The Relative *cis/trans* Reactivity in the Hydrochlorination of 1-Arylpropenes

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Hydrochlorination of *cis*- and *trans*-1-phenylpropenes and their ring-substituted derivatives (*p*-CH_3O, *p*-CH_3, and *p*-Cl) has been studied in acetic acid at 16—35°C. 1-Phenylpropene gave predominantly a *cis*-adduct while the *p*-CH_3O derivative yielded a non-stereospecific product. For the *p*-CH_3O and *p*-CH_3 derivatives, the *cis* isomer was found to be more reactive than the corresponding *trans* isomer, while for the *p*-Cl derivative the opposite relative reactivity was observed. The origins of these *cis/trans* reactivities have been discussed in terms of the electronic and steric effects on stability of the solvated transition state.

The question of the relative reactivity of the geometrical isomers of an olefin in addition reactions is one of the problems remaining to be solved. We have studied the acid-catalyzed hydrolyses of various alkenyl alkyl ethers and found that all the *cis* isomers are more reactive than the corresponding *trans* isomers.[1] Since most of the *cis* ethers are thermochemically less stable than the *trans* isomers, the reactivity difference was at first ascribed to the difference in the ground-state stability.[2] A similar reasoning of the relative reactivities in some electrophilic additions was presented previously.[3] However, we have later found that *cis*-β-chlorovinyl ethyl ether[4] and *cis*-1,2-dialkoxyethylenes,[5] which are more stable than the *trans* isomers, are more reactive than the *trans* isomers. An alternative explanation for this reactivity has tentatively been presented but is not general.[4,5] Furthermore, we have found that *trans*-styryl ethyl ether is less reactive than the *cis* isomer at ordinary temperatures but the activation enthalpy for the former is smaller than that for the latter, despite the greater stability of the former at the ground state.[6] The reactivity difference in this case is controlled by the entropy term at higher temperatures and the origin of this observation is still ambiguous.

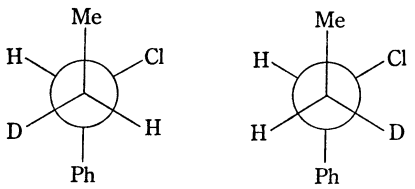
Addition reactions of various electrophiles have already been studied with *cis*- and *trans*-1-phenylpropenes (**1c** and **1t**).[7-11] The reactivity difference between **1c** and **1t** was found to be very small and vary depending on the electrophile. Thus, the *trans* isomer is slightly more reactive in bromination[7] and sulfenylation[8] but less reactive in methoxymercuration[9] and hydrobromination.[10] Results on cationic polymerization are not definite.[11]

In the present investigation, the relative reactivities of *cis* and *trans* isomeric pairs of **1c** and **1t** and their ring-substituted derivatives have been measured for their hydrochlorination in acetic acid in the temperature range of 16—35 °C. Possible origins of these reactivities are discussed.

Results

The hydrochlorination of both **1c** and **1t** in glacial acid acetic gave predominantly 1-phenylpropyl chloride (**2**) with a contamination by 1-phenylpropyl acetate (**3**).

In order to confirm the stereochemistry of the present reaction, the deuteriochlorination was carried out in acetic acid-*O*-*d*. The *cis* isomer **1c** gave predominantly an *erythro* adduct **2c** while **1t** yielded a *threo* adduct **2t**, in agreement with the results obtained in hydrobromination.[10] The most favorable conformations of **2c** and **2t** are shown below.



2c **2t**

The stereochemistry of the adducts was determined by NMR spectra. The vicinal H-H coupling constants were 7.5 and 4.5 Hz for **2c** and **2t**, respectively. It is known that the spin-spin coupling constant between vicinal hydrogens is greatly dependent on the dihedral angle of their bonds.[12] The coupling constant between trans protons is greater than that between gauche protons. Consequently, **2c** should have a greater coupling constant than **2t**. A similar pair of compounds, *erythro*- and *threo*-1-phenyl-2-methylaminopropyl alcohols, have $J=8.2\pm0.2$ and 4.0 ± 0.2 Hz, respectively.[13]

By contrast, the products from both the *p*-methoxy derivatives of **1c** and **1t** gave the same NMR spectrum, suggesting the formation of nonstereospecific adducts. This observation is consistent with the observation that the geometrical isomerization of *p*-CH_3O-**1c** to *p*-CH_3O-**1t** is taking place during the reaction. Other derivatives suffered little geometrical isomerization under the reaction conditions adopted here.

During the reaction of **1c**, no trace of the *trans* isomer **1t** was found by vpc. With the *p*-CH_3 derivative, the relative concentration of the *trans* isomer (*ca.* 5%) concomitant with the *cis* isomer did not increase during the reaction. But geometrical isomerization of *p*-CH_3-**1c** to *p*-CH_3-**1t** seems to take place to some extent. However, it did not affect rate-determination under low conversion.

The kinetic measurements were carried out gas-chromatographically with a pure isomer or with a

Table 1. Pseudo-first order rate constants in the hydrochlorination of substituted 1-phenylpropenes in acetic acid[a)]

Substituent	Temp., °C	$10^4 k_1$, s^{-1}	
		cis	*trans*
p-CH_3O	25	329	244
	16	188	124
p-CH_3	25	0.416	0.331

a) [Olefin]=0.45 M; [HCl]=0.65 M.

Table 2. Relative *cis/trans* reactivity of substituted 1-phenylpropenes

Substituent	Rel. reactivity[a)]			$\delta\Delta H^{\neq}$,[c)] kcal/mol	$\delta\Delta S^{\neq}$,[c)] e.u.
	16°C	25°C	35°C		
p-CH_3O	1.52[b)]	1.35[b)]		-2.2_7	-7.0_2
p-CH_3		1.25[b)]			
		1.31	1.46	$+1.9_7$	$+7.1_5$
H		0.97	1.97	$+2.3_1$	$+1.6_9$
p-Cl		0.30	0.35	$+2.8_2$	$+7.0_5$

a) By the competitive method. b) Calcd from the k_1 values listed in Table 1. c) $2.303\,R \log (k_{cis}/k_{trans}) = -\delta\Delta H^{\neq}(1/T)+\delta\Delta S^{\neq}$, $\delta\Delta H^{\neq}=\Delta H^{\neq}(cis)-\Delta H^{\neq}(trans)$ $\delta\Delta S^{\neq}=\Delta S^{\neq}(cis)-\Delta S^{\neq}(trans)$

mixture of isomeric olefins. Because of the complexity of kinetic order in [HCl],[14] the pseudo-first order rate constants were determined under low conversion (5—10 %) for isomerically pure *p*-CH_3O and *p*-CH_3 derivatives. The results are given in Table 1. Although the isomerization accompanied the reaction of *p*-CH_3O-**1c**, the rate of decay of the substrate is considered to be that of protonation and recorded as such in Table 1.

The relative rates of geometrical isomers were measured mostly by the competitive method with an isomeric mixture. The results are given in Table 2. The *cis* isomers are more reactive in the case of 1-phenylpropenes bearing an electron-donating group (*p*-CH_3O and *p*-CH_3) while the *trans* isomer of the *p*-Cl derivative is more reactive than its *cis* isomer. Unsubstituted **1c** and **1t** are similar in reactivity; relative reactivity is reversed between 25 and 35 °C.

The relative *cis/trans* reactivity tends to increase with the rise in temperature except for the *p*-CH_3O derivative. The differences in activation enthalpy $\delta\Delta H^{\neq}$ and activation entropy $\delta\Delta S^{\neq}$ between the *cis* and *trans* isomers were calculated and are listed in Table 2. The activation enthalpies of *cis* isomers are greater than those for the corresponding *trans* isomers except for the *p*-CH_3O derivative. The apparently greater reactivity of the *cis* isomer of the *p*-CH_3 derivative in the present temperature range is entropy-controlled. Negative $\delta\Delta H^{\neq}$ obtained for the *p*-CH_3O derivative implies that the *cis* isomer is energetically more reactive.

Discussion

Stereochemistry. Deuteriochlorination of **1c** and **1t** in DCl-DOAc gave mainly *erythro*- and *threo*-adducts, respectively. That is, hydrochlorination of **1c** and **1t** takes place preferentially through *syn*-addition. Similar results were obtained in the hydrobromination of **1c** and **1t** and interpreted in terms of the mechanism involving carbonium halide ion-pair intermediates.[10]

The *p*-CH_3O derivative reacts non-stereospecifically, being accompanied by geometrical isomerization. The intermediate carbonium ion, which should be stabilized by *p*-CH_3O group, would be reluctant to collapse by the attack of the chloride ion and hence could rotate freely before completion of the reaction. Thus, the isomerization accompanies the reaction of the *cis* isomer.

Relative cis/trans *Reactivities.* Relative reactivities of geometrically isomeric pairs vary depending on the ring substituent and reaction temperature. As has been described above,[7,8,11] *trans* isomers are often more reactive in styryl compounds. Similar observations were previously made for another class of styryl derivatives, styryl ethyl ether.[6] On the other hand, it was found that the *cis* isomers of α,β-unsaturated ethers are usually more reactive than the corresponding *trans* isomers toward some electrophiles, irrespective of ground-state stability.[1,2,4,5,15] Clearly, relative reactivities cannot be interpreted by the ground-state stability differences alone.

Yamaguchi *et al.*[16] have theoretically made general considerations on the origin of the *cis/trans* reactivities of olefins. It was concluded that the *cis* isomer should generally be more reactive in ionic reactions irrespective of the ground-state stability and that the Coulombic interaction in the transition state plays a predominant role in determining the greater reactivity of *cis* isomer relative to the *trans* counterpart. The observations on styryl compounds are however outside this scope, and another factor has to be taken into account to interpret the reactivities.

Relative *cis/trans* reactivity increases with increasing electron-donating character of a ring substituent as is seen in Table 2. This implies that the *cis* isomer is more sensitive to the electronic effects of ring substituents. It was suggested earlier that the diminished reactivity of **1c** is due to steric hindrance against electrophilic attack because of nonplanar conformation of **1c**.[11] This view implicitly presumes that the transition state for **1c** is less bonding (between an electrophile and the reaction site of olefin) than that for **1t**. However, this interpretation seems to contradict the present result that **1c** is more sensitive to the substituent effects than **1t**.

Alternatively, a steric effect against solvation of intermediate ion-pair in the *cis* isomers seems to account for all the results available. Effective solvation of intermediate carbonium-chloride ion-pair derived from the *trans* isomer stabilizes the transition state and hence enhances the reactivity of **1t** on one hand. Charge dispersion by solvation, on the other hand, would result in lower sensitivity of **1t** to substituent effects.[17] For very reactive derivatives like *p*-CH_3O-**1**, the electronic effects will overcome the steric effects, thus allowing the *cis* isomer to be more reactive.

In conclusion, the *cis* isomers of any olefins including styryl compounds should be intrinsically (or electro-

nically) more reactive in protonation than are the *trans* counterparts. The Coulombic interaction at the transition state contributes mainly to this reactivity. In the protonation and probably in other types of reactions also, the steric inhibition against intermediate solvation should more or less reduce the reactivity of *cis* isomers. The relative *cis/trans* reactivities experimentally observed are probably a reflection of the relative importance of these two opposing contributions.

Experimental

Materials. Preparation of *cis*- and *trans*-1-phenylpropenes (**1c** and **1t**) and their derivatives will be described elsewhere.[8]

1-Phenylpropyl chloride was prepared as an authentic sample by treatment of 1-phenylpropyl alcohol with thionyl chloride. NMR (CCl_4); δ 1.02 (3H, t, J=7.5 Hz, CH_3), 2.10 (2H, q, J=7.5 Hz, CH_2), 4.70 (1H, t, J=7.5 Hz, CH–Cl), 7.3 (5H, s, C_6H_5).

Hydrochlorination. Procedure of the reaction and the method of kinetic measurements were described previously.[18] The reaction procedure for deuteriochlorination was also described before.[19]

NMR spectra of the products were recorded on a JNM-4H-100 spectrometer. NMR (CCl_4): **2t**. δ 0.96 (3H, d, J=7 Hz, CH_3), ~2.0 (1H, m, CH–Me), 4.63 (1H, d, J=4.5 Hz, CH–Cl), ~7.25 (5H, m, C_6H_5). **2c**: δ 0.98 (3H, d, J=7 Hz, CH_3), ~2.0 (1H, m, CH–Me), 4.66 (1H, d, J=7.5 Hz, CH–Cl), ~7.22 (5H, m, C_6H_5). Product from *p*-CH_3O-**1t**; δ 0.96 (3H, d, J=7 Hz, CH_3), ~2 (1H, m, CH–Me), 3.73 (3H, s, CH_3O), 4.63 (1H, d, J=6.0 Hz, CH–Cl), 6.7—7.25 (4H, m, C_6H_4). Product from *p*-CH_3O-**1c**; δ 0.96 (3H, d, J=7 Hz, CH_3), ~2 (1H, m, CH–Me), 3.70 (3H, s, CH_3O), 4.65 (1H, d, J=6.0 Hz, CH–Cl), 6.72—7.27 (4H, m, C_6H_4).

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