitate was formed. After stirring 30 min, the mixture was filtered and washed with water (3 x 30 ml). The filtered cake was dried and recrystallised from $CHCl_3$ to give **3** as yellow crystals (53.4 g, 90% yield), m.p.: 136–137°C. Anal Calcd for $C_{25}H_{22}Br_3P$: C: 50.84%, H: 3.72%. Found C: 50.74%, H: 3.60%.

Bromination of phenols (**4a–o**)*:* The regeant **3** (3.56 g, 6 mmol) was added to a solution of phenol (**4a**) (0.19 g, 2 mmol) in dichloromethane (20 ml)-methanol (10 ml). The mixture was stirred for 30 min at room temperature whilst decolorisation of the orange solution took place. When TLC showed the complete disappearance of phenol, the solvent was evaporated and the solid residue was washed with ether (4 x 40 ml) and filtered off. The combined organic layer was dried on magnesium sulfate, and evaporated under vacuum to give 2,4,6-tribromophenol **5a′**, which was recrystallised in (methanol/water) (1:3) as a colourless needles m.p. 90–91° in 95% yield (0.63 g).

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References

1 (a) R.C. Fuson, *Reaction of Organic Compounds,* New York, Wiley, 1962, **58**, 98; (b) R.O.C. Norman and R. Taylor, *Electrophilic Substitution in Benzenoid Compounds*, New York, American Elsevier, **1965**, 130.
2 D. Dey, W. Kharmawophlang, T.R. Lakshmiprabha and G.C. Mandal, *Tetrahedron Lett*., 1998, **39**, 8163.
3 (a) F.D. Gattaway; G. Hoyle, *J. Chem. Soc,* 1923, 654; (b) M. Avramoff, J. Weiss and O. Schaechter, *J. Org. Chem.,* 1963, **28,** 3256.
4 S. Kajigaeshi, T. Kakinami, H. Yamasaki, S. Fujisaki and T. Okamoto, Bull. Chem. Soc. Jpn., 1988, **61,** 2681.
5 H.A. Muathen, *J. Org. Chem*., 1992, **57,** 2740.
6 S. Kajigaeshi, T. Kakinami, H. Tokiyama,T. Hirakava and T. Okamoto*, Chem. Lett.,* 1987, 627.
7 H.J. Cristau, E. Torreilles, P. Morand, and H. Cristol, *Phosphorus Sulfur*, 1985, **25**, 357–368.
8 V.W. Armstrong, N.H. Chishti and R. Ramage*, Tetrahedron Lett*., 1975, **6**, 373.
9 D. Xin-teng, T. Gue-bin, *Synth. Commun*., 1989, **19**, 1261.
10 R.C. Thampson, *Adv. Inorg. Bioinorg. Mech*., 1986,**4**, 65
11 C.O. Obenland, *.J Chem.Edu*., 1964, **41**, 566.
12 R. Adams, C.S. Marrei, H.T. Clarke, C.R. Nooller, J. Bconant, F.C. Whitmore, *Organic. Syntheses*, New York, John Wiley and Sons. 1941, Coll. Vol.**1**,194.
13 L. Cohnand, and F. Schultse, *Ber*. 1905, **38**, 3297.
14 J. Buckingham and S.M. Donagy, *Dictionary of Organic Compounds*, 5th edn, New York, Chapman and Hall, 1982, D-01927.
15 J. Buckingham and S.M. Donaghy*, Dictionary of Organic Compounds*, 5th edn, New York, Chapman and Hall, 1982, B-023.
16 M. Fojio, *Bull. Chem. Soc. Jpn*., 1975, **48,** 217.
17 J. Buckingham and S.M. Donaghy, *Dictionary of Organic Compounds*, 5th edn, New York, Chapman and Hall, 1982**,** B-02145.
18 A.R. Ling, J. Chem. Soc., 1989, **55,** 585.
19 R.L. Datta and J.C. Bhoumik, J. Am. Chem. Soc., 1921, **43**, 309.
20 J. Buckingham and S.M. Donaghy, *Dictionary of Organic Compounds*, 5th edn, New York, Chapman and Hall,1982, T-10204.
21 J. Buckingham and S.M. Donaghy, *Dictionary of Organic Compounds*, 5th edn, New York, Chapman and Hall, 1982, D-01461.
22 J. Buckingham and S.M. Donaghy, *Dictionary of Organic Compounds*, 5th edn, New York, Chapman and Hall, 1982, B-03050.
23 J. Kryaski, CA, 1928, **22**, 4120.in J. Buckingham and S.M. Donaghy, *Dictionary of Organic Compounds*, 5th edn, New York, Chapman and Hall, 1982, D-01940.
24 Aldrich, Catalogue Handbook of Fine Chemical, pp. 1198, 1994–1995
25 Aldrich, Catalogue Handbook of Fine Chemical, pp. 777, 1994–1995