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Torquoselectivity in the electrocyclic ring-opening of cyclopropyl anions

Olalla Nieto Faza[a]*, Carlos Silva López[a], Adán B. González-Pérez[a], Martín Pérez-Rodríguez[a] and Ángel Rodríguez de Lera[a]*

Ring-opening reactions of substituted cyclopropanes are a convenient synthetic method for the preparation of functionalized alkenes. The Woodward–Hoffmann-DePuy rule governs the selectivity of the cationic process, as exemplified by the solvolysis of substituted halocyclopropanes but, although the reaction has been studied in detail, the torquoselectivity in the ring-opening of cyclopropyl anions has never been addressed. In this work, we use DFT calculations to study the two Woodward–Hoffmann allowed ring-opening paths available to cyclopropyl anions with different substitution patterns. We find that the reaction proceeds with torquoselectivity, evaluate the applicability of Houk's model to explain the effect of the substituents in the product distribution and correlate this effect with the aromaticity of the corresponding transition states. Copyright © 2008 John Wiley & Sons, Ltd.

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Keywords: torquoselectivity; electrocyclization; cyclopropyl anions; substituent effects; density functional theory

INTRODUCTION

Ring-opening reactions of substituted cyclopropanes are a good synthetic method to obtain functionalized alkenes. The application of the Woodward–Hoffmann–DePuy rule[1–3] leads to complete control of the geometry of the resultant alkene in the solvolysis of substituted halocyclopropanes, a cationic process. A number of papers have addressed in detail the mechanism of the parallel anionic ring-opening reaction[4,5] not without some degree of controversy regarding the Woodward–Hoffmann rules binding/defying nature of these reactions.[6,7] However, to this day, the issue of torquoselectivity (the preference for one of the two allowed rotations of the substituents in an electrocyclic reaction) has not been addressed. The finding of torquoselectivity and the extension to these systems of the predictive power available for the cationic reaction would be of great interest, resulting in a wide scope of synthetic possibilities.

Based on precedents on the solvolytic ring openings of substituted halo or tosyl-cyclopropanes,[3,8] and our previous work on conrotatory ring-opening reactions of cyclopropyl anions,[7] we set out to assess the substituent effects on this reverse electrocyclization.

The extensive work of Rondan and Houk on the preference for one of the two symmetry allowed paths in the electrocyclic ring-opening of C_3 substituted cyclobutenes first established the electronic, rather than steric, origin of this selectivity: electron donors tend to rotate away (outwards) from the breaking bond in order to avoid destabilizing four-electron two-orbital interactions, and conversely, strong electron acceptors rotate inwards (even overcoming "incredible steric odds"),[9] resulting in stabilizing two-electron two-orbital interactions.[10–20] The effect of substituents on the course of electrocyclizations, thus rationalized and systematized, was extended to systems other than cyclobutenes, such as the ring-opening reaction of cyclobutenones,[15] the pentadienyl cation cyclization,[16,17] the electrocyclic ring-opening of azetines, oxetenes and tietenes,[21] the opening of cyclopropenes,[22] or the ring opening of aziridines and oxiranes.[23] In longer chain systems, such as the cyclooctatetraene[24] ring-closure, however, the substituent effects are modest and not correlated with their donor or acceptor properties. A similar example on the electrocyclic reactions of polyenes points toward the loss of torquoselectivity in large systems: while there is a strong preference for inwards rotation of the terminal nitrogen in the $4\pi e^-$ and $6\pi e^-$ systems, there is barely any selectivity in the $8\pi e^-$ electrocyclization.[19]

Since there are also other examples where torquoselectivity is achieved through more specific and sometimes subtler interactions such as (hyper)conjugation,[17,25] steric effects or frontier orbital interactions, the extrapolation of these rules to the ring-opening of cyclopropyl anions is not straightforward.

In the disrotatory solvolytic ring-opening of halocyclopropanes the geometry of the product is solely dependent on the configuration of the center supporting the leaving group, as the effect of the charge donation from the breaking bond to the σ^*_{C-X} completely eclipses any hypothetical orbital interaction from the substituents (Fig. 1). The anionic transition state, corresponding to a conrotatory process, however, would at the

* *Correspondence to: O. N. Faza and Á. R. de Lera, Departamento de Química Orgánica, Universidade de Vigo, Lagoas-Marcosende s/n Vigo-36310, Spain. E-mail: faza@uvigo.es; qolera@uvigo.es*

a *O. N. Faza, C. S. López, A. B. González-Pérez, M. Pérez-Rodríguez, Á. R. de Lera Departamento de Química Orgánica, Universidade de Vigo, Lagoas-Marcosende s/n Vigo-36310, Spain*

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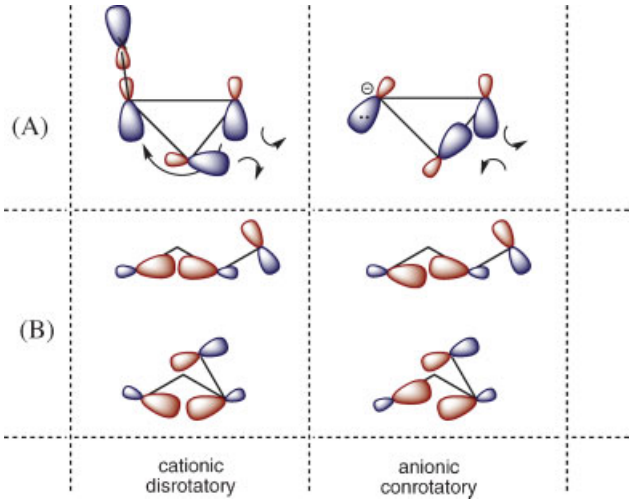

Figure 1. Orbital interactions in the ring-opening of cyclopropyl cations (left) and anions (right). There is a strong interaction between the breaking bond and the σ^*_{C-X} in the cationic reaction that is not present in the anionic system (A). This, together with the better overlap of the substituent's orbitals in a conrotation (B) would allow for noticeable substituent effects on the torquoselectivity in cyclopropyl anion ring-opening

same time provide a better overlap of the orbitals of the breaking bond with those on the substituents, and a less favorable interaction with the carbon supporting the anion. Both arguments allow us to contemplate the possibility of torquoselectivity induced by the substituents on C_2 and C_3 in the ring-opening of cyclopropyl anions.

RESULTS AND DISCUSSION

Cyclopropyl anions have a relatively high configurational stability, but the inversion barriers range from 0.7 to 20.3 kcal/mol depending on the substituent geminal to the lone pair (the lowest value corresponds to formyl R = CHO, and the highest to isonitrile R = NC).[26] Both this stability and the barrier fluctuations are explained because of the increasing angle strain when going from tetrahedral to planar anions. While the lone pairs are well defined for substituents like H or CN, they are not so with groups like NO_2 or CHO, where the anion is more delocalized over the substituent, the resulting conjugation favoring a more planar structure.

We have chosen a model (Fig. 2) with a nitrile group on the carbon supporting the anion, to stabilize it and make it more similar to the systems used in experimental settings, and a methyl group on the adjacent carbon, to use as a reference against which to check the effect of the substituents (R) on the remaining carbon. With this, we are trying to isolate single substituent effects. For the study of torquoselectivity, we extended our choice of substituents to include some very unrealistic options (groups that are not compatible with the existence of an anion in the vicinal carbon) so that we could test the effect of a wide range of donor–acceptor properties.

Cyclopropyl anions

The most stable configuration in the manifold in Fig. 2 is shown to depend on the nature of R. For most substituents it places the methyl group and R *cis* to each other (except for CF_3, NO_2, and ^{t}Bu), and the anion *cis* to R (except for $CHCH_2$ and CHO). The preferred configuration (Me/anion lone pair-Me/R) is *cis/cis* for CH_2CH_3, CN, F, Me, NH_2, OH, and OMe, *cis/trans* for $CHCH_2$ and CHO, and *trans/trans* for CF_3, NO_2, and ^{t}Bu. Results could not be compared for BH_2, Cl, and Br since in the first case, the lone pair attacked R and formed a new C—B bond and, in the latter two, a β-elimination is observed (E1cB) in an apparently barrierless process, resulting in the formation of 1-cyano-3-methyl-cyclopropene.

The general preference for a *cis/cis* configuration of the Me/R/lone pair triad can be rationalized in terms of the polarizability of these substituents, that could better offset the large electrostatic effects of the negative charge concentrated on C_1. The *trans/trans* configuration favored when R = CF_3, NO_2, and ^{t}Bu can be rationalized through steric arguments favoring the *trans* disposition of Me and R (Notice that in these cases the lone pair is still *cis* to R (with larger electron clouds than a methyl group), thus maintaining the stabilization provided by the polarizability of the substituent).

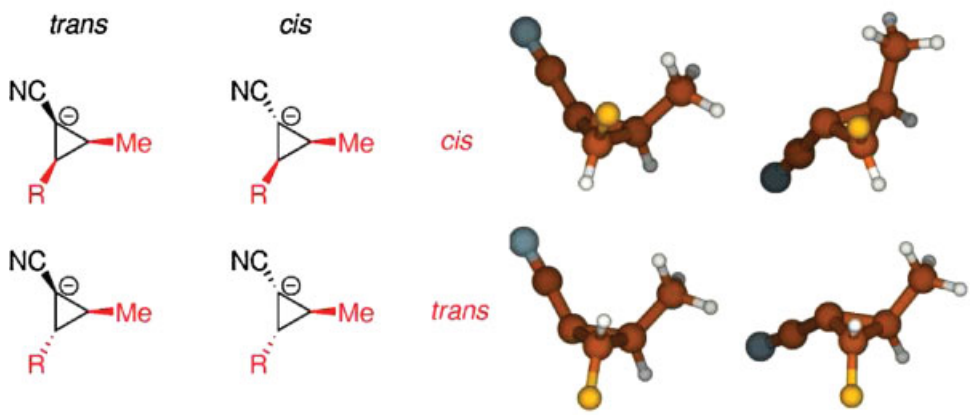

Figure 2. Model with a nitrile group on the carbon supporting the anion, a methyl group as a common function in all anions, and a range of substituents R with different electronic demands. For the cyclopropyl anions there are four available configurations: *cis/cis, cis/trans, trans/cis, trans/trans*, the descriptors denoting the relative positions of Me/lone pair and Me/R

If the $\Delta\Delta G_{t-c}$ values are analyzed for each relative configuration of the methyl group and R (Table 1) the following order for descending energy differences between the *trans*- and *cis*-configurations of the anion is found: OH > OMe > ^{t}Bu > CF_3 > NH_2 > F > Me > CH_2CH_3 > CN > NO_2 > $CHCH_2$ > CHO when Me and R are *cis* to each other, and CHO > $CHCH_2$ > CN > NO_2 = CH_2CH_3 > NH_2 > CF_3 > F > ^{t}Bu > OMe > OH for the systems with a *trans*-Me/R configuration, where negative and positive values indicate a preference for the anion to be *cis* to R or *cis* to the methyl group, respectively.

The correlation with the conventional electronic donor or acceptor character and the $\Delta\Delta G_{t-c}$ values in Table 1 is consistent albeit rough. No linear relationship is found when using empirical parameters such as Hammett's σ values to describe the electronic demands of substituents, but the trends are clear and consistent bor both *cis*- and *trans*-Me/R configurations.

For the *cis*-Me/R systems, the *cis*-configuration of the anion lone pair is always favored, but the energy difference is noticeably higher when R is a donor group than for acceptors. The abnormal (with respect to their electronic properties) position of ^{t}Bu and CF_3 on these lists can be rationalized again in terms of the polarizability of these larger substituents favoring a *cis*-R/lone pair orientation. An stereoelectronic origin of this effect is inferred from the variation in the C—R bond distance between the two lone pair configurations (Table 1), even if inspection of the second order interactions between natural bond orbitals (NBOs) shows no clear evidence of any charge delocalization relevant to this phenomenon. C—R bonds are shorter for the *cis*-isomer when R is a donor (OH, OMe, F) and shorter for the *trans*-isomer when R is an acceptor (CHO, NO_2, or $CHCH_2$). In all cases the *trans*-isomer is more planar than its *cis* counterpart, but the difference in the values of α is noticeably larger for the clearly donor (OH, OMe, F) or clearly acceptor (CHO, NO_2) than for the other substituents, with the highest values corresponding to R with donor character.

For the *trans*-Me/R systems, the lone pair is always going to be *cis* to either the reference Me or to R, and as a result, there is no longer a single favored conformation for the anion. Thus, the trends described in the previous paragraphs are enhanced, with donor groups favoring the *trans* configuration (it means that the lone pair will prefer being *cis* to R) and acceptors (CHO, $CHCH_2$, CN) favoring a *trans* disposition of R/lone pair (corresponding to the *cis* descriptor for the Me/lone pair, as depicted in Fig. 2), but with much lesser variation in the geometric parameters between the two alternatives.

Transition structures

In Fig. 3, the two ring-opening reaction paths allowed by the Woodward–Hoffmann rules are depicted for the two sets of reactants (*cis*- and *trans*-Me/R systems). They are labeled *in* and *out* depending on whether the methyl group on the cycle is rotating inwards or outwards during the process. Upon conrotation, the *cis*-Me/R systems always lead to a *Z*,*E*-allyl anion, while the *trans*-Me/R systems can lead to a *E*,*E*- (through ts-*in*) or a *Z*,*Z*-allyl anion (through ts-*out*). The effect of substituents in the preference for either path will depend on both their electronic character and steric demands. Despite the existence of two different lone pair configurations for each diastereomer (for *cis*-Me/R or *trans*-Me/R) of the cyclopropyl

Table 1. Energy differences (kcal/mol) between the *trans*- and *cis*-cyclopropyl anions, activation barriers for anion inversion (the most stable anion configuration is chosen as reference) and variation of α and the C—R bond distance (in Ångstroms) upon configuration inversion of the anion (*trans*/*cis*). *Cis* and *trans* refer here to the relative configuration of the anion lone pair and the methyl group. α is a measure of the planarization at the anion center, and is calculated as $\alpha = 360° - (\widehat{213} + \widehat{214} + \widehat{314})$

	cis-Me/R				*trans*-Me/R			
R	$\Delta\Delta G_{t-c}$	$\Delta\Delta G^{\ddagger}_{inv}$	α_{t-c}	d(C–R)$_{t-c}$	$\Delta\Delta G_{t-c}$	$\Delta\Delta G^{\ddagger}_{inv}$	α_{t-c}	d(C–R)$_{t-c}$
BH_2[a]	22.33		10.3	−0.190	−20.26		0.3	0.080
Br[b]	0.00		0.0	0.000	0.00		0.0	0.000
CF_3	4.93		−9.3	−0.001	−1.08		7.8	0.000
CH_2CH_3	3.69		−1.8	0.000	−0.34		0.1	0.000
$CHCH_2$	2.24	6.47	−3.5	−0.006	1.62	6.44	2.0	0.004
CHO	1.83		−5.8	−0.007	2.01		5.3	0.002
Cl[b]	0.00		0.0	0.000	0.00		0.0	0.000
CN	3.22	7.30	−6.5	0.000	0.22	5.92	4.8	−0.001
F	4.29		−20.7	0.020	−1.76	3.12	9.0	−0.006
H	2.06		−1.2	0.002	2.06		−1.2	−0.001
Me	3.88	6.85	−1.1	0.000	0.00	5.24	0.0	0.000
NH_2	4.65		−4.5	−0.002	−0.71		−2.9	0.003
NO_2	3.08		−12.8	−0.016	−0.34		10.1	−0.001
OH	9.23		−22.2	0.048	−2.38		−5.4	0.001
OMe	6.70	6.57	−12.7	0.005	−2.29	4.91	4.6	−0.001
^{t}Bu	6.54	8.04	−6.5	0.001	−1.93	5.57	7.8	−0.001

[a] When *cis* to the lone pair, BH_2 forms a C—B bond during optimization.
[b] The cyclopropyl anion is not stable, resulting in C—R bond cleavage during optimization and the formation of 1-cyano-3-methyl-cyclopropene.

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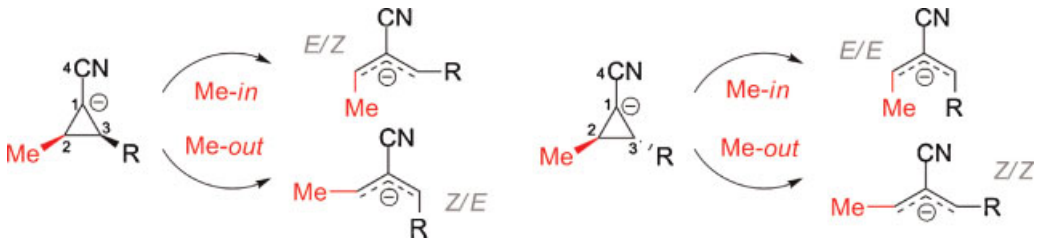

Figure 3. Conrotatory reaction paths for the *cis*-Me/R and *trans*-Me/R cyclopropyl anions

anions, the configuration of the anionic carbon on the ring-opening transition structures is not so well defined. In most cases either a (nearly)planar backbone or a single non-planar ring-opening path where the ring-opening transition state has a single defined lone pair configuration is accessible from both *cis*- and *trans*-Me/lone pair due to the release of the aforementioned ring-strain on the transition state.

The anionic center is almost planar (we have arbitrarily set an α value lesser than 10 as a definition of planarity) for every substituent besides those with more marked electron–acceptor properties: BH_2, NO_2, CHO, CN, $CHCH_2$ and, partially, CF_3. From the data in Tables 2 and 3, we can conclude that in the *in* transition structures, the methyl group and the lone pair are *cis* to each other, and that a *trans*- Me/lone pair relative configuration is found for the *out* transition states, both for the *cis*- and *trans*-Me/R systems. This translates into a preferred *cis* disposition of R and the lone pair when R is rotating outwards, that becomes *trans* upon inwards rotation of R. For the other groups no such distinction is found between trajectories, since the two accessible transition states involve a wholly planarized carbanion.

Table 2. Relevant geometrical parameters of the minima and transition structures for the *cis*-Me/R system: C—C distance of the bond being broken (d_{23}), values of α and their variation when going from the most stable minima to the transition state

R	ts	d_{23} (min)	α (min)	d_{23} (ts)	α (ts)	d_{23} (ts-min)	α (ts-min)
				cis			
BH_2	in	1.50	48.5	2.01	27.8	0.51	−20.7
	out	1.50	48.5	1.97	22.0	0.47	−26.5
Br	in	1.51	25.7	2.05	0.4	0.55	−25.3
	out	1.51	25.7	2.10	0.9	0.59	−24.8
CF_3	in	1.52	65.3	2.01	14.0	0.48	−51.3
	out	1.52	65.3	1.96	1.9	0.44	−63.4
CH_2CH_3	in	1.52	64.5	2.07	3.5	0.54	−61.0
	out	1.52	64.5	2.06	2.9	0.54	−61.6
$CHCH_2$	in	1.54	67.2	2.04	16.0	0.50	−51.2
	out	1.54	67.2	1.99	5.5	0.45	−61.7
CHO	in	1.54	68.1	1.99	22.3	0.45	−45.8
	out	1.54	68.1	1.95	15.4	0.41	−52.7
Cl	in	1.51	32.7	2.04	0.6	0.53	−32.1
	out	1.51	32.7	2.09	0.6	0.58	−32.1
CN	in	1.54	70.9	2.01	17.0	0.48	−53.9
	out	1.54	70.9	1.97	11.2	0.44	−59.7
F	in	1.50	64.7	2.04	0.8	0.54	−63.9
	out	1.50	64.7	2.08	0.0	0.58	−64.7
H	in	1.52	70.6	2.05	3.4	0.54	−67.2
	out	1.52	70.6	2.03	0.1	0.51	−70.5
Me	out	1.52	64.1	2.07	2.8	0.55	−61.3
	in	1.52	64.1	2.07	2.8	0.55	−61.3
NH_2	in	1.52	65.6	2.10	0.3	0.57	−65.3
	out	1.52	65.6	2.17	4.3	0.64	−61.3
NO_2	in	1.54	68.9	1.96	22.6	0.42	−46.3
	out	1.54	68.9	1.93	15.7	0.40	−53.2
OH	in	1.52	67.7	2.08	0.3	0.56	−67.4
	out	1.52	67.7	2.10	0.8	0.58	−66.9
OMe	in	1.51	69.1	2.06	0.8	0.55	−68.3
	out	1.51	69.1	2.10	0.5	0.59	−68.6

Table 3. Relevant geometrical parameters of the minima and transition structures for the *trans*-Me/R system: C—C distance of the bond being broken (d_{23}), values of α and their variation when going from the most stable minima to the transition state

R	ts	d_{23} (min)	α (min)	d_{23} (ts)	α (ts)	d_{23} (ts-min)	α (ts-min)
				trans			
BH_2	in	1.50	50.4	2.01	22.1	0.51	−28.3
	out	1.50	50.4	1.99	27.0	0.49	−23.4
Br	in	1.49	58.7	2.08	1.7	0.59	−57.0
	out	1.49	58.7	2.04	0.2	0.54	−58.5
CF_3	in	1.52	69.1	2.01	6.5	0.49	−62.6
	out	1.52	69.1	1.98	11.1	0.46	−58.0
CH_2CH_3	in	1.51	66.2	2.05	0.2	0.54	−66.0
	out	1.51	66.2	2.03	2.7	0.52	−63.5
$CHCH_2$	in	1.53	71.4	2.02	10.9	0.49	−60.5
	out	1.53	71.4	1.99	14.0	0.46	−57.4
CHO	in	1.54	72.7	1.99	16.7	0.45	−56.0
	out	1.54	72.7	1.96	21.3	0.42	−51.4
Cl	in	1.51	32.4	2.08	1.3	0.57	−31.1
	out	1.51	32.4	2.02	0.5	0.51	−31.9
CN	in	1.53	72.9	2.01	12.6	0.47	−60.3
	out	1.53	72.9	1.97	15.0	0.44	−57.9
F	in	1.50	64.4	2.08	0.3	0.58	−64.1
	out	1.50	64.4	2.02	0.4	0.52	−64.0
H	in	1.52	74.6	2.05	3.4	0.54	−71.2
	out	1.52	74.6	2.02	0.1	0.51	−74.5
Me	in	1.51	70.5	2.06	0.1	0.54	−70.4
	out	1.51	70.5	2.03	0.0	0.52	−70.5
NH_2	in	1.50	68.3	2.13	2.4	0.62	−65.9
	out	1.50	68.3	2.04	0.3	0.54	−68.0
NO_2	in	1.52	73.1	1.97	16.3	0.45	−56.8
	out	1.52	73.1	1.92	20.3	0.40	−52.8
OH	in	1.51	63.4	2.10	2.7	0.59	−60.7
	out	1.51	63.4	2.04	0.1	0.53	−63.3
OMe	in	1.50	69.8	2.10	0.1	0.60	−69.7
	out	1.50	69.8	2.03	0.2	0.53	−69.6
^{t}Bu	in	1.52	63.3	2.07	0.1	0.56	−63.2
	out	1.52	63.3	2.04	2.8	0.52	−60.5

Torquoselectivity

Due to the existence of common transition structures for the *cis* and *trans* anions (differing only in the configuration of the anionic center), we will refer the activation energies and all other comparisons to the most stable of the two.

From what can be seen in Table 4, the ring-opening is easier when R is an acceptor, as can be expected for a process where the negative density charge is being shifted from C_1 to C_2 and C_3. The consistently higher $\Delta G^{\ddagger}$ values obtained for the *cis* paths for a given R are no surprise either, due to the steric hindrance found by the unavoidable *in*-rotating substituent (Figure 3).

When one looks at the energy difference between the two alternate conrotatory transition structures for the ring-opening of a given anion ($\Delta\Delta G^{\ddagger}_{\text{out}-\text{in}}$ in Table 4), two facts are made patent: the *trans*-isomers always prefer to travel the *out* path, instead of the *in*, and the rotation selection in the *cis*-isomers depends on the substituent R under consideration. Thus, *there is torquoselectivity in the electrocyclic ring-opening reaction of cyclopropyl anions*, and for most substituents, the energy differences between the two available paths are high enough to be synthetically useful (if the geometrical stability of the resulting allyl anion is preserved until it can be protonated or trapped by a suitable electrophile). The situations for which these energy differences are too small ($R = CH_2CH_3$ for the *cis* system and $R = CHO$ for the *trans*) can be easily explained by the confluence of the steric and electronic effects that provide selectivity for this reaction and they are not outsider points in the general trend.

The preference for the outwards rotation in the *trans*-isomers originates in the large difference in steric interactions between a path where the two substituents at the extremes of the breaking bond are rotating away from this bond and a path where these two groups rotate inwards. This lower barrier for the *out* path is accompanied by shorter C_2—C_3 bond distances and less planar carbanions when applicable (Table 3), sign of an earlier transition state. Despite this apparent lack of substituent effect on the selectivity of the reaction, the substituents have a large impact in the energy gap between the two mechanisms, a gap that can go from 0.01 kcal/mol for $R = CHO$ (the inwards and outwards paths are quasidegenerate) to the maximum value of 13 kcal/mol found

Table 4. Activation energies (in kcal/mol, referred to the most stable anion) corresponding to the *in* and *out* conrotatory paths available for the studied systems, and the energy difference between the two ($\Delta G^{\ddagger}_{out} - \Delta G^{\ddagger}_{in}$)

		cis		*trans*	
R	ts	$\Delta G^{\ddagger}$	$\Delta\Delta G^{\ddagger}_{out-in}$	$\Delta G^{\ddagger}$	$\Delta\Delta G^{\ddagger}_{out-in}$
BH_2[a]	in	37.08		33.53	
	out	30.30	−6.78	35.00	1.47
Br[a]	in	38.36		44.60	
	out	42.29	3.94	31.59	−13.00
CF_3	in	24.59		25.46	
	out	21.88	−2.70	21.31	−4.15
CH_2CH_3	in	27.91		31.49	
	out	27.45	−0.46	24.93	−6.56
$CHCH_2$	in	20.02		22.18	
	out	18.07	−1.95	18.65	−3.53
CHO	in	17.13		16.51	
	out	12.69	−4.44	16.52	0.01
Cl[a]	in	35.61		44.90	
	out	40.27	4.66	32.33	−12.57
CN	in	20.60		21.19	
	out	18.29	−2.31	16.72	−4.46
F	in	26.80		34.28	
	out	30.84	4.04	22.62	−11.65
H[b]	in	29.83		29.83	
	out	25.89	−3.94	25.89	−3.94
Me[c]	in	28.39		31.99	
	out	28.39	0.00	23.75	−8.23
NH_2	in	24.15		32.50	
	out	27.30	3.15	21.10	−11.40
NO_2	in	15.97		18.24	
	out	13.19	−2.78	13.27	−4.98
OH	in	29.94		35.00	
	out	33.85	3.91	26.23	−8.77
OMe	in	26.72		33.74	
	out	30.01	3.29	22.69	−11.05
^{t}Bu	in			32.18	
	out			24.12	−8.06

[a] The $\Delta G^{\ddagger}$ values are not reliable for these systems due to the problems described for the minimization of the corresponding minima.
[b] The *cis*- and *trans*-isomers are the same when R = H.
[c] When R = Me, the *in* and *out* paths are equivalent for the *cis*-isomer.

for chlorine. Even if steric reasons favor the *out* path for all the systems, steric arguments alone cannot justify why the $\Delta\Delta G^{\ddagger}_{(o-i)}$ is much larger for Br, F, or OMe than for ^{t}Bu, and electronic arguments have to be invoked to explain why the preference for the *out* mechanisms is greatly enhanced for donor groups at R, and dampened when R is an acceptor, to the point of reversal in the case of R = CHO.

When the excessive crowding is removed from one of the paths, as in the *cis* series (there is always one substituent rotating inwards), and the steric demands on the two transition states are more balanced, the electronic effects are more clearly appreciated. In Table 4 and Fig. 4, the same preference for the outwards rotation of donor groups and inwards rotation of acceptors is shown, but now this preference has consequences on the distribution of products: NH_2, OH, OMe, F, Cl, and Br steer the reaction through a lower energy *in* earlier transition state (with shorter C_2—C_3 bond lengths), while the other groups (either good acceptors or bulky groups with no well defined electronic demand) proceed through *out* transition states that now are lower energy and earlier (in terms of C_2—C_3 bond distances, albeit not in terms of anion planarity, with noticeable disparities between the two paths for CF_3 and $CHCH_2$) than their *in* counterparts.

In Fig. 4, the difference in the barriers for the *out* and *in* mechanisms ($\Delta\Delta G^{\ddagger}_{(o-i)}$) is plotted against Hammett's σ_p[27] for the two series of *cis*- and *trans*-Me/R anions with different substituents (Table 4). There is a very rough linear fit between the two (we would not expect more than that, since the reactions used are very different from the model and steric factors play an important role here as well), summarizing well the previously discussed trends. The most outlying points in the plots correspond to R = F, Cl, Br, which despite their low positive values of σ_p and their usual behavior as electron-withdrawing groups through inductive effect, are in fact good donors (through resonance) in the context of small charged systems.[8]

Aromaticity of minima and transition structures

For longer chain electrocyclizations,[28] the inwards rotation of a donor group distorts the nucleus independent chemical shift (NICS) pattern along the axis normal to the ring plane, making it resemble that of a non-aromatic system. However, when dealing with three-membered rings, the use of NICS as probes for the pericyclic character of a transition structure (a pericyclic transition structure is supposed to have aromatic character and thus, according to a ring-current model,[29] display high negative NICS values at the ring center) is somehow problematic, due to the combined effects of the σ and π aromaticities, the first a residue from the closed cycle in-plane conjugation, the second arising

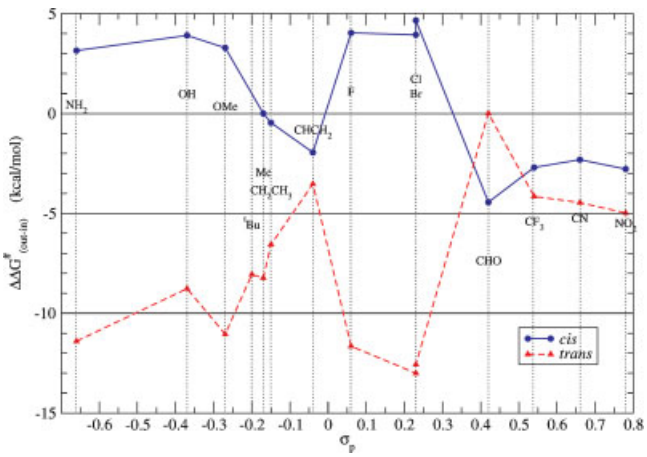

Figure 4. $\Delta\Delta G^{\ddagger}$ (out-in) against Hammett's σ_p for different R on the *cis*/*trans*-Me/R anions. There is a marked preference for donors to rotate outwards and acceptors to rotate inwards, which determines the preference for one of the two available paths for the *cis* substrates and modulates the *out* preference of the *trans*

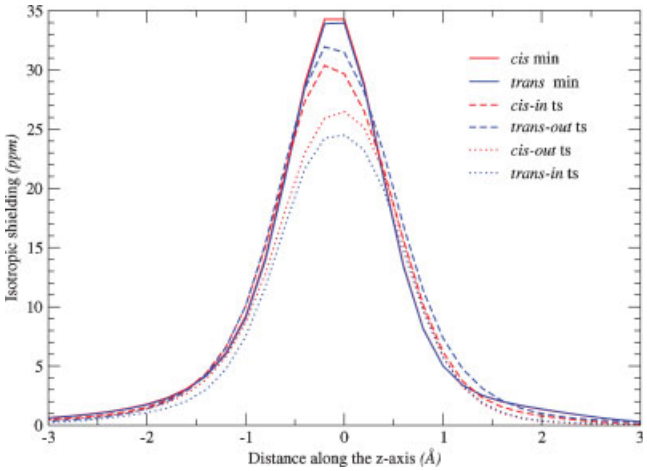

Figure 5. Isotropic shielding (= –NICS) along an axis normal to the ring plane, for the minima and transition structures corresponding to the ring opening of the cyclopropyl anions where R = F. The high values reached in all the systems are remarkable, due to the σ contribution to the overall aromaticity

Table 5. Main divergences in the orbital interaction energies (kcal/mol) obtained for the competing transition structures with second order perturbation theory on the NBO. The interaction is more favorable in the preferred path for each cyclopropyl anion

Anion	R	Interaction	*in*	*out*
cis	OH	$n_O - \sigma^*_{C_2-C_3}$	24.87	7.09
trans	OH	$n_O - \sigma^*_{C_2-C_3}$	19.72	23.80
cis	NH_2	$n_N - \sigma^*_{C_2-C_3}$	19.70	13.71
trans	NH_2	$n_N - \sigma^*_{C_2-C_3}$	12.07	17.41
cis	OMe	$n_O - \sigma^*_{C_2-C_3}$	24.89	9.32
trans	OMe	$n_O - \sigma^*_{C_2-C_3}$	6.84	23.68
cis	F	$n_F - \sigma^*_{C_2-C_3}$	14.96	8.36
trans	F	$n_F - \sigma^*_{C_2-C_3}$	8.22	14.42
cis	BH_2	$\pi_{(C_1-C_3)} - \pi^*_{C_2-B}$	6.68	22.43
trans	BH_2	$\pi_{(C_1-C_3)} - \pi^*_{C_2-B}$	<5	9.71

from the cyclic array of overlapping π orbitals expected from an aromatic transition structure. As a result, we find in our system that NICS values are higher in the reactants than in the transition structures (Fig. 5), that both available transition structures have very high NICS values and that the higher energy transition structure has lower NICS values. This last fact, however, can be attributed both to the effect of the inwards-rotating donor group, responsible of a destabilizing two-orbital four-electron antiaromatic interaction,[11] and to the position of the transition state along the reaction coordinate (early of late), as the lower-energy paths corresponding to earlier transition structures (where more features from the reactants remain) are those where the offending donor groups are rotating outwards. Although the similar decrease in NICS values when going from the minima to the transition states is found when R is an acceptor, the differences between the NICS profile between the favored and more energetic pathways are negligible.

NBO analysis

The substituent effects are better assessed in the competing transition structures by comparing the orbital interactions obtained through the use of second order perturbation theory on the orbitals resultant from a NBO analysis of their wavefunctions. While there is no significant difference in the interactions (in fact, there are no such interactions over a threshold of 5 kcal/mol) between the two transition structures when R = ^{t}Bu or Me for example, for substituents with more defined electronic characteristics, the effects are clear, as can be seen in Table 5. Donor groups favor an outwards rotation by donating charge to the antibonding orbital corresponding to the breaking bond, while acceptors lower the energy of the transition structure that makes them rotate inwards, through charge donation of the $\pi_{(C1-C2)}$ bond to a vacant π orbital on the substituent, in accord with the well-described model for cyclobutane openings.[11] BH_2 is the only acceptor considered here, as the NBO analysis of other systems resulted in different Lewis structures for the *in* and *out* transition structures, making the comparison of the orbital interactions difficult.

SUMMARY

This study of the electrocyclic ring-opening of cyclopropyl anions has been organized in five sections having to do with the structure and relative stability of the cyclopropyl anions themselves, the structure of the corresponding ring-opening transition structures and the factors affecting their energy (exploring the torquoselectivity of the process) and their characterization in terms of aromaticity and NBO orbitals.

The relative stability of the different configurations of substituted cyclopropyl anions has been studied in detail for the systems in Fig. 2. We have found that the most stable configurations tend to place the lone pair and donor substituents *cis* to each other with a general preference for the *cis*/*cis* configuration of Me/lone pair/R based on polarizability and the stereoelectronic effects of R, as reflected in the variation of geometric parameters between the *cis* and *trans* configurations of the lone pair for a set Me/R arrangement.

The configuration of the anionic center is not so well defined in the transition state, and only one structure is found for each allowed path. Thus, we find planar transition structures for most substituents, while for electron-withdrawing groups a *cis* arrangement of R and the lone pair is prefered when R is rotating outwards which becomes *trans* upon inwards rotation of R.

Analysis of the energy difference between the *in* and *out* paths available for each Me/R configuration, lets us conclude that the electrocyclic ring-opening of cyclopropyl anions is torquoselective and that this selectivity can be modulated by the electronic demand of the R substituents. Torquoselectivity for this system conforms to Houk's model for the ring-opening of substituted cyclobutanes as can be confirmed by the energetic trends and by the difference between the second order orbital interactions found in the transition structures of the competing paths.

In the transition structures of electrocyclizations, NICS values at the center of the ring sometimes reflect the unfavorable interactions upon inwards rotation of donor substituents as a decrease in the aromaticity of the transition state. Substituent-induced torquoselectivity is found in this system, together with

this decrease in the NICS values for the more energetic path. However, the in-plane aromaticity and very large NICS values found in the reactants can skew the results making this reduced aromaticity a result of a later transition state instead.

METHODS

Throughout this study, all the calculations have been performed with the Gaussian 03 suite of programs.[30] Density functional theory,[31] was used with Becke's three-parameter exchange functional[33] and the non-local correlation functional of Lee *et al*.[34] (B3LYP). The choice of functional was made based on the previous successful application of this methodology to describe other pericyclic mechanisms,[35] and our experience with cyclopropyl anions and other electrocyclic ring-opening reactions.[7,28,36] The basis set used, Pople's 6-31++G(d,p), includes polarization and diffuse functions, useful in the description of the extended electron clouds of anions. All stationary points were characterized by means of harmonic analysis, and for all the transition structures, the vibration related to the imaginary frequency corresponds to the nuclear motion along the reaction coordinate under study. The stability of the wavefunction was checked, and in all structures it was found to correspond to a minimum. Bond orders, atomic charges, and second order orbital interactions were calculated with the NBO[37] method.

For the characterization of aromaticity of some transition structures and minima, Schleyer's NICS[38] values were computed using gauge-independent atomic orbitals (GIAO method).[39]

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