Pergamon

Tetrahedron 55 (1999) 11127–11142

TETRAHEDRON

Simple and Practical Halogenation of Arenes, Alkenes and Alkynes with Hydrohalic Acid/H_2O_2 (or TBHP)

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Received 11 January 1999; revised 29 June 1999; accepted 15 July 1999

Abstract: A simple protocol for the halogenation of arenes utilizing a combination of aqueous hydrogen peroxide (34 %) or *tert*-butylhydroperoxide (70 %) and hydrohalic acid is presented. A similar procedure of oxyhalogenation involving the *in situ* generation of positive halogen reagents is applied for the preparation of vicinal *trans*-dibromoalkanes and dichloroalkanes from alkenes. The reaction of alkenes with a combination of hydrochloric acid and hydrobromic acid with hydrogen peroxide gave a mixture of 1-bromo 2-chloro alkanes and 1,2-dibromoalkanes. Oxidative bromination of alkynes is also reported under similar conditions.

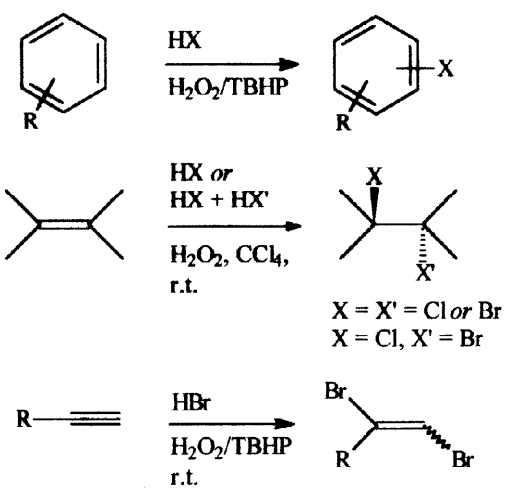
Keywords: Oxyhalogenation; arenes; alkenes; alkynes.

Introduction

Halogenated organic compounds form an important class of intermediates as they can be converted efficiently into other functionality by simple chemical transformations. Halogenated arenes and alkanes are precursors to organometallic reagents [1] useful in synthetic organic chemistry. Preparation of halogenated compounds using molecular halogen with or without transition metal based catalysts has several environmental drawbacks [2] arising out of the toxic nature of the reagents/catalysts. The use of *tert*-butylhypohalite and hypohalous acid for halogenation [3,4] and oxidation [5] reactions has received considerable attention. The preparation of *tert*-butylhypohalite is available in the literature [6] but is known to pose some handling problems due to its hazardous nature. To overcome these difficulties some researchers [7,8,9] have utilized a combination of hydrohalic acid and suitable oxidant such as *tert*-butylhydroperoxide (TBHP) or hydrogen peroxide, which *in situ* generates positive halogen

0040-4020/99/$ - see front matter
PII: S0040-4020(99)00628-6

species for the halogenation of organic substrates. In this reaction system full utilization of halogen is achieved with little environmental problems as the waste is only water. In our preliminary communication [10] we have demonstrated efficient chlorination and bromination of the aromatic nucleus with this reagent system. In their work on the halogenation of olefins, Olah and coworkers [8] have reported the use of hydrogen peroxide and hydrohalic acid but require one equivalent of calcium halide and a phase-transfer catalyst for efficient reaction. In the present work we wish to elaborate on our comprehensive study on the oxyhalogenation of aromatic compounds, alkenes and alkynes with the combination of hydrohalic acid and a suitable oxidant such as TBHP or hydrogen peroxide (Scheme 1) without the use of calcium halide or any catalyst. We further investigate the possibility to introduce two different halogen atoms on alkanes by this reaction system when two different hydrohalic acids are utilized in the dihalogenation of alkenes.



Scheme 1

Results and discussions

A number of aromatic substrates were subjected to the oxyhalogenation conditions where the positive halogen reagents were to be produced *in situ* for the electrophilic halogenation of the aromatic ring. We selected methanol as the solvent because of good solubility of all the reagents as well as its suitable polarity. Bromination of anisole was achieved in good yield and high regioselectivity using one equimolar mixture of TBHP (70%) and HBr (48% aq.) in boiling methanol (Table 1; entry 1). The chlorination of anisole, however, required a large excess of reagents (4 eq.) resulting in substantial drop in the efficiency (50 % yield; with *ortho:para* ratio 35:65). Similarly 1,4-dimethoxybenzene furnished the mono bromo compound in good yield when treated with one equimolar mixture of TBHP and HBr (entry 2). Electrophilic bromination of 1,4-dimethoxybenzene with *in situ* generated bromonium ion was observed to be more efficient compared to anisole as the former is a more electron rich system.

Bromination of 4-methylphenol was directed *ortho* to the hydroxyl (entry 3) and exclusively *para* to methoxy in 3-methoxy methylbenzoate (entry 4). Further examples of regioselective halogenation were observed in reactions with 2- and 3-methoxy-*N,N*-dimethylbenzamide with halogenation being directed *para* to the electron donating methoxy group (entries 5 to 7).

Table 1: Halogenation of aromatic compounds:

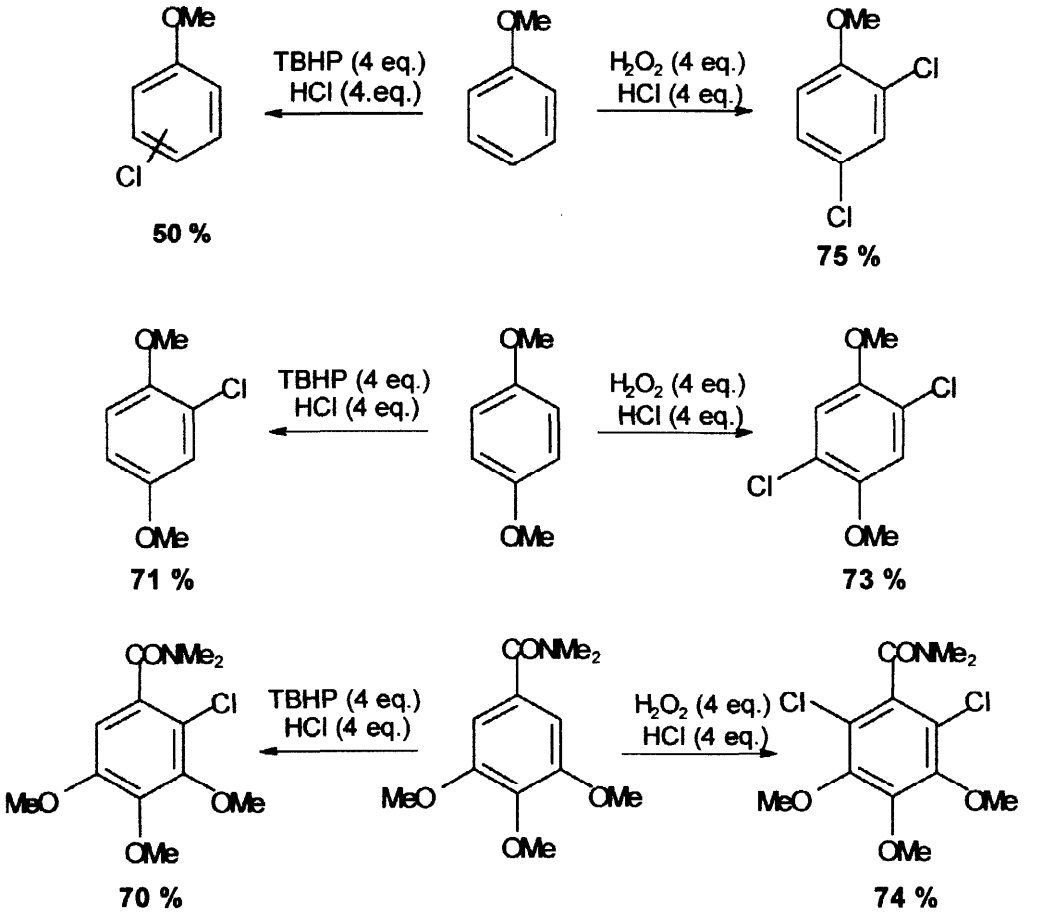
Entry	Aromatic nucleus	Reaction condition	Product[a]	Yield[b] in %
1	Anisole	TBHP (1.0 eq.) HBr (1.0 eq.)	4-Bromoanisole	76
2	1,4-Dimethoxybenzene	TBHP (1.0 eq.) HBr (1.0 eq.)	2-Bromo-1,4-dimethoxybenzene	89
3	4-Methylphenol	TBHP (1.0 eq.) HBr (1.0 eq.)	2-Bromo-4-methyl phenol	74
4	3-Methoxy methybenzoate	TBHP (1.0 eq.) HBr (1.0 eq.)	2-Bromo-5-methoxy methylbenzoate	73
5	*N,N*-Dimethyl (2-methoxy)benzamide	TBHP (4.0 eq.) HCl (4.0 eq.)	*N,N*-Dimethyl(3-chloro-6-methoxy)benzamide	88
6	*N,N*-Dimethyl (3-methoxy)benzamide	TBHP (1.0 eq.) HBr (1.0 eq.)	*N,N*-Dimethyl(2-bromo-5-methoxy)benzamide	98
7	*N,N*-Dimethyl (3-methoxy)benzamide	TBHP (4.0 eq.) HCl (4.0 eq.)	*N,N*-Dimethyl(2-chloro-5-methoxy)benzamide	38
8	*N,N*-Dimethyl (3,4,5-trimethoxy)benzamide	TBHP (1.0 eq.) HBr (1.0 eq.)	*N,N*-Dimethyl(2-bromo-3,4,5-trimethoxy)benzamide	93
9	*N,N*-Dimethyl(2-methyl-3,4,5-trimethoxy)benzamide	TBHP (4.0 eq.) HCl (4.0 eq.)	*N,N*-Dimethyl(2-chloro-3,4,5-trimethoxy-6-methyl)benzamide	70
10	1,4-Dimethoxybenzene	TBHP (4.0 eq.) HBr (4.0 eq.)	2,5-Dibromo-1,4-dimethoxybenzene	98
11	1,4-Dimethoxybenzene	H_2O_2 (4.0 eq.) HBr (4.0 eq.)	2,5-Dibromo-1,4-dimethoxybenzene	99
12	*N,N*-Dimethyl (3,4,5-trimethoxy)benzamide	TBHP (4.0 eq.) HBr (4.0 eq.)	*N,N*-Dimethyl(2,6-dibromo-3,4,5-trimethoxy)benzamide	93

[a]*Characterised by usual spectral and analytical methods;* [b]*isolated yield.*

It was interesting to note that only dibromination of 1,4-dimethoxybenzene was observed in nearly quantitative yield when treated with excess (4 eq) of TBHP or H_2O_2 with HBr

(entries10 & 11). The absence of halogenation of the ring methyl group (entry 3 and 9) is indicative of the electrophilic mechanism of the reaction rather than a radical pathway.

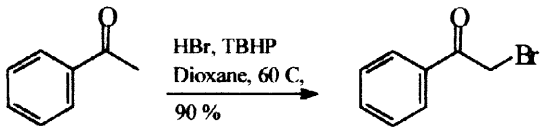
The bromination of 1,4-dimethoxybenzene with excess (4 eq. each) of HBr and TBHP as well as H_2O_2 as oxidant afforded a dibrominated product. However, a similar set of reactions with HCl gave quite a different result. The chlorination of 1,4-dimethoxybenzene with excess of TBHP and HCl (4 eq. each) afforded the 2-chloro-1,4-dimethoxybenzene in 71% yield without formation of detectable amounts of the dichloro compound, whereas H_2O_2 furnished 2,5-dichloro-1,4-dimethoxybenzene as the single product in 73 % yield (Scheme 2). This interesting selectivity between the oxidant was confirmed by performing the reaction on anisole and *N,N*-dimethyl(3,4,5-trimethoxy)benzamide (Scheme 2).



Scheme 2

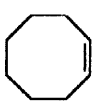
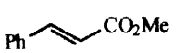
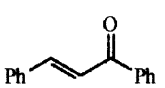
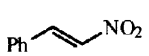
It is believed that the chlorination proceeds *via* the formation of *tert*-butylhypochlorite when the combination of TBHP/HCl was used while *via* hypochlorous acid when H_2O_2/HCl was used. The hypochlorous acid has higher instability [11] due to pronounced ionic nature compared to *tert*-butylhypochlorite and thus more reactivity towards the aromatic nucleus. The lack of similar selectivity for HBr could be because of much higher reactivity of the bromonium ion due to its superior electrophilic nature.

We attempted the bromination of acetophenone with hydrobromic acid and TBHP (eq. each). Careful GLC and proton NMR spectroscopic analysis of the reaction product indicated that the bromination did not occur on the ring but on the methyl group giving 2-bromoacetophenone. This reaction was performed in dioxane since an impurity of 2-methoxyacetophenone was detected in methanol.



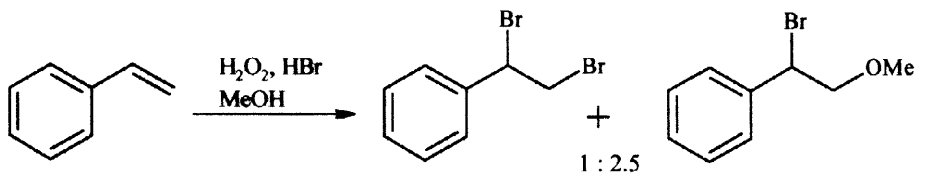
Vicinal dihalogenation of alkenes is often reported with complicated reagents as the source of positive halogen [12]. After the successful implementation of this methodology for aromatic halogenation we were interested in extending it to the halogenation of alkenes. In order to test the reaction, a solution of alkene in carbon tetrachloride or in dioxane was treated with a mixture of aqueous hydrochloric acid or hydrobromic acid and hydrogen peroxide at ambient temperature. We believe that the reaction of halonium ion generated *in situ* reacts with the alkene to give a cyclic halonium ion intermediate which is attacked by halide from the reverse side giving selectively the *trans* vicinal dihalo compound. After usual work-up the dihalogenated compounds are isolated in good yields and the results are summarized in Table 2

Table 2: Vicinal dihalogenation of alkenes.

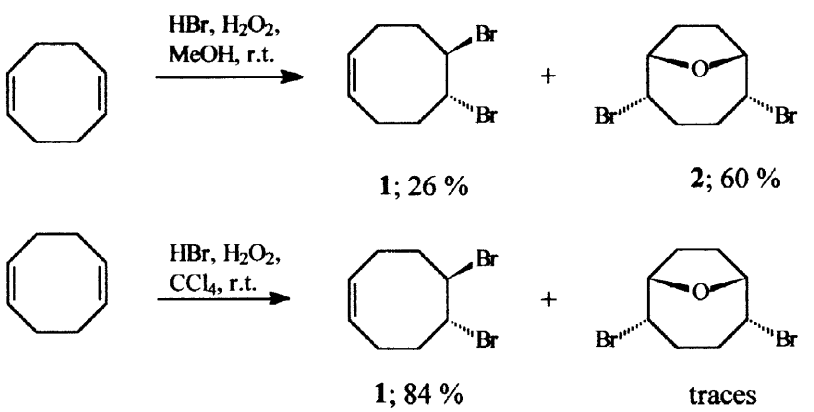
Entry	Olefin	% Yield[a]	
		vic-Dichloro[b]	*vic*-Dibromo[c]
1		75	86
2		64	82
3	1-Decene	80	95
4		70	99
5		54	97
6		--	98

[a]*Isolated yield. All the products are characterised by usual analytical methods;* [b]*With 2 eq. H_2O_2 and 6 eq. HCl ;* [c]*With 2 eq. H_2O_2 and 2 eq. HBr.*

The reaction with hydrochloric acid furnished *trans*-dichloro products in slightly low yield compared to the reaction with hydrobromic acid in all cases. The reaction is also extended to α,β-unsaturated carbonyl systems like methyl cinnamate and chalcone with good efficiency. Dibromination of β-nitrostyrene was also achieved with almost quantitative conversion with H_2O_2/HBr system, however the corresponding dichlorination could not be carried out. This transformation was also investigated with aqueous *tert*-butylhydroperoxide (TBHP) in place of hydrogen peroxide. The results with both oxidants were found to be comparable. The reaction of styrene with H_2O_2/HBr system in methanol as solvent revealed interesting results. Careful analysis of the reaction products suggested the formation of 1-bromo-1-phenyl-2-methoxy ethane along with vicinal dibromo product.



Haufe and coworkers [13] have reported the reaction of Z,Z-1,5-cyclooctadiene with the bromonium ion generated from *N*-bromosuccinimide. The reaction in methanol proceeds via an intermediate bromohydrin and finally gives dibromo oxabicyclic product **2** instead of the expected *trans*-5,6-dibromo-(*Z*)-cyclooctene **1**, (Scheme 3). We investigated this reaction with our reagent system. The reaction of *Z,Z*-1,5-cyclooctadiene with aqueous HBr (2 eq.) and hydrogen peroxide (2 eq.) in methanol indeed followed the same course and resulted in the formation of **2** as the major product. However, in carbon tetrachloride the dibromo product **1** was formed as a major product (Scheme 3) with only traces of compound **2**. We assume that the reaction in methanol proceeds via an intermediate bromohydrin, *trans*-6-bromo-(Z)-cycloocten-5-ol while in CCl_4 some amount of Br_2 is formed which might be responsible for the formation of **1** as a major product.

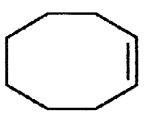
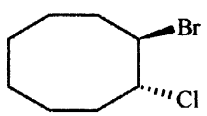
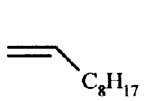
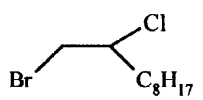
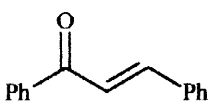
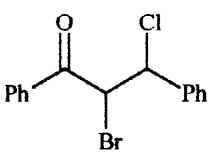
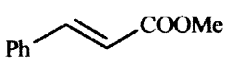
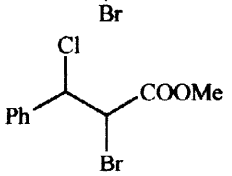


Scheme 3

Saturated halogenated compounds with two different halogens are an important class of substances. The heterohalogenated alkanes can be converted into a variety of functional groups taking advantage of the reactivity difference of halogens towards nucleophilic substitution reactions. The presently available methods of converting the alkenes into 1,2-heterohalogenated alkanes involve the use of positive halogen reagents [14] in combination with halides. We wish to present our findings on the preparation of *trans*-1-bromo-2-chloro alkanes from alkenes and *in situ* generated positive reagents.

A solution of alkene and an excess of aqueous hydrochloric acid (10 eq.) in dioxane is treated with a mixture of hydrogen peroxide (1.5 eq.) and hydrobromic acid (1.0 eq.) and the results are presented in Table 3. The reaction mixture showed the presence of some amount of *trans*-1,2-dihalo alkane along with the *trans*-1-bromo-2-chloro alkane as the main product. The ratio of bromochloro alkane was much higher for methyl cinnamate and chalcone than for the other examples studied. The attack of chloride ion on the intermediate bromonium ion proceeds with regioselectivity to give a single isomer of bromo chloro products.

Table 3: Preparation of bromo-chloro alkanes from alkenes.

Entry	Alkene	Chloro-bromo alkane	Yield[a] in % (chloro-bromo:dibromo:dichloro)[b]
1.			97 (76:11:13)
2.			98 (78:11:11)
3.			89 (93:4:3)
4.			92 (94:4:2)

[a]*Isolated Yield;* [b]*Determined by* ^1H *NMR spectroscopy.*

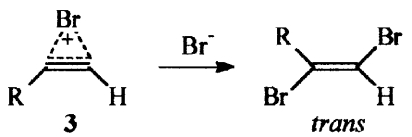
This protocol of dibromination was then applied to the preparation of dibromoalkenes from alkynes as this conversion has received relatively less attention [15, 16]. Action of a mixture of aqueous hydrobromic acid and the oxidant on various alkynes was studied and the results are presented in Table 4.

Table 4: Dibromination of alkynes with aqueous hydrobromic acid and hyrogen peroxide or *tert*-butylhydroperoxide.

Entry	Alkyne	Oxidant[a]	% Yield[b] of dibromoalkene (*trans*:*cis*)[c, ref.]
1	1-Hexyne	H_2O_2	78 (76:24)[14]
2	1-Hexyne	TBHP	71 (92:8)[14]
3	1-Octyne	H_2O_2	95 (50:50)[15]
4	1-Octyne	TBHP	96 (93:7)[15]
5	Phenylacetylene	H_2O_2	18 dibromo (76:24) + 82 tetrabromo[d]
6	Phenylacetylene	TBHP	79 dibromo (74:26) + 21 tetrabromo[d]

[a] *With HBr (2 eq.) and oxidant (2 eq.);* [b] *Isolated yield;* [c] *Determined by* ^{1}*H NMR spectroscopy of crude sample and comparison with the literature values.* [d] *Determined by NMR spectroscopy.*

The reaction of acetylenes with hydrobromic acid and hydrogen peroxide or TBHP furnished a mixture of dibromo alkenes where the *trans* isomer was formed in excess. This is in accordance with the mechanism proposed by Pincock and Yates [17] which involves the cyclic "bromonium" ion intermediate **3** on which unoxidised bromide ion attacks from the reverse side *via* an Ad_E2 pathway resulting in the formation of the *trans*-dibromoalkene in excess.



3 *trans*

In the case of phenylacetylene further bromination was observed furnishing the tetrabromo product. When the oxidant was hydrogen peroxide the formation of this product was pronounced. However, when TBHP was used the tetrabromo formation was reduced probably due to lower reactivity of the oxidant (Table 4, entries 5 and 6).

Conclusion

An efficient and practical method for the halogenation of aromatic compounds and for the preparation of vicinal *trans*-dihalogenated alkanes and 1,2-dihalo alkenes utilizing an environmentally safe procedure is presented. The positive halogen reagents are prepared *in situ* from aqueous hydrohalic acid and suitable oxidant. We have observed a novel selectivity in the chlorination of aromatic compounds with TBHP and H_2O_2 as the oxidant. An efficient and simple method for preparation of 1-bromo-2-chloro alkanes from alkenes has been developed through this methodology.

Experimental

Melting points were recorded on Electrothermal melting point apparatus and are uncorrected. The NMR spectra were recorded in $CDCl_3$ with TMS as an internal standard on Bruker WM 200 NMR spectrometer (^1H NMR at 200 MHz and ^{13}C NMR at 50 MHz). Mass spectra were recorded on Finnigan MAT 1020B GC-MS (EI) instrument. Flash chromatography was performed on TLC grade silica gel and analytical TLC were performed on Merck silica gel 60 F254 pre-coated plates and the spots were visualized under UV light or in iodine vapors. Carbon tetrachloride, methanol and dioxane were distilled before use. Hydrogen peroxide (30 % w/v) was procured from Asian Chemicals, India and *tert*-butylhydroperoxide (TBHP) (70 % w/v) was obtained from Aldrich Chemicals. Aqueous hydrobromic acid (47 %) and hydrochloric acid (35 %) were purchased from S.D. Fine chemicals, India. The aromatic *N,N*-dimethylamides were prepared from the corresponding acids *via* acid chlorides while the commercial substrates in all cases were purchased from standard sources, most from Aldrich Chemicals, and used as such.

Standard procedure for aromatic halogenation:

N,N-Dimethyl-(2-bromo-5-methoxy)benzamide (Table 1; entry 6): A solution of TBHP (70 % aq.; 0.15 mL; 1.17 mmol) was added to a cooled mixture of HBr (48 % aq.; 0.20 mL; 1.17 mmol) in methanol (5 mL) and the mixture stirred for 5 min. To this cold solution *N,N*-dimethyl(3-methoxy)benzamide (0.21 g; 1.17 mmol) was added, stirred for 30 min. and then refluxed for 6 h. On completion of the reaction (TLC) the solvent was evaporated and the product was taken in 5 mL water, extracted with dichloromethane (3 X 15 mL) and residue was purified by flash column chromatography over silica gel (10 % EtOAc in Pet. ether) to afford pure product as thick yellow oil (0.28 g; 98 %).

IR ν 3460, 2900, 1705, 1590, 1440, 1270, 1010, 940, 860, 810, 590 $cm.^{-1}$ **NMR** δ_H 2.85 (s, 3H), 3.10 (s, 3H), 3.80 (s, 3H), 6.80 (m, 2H), 7.45 (m, 1H). δ_C 35.0, 39.0, 56.0, 110.0, 113.0, 117.0, 134.0, 139.0, 159.0, 169.0. **MS** (m/z) 259 (M^++2, 31), 258 (34), 257 (M^+, 35), 256 (M^+-1, 38), 215 (85), 213 (100), 187 (23), 185 (28), 172 (15), 170 (17). **Analysis**: Calculated for $C_{10}H_{12}BrNO_2$; C: 46.51; H: 4.65; N: 5.43; Br: 31.39 %, found, C: 46.34; H: 4.60; N: 5.22; Br: 31.62 %.

The following compounds were prepared in the same way and purified by chromatography with 5 - 10 % EtOAc in Pet. ether as eluent.

4-Bromoanisole (Table 1, entry 1) [18]: **IR** ν 3120, 2990, 1630, 1560, 1300, 1060, 885 $cm.^{-1}$ **NMR** δ_H 3.80 (s, 3H), 6.80 (d, J=10.0 Hz, 2H), 7.4 (d, J=10.0 Hz, 2H).

1-Bromo-2,5-dimethoxybenzene (Table 1, entry 2) [18]: **IR** ν 3350, 1590, 1060, 740 cm.$^{-1}$ **NMR** δ_H 3.75 (s, 3H), 3.85 (s, 3H), 6.85 (m, 2H), 7.15 (m, 1H). **MS** (m/z) 216 (M^+, 92), 218 (M^++2, 90), 203 (100), 201 (90), 187 (10), 173 (48), 157 (15), 107 (55).

2-Bromo-4-methylphenol (Table 1, entry 3): **IR** ν 3650, 3100, 1560, 1240, 1150, 830 740 cm.$^{-1}$ **NMR** δ_H 2.30 (s, 3H), 5.40 (bs, 1H), 6.92 (d, J=8.0 Hz, 1H), 7.00 (d, J=8.0 Hz, 1H), 7.30 (s, 1H).

2-Bromo-5-methoxy methylbenzoate (Table 1, entry 4): Colorless oil. **IR** ν 2951, 1732, 1593, 976, 817, 609 cm.$^{-1}$ **NMR** δ_H 3.80 (s, 3H), 3.90 (s, 3H), 6.90 (dd, J=2.7 & 8.6 Hz, 1H), 7.30 (d, J=2.7 Hz, 1H), 7.55 (d, J=8.6 Hz, 1H).

N,N-Dimethyl-(3-chloro-6-methoxy)benzamide (Table 1, entry 5): Pale yellow solid. m.p. = 77 °C **IR** ν 2937, 1643, 1250, 1072, 650 cm.$^{-1}$ **NMR** δ_H 2.85 (s, 3H), 3.10 (s, 3H), 3.80 (s, 3H), 6.82 (d, J=8.8 Hz, 1H), 7.20 (d, J=2.6 Hz, 1H), 7.25-7.35 (dd, J=2.6 & 8.8 Hz, 1H). **Mass** (m/z) 213 (M^+, 10), 198 (2), 169 (100), 154 (6), 135 (5), 126 (15), 111 (14).

N,N-Dimethyl-(2-chloro-5-methoxy)benzamide (Table 1, entry 7): Thick yellow oil. **IR** ν 2924, 1643, 1567, 815, 601 cm.$^{-1}$ **NMR** δ_H 2.85 (s, 3H), 3.05 (s, 3H), 3.85 (s, 3H), 6.75-6.85 (m, 2H), 7.15 (d, J=8.5 Hz, 1H). **MS** (m/z) 213 (M^+, 10), 198 (2), 169 (100), 154 (6), 135 (5), 126 (15), 111 (14). **Analysis:** Calculated for $C_{10}H_{12}ClNO_2$; C: 56.20; H: 5.62; N: 6.55; Cl: 16.62 %, found, C: 56.55; H: 5.95; N: 6.15; Cl: 15.81 %.

*N,N-Dimethyl-(2-chloro-3,4,5-trimethoxy-6-meythyl)benzamide (Table 1, entry 9):*Thick yellow oil. **IR** ν 1610, 1200, 740 cm.$^{-1}$ **NMR** δ_H 2.15 (s, 3H), 2.85 (s, 3H), 3.15 (s, 3H), 3.85 (s, 3H), 3.90 (s, 3H), 3.95 (s, 3H). δ_C 12.0, 34.0, 37.0, 60.0, 60.5, 61.0, 118.0, 124.0, 132.0, 147.0, 148.0, 151.0, 167.0. **MS** (m/z) 290 (2), 289 (12), 287 (M^+, 45), 272 (15), 252 (5), 243 (100), 227 (3), 214 (3), 200 (8), 72 (2). **Analysis:** Calculated for $C_{13}H_{18}ClNO_4$; C: 54.35; H: 6.27; N: 4.89; Cl: 12.36 %, found, C: 54.55; H: 6.57; N: 4.39; Cl: 11.83 %.

1,4-Dibromo-2,5-dimethoxybenzene (Table 1, entry 10 & 11) [18]: Pale yellow solid. m.p. = 147 °C **IR** ν 2926, 2050, 1674, 860, 760 cm.$^{-1}$ **NMR** δ_H 3.85 (s, 6H), 7.10 (s, 2H). **MS** (m/z) 298 (50), 296 (100), 294 (42), 281 (95), 185 (40).

2,4-Dichloroanisole (Scheme-2): Pale yellow oil. **IR** ν 3100, 1615, 1320, 790 cm.$^{-1}$ **NMR** δ_H 3.85 (s, 3H), 6.82 (d, J=9.0 Hz, 1H), 7.18 (d, J=9.0 Hz, 1H), 7.35 (d, J=2.0 Hz, 1H).

1-Chloro-2,5-dimethoxybenzene (Scheme 2): Light yellow oil. **IR** ν 2924, 1500, 1047, 739 cm.$^{-1}$ **NMR** δ_H 3.75 (s, 3H), 3.85 (s, 3H), 6.75 (d, J=2.9 Hz, 1H), 6.85 (s, 1H), 6.95 (d, J=2.9 Hz, 1H). **MS** (m/z) 174 (M^++1, 10), 173 (M^+, 4), 172 (32), 157 (60), 138 (80), 123 (100).

1,4-Dichloro-2,5-dimethoxybenzene (Scheme 2): m.p. = 139 °C. **IR** ν 2980, 1620, 1220, 680 cm.$^{-1}$ **NMR** δ_H 3.85 (s, 6H), 7.00 (s, 2H).

N,N-Dimethyl(2-chloro-3,4,5-trimethoxy)benzamide (Scheme 2): Thick yellow oil. **IR** ν 2939, 1645, 1390, 1109, 793, 658 cm.$^{-1}$ **NMR** δ_H 2.85 (s, 3H), 3.10 (s, 3H), 3.82 (s, 3H), 3.87 (s, 3H), 3.90 (s, 3H), 6.60 (s, 1H). **MS** (m/z) 275 (12), 274 (7), 273 (42), 258 (4), 231(40), 230 (15), 229 (100), 186 (12), 171 (8), 119 (5), 72 (8).

N,N-Dimethyl(2,6-dichloro-3,4,5-trimethoxy)benzamide (Scheme 2): Thick yellow oil. **NMR** δ_H 2.90 (s, 3H), 3.15 (s, 3H), 3.95 (s, 6H), 4.00 (s, 3H). **MS** (m/z) 308 (M^+, 28), 272 (22), 263 (100), 256 (3), 246 (5), 236 (2), 220 (12), 157 (5), 129 (5), 72 (22).

N,N-Dimethyl(2,6-dibromo-3,4,5-trimethoxy)benzamide (Table 1; entry 12): Pale yellow solid. m.p. = 146 °C **IR** ν 2924, 1639, 1377, 1014, 999, 723 654 cm.$^{-1}$ **NMR** δ_H 2.90 (s, 3H), 3.18 (s, 3H), 3.92 (s, 6H), 3.95 (s, 3H). **MS** (m/z) 399 (M^++2, 18), 397 (M^+, 35), 395 (M^+-2, 18), 355 (52), 353 (100), 318 (15), 310 (5), 229 (5), 201 (5).

Standard procedure for the preparation of 1,2-dihaloalkanes:

trans-2,3-Dibromo-3-phenyl methylpropanoate (Table 2; entry 4):

To a stirred solution of methyl cinnamate (162 mg, 10.0 mmol) in CCl_4 (5 mL) (or dioxane) held at ambient temperature, a mixture of hydrogen peroxide (0.20 mL, 20.0 mmol) and hydrobromic acid (0.34 mL, 20 mmol; mixed at 0 °C) was added over 10 min. After the completion of the reaction (2 h, by tlc) organic layer was separated and washed with water, brine and dried over anhydrous sodium sulphate. On evaporation of solvent the sample of *trans*-2,3-dibromo-3-phenyl methylpropanoate (319 mg, 99 %) was obtained and found to be pure by proton NMR analysis. For the preparation of vicinal dichloro compounds similar method was employed with excess (6 eq.) of hydrochloric acid and the reaction was continued overnight.

trans-2,3-Dibromo-3-phenyl methylpropanoate: Light yellow solid. m.p. = 114 °C. **IR** ν 2852, 1738, 1435, 1377, 1145, 981, 700 cm.$^{-1}$ **NMR** δ_H 3.90 (s, 3H); 4.85 (d, J = 14.0 Hz, 1H); 5.35 (d, J = 14.0 Hz, 1H), 7.40 (s, 5H). δ_c 46.8, 50.8, 53.3, 128.5, 129.0, 130.0, 137.7, 168.2. **MS** (m/z) 243 (2), 197 (20), 182 (3), 161 (31), 131 (50), 125 (100), 103 (45).

trans-2,3-Dichloro-3-phenyl methylpropanoate (Table 2; entry 4) [20]: Pale yellow solid. m.p. = 96 °C **IR** ν 3005, 1730, 1620, 1180,990, 620 cm.$^{-1}$ **NMR** δ_H 3.85 (s, 3H); 4.65 (d, J = 11.0 Hz, 1H); 5.18 (d, J = 11.0 Hz, 1H), 7.45 (s, 5H). δ_c 53.0, 58.2, 60.8, 128.0, 129.5, 130.0, 136.0, 167.8. **MS** (m/z) 234 (M^++1, 2.5), 232 (M^+-1, 3.0), 196 (37), 173 (7), 165 (15), 125 (100), 103 (45).

trans-1,2-Dibromocyclohexane (Table 2; entry 1) [8]: Yellow oil. **IR** ν 2935, 1643, 1468, 1288, 814, 560 cm.$^{-1}$ **NMR** δ_H 1.40-1.60 (m, 2H), 1.70-2.00 (m, 4H), 2.35-2.55 (m, 2H), 4.40-4.50 (m, 2H).

trans-1,2-Dichlorocyclohexane (Table 2; entry 1) [8]: Yellow oil. **IR** ν 2941, 1450, 1078, 735 cm.$^{-1}$ **NMR** δ_H 1.35-1.50 (m, 2H), 1.65-1.85 (m, 4H), 2.25-2.40 (m, 2H), 3.95-4.05 (m, 2H).

trans-1,2-Dibromocyclooctane (Table 2; entry 2) [8]: Colorless oil. **NMR** δ_H 1.40-1.60 (m, 6H), 1.80-2.00 (m, 2H), 2.00-2.20 (m, 2H), 2.20-2.60 (m, 2H), 4.60-4.70 (m, 2H).

trans-1,2-Dichlorocyclooctane (Table 2; entry 2) [8]: Pale yellow oil. **IR** ν 2925, 1640, 1014, 730, 654 cm.$^{-1}$ **NMR** δ_H 1.35-1.45 (m, 2H), 1.50-1.80 (m, 4H), 1.80-1.90 (m, 2H), 2.00-2.10 (m, 2H), 2.20-2.35 (m, 2H), 4.20-4.25 (m, 2H).

1,2-Dibromodecane (Table 2; entry 3): Colorless oil. **IR** ν 2926, 1465, 1145, 723, 571 cm.$^{-1}$ **NMR** δ_H 0.90 (t, J=3.0 Hz, 3H), 1.30 (bs, 8H), 1.40-1.60 (m, 2H), 1.70-1.90 (m, 2H), 2.10-2.20 (m, 2H), 3.60 (t, J=11.0 Hz, 1H), 3.80 (dd, J=5.5, 6.0 Hz, 1H), 4.10-4.20 (m, 1H). **MS** (m/z) 302 (M^++4, 1), 300 (M^++2, 0.5), 298 (M^+, 1), 219 (1), 176 (2), 163 (6), 148 (4), 135 (8), 119 (8), 105 (8), 97 (45), 83 (100), 71 (58).

1,2-Dichlorodecane (Table 2; entry 3) [19]: Colorless oil. **IR** ν 2926, 1466, 1174, 731, 663 cm.$^{-1}$ **NMR** δ_H 0.90 (t, J=3.0 Hz, 3H), 1.20-1.60 (bs, 10H), 1.65-1.80 (m, 2H), 1.90-2.10 (m, 2H), 3.60-3.80 (m, 2H), 4.00-4.10 (m, 1H).

trans-2,3-Dibromo-1,3-diphenyl-1-propanone (Table 2; entry 4): Pale yellow solid. m.p. = 164 °C. **IR** ν 2930, 1620, 1160, 720 cm.$^{-1}$ **NMR** δ_H 5.68 (d, J=10.8 Hz, 1H), 5.82 (d, J=10.8 Hz, 1H), 7.30-7.70 (m, 8H), 8.05-8.15 (m, 2H). **MS** (m/z) 289 (0.5), 207 (8), 131 (10), 105 (100), 77 (70).

trans-2,3-Dichloro-1,3-diphenyl-1-propanone (Table 2; entry 4): Pale yellow solid. m.p. = 116 °C. **IR** ν 1610, 1440, 970, 680 cm.$^{-1}$ **NMR** δ_H 5.50 (m, 2H), 7.35-7.70 (m, 8H), 8.05-8.15 (m,

2H). **Analysis:** Calculated for $C_{15}H_{12}Cl_2O$; C: 64.57; H: 4.30; Cl: 25.45 %, found, C: 64.78.40; H: 4.15; Cl: 25.95 %. **MS** (m/z) 243 (M+, 15), 207 (25), 105 (100), 77 (75).

trans-1,2-Dibromo-2-phenyl-nitroethane (Table 2; entry 5): Pale yellow solid. m.p. = 89 °C. **IR** ν 2924, 1578, 1494, 1456, 1357, 1153, 698, 605 cm.$^{-1}$ **NMR** δ_H 5.50 (d, J=10.8 Hz, 1H), 6.60 (d, J=10.8 Hz, 1H), 7.45 (m, 5H). **MS** (m/z) 311 (M^+ +4, 4), 309 (M^+ +2, 8), 307 (M^+, 4), 262 (6), 261 (5), 228 (18), 182 (100), 171 (3), 103 (85), 77 (65). **Analysis:** Calculated for $C_8H_7Br_2NO_2$; C: 31.07; H: 2.26; N: 4.53; Br: 51.78 %, found, C: 31.40; H: 2.09; N: 4.41; Br: 51.70 %.

trans-5,6-Dibromo-(Z)-cyclooctene (Scheme 3) [13]: Colorless oil. **IR** ν 2927, 1440, 1217, 997, 737 536, cm.$^{-1}$ **NMR** δ_H 2.10-2.40 (m, 4H), 2.55-2.70 (m, 4H), 4.70 (t, J=2.0 Hz, 2H), 5.70 (t, J=2.0 Hz, 2H). δ_C 24.98, 35.4, 59.5, 128.8. **MS (m/z)** 207 (M^+ +4, 1), 268 (M^+ +2, 2), 266 (M^+, 0.5), 203 (0.5), 189 (2), 159 (1), 145 (2), 121 (4), 109 (7), 107 (85), 91 (25), 79 (100).

endo,endo-2,5-Dibromo-9-oxabicyclo[4.2.1]nonane (Scheme 3) [13]: Colorless oil. **IR** ν 2949, 1477, 1433, 1049, 717, 599 cm.$^{-1}$ **NMR** δ_H 1.90-2.10 (m, 2H), 2.15-2.35 (m, 4H), 2.30-2.50 (m, 2H), 4.30-4.40 (m, 2H), 4.50-4.60 (m, 2H). **MS** (m/z) 286 (M^+ +4, 1), 284 (M^+ +2, 2), 282 (M^+, 1), 203 (18), 187 (1), 163 (2), 149 (1), 135 (2), 123 (32), 105 (28), 95 (55), 79 (100), 96 (70).

Standard procedure for the preparation of mono bromo mono chloro alkanes:

trans-2-Bromo-3-chloro-3-phenyl methylpropanoate (Table 3; entry 4):

To a well stirred solution of methyl cinnamate (162 mg, 10.0 mmol) and hydrochloric acid (1.05 mL, 100 mmol) in dioxane (5 mL) held at *ca* 5 °C, a mixture, prepared at 0 °C, of hydrogen peroxide (0.15 mL, 15.0 mmol) and hydrobromic acid (0.172 mL, 10 mmol) was added over 60 min. After the completion of the reaction (overnight, tlc) and usual work-up the product was separated. The proton NMR and GLC analysis of the crude product indicated the ratio of *trans*-2-bromo-3-chloro-3-phenyl methylpropanoate, *trans-2,3-dibromo-3-phenyl methylpropanoate* and *trans-2,3-dichloro-3-phenyl methylpropanoate* to be 94:4:2.

trans-2-Bromo-3-chloro-3-phenyl methylpropanoate [21]: White solid. m.p. = 117 °C. **IR** ν 2924, 1738, 1500, 1275, 708, 609. cm.$^{-1}$ **NMR** δ_H 3.90 (s, 3H), 4.67 (d, J = 11.0 Hz, 1H), 5.27 (d, J = 11.0 Hz, 1H), 7.40 (s, 5H). δ_C 47.5, 53.2, 61.0, 128.0, 129.0, 129.5, 136.9, 168.0. **MS** (m/z) 243 (2), 197 (17), 182 (3), 161 (30), 138 (5), 131 (50), 125 (100), 103 (40), 77 (5).

trans-1-Bromo-2-chloro-cyclooctane (Table 3; entry 1): Pale yellow oil. **IR** ν 2939, 1447, 1014, 768, 619 cm.$^{-1}$ **NMR** δ_H 1.52-1.70 (m, 2H), 1.87-2.05 (m, 2H), 2.10-2.40 (m, 6H), 2.40-

2.60 (m, 2H), 4.20-4.35 (m, 1H), 4.40-4.55 (m, 1H). **MS** (m/z) 225 (M^++1, 0.5), 189 (2), 177 (0.5), 143 (35), 116 (3), 107 (100), 91 (12), 79 (18).

*trans-1-Bromo-2-chlorodecane (Table 3; entry 2):*Light yellow oil. **IR** ν 2926, 1468, 1146, 721 cm.$^{-1}$ **NMR** δ_H 0.85 (t, J=3.0 Hz, 3H), 1.10-1.35 (bs, 8H), 1.40-1.60 (m, 2H), 1.70-1.90 (m, 2H), 1.95-2.20 (m, 2H), 3.55-3.95 (m, 2H), 4.00-4.25 (m, 1H). **MS** (m/z) 256 (M^++2, 1), 255 (M^++1, 0.5), 254 (M^+, 1), 219 (1), 176 (2), 163 (5), 148 (4), 135 (6), 119 (8), 105 (8), 97 (45), 83 (100), 71 (60).

trans-2-Bromo-3-chloro-1,3-diphenyl-1-propanone (Table 3; entry 3): **IR** ν 2924, 1680, 1595, 986, 685 cm.$^{-1}$ **NMR** δ_H 5.60 (s, 2H), 7.35-7.70 (m, 8H), 8.05-8.15 (m, 2H). **MS** (m/z) 326 (M^++4, 0.5), 287 (9), 243 (6), 207 (18), 182 (10), 165 (2), 131 (4), 105 (100), 77 (25).

Standard procedure for bromination of Alkynes:

cis/trans-1,2-Dibromophenylethylene (Table 3; entry 6):

To a stirred solution of phenylacetylene (1.02 gm, 10 mmol) in CCl_4 (20 mL), TBHP (2.57 mL, 20 mmol) was added. To this mixture aqueous hydrobromic acid (3.45 mL, 20 mmol) was added drop wise over a period of 10 min. After the completion of the reaction (2 h, tlc) organic layer was separated and the products isolated by the procedure described above. The ratio of *cis/trans* isomers was established by NMR analysis of the crude sample [16].

trans-1,2-Dibromophenylethylene: Pale yellow oil. **IR** ν 3062, 1595, 1191, 629, 567 cm.$^{-1}$ **NMR** δ_H 6.65 (s, 1H); 7.45-7.55 (m, 2H); 7.60-7.70 (m, 1H), 8.05-8.15 (m, 2H). **MS** (m/z) 264 (M^++4, 10), 262 (M^++2, 20), 260 (M^+, 10), 183 (50), 171 (10), 105 (100), 90 (21), 77 (45). **Analysis:** Calculated for $C_8H_6Br_2$; C: 36.64; H: 2.29; Br: 61.06 %, found, C: 36.12; H: 2.40; Br: 61.48 %.

cis-1,2-Dibromophenylethylene: Pale yellow oil. **IR** ν 2995, 1444, 1138, 615 cm.$^{-1}$ **NMR** δ_H 7.05 (s, 1H); 7.45 – 6.70 (m, 3H); 8.05 – 8.15 (m, 2H). **MS** m/z 264 (M^++4, 18), 262 (M^++2, 36), 260 (M^+, 18), 183 (50), 171 (10), 105 (100), 90 (21), 77 (45). **Analysis:** Calculated for $C_8H_6Br_2$; C: 36.64; H: 2.29; Br: 61.06 %, found, C: 36.82; H: 2.28; Br: 61.56 %.

1,1,2,2-Tetrabromo-1-phenylethane: White solid. m.p. = 72 °C. **IR** ν 2855, 1443, 1176, 615, 526 cm.$^{-1}$ **NMR** δ_H 6.40 (s, 1H); 7.40 – 7.45 (m, 3H); 7.85 – 7.95 (m, 2H). δ_C 54.5, 72.6, 128.2, 128.7, 129.9, 139.9. **MS** m/z (%) 422 (M^++4, trace), 344 (10), 343 (12), 342 (65), 340 (63), 338 (11), 264 (28), 262 (50), 260 (28), 183 (50), 102 (100), 77 (35). **Analysis:** Calculated for $C_8H_6Br_4$; C: 22.74; H: 1.42; Br: 75.82 %, found, C: 22.50; H: 1.51; Br: 75.20 %.

trans-1,2-Dibromo-1-hexene (Table 4; entry 1)[17]: Pale yellow oil. **IR** ν 2932, 1708, 1464, 1141, 609 cm.$^{-1}$ **NMR** δ_H 0.95 (t, J=8.0 Hz, 3H); 1.25 – 1.65 (m, 4H); 2.65 (t, J=8.0, 2H), 6.40 (s, 1H). **MS** (m/z) 244 (M^++4, 1), 243 (M^++3, 8), 242 (M^++2, 2), 241 (M^++1, 16), 240 (M^+, 2), 239 (8), 199 (12), 197 (8), 185 (3), 173 (8), 161 (49), 159 (55), 133 (35), 119 (40), 79 (100).

trans-1,2-Dibromo-1-octene (Table 4; entry 2): Pale yellow oil. **IR** ν 2954, 1734, 1465, 779, 636 cm.$^{-1}$ **NMR** δ_H 0.80 – 0.95 (t, J=<1 Hz, 3H); 1.15 – 1.70 (m, 8H); 2.60 (t, J=6.0 Hz, 2H), 6.40 (s, 1H). **MS** (m/z) 272 (M^++4, 5), 270 (M^++2, 15), 268 (M^+, 5), 199 (10), 189 (5), 173 (5), 147 (8), 132 (8), 105 (100), 67 (65).

Acknowledgements We are grateful to Dr. T. Ravindranathan and Dr. V.H. Deshpande for helpful suggestions and encouragement. We wish to thank CSIR, New Delhi for the award of a Pool Officership to AVB, Research Associateship to ASG and Senior Research Fellowship to NBB.

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