The Behavior of Stereoisomeric Cyclohexane- 1,2-, 1,3-, and 1,4-dicarboxylates under Chemical Ionization and Collision Induced Dissociation. Conformational Effects in Gas-Phase Cations

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Abstract: Dimethyl and diethyl esters of *cis*-cyclohexane- 1,2- 1,3-, and 1,4-dicarboxylic acids *cis*-**1**, *cis*-**2**, and *cis*-**3** give rise to major MH^+ ions under ammonia chemical ionization (NH_3-CI) conditions (minor $[M + NH_4]^+$) and to abundant $[MH - ROH]^+$ ions under isobutane chemical ionization (i-Bu-CI) and collision induced dissociation (CID) conditions, indicating interaction between the two adjacent ester groups (stabilization of MH^+ ion by hydrogen bridging and facilitating the ROH elimination by proton transfer between the two alkoxycarbonyl groups). Cyclohexane-*trans*-1,2-dicarboxylates *trans*-**1** exhibit a similar interaction giving rise to major MH^+ ions under NH_3-CI and to abundant $[MH - ROH]^+$ ions upon i-Bu-CI and CID. *trans*-1,4-Bis(alkoxycarbonyl)cyclohexanes *trans*-**3**, in which the two remote alkoxycarbonyl groups cannot interact, give rise to major $[M + NH_4]^+$ ions under NH_3-CI (minor MH^+) and to negligible $[MH - ROH]^+$ ions under i-Bu-CI and CID. *trans*-1,3-Diesters *trans*-**2** behave in an unexpected way: They exhibit not only major $[M + NH_4]^+$ and minor MH^+ ions under NH_3-CI, in consistency with the large distance between the two ester groups, but also abundant $[MH - ROH]^+$ ions under i-Bu-CI and upon CID conditions, indicating occurrence of a proton migration between the two alkoxycarbonyl groups. This behavior is explained in terms of a strained transition state or intermediate involved in the ROH elimination from MH^+ of the *trans*-1,3-diesters. Methyl substituents at the two α-positions 1 and 3 increase the barrier for the proton transfer resulting in suppression of the ROH elimination from the MH^+ ions of *trans*-1,3-dimethyl-1,3-bis(carboalkoxy)cyclohexanes *trans*-**4** under i-Bu-CI and CID conditions.

Introduction

The effect of configuration on the fragmentation pattern of esters of various stereoisomeric dicarboxylic acids under electron ionization (EI) has been explored by several research groups.[1] A variety of stereospecific fragmentation processes have been observed in numerous diastereomeric pairs of diesters which are specific to the particular systems.[1]

The present knowledge of the behavior of stereoisomeric diesters under chemical ionization (CI) conditions is limited to a few systems, but the reported results suggest two typical stereospecific features in the CI-induced behavior, which can be rationalized in terms of an effect of the distance between the two ester groups in the particular stereoisomers.[2,3] Dialkyl maleates and fumarates exhibit a pronounced difference in the extent of alcohol elimination from their MH^+ ions upon chemical ionization. The carbonyl oxygen atom is the favored site of protonation in esters. Elimination of ROH from MH^+ ions of fumarates requires a symmetry forbidden 1,3-hydrogen transfer resulting in a very low abundance of $[MH - ROH]^+$ ions. These ions are abundant

Table I. i-Bu-CI Mass Spectral Data of Stereoisomeric Pairs of Cyclohexanedicarboxylates and of Cyclohexanecarboxylates

	MH^+		$[MH - ROH]^+$	
	m/z	RA (%)	*m/z*	RA (%)
cis-**1a**[a]	201	68	169	100
trans-**1a**[b]	201	63	169	100
cis-**1b**[c]	229	9	183	100
trans-**1b**[d]	229	12	183	100
cis-**2a**[e]	201	75	169	100
trans-**2a**[f]	201	88	169	100
cis-**2b**[g]	229	55	183	100
trans-**2b**[h]	229	100	183	89
cis-**3a**[i]	201	100	169	62
trans-**3a**[j]	201	100	169	2
cis-**3b**[k]	229	100	183	67
trans-**3b**[l]	229	100	183	1
cis-**4a**[m]	229	10	197	100
trans-**4a**[n]	229	100	197	0.4
cis-**4b**[o]	257	17	211	100
trans-**4b**[p]	257	100	211	<0.1
cis-**5a**[q]	215	14	183	100
trans-**5a**[r]	215	74	183	100
cis-**5b**[s]	243	24	197	100
trans-**5b**[t]	243	100	197	71
c-$C_6H_{11}COOMe$[u]	143	100	111	1
c-$C_6H_{11}COOEt$[a]	157	100	111	0.4

[a] No additional ions above 1%. [b] An additional ion at *m/z* 141 (1%). [c] Additional ions above 1%: *m/z* 155 (28%), 127 (7%), 109 (41%), 81 (26%). [d] *m/z* 155 (48%), 127 (5%), 109 (36%), 81 (24%). [e] *m/z* 141 (1%), 140 (1%), 139 (1%). [f] *m/z* 141 (1%). [g] *m/z* 155 (2%). [h] *m/z* 155 (13%). [i] *m/z* 141 (1%), 140 (1%). [j] *m/z* 141 (1%), 140 (1%). [k] *m/z* 155 (3%), 154 (3%). [l] *m/z* 155 (3%), 154 (2%). [m] *m/z* 169 (7%), 167 (2%). [n] *m/z* 169 (5%), 167 (1%). [o] *m/z* 183 (3%), 109 (3%). [p] *m/z* 183 (4%), 109 (2%). [q] *m/z* 155 (8%). [r] *m/z* 155 (23%). [s] *m/z* 169 (10%). [t] *m/z* 169 (31%). [u] *m/z* 111 (1%).

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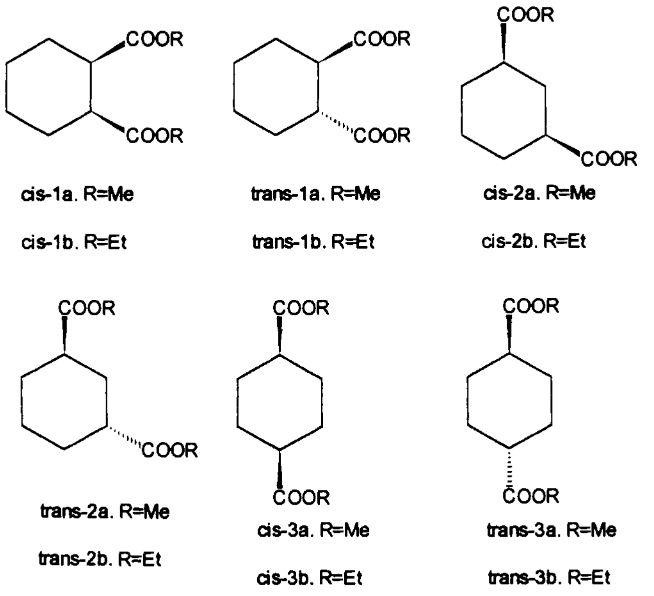
Table II. NH_3-CI Mass Spectral Data of Stereoisomeric Pairs of Cyclohexanedicarboxylates and of Cyclohexanecarboxylates

	MH^+		$[M + NH_4]^+$	
	m/z	RA (%)	*m/z*	RA (%)
cis-**1a**[a]	201	100	218	2
trans-**1a**[b]	201	100	218	21
cis-**1b**[c]	229	100	246	2
trans-**1b**[d]	229	100	246	12
cis-**2a**[e]	201	100	218	3
trans-**2a**[f]	201	11	218	100
cis-**2b**[g]	229	100	246	2
trans-**2b**[h]	229	21	246	100
cis-**3a**[i]	201	100	218	51
trans-**3a**[j]	201	12	218	100
cis-**3b**[k]	229	100	246	33
trans-**3b**[l]	229	43	246	100
cis-**4a**[m]	229	56	246	3
trans-**4a**[n]	229	27	246	100
cis-**4b**[o]	257	71	274	<1
trans-**4b**[p]	257	96	274	100
cis-**5a**[q]	215	100	232	4
trans-**5a**[r]	215	10	232	100
cis-**5b**[s]	243	100	260	1
trans-**5b**[t]	243	24	260	100
c-$C_6H_{11}COOMe$[u]	143	14	160	100
c-$C_6H_{11}COOEt$[v]	157	44	174	100

[a] Additional ions in the mass spectrum (above 1%): *m/z* 186 (12%), 169 (37%), 154 (4%), 140 (5%), 81 (5%). [b] *m/z* 186 (8%), 169 (9%), 168 (8%), 154 (9%). [c] *m/z* 183 (28%), 154 (9%). [d] *m/z* 200 (15%), 183 (16%), 182 (6%), 154 (29%), 109 (3%). [e] *m/z* 200 (8%), 186 (10%), 169 (16%), 154 (4%). [f] *m/z* 186 (6%), 185 (5%), 169 (5%), 168 (7%), 141 (3%), 140 (4%), 81 (2%). [g] *m/z* 200 (11%), 183 (24%), 182 (3%), 155 (2%), 154 (8%). [h] *m/z* 200 (7%), 199 (5%), 183 (4%), 182 (5%), 155 (4%), 154 (7%). [i] *m/z* 186 (10%), 185 (4%), 169 (16%), 168 (5%), 154 (7%), 141 (5%), 140 (9%), 109 (8%), 108 (16%). [j] 186 (3%), 185 (12%), 169 (5%), 168 (13%), 141 (8%), 140 (28%), 109 (9%), 108 (11%). [k] *m/z* 200 (7%), 183 (15%), 182 (3%), 155 (5%), 154 (13%), 109 (3%), 108 (4%). [l] *m/z* 199 (6%), 182 (5%), 155 (8%), 154 (21%), 109 (3%), 108 (3%). [m] *m/z* 214 (29%), 197 (100%), 182 (13%), 169 (10%), 168 (5%), 109 (13%), 95 (3%). [n] *m/z* 169 (16%), 168 (3%), 109 (16%). [o] *m/z* 228 (15%), 211 (100%), 210 (8%), 183 (11%), 182 (14%), 142 (5%), 109 (15%), 95 (4%). [p] *m/z* 210 (3%), 183 (22%), 109 (19%). [q] *m/z* 200 (25%), 183 (60%), 168 (11%), 155 (23%), 123 (7%), 95 (12%). [r] *m/z* 200 (5%), 199 (3%), 183 (6%), 182 (5%), 155 (6%), 154 (5%), 95 (7%). [s] *m/z* 214 (18%), 197 (61%), 169 (16%), 168 (11%), 123 (6%), 95 (11%). [t] *m/z* 214 (6%), 213 (4%), 197 (5%), 196 (3%), 169 (8%), 168 (7%), 95 (6%). [u] *m/z* 142 (5%), 111 (4%), 110 (3%). [v] *m/z* 156 (5%).

Chart I



cis-1a. R=Me

cis-1b. R=Et

trans-1a. R=Me

trans-1b. R=Et

cis-2a. R=Me

cis-2b. R=Et

trans-2a. R=Me

trans-2b. R=Et

cis-3a. R=Me

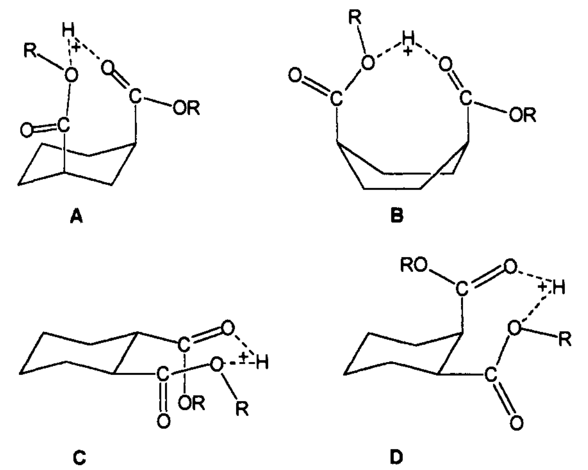
cis-3b. R=Et

trans-3a. R=Me

trans-3b. R=Et

in the CI mass spectra of maleates, which eliminate ROH via an interaction of the two adjacent ester groups.[2] Elimination of ethylene from the MH^+ ions of diethyl fumarates takes place under CID conditions, while the corresponding maleates undergo an exclusive elimination of alcohol.[2b]

Chart II



Another stereochemical feature observed in maleates and fumarates is connected with the different proton affinities (PA) of the stereoisomers. Thus the higher PA maleates are protonated even by high PA reagent gases giving rise to the hydrogen bridged MH^+ ions, while fumarates undergo preferable reagent ion attachment processes giving rise to attachment ions such as $[M + NH_4]^+$, $[M + H_3O]^+$, and others.[3] The high stereospecificity of the above two processes, namely preferential protonation and alcohol elimination in the cis isomers, clearly indicates retention of the original double bond geometry in the gas-phase MH^+ ions of the maleates and fumarates.

In the present work we examined the CI-induced behavior of stereoisomeric cyclohexane dicarboxylates. Since the stereospecificity of the above processes results from the different distances between the two ester groups, the CI-induced behavior of cyclic diesters could provide information on the conformations of gas-phase cations.

Results and Discussion

The isobutane-CI and NH_3-CI mass spectral data of the diastereomeric pairs of dimethyl and diethyl esters of cyclohexane-1,2-, 1,3-, and 1,4-dicarboxylic acids **1**, **2**, and **3** are listed in Tables I and II.

NH_3-CI of the Stereoisomeric Diesters. The NH_3-CI data are consistent with the expected behavior of the stereoisomers. Cis-1,3- and -1,4-diesters (*cis*-**2** and *cis*-**3**, respectively) exhibit most abundant MH^+ ions, while formation of the $[M + NH_4]^+$ attachment ions is preferred in the corresponding trans isomers. This stereospecific behavior suggests hydrogen bridged structures A and B for the MH^+ ions of *cis*-**2** and *cis*-**3**. The two alkoxycarbonyl groups attain an axial conformation A and the cyclohexane ring has the twist boat conformation in B. These conformations are apparently stabilized by the intramolecular hydrogen bond. The trans isomers behave in a similar way to methyl and ethyl cyclohexanecarboxylates (monoesters), which also afford major $[M + NH_4]^+$ ions in their NH_3-CI mass spectra.

Both *cis*- and *trans*-1,2-diesters (*cis*-**1** and *trans*-**1**) give rise to the most abundant MH^+ ions under NH_3-CI conditions indicating occurrence of hydrogen bridging in the two stereoisomers. This behavior is consistent with the short distances between the two ester groups in both stereoisomers (diequatorial conformation in *trans*-**1**) which enable formation of hydrogen bridged MH^+ ions C and D.

The difference between the *cis*- and *trans*-1,2-diesters is demonstrated by the relative abundances of the $[M + NH_4]^+$ attachment ions (which are low for both isomers). They are higher in the trans isomers (21% of MH^+ in *trans*-**1a** and 12%

Table III. CID[a] Mass Spectral Data[b] of MH⁺ Ions of Stereoisomeric Pairs of Dimethyl Esters of Cyclohexanedicarboxylic Acids

m/z	ion	*cis*-**1a**	*trans*-**1a**	*cis*-**2a**	*trans*-**2a**	*cis*-**3a**	*trans*-**3a**
201	parent	16	14	17	9	39	100
183	$[MH - H_2O]^+$	*c*	*c*	*c*	*c*	0.3	16
169	$[MH - MeOH]^+$	100	100	100	64	95	3
141	$[169 - CO]^+$	16	47	37	100	81	3
137	$[MH - 2MeOH]^+$	*c*	*c*	*c*	*c*	0.7	34
123	$[183 - HCO_2Me]^+$	*c*	*c*	*c*	*c*	0.1	10
109	$[169 - HCO_2Me]^+$	43	59	57	87	100	28
81	$[109 - CO]^+$	40	53	41	77	71	30

[a] 30 eV collision energy. [b] Relative ion abundances (%). [c] Below detection level, <0.1%.

Table IV. CID[a] Mass Spectral Data[b] of MH⁺ Ions of Stereoisomeric Pairs of Diethyl Esters of Cyclohexanedicarboxylic Acids

m/z	ion	*cis*-**1b**	*trans*-**1b**	*cis*-**2b**	*trans*-**2b**	*cis*-**3b**	*trans*-**3b**
229	parent	18	16	16	7	32	54
211	$[MH - H_2O]^+$	*c*	*c*	*c*	*c*	*c*	0.8
201	$[MH - C_2H_4]^+$	*c*	*c*	*c*	*c*	*c*	24
183	$[MH - EtOH]^+$	100	100	100	48	93	8
173	$[MH - 2C_2H_4]^+$	*c*	*c*	*c*	*c*	*c*	20
155	$[183 - C_2H_4]^+$	35	57	46	100	100	20
137	$[MH - 2EtOH]^{+\,d}$	*c*	*c*	*c*	*c*	*c*	100
109	$[183 - HCO_2Et]^+$	20	46	34	54	70	15
81	$[109 - CO]^+$	9	30	22	33	40	7

[a] 30 eV collision energy. [b] Relative ion abundances (%). [c] Below detection level, <0.1%. [d] Formal assignment. Parent mass spectrum indicates the following sequence (multiple collision conditions): $MH^+ \rightarrow [MH - H_2O]^+ \rightarrow [MH - H_2O - C_2H_4]^+ \rightarrow [MH - H_2O - C_2H_4 - EtOH]^+$.

Scheme I

$$MH^+ \xleftarrow{(c)} cis\text{-}1 \xrightarrow{(a)} MH^+ \xrightarrow{(b)} [MH - ROH]^+$$

$$MH^+ \xleftarrow{(c)} trans\text{-}1 \xrightarrow{(a)} MH^+ \xrightarrow{(b)} [MH - ROH]^+$$

$$MH^+ \xleftarrow{(c)} cis\text{-}3 \xrightarrow{(a)} MH^+ \xrightarrow{(b)} [MH - ROH]^+$$

$$[M + NH_4]^+ \xleftarrow{(c)} trans\text{-}3 \xrightarrow{(a)} MH^+ \overset{(b)}{\not\longrightarrow} [MH - ROH]^+$$

$$MH^+ \xleftarrow{(c)} cis\text{-}2 \xrightarrow{(a)} MH^+ \xrightarrow{(b)} [MH - ROH]^+$$

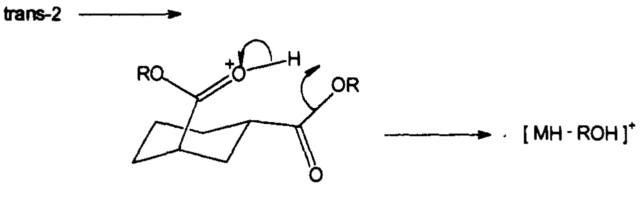
$$[M + NH_4]^+ \xleftarrow{(c)} trans\text{-}2 \xrightarrow{(a)} MH^+ \xrightarrow{(b)} [MH - ROH]^+$$

$$MD^+ \xleftarrow{(f)} cis\text{-}2 \xrightarrow{(d)} MD^+ \xrightarrow{(e)} [MD - ROD]^+$$

$$[M + ND_4]^+ \xleftarrow{(f)} trans\text{-}2 \xrightarrow{(d)} MD^+ \xrightarrow{(e)} [MD - ROD]^+$$

[a] (a) i-Bu-CI; (b) fragmentation under CI and under CID conditions; (c) major ion upon NH_3-CI; (d) ND_3-CI; (e) CID; (f) major ion upon ND_3-CI

Scheme II

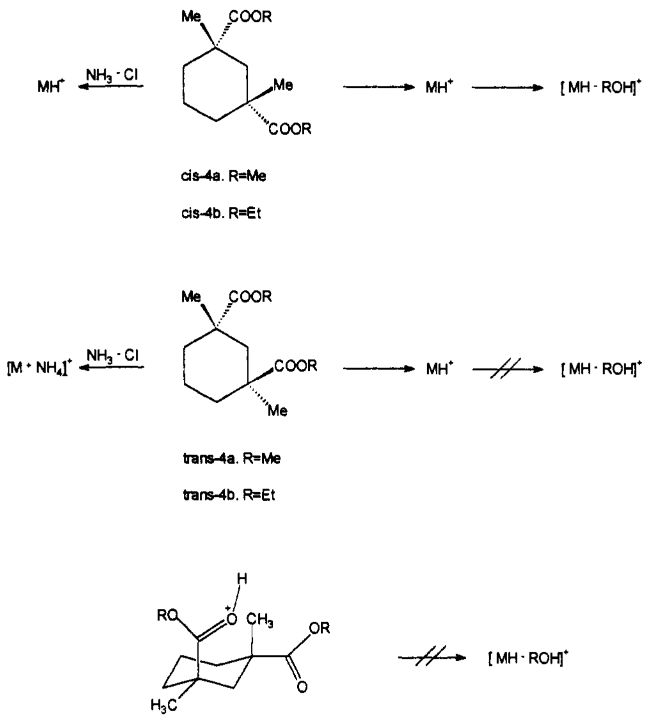


E

in *trans*-**1b**), in which the hydrogen bridging between the two equatorial ester groups restricts conformational freedom in the MH⁺ ions, than in the *cis*-diesters (2% in both *cis*-**1a** and *cis*-**1b**), where an interaction between the two alkoxycarbonyl groups is possible in both conformations.

Alcohol Elimination under i-Bu-CI and CID Conditions. The elimination of alcohol follows the expected pattern in the 1,4- and 1,2-diesters. *cis*-Cyclohexane-1,4-dicarboxylates *cis*-**3a** and *cis*-**3b** give rise to abundant [MH – ROH]⁺ ions under i-Bu-CI conditions. These ions are practically absent in the i-Bu-CI spectra of *trans*-**3a** and *trans*-**3b** (in analogy with methyl and ethyl cyclohexanemonocarboxylates). This highly stereospecific behavior is reproduced in the CID measurements of MH⁺ ions of the above two pairs of stereoisomers obtained under i-Bu-CI and NH_3-CI conditions: The elimination of one molecule of methanol and ethanol gives rise to abundant product ions only in the cis isomers. MD⁺ ions obtained by ND_3-CI of these isomers exhibit exclusive elimination of ROD. The MH⁺ ions of the *trans*-1,4-diesters (*trans*-**3**) undergo some unusual fragmentation processes under CID conditions (e.g., elimination of H_2O, C_2H_4, 2ROH) which have not been observed in all the other examined isomeric diesters (see Tables III and IV). This highly stereospecific behavior clearly indicates retention of the original configuration of the stereoisomers upon CI, and it reflects the interaction between the two ester groups which is possible only in the cis isomers in analogy to that suggested for protonated maleates.[2]

Scheme III



F

Scheme IV

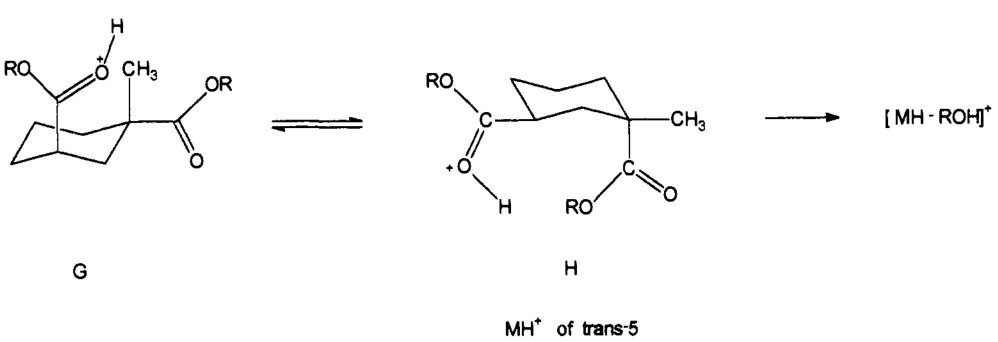


Table V. CID[a] Mass Spectral Data[b] of MH$^+$ Ions of Stereoisomeric 1-Methyl- and 1,3-Dimethyl-1,3-dimethoxycarbonylcyclohexanes 4a and 4b

ion	*m/z*	*cis*-**4a**	*trans*-**4a**	*m/z*	*cis*-**5a**	*trans*-**5a**
parent	229	2	33	215	3	3
$[MH - MeOH]^+$	197	61	*c*	183	71	53
$[MH - HCO_2Me]^+$	169	79	22	155	100	100
$[MH - MeOH - HCO_2Me]^+$	137	14	46	123	47	34
$[MH - 2HCO_2Me]^+$	109	100	100	95	56	96

[a] 30 eV collision energy. [b] Relative ion abundances (%). [c] Below detection level, <0.1%.

Table VI. CID[a] Mass Spectral Data[b] of MH$^+$ Ions of Stereoisomeric 1-Methyl- and 1,3-Dimethyl-1,3-diethoxycarbonylcyclohexanes 4b and 5b

ion	*m/z*	*cis*-**4b**	*trans*-**4b**	*m/z*	*cis*-**5b**	*trans*-**5b**
parent	257	22	28	243	9	0.1
$[MH - EtOH]^+$	211	65	0.8	197	65	37
$[MH - HCO_2Et]^+$	183	100	35	169	100	100
$[MH - HCO_2Et - C_2H_4]^+$	155	*c*	15	141	0.2	4
$[MH - HCO_2Et - EtOH]^+$	137	16	60	123	34	18
$[MH - 2HCO_2Et]^+$	109	89	100	95	38	56

[a] 30 eV collision energy. [b] Relative ion abundances (%). [c] Below detection level, <0.1%.

As expected the stereoisomeric pairs of cyclohexane-1,2-carboxylates **1** give rise to abundant [MH − ROH]$^+$ ions upon i-Bu-CI and under CID conditions almost independent of the configuration. MD$^+$ ions obtained upon ND_3-CI of both cis and trans isomers exhibit exclusive elimination of ROD. This nonstereospecific behavior results from the interaction between the two ester groups, which is possible in both the cis and trans isomers.

An unexpected behavior was observed in the i-Bu-CI-induced elimination of ROH from MH$^+$ ions of the stereoisomeric pairs of the 1,3-diesters **2**: Both stereoisomers within each pair gave rise to comparable [MH − ROH]$^+$ ions. A similar behavior takes place in the fragmentation of the MH$^+$ ions of *cis*-**2** and *trans*-**2** under CID conditions: Again both stereoisomers in each pair eliminate ROH to a comparable extent. CID measurement of MD$^+$ ions obtained upon ND_3-CI showed that the external deuteron was quantitatively abstracted in the course of alcohol elimination in both the cis and trans isomers. The above results are summarized in Scheme I.

As stated above the formation of major MH$^+$ ions under NH_3-CI and the elimination of ROH in both *cis*- and *trans*-1,2-diesters **1** and in the *cis*-1,3- and -1,4-diesters results from the interaction between the two ester groups. The absence of the [MH − ROH]$^+$ ions in the *trans*-1,4-diesters (*trans*-**3**) clearly demonstrates the inability of the esters to undergo the CI and CID-induced alcohol elimination (e.g., via ring open intermediates) when such an interaction does not exist.

Hydrogen Transfer via Strained Transition Structures. In contrast to the above systems the behavior of *trans*-1,3-diesters (*trans*-**2**) is inconsistent. The large distance between the two alkoxycarbonyl groups effectively hinders formation of the MH$^+$ ions in the NH_3-CI spectra of *trans*-**2**. However the facile elimination of alcohol, which is comparable to that of the cis isomers and exclusively involves the external proton, indicates presence of an interaction between the two groups. This inconsistent behavior suggests intermediacy of a strained conformation (such as structure E) in the elimination of ROH from *trans*-**2**, which enables a proton transfer between the two alkoxycarbonyl groups (Scheme II). The low abundance of MH$^+$ ions in the NH_3-CI mass spectra of *trans*-**2** indicates that the energy of the hydrogen bridging is insufficient to stabilize the highly strained conformation in which the two remote ester groups are brought within the suitably short distance.

Introduction of alkyl substituents at the two α-positions 1 and 3 should significantly increase the strain energy of the intermediate conformation F and thus increase the barrier for the hydrogen transfer between the two alkoxycarbonyl groups. Esters of the stereoisomeric 1,3-dimethylcyclohexane-1,3-dicarboxylic acids *cis*-**4** and *trans*-**4** were prepared in order to determine whether the increase of the strain energy caused by the α-methyl substituent will be sufficient to hinder the hydrogen transfer and consequently suppress the alcohol elimination in the trans isomers. The results of the CI measurements of these stereoisomeric pairs are shown in Scheme III. The behavior of *cis*-**4** is similar to the other *cis*-diesters. *trans*-**4** undergo negligible elimination of ROH under i-Bu-CI and under CID conditions indicating the effect of α-substitution on the strain energy.

α-Substitution by one methyl group is not sufficient for suppression of the hydrogen migration between the two ester groups. Only conformation G with the axial methyl substituent is expected to have a high barrier for the hydrogen transfer, while the other favored conformation H with the equatorial methyl group is similar to the unsubstituted *trans*-**2** (structure E) in this respect. Indeed, *trans*-1-methyl-1,3-bis(alkoxycarbonyl)cyclohexanes *trans*-**5** give rise to abundant [MH − ROH]$^+$ ions under i-Bu-CI and CID conditions (Scheme IV and Tables I, V, and VI).

Conclusion

Results obtained in this work suggest the correlation of the CI and CID behavior of diesters with the distance between the two alkoxycarbonyl groups as a useful way for configurational assignments. When this distance is small, major MH^+ and minor $[M + NH_4]^+$ ions are obtained under NH_3-CI, and high abundance $[MH - ROH]^+$ ions are observed under i-Bu-CI and CID conditions. A large interfunction distance results in formation of major attachment $[M + NH_4]^+$ ions upon NH_3-CI and negligible $[MH - ROH]^+$ under i-Bu-CI and CID. In intermediate cases, such as *trans*-**2** and *trans*-**5**, relatively abundant $[MH - ROH]^+$ are formed upon i-Bu-CI and CID via strained conformations which enable proton transfer between the two ester functions. Formation of major $[M + NH_4]^+$ attachment ions under NH_3-CI from *trans*-**2** and *trans*-**5** indicates that the energy of the strained conformation with a shorter distance between the two ester groups cannot be effectively compensated by hydrogen bridging in a MH^+ ion.

Experimental Section

Mass Spectrometry. CI-GC-MS analyses and CID measurements were carried out on a Finnigan TSQ-70B triple stage quadrupole mass spectrometer. The stereoisomeric pairs were introduced as mixtures (with the exception of **3a**), and separations were performed on a DB-5 (0.25 μm film) 30 m × 0.25 mm (i.d.) capillary column. Temperature was programmed from 60° to 250° at 20 °C/min for materials **1**, **2**, and **3** and at 4 °C/min for the mixtures containing **4**. The scan rate was 1 scan/s. The elution sequences were *trans*-**1** followed by *cis*-**1**, *trans*-**2** by *cis*-**2**, *cis*-**3b** by *trans*-**3b**, and *cis*-**4** by *trans*-**4**. *Cis*-**3a** and *trans*-**3a** had identical retention times and were introduced separately. The elution sequence of the mixtures containing **4** and **5** was *cis*-**4**, *trans*-**2**, *trans*-**5**, *cis*-**2**, *trans*-**4**, and *cis*-**5**.

CI measurements were performed at 150 °C ion source temperature and 0.4 Torr (indicated) reagent gas pressure (isobutane and ammonia). CID measurements were performed with argon as the target gas (0.3 mTorr, indicated) at 30 eV collision energy (indicated). All data presented in each table were obtained on a single day under identical conditions in order to assure reliable comparisons.

Materials. Stereoisomeric cyclohexane-1,2-, 1,3-, and 1,4-dicarboxylic acids from a previous study[1b] were used in this work. Methyl and ethyl esters **1**, **2**, and **3** were prepared by heating the acids with methanol or ethanol in the presence of catalytic amounts of sulfuric acid. 1,3-Dimethyl-1,3-bis(alkoxycarbonyl)cyclohexanes **4** (mixtures of cis and trans isomers) were prepared by methylation of **2** (mixtures of stereoisomers) with iodomethane and lithium diisopropylamide (LDA) in tetrahydrofuran.[4] The monoalkylation products **5** were also obtained in this reaction and were separated by gas chromatography.

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