Table IV. ^{7}Li Quadrupole Scalar Coupling Constants for Enolates and Phenoxides in Ether Solvents (kHz)

	form[a]	THF	dioxolane	$MeOCH_2$-CH_2OMe	ref
I	T	65			this work
LiIBP[b]	T	136	133	178	8
LiOPh	T		69	66	6
lOPh (2,6-Me_2)	D		147	154	6
LiOPh (2,6-di-*t*-Bu)	M		212		6

[a] T = tetramer; D = dimer; M = monomer. [b] Lithium isobutyrophenone enolate.

resulted in comparable changes which were correlated with the change in electronic environment of the cation on conversion of tetramer to dimer and monomer. Two plausible explanations for the variation in lithium QSC between these two enolates are that the increased bulk of IBP increases the Li–solvent distance producing a more anisotropic electronic environment or that IBP is undergoing rapid internal rotation in the tetramer. Since the para C–H dipole and the Li–O quadrupole axis are not parallel, rapid internal rotation would lead to an apparently smaller τ_c and produce a larger QSC on substitution in eq 10.[24] Both effects may be operating.

Conclusion

The simplest lithium enolate **1** has been shown to exist as a solvated tetramer in THF solution–structure **2**. Remarkably, it is found that the enolate rotates more rapidly about its C–O axis than the aggregate reorients in solution. Lithium phenoxide behaves analogously, and the analogy is strengthened by the finding that the electronic environment around the lithium cation is the same in both compounds as reflected in their equivalent quadrupole scalar coupling constants. The structure of **1** in THF should thus be written

$$(CH_2{=}CHOLi)_4$$

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Comparison of Molecular Bromine and Tribromide Ion as Brominating Reagents. 2. Kinetic and Product Investigation of the Bromination of 3-Substituted Cyclohexenes

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The kinetics and products of bromination of several 3-substituted cyclohexenes with molecular Br_2 and with tetrabutylammonium tribromide have been investigated in 1,2-dichloroethane and chloroform. In both solvents the reactions of the unsubstituted, 3-alkyl-substituted, and 3-halogen-substituted olefins followed a third-order rate law (second order in Br_2). Changing the solvent from 1,2-dichloroethane to chloroform caused a 13- to 41-fold decrease in k_3. A *tert*-butyl group produced a 6- or 3-fold deceleration in k_3 in the two solvents, whereas a 3-bromo or 3-chloro substituent reduced the k_3 by five orders of magnitude. Tetrabutylammonium tribromide reacted with all investigated substrates following a second-order rate law in both solvents. Added bromide had no significant effect on the rates nor on the products. These reactions were 6- to 18-fold faster in chloroform than in 1,2-dichloroethane. A *tert*-butyl group caused a 35- to 36-fold decrease, a 3-bromo and a 3-chloro substituent an about three orders of magnitude decrease, and a benzoyloxy or para-substituted benzoyloxy group an about two orders of magnitude decrease in k_2. The products of the molecular Br_2 reactions consisted of mixtures of diaxial and diequatorial dibromo adducts in ratios depending on the substituent. 3-Benzoyloxy-substituted substrates gave, in addition, cis 1,2- and cis 1,3-dibromides. Only diaxial and diequatorial dibromo adducts, with a large prevalence (70–90%) of the former, were always obtained in all tribromide reactions. The kinetic and product results are consistent with an addition mechanism of molecular Br_2 involving a rate-determining ionization of olefin–Br_2 charge-transfer complexes (CTC's) to bromonium–tribromide ion pairs, followed by fast collapse to dibromo adducts. For the tribromide reactions they suggest instead a rate- and product-determining nucleophilic attack by bromide on olefin–Br_2 CTC's in equilibrium with the olefin and tribromide ions.

The use of organic tribromide salts in low polarity aprotic solvents as brominating reagents for conjugated carbon–carbon double bonds always gives more stereoselective anti 1,2-addition relative to molecular bromine.[1] This difference has been attributed to a change in the addition mechanism, and kinetic evidence for this has been produced in a recent investigation of the bromination of cyclohexene.[2] Of course, no difference in product could be observed with this substrate, *trans*-1,2-dibromocyclohexane being the only product.

Previous investigations had, however, shown[3] that in the case of allylically substituted cyclohexenes both diaxial and diequatorial adducts are obtained and that the product

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Table I. Third-Order and Second-Order Rate Constants for the Bromination of 3-Substituted Cyclohexenes at 25 °C with Molecular Br_2 and with TBAT[a]

R	$k_{3\,Br_2}$, M^{-2} s^{-1}		$k_{2\,Br_3^-}$, M^{-1} s^{-1}	
	$(CH_2Cl)_2$	$CHCl_3$	$(CH_2Cl)_2$	$CHCl_3$
H (**1a**)	2.40×10^5 (0.11)	5.80×10^3 (0.25)	7.20×10^{-1} (0.02)	13.41 (0.25)
Me (**1b**)	3.00×10^5 (0.15)	1.15×10^4 (0.06)	4.40×10^{-1} (0.08)	7.72 (0.11)
t-Bu (**1c**)	3.72×10^4 (0.12)	1.80×10^3 (0.07)	2.10×10^{-2} (0.05)	3.85×10^{-1} (0.07)
Br (**1d**)	1.64 (0.07)	1.20×10^{-1} (0.08)	9.75×10^{-4} (0.03)	7.35×10^{-3} (0.025)
Cl (**1e**)	8.80×10^{-1} (0.35)	6.60×10^{-2} (0.35)	1.30×10^{-3} (0.03)	1.20×10^{-2} (0.02)
C_6H_5COO (**1f**)			4.21×10^{-3} (0.05)	2.68×10^{-2} (0.02)
p-$CH_3C_6H_4COO$ (**1g**)			4.45×10^{-3} (0.03)	
p-$CH_3OC_6H_4COO$ (**1h**)			5.71×10^{-3} (0.04)	
p-$NO_2C_6H_4COO$ (**1i**)			4.05×10^{-3} (0.02)	

[a] Rate constants are the average of at least four independent measurements. Errors are given as standard deviations obtained from the deviations of individual measurements from the average value.

ratios change considerably when the free halogens or charge-transfer complexes (CTC's) of halogens are employed. On the other hand, most of the amine–Br_2 CTC's that could be used have rather low formation constants[4] and give mechanistically very complicated reactions[5] which can involve both the free and the complexed halogen depending on the reaction conditions. Furthermore, tribromide salts arising from amine incorporation in the bromination products are also formed, and the Br_3^- ion is responsible for part of the bromine addition reaction.[1d,5,6] The use of preformed organic tribromide salts seemed, therefore, to be a more simple and promising way also to perform stereoselective anti-diaxial addition of bromine to cyclohexene derivatives.

In the present paper we are reporting the results of a comparative study of the bromination of several allylically substituted cyclohexenes with molecular bromine and with tetrabutylammonium tribromide (TBAT). In order to put the observed product differences on a rational mechanistic base, we have first carried out an investigation of the substituent and solvent effects on the bromination kinetics with both these reagents.

Results

Kinetics. The rate constants for the bromination of cyclohexene derivatives bearing substituents in the allylic position with molecular Br_2 and with TBAT are reported in Table I.

All brominations were examined in two aprotic solvents of different dielectric constant, 1,2-dichloroethane (ϵ 10.7) and chloroform (ϵ 4.6),[7] at 25 °C in the presence of a large excess of olefins. A relevant solvent effect on the rates was observed. However, in general, cyclohexene and its 3-alkyl derivatives reacted very fast with molecular Br_2 in both solvents. The reactions of these substrates with TBAT were slower but still too fast to be followed with conventional spectrophotometric techniques. All reaction rates of compounds **1a–c** were therefore measured with a stopped-flow apparatus. All reactions of 3-halogen-substituted derivatives **1d** and **1e** were instead sufficiently slow to be monitored with a conventional UV–vis spectrophotometer.

Hydroxy or alkoxy derivatives were not included in the present investigation because of their peculiar behavior in the bromination reaction, which is thought to involve extensively CTC's of bromine with the oxygen substituent.[8] This effect is not important with benzoyloxy-substituted cyclohexenes. These compounds (**1f–i**) reacted fast with molecular Br_2 but slowly with TBAT, so that the stopped-flow and the conventional technique had to be used, respectively.

The reactions of molecular Br_2 with substrates **1b–e** obeyed cleanly the simple third-order rate law of eq 1, as already found for the parent olefin **1a**.[2] Only in chloroform the kinetics of the least reactive substrates **1d** and **1e** showed, usually after about 1 h of reaction, an increase in rate inconsistent with rate eq 1 or with a modified equation containing an additional term first order in Br_2 of the type found in protic solvents.[9] These deviations were attributable to the incursion of free radical processes, as shown by the fact that kinetic runs carried out in the presence of *n*-pentyl nitrite as free radical inhibitor obeyed cleanly eq 1 for at least two half-lives. The rate constants so obtained were well reproducible and coincident with those measured in runs performed in the absence of the inhibitor, before the start of the free radical reaction.

$$-\frac{d[Br_2]}{dt} = k_3[Br_2]^2[ol] \quad (1)$$

The reaction of the benzoyloxy derivatives **1f–i** with Br_2 exhibited peculiar kinetic curves showing a fast initial increase in absorbance up to a maximum, followed by a slower decay. This has been attributed[10] to the accumulation of Br_3^- anions formed as counterions of relatively stable 2-aryl-1,3-dioxolan-2-ylium cations arising from nucleophilic participation by the carbonyl oxygen in the opening of trans bromonium ion intermediates. Third-order rate constants could not be obtained for these substrates. These aspects will be discussed in detail in a forthcoming publication.

In contrast, the reactions of TBAT with all examined substrates, including the benzoyloxy derivatives **1f–i**, followed very cleanly the second-order rate law of eq 2 in both solvents up to over 90% conversion.

$$-\frac{d[Br_3]}{dt} = k_2[Br_3^-][ol] \quad (2)$$

An investigation of the effect of added bromide ions in the latter reaction was carried out with an alkyl-substituted substrate, 3-*tert*-butylcyclohexene, and a halogen-substi-

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Table II. Second-Order Rate Constants and Product Ratios for the Bromination of 3-*tert*-Butylcyclohexene and 3-Bromocyclohexene at 25 °C in the Presence of TBAB[a]

10^2[1c], M	10[1d], M	10^4[Br_2], M	10^4[TBAB], M	solvent	k_2, M^{-1} s^{-1}	products[b] 4:5
3.62		2.22	3.02	$(CH_2Cl)_2$	2.10 (0.03)	70:30
3.64		2.22	9.70	$(CH_2Cl)_2$	1.91 (0.03)	70:30
3.20		2.22	51.60	$(CH_2Cl)_2$	1.84 (0.02)	71:29
3.62		2.22	110.0	$(CH_2Cl)_2$	1.59 (0.02)	69:31
	1.09	93.0	200.0	$CHCl_3$	7.35 (0.06)	72:28
	1.23	41.0	410.0	$CHCl_3$	8.35 (0.06)	71:29
	1.23	41.0	2080.0	$CHCl_3$	8.55 (0.07)	73:27
	1.23	41.0	4070.0	$CHCl_3$	9.60 (0.11)	75:25

[a] Errors on rate constants are given as standard deviations estimated from the deviations of experimental points from the best-fit pseudo-first-order straight lines. [b] Products ratios have been determined by NMR for the bromination of 1c and by GLC for the bromination of 1d.

tuted one, 3-bromocyclohexene, in 1,2-dichloroethane and chloroform, respectively. A similar study had already been reported for the parent olefin **1a**,[2] but the use of its 3-substituted derivatives has the advantage that the effect of added bromide can be checked on both the rates and the product distributions. The Br_3^- ion was generated in situ from Br_2 and tetrabutylammonium bromide (TBAB). Rate eq 2 was again very cleanly obeyed in all runs. The second-order rate constants are reported in Table II, which also includes the ratios of diaxial to diequatorial dibromo adducts.

Added bromide had opposite effects on the rates of bromination of **1c** and **1d**, causing a decrease in k_2 in the former case but an increase in the latter. However, for both substrates the magnitude of the effect was extremely modest, a 50-fold excess of TBAB producing only a 25% decrease in k_2 for 3-*tert*-butylcyclohexene and a 100-fold excess only a 30% increase for 3-bromocyclohexene. Furthermore, no significant effect was found for either substrates on the products ratios.

The inspection of Table I shows that a change in solvent from 1,2-dichloroethane to the less polar chloroform always caused a decrease in k_3 for the free Br_2 reaction. This effect is highest for the most reactive substrate (41-fold decrease in the case of **1a**) and smallest for the least reactive ones (13- to 14-fold decrease for **1d** and **1e**). On the contrary, the same change in solvent produced an increase in k_2 for all the TBAT reactions. Even if this opposite solvent effect is again slightly higher for the most reactive unsubstituted or 3-alkyl-substituted substrates **1a–c** (about 18-fold increase on passing from 1,2-dichloroethane to chloroform) than for the least reactive 3-halogen and 3-benzoyloxy derivatives **1d–f** (6- to 9-fold increase), it appears to be quite general and therefore speaks in favor of different addition mechanisms for molecular Br_2 and Br_3^-.

Concerning the substituent effect, it can be observed that an allylic methyl had no influence on the k_3 for the Br_2 reaction in 1,2-dichloroethane but doubled the rate constant for this reaction in chloroform. On the other hand, a *tert*-butyl group always retarded the Br_2 reaction, causing an about 6-fold decrease in k_3 in 1,2-dichloroethane and an about 3-fold decrease in chloroform. On the contrary, a methyl group produced identical 1.7-fold decelerations in the k_2 for the Br_3^- reaction in 1,2-dichloroethane and in chloroform, while a *tert*-butyl group was responsible for a much larger 35- to 36-fold decrease in k_2 in both these solvents. The comparison of all these data indicates that, although both reactions are subjected to steric effects by the 3-substituent, these effects play a more important role in the Br_3^- than in the Br_2 reaction.

A bromine and a chlorine substituent caused dramatic decelerations in the Br_2 reactions, the $k_{3\,Br_2}$ of compounds **1d** and **1e** being reduced by about five orders of magnitude relative to the parent olefin **1a** in both solvents. The same halogen substituents produced instead a decrease of only about three orders of magnitude in the k_2 for the Br_3^- reactions. A benzoyloxy group decreased similarly the $k_{2\,Br_3^-}$ by about two orders of magnitude. Furthermore, this effect was practically independent of the presence and nature of para substituents on the benzoyloxy group.

The whole comparative kinetic data show that the Br_3^- reaction is much less affected than the Br_2 one by the inductive effects of electron-withdrawing 3-substituents.

Table III. Product Ratios for Brominations Performed with Molecular Br_2 and with TBAT[a]

R	brominating reagent	products 4:5 $(CH_2Cl)_2$	products 4:5 $CHCl_3$
Me (**1b**)	Br_2	76:24	77:23
	TBAT	86:14	90:10
t-Bu (**1c**)	Br_2	45:55	44:56
	TBAT	70:30	67:33
Br (**1d**)	Br_2	27:73	26:74
	TBAT	73:27	71:29
Cl (**1e**)	Br_2	47:53	48:52
	TBAT	77:23	83:17
C_6H_5COO (**1f**)	TBAT	78:22	83:17
p-$CH_3C_6H_4COO$ (**1g**)	TBAT	81:19	81:19
p-$CH_3OC_6H_4COO$ (**1h**)	TBAT	75:25	82:18
p-$NO_2C_6H_4COO$ (**1i**)	TBAT	74:26	68:32

[a] Product ratios have been determined by GLC for **1b**, **1d**, and **1e**, by NMR for **1c** and by HPLC for **1f–i**. The quoted values are averages of at least three experiments and were reproducible within ±1%.

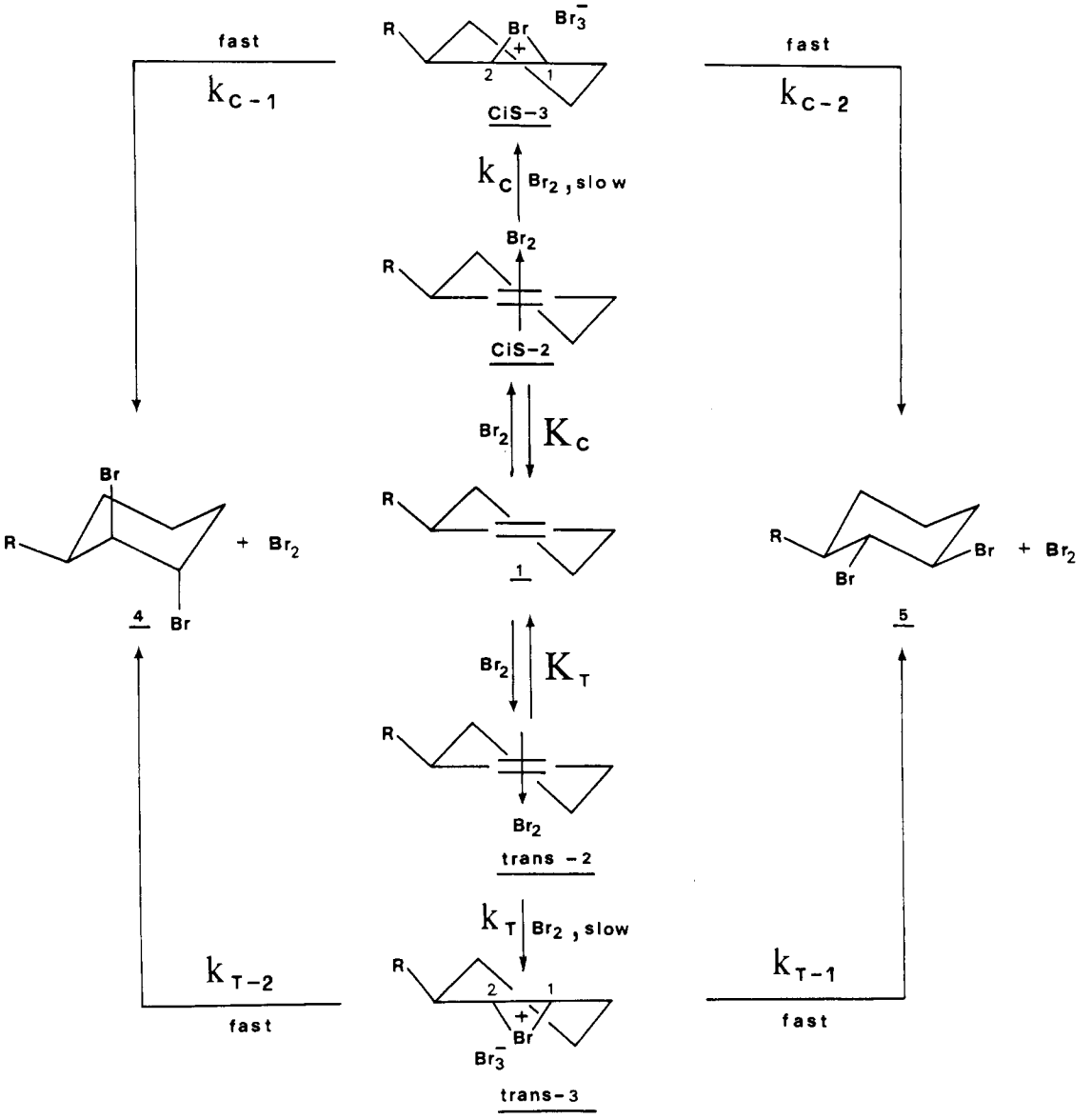
Products. The ratios of diaxial to diequatorial dibromides **4** and **5** obtained in the bromination of 3-substituted cyclohexene derivatives with molecular Br_2 and with TBAT in 1,2-dichloroethane and in chloroform are reported in Table III.

The products arising from olefins **1b–d** had been described previously.[3a,c,11] Those formed from **1e–i** have been separated from preparative reactions and identified by their ^1H NMR spectra (see Experimental Section). The reactions of benzoyloxy derivatives **1f–i** with molecular Br_2, which exhibited an unusual kinetic behavior (see above), also gave complex product mixtures containing up to about 40–50% of cis 1,2- and cis 1,3-dibromo adducts, besides the normal diaxial and diequatorial addition products **4** and **5**.[10] These cis dibromides and their distributions under several conditions will be described in detail elsewhere.

It can be observed that the results reported in Table III for the Br_2 addition to substrates **1b–e** cover a wide range of diaxial to diequatorial dibromide ratios. These ratios appear to be substantially affected by steric and electronic

(11) (a) Barili, P. L.; Bellucci, G.; Berti, G.; Marioni, F.; Marsili, A.; Morelli, I. *J. Chem. Soc. Perkin Trans. 2* **1972**, 58. (b) Barili, P. L.; Bellucci, G.; Ingrosso, G.; Marioni, F.; Morelli, I. *Tetrahedron* **1972**, *28*, 4583.

Scheme I



effects of substituents, changing from a large excess of diaxial dibromide with a 3-methyl to a large excess of diequatorial with a 3-bromine substituent.

In contrast with molecular Br_2, TBAT, which showed clean second-order kinetics in its reactions with all substrates **1a–i**, gave clean product distributions consisting only of diaxial and diequatorial trans dibromides also with the benzoyloxy derivatives **1f–i**. In all cases the products ratios obtained with the two brominating reagents were different. In particular, with **1d** these ratios were exactly inverted. Furthermore, in the TBAT additions the 3-substituents always led to preferential formation of the diaxial dibromide (~70–90%) with all examined substrates.

Finally, the data of Table III show that solvents which display a relevant and opposite effect on the kinetics of the Br_2 and of the TBAT reactions were instead devoid of any significant effect on the product ratios of both these reactions.

Discussion

The results of the present investigation definitely confirm that in aprotic solvents of moderate to low polarity molecular Br_2 and quarternary ammonium tribromides react with olefins by different mechanisms.

The second-order dependence on Br_2 of the reaction rates of the molecular halogen and the deceleration produced by a decrease in solvent polarity for all investigable 3-substituted cyclohexene derivatives lend general validity to the mechanistic rationalization given for the reaction of parent compound **1a**.[2] For the presently examined substrates this mechanism is sketched in Scheme I, where a Br_2 assisted ionization of olefin–Br_2 CTC's **2**, formed on the two faces of the double bond, to give cis and trans bromonium–tribromide ion pair intermediates **3** is considered to be the rate-limiting step.[12] A fast collapse of the latter ion pairs to dibromo adducts **4** and **5** and molecular Br_2 completes the addition.

Linear free energy relationships have been extensively used to prove the ionic nature of the bromination mechanism.[9,13] In the present case, this treatment is prevented

(12) As a matter of fact, evidence has been produced (see ref 15) for the involvement of Br_2–alkene complexes of stoichiometry higher than 1:1 (probably 2:1) in the ionization step of the overall third-order bromination of cyclohexene. Even if CTC's of the latter type are likely involved also in the reaction of Br_2 with substituted cyclohexenes, for simplicity they are not shown in Scheme I, it being understood that they lie along the reaction coordinate between the 1:1 CTC's and the bromonium–tribromide ion pairs.

(13) Ruasse, M. F.; Dubois, J. E. *J. Am. Chem. Soc.* **1984**, *106*, 3230 and references cited therein.

by the impossibility of obtaining values of k_3 for substrates bearing oxygen-containing substituents, as well as by the observed importance of steric effects by 3-alkyl groups. Furthermore, substituent effects on the formation constants of the involved CTC's may possibly interfere with this approach.[14] We want, however, to stress that at least a large part of the five orders of magnitude decrease in the rate of molecular Br_2 addition by a 3-halogen substituent is attributable to the kinetic substituent effect on the ionization of the CTC's to bromonium ions expected for a mechanism of type shown in Scheme I.

The rate law expected for this mechanism[15] is given by eq 3, where K_C and K_T are the formation constants of the cis and trans CTC and k_C and k_T the rate constants for their Br_2-assisted ionizations. At alkene concentrations

$$-\frac{d[Br_2]}{dt} = \left(\frac{K_C k_C}{1 + K_C[ol]} + \frac{K_T k_T}{1 + K_T[ol]}\right)[Br_2]^2[ol] \quad (3)$$

such that $K_C[ol]$ and $K_T[ol] \ll 1$, eq 3 is reduced to eq 4, which is related to the observed rate law 1 by eq 5.

$$-\frac{d[Br_2]}{dt} = (K_C k_C + K_T k_T)[Br_2]^2[ol] \quad (4)$$

$$k_3 = K_C k_C + K_T k_T \quad (5)$$

On the other hand, the results of the investigation of the effect of added bromide in the TBAT reactions allow one to rule out the hypothesis that the brominations performed with the latter reagent are actually carried out by the free Br_2 released by equilibrium 6. In fact, although in protic

$$Br_2 + Br^- \rightleftharpoons Br_3^- \quad (6)$$

solvents at sufficiently low Br_2 concentration the brominations are first order in halogen,[9] no contribution by such a first-order process was detected in brominations performed with molecular Br_2 in the solvents used in this work even at the lowest attainable halogen concentrations. Furthermore, under the above hypothesis the observed rate constants should actually be given by eq 7, where $k_{2\,Br_2}$ is the true rate constant for the bromination process first order in Br_2 and $K_{Br_3^-}$ is the formation constant of the Br_3^- ion. Since the latter has very high values in the used

$$k_{2\,obsd} = \frac{k_{2\,Br_2}}{1 + K_{Br_3^-}[Br^-]} \quad (7)$$

solvents ($K_{Br_3^-} \geq 2 \times 10^7\ M^{-1}$ in 1,2-dichloroethane,[5] $K_{Br_3^-} = 1.2 \times 10^5\ M^{-1}$ in chloroform[16]), $K_{Br_3^-}[Br^-] \gg 1$ and an inverse linear dependence of $k_{2\,obsd}$ on the bromide concentration would be expected, in contrast with the negligibly small rate deceleration observed in the case of 3-*tert*-butylcyclohexene and with the negligibly small acceleration found for 3-bromocyclohexene. These two different effects are likely to be attributed to minor changes in the properties of the reaction media.

The occurrence of free Br_2 additions in the brominations carried out with TBAT is also ruled out by the product distributions reported in Table II. For both substrates **1c** and **1d** these distributions are not only different from those obtained with molecular Br_2 (Table III) but also constant with increasing bromide concentration. This shows that a single bromination process, different from the free Br_2 addition, is always operating in these reactions also in the absence of an excess of TBAB. These conclusions are in agreement with those inferred for the reaction of the parent olefin **1a**[2] and can therefore be assumed as generally valid.

The rate increase generally observed for all TBAT brominations on changing the solvent from 1,2-dichloroethane to chloroform can instead be attributed to a specific solvation effect by chloroform. As shown for the same reaction of the unsubstituted compound **1a**,[2] this effect consists of hydrogen bonding to a leaving bromide ion. This is consistent with a mechanism involving in the TS of the slow step the breaking of the Br–Br bond of an olefin–Br_2 CTC without the intervention of a second Br_2 molecule, to give a Br^- ion.

This step cannot, however, lead to bromonium–bromide-type intermediates. Such a process would coincide with a simple bromination first order in halogen, which has been ruled out on the basis of the above discussed arguments. It is furthermore disproved by the higher incidence of steric effects and by the much lower importance of inductive effects of 3-substituents in the TBAT as compared to the overall third-order Br_2 reactions. In fact, on the one hand a bromination process having as the slow step the unimolecular ionization of 1:1 olefin–Br_2 CTC's would be expected to suffer substituent steric effects less than the corresponding reaction second order in Br_2, where 1:2 olefin–Br_2 aggregates seems to be involved.[12] On the other hand, a quantitatively similar dependence on substituent electronic effects would be expected for two processes leading to ion couple intermediates consisting of identical cationic moieties (bromonium ions).

All above observations suggest for the TBAT reactions a slow step of the type indicated in the Scheme II. According to this mechanism, in the case of substituted cyclohexenes the first reaction step should consist in the equilibrium between Br_3^- and the two 1:1 olefin–Br_2 CTC's *cis*-**2** and *trans*-**2**. The respective equilibrium constants are given by the ratios of the formation constants of the cis and trans CTC from olefin and Br_2 (K_C and K_T in Scheme I) to the stability constant of Br_3^- ($K_{Br_3^-}$). This is followed by rate- and product-determining nucleophilic attack on the two CTC's by the Br^- of the ammonium bromide ion pair formed in the equilibrium step or present as added salt, while a Br–Br bond is broken and a new Br^- is formed.

The rate law expected for this mechanism in the case of substituted cyclohexenes should have the form of eq 8, where K_C, K_T, and $K_{Br_3^-}$ are the above defined formation constants and $k_{C\text{-}1}'$, $k_{C\text{-}2}'$, $k_{T\text{-}1}'$, and $k_{T\text{-}2}'$ are the rate constants for nucleophilic attack by Br^- at C(1) and C(2) of the cis and trans CTC. Equation 8 is related to the experimentally observed eq 2 by eq 9. Since added bromide

$$-\frac{d[Br_3^-]}{dt} = (k_{C\text{-}1}' + k_{C\text{-}2}')[\text{cis CTC}][Br^-] + (k_{T\text{-}1}' + k_{T\text{-}2}')[\text{trans CTC}][Br^-] = \frac{1}{K_{Br_3^-}}\{(k_{C\text{-}1}' + k_{C\text{-}2}')K_C + (k_{T\text{-}1}' + k_{T\text{-}2}')K_T\}[ol][Br_3^-] \quad (8)$$

$$k_2 = \frac{1}{K_{Br_3^-}}\{(k_{C\text{-}1}' + k_{C\text{-}2}')K_C + (k_{T\text{-}1}' + k_{T\text{-}2}')K_T\} \quad (9)$$

proportionally reduces the amount of CTC's at equilibrium, no significant net effect is to be expected, apart from the small ones arising from modifications in the reaction medium.

(14) Although it has been argued that the latter effects are negligible relative to the substituent effects on the rate of the ionization step (see ref 13, footnote 19), no direct experimental evidence is yet available to support this assumption.

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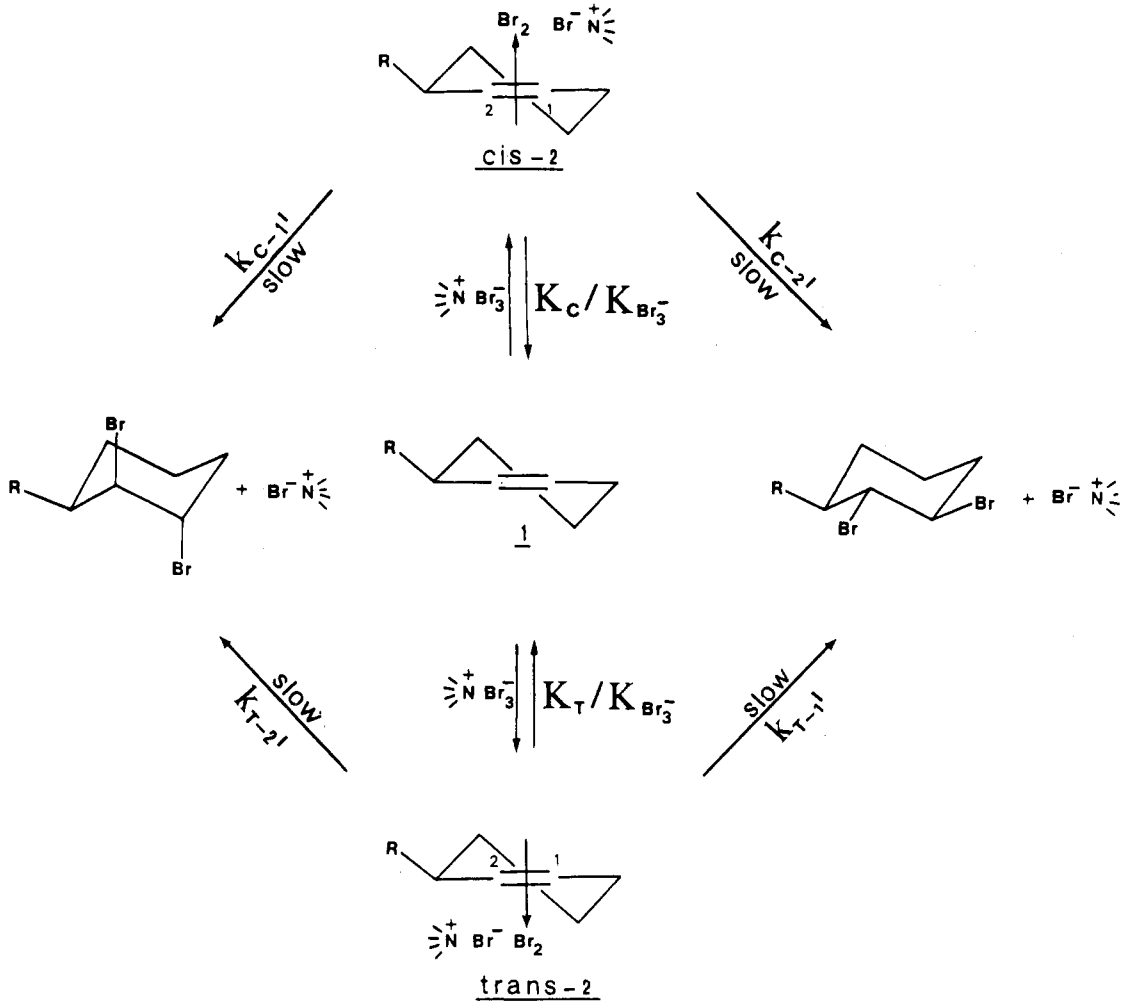
Scheme II



At variance with the reaction of molecular Br_2, the proposed slow step of the TBAT reaction should be a concerted process not involving a development of positive charge on carbons, and this explains the much lower retarding effect of electron-withdrawing substituents on the rates of the latter relative to the former reaction. It can also be observed that, as shown by eq 9, the actual effect on the rate constants of the slow step, $k_{C\text{-}1}'$, $k_{C\text{-}2}'$, $k_{T\text{-}1}'$, and $k_{T\text{-}2}'$, may well be smaller than that appearing from the measured composite rate constants k_2, if electron-withdrawing or bulky substituents reduce the values of K_C and K_T, too.

We can now come to our initial goal, that is, to rationalize the differences in products obtained from the various substrates with molecular Br_2 and with TBAT.

As far as the free Br_2 additions are concerned, it can be stressed that the formation of substantial amounts of cis 1,2- and cis 1,3-dibromo adducts from the benzoyloxy derivatives **1f–i** is consistent with the intervention of bromonium ions as the intermediates of these reactions. In fact, as will be discussed in more detail elsewhere, these cis dibromides arise from the collapse of the 2-aryl-1,3-dioxolan-2-ylium tribromide intermediates, whose formation by intramolecular attack of the carbonyl oxygen on first formed trans bromonium–tribromide ion pairs was detected by the above-mentioned spectrokinetic measurements.[10]

With reference to Scheme I, the distribution between the two bromonium–tribromide ion pair intermediates is determined by the ratio K_Ck_C/K_Tk_T. While inductive effects of substituents are expected to affect similarly K_C and K_T as well as k_C and k_T, steric effects should reduce the product K_Ck_C more than K_Tk_T, favoring the formation of the trans intermediate. A prominent steric effect of this type is expected by a pseudoequatorial *tert*-butyl group or by substituents situated in a pseudoaxial position like bromine in 3-bromocyclohexene.[17]

It has been previously shown[3,18–20] that the stereochemistry and regiochemistry of nucleophilic attack on cyclohexene bromonium ions are determined by the same conformational, steric, and electronic factors conditioning the opening of the corresponding protonated epoxycyclohexanes. Thus, the conformational preference for an antiparallel nucleophilic attack (chairlike TS)[21] at C(1) of the cis bromonium ion, reinforced by the unfavorable inductive effect of electron-withdrawing 3-substituents on attack at C(2),[3c,19,20] should make $k_{C\text{-}1} \gg k_{C\text{-}2}$. On the other hand, both the inductive[3c,19,20] and the steric effects[18] of 3-substituents should decrease the rate of antiparallel attack[21] at C(2) on the trans bromonium ion, $k_{T\text{-}2}$, making $k_{T\text{-}1}$ competitive or even prevailing. It can be observed that the last process requires a conformationally unfavorable

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parallel attack (boatlike TS) at C(1) in the case of the 3-*tert*-butyl derivative but likely involves a more easy antiparallel attack on conformers with a pseudoaxial substituent (for simplicity not shown in Scheme I) for the other conformationally mobile substrates.

If the rates of collapse of the bromonium–tribromide intermediates *cis*-**3** and *trans*-**3** to products **4** and **5** are higher than those of reversion to CTC's **2** and olefins **1**, the largest amounts of diequatorial dibromides should be formed, as actually found, from the addition of molecular Br_2 to substrates bearing electron-withdrawing and bulky substituents, 3-bromo- and 3-*tert*-butylcyclohexene, where the $K_T - k_T - k_{T\text{-}1}$ pathway is most favored. 3-Chlorocyclohexene, where the inductive effect is large but the steric effect is smaller, is expected and actually found to give an intermediate product distribution, arising from pathways $K_T - k_T - k_{T\text{-}1}$ and $K_C - k_C - k_{C\text{-}1}$. 3-Methylcyclohexene, where only a modest steric effect can affect all steps of the addition, gives instead the largest amount of diaxial dibromide, formed by both pathways $K_T - k_T - k_{T\text{-}2}$ and $K_C - k_C - k_{C\text{-}1}$.[22]

On the other hand, the lack of formation of cis 1,2- and cis 1,3-dibromo adducts from the reactions of compounds **1f–i** with TBAT is conclusive evidence against the involvement of ionic intermediates of bromonium-type and in favor of the exclusive intervention of CTC's in the Br_3^- additions. Following the mechanistic picture of Scheme II and the derived eq 8, the final dibromide distribution in these reactions should be determined only by the relative values of products $K_C k_{C\text{-}1}'$, $K_C k_{C\text{-}2}'$, $K_T k_{T\text{-}1}'$, and $K_T k_{T\text{-}2}'$. The rate constants appearing in these products are likely affected by the same conformational and steric effects operating in the molecular Br_2 reactions, while electronic effects should be less important, owing to the lower charge localization in the TS for the nucleophilic attack of the TBAT reactions. The rate constant $k_{T\text{-}2}'$ is expected to be reduced relative to $k_{C\text{-}1}'$ mainly by the steric effect of the substituent, while both $k_{T\text{-}1}'$ and $k_{C\text{-}2}'$ are reduced by unfavorable conformational effects. If these effects outweight the unfavorable steric effect on K_C, then $K_C k_{C\text{-}1}' > K_C k_{C\text{-}2}'$, $K_T k_{T\text{-}1}'$, and $K_T k_{T\text{-}2}'$, and most of the reaction can proceed through the $K_C - k_{C\text{-}1}'$ pathway to give the diaxial dibromide as the main product, as actually found in all TBAT reactions.

The remarkably lower reaction rate of the 3-*tert*-butyl derivative **1c** with TBAT relative to that of the parent compound is thus due to an unfavorable steric influence both on $k_{T\text{-}2}'$ and, to a lesser degree, on K_C. In our opinion the much higher rate reduction observed in the TBAT reactions of 3-halogen-substituted compounds should instead be mainly due to an unfavorable inductive effect of the electron-withdrawing substituent on both K_C and K_T. This point requires further investigation.

In conclusion, TBAT has been proved to be a very suitable reagent for stereoselective anti diaxial additions of Br_2 to cyclohexene derivatives. Futhermore, the obtained product distributions, along with the observed kinetic and product differences with respect to the reactions of molecular Br_2, have provided further convincing evidence for a Br_3^- addition mechanism involving rate- and product-determining attack by Br^- on olefin–Br_2 CTC's formed in a preequilibrium step.

(22) It could appear that the differences in overall free energies of activation for the formation of the two dibromo adducts **4** and **5** from olefins **1** and Br_2 do not change enough (1.3 kcal mol^{-1} on passing from **1b** to **1d**) to allow a trustworthy dissection of the steric, electronic, and conformational effects whose balance is responsible for the steric course of these additions. In our opinion, however, the fact that the observed product distributions can be consistently anticipated, in a qualitative way, throughout the entire series **1b–e** by a consideration of the effects by the different substituents first on the electrophilic and then on the nucleophilic step of the reactions provides confidence in the above discussed analysis. Work is in progress using interhalogens in place of Br_2 in order to obtain a more direct information on this.

Experimental Section

Materials and Methods. Melting points were determined on a Kofler apparatus and are uncorrected. IR spectra were registered on a Pye-Unicam SP3-300 spectrophotometer. UV spectra were recorded on a Pye-Unicam SP8-400 UV–vis spectrophotometer. ^1H NMR spectra were taken on a EM 360A or a CFT 20 Varian instrument from $CDCl_3$ solutions unless otherwise stated, using Me_4Si as internal standard.

Fast kinetic measurements were performed on a Durrum D-110 stopped-flow apparatus having a mixing time of 3 ms, equipped with a 2-cm observation cell. The instrument was coupled to a Tektronix 5103 storage oscilloscope and to a data acquisition system built around a 12-bit A/D converter, interfaced to a Commodore 4032 personal computer. Slow kinetics were followed in 1-cm cells on the UV–vis spectrophotometer equipped with a thermostated cell holder.

GLC analyses were carried out on a Dani 2000 instrument, equipped with a 1.8-m glass column, 3 mm i.d., packed with 3% neopentyl glycol succinate (NPGS) on sylanized Chromosorb W 80–100 mesh and a flame-ionization detector. HPLC analyses were performed on a Pye-Unicam 4000 chromatograph using a Lichrosorb Si 60-10 column (25 cm, Chrompack) and monitoring at 254 nm.

Preparative chromatographic separations were carried out by TLC on 20 × 20 cm glass-supported silica gel 60 plates (1-mm layer, F-254, Merck) or by column chromatography on silica gel 60 (70–230 mesh, ASTM, Merck).

1,2-Dichloroethane was treated as previously reported.[5] Chloroform was washed with concentrated sulfuric acid, water, saturated aqueous sodium hydrogen carbonate, and water until neutral, dried ($MgSO_4$), and distilled under reduced pressure. The fraction with bp 27–30 °C (40–50 mm) was collected, stored under argon in the dark, and used within 12 h. The best quality commercial bromine (C. Erba RPE, >99.5%) was kept in 1-mL sealed vials, which were opened immediately before use and employed without further purification. Commerical tetrabutylammonium bromide (TBAB) (EGA, ca. 99%) was crystallized from ethyl acetate–toluene [mp 115–116 °C (lit.[23] mp 116–116.5 °C)].

Cyclohexene (**1a**, >99.5%) and 3-methylcyclohexene (**1b**, >99%) were purchased from Fluka AG, 2-cyclohexen-1-ol (≥96%) from Aldrich Chemical Co. 3-*tert*-Butylcyclohexene (**1c**) was obtained from 2-*tert*-butylcyclohexanone tosylhydrazone with butyllithium;[24] 3-bromocyclohexene (**1d**) was prepared from cyclohexene and *N*-bromosuccinimide[25] and 3-chlorocyclohexene (**1e**) from 2-cyclohexen-1-ol and thionyl chloride.[26]

2-Cyclohexen-1-yl benzoate (**1f**), *p*-methylbenzoate (**1g**), *p*-methoxybenzoate (**1h**), and *p*-nitrobenzoate (**1i**) were prepared by reacting 2-cyclohexen-1-ol with the corresponding benzoyl chlorides in dry pyridine.[27]

1f: bp 105 °C (0.3 mm) [lit.[28] bp 100–105 °C (0.25 mm)]; ^1H NMR δ 8.15, 7.50 (m, 2 and 3 Ar H), 5.95 (m, CH=, 2 H), 5.55 (m, $W_{1/2}$ = 12 Hz, CHO, 1 H), 2.45–1.45 ppm (6 cyclohexane H); IR 3040, 2940, 2880, 1710, 1600, 1580, 1490, 1450, 1340, 1310, 1260, 1170, 1100, 1060, 1010, 915, 700, 680, 650 cm^{-1}.

1g, bp 76–78 °C (10^{-5} mm); ^1H NMR δ 8.05, 7.25 (AA'BB' system, 4 Ar H), 5.95 (m, CH=, 2 H), 5.60 (m, $W_{1/2}$ = 12 Hz, CHO, 1 H), 2.40 (s, CH_3), 2.30–1.55 (6 cyclohexane H); IR 3060, 2960, 2900, 2860, 1720, 1625, 1520, 1460, 1320, 1280, 1190, 1130, 1070, 1030, 930, 850, 760, 735, 700, 680 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_2$: C, 77.75; H, 7.46. Found: C, 77.86; H, 7.53.

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1h: bp 132–133 °C (10^{-4} mm); ^{1}H NMR δ 8.10, 6.95 (AA'BB' system, 4 Ar H), 5.95 (m, CH=, 2 H), 5.55 (m, $W_{1/2}$ = 11 Hz, CHO, 1 H), 3.80 (s, OCH_3), 2.35–1.35 (6 cyclohexane H); IR 3050, 2950, 2880, 2850, 1715, 1610, 1510, 1460, 1315, 1260, 1165, 1095, 1025, 915, 845, 770, 730, 695, 610 cm^{-1}. Anal. Calcd for $C_{14}H_{16}O_3$: C, 72.39; H, 6.94. Found: C, 72.45; H, 7.01.

1i: mp 76–77 °C (from petroleum ether) (lit.[27] mp 77–78 °C).

Olefins **1a–c** were refluxed over $LiAlH_4$ and distilled, while **1d–i** were simply distilled immediately before each kinetic run.

Kinetic Measurements. (a) Reactions with Molecular Bromine. Stock solutions [(1–3) × 10^{-3} M)] of Br_2 in 1,2-dichloroethane and chloroform were prepared by using freshly distilled solvents and stored under protection from external light. Concentrations were determined from the UV spectra and frequently checked during use. The chloroform solutions were rather unstable and were used immediately after the preparation. All reactions were carried out at 25 °C under pseudo-second-order conditions, at (3–10) × 10^{-2} M olefin concentrations.

The stopped-flow technique was used for the kinetic measurements with olefins **1a–c** in both solvents,[2] monitoring the disappearance of Br_2 at 410 nm (ε 211 M^{-1} cm^{-1} in 1,2-dichloroethane, ε 196 M^{-1} cm^{-1} in chloroform).

The conventional UV–vis spectrophotometer was used for the kinetic measurements with olefins **1d–e**. Prethermostated solutions of Br_2 in 1,2-dichloroethane [(2–6) × 10^{-3} M] or in chloroform [(1–2.5) × 10^{-2} M] were mixed with equal volumes of olefin solutions [(5–10) × 10^{-2} M in 1,2-dichloroethane and (1–5) × 10^{-1} M in chloroform]. In the case of **1d** and **1e** the chloroform used as the solvent contained *n*-pentyl nitrite (10^{-3} M) as free radical inhibitor. The reactions were followed by monitoring the disappearance of Br_2 at 410 nm in 1,2-dichloroethane and at 480 and at 510 nm in chloroform (ε 110 and 69 M^{-1} cm^{-1}, respectively). Reproducible results were obtained in all cases.

(b) Reactions with Tetrabutylammonium Tribromide. A 10–20% excess of TBAB was dissolved into (1.5–3) × 10^{-3} M Br_2 solutions in 1,2-dichloroethane or chloroform. The UV spectra of the resulting solutions showed that all initial Br_2 was transformed into Br_3^- ion (λ_{max} 273 nm in 1,2-dichloroethane, λ_{max} 274 nm in chloroform). These solutions were reacted at 25 °C with (3–10) × 10^{-2} M olefin solutions in the same solvent, under pseudo-first-order conditions.

The reactions of **1a–c** were carried out in the stopped-flow apparatus monitoring the disappearance of Br_3^- at 410 (ε 530 M^{-1} cm^{-1} in 1,2-dichloroethane, ε 505 M^{-1} cm^{-1} in chloroform), at 430 (ε 275 M^{-1} cm^{-1} in 1,2-dichloroethane, ε 265 M^{-1} cm^{-1} in chloroform), and at 440 nm (ε 190 M^{-1} cm^{-1} in 1,2-dichloroethane, ε 182 M^{-1} cm^{-1} in chloroform).

The reactions of olefins **1d–i** were followed on the conventional UV–vis spectrophotometer, monitoring the disappearance of Br_3^- at 380 (ε 990 M^{-1} cm^{-1} in 1,2-dichloroethane, ε 940 M^{-1} cm^{-1} in chloroform) and at 450 nm (ε 130 M^{-1} cm^{-1} in 1,2-dichloroethane, ε 124 M^{-1} cm^{-1} in chloroform). Reactions in chloroform were carried out both in the absence and in the presence of *n*-pentyl nitrite. Identical results were always obtained.

Preparative Brominations. (a) With Bromine. In a typical experiment a freshly prepared 0.1 M solution of Br_2 in 1,2-dichloroethane or chloroform (10 mL) was added dropwise to 10 mL of a solution of olefin (10% excess) in the same solvent at 25 °C. The mixture was allowed to react in the dark until it became colorless. The solvent was removed under reduced pressure (20 mm), and the residue was subjected to analysis and chromatographic separation of the products.

(b) With Tetrabutylammonium Tribromide. In a typical experiment 10 mL of a freshly prepared solution of Br_2 (0.1 M) and TBAB (5–10 M) in 1,2-dichloroethane or chloroform was added dropwise to 10 mL of a solution of olefin (10% excess) in the same solvent at 25 °C. The mixture was kept in the dark until it became colorless and then was repeatedly washed with water and dried. The solvent was removed under reduced pressure and the residue subjected to analysis and chromatographic separation of the products.

***c*-2,*t*-3-Dibromo-*r*-1-chlorocyclohexane (4e) and *t*-2,*c*-3-Dibromo-*r*-1-chlorocyclohexane (5e).** The mixture obtained by bromination of **1e** with TBAT in 1,2-dichloroethane was separated by column chromatography on silica gel. Elution with petroleum ether gave the following.

4e: oil; ^{1}H NMR (C_6D_6) δ 4.35 and ~4.25 (2 narrow and 1 structured partially overlapping m, CHBr and CHCl, 3 H), 2.27–1.24 (6 cyclohexane H); IR 2950, 2870, 1450, 1355, 1340, 1285, 1210, 1160, 1055, 960, 880, 820, 770, 660, 635 cm^{-1}. Anal. Calcd for $C_9H_9Br_2Cl$: C, 26.07; H, 3.28; Br, 57.82; Cl, 12.83. Found: C, 25.96; H, 3.24; Br, 57.94; Cl, 12.92.

Further elution with petroleum ether yielded **5e**: mp 37–38 °C (from petroleum ether, bp 60–80 °C); ^{1}H NMR (C_6D_6) δ 3.72 (distorted t, *J* = 9.5 Hz, CHBr, 1 H), 3.60–3.26 (2 overlapping m, CHBr and CHCl, 2 H), 1.86–0.90 (6 cyclohexane H); IR (Nujol) 2950, 2870, 1445, 1325, 1265, 1210, 1170, 1150, 1120, 1030, 945, 850, 770, 690, 670 cm^{-1}. Anal. Found: C, 25.98; H, 3.25; Br, 57.98; Cl, 12.93.

***c*-2,*t*-3-Dibromo-*r*-1-cyclohexyl Benzoate (4f) and *t*-2,*c*-3-Dibromo-*r*-1-cyclohexyl Benzoate (5f).** These products were separated by preparative TLC from the mixture obtained by bromination of **1f** with TBAT in 1,2-dichloroethane, using 90:10 hexane–ethyl ether as the eluant (relative R_f of **4f** and **5f** on analytical plate, 1.5:1).

4f: oil; ^{1}H NMR δ 8.15, 7.50 (m, 2 and 3 Ar H), 5.50 (m, $W_{1/2}$ = 16 Hz, CHO, 1 H), 4.70 (2 overlapping m, $W_{1/2}$ = 8 Hz, CHBr, 2 H), 2.75–1.10 (6 cyclohexane H); IR 2940, 2860, 1720, 1600, 1450, 1330, 1270, 1160, 1105, 1065, 1025, 935, 840, 800, 705, 680, 665, 650 cm^{-1}. Anal. Calcd for $C_{13}H_{14}Br_2O_2$: C, 43.12; H, 3.90; Br, 44.14. Found: C, 43.33; H, 4.01; Br, 44.33.

5f: mp 152–154 °C (from ethanol); ^{1}H NMR δ 8.15, 7.50 (m, 2 and 3 Ar H), 5.25 (m, $W_{1/2}$ = 17 Hz, CHO, 1 H), 4.35 (2 overlapping m, *W* = 25 Hz, CHBr, 2 H), 2.75–1.10 (6 cyclohexane H); IR (Nujol) 2940, 2860, 1705, 1600, 1450, 1370, 1310, 1280, 1215, 1160, 1120, 1060, 1020, 950, 910, 830, 700, 690, 670 cm^{-1}. Anal. Found: C, 43.28; H, 3.99; Br, 44.36.

Products **4f** and **5f** proved to be identical with those prepared by esterification of *c*-2,*t*-3-dibromo-*r*-1-cyclohexanol and *t*-2,*c*-3-dibromo-*r*-1-cyclohexanol[8a] with benzoyl chloride.

***c*-2,*t*-3-Dibromo-*r*-1-cyclohexyl *p*-Methylbenzoate (4g) and *t*-2,*c*-3-Dibromo-*r*-1-cyclohexyl *p*-Methylbenzoate (5g).** These compounds were separated by preparative TLC from the mixture obtained by bromination of **1g** with TBAT in 1,2-dichloroethane eluting with 85:15 hexane–ethyl ether (relative R_f of **4g** and **5g** on analytical plate, 1.5:1).

4g: mp 46–48 °C (from methanol); ^{1}H NMR δ 8.05, 7.30 (AA'BB' system, 4 Ar H), 5.60 (m, $W_{1/2}$ = 16 Hz, CHO, 1 H), 4.75 (2 overlapping m, $W_{1/2}$ = 6 Hz, CHBr, 2 H), 2.35 (s, CH_3), 2.30–1.65 (6 cyclohexane H); IR (Nujol) 2940, 2860, 1720, 1610, 1460, 1370, 1340, 1330, 1270, 1170, 1160, 1100, 1020, 940, 840, 750, 660 cm^{-1}. Anal. Calcd for $C_{14}H_{16}Br_2O_2$: C, 44.71; H, 4.29; Br, 42.49. Found: C, 44.92; H, 4.39; Br, 42.61.

5g: mp 108–110 °C (from ethanol); ^{1}H NMR δ 8.10, 7.35 (AA'BB' system, 4 Ar H), 5.30 (m, $W_{1/2}$ = 16 Hz, CHO, 1 H), 4.35 (2 overlapping m, W = 24 Hz, CHBr, 2 H), 2.35 (s, CH_3), 2.30–1.25 (6 cyclohexane H); IR (Nujol) 2940, 2860, 1705, 1610, 1460, 1375, 1315, 1275, 1215, 1175, 1120, 1100, 1080, 830, 740, 700, 685 cm^{-1}. Anal. Found: C, 44.89; H, 4.41; Br, 42.63.

***c*-2,*t*-3-Dibromo-*r*-1-cyclohexyl *p*-Methoxybenzoate (4h) and *t*-2,*c*-3-Dibromo-*r*-1-cyclohexyl *p*-Methoxybenzoate (5h).** The products were separated by preparative TLC from the mixture obtained by bromination of **1h** with TBAT in 1,2-dichloroethane eluting with 70:30 hexane–ethyl ether (relative R_f of **4h** and **5h** on analytical plate, 1.4:1).

4h: mp 99–101 °C (from methanol); ^{1}H NMR δ 8.10, 6.95 (AA'BB' system, 4 Ar H), 5.55 (m, $W_{1/2}$ = 16 Hz, CHO, 1 H), 4.75 (2 overlapping m, $W_{1/2}$ = 7 Hz, CHBr, 2 H), 3.85 (s, OCH_3), 2.80–1.45 (6 cyclohexane H); IR (Nujol) 2940, 2860, 1710, 1605, 1510, 1460, 1375, 1325, 1270, 1250, 1170, 1100, 1020, 940, 840, 760, 720, 685, 660 cm^{-1}. Anal. Calcd for $C_{14}H_{16}Br_2O_3$: C, 42.89; H, 4.11; Br, 40.76. Found: C, 43.01; H, 4.25; Br, 40.94.

5h: mp 103–105 °C (from ethanol); ^{1}H NMR δ 8.10, 6.95 (AA'BB' system, 4 Ar H), 5.20 (m, $W_{1/2}$ = 17 Hz, CHO, 1 H), 4.25 (2 overlapping m, *W* = 24 Hz, CHBr, 2 H), 3.75 (s, OCH_3), 2.80–1.35 (6 cyclohexane H); IR (Nujol) 2940, 2860, 1700, 1605, 1510, 1460, 1370, 1275, 1255, 1165, 1125, 1100, 1020, 840, 760, 715, 690 cm^{-1}. Anal. Found: C, 43.02; H, 4.26; Br, 40.88.

***c*-2,*t*-3-Dibromo-*r*-1-cyclohexyl *p*-Nitrobenzoate (4i) and *t*-2,*c*-3-Dibromo-*r*-1-cyclohexyl *p*-Nitrobenzoate (5i).** These products were separated by preparative TLC from the mixture obtained by bromination of **1i** with TBAT in 1,2-dichloroethane,

using 85:15 hexane–ethyl ether (relative R_f of **4i** and **5i** on analytical plate, 1.9:1) as the eluant.

4i: mp 111–113 °C (from methanol); ^{1}H NMR δ 8.30 (s, 4 Ar H), 5.60 (m, $W_{1/2}$ = 14 Hz, CHO, 1 H), 4.75 (2 overlapping m, $W_{1/2}$ = 8 Hz, CHBr, 2 H), 2.75–1.45 (6 cyclohexane H); IR (Nujol) 2920, 2860, 1730, 1605, 1520, 1460, 1375, 1350, 1275, 1160, 1105, 1015, 940, 875, 835, 720, 660 cm^{-1}. Anal. Calcd for $C_{13}H_{13}Br_2NO_4$: C, 38.36; H, 3.22; Br, 39.26; N, 3.44. Found: C, 38.42; H, 3.31; Br, 39.46; N, 3.38.

5i: mp 105–107 °C (from ethanol) (lit.[8a] mp 103–105 °C, lit.[3c] mp 108–110 °C); ^{1}H NMR δ 8.30 (s, 4 Ar H), 5.30 (m, $W_{1/2}$ = 16 Hz, CHO, 1 H), 4.35 (2 overlapping m, W = 25 Hz, CHBr, 2 H), 2.75–1.35 (6 cyclohexane H); IR (Nujol) 2930, 2860, 1720, 1600, 1520, 1460, 1370, 1350, 1310, 1280, 1120, 1100, 1010, 830, 710, 690 cm^{-1}. Anal. Found: C, 38.51; H, 3.30; Br, 39.38; N, 3.49.

Product Analyses. The mixtures of **4b–5b**, **4d–5d**, and **4e–5e** were analyzed by GLC.[3a,c] The relative retention times were as follows: **4b** and **5b**, 1:2.3; **4d** and **5d**, 1:1.4; **4e** and **5e**, 1:1.5. Identical products ratios were found for mixtures obtained both under the conditions of the kinetic runs and under the preparative conditions.

The analyses of the mixtures of **4c–5c** obtained under preparative conditions were carried out by integration of the signals of the protons α to bromine in the NMR spectra.[11a]

The mixtures of **4f–5f**, **4g–5g**, **4h–5h**, and **4i–5i** were analyzed by HPLC using respectively 99:1, 96:4, 96:4, and 98:2 mixtures of hexane–ethyl acetate as the eluants. The relative retention times were as follows: **4f** and **5f**, 1:1.6; **4g** and **5g**, 1:2; **4h** and **5h**, 1:1.5; **4i** and **5i**, 1:1.3. Also in these cases identical product ratios were found for mixtures obtained under the conditions of the kinetic runs and under the preparative conditions.

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Registry No. **1a**, 110-83-8; **16**, 591-48-0; **1c**, 14072-87-8; **1d**, 1521-51-3; **1e**, 2441-97-6; **1f**, 3352-93-0; **1g**, 103437-97-4; **1h**, 103437-98-5; **1i**, 38313-01-8; **4e**, 103437-99-6; **4f**, 103438-00-2; **4g**, 103438-01-3; **4h**, 103438-02-4; **4i**, 103530-08-1; **5e**, 103530-04-7; **5f**, 103530-05-8; **5g**, 103530-06-9; **5h**, 103530-07-0; **5i**, 53119-31-6.

Mechanism of Base-Promoted Eliminative Fragmentations of 2-Alkyl-3-Phenyloxaziridines

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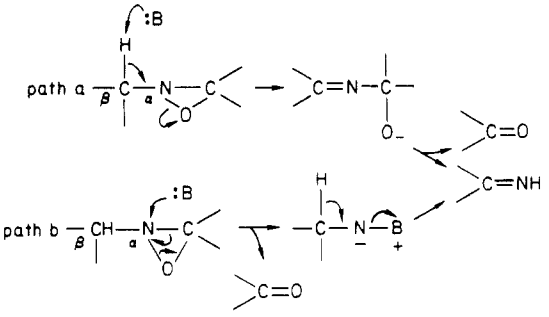
The base-promoted fragmentations of 2-benzyl-3-(4-substituted-phenyl)oxaziridines **1** and 2-(4-substituted-benzyl)-3-phenyloxaziridines **2** in anhydrous organic solvents give benzaldehydes and unstable benzylideneimines. The subsequent trimerization of the imines provides the benzylidene animals with the liberation of ammonia. The fragmentations can be regarded as an α,β-elimination and have been studied kinetically with triethylamine in acetonitrile at 40 °C. The (*Z*)-oxaziridines react more rapidly than the corresponding (*E*)-oxaziridines. The Hammett ρ values for the *E* isomers of **1** and **2** are 0.68 and 0.89, respectively. The primary kinetic β-deuterium isotope effects (k_H/k_D) are 6.1 for (*E*)-2-benzyl-3-(4-nitrophenyl)oxaziridine [(*E*)-**1a**] and 6.9 for (*E*)-2-benzyl-3-(4-methoxyphenyl)oxaziridine [(*E*)-**1e**]. From these results and considerations on the magnitudes of the Brønsted β (0.46), the activation parameters and the Arrhenius parameters for (*E*)-**1a**, the triethylamine-promoted fragmentations of **1** and **2** are best interpreted in terms of a near central E2 mechanism; for the transition state of (*E*)-**1a** the N_α–O bond breaking is slightly ahead of the β-proton removal. The triethylamine-promoted fragmentations of (*E*)- and (*Z*)-2-methyl-3-(4-nitrophenyl)oxaziridines (**9**) in acetonitrile are slower than those of **1a**, but give comparable primary isotope effects; k_H/k_D = 6.1 for (*Z*)-**9** and 6.6 for (*E*)-**9**. The Arrhenius plot for (*Z*)-**9** shows excellent linearity, suggesting neither change in mechanism nor the necessity for a tunneling correction. The fragmentation of (*Z*)-**9** in chloroform is slightly slower than that in acetonitrile, with k_H/k_D = 6.2. These data suggest that the tertiary amine promoted fragmentations of 2-alkyl-3-phenyloxaziridines with β-hydrogen exclusively proceed through an E2 mechanism.

Oxaziridines represent a unique class of three-membered heterocyclic compounds of which three bonds are severed respectively under appropriate conditions.[1] The chemistry of these compounds is relatively new and, at present, has received considerable attention in connection with some biological processes.[2] Oxaziridines with a proton on the carbon adjacent to the ring nitrogen undergo a base-promoted fragmentation to aldehydes or ketones and imines.[3]

Scheme I



The transformation of amino acids to oxaziridines via the corresponding imines and the subsequent fragmentation of the oxaziridines are of interest in connection with a biological oxidative deamination of amino acids.

For the base-promoted fragmentation of 2-alkyloxaziridines mainly two reaction pathways concerning the rupture of the N-O bond have been suggested (Scheme

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