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Chiral Induction in Photochemical Reactions. 14.[1]

Linear Free Energy Relationships as an Instrument for the Prediction of either *de* values or Conformation Energies of the Auxiliary in the Diastereoselective Paternò-Büchi Reaction.

This work is dedicated to G. Büchi on the occasion of his 70th birthday.

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Key Words: Chiral Induction, Paternò-Büchi Reaction, Conformation Energies, Linear Free Energy Relationship

Abstract *- To value a stoichometric asymmetric synthesis it is important for a synthetic chemist to gain information about those structural elements of a chiral auxiliary which are responsible for high diastereomeric excesses in a particular reaction. Furtheron it is desirable to have detailed knowledge about the mechanism of the chirality transfer. In this paper an empirical relation is formulated for the correlation of structural variations of a chiral auxiliary and its influence of the diastereomeric excess in the photochemical oxetane formation in correspondance to the Ugi/Ruch concept. For this purpose we use a Linear Free Energy Relationship (LFER) which we have adjusted to reaction (2) in order to obtain quantitative information about the selectivity of this reaction on the basis of special parameters of the auxiliary applied.*

Introduction:

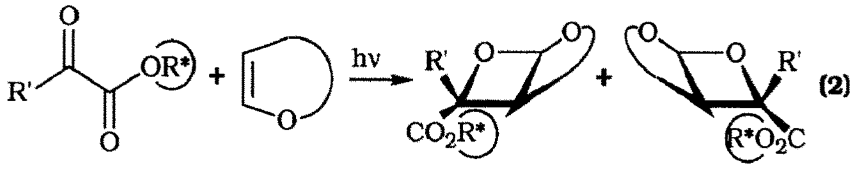
Generally a Linear Free Energy Relationship is a correlation between rate or equilibrium constants (or related parameters which describe the kinetic - or thermodynamic behaviour of a series of systems (reaction partners) of a definite reaction with other quantities which have been determined by other reactions.[2] Such an empirical correlation[3] corresponds to the general Equation (1).[4]

$$P_i = a \cdot Q_i \qquad (1)$$

$\mathbf{P_i}$ represents the property of a system under the influence of a factor **i**, whereas $\mathbf{Q_i}$ is a characteristic figure of its respond on **i**. **a** is a specific proportionality factor. Other examples which obey the Relation (1) are for instance the *Brönstedt*[5] or the *Hammett* relation.[6]

For the diastereoselective Paternò-Büchi reaction[7] according to (2)[8,9,11] a Hammett-analogous relation was observed, when phenyl substituted-phenylglyoxylates of type **1** were converted photochemically with furan **3** as the olefinic partner. The logarithmic parameters of selectivity $(k/k')(k_H/k'_H)$ for this reaction correlate with the σ-Hammett constants of the *para* substituents R" of phenyl group.[10]

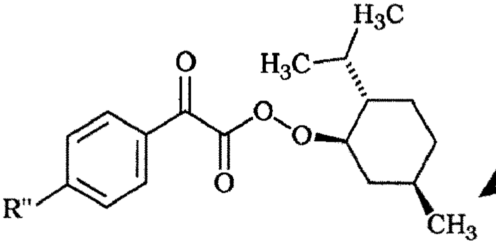
However a corresponding relation for the auxiliary Ⓡ* in (2) is not observed, if *para* substituted *trans*-2-phenylcyclohexanols of type **2** are used as chiral auxiliaries.[11]



(2)

8 **10** **10'**

R* = chiral Auxilary



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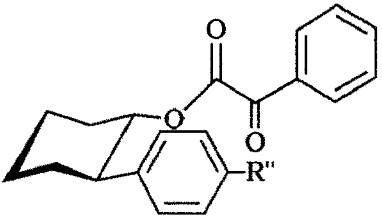


2

The comparison of the auxiliary structure of the cyclohexanol derivatives shows no correlation of the selectivities with the stereic demand of the shielding substituents.[9,11] According to common conceptions a steric anlargement of the auxiliary should favour for high diasteremeric excesses in agreement with the "*concave/convex-model*" of *Helmchen* and *Schmierer*[9,12], but however very often the contrary happens.

This is demonstrated by the dependence of the diastereoselectivities from the auxiliary structure and the olefinic partner in the investigated reaction (2) (Table 1).

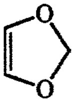
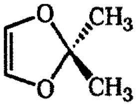
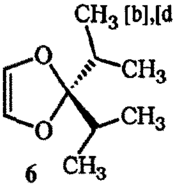
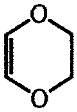
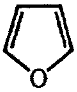
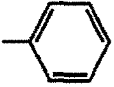
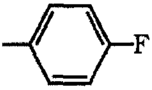
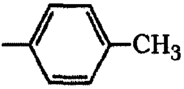
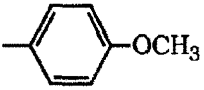
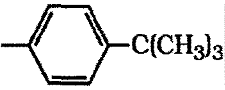
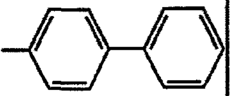
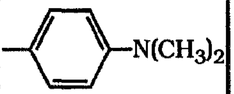
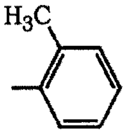
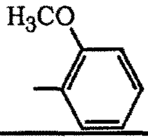
Conformation Energies of Substituted Cyclohexanols

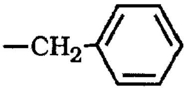
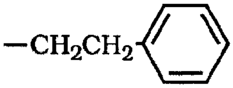
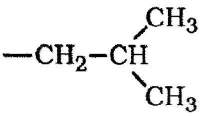
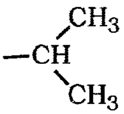
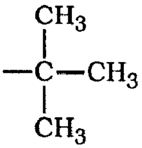
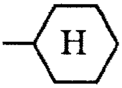
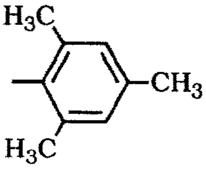
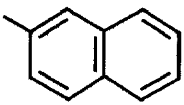
To find a Linear Free Energy Relationship between structural parameters of the cyclohexanol auxiliaries and the selectivities of the reaction we tried to correlate the free enthalpy of activation $\Delta G^{\neq}$ of a system to the free enthalpy $\Delta G°$ of the ground state conformers according to Equation (3).[4]

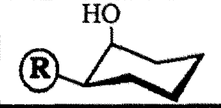
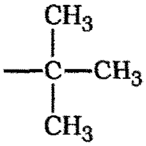
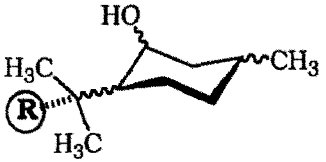
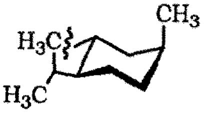
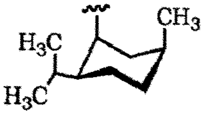
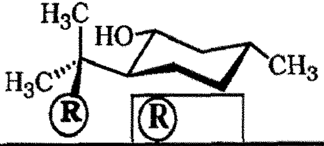
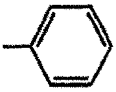
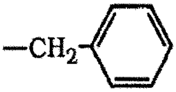
$$\delta\,(\Delta G^{\neq}) = \rho \cdot \delta(\Delta G^{\circ}) \tag{3}$$

The operator δ describes the influence of the substituent variation in Equation (3). The differences of free enthalpies of activation for the Reaction (2) on the basis of the product ratio of the diastereomeric oxetanes for a given temperature are available by $\Delta\Delta G^{\neq}$ values.[8,9,11]

Table 1: Diastereoselectivity in terms of % *de* values[a] for the photochemically oxetane formation (2), if chiral phenylglyoxylates are added to olefines of type **8** (T = 14°C).

Ⓐ		***trans*-2-substituted cyclohexanols[a]**				
No.	 **8** —Ⓡ	***de* value (%)**				
		[b],[d]  **4**	[b],[d]  **5**	[b],[d]  **6**	[b],[e]  **7**	[c],[e]  **3**
1		**49,8**	**56,4**	**52,4**	**67,0**	**65,4**
2		**40,7**	**39,8**	**35,6**	**40,4**	**50,8**
3		**45,4**	**46,0**	**42,6**	**52,4**	**59,4**
4		**28,2**	**55,0**	**43,1**	**71,0**	**63,6**
5		**49,6**	**51,2**	**47,4**	**61,0**	**72,6**
6		**43,1**	**42,0**	**37,2**	**49,2**	**59,8**
7		**no reaction**				
8		**53,8**	**52,2**	**55,2**	**60,9**	**68,6**
9		**53,2**	**53,8**	**41,9**	**63,8**	**65,0**

10	$-CH_3$	35,6	41,8	25,2	41,4	44,2
11		45,7	48,7	22,0	44,1	52,1
12		39,2	39,1	31,4	48,6	50,8
13	 $-CH_2-CH(CH_3)_2$	35,6	38,6	19,0	39,2	47,6
14	$-CH_2CH_2CH_2CH_3$	36,8	43,2	23,4	43,6	46,4
15	 $-CH(CH_3)_2$	48,4	59,1	27,8	60,1	59,0
16	 $-C(CH_3)_3$	91,0	92,0	90,6	95,4	95,6
17		45,8	49,3	14,2	51,8	51,4
18		38,3	39,8	28,2	51,2	61,8
19		33,8	40,4	33,4	53,0	41,0
20	—Cl	32,4	23,8	29,5	36,0	42,8
21	—Br	—	29,4	40,0	43,0	48,8

Ⓑ	Ⓡ 	**cis-2-substituted cyclohexanols**				
22	$—CH_3$	—	25,6	18,3	24,2	24,6
23	 $—\overset{CH_3}{\underset{CH_3}{C}}—CH_3$	81,6	90,8	81,4	93,9	94,4
Ⓒ		**configuration isomers of the menthol type**				
24		48,2	56,8	26,8	58,1	58,5
25		22,1	22,8	21	22,1	24,5
26		24,5	26	23,4	28,6	25
27		25	21,4	25,6	19,6	20
Ⓓ		**menthol and 8-substituted mentholderivatives**				
28	$—CH_3$	—	92	83,6	95,6	94,8
29	$—CH_2CH_2CH_2CH_3$	—	90	87,8	90,9	94,4
30		90	> 96	90	> 96	> 96
31		—	95	—	—	—

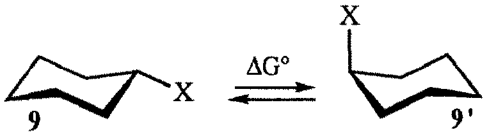
[a] The ratio of diastereomers is derived from the ^{13}C-NMR spectra of the oxetane mixture; [b] for the photochemically addition to olefines 4-7 benzene as solvent was used; [c] in the case of furan^3 the olefine itself was used as solvent; [d] irradiation time 6 hours; [e] irradiation time 15 hours (mercury high pressure lamp: Philips HPK 125).

Generally molecules exist in different conformers .Thus the conformation energy[13] seems to us to be a suitable figure for the representation of the ground state enthalpy ΔG° which would characterize the influence of the auxiliary in a certain sence. A conformation of a molecule designates the alteration of its structure by simply rotation around single bonds.[13a]

Monosubstituted cyclohexanols exist as two stable conformers which are distinguished by either axial or equatorial positions of a substituent. They interchange easily by rotation of single bonds, weak deformation of bond angles and by subduing torsional stress of hydrogen atoms. The two chair conformations **9** and **9'** are discriminated by a considerable amount of energy depending whether the substituent X is in an axial or in an equatorial position, however. *Eliel*[13a] defines in general the conformation energy of a cyclohexanol derivative as the free energy ΔG° of a conformer relative to the item of lowest energy.

For example the negative value of the free energy ΔG° for the equilibrium **9**/**9'** is the conformation energy of the axial conformer **9'**. These energy values are available in literature at least for monosubstituted cyclohexanol derivatives (Table 2).[14]

Table 2: Conformation energies[a] (changes of free enthalpie in the axial/equatorial equilibrium of mono substituted cyclohexane derivatives **9**/**9'** in aprotic solvents).



X	$-\Delta G^\circ$ / $\mathrm{kJmol^{-1}}$	X	$-\Delta G^\circ$ / $\mathrm{kJmol^{-1}}$
F	0.63	Ph	125.40
Cl	1.80	*cyclo*-C_6H_{11}[34]	9.20
Br	1.57	OH	2.17
I	1.80	OAc	2.51
CN	0.71	OCH_3	2.51
CH_3	7.11	OCH_2CH_3	3.72
CH_2CH_3	7.35	OTs	2.09
$CH_2CH_2CH_3$[34]	8.79	SH	3.76
$CH_2CH_2CH_2CH_3$[34]	8.79	SCH_3	2.93
$CH(CH_3)_2$	8.99	SPh	3.34
$C(CH_3)_3$	50.20		

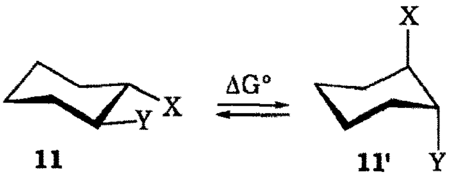
[a] Literature data ("*the best values*" determined by different methods) taken from *Ref.* 14 if not otherwise noted.

It is obvious from Table 2 that conformation energies mainly depend on the atom of a substiuent which is directly linked to the cyclohexanol ring.[13a] Consequently cyclohexanol derivatives having substituents like: OH, OAc, OCH_3, OCH_2CH_3or OTs resamble in their conformation energy. The same is true for derivatives having groups like: SH, SCH_3, SPh, respectively CH_3, CH_2CH_3, $CH(CH_3)_2$.

As long as the direct linked atom carries at least one H-atom respectively an electron lone pair the syn-axial repulsion does not increase. If the *tert* butyl group is in an axial position in any case one methylgroup of it is directed towards the middle of the ring. Consequently its repulsion potential with syn-axial H-atoms increase considerably. This explains the strong aversion of the *tert* butyl group of a cyclohexane ring to occupy an axial position (anchor function of a *tert* butyl group).[15,16] The collected values in Table 2 represent the differences in free enthalpy. There are only a few investigations known which give information about the share of these values in terms of enthalpy and entropy. An entropy differences is certainly expected for unsymmetric substituents. For instance the differences in ΔG° values for methyl, ethyl and *iso* propyl cyclohexane is completely reduced to entropy differences.[17]

What about the conformation energy of multisubstituted cyclohexanes? For the first approach *Eliel* assumes, that the conformation energies behaves additively.[13a] The conformative behaviour (4) of *trans*-1,2-disubstituted cyclohexanes **11** demonstrates the preferential occupation of the bisequatorial position. This can be additionally stabilzed or destabilized by *gauche*-interactions of X and Y considerably.[18,19]

According to *Zefirov* [19] the total conformation energy ΔG° of the *trans*-1,2-disubstituted cyclohexanes constituents is composed additively of the free enthalpy of the conformation equilibria of the corresponding monosubstituted cyclohexanes ΔG°_x and ΔG°_y according to Equation (5) considering also the *gauche*-interaction $\Delta G^\circ_{x/y}$ of the substituents in the bisequatorial position **11**.[20]



11 **11'** (4)

$$\Delta G^\circ = \Delta G^\circ_x + \Delta G^\circ_y + \Delta G^\circ_x{}_{/y} \qquad (5)$$

In the case of repulsion the energy of *gauche*-interaction becomes positiv. It is negativ, if attraction between the substituents occur (e.g. in the case of strongly electronegative substituents). The determination of *gauche*-interactions is however very difficult to achieve. Therefore it has been executed for a few examples only. Since the conformation energy of the applied auxiliaries (Table 1) were unknown, we used the additivity principle for their calculation as the first approach.

The phenylglyoxylate residue of the auxiliaries in Table 1 is the unchanged structural feature of this compounds, so its *gauche*-interactions with the adjacent substituents (axial or equatorial) will certainly be in a comparable order of magnitude. This allows us to compare the conformation energies with each other.[13a] In Table 3 we present these energies which have been calculated by the additive procedure. Instead of the unknown conformation energy of the cyclohexylphenylglyoxylate we used the ΔG°- value of the acetate residue[14] because of the same primarily to the ring linked atom. Therefore the conformation energy difference of the cyclohexylesters should be low.[13a] The influence of temperature and solvents on the ΔG° term has been neglected.

Consequently the values in Table 3 have the character of standardized relative figures with the advantage to be comparable.

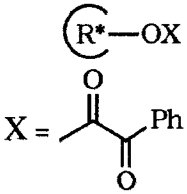
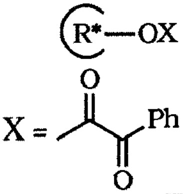
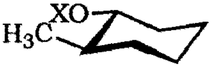
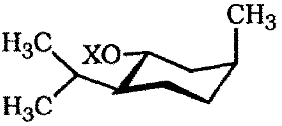
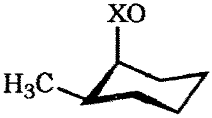
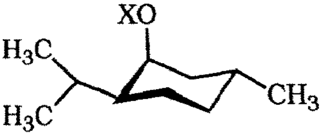
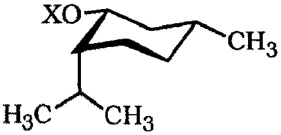
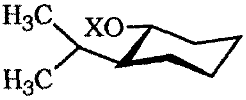
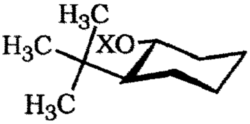
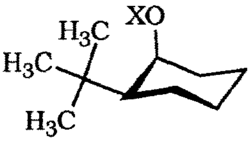
The ($\Delta\Delta G^{\neq}/\Delta G^\circ$)-Relation for the Diastereoselevtive Paternò-Büchi Reaction

The ΔG°-values of the auxiliaries, determinated according to this procedure and summerized in Table 3 yield for a given olefin **4**-**7** at constant temperature in the -$\Delta\Delta G^{\neq}$/-ΔG°-diagram a linear plot which is demonstrated for 2,2-dimethyl-1,3-dioxol **5** as a typical olefinic partner for T = 14°C in Scheme 1.

From this diagram which reflects the influences of the olefinic partners as well as the reaction conditions the intercept reveal the $\Delta\Delta G^{\neq}_0$ value and the ρ constant is evaluated from the slope. For the olefines **3**-**7** the values have been summerized in Table 4.

The induced absolut configuration of the major oxetane depends on the configuration of the C-atom of the cyclohexane ring carrying the OH-group.[11,21] Consequently a factor "a" is defined +1 for (1*R*) configurated auxiliaries and -1 for cyclohexane derivatives with (1*S*)-configuration.

Table 3: Conformation energies ΔG°[a] for the auxiliaries with cyclohexane structure applied in the photochemical oxetane formation (2).

	$\frac{-\Delta G^{\circ}}{kJmol^{-1}}$		$\frac{-\Delta G^{\circ}}{kJmol^{-1}}$
	**10.30**		**4.70**
	**4.30**		**13.3**
	**11.80**		**1.30**
	**12.00**		**15.60**
	**12.00**		**4.60**
	**53.00**		**4.80**
	**47.00**		**19.20**

[a] The ΔG° values are composed of literature data shown in Table 2 according to the additivity-principle ($\Delta G^{\circ} = \sum a_i \Delta G^{\circ}_i$, $a_i = +1$ for equatorial substituents X and $a_i = -1$ for axial groups X of the most stable chair conformation); *gauche* interactions described by *Zefirov*[19] are neglected. Instead of the ΔG°_i-value for the phenylglyoxylate substituent the conformation energy of the acetate is used.[14] The temperature and solvent dependencies of the ΔG°-term are neglected too.

Thus a Linear Free Energy Relation (Equation (6)) can be formulated for the stereoelectronic influences of substituents on the cyclohexane auxiliaries. This is in accordance with the *Ugi/Ruch* model.[35]

$$\Delta\Delta G^{\neq} = a\,(\rho \cdot \Delta G^{\circ} + \Delta\Delta G^{\neq}_{0}) \qquad (6)$$

$$a = \begin{cases} -1, \text{ for } (1R) \text{ configurated cyclohexanols} \\ +1, \text{ for } (1S) \text{ configurated cyclohexanols} \end{cases}$$

Scheme 1: ($-\Delta\Delta G^{\neq}$/$-\Delta G^\circ$)-Diagram for the reaction of phenylglyoxylates of substituted cyclohexanols with 2,2-dimethyl-1,3-dioxol **5** in benzene at T = 14°C.[11]

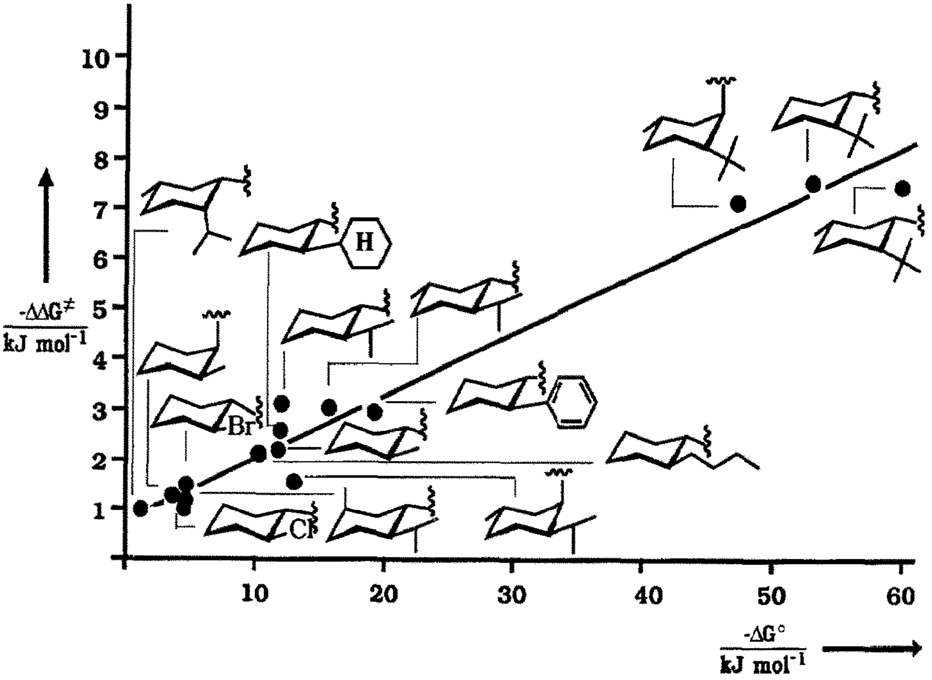
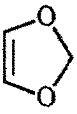
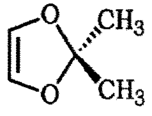
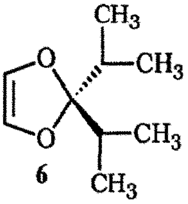
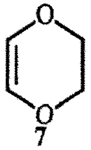


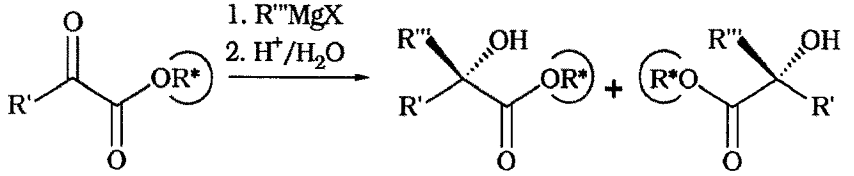
Table 4: The $\Delta\Delta G^{\neq}_0$- and ρ-values for a given olefine derived from the corresponding $\Delta\Delta G^{\neq}$/ΔG°-diagram.

 8	 4	 5	 6	 7	 3
ρ	0.11	0,13	0,12	0,15	0,15
$-\Delta G^{\neq}_0$ / kJmol^{-1}	0,87	0,87	0,36	1,01	1,11

According of this relation $\Delta\Delta G^{\neq}$ is a function of $\Delta\Delta G^{\neq}_0$ and ΔG° (7).[36]

$$\Delta\Delta G^{\neq} = f\,(\Delta G^\circ, \Delta\Delta G^{\neq}_0) \qquad (7)$$

Scheme 2 demonstrates the derivation of the relevant parameters of Equation (6) for the Paternò-Büchi reaction. Principally this procedure should be extended also to other reactions as far as diastereoselectivity in a stoichometric asymmetric synthesis is induced by a chiral auxiliary of the cyclohexane typ . The atrolactinat formation (8)[11,22,23] is a further example in this line.[37]



(8)

With the reaction specific parameters ρ and $\Delta\Delta G^{\neq}_0$ and subsequent application of Equation (6) the extent of diastereoselectivity and the direction of chiral induction should be calculable as far as the conformation energies, the olefine and the reaction conditions are known. On the other hand Equation (6) and Reaction (2) can be applied for the calculation of an unknown conformation energy $\Delta G°$ of a mono substituted cyclohexane auxiliary .

Beside numerous spectroscopic and kinetic methods for the determination of conformation energies it is now possible to use additionally a selectivity parameter of a stereoselective reaction.

In Table 5 we have collected the hithero unknown ΔG^0-values for monosubstituted cyclohexane derivatives which we have evaluated with Equation (6). The items in Table 5 are averages resulting from independent determinations for the olefines **3-7**. As published data from Table 2 were used as basis for calculated values, both data sets are comparable.

Additionally an electronic influence on the conformation energies is observed, since steric interactions remain more or less unchanged. However, the steric effect seems to be large enough that a Hammett relationship is not obtained.

Furthermore the increase of the steric interaction for the mesityl- and naphthyl substituents compared to the phenyl residue is evident. If one compares the similar conformation energies of the benzyl, 2-phenylethyl and *iso* butyl group with each other, again the dominance of the atom primarily linked to the cyclohexane ring becomes obvious.

In line with the $\Delta\Delta G^{\neq}/\Delta G^0$-correlation one can conclude that the selectivity of the Reaction (2) exhibits not a simple functionality of the sterical properties of the shielding group but is essentially determined by intermolecular stereoelectronic effects in the auxiliary - as it definitely should be expected.

Origins and Reasons for Selectivity Control Caused by Conformational Influence of the Auxiliary

The product ratio is either influenced by the population of conformers in the educts or by those in the reactive intermediates within a chemical reaction.[24, 25, 26, 27] For the former there are only a few examples known, however. As an example *Still* and *Jalynker* [28]described the educt conformation controled selectivity in the kinetically controled hydrogenation of macrocyclic exo-methyleneketones. The basis of their arguments is a quantum mechanical study of equilibria of educt conformations. In the vast number of kinetically controled stereoselective reactions in the ground state the *Curtin-Hammett* principle[24, 26]is valid. This principle affirms that the major product is formed via the transition state of the lowest energy. The principle explains, why the prefered conformation of an educt is not necessarily its most reactive one. If the free enthalpy of activation is much higher than the energy of conformation interchange for the educt, the prediction of the product ratio on the basis of the prefered educt conformation is no more possible. This is expected for most reactions.

Photochemical and photophysical processes should be typical examples for application of the *Curtin-Hammett* principle, because in this cases the excitation energies are much larger than the energy of activation for conformation interchange. Nevertheless, examples are known, where different photoreactions result from different educt conformations.[29, 30]

A proved example has been investigated by *Havinga*.[31] It is the photocyclzation of 1,3,5-hexatriene derivatives. Further arguments have been collected by *Lewis* and *Johnson* (*"Can Molecular Conformation Control Photochemical Behavior ?"*).[32] If two conformers **A** and **B** according Equation (9) would lead to two different photoproducts **X** resp. **Y** one can discuss two borderline cases.

$$\begin{tikzcd}
 & A^* \arrow[r, shift left, "k^*_{AB}"] \arrow[dl, "k_A"'] & B^* \arrow[l, shift left] \arrow[dr, "k_B"] & \\
X & & & Y \\
 & A \arrow[uu, "h\nu"] \arrow[r, shift left, "k_{AB}"] & B \arrow[l, shift left] \arrow[uu, "h\nu"'] &
\end{tikzcd} \tag{9}$$

Due to the Franck-Condon principle the population of A* and B* is first determined by the population of the conformers A and B in the ground state and by the extinction coefficients of each one.

Scheme 2: Schematic presentation of the derivation of **a**, $\Delta G°$, $\Delta\Delta G^{\neq}_0$ and ρ in Equation (6). $\Delta G°$ and **a** are specific constants of the auxiliary. $\Delta G°$ is compares of literature data[14] according to the additivity-principle ($\Delta G° = \Sigma a_i\, \Delta G°_i$). **a** may be derived empirically from comparative considerations of the structure of the auxiliary and the absolute configuration of the major diastereomer: **a** = +1 if the auxiliary is (1*R*)-configurated (oxetane **10** is the major diastereomer), **a** = -1 if the auxiliary is (1*S*)-configurated (oxetane **10'** is the major diastereomer). $\Delta\Delta G^{\neq}$ is deduced from the product ratio ($\ln(k/k') = -RT\,\Delta\Delta G^{\neq}$, $k/k' = [\mathbf{10}]/[\mathbf{10'}]$ for $k>k'$). The olefinic partner, the temperature and further reaction conditions keep constant. From the $\Delta\Delta G^{\neq}/\Delta G°$-plot the reaction specific parameters $\Delta\Delta G^{\neq}_0$ and ρ are derived. They depend on the reaction conditions and the olefinic partner. The product ratio can be predicted, if the $\Delta G°$ is known. On the other hand the de values can be used to determin the conformation energy $\Delta G°$ of mono substituted cyclohexane derivatives with substituents **X**.

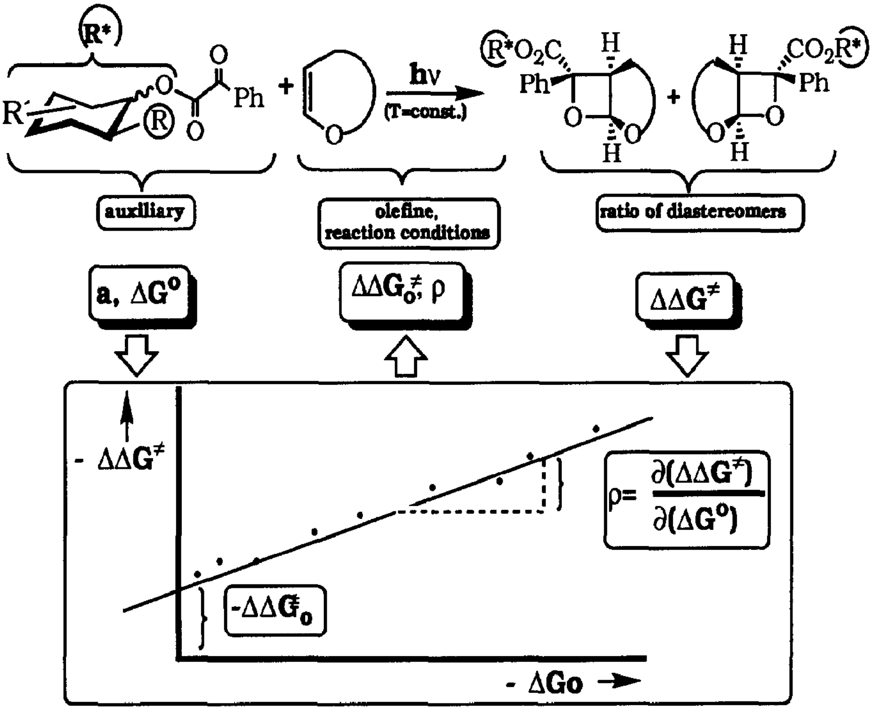
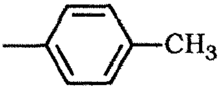
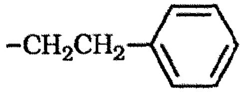
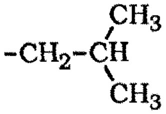
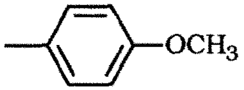
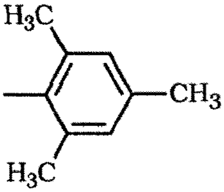
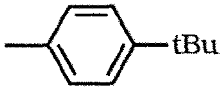
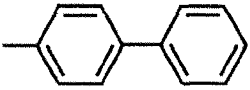
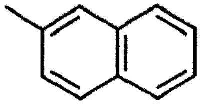
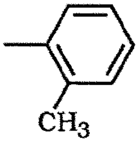
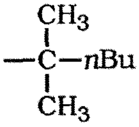
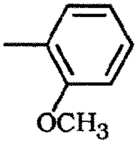
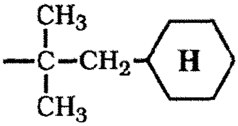
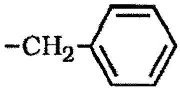
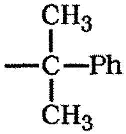


Table 5: The ΔG°-values [a] for monosubstituted cycohexane derivatives with a substituent X derived from Equation (6) because of the determined de values in the photochemical oxetane formation (2).

X	$\frac{-\Delta G^{\circ}}{kJmol^{-1}}$	X	$\frac{-\Delta G^{\circ}}{kJmol^{-1}}$
	6.7 ± 1.5		6.8 ± 1.0
	10.3 ± 2.0	 $-CH_2-CH(CH_3)_2$	4.3 ± 1.0
	11.7 ± 3.0		7.8 ± 1.5
	14.0 ± 2.0		
	8.9 ± 1.5		6.2 ± 2.0
	14.9 ± 3.0	 $-C(CH_3)_2-nBu$	37.2 ± 4.0
	12.4 ± 2.0		50.4 ± 4.0
	7.3 ± 2	 $-C(CH_3)_2-Ph$	60.3 ± 2.0

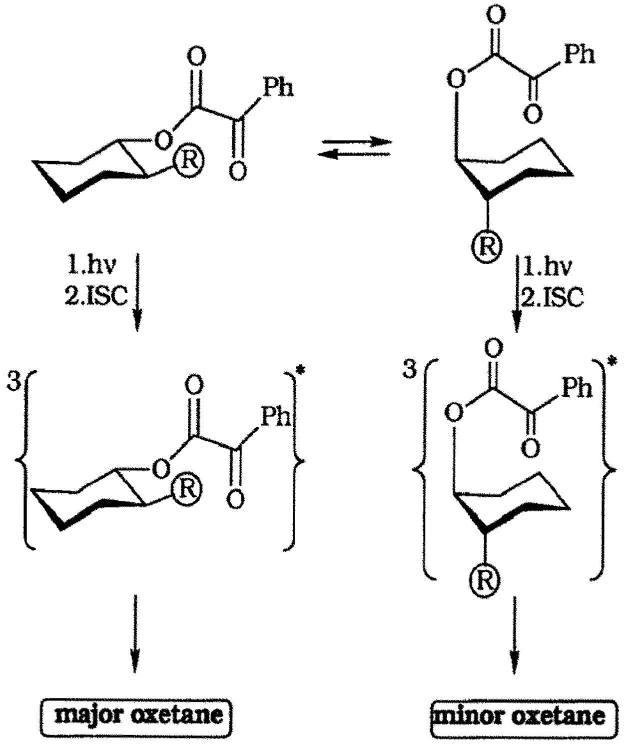
[a] The given ΔG°-values are averages, which are confirmed by independent determinations for the olefines **3-7**

In the first case the conformation barrier $(\Delta G^{0}_{AB})^{*}$ in the excited state is lower than the energy of activation for the formation of the products X and Y ($k^{*}_{AB} >> k_A, k_B$). The *Curtin-Hammett* principle is valid since the product distribution is determined by the difference of the energies of activation for the products X and Y.

In the second case the energy of activation of the equilibrium of the conformers A*/B* is higher as the energy of activation for the formation of the products X and Y ($k^{*}_{AB} < k_A, k_B$). In this case the product distribution is determined by the relative population of the conformers A* and B*. The lifetime of the latter can be naturally different.

The $\Delta\Delta G^{\neq}/\Delta G^{0}$-correlation doesn't imply, that the diastereoselectivity is directly controled by the ground state conformation equilibrium, because this conformation ratio doesn't determine the *de* value in the oxetane mixture. The observed $\Delta\Delta G^{\neq}/\Delta G^{0}$- correlation means at least, that a certain of relation between the conformation energies of the auxiliary and the observed ratio of diastereomers in the product exists.The conformations can influence the product ratio on different levels of diastereoselection.

Scheme 3



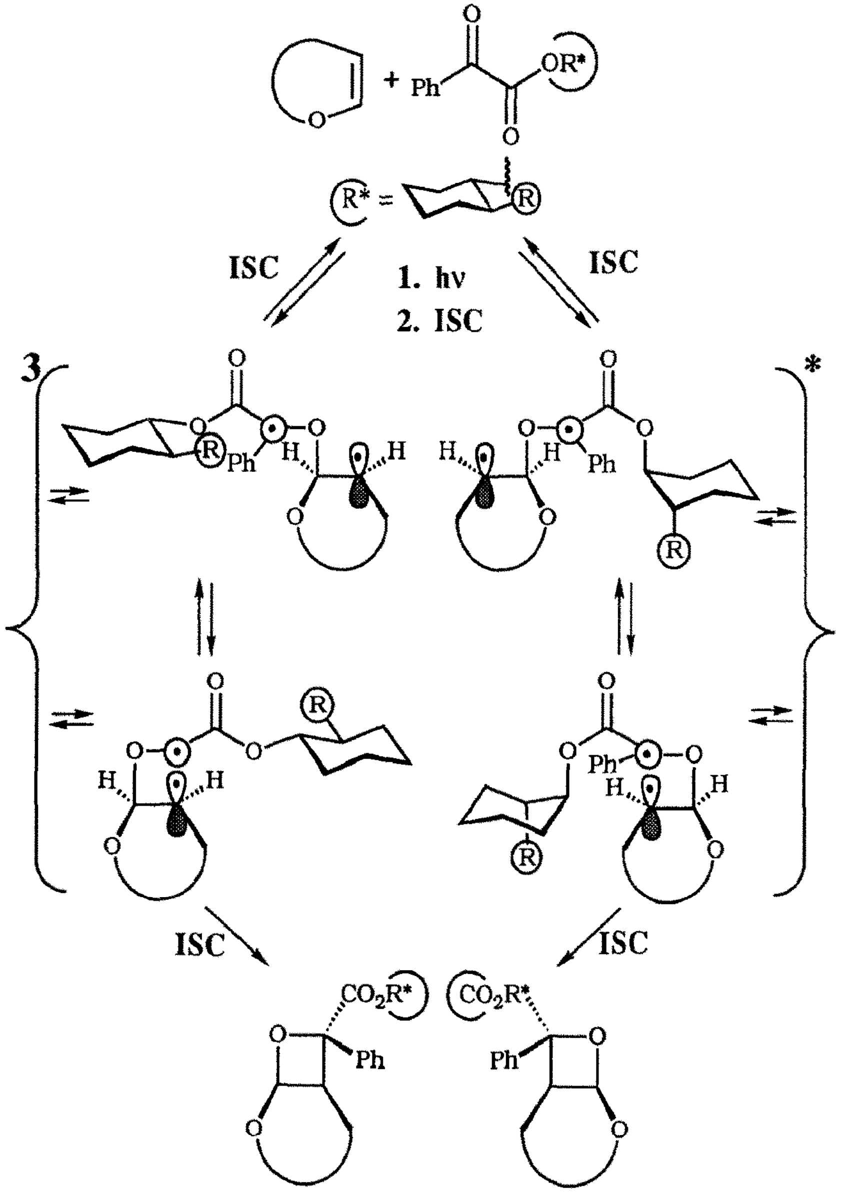
In line with the classification of *Lewis* and *Johnson*[32] the photooxetane formation is thus assigned to the first case if only the overal process is considered - this means that a fast equilibration of conformers and the determination of the product ratio by the differences of activation energies of the subsequent processes exists.

If one discusses the selection mechanism in terms of the *Isoinversion Principle*[8,9] the influence of the auxiliary conformations can take place either on the first level (formation of the 1,4-biradical intermediates) or on the second level (retrocleavage of the biradical intermediates). Since the population of auxiliary conformations is not directly reflected in the ratio of the oxetane diastereomers, the influence on the first level of selection according to Scheme 3 is of minor importance. This is a supplementary hint for the assumption that the *Curtin-Hammett* principle is not violated.

A control of the cyclisation/retrocleavage ratio on the level of the triplet biradicals by the conformation energies of the auxiliaries is much more likely (Scheme 4). This may happen through the control of biradical conformations by the auxiliary which means that conformers which are energetically unfavorable for ring closure to the relevant oxetane better split into the educts whereas the favourable conformations of the biradicals easier undergo ring closure. Alternatively the influence of auxiliary conformations at the lavel of the 1,4-biradicals can also be discussed in that way that intermediates with bisequatorial conformers preferentially split into the educts (*stereoelectronic gauche effect*), which also would explain that selectivity is produced.

The dominance of these both alternatives may possibly be temperature dependent.

Scheme 4: Conformation control of the auxiliary in the triplett 1,4-biradical intermediates as a consequence of stereoelectronic regulation of the cyclization/retrocleavage ratio for the case of *trans*-2-substituted cyclohexanol auxiliaries. The bisequatorial auxiliary conformation favors a cisoid 1,4-biradical conformation, which predominantly gives oxetanes. In this case the bisaxial auxiliary conformation favors the transoid geometry of the 1,4-biradical intermediate, which predominently undergoes retrocleavage. Alternatively the bisequatorial auxiliary conformation may also favor the retrocleavage of the 1,4-biradical. In this case the selection is increased by efficient retrocleavage.



Conclusion

We could demonstrate that diastereomeric selectivities of the stoichometric asymmetric Paternò-Büchi reaction can be projected to structural items of an auxiliary of the cyclohexane type via a Linear Free Energy Relationship. Now, we are able to predict either *de* values or conformation energies of the auxiliary.

A more detailed investigation of the corresponding influence of enthalpy resp. entropy on the basis of the *Isoinversion Principle*[9] is possible and would give more detailed insight in the selection mechanism of this reaction. Further studies are on the way.

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3. It is an common rule in organic chemistry that similar systems act in similar ways. This principle was already clearly formulated in organic chemistry in the middle of the 19th century. See, for instance: Kekulé, A., *Lehrbuch der Organischen Chemie*, Band 1, pp 124-132; Verlag von Ferdinand Enke: Erlangen 1861.
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36. The dependence of the $\Delta\Delta G^{\neq}$ term on $\Delta\Delta G_0^{\neq}$ and ΔG^0 is comparable to empirically deduced *Marcus* equation (see *Ref.* 5b,c).
37. For $R''' = CH_3$ and $T = O°C$: $\rho = 0.08$, $-\Delta\Delta G_0^{\neq} = 0{,}25$ kJmol^{-1} (further reaction conditions see *Ref.* 23).