Retentive Friedel-Crafts Alkylation

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Summary The Friedel Crafts alkylation of benzene with *R*-(−)-2-chloro-1-phenylpropane gave *R*-(−)-1,2-diphenylpropane with almost complete retention of configuration below room temperature.

THE stereochemical course of Friedel-Crafts alkylation has been thought to proceed with almost complete racemization.[1] Recently, however, some instances of stereospecific alkylation which proceed with inversion of configuration have been reported[2] and we now report a novel alkylation reaction which proceeds with almost complete retention of configuration.

In the presence of ferric chloride, alkylation of benzene with (−)-2-chloro-1-phenylpropane (I) gave a mixture of (−)-1,2-diphenylpropane (II), 1,1-diphenylpropane (III) and polymer below room temperature. The results obtained under several conditions are shown in the Table.

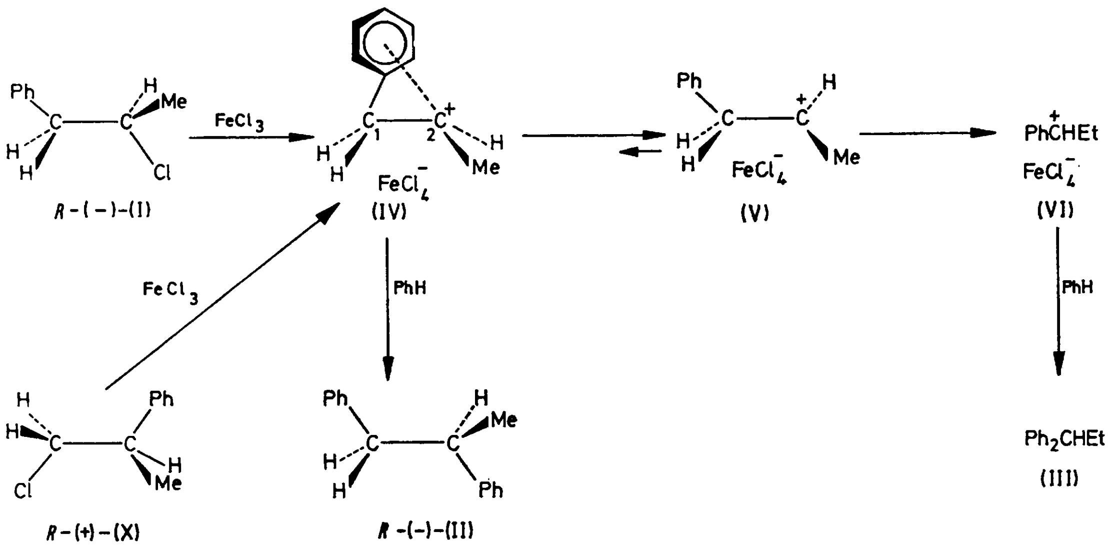
Table. Alkylation of benzene with (−)-2-chloro-1-phenylpropane (I) and (+)-1-chloro-2-phenylpropane (X)[a]

	Starting chloride[b] (4·5 mmol)	Lewis acid (0·45 mmol)	Temp /°C	Time /h	Yield[c] /%	Alkylated products Isomer/%[d] (II)	(III)	$[\alpha]^{25}_D$ (c 5,$CHCl_3$)	Optical purity of (II)/%[e]	Optical yield of (II)/%	Polymer yield /%
1	(−)-(I)	$FeCl_3$	20	1·0	69·2	53	47	−20·0°	59·4	69·7	30·8
2	(−)-(I)	$FeCl_3$	0	3·0	60·0	65	35	−30·1°	72·9	85·6	40·1
3	(−)-(I)	$AlCl_3$	−20	1·0	70·9	80	20	−41·7°	82·1	96·4	29·1
4	(+)-(X)	$FeCl_3$	20	1·0	75·6	52	48	−21·9°	66·3	70·5	24·4

[a] The reaction was conducted in 15 ml (0·16 mol) of benzene. In **2** and **3**, carbon disulphide (8 ml) was added as solvent. [b] (−)-(I): $[\alpha]^{25}_D$ −18·3° (neat), optical purity 85·2%; (+)-(X): $[\alpha]^{25}_D$ +14·0°, optical purity 94·0%. [c] Based on (−)-(I) or (+)-(X) used. [d] Determined by n.m.r. [e] Calculated from the reported rotation of (−)-(II) (−63·5°)[4] and corrected by isomer percentage.

The absolute configuration of (−)-(I)[3] and (−)-(II)[4] has been assigned as *R* and *R*, respectively. Thus, the stereochemical course of the reaction can be formulated as a series of reactions as shown in the Scheme.

The optical yields of (−)-(II) decrease with rise in temperature. When (−)-(II) was treated with ferric chloride in benzene at 30°, the optical rotation of (−)-(II) remained unchanged and thus, successive racemization of (−)-(II) should not occur in this reaction. The stereochemical results suggest that the reaction takes place through an intermediate of the phenonium ion type, and attack of benzene on either of the two bridged carbon atoms in this intermediate would produce two enantiomers and decrease the optical yield of (II). Thus the alkylation of *p*-xylene with (I) in the presence of ferric chloride at room temperature should give 1-phenyl-2-(2,5-dimethylphenyl)propane (VII) and 1-(2,5-dimethylphenyl)-2-phenylpropane (VIII) as products of C-2 and C-1 attack of *p*-xylene respectively. However, the reaction products obtained were (VII), 1-phenyl-1-(2,5-dimethylphenyl)propane (IX), and polymer. The C-2 atom has such a strong carbonium ion character that each nucleophile attacks the C-2 position exclusively. 1,1-Diarylpropane [(III) or (IX)] is formed from the 1-phenylpropyl carbonium ion intermediate (VI) produced from the open carbonium ion intermediate (V) accompanied by a 1,2-hydride shift. At low temperature, the rate of reaction (V) → (IV) is so much slower than that of reaction (V) → (VI), that the configuration of (IV) remains unchanged. At elevated temperature, racemization of (IV) takes place by the reversible formation of inactive intermediate (V). This could account for the decrease of the optical yields of (−)-(II) obtained.



Scheme

Alkylation of benzene with *R*-(+)-1-chloro-2-phenylpropane (X)[5] also gave *R*-(−)-(II). This can be explained in terms of a Wagner-Meerwein rearrangement of the phenyl group in (X) which results in the formation of the intermediate (IV).†

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† We found that *R*-(+)-(X) was converted stereospecifically into *R*-(−)-(I) by a trace amount of Lewis acid.

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