ORGANIC
LETTERS

2004
Vol. 6, No. 22
3945−3948

Hyperconjugative Effects in the Stereoselective Ring-Opening Reactions of Oxetenoxides

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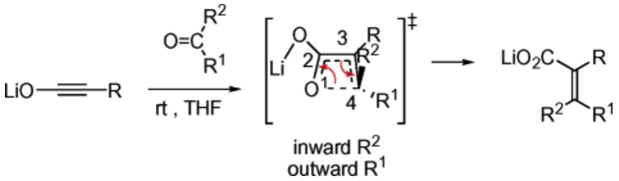
Received July 29, 2004

ABSTRACT

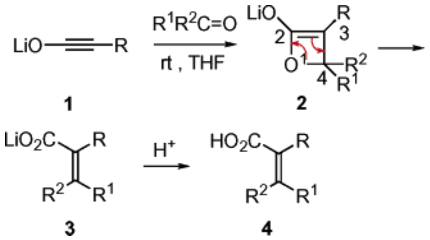


Unexpectedly, the pattern of the stereoselectivity in the ring-opening reactions of lithium oxetenoxides is not consistent with the bulkiness of substituents, and both the bulkier *tert*-butyl and silyl substituents favor inward rotation. With the aid of B3LYP calculations, the hyperconjugative interaction between the breaking C^1–O σ and its *anti*-periplanar Z-Me (Z = Si or C) σ^* orbital is found to be responsible among the secondary orbital interactions of the substituents and the oxetene moiety.

Ring opening of four-membered rings is of particular interest in organic chemistry to control the stereoselectivity in the synthesis of multisubstituted alkenes.[1] Due to the efforts of Houk et al., the stereoselectivity in the ring opening of substituted cyclobutenes can be explained by stereoelectronic effects.[2] Recent studies of the reaction of silyl- and stannylcyclobutenes by Murakami and co-workers suggest that hyperconjugative interaction between Sn−C or Si−C σ^* and the breaking C−C σ orbital is much more responsible for this effect than in the *tert*-butylcyclobutene ring opening.[3−5]

Shindo and co-workers developed highly stereoselective syntheses of multisubstituted alkenes using lithium ynolates and found that the stereoselectivity was controlled by the stereoelectronic effects of the ring opening of lithium oxetenoxides **2** as intermediates (Scheme 1).[6,7]

Scheme 1



Several recent results with substituents on the carbonyl substrates are shown in Table 1.[8] Interestingly, the bulkier

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10.1021/ol048499f CCC: $27.50

Table 1. Experimental Selectivities for Alkenes **4**[7,8]

entry	**2**	R^1	R^2	R	*E*:*Z*
1	**2a**	Me	*t*-Bu	Me	19:81
2	**2b**	Me	*t*-Bu	Bu	1:8
3	**2c**	Me	$SiMe_3$	Me	1:>99

t-Bu group favors inward rotation over the Me group (Table 1, entries 1 and 2). This is different from the trend of the ring opening of *tert*-butylmethylcyclobutene, in which the *t*-Bu group favors outward rotation.[9] Natural bond orbital (NBO) theory[10] is useful to analyze the stereoelectronic effects of conformations and organic reactions.[11] It has been reported that the donating ability of the C−H σ orbital is higher than the C−C and C−O σ orbitals because of its high-lying NBO energy.[12] Therefore, we employed the B3LYP hybrid functional[13] with the 6-31G(d) basis sets[14] for the oxetene intermediate, the transition states (TSs) of the ring-opening process, and the products.[15,16] The normal coordination analyses were performed for stationary points; no imaginary frequency was confirmed at each stable structure, and one imaginary frequency was confirmed at each optimized TS structure. The origin of the stereoelectronic effects of the ring-opening of oxetene derivatives was examined with the aid of NBO analysis.[17] The transition states of the ring opening are reactantlike rather than productlike by the optimal Lewis structure search.

In a series of reactions, the energy differences of the two transition states, **TSE** and **TSZ**, which give the (*E*)- and (*Z*)-isomers, respectively, are summarized in Table 2. **TSZa** is more stable than **TSEa** by 1.8 and 7.2 kJ/mol in electronic and Gibbs free energies, respectively (entry 1), as expected. The larger difference of Gibbs free energies than electronic energies is due to the difference of the vibrational entropies. The preference for (*Z*)-alkene formation in silyloxetenoxides **2c** is larger than that for **2a** (entry 2).

Table 2. Relative Activation Energies ($\Delta\Delta E^\ddagger$) and Gibbs Free Energies of Activation ($\Delta\Delta G^\ddagger$) at 298.15 K of **TSZ** Relative to **TSE** in kJ/mol at the B3LYP/6-31G(d) Level

entry	**2**	R^1	R^2	$\Delta\Delta E^\ddagger$	$\Delta\Delta G^\ddagger$
1	**2a**	Me	*t*-Bu	−1.8	−7.2
2	**2c**	Me	$SiMe_3$	−13.8	−17.8

The TS structures **TSE** and **TSZ** for substrates **2a** and **2c** (entry 4) and representative geometric parameters are shown in Figure 1 and Table 3, respectively.[18] Notably, in the more stable **TSZa**, with the inward *t*-Bu group, the $C^5{-}C^6H_3$ bond length of 1.559 Å is somewhat longer than the other two $C^5{-}CH_3$ ($C^5{-}C^bH_3$ and $C^5{-}C^cH_3$) lengths of 1.538 and

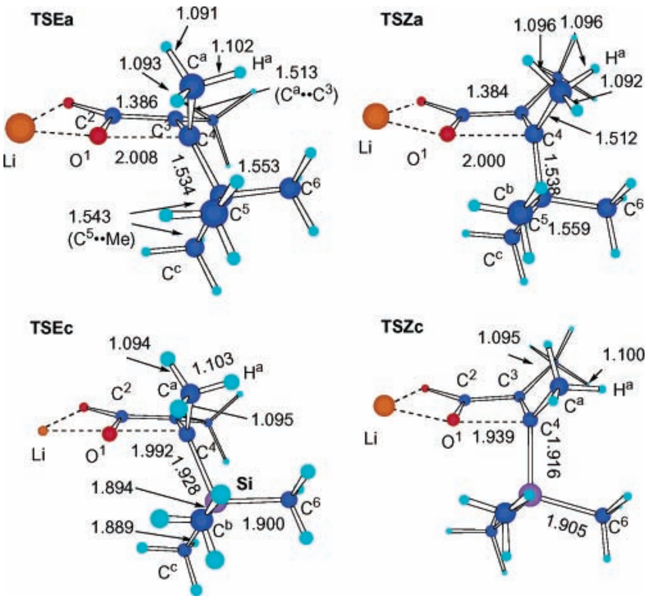

Figure 1. Structures of **TSE** and **TSZ**. Bond lengths are shown in Å.

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(17) *NBO*, Version 5.0, as implemented by Glendening, E. D.; Reed, A. E.; Carpenter, J. E.; Weinhold, F.

(18) Coordination of two Me_2O molecules to the lithium atom does not change the geometries and the relative energies of TSs very much. See Supporting Information.

Table 3. Several Geometric Parameters for **TSE** and **TSZ**[a]

TS	Z−C^6	Z−C^b	Z−C^c	O^1−C^4−Z−C^6H_3
TSEa	1.553	1.543	1.543	170
TSZa	1.559	1.541	1.538	174
TSEc	1.900	1.894	1.889	172
TSZc	1.905	1.895	1.888	174

[a] Distances are shown in Å and dihedral angles in degrees. Z = C or Si.

1.541 Å, respectively. The $O^1-C^4-C^5-C^6H_3$ dihedral angle of 174° indicates that the $C^5-C^6H_3$ bond and the breaking $C^4\cdots O^1$ bond are mutually *anti*-periplanar. In **TSEa**, the C^a-H^a bond length of 1.102 Å at the inward C^aH_3 group is longer than the other two, 1.091 and 1.093 Å. The C^5-C^6 bond length of 1.553 Å is somewhat longer than the others. These results suggest that competition of the interaction with the hyperconjugative $C^4\cdots O^1$ σ bond between the C^aH_3 and the *t*-Bu groups occurs. The C^a-H^a, C^5-C^6, and $Si-C^6$ bonds are stretched in all the transition states in Figure 1.

Second-order perturbation analysis of bonding NBOs and antibonding NBOs was carried out for these transition states. The second-order interaction energy is expressed as follows.

$$E_{\sigma\sigma^*}{}^{(2)} = 2\frac{\langle\sigma|F|\sigma^*\rangle^2}{\epsilon_{\sigma^*}-\epsilon_{\sigma}}$$

Notice that σ/σ^* and F refer to filled/vacant NBO and Fock matrixes, respectively, and that ϵ_σ and ϵ_{σ^*} refer to the NBO energies of the bonding/lone pair and those of antibonding/Rydberg, respectively.

A representation of the orbital interactions is shown in Figures 2 and 3, and the second-order perturbation energies are shown in Table 4. In the case of the reaction of **2a** (X = *t*-Bu, Y = CH_3), the higher stability of **TSZa** is due partly to the differences of 12.1 and 16.4 kJ/mol of the σ (C^2-C^3) ↔ σ^* (C^4-Y) interaction (**A**) and the π (C^2-C^3) ↔ σ^* (C^4-X) interaction (**D**), respectively. These differences are attributed more to the differences of the interaction integrals $\langle\sigma|F|\sigma^*\rangle$ and rather that of the NBO energies $\epsilon_{\sigma^*}-\epsilon_\sigma$ between the C−Me and C−*t*Bu bonds. The opposite trend of the energetic differences ΔE of the TSs is seen in the $\sigma(C^2-C^3)$ ↔ σ^*(C−X) interaction (**B**) and the $\pi(C^2-C^3)$ ↔ σ^*(C−Y) interaction (**C**). The $\sigma(C^4-O^1)$ ↔ σ^*(Z−Me, Z = C) interaction (**G**) in **TSZa** is more stable by 7.7 kJ/mol than that in **TSEa**. The magnitude of the $\sigma^*(C^4-O^1)$ ↔ σ (Z−Me) interaction (**I**) is larger (Table 4), but these results suggest that the C−Me bond in the *t*-Bu group acts as both an electron donor and an electron acceptor. The preference of interaction **I** in **TSEa** over that in **TSZa** is opposite to the actual $\Delta\Delta E^\ddagger$. The preference of the σ (C^a-H^a) bond ↔ σ^* (C^4-O^1) interaction (**J**) in **TSZa** is as large as 12.0 kJ/mol.

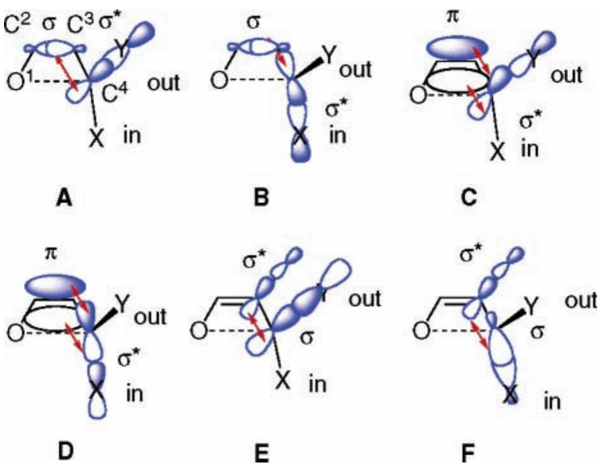

Figure 2. Representative secondary interactions between NBOs in TSs. (X/Y = CH_3, $SiMe_3$). “In” refers to the inward position and “out” to the outward position.

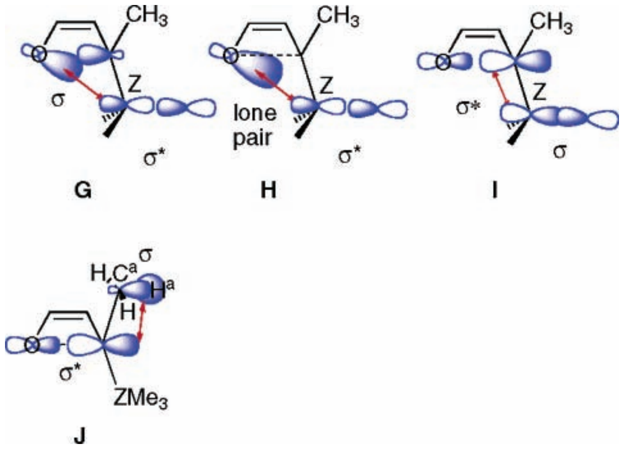

Figure 3. Representative secondary interactions between NBOs in TSs (Z = C or Si).

The NBO analysis was also performed for the ring-opening reaction of the silyl oxetenoxide **2c** (X = $SiMe_3$, Y = CH_3). The largest and the second largest energy preferences of **TSZc** over **TSEc** are the interaction of $n(O^1)$ ↔ σ^* (Z−Me) (**H**) and the σ (C^4-O^1) ↔ σ^* (Z−Me, Z = Si) (**G**) interactions of 14.5 and 9.7 kJ/mol, respectively. The larger secondary interaction energies for **H** in **2c** than in **2a** suggest that the acceptor ability of the Si−C bond is higher than that of the C−C bond. The interaction energies for **I** in **TSEc** and **TSZc** are smaller than those in **TSEa** and **TSZa** (Table 4). As Houk and Murakami proposed in the cyclobutene ring-opening, the interaction of vacant Si orbitals and the breaking O^1-C^4 σ orbital in the silyloxetenoxide ring opening is responsible.[3,4] Both Boys and the natural localized MO analysis[19] give essentially the same conclusion.[8e] The energy of the interaction **B** in **TSZc** of 6.3 kJ/mol is larger than that in **TSZa** of 1.8 kJ/mol, also resulting in a much larger preference of (*Z*)-alkene formation from **2c**, because of its

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Table 4. Second-Order Interaction Energies between NBOs of the Transition States in kJ/mol[a]

TSs	X	Y	Z	**A**	**B**	**C**	**D**	**E**	**F**	**G**	**H**	**I**	**J**
TSEa	Me	tBu	C	0.8	16.4	25.5	14.1	0. 8	6.0	5.1	<0.4	26.8	8.1
TSZa	tBu	Me	C	12.9	1.8	13.8	30.5	5.2	<0.4	12.8	1.5	22.8	20.1
ΔE				12.1	−14.6	−11.7	16.4	4.4	~ −5.6	7.7	~1.1	−4.0	12.0
TSEc	Me	$SiMe_3$	Si	0.7	16.1	25.2	7.3	<0.4	<0.4	5.2	28.7	10.1	0.9
TSZc	$SiMe_3$	Me	Si	12.6	6.3	12.7	14.5	9.0	<0.4	14.9	43.2	6.9	8.6
ΔE				11.9	−9.8	−12.5	7.2	~8.6	~0	9.7å	14.5	−3.2	7.7

[a] Transition state underlined is the more stable of **TSE** and **TSZ**. ΔE refers to the energy difference between **TSZ** and **TSE**.

lower $\epsilon_{\sigma^*} - \epsilon_\sigma$ (lower acceptor ability of a C−C bond than a C−Si bond) and larger $\langle\sigma|F|\sigma^*\rangle$. The difference between the σ ($C^3{-}CH_3$) ↔ σ^* ($C^4{-}Y$) interaction (**E**) and the σ ($C^3{-}CH_3$) ↔ σ^* ($C^4{-}X$) interaction (**F**) is also responsible. The preference of the σ ($C^a{-}H^a$) bond ↔ σ^* ($C^4{-}O^1$) interaction (**J**) in **TSZc** is as large as 7.7 kJ/mol.

Finally, to shed light on the role of the oxygen atom, the ring-opening TSs of 4-*tert*-butyl-1,4-dimethylcyclobut-1-ene were examined (See Supporting Information). The inward rotation of the *tert*-butyl group is preferred by only 0.49 kJ/mol in electronic energy (B3LYP/6-31G(d)). Those results clearly show that more electron-rich oxygen atom in the oxetene system favors more inward rotation of *tert*-butyl group in the cyclobutene.

In summary, the stereoselectivities of the formation of (*E*)- or (*Z*)-alkenes by the reaction of aliphatic ketones with lithium ynolates are in agreement with the energy preferences of the ring opening of the lithium oxetenoxide intermediates. The order of the outward preferences of silyl < *t*-Bu < Me in the transition state do not agree with the size of the substituents. *Even in the ring opening of the alkyloxetenoxides*, as well as in the silyl analogue case, the interaction between a lone pair orbital of O and the Z−Me σ^* orbital (Z = C or Si) and the interaction between the C−O σ and its *anti*-periplanar Z−Me σ^* orbital (Figure 3) are found to be *the most important contributions* among the many secondary orbital interactions on the basis of the semiquantitative NBO analysis.

Acknowledgment. This work was supported by a Grant-in-Aid for Young Scientists (B) and in the Priority Area (A) “Exploitation of Multi-Element Cyclic Molecules” from the Ministry of Education, Culture, Sports, Science and Technology (Mombukagakusho). Generous allotment of computational time from the Institute for Molecular Science, Japan, is gratefully acknowledged.

Supporting Information Available: Cartesian coordinates of stationary points, three-dimensional structures of the reactants, products of the ring opening of **2a** and **2c**, and transition states of the ring opening of **2a** and **2c** with two Me_2O molecules, in addition to the TSs of ring opening of 4-*tert*-butyl-1,4-dimethylcyclobut-1-ene. This material is available free of charge via the Internet at http://pubs.acs.org.

OL048499F