Anion-Exchange Resins as Halogen Carriers in the Bromination and Chlorobromination of Organic Compounds

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Several polymeric reagents[1,2,3] have been recently described as useful in the halogenation of organic compounds, although they always require the preparation of a specific macromolecular backbone[1,3] or tedious modification of a commercial one[2]. Moreover, the yields are often moderate[3] or the choice of solvents severely restricted[1].

Recently, a paper[4] appeared reporting the use, as brominating agent for ketones, of the commercially available anion-exchange resin Amberlyst A-26 (Rohm and Haas Co.) in the perbromide form. We now demonstrate that this reagent has a wider applicability in organic synthesis than that reported[4]. Moreover, we have found that a modification of Amberlyst A-26, bromide form, can also be used in the direct chlorobromination of alkenes and alkynes (see Scheme B).

Amberlyst A-26, bromide form, was converted to the perbromide form **1** by action of a carbon tetrachloride solution of bromine (see experimental part) giving orange, odorless beads, probably carrying benzyltrimethylammonium perbromide groups[5], that proved to be effective in the bromination of various substrates (Scheme A). The content of active bromine was evaluated by iodometry to be 2.5 mmol/g and only a small decrease (less than 10%) was observed after a three months storage at room temperature.

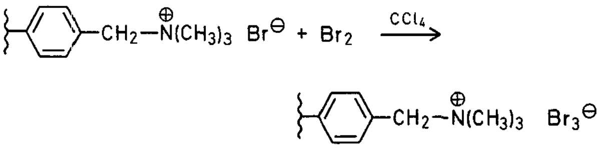

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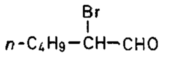
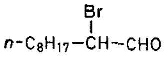
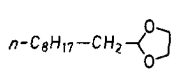
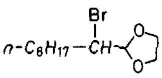
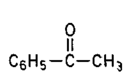
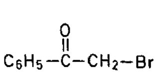
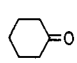
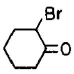
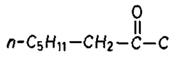
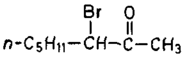
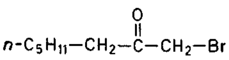
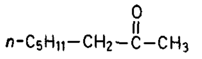
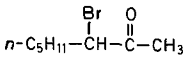
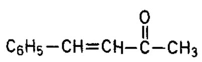
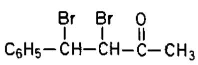
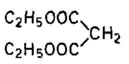
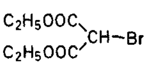
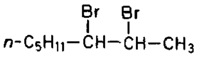
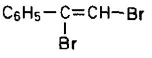
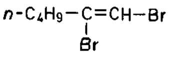
Table 1. Brominations with Amberlyst A-26, Perbromide Form (1)

Substrate	Product	Yield[a] [%]	Reaction Conditions (solvent/temp./time)	m.p. or b.p./torr	Lit. m.p. or b.p./torr	Reference
$n\text{-}C_4H_9{-}CH_2{-}CHO$	 $n\text{-}C_4H_9{-}\overset{Br}{CH}{-}CHO$	95[b]	CCl_4/reflux/15 min	62–64°C/12	63°C/12	16
$n\text{-}C_8H_{17}{-}CH_2{-}CHO$	 $n\text{-}C_8H_{17}{-}\overset{Br}{CH}{-}CHO$	97[a,b]	CH_2Cl_2/reflux/1h	80–83°C/1	72–76°C/0.5	6
		70	CH_2Cl_2/r.t./24 h	92–95°C/1	–[f]	–[f]
 $C_6H_5{-}\overset{O}{C}{-}CH_3$	 $C_6H_5{-}\overset{O}{C}{-}CH_2{-}Br$	70	THF/r.t./12 h	50°C	50–51°C	17
		65	THF/r.t./5 h	85–86°C/10	85–86°C/10	18
		90	H_2O/r.t./24 h			
 $n\text{-}C_5H_{11}{-}CH_2{-}\overset{O}{C}{-}CH_3$	 $n\text{-}C_5H_{11}{-}\overset{Br}{CH}{-}\overset{O}{C}{-}CH_3$ (65%)  $n\text{-}C_5H_{11}{-}CH_2{-}\overset{O}{C}{-}CH_2{-}Br$ (35%)	74[c]	CH_2Cl_2/reflux/1 h	–	–	–
 $n\text{-}C_5H_{11}{-}CH_2{-}\overset{O}{C}{-}CH_3$	 $n\text{-}C_5H_{11}{-}\overset{Br}{CH}{-}\overset{O}{C}{-}CH_3$	70	hexane/reflux/30 min[d]	91–93°C/11	92–92.5°C/11	19
 $C_6H_5{-}CH{=}CH{-}\overset{O}{C}{-}CH_3$	 $C_6H_5{-}\overset{Br}{CH}{-}\overset{Br}{CH}{-}\overset{O}{C}{-}CH_3$	95	hexane/r.t./1 h	125–126°C	125–126°C	20
		96	CH_2Cl_2/reflux/1 h	123°C/20	123°C/20	21
$n\text{-}C_5H_{11}{-}CH{=}CH{-}CH_3$	 $n\text{-}C_5H_{11}{-}\overset{Br}{CH}{-}\overset{Br}{CH}{-}CH_3$	85	CH_2Cl_2/r.t./10 min	114–116°C/20	114–116°C/20	22
$C_6H_5{-}C{\equiv}CH$	 $C_6H_5{-}\underset{Br}{C}{=}CH{-}Br$	92[e]	CH_2Cl_2/r.t./1 h	118–121°C/10	–	–
$n\text{-}C_4H_9{-}C{\equiv}CH$	 $n\text{-}C_4H_9{-}\underset{Br}{C}{=}CH{-}Br$	94[e]	CH_2Cl_2/reflux/3 h	74–77°C/15	–	–

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[a] Yield of isolated product of ≥97% purity, unless otherwise stated.

[b] Yield estimated by G.L.C. and ^{1}H-N.M.R.

[c] Product distribution estimated from ^{1}H-N.M.R. spectrum.

[d] Ratio of resin:ketone:methyloxirane = 2:1:1; catalytic amount of AIBN added.

[e] cis/trans mixtures (~1:3) as estimated from ^{1}H-N.M.R. spectrum.

[f] $C_{12}H_{23}BrO_2$ calc. C 51.62 H 8.30 Br 28.62
(279.2) found 51.99 8.22 28.75
M.S.: m/e = 280, 278 (M^+).
^{1}H-N.M.R.: δ=0.95 (t, 3H); 1.20 (m, 14H); 3.7–4.1 (m, 5H); 4.90 ppm (d, 1H).

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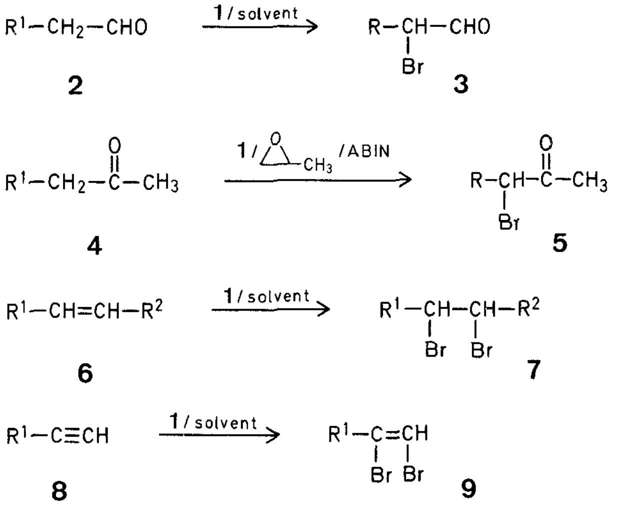


Scheme A

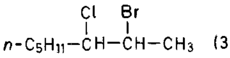
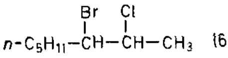
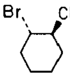
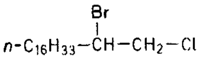
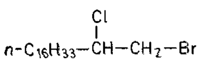
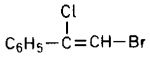
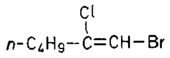
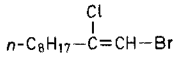
Reactions were usually carried out by the batch technique, by stirring the organic compound with ~50% excess of the polymer, until complete conversion of the starting material was observed. A column technique can also be used but, in some instances, it is more time consuming as the solution of the organic compound has to be percolated many times through the brominating polymer. By filtration of the resin and removal of the solvent, we isolated the products in good yields.

Identification was carried out by spectral data and by comparison with authentic samples. Results are collected in Table 1. A wide choice of solvents is allowed as the reaction was performed in hydrocarbons, ether, chlorinated solvents, and even in water. Direct bromination of saturated aldehydes **2** was quickly achieved under mild conditions and the ease and simplicity of our method seems to provide an improvement over other existing routes to α-bromoaldehydes[6,7]. Also the diethylene acetal of *n*-decanal was successfully brominated in the α-position whereas dioxolanes of ketones were readily hydrolyzed in the acidic medium. Unsymmetrical ketones **4** were selectively brominated at the more highly substituted position in the presence of a free radical initiator (azo-bis-isobutyronitrile), and methyloxirane as scavanger of the hydrobromic acid produced in the reaction[8]. α,β-Unsaturated ketones, however, were readily and completely converted to the corresponding dibromo-saturated product. Alkenes **6** and alkynes **8** were converted respectively to vicinal dibromoalkanes **7** and dibromoalkenes **9**, the latter as a mixture of (*Z*)- and (*E*)-isomers. Esters, other than diethyl malonate, failed to react.

Regeneration of the reagent was simply accomplished by suspending the exhausted resin in a carbon tetrachloride solution of bromine to give a reagent as effective as the original one.

As previously mentioned, we succeeded also in the chlorobromination of unsaturated carbon compounds **6** and **8**, by means of the following polymeric reagent. Amberlyst A-26,

Table 2. Chlorobrominations with Amberlyst A-26, $(BrCl_2)^{\ominus}$ Form (**10**)

Substrate	Product	Yield [%]	Reaction Time[a]	b.p./torr
$n\text{-}C_5H_{11}\text{-}CH{=}CH\text{-}CH_3$	 $n\text{-}C_5H_{11}\text{-}\overset{Cl}{C}H\text{-}\overset{Br}{C}H\text{-}CH_3$ (35%)  $n\text{-}C_5H_{11}\text{-}\overset{Br}{C}H\text{-}\overset{Cl}{C}H\text{-}CH_3$ (65%)	85[c]	2 h	112–115°C/17
		71	2 h	93–95°C/17
$n\text{-}C_{16}H_{33}\text{-}CH{=}CH_2$	 $n\text{-}C_{16}H_{33}\text{-}\overset{Br}{C}H\text{-}CH_2\text{-}Cl$ (50%)  $n\text{-}C_{16}H_{33}\text{-}\overset{Cl}{C}H\text{-}CH_2\text{-}Br$ (50%)	62[c]	12 h	165–170°C/0.1
$C_6H_5\text{-}C{\equiv}CH$	 $C_6H_5\text{-}\overset{Cl}{C}{=}CH\text{-}Br$	96 (*Z*: 95)[f]	3 h	42–45°C/0.15
$n\text{-}C_4H_9\text{-}C{\equiv}CH$	 $n\text{-}C_4H_9\text{-}\overset{Cl}{C}{=}CH\text{-}Br$	91 (*E*: 95)[f]	1 h	23–25°C/0.25
$n\text{-}C_8H_{17}\text{-}C{\equiv}CH$	 $n\text{-}C_8H_{17}\text{-}\overset{Cl}{C}{=}CH\text{-}Br$	85 (*E*: 95)[f]	3 h	58–60°C/0.25

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[a] Reactions in dichloromethane at room temperature.

[b] All products gave satisfactory microanalyses (C ± 0.32, H ± 0.09, Br ± 0.37, Cl ± 0.18).

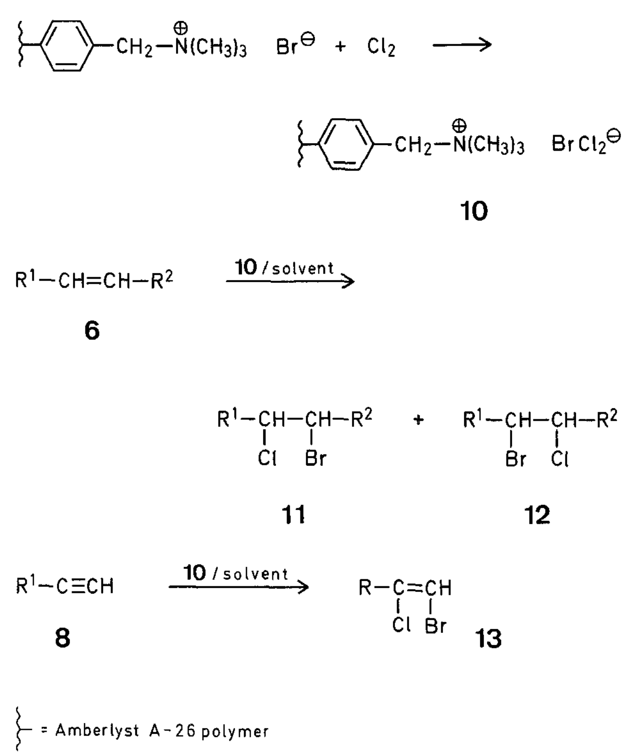
[c] Isomer ratio estimated from ^{13}C-N.M.R. spectra.

[d] *erythro* and *threo* form.

[e] Compare with Lit.[11].

[f] Estimated from G.L.C. and N.M.R. data.

[g] As chloro and bromo substituents exhibit the same geminal effect[10], we can compare our values with those of the dichloro analogues[12].



Scheme **B**

bromide form, was converted to a chlorobromide form **10** by action of a dichloromethane solution of chlorine (see experimental part) giving yellow-greenish, lightly chlorine smelling beads probably carrying, as counterions of the benzyltrimethylammonium groups, anions of the type[5] $(BrCl_2)^{\ominus}$ (Scheme **B**).

Molecular formula[b]	^1H- and ^{13}C-N.M.R. data δ [ppm]
$C_8H_{16}BrCl$ (227.6)	^{13}C: 52.2, 52.3 (CHBr); 66.3, 67.6 (CHCl)[d] ^{13}C: 60.2, 61.4 (CHBr); 60.0 (CHCl)[d]
$C_6H_{10}BrCl$ (197.5)	^{13}C: 55.2 (CHBr); 62.7 (CHCl) ^1H: 4.25 (d, $\Delta\nu/2 = 10$ Hz, CHBr, CHCl)[e]
$C_{18}H_{36}BrCl$ (367.8)	^{13}C: 53.1 (CHBr); 48.0 (CH_2Cl) ^{13}C: 36.0 (CH_2Br); 60.6 (CHCl)
C_8H_6BrCl (217.5)	^{13}C: 101.7 (CHBr); 132.7 (CCl) ^1H: 6.65 (= CH)
$C_6H_{10}BrCl$ (197.5)	^{13}C: 101.1 (CHBr); 137.0 (CCl) ^1H: 6.25 (= CH); 2.45–2.70 (CH_2)[g]
$C_{10}H_{18}BrCl$ (253.6)	^{13}C: 101.1 (CHBr); 137.1 (CCl) ^1H: 6.25 (= CH); 2.45–2.70 (CH_2)[g]

The content of the halogenating species was determined by iodometry to be 2.5 mmol/g and the reagent is well storable at room temperature.

The reactions were usually carried out in dichloromethane at room temperature, by treating the organic substrate with 50% excess of the resin. Regeneration of the resin was accomplished by washing the exhausted reagent with aqueous sodium hydroxide followed by neutralization with hydrogen bromide and suspension in a dichloromethane solution of chlorine.

Products were isolated in good yields and were identified by G.L.C., ^1H-N.M.R., and ^{13}C-N.M.R. data, in comparison with data for the dichloro and dibromo analogues or calculated chemical shifts[9–12]. The results are reported in Table 2 together with the more significant data.

Chlorobromination of alkenes has been described to occur using copper(II) chloride/bromine[13] or antimony(V) chloride/bromine[14] mixtures, but we think that, even if the yields are comparable, the ease of work-up makes our reagent the method of choice to perform such reactions. Moreover, a wider applicability is allowed as we obtained chlorobromoalkenes from alkynes and we are not aware of any data from the literature to achieve such a result.

G.L.C. analyses were performed on a Hewlett-Packard 5750 instrument equipped with 5% SE 30 stainless steel column 10 ft × 0.25 in. ^1H-N.M.R. spectra were measured at 60 MHz on a Perkin-Elmer R12B instrument. ^{13}C-N.M.R. spectra were measured on a Varian XL-100 Fourier transform instrument. In both cases the substances were in $CDCl_3$ solution with TMS as internal standard. Mass spectra were recorded with a Varian Mat III instrument at 70 eV.

Brominating (1) and Chlorobrominating (10) Reagents:
Amberlyst A-26, chloride form, is converted to the basic form by washing with 1 normal aqueous sodium hydroxide solution and then rinsing with water to neutrality. The resin is then converted to the bromide form by neutralization with 10% aqueous hydrobromic acid and dried by azeotropic extraction[15]. This polymer (10 g) is suspended in a 4% carbon tetrachloride solution of bromine (100 ml) and shaken at room temperature overnight. The resin is filtered off, washed with carbon tetrachloride (50 ml), and dried under reduced pressure. The bromine content is evaluated by extracting a sample of the polymer (1.0 g) with 1 normal aqueous sodium hydroxide and, after acidification, titrating by iodometry. A mean value of 2.5 mmol bromine/g of polymeric reagent is obtained for **1**.

Amberlyst A-26, bromide form, (10 g) is similarly suspended in a 1.2 normal solution of chlorine in dichloromethane (100 ml) and shaken overnight. The resin is filtered off, washed with dichloromethane, dried under reduced pressure, and stored in a tightly stoppered flask. To estimate the capacity of the reagent, a sample of the polymer (1.0 g) is extracted with 1 normal aqueous sodium hydroxide; the iodometric titration of this solution gives a mean value of 2.5 mmol of halogenating species per gram of reagent **10**.

α-Bromodecanal: Typical Procedure:
Decanal (0.78 g, 5 mmol) and Amberlyst A-26, perbromide form (3 g, 7.5 mmol) are stirred and heated under reflux in dichloromethane (10 ml), the reaction being followed by G.L.C. After 1 h the resin is filtered off, thoroughly washed with dichloromethane and the solvent removed under reduced pressure. Bulb-to-bulb distillation of the crude product affords pure α-bromodecanal; yield: 1.14 g (97%); b.p. 80–83 °C/1 torr.

$C_{10}H_{19}BrO$	calc.	C 51.08	H 8.12	Br 33.99
(235.1)	found	50.73	8.20	34.29

M.S.: $m/e = 234, 236$ (M^{+}).

I.R. (liquid film): $\nu_{C=O} = 1725\ cm^{-1}$.

^1H-N.M.R. ($CDCl_3$): $\delta = 0.9$ (t, 3H); 1.3 (m, 12H); 1.85 (m, 2H); 4.25 (d, t, 1H); 9.6 ppm (d, 1H).

We acknowledge the help of Dr. A. G. Giumanini for mass spectra.

Received: June 11, 1979
(Revised form: August 6, 1979)

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[1] J. M. J. Frechet, M. J. Farral, L. J. Nuyens, *J. Macromol. Sci. Chem.* **11**, 507 (1977).

[2] M. Zupan, A. Pollak, *J. Chem. Soc. Chem. Commun.* **1975**, 715.

[3] G. Manecke, M. Stark, *Makromol. Chem.* **176**, 285 (1975).

[4] S. Cacchi, L. Caglioti, E. Cerna, *Synthesis* **1979**, 64.

[5] H. McCombie, T. H. Reade, *J. Chem. Soc.* **1923**, 141.

[6] R. H. Reuss, A. Hassner, *J. Org. Chem.* **39**, 1785 (1974).

[7] R. Bloch, *Synthesis* **1978**, 140.

[8] V. Calò, L. Lopez, G. Pesce, *J. Chem. Soc. Perkin Trans. 1* **1977**, 501.

[9] F. W. Wehrli, T. Wirthlin, *Interpretation of Carbon 13 NMR Spectra,* Heyden, London, 1976.

[10] U. E. Matter et al., *Tetrahedron* **25**, 691 (1969).

[11] H. M. VanDort, T. J. Sekuur, *Tetrahedron Lett.* **1963**, 1301.

[12] A. Debon, S. Masson, A. Thuillier, *Bull. Soc. Chim. Fr.* **1975**, 2493.

[13] W. C. Baird, Jr., J. H. Surridge, M. Buza, *J. Org. Chem.* **36**, 3324 (1971).

[14] S. Uemura, A. Onoe, M. Okano, *Bull. Chem. Soc. Jpn.* **47**, 143 (1974).

[15] G. A. Crosby, N. M. Weinshenker, H. S. Uh, *J. Am. Chem. Soc.* **97**, 2232 (1975).

[16] A. Kirrmann, *Ann. Chim. (Paris)* **11**, 229 (1929).

[17] C. F. Ward, *J. Chem. Soc.* **1923**, 2211.

[18] F. Schmidt, V. Knilling, A. Scherl, *Ber. Dtsch. Chem. Ges.* **59**, 1280 (1926).

[19] K. Ganafathi, V. Shirsat, V. Deliwala, *Proc. Indian Acad. Sci.* **14**, 630 (1941); *C. A.* **36**, 4102 (1942).

[20] C. Weigand, *Ber. Dtsch. Chem. Ges.* **58**, 1478 (1925).

[21] F. C. Whitmore, E. N. Thurman, *J. Am. Chem. Soc.* **51**, 1499 (1929).

[22] A. J. Houssa, J. Kenyon, H. Phillips, *J. Chem. Soc.* **1929**, 1710.

0039-7881/80/0232-0146 $ 03.00