turned blue, and an excess pressure of about 0.5 bar was applied. The suspension was stirred magnetically at 35 °C for 48 h. The bacteria were removed by centrifuging, and the liquid was continuously extracted with ether for 24 h.

The residue contained only sulcatol, complete conversion having taken place. Optical purity was determined on the crude extract. The optical rotation was not measured. Chromatography on chiral column: 94% *S* and 6% *R*.

5. *Aspergillus niger* (ATCC 9142). The following culture medium was used. For 1 L of water: glucose, 20 g; yeast extract, 5 g; soya meal, 5 g; NaCl, 5 g; K_2HPO_4, 5 g; pH adjusted to 6.5.

The culture was set up in 500-mL conical flasks containing 100 mL of medium stirred at 200 rpm at 27 °C. After 24 h the contents of the flasks were filtered and the mycelium washed repeatedly with 8% NaCl solution. The bioconversion was carried out under the following conditions: in a conical flask containing 50 mL of water were placed 5 g of wet mycelium and 50 μL of 6-methylhept-5-en-2-one. The mixture was stirred at 200 rpm at 27 °C.

After a 24-h reaction the mixture was filtered and the filtrate extracted continuously with ether overnight.

The crude extract contained 80% sulcatol and 20% unreacted ketone.

From 10 flasks 2.5 g of purified sulcatol was recovered (yield 80%): $[\alpha]^{25}_J$ −14.3° (*c* 0.05, EtOH). Chromatography on chiral column: 98% *R* and 2% S.

6. *Geotrichum candidum* (CBS 233-76). This microorganism is generally classified among the fungi even though it may occur under various forms. The strain used is a yeast-like strain giving large isolated cells.

The following culture medium was used: glucose, 50 g; yeast extract, 10 g; bactopeptone, 10 g; H_2O, 1000 mL. The culture was grown in a 2-L fermenter containing 1 L of medium, well-aerated and maintained at 27 °C. After 48 h growth the mixture was filtered, and the cells were washed repeatedly with 8% NaCl solution.

The bioconversion conditions were identical with those used with *A. niger* except that the water was replaced by 5% glucose solution to prevent high metabolization.

After a 17-h reaction the mixture was filtered and the filtrate extracted continuously with ether overnight. The residue consisted of 70% sulcatol and 30% unreacted ketone. The yield, determined with the aid of an internal standard was 50%. The optical rotation was not measured. The optical purity was determined on the crude extract. Chromatography on chiral column: 96% *R* and 4% *S*.

7. *Clostridium tyrobutyricum* (DSM 1460). To obtain the *R*-(−) enantiomer, the bacterium was grown on a medium containing glucose (10 g/L) as sole carbon source as described by J. Bader et al.[17] Growth was monitored as previously and filtration carried out under anaerobic conditions when the optical density was maximal (2.0 to 2.1).

Recovery of *C. tyrobutyricum* cells and the bioconversion of 6-methylhept-5-en-2-one were carried out under the conditions described previously for the microorganism grown on crotonic acid. The residue consisted of 76% sulcatol and 24% unreacted ketone. After purification, 0.26 g of sulcatol was recovered (yield 70%): $[\alpha]^{25}_J$ −11° (*c* 0.015, EtOH). Chromatography on chiral column: 90% *R* and 10% *S*.

8. Resolution of Racemic Sulcatol with Pig Pancreatic Lipase. The resolution of racemic sulcatol was performed as follows: A mixture of 1.3 g (10 mM) of racemic 6-methylhept-5-en-2-ol obtained by $LiAlH_4$ reduction of the corresponding ketone, 2.4 g of trichloroethyl butyrate (11 mM), 2 g of pig pancreatic lipase (Sigma, activity 35 U/mg protein), and 10 mL of anhydrous ether was placed in a vessel sealed with a septum cap and stirred at 27 °C. The degree of completion of the reaction was monitored by gas-phase chromatography. Once the required extent of transesterification had been reached, the lipase was filtered and the ether evaporated off. The residue was chromatographed on a silica gel column with dichloromethane as eluant, giving butyrates and unreacted sulcatol. The butyrates were hydrolyzed with 1 N potassium hydroxyde in alcohol. The alcohol was then evaporated, water added, and the mixture extracted with ether, giving the sulcatol which had reacted.

(a) Reaction time, 48 h: transesterification, 30%; unreacted sulcatol, chromatography on chiral column, 83% *S* and 17% *R*; sulcatol from butyrate, chromatography on chiral column, 94% *R* and 6% *S*.

(b) Reaction time, 96 h: transesterification, 65%; unreacted sulcatol, $[\alpha]^{25}_J$ +15.6° (*c* 0.015, EtOH), chromatography on chiral column, *S* >99%; sulcatol from butyrate, chromatography on chiral column, 90% *R* and 10% *S*.

Aryl-Assisted Halogen Exchange and Rearrangements of 2-Bromo-1-chloro-3-arylpropanes and 1-Bromo-3-chloro-2-arylpropanes. Evidence for a Competitive Bromine-Assisted Pathway in the Case of 1,2-Dibromo-3-arylpropanes

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Received May 22, 1986

Ion pairing, ring opening, and the rates of formation of aryl-bridged chlorinated intermediates are investigated through reactions of mixed 1,2-dihalo-3-arylpropanes and 1,3-dihalo-2-arylpropanes (aryl = C_6H_4X with X = H and X = *p*-Me) and are compared with previous results for X = *p*-OMe; this allows an estimation of the free energy difference between isomeric aryl-bridged (3-bromopropylene)benzenium ions and bromine-bridged 3-arylpropylenebromonium ions.

Bromonium ions and benzenium ions are well-known intermediates: the former were originally proposed to account for the anti stereochemistry of the addition of bromine to olefins;[1] the latter play an important part in the solvolysis of primary and secondary β-arylalkyl tosylates.[2]

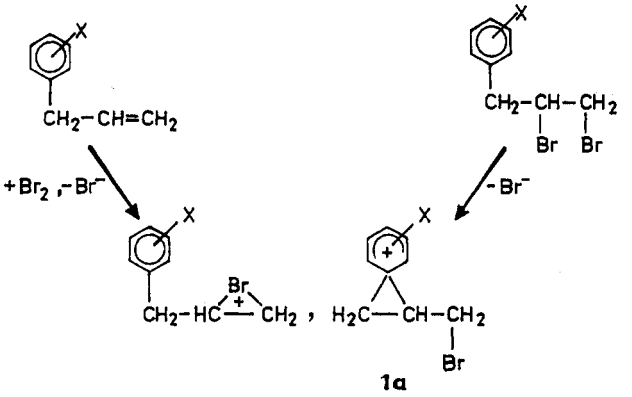
Here we examine an original situation where aryl and bromine groups are present simultaneously and can compete to delocalize a positive charge. This situation is ob-

(1) (a) Roberts, L.; Kimball, J. E. *J. Am. Chem. Soc.* **1937**, *59*, 947. (b) Olah, G. A. *Halonium Ions*; Wiley: New York, 1975; pp 97-124. (c) Freeman, F. *Chem. Rev.* **1975**, *75*, 439. (d) Dubois, J.-E.; Chretien, J. R. *J. Am. Chem. Soc.* **1978**, *100*, 3506. (e) Bienvenüe-Goetz, E.; Dubois, J.-E. *Tetrahedron* **1978**, *34*, 2021. (f) Angelini, G.; Speranza, M. *J. Am. Chem. Soc.* **1981**, *103*, 3792.

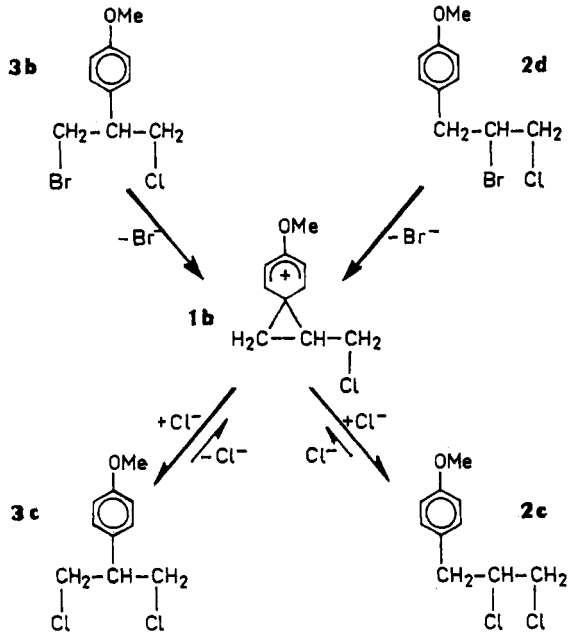
(2) (a) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2129. (b) Olah, G. A.; Schleyer, P. v. R. *Carbonium Ions*; Wiley: New York, 1972; pp 1347-1383. (c) Schadt, F. L.; Lancelot, C. J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1978**, *100*, 228.

0022-3263/87/1952-0260$01.50/0

Scheme I

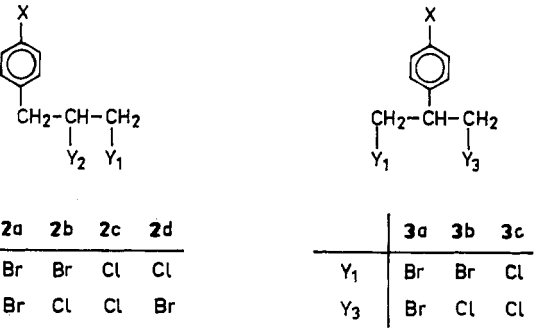


Scheme II



tained by bromination of a 3-arylpropene or by abstracting a bromide ion from a 1,2-dibromo-3-arylpropane. Two isomeric intermediates can be envisaged: a 3-arylpropylenebromonium ion and the (3-bromopropylene)benzenium ion **1a** (Scheme I). Not a great deal is known about benzenium ions bearing electron-withdrawing groups.[3,4] (3-Halopropylene)benzenium ions themselves were revealed primarily by our work.[5,6] Recently, we demonstrated the nonregioselectivity of the addition of a halide ion to 1-(3-halopropylene)-4-methoxybenzenium ions.[6] One of the various methods used consisted of studying the reaction products of 2-bromo-1-chloro-3-(4-methoxyphenyl)propane (**2d**-OMe) and of 1-bromo-3-chloro-2-(4-methoxyphenyl)propane (**3b**-OMe) in tin tetrachloride at 100 °C. It was shown that, under these conditions, a 1-(3-chloropropylene)-4-methoxybenzenium ion (**1b**-OMe) is formed irreversibly from one or the other of these substrates by loss of a bromide ion (Scheme II). The benzenium ion then reacts with Cl^-; the nucleophilic attack takes place with the same rate at the two electrophilic sites of the benzenium ion, whatever the precursor, leading to the formation of 1,3-dichloro-2-arylpropane

(3) Lambert, J. B.; Mark, H. W.; Stedman Magyar, E. *J. Am. Chem. Soc.* **1977**, *99*, 3059.
(4) Lambert, J. B.; Mark, H. W.; Holcomb, A. G.; Stedman Magyar, E. *Acc. Chem. Res.* **1979**, *12*, 317.
(5) Dubois, J.-E.; Toullec, J.; Fain, D. *Tetrahedron Lett.* **1973**, 4859.
(6) Fain, D.; Dubois, J.-E. *J. Org. Chem.* **1982**, *47*, 4855.



	2a	2b	2c	2d
Y_1	Br	Br	Cl	Cl
Y_2	Br	Cl	Cl	Br

	3a	3b	3c
Y_1	Br	Br	Cl
Y_3	Br	Cl	Cl

Figure 1. Compounds encountered in this study.

Table I. Rate Constants for Interconversion of 1,3-Dichloro-2-arylpropanes 3c and 1,2-Dichloro-3-arylpropanes 2c in $SnCl_4$ at 100 °C

aryl group	10^8k_{32}, s^{-1}	10^8k_{23}, s^{-1}	K^a
p-$MeOC_6H_4$	18600[b]	1830[b]	10.1
p-MeC_6H_4	725	66.5	10.9
C_6H_5	35.8	3.17	11.3

[a] **3c** to **2c** equilibrium constant. [b] Data taken from ref 6.

3c-OMe and of 1,2-dichloro-3-arylpropane **2c**-OMe in equal amounts. This addition is reversible; the dichlorides slowly give an equilibrium mixture. The influence of an electron-withdrawing substituent in a reaction taking place via a benzenium ion is therefore most important. The usual rearrangement of a primary system into a secondary system is limited here to 50% (**3b** → **2c**), and we see the quite unusual rearrangement of a secondary system into a primary one (**2d** → **3c**). Our intention was, on the one hand, to carry out an analogous study of the formation and behavior of (3-halopropylene)benzenium ions with a less electron-donating aromatic substituent than p-OMe, and, on the other hand, to measure the relative stability of (3-bromopropylene)benzenium and 3-arylpropylenebromonium ions. This latter may be an important reaction intermediate when the stability of benzenium ion is lessened. To obtain the desired ions, we used halogen exchange reactions of 1,2-dihalo-3-arylpropanes and 1,3-dihalo-2-arylpropanes with tin tetrachloride.[6] Product distributions and rate constants are examined.

Results

The designation of the compounds encountered in this study is indicated in Figure 1.

Equilibration. It was previously reported that, at 100 °C, in $SnCl_4$, 1,2-dichloro-3-(4-methoxyphenyl)propane (**2c**-OMe) or 1,3-dichloro-2-(4-methoxyphenyl)propane (**3c**-OMe) gives an equilibrium mixture of both compounds (eq 1).[6]

$$\textbf{2c} \text{ or } \textbf{3c} \xrightarrow{k_{eq}} \text{equilibrium mixture} \qquad (1)$$

Identical reactions are observed with dichloroarylpropanes **2c**-H and **3c**-H, **2c**-Me and **3c**-Me (aryl = C_6H_4X with X = H or p-Me). The first-order rate constants k_{32} and k_{23} for reaction 2 were determined from the rate constant for eq 1 ($k_{eq} = k_{32} + k_{23}$) and the equilibrium constant for eq 2 ($K = k_{32}/k_{23}$). The results are given in Table I.

$$\textbf{3c} \underset{k_{23}}{\overset{k_{32}}{\rightleftharpoons}} \textbf{2c} \qquad (2)$$

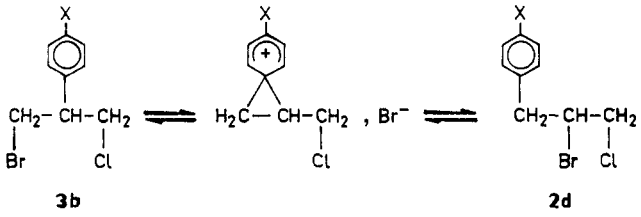
Halogen Interchange and Rearrangements. A series of halogenated compounds (2-bromo-1-chloro-3-arylpropanes **2d**-H and **2d**-Me, 1-bromo-3-chloro-2-arylpropanes **3b**-H and **3b**-Me, 1,2-dibromo-3-phenylpropane **2a**-H) was treated with $SnCl_4$ at 100 °C. The first-order

Table II. Halogen Exchange with $SnCl_4$ at 100 °C: Rate Constants and Product Distributions

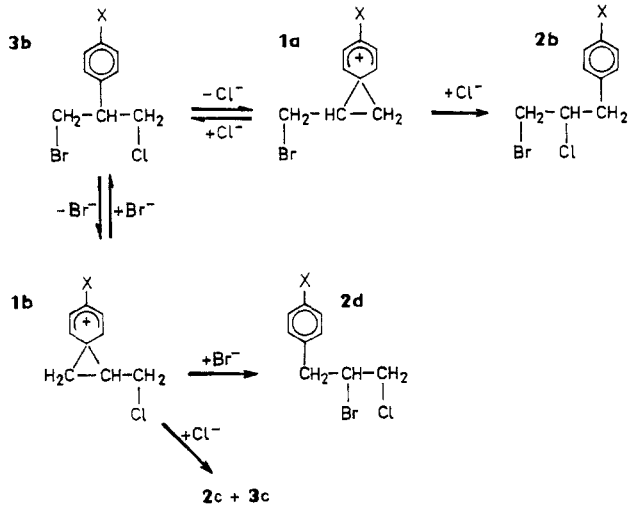
		yields of products, %			
		1,2-dihalo-3-arylpropanes		1,3-dihalo-2-arylpropanes	
compd	$10^8 k_{exptl}$, s^{-1}	chloro bromides **2b** + **2d**	dichloride **2c**	chloro bromide **3b**	dichloride **3c**
1-bromo-3-chloro-2-arylpropanes **3b**					
3b-OMe	101000[a]	11[a,b]	46[a,b]		43[a,b]
		11[a,c]	50[a,c]		39[a,c]
3b-Me	2840	26[b]	41[b]		33[b]
		25[c]	46[c]		29[c]
3b-H	120	40[b]	33[b]		27[b]
		38[c]	38[c]		24[c]
2-bromo-1-chloro-3-arylpropanes **2d**					
2d-OMe	14500[a]		58[a,b]	0[a,b]	42[a,b]
			74[a,c]	0[a,c]	26[a,c]
2d-Me	500		65[b]	6[b]	29[b]
			81[c]	1[c]	18[c]
2d-H	15.3		76[b]	11[b]	13[b]
			85[c]	3.5[d]	11.5[d]
1,2-dibromo-3-phenylpropane **2a**-H	100				
1,3-dibromopropane	0[e]				

[a] Data taken from ref 6. [b] At 25% reaction. [c] At 70% reaction. [d] At 57% reaction. [e] 98% of the starting material is recovered after 48 h at 140 °C.

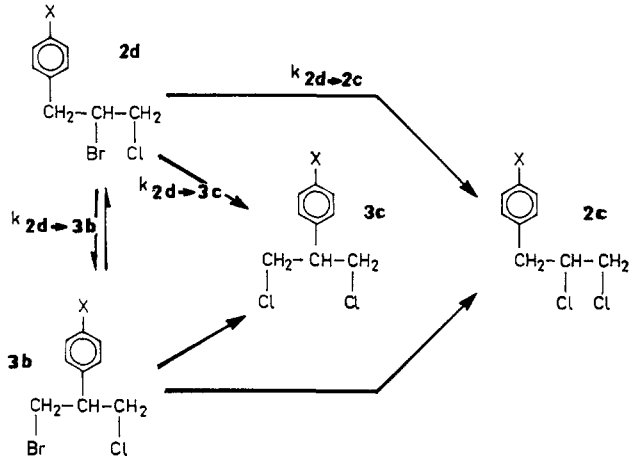
Scheme III



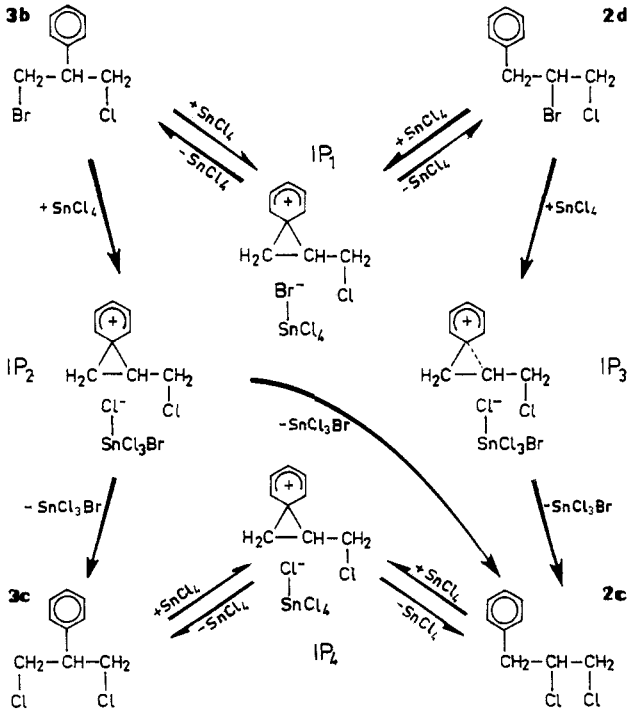
Scheme IV



Scheme V



Scheme VI



rate constants for disappearance of the substrates, k_{exptl}, are given in Table II. The reaction products were exclusively mixtures of other dihaloarylpropanes **2** and **3** (no elimination product was detected). The composition of each mixture, which changed with time, is given in Table II for 25% and 70% reaction (in our GLC analyses, the 1-bromo-2-chloro-3-arylpropane **2b** and its isomer, 2-bromo-1-chloro-3-arylpropane **2d**, are not separated). Product recovery was nearly 100%. Previous results for **2d**-OMe, **3b**-OMe, and 1,3-dibromopropane are also listed in Table II.

Discussion

The set of reactions given by bromochloroarylpropanes **2d** and **3b** is complex. Transformation of the substrate into dichlorides **2c** and **3c** competes with its isomerization (**2d** → **3b** or **3b** → **2d**). Moreover, the dichlorides obtained

evolve toward a state of equilibrium. Comparing these reactions raises interesting problems. In Scheme VI, we show that **3b**-H and **2d**-H interconvert and that their evolution toward dichloro products is not parallel in the absence of a direct transformation **2d**-H → **3c**-H. This pathway intervenes more or less depending on the group X on the aromatic ring. Analysis of the experimental results is based on the partial rate constants for formation of the various products from each bromo chloride. Equilibration of dichlorides **2c** and **3c** was studied so as to take into account its influence during reactions of **2d** and **3b**, but also to measure indirectly the difference in the standard molar free energies of these two compounds.

Mechanism, Rate Constants, and Equilibrium Constants for 3c ⇌ 2c. The formation of 1,3-dichloro-2-arylpropane **3c** from 1,2-dichloro-3-arylpropane **2c** (as well as the reverse reaction, according to the principle of microreversibility) can only be reasonably explained by the intervention of a (3-chloropropylene)benzenium ion wherein the positive charge is extensively delocalized. The alternative of direct migration of the aromatic ring would lead to a highly unstable primary chlorocarbenium ion. The aromatic substituent markedly affects the rate constant k_{32}. The relative reactivity *p*-OMe/H reaches 520,[7] while it is usually between 30 and 70 for solvolysis reactions via a propylenebenzenium ion.[8,9] The positive charge transferred to the aromatic ring is therefore particularly great in the present case. Thus the presence of an electron-withdrawing halogen atom in the benzenium ion enhances the participation of the aromatic ring. In contrast, K, the equilibrium constant for **3c** ⇌ **2c**, depends only very slightly on the aromatic substituent. This result was to be expected since in **2c** and **3c** there is little charge at the benzylic position. The vicinal dihalide **2c** is more stable than its isomer **3c**.

Standard Free Energy Difference between 3b and 2d. The standard molar free energy difference between a 2-bromo-1-chloro-3-arylpropane **2d** and the isomeric 1-bromo-3-chloro-2-arylpropane **3b**, $\Delta G°_{2d} - \Delta G°_{3b}$, can be obtained from the equilibrium constant K, given two assumptions: (i) The equilibration of 1,3-dihalo-2-(4-methoxyphenyl)propane and 1,2-dihalo-3-(4-methoxyphenyl)propane is carried out in $SnCl_4$ when the halogen is chlorine, in $SnBr_4$ when the halogen is bromine; the two equilibrium constants are equal.[6] We shall assume that this result is also valid when the group *p*-$MeOC_6H_4$ is replaced by *p*-MeC_6H_4 or C_6H_5. (ii) When a benzenium ion is formed from one of our dihalides, one halogen behaves as a leaving group, the other as an electron-withdrawing substituent. We shall assume that the rate constant is the same whatever the halogen (chlorine or bromine) acting as an electron attractor. The small difference in the inductive effects of the CH_2Cl and CH_2Br groups would appear to justify this assumption.[10]

Table III. Reactions of 1-Bromo-3-chloro-2-arylpropanes 3b and 2-Bromo-1-chloro-3-arylpropanes 2d in $SnCl_4$ and Related Kinetic Parameters[a]

	aryl group		
	p-MeO-C_6H_4[b]	*p*-MeC_6H_4	C_6H_5
isomerization (**3b** → **2d** and **2d** → **3b**)	no	yes	yes
halogen interchange with rearrangement (**3b** → **2c** and **2d** → **3c**)	yes	yes	only **3b** → **2c**
halogen interchange without rearrangement (**3b** → **3c** and **2d** → **2c**)	yes	yes	yes
$10^8 k_{3b\to 2d}$, s^{-1}		388	30.6
$10^8 k_{3b\to 3c}$, s^{-1}	44 000	960	34.0
$10^8 k_{3b\to 2c}$, s^{-1}	46 000	1130	37.5
$10^8 k_{3b}$,[c] s^{-1}	90 000	2810	130
$F_{3b} = (k_{3b\to 3c} + k_{3b\to 2c})/k_{3b}$	1	0.745	0.55
$10^8 k_{2d\to 3b}$, s^{-1}		51	4.9
$10^8 k_{2d\to 3c}$, s^{-1}	7 250	124	0.4
$10^8 k_{2d\to 2c}$, s^{-1}	7 250	333	11.4
$10^8 k_{2d}$,[d] s^{-1}	14 500	568	22.1
$F_{2d} = (k_{2d\to 3c} + k_{2d\to 2c})/k_{2d}$	1	0.80	0.54

[a] The rate constants k are related to the process subscripted, unless noted otherwise. **2c** is the 1,2-dichloro-3-arylpropane. **3c** is the 1,3-dichloro-2-arylpropane. [b] Data for *p*-methoxyphenyl compounds taken from ref 6. [c] k_{3b} is the rate constant of **3b** ionization. [d] k_{2d} is the rate constant of **2d** ionization.

Let us suppose now that the equilibration of **3b** and **2d** occurs through a common **1b**,Br^- ion pair (Scheme III), and let us compare it to the equilibration of the corresponding dibromides (1,3-dibromo-2-arylpropane **3a** and 1,2-dibromo-3-arylpropane **2a**). According to our second hypothesis, the ratio of the rate constants for **3b** → **2d** and **3a** → **2a** will be 0.5, as a result of the suppression of one of the two leaving groups, while the rate constants for **2d** → **3b** and **2a** → **3a** will be identical. The equilibrium constant for **3b** ⇌ **2d** is therefore half that of **3a** ⇌ **2a**; this latter is presumed to be equal to K. Whence: $\Delta G°_{2d} - \Delta G°_{3b} = -RT \ln (K/2)$.

Rate Constants for the Formation of Products from 1-Bromo-3-chloro-2-arylpropanes 3b. For three 1-bromo-3-chloro-2-arylpropanes **3b** (aryl = C_6H_4X with X = *p*-OMe, *p*-Me, H), the product distribution is given for 25% and 70% reaction in $SnCl_4$ (Table II). The only products discovered are 1,2-dichloro-3-arylpropane **2c**, 1,3-dichloro-2-arylpropane **3c**, and 1-bromo-2-chloro-3-arylpropane **2b** and/or 2-bromo-1-chloro-3-arylpropane **2d**. The influence of the extent of reaction seems limited. It bears on the relative proportions of dichlorides **2c** and **3c**. It is quite clear, however, that these two dichlorides are formed in similar quantities whatever the aromatic substituent X. Obviously, the interpretation previously given for **3b**-OMe[6] and recalled in Scheme II (nonregioselective nucleophilic attack of a (3-chloropropylene)benzenium ion **1b**) applied to all substrates. As for the proportion of **2b** and/or **2d** in the reaction products of **3b**, this depends considerably on the ring substituent. It increases when the latter becomes less electron-donating. A first mechanism for forming a bromo chloride is the reversible departure of Cl^- leading to **2b** via a (3-bromopropylene)benzenium ion **1a** (Scheme IV, first line). This transformation **3b** → **2b** is closely analogous to the dichloride **3c** reaction leading to its isomer **2c** (eq 2, direct reaction). Since substituents CH_2Br and CH_2Cl are approximately equally electron-withdrawing,[10] and since **3b** has only one chlorine atom, the **3b** → **2b** rate constant $k_{3b\to 2b}$ can be taken as equal to $k_{32}/2$. We thus calculate that $k_{3b\to 2b}$

(7) There is a satisfactory correlation with a slope of 1.38 between log k_{32} and the logarithms of the rate constant for acetolysis of neophyl tosylates given by Coke and Jones (Coke, M. G.; Jones, J. L. *J. Am. Chem. Soc.* **1969**, *91*, 4284); this acetolysis is considered as a model for aromatic ring participation. For the acetolysis of *meso*-1,4-diaryl-2,3-butyl ditosylates via a benzenium ion destabilized by an electron-withdrawing substituent, Lambert and co-workers have reported rate constants Fk_Δ whose logarithms do not really satisfy such a correlation. The point *p*-OMe deviates significantly from the line drawn through the points for *p*-Me, H, and *p*-Cl.[3]

(8) Lancelot, C. J.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1969**, *91*, 4291.

(9) Raber, D. J.; Harris, J. M.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1971**, *93*, 4829.

(10) (a) Taft, R. W. *J. Am. Chem. Soc.* **1953**, *75*, 4855. (b) In ref 6, the rate constants k_{exptl} reported for 2-bromo-1-chloro-3-(4-methoxyphenyl)propane and 1,2-dibromo-3-(4-methoxyphenyl)propane are similar.

represents nearly 10%, 13%, and 15% of $(k_{exptl})_{3b}$ for X = *p*-OMe, *p*-Me, and H, respectively.[11] The reaction **3b** → **2b** thus accounts for the presence of the whole of the 11% of **2b** and/or **2d** found in the products of **3b**-OMe, while for **3b**-H and **3b**-Me a second phenomenon is involved. We suggest that the departure of Br^- leading to the (3-chloropropylene)benzenium ion **1b** is now reversible and that 2-bromo-1-chloro-3-arylpropane **2d** is thus formed (Scheme IV, second line).[12] 1-Bromo-3-chloro-2-arylpropane **3b** must, at the same time, be reformed from the benzenium ion since nucleophilic attack on the latter is not regioselective.

Table III reports the rate constants $k_{3b\rightarrow 2d}$, $k_{3b\rightarrow 3c}$, and $k_{3b\rightarrow 2c}$ concerning processes **3b** → **2d**, **3b** → **3c**, and **3b** → **2c**, respectively. The rate constant $k_{3b\rightarrow 2d}$ is obtained from eq 3 by taking $k_{3b\rightarrow 2b} = k_{32}/2$ (small changes in product distribution with the extent of reaction are allowed for).[13]

$$k_{3b\rightarrow 2d} = (k_{exptl})_{3b} \times \frac{[2d] + [2b]}{[2d] + [2b] + [2c] + [3c]} - k_{3b\rightarrow 2b} \quad (3)$$

$k_{3b\rightarrow 2d}$ represents 14% of $(k_{exptl})_{3b}$ for X = *p*-Me and 26% for X = H. Constant $k_{3b\rightarrow 3c}$ is obtained by taking account of the equilibration between reaction products **3c** and **2c**.[13] Constant $k_{3b\rightarrow 2c}$ is the difference between $(k_{exptl})_{3b}$ and the sum of the other constants. We see in Table III that $k_{3b\rightarrow 3c}/(k_{3b\rightarrow 3c} + k_{3b\rightarrow 2c})$ remains between 0.50 and 0.46. The nucleophilic addition on the intermediate is nonregioselective whatever the aryl group.

Rate Constants for the Formation of Products from 2-Bromo-1-chloro-3-arylpropanes 2d. It is very important to study the behavior of compounds **2d** in $SnCl_4$. We shall transpose the results to the aryl-assisted reaction pathway of 1,2-dibromo-3-arylpropanes **2a** with $SnCl_4$ so as to measure the difference in free energy between isomeric benzenium and bromonium ions shown at the bottom of Scheme I.

Elsewhere, we have studied the reaction of **2d**-OMe with $SnCl_4$.[6] The irreversible loss of a bromide ion gives a (3-chloropropylene)benzenium ion. From this ion, only two products are formed, the **2c**-OMe and **3c**-OMe dichlorides (Scheme II). In Table III, we report the rate constants $k_{2d\rightarrow 2c}$ and $k_{2d\rightarrow 3c}$ relative to their formation. In order to calculate these constants from the quantities of **2c**-OMe and **3c**-OMe present in the reaction mixture, we have taken into account the slow equilibration of these two compounds. We find that, for X = *p*-OMe, the ratio $k_{2d\rightarrow 2c}/k_{2d\rightarrow 3c}$ is very close to unity, like $k_{3b\rightarrow 2c}/k_{3b\rightarrow 3c}$. This similarity of the reactions of **2d**-OMe and **3b**-OMe with $SnCl_4$ argues for the existence of an identical intermediate.

When the aryl group is *p*-MeC_6H_4 or C_6H_5, the experimental results of Table II show three products for the reaction of 2-bromo-1-chloro-3-arylpropanes **2d** with $SnCl_4$. These compounds are shown in Scheme V. As for **2d**-OMe, we obtain the dichlorides **2c** and **3c** but also a small amount of bromo chloride **3b**. This compound, which clearly results from the recombination of the leaving group and a (3-chloropropylene)benzenium ion, is distinctly more reactive with regard to $SnCl_4$ than the starting compound **2d**. We have seen above that **3b** leads primarily to **3c**, **2c**, and **2d**. Therefore, during the reaction of a bromo chloride **2d** (X = *p*-Me or X = H) with $SnCl_4$, the dichlorides **2c** and **3c** are formed in part via **3b**. This complex situation is shown in Scheme V, where the arrows do not denote a mechanistic pathway but refer to overall rates. Our immediate concern is to determine the rate constants $k_{2d\rightarrow 2c}$ and $k_{2d\rightarrow 3c}$ for the direct transformations **2d** → **2c** and **2d** → **3c** (the formation of **2c** and **3c** via **3b** will not be taken into account, therefore) as well as $k_{2d\rightarrow 3b}$ relative to the transformation **2d** → **3b**.

We have noted that for **2d**-H from 35% reaction onward the **3b**/**2d** concentration ratio is constant. It is possible to show that this ratio is equal to $k_{2d\rightarrow 3b}/[(k_{exptl})_{3b} - (k_{exptl})_{2d}]$; one can thereby obtain $k_{2d\rightarrow 3b}$.[13] We have nonetheless used a more complex relationship that makes it possible to use the value of [**3b**]/[**2d**] from the start of the reaction.[13] The constants $k_{2d\rightarrow 3b}$ thus calculated for **2d**-H and **2d**-Me are reported in Table III. $k_{2d\rightarrow 3b}$ represents 32% of $(k_{exptl})_{2d}$ for **2d**-H and 10% for **2d**-Me. Since **3b** itself constitutes only a small fraction of the reaction products, it seems that, primarily for X = H, significant amounts of the dichlorides **2c** and **3c** are formed via **3b**; **2d** is also reformed from **3b**. The result is that $k_{2d\rightarrow 3c} + k_{2d\rightarrow 2c} + k_{2d\rightarrow 3b}$ is not quite equal to $(k_{exptl})_{2d}$: a supplementary term is needed, as shown in eq 4.[13,14] $k_{2d\rightarrow 3c}$ was

$$k_{2d\rightarrow 3c} + k_{2d\rightarrow 2c} + k_{2d\rightarrow 3b} = (k_{exptl})_{2d} + k_{2d\rightarrow 3b} \times \frac{k_{3b\rightarrow 2d}}{(k_{exptl})_{3b} - (k_{exptl})_{2d}} \quad (4)$$

roughly calculated from $(k_{exptl})_{2d}$, the product distribution at 25% reaction, and $k_{2d\rightarrow 3b}k_{3b\rightarrow 3c}/[(k_{exptl})_{3b} - (k_{exptl})_{2d}]$, the rate constant for the formation of **3c** via **3b**.[15] $k_{2d\rightarrow 2c}$ is then calculated by eq 4. The results (Table III) show a marked variation of the ratio $k_{2d\rightarrow 2c}/k_{2d\rightarrow 3c}$. Close to unity for X = *p*-OMe, this ratio reaches 2.7 for X = *p*-Me and 28 for X = H.[16] For 2-bromo-1-chloro-3-phenylpropane (**2d**-H), the substitution of Br by Cl takes place with practically no rearrangement. This situation is unexpected, since at the same time **2d**-H rearranges to give the isomeric bromo chloride **3b**-H ($k_{2d\rightarrow 3b}$ represents 32% of $(k_{exptl})_{2d}$).

Mechanism of the Reaction of Bromochloroarylpropanes 2d-H and 3b-H. The almost total absence of rearrangement during the transformation of **2d**-H to dichlorides makes the dihalophenylpropanes a most interesting and borderline case. For **3b**-H, we shall only examine the consequences of bromide ion loss.

We thus observe transformations **2d**-H → **3b**-H and **3b**-H → **2d**-H. We have shown above that the difference in standard free energy between **3b**-H and **2d**-H is equal to $-RT \ln (K/2)$, K being the equilibrium constant for **3c**-H ⇌ **2c**-H. Constants $k_{3b\rightarrow 2d}$ and $k_{2d\rightarrow 3b}$ must therefore be in a ratio close to $K/2$ to be in agreement with this ther-

(11) In what follows, we shall consider that the fraction of **2b** in the reaction products of **3b** remains equal to $k_{32}/2(k_{exptl})_{3b}$, since **2b** is unreactive at 100 °C in $SnCl_4$: **2b** can only give **3b** again with a rate constant practically equal to k_{23} and therefore small compared to $(k_{exptl})_{3b}$.

(12) This collapse of the leaving group and of the intermediate leading to a rearranged product appears most strikingly when 1,3-dibromo-2-arylpropane **3a** is dissolved in $SnCl_4$ at 100 °C. For X = H and X = *p*-Me, large amounts of 1,2-dibromo-3-arylpropane are formed (Fain, D.; Dubois, J.-E., unpublished results); this phenomenon does not exist for X = *p*-OMe.[6]

(13) See Supplementary Material.

(14) Although eq 4 is rigorously exact only when the ratio [**3b**]/[**2d**] has become constant, the plot of log [**2d**] vs. time is nearly linear for X = H and X = *p*-Me.

(15) Constants $k_{2d\rightarrow 3b}$, $k_{2d\rightarrow 2c}$, and $k_{2d\rightarrow 3c}$ are known only roughly, since their calculation depends on the small amount of **3b** observed in the reaction products of **2d**.

(16) Lambert and co-workers seem to have found an analogous phenomenon in acetolysis of *meso*-1,4-diaryl-2,3-butyl ditosylates.[3] In the first and rate-determining stage of this acetolysis, one tosylate group plays the part of the leaving group, the other that of electron-withdrawing substituent. The occurrence of a destabilized benzenium ion is demonstrated for aromatic substituent *p*-OMe, *p*-Me, H, and *p*-Cl by a Hammett correlation. However, rearranged reaction products are observed only when this substituent is *p*-OMe.

modynamic datum. This is verified since for X = H, $K/2$ = 5.64 and $k_{3b\rightarrow 2d}/k_{2d\rightarrow 3b}$ = 6.27.

For all 1-bromo-3-chloro-2-arylpropanes **3b**, as well as for **2d**-OMe, we observe the formation of dichlorides **2c** and **3c** in equal amounts. We have attributed this to the intervention of an intermediate on which the nucleophilic addition is nonregioselective, the (3-chloropropylene)-benzenium ion **1b**. We shall examine below whether the ion **1b**-H is also an intermediate in the transformation of **2d**-H to dichlorides. Two aspects will be investigated: the rate constant and the composition of the mixture obtained.

$k_{2d\rightarrow 2c} + k_{2d\rightarrow 3c}$, the overall rate constant for transforming **2d**-H into dichlorides, is in agreement with the idea that only ions **1b**-H are involved in this process. The ratio $(k_{3b\rightarrow 2c} + k_{3b\rightarrow 3c})/(k_{2d\rightarrow 2c} + k_{2d\rightarrow 3c})$ is indeed equal to 6.06. Given a difference of standard free energy between **3b**-H and **2d**-H equal to $-Rt \ln (K/2)$, with $K/2$ = 5.64, the rate-limiting transition states that can be associated with transformations **3b**-H → **2c**-H + **3c**-H and **2d**-H → **2c**-H + **3c**-H have identical standard free energies. This is in agreement with there being a common intermediate able to undergo a nonregioselective nucleophilic addition. The first transition state of reaction **2d**-H → **2c**-H + **3c**-H thus has a free energy close to that of the ion **1b**-H and most certainly resembles it.

On the other hand, the composition of the dichloride mixture obtained from **2d**-H leads to $k_{2d\rightarrow 2c}/k_{2d\rightarrow 3c}$ = 28, whereas the involvement of **1b**-H corresponds to a value of this ratio close to unity. Thus, from **2d**-H, after a transition state close to the ion **1b**-H, this ion is not obtained. The nucleophilic addition occurs at an intermediate **4**, which will be very short-lived.

In Scheme VI, we propose a reaction mechanism accounting for the results observed for **3b**-H and **2d**-H. Four intimate ion pairs IP_1, IP_2, IP_3, and IP_4 are shown. IP_1 occurs in reaction **2d**-H → **3b**-H and **3b**-H → **2d**-H (first line of Scheme VI). It seems highly probable that it includes a bromide ion solvated by $SnCl_4$ with a (3-chloropropylene)benzenium ion (**1b**-H). The collapse of IP_1 undoubtedly leads, therefore, to equal amounts of **2d**-H and **3b**-H, but this cannot be proven experimentally. IP_2 is involved in the transformation of **3b**-H to **3c**-H and **2c**-H. It consists of the cation **1b**-H associated with a chloride ion solvated by $SnCl_3Br$; collapse gives dichlorides. IP_3, involved in the reaction of **2d**-H to **2c**-H, is made up of intermediate **4** and a chloride ion solvated by $SnCl_3Br$. The formation of IP_1 and IP_2 is certainly irreversible, since otherwise these ion pairs would be in rapid equilibrium, or even indiscernible, and the products resulting from reactions of **2d**-H and **3b**-H would be identical. IP_4, which ensures the slow equilibration of **2c**-H and **3c**-H, differs from IP_1 and IP_2 only by the anion, which is here a chloride ion solvated by $SnCl_4$.

Scheme VI shows that for compounds **3b**-H and **2d**-H, the processes of isomerization and of transformation to dichlorides are distinct. This separation can be demonstrated, for example, for **3b**-H. We have seen that reaction of **2d**-H to **3b**-H is important; thus **2d**-H gives IP_1. IP_2, on the other hand, leads to equal amounts of **2c**-H and **3c**-H. Since conversion of **2d**-H to **3c**-H is practically inexistent, IP_2 is not formed from IP_1. We therefore deviate here from the usual nucleophilic substitution patterns in which different varieties of ion pairs are formed successively.[17] For **3b**-H, a common mechanism for isomerization and replacement of bromine by chloride is thus excluded. The nucleophile is chosen before the first transition state.[18] These facts reveal a great instability of the ion **1b**-H, which could only exist in a complex with a halide ion that will be the nucleophile. The lifetime of such an entity can only be very short.

It is difficult to define why intermediate **4** of transformation **2d**-H → **2c**-H is different from **1b**-H. The involvement of **4** corresponds to an extremely rapid, nearly concerted process of nucleophilic substitution. The formation of **4** is irreversible and is found only during the replacement of bromine by chlorine (reactions **2d**-H → **3b**-H and **2c**-H ⇌ **3c**-H involve **1b**-H). Since, in our conditions, bromine is a better leaving group than chlorine,[19] one can reasonably assume that, in the **2d**-H → **2c**-H process, the first transition state is further from the **1b**-H ion than the second. One can then imagine that early addition of Cl^- leads primarily to **2c**-H. The involvement of **1b**-H in the transformation **3b**-H → **3c**-H + **2c**-H could not, on the other hand, be avoided because of a great resemblance between the first transition state and this ion.

Mechanism of the Reactions of Bromochloroarylpropanes 2d-Me and 3b-Me. For X = *p*-Me, the situation is intermediate between what is observed for X = H and what is observed for X = *p*-OMe. 1-Bromo-3-chloro-2-(4-methylphenyl)propane (**3b**-Me) is isomerized but less than **3b**-H, since $k_{3b\rightarrow 2d}$ represents only 14% of $(k_{exptl})_{3b}$. It gives dichlorides **2c**-Me and **3c**-Me at similar rates: $k_{3b\rightarrow 2c}/k_{3b\rightarrow 3c}$ = 1.18. These reactions involve the (3-chloropropylene)-4-methylbenzenium ion (**1b**-Me). From 2-bromo-1-chloro-3-(4-methylphenyl)propane (**2d**-Me) are formed **3b**-Me, **3c**-Me, and above all, **2c**-Me. The ratio $k_{2d\rightarrow 2c}/k_{2d\rightarrow 3c}$ is equal to 2.7 (as against 28 for X = H) and approaches unity corresponding to a nonregioselective nucleophilic addition to the intermediate. The reaction mechanism established for X = H, and shown in Scheme VI, accounts for these observations if we accept that IP_3 now leads to a certain amount of **3c**-Me. This variation of the mechanism with the electron-donating capacity of the substituent X leads to the coalescence of IP_1, IP_2, and IP_3 into a very dissociated ion pair for X = *p*-OMe.

Kinetic Parameters for Ionization of Bromochloroarylpropanes 2d and 3b. In Table III, we gave the rate constants k_{3b} and k_{2d} for the ionization of 1-bromo-3-chloro-2-arylpropanes **3b** and 2-bromo-1-chloro-3-arylpropanes **2d** (X = H, *p*-Me, *p*-OMe) by bromide ion loss. They were calculated by eq 5 and 6 on the assumption that the ring opening of the benzenium ions involved in the processes **3b** → **2c** + **3c** and **3b** ⇌ **2d** is of similar regioselectivity. The influence of the aromatic substituent

$$k_{3b} = k_{3b\rightarrow 2c} + k_{3b\rightarrow 3c} + k_{3b\rightarrow 2d} \times \frac{k_{3b\rightarrow 2c} + k_{3b\rightarrow 3c}}{k_{3b\rightarrow 2c}} \quad (5)$$

$$k_{2d} = k_{2d\rightarrow 2c} + k_{2d\rightarrow 3c} + k_{2d\rightarrow 3b} \times \frac{k_{3b\rightarrow 2c} + k_{3b\rightarrow 3c}}{k_{3b\rightarrow 3c}} \quad (6)$$

is considerable; the relative reactivity *p*-OMe/H is over 600. On the other hand, the ratio k_{3b}/k_{2d} is practically constant. Now, for all 1-bromo-3-chloro-2-arylpropanes

(17) Raber, D. J.; Harris, J. M.; Schleyer, P. v. R. In *Ions and Ion Pairs in Organic Reactions*; Szwarc, M., Ed.; Wiley: New York, 1974; Vol. 2, p 247. This review gives considerable attention to reactions with aromatic ring participation.

(18) Jencks has examined reactions involving a short-lived intermediate, or even one whose existence is uncertain, and has demonstrated that for these reactions a preassociation mechanism predominates: Jencks, W. P. *Chem. Soc. Rev.* **1981**, *10*, 345 and references therein.

(19) The ionization rate constant of **2d**-OMe is equal to 14 500 × 10^{-8} s^{-1}. That of **2c**-OMe can be estimated as 3660 × 10^{-8} s^{-1} ($2k_{23}$). The relative rate constant Br/Cl is thus close to 4.

3b, the ionization process involves the aromatic ring; this is shown by the stability of 1,3-dibromopropane in the same conditions. The invariance of the ratio k_{3b}/k_{2d} indicates that the ionization of **2d**-H and **2d**-Me, like **2d**-OMe, is assisted by the aromatic ring. Even for X = H, no other process such as the formation of a chloronium ion or a secondary carbocation contributes significantly.

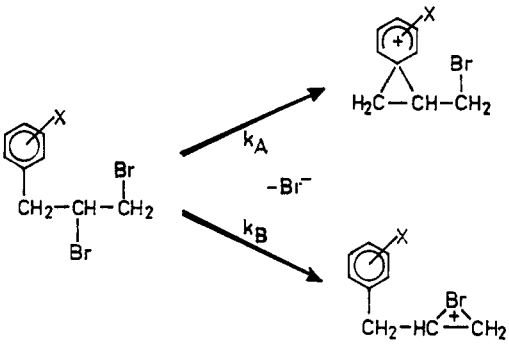
In Table III, we propose a factor F_{3b} defined by $F_{3b} = (k_{3b\rightarrow 2c} + k_{3b\rightarrow 3c})/k_{3b}$. F_{3b} indicates the fraction of ion pairs obtained from **3b** that lead to dichloro products. F_{3b} falls from 1 for X = *p*-OMe to 0.55 for X = H. The influence of the aromatic substituent is appreciable, whereas this is not usually the case for ion pair return in solvolysis reactions via a nondestabilized benzenium ion.[20] A factor F_{2d} also reported in Table III, $F_{2d} = (k_{2d\rightarrow 2c} + k_{2d\rightarrow 3c})/k_{2d}$, is related to the ionization of **2d**. Because of the small quantity of **3b** observed in the reaction products of **2d**, F_{2d} is relatively imprecise. We see, however, in Table III that F_{2d} is close to F_{3b}. Reactivity distribution between isomerization and transformation in dichlorides is identical in both systems **3b** and **2d**.

Summary of the Reactions of Bromochloroarylpropanes 2d and 3b. The results show that all 1-bromo-3-chloro-2-arylpropanes **3b** studied are transformed into dichlorides **2c** and **3c** via (3-chloropropylene)benzenium ions. Nucleophilic addition on these ambident ions is nonregioselective whatever the aromatic substituent. The behavior of **3b**-H and **3b**-Me differs from that of **3b**-OMe by the existence of an isomerization, caused by the fact that some of the benzenium ions formed recombine with the leaving group. At least for **3b**-H, the nucleophile which should react with a benzenium ion is specified during the appearance of this latter; the processes of isomerization and of the formation of dichloro compounds are thus discrete.

All the 2-bromo-1-chloro-3-arylpropanes **2d** studied ionize in $SnCl_4$ with assistance by the aromatic ring. When the aromatic substituent is *p*-OMe, a (3-chloropropylene)benzenium ion is formed and leads to the dichloro compounds **2c** and **3c** in equal amounts. With a less activating aromatic substituent, an isomerization involves the (3-chloropropylene)benzenium ion, leading this time to **3b**. In addition, dichloro products **2c** and **3c** are formed without the intermediacy of the same benzenium ions found in the **3b** reactions. As a result, the nonrearranged dichloride **2c** is the principal product in the absence of a strongly electron-donating substituent. Thus, during the S_N1 reaction of a very unreactive substrate, internal return and nucleophilic substitution can occur without a true common intermediate.

Standard Free Energy Difference between (3-Bromopropylene)benzenium Ions and 3-Arylpropylenebromonium Ions. We have shown that the ionization of the three 2-bromo-1-chloro-3-arylpropanes **2d** studied is aryl-assisted, although the intermediates obtained do not show the same regioselectivity to the addition of a nucleophile. We shall now be able to compare the stability of (3-bromopropylene)benzenium ions with that of 3-arylpropylenebromonium ions. To this end, 1,2-dibromo-3-arylpropanes **2a** were studied. From these compounds, two intermediates, benzenium and bromonium, are formed with rate constants k_A and k_B, respectively (Scheme VII), and thence give various bromo chlorides and

Scheme VII



dichlorides. It is generally accepted that, for an ionization process, the free energy of activation is a good estimate of the free energy difference between the ground state and the ion pair. It follows that the standard free energy difference between benzenium and bromonium ions arising from **2a** is well-represented by $-RT \ln (k_A/k_B)$. k_A can be equated with k_{2d}, the rate constant for the ionization of 2-bromo-1-chloro-3-arylpropane **2d**. We have established that under our conditions these compounds react with assistance by the aromatic ring only, and that the inductive effect of chlorine is close to that of bromine. k_B can be most precisely determined for 1,2-dibromo-3-phenylpropane. For this compound, k_A is taken equal to 22.1×10^{-8} s^{-1}. k_B is the difference between $(k_{exptl})_{2a}$ and $(k_{exptl})_{2d}$, i.e., 84.7×10^{-8} s^{-1}. It follows that the bromonium ion is 1.0 kcal mol^{-1} more stable than the benzenium ion. However, this greater stability of the bromonium ion does not appear when the aromatic ring is para substituted by a methyl or a methoxy group. Indeed, benzenium ions are seen to be more stable than the competing bromonium ions, 1.4 kcal mol^{-1} for X = *p*-Me and 3.9 kcal mol^{-1} for X = *p*-OMe. These values are obtained from the k_{2d} constants of Table III by assuming $k_B = 84.7 \times 10^{-8}$ s^{-1} for all 1,2-dibromo-3-arylpropanes. The existence of different ions depending on the aromatic ring substituent is not surprising in view of the various possibilities for assistance.

Conclusion

Through this study of the behavior of 2-bromo-1-chloro-3-arylpropanes **2d** and 1-bromo-3-chloro-2-arylpropanes **3b** in $SnCl_4$, we have shown that for a nucleophilic substitution reaction involving a benzenium ion destabilized by an electron-withdrawing halide group, the influence of a substituent situated on the aromatic ring is especially important. The polar effect on the reaction rates is very large. There are considerable mechanistic differences depending on whether the aryl group is *p*-$MeOC_6H_4$, *p*-MeC_6H_4, or C_6H_5. In the first case, for the two systems studied, there is a real common intermediate, which behaves as a free carbocation. Its lifetime is no doubt sufficient to enable the corresponding anion $SnCl_4Br^-$ to be transformed into $SnCl_5^-$. On the other hand, with the groups *p*-MeC_6H_4 and especially C_6H_5, intimate ion pairs are clearly involved. Somewhat disconcerting results associate the substrate isomerization with a poor yield in rearranged substitution product from 2-bromo-1-chloro-3-arylpropane. In order to interpret this, we have proposed the competitive formation of several intermediate ion pairs IP_1, IP_2, IP_3, and IP_4, very similar and very short-lived. Finally, with regard to the ionization of 1,2-dibromo-3-arylpropanes in the presence of a Lewis acid, depending on whether the aryl group is *p*-$MeOC_6H_4$ or C_6H_5, benzenium or bromonium intermediates will predominate. Several interesting competitive behaviors are

(20) From carbon-14 scrambling data, Coke and Jones determined a factor *F* for 2-arylethyl tosylate acetolysis via an ethylenebenzenium ion (see ref 7). *F* is the fraction of the ion pair that yields solvolysis product. These authors have obtained *F*-values that increase only very slightly with the electron-donating character of the aromatic substituent: 0.32, 0.32, 0.35, and 0.47 for *p*-Cl, H, *p*-Me, and *p*-OMe, respectively.

thus demonstrated in this always up-to-date field of nucleophilic substitution.[21]

Experimental Section

The preparation of the *p*-OMe-substituted derivatives and the techniques for identifying products and measuring rates have already been described.[6] The same procedures are used here.

Products. 1,2-Dichloro-3-arylpropanes 2c and 1,3-Dichloro-2-arylpropanes 3c. The mixture of **2c** and **3c** dichlorides obtained by the action of chlorine on $XC_6H_4CH_2CH{=}CH_2$ (K & K) contains 18% and 27% of **3c** for X = H and X = *p*-Me, respectively (50% for X = *p*-OMe).[6]

1-Bromo-3-chloro-2-arylpropanes 3b. Of the bromo chlorides obtained by the action of a mixture of bromine and chlorine on $XC_6H_4CH_2CH{=}CH_2$, **3b** represents 22% and 45% for X = H and X = *p*-Me, respectively (50% for X = *p*-OMe).[6]

2-Bromo-1-chloro-3-arylpropanes 2d. The procedure given for **2d**-OMe is used.[6] The amount of bromo chloride **2d** in the crude product is the same (86%) whatever the aromatic substituent.

1,2-Dibromo-3-phenylpropane (2a-H). To 3-phenylpropene (0.1 mol) in $CHCl_3$ (50 mL) is added bromine (0.1 mol) in the same solvent (25 mL). After the crude product is washed with a $NaHCO_3$ solution and dried on $MgSO_4$ and the solvent evaporated, the crude product, which contains 95% 1,2-dibromo-3-phenylpropane, is purified by GLC.

Kinetic Studies. For unreactive compounds, sealed tubes containing substrate (4 μL), $SnCl_4$ (200 μL), and a reference substance are suspended in a steam bath for the appropriate time. Because of the slow rate of reaction of **2d**-H, product formation for this compound was only followed up to 60% conversion. The equilibrium mixture of **3c**-H and **2c**-H in $SnCl_4$ was obtained from each dichloride by heating, first for 90 h at 161 °C, then for 80 days at 100 °C. The formation of **3b** in the reaction of **2d** with $SnCl_4$ was determined by GLC on a Varian 1400 chromatograph (0.125 in. × 10 ft column packed with 10% DEGS on Chromosorb).

Supplementary Material Available: Derivation of rate constants $k_{3b\rightarrow 2d}$, $k_{3b\rightarrow 3c}$, and $k_{2d\rightarrow 3b}$ and eq 4 (5 pages). Ordering information is given on any current masthead page.

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Functionalized 2-Azabicyclo[3.3.1]nonanes. 6.[1] Studies Directed to the Synthesis of Pentacyclic *Strychnos* Indole Alkaloids[2]

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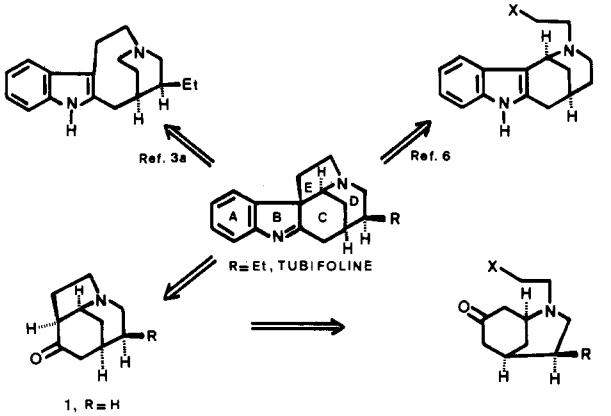
Received April 1, 1986

A new synthetic entry to the pentacyclic ring system of *Strychnos* indole alkaloids, based on the elaboration of the indolenine ring by Fischer indole synthesis in the last step, is investigated. The required tricyclic amino ketone **1** was prepared from N-(hydroxyethyl) ketone **2g** by closure of the five-membered ring by treatment with mesyl chloride and further base-catalyzed cyclization. In turn, morphan **2g** was obtained through a new method for the synthesis of 2-azabicyclo[3.3.1]nonan-7-ones, consisting in the oxidative cyclization of 4-piperidineacetoacetates **4**. Unfortunately, indolization of unsymmetrical ketone **1** afforded the unnatural regioisomer **11** instead of the *Strychnos*-type indolenine **12**.

Pentacyclic *Strychnos* indole alkaloids, exemplified by tubifoline, possess a characteristic 4-azatricyclo-[5.2.2.$0^{4,8}$]undecane ring system fused to the indole nucleus. These alkaloids have been synthesized by means of a common strategy based on the elaboration of a tetracyclic stemmadenine-type system followed by its transanular cyclization through an iminium salt.[3,4] In our search to new and general synthetic entries to pentacyclic *Strychnos* alkaloids,[5] we recently reported[6] an alternative route for the elaboration of the ring skeleton of these alkaloids consisting in the closure of the five-membered E ring by cyclization upon the indole 3-position from an appropriately N-substituted 1,2,3,4,5,6-hexahydro-1,5-methanoazocino[4,3-*b*]indole system.



With the same synthetic goal, we decided to explore another synthetic alternative to the *Strychnos* alkaloids based on the elaboration of the indolenine moiety in the

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