The Participation Effect of Halogen Atoms in Stereospecific Friedel–Crafts Alkylations

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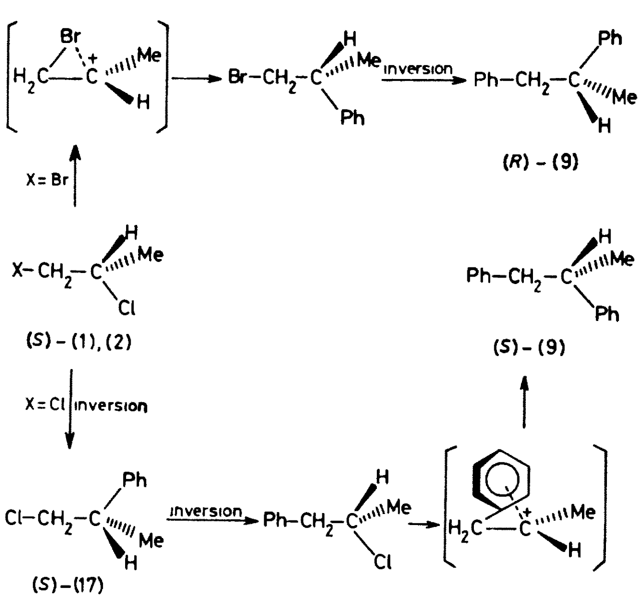
Summary The Friedel–Crafts alkylation of benzene with optically active 1,2-, 1,3-, 1,4-, and 1,5-dihalogenoalkanes gave the corresponding primary phenylalkyl halides with a stereospecificity which depended primarily on the type of terminal halogen or the variation in carbon chain length.

The stereochemical course of Friedel–Crafts alkylation has been assumed to proceed with almost complete racemization.[1] Recently, however, some instances of stereospecific alkylations which proceed with inversion or retention of configuration have been reported.[2] This communication describes new Friedel–Crafts alkylations of benzene with optically active 1,2-, 1,3-, 1,4-, and 1,5-dihalogenoalkanes, which gave the corresponding primary phenylalkyl halides with inversion or retention of configuration without skeletal rearrangement. The results are summarized in the Table. The alkylation of benzene with (*S*)-1,2-dichloropropane (**1**) and aluminium chloride gave (*S*)-1,2-diphenylpropane (**9**) with apparently, retention of configuration, and 1,1-diphenylpropane (**16**). The first stage of the reaction would yield (*S*)-1-chloro-2-phenylpropane (**17**) followed by benzene alkylation to give (*S*)-(**9**).[3] Thus the reaction of (**1**) to (**17**) proceeded with almost complete inversion of configuration as shown in Scheme 1. In contrast, the reaction of benzene with (*S*)-1-bromo-2-chloropropane (**2**) afforded a mixture of (*R*)-(**9**) and (**16**). Thus the first stage in the conversion of (**2**) into (**9**) proceeded with retention of configuration *via* a propylene bromonium ion intermediate as shown in Scheme 1.[4,5] Although the Friedel–Crafts alkylations of aromatic hydrocarbons with secondary species such as optically active $CD_3CHOHMe$ and 2-butanol have been shown to proceed through carbonium ion intermediates with almost complete racemization or rearrangement of products,[1,6] the reaction of (**1**) and (**2**) proceeded with high stereospecificity.

$$\mathrm{Me{\cdot}CHCl{\cdot}CH_2X} \xrightarrow{\mathrm{PhH,\ AlCl_3}} \mathrm{Me{\cdot}CHPh{\cdot}CH_2X}$$

	X		X
(**1**)	Cl	(**9**)	Ph
(**2**)	Br	(**10**)	$ClCH_2$
(**3**)	$ClCH_2$	(**11**)	$BrCH_2$
(**4**)	$BrCH_2$	(**12**)	ICH_2
(**5**)	ICH_2	(**13**)	$Cl[CH_2]_2$
(**6**)	$Cl[CH_2]_2$	(**14**)	$Br[CH_2]_2$
(**7**)	$Br[CH_2]_2$	(**15**)	$Cl[CH_2]_3$
(**8**)	$Cl[CH_2]_3$		



Scheme 1.

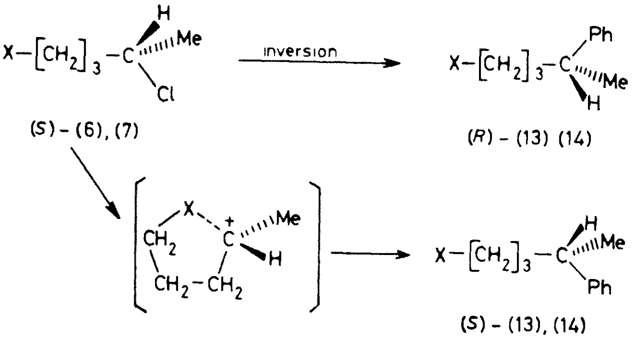
Table. Alkylation of benzene with optically active dihalogenoalkanes in the presence of aluminium chloride[a]

	Starting dihalide[b]				Alkylated products[c]			
Comp.	$[\alpha]_D^{25}$ (*c* 10, $CHCl_3$)	Absolute config.	Temp /°C	Time /h	Comp.	Yield /%	$[\alpha]_D^{25}$ (*c* 10, $CHCl_3$)	Optical yield/%
(**1**)	−5·58° (neat)	*S*	10	1·0	(**9**)	66	+36·0°	60
(**2**)	−6·16° (neat)	*S*	10	1·0	(**9**)	64	−23·4°	36
(**3**)	−63·4°	*R*	7	0·5	(**10**)	86	+35·5°	47
(**4**)	−33·6°	*R*	10	0·5	(**11**)	88	+21·8°	29
(**5**)	−47·5°	*R*	10	0·5	(**12**)	69	+21·0°	22
(**6**)	+32·3°	*S*	0	0·2	(**13**)	23	+2·4°	15
(**6**)	+32·3°	*S*	−20	0·7	(**13**)	85	−2·7°	17
(**7**)	+21·6°	*S*	−10	0·1	(**14**)	85	+2·9°	17
(**8**)	+27·7°	*S*	−20	1·2	(**15**)	95	−6·1°	26

[a] Reactions were conducted with 4·5 mmol of dihalogenoalkane and 0·45 mmol of aluminium chloride in 15 ml of benzene. Carbon disulphide (8 ml) was added at below 0 °C. [b] Dihalogenoalkanes were prepared by chlorination of corresponding halogenohydrines with thionyl chloride in pyridine. The reported rotation of the dihalogenoalkane (*S*)−(**1**) is −5·87° (neat) (W. Fickett, H. K. Garner, and H. J. Lucas, *J. Amer. Chem. Soc.*, 1951, **73**, 5063). [c] The absolute configuration and maximum rotation of the following primary phenylalkyl halides were determined: (*S*)−(**10**) +77·2°; (*S*)−(**12**) +114·1°; (*S*)−(**13**) + 16·3°; (*R*)−(**15**),−23·9°. The following reported values were used for the others: (*S*)−(**9**), + 63·5° (R. A. Barnes and B. R. Juliano, *J. Amer. Chem. Soc.*, 1959, **81**, 6462); (*R*)−(**11**), −74·0° and (*R*)−(**14**), − 16·6° (P. A. Levene and R. E. Marker, *J. Biol. Chem.*, 1935, **110**, 329).

The alkylation of benzene with (*R*)-1,3-dichlorobutane (**3**) and (*R*)-1-bromo-3-chlorobutane (**4**) gave (*S*)-1-chloro-3-phenylbutane (**10**) and (*S*)-1-bromo-3-phenylbutane (**11**), respectively as the main products with inversion of configuration, without skeletal rearrangement under the reaction conditions The lower optical yield of (**10**) or (**11**) than that of (*S*)-(**9**) could be caused by the increase in ionic character of the intermediate in the reaction of (**3**) or (**4**) In the reaction of (*R*)-3-chloro-1-iodobutane (**5**), (*S*)-1-iodo-3-phenylbutane (**12**) was obtained with inversion of configuration, along with 1-iodo-2-phenylbutane in 10% yield

The reaction with (*S*)-1-bromo-4-chloropentane (**7**) proceeded with some retention of configuration to give 1-bromo-4-phenylpentane (**14**) as shown in the Table The stereochemical course of the reaction of 1,4-dichloropentane (**6**) to 1-chloro-4-phenylpentane (**13**) varied with reaction temperature, *i e* , retention at 0 °C and inversion at −20 °C Therefore, two paths at least are competing in the alkylation of benzene with 1,4-dihalogenopentanes and they involve direct substitution of benzene and halogen participation to give a five-membered halonium ion intermediate as shown in Scheme 2 [5,7] However, the possibility of a carbonium ion intermediate should not be excluded



SCHEME 2

Finally, the alkylation of benzene with (*S*)-1,5-dichlorohexane (**8**) at −20 °C gave (*R*)-1-chloro-5-phenylhexane (**15**) with inversion of configuration

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