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α-Fluoro decalones as chiral epoxidation catalysts: fluorine effect

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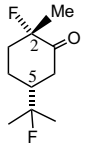
Abstract—Three rigid monofluorinated *trans*-decalones **4a**, **5e**, and **6e** (90% ee) have been synthesized from commercially available (−)-(*R*)-methyl naphthalenone (90% ee). Their structures have been fully characterized (NMR, X-ray): ketones **4a** and **5e** are Me,F-disubstituted α to the carbonyl with the fluorine axial and equatorial, respectively, while ketone **6e** is F-monosubstituted α to the carbonyl with the fluorine equatorial. The use of these ketones as chiral catalysts for the epoxidation of *trans*-olefins (such as stilbene, β-methylstyrene and *p*-methoxy cinnamate) through the formation of dioxiranes shows (i) that dioxiranes with an equatorial fluorine α to the dioxirane ring are less reactive and provide lower ee's than dioxiranes with an axial fluorine and having the same chirality and (ii) that an axial methyl α to the dioxirane ring is significantly less efficient than a fluorine. The results corroborate Armstrong and Houk's theoretical model and our first hypothesis to rationalize the inverted enantioselectivities observed using α-fluorinated cyclohexanones having the same chirality, i.e.: rapid ring inversion (Curtin–Hammett principle) allows the dioxirane conformation to have the fluorine axial (even if less populated than the other) to contribute significantly to the epoxidation reaction.

1. Introduction

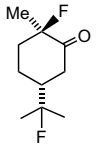
Since the first use by Curci et al. in 1989[1] of trifluoromethyl acetone as a dioxirane precursor for the epoxidation of olefins, the observed activating effect of fluorine substitution has been extended to asymmetric epoxidation while various chiral fluorinated ketones have been designed.[2–9]

During work on the epoxidation of *trans*-methyl *p*-methoxy cinnamate[10] and other *trans*-olefins using chiral dioxiranes generated in situ from tri- and tetra-substituted α-fluoro cyclohexanones it was found that

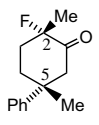
- (2*S*,5*R*)-ketones, called F-axial, were more efficient,[5,6] providing epoxides with higher yields and higher ees than (2*R*,5*R*)-ketones, called F-equatorial, (e.g., ketone **1a** vs ketone **1e**). It is noteworthy that ketones are named F-axial and/or F-equatorial for convenience and according to the NMR data (in benzene-d_6), which fit with F-axial or F-equatorial.



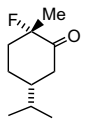
1a
F-axial
stilbene
90%conv.
90% ee(-)-(*S*,*S*)



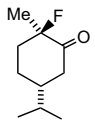
1e
F-equatorial
stilbene
70% conv.
20% ee (+)-(*R*,*R*)



2a
F-axial
stilbene
95% conv.
90% ee (-)-(*S*,*S*)



3a
F-axial
stilbene
78% conv.
60% ee (-)-(*S*,*S*)



3e
F-equatorial
stilbene
69% conv.
18% ee (+)-(*R*,*R*)

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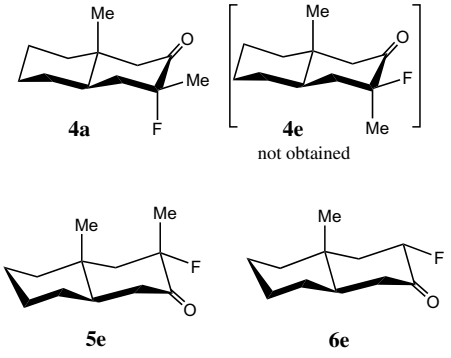
- Di-substitution at C5 increased the enantioselectivity by 25–30%,[9] suggesting that *axial* approaches of the olefin towards the corresponding dioxirane could contribute significantly (e.g., compare ketones **2a** and **3a**).
- Inversions of enantioselectivity were observed in the case of dioxiranes derived from (2*R*,5*R*)-ketones (F-equatorial). This behavior was ascribed to the contribution of both conformers **C1** (providing enantiomer 1) and **C2** (providing enantiomer 2) to the reaction due to rapid ring inversion in the dioxiranes (Scheme 1), and to better reactivity of **C2**.[6]

Rigid *trans*-decalones **4a**, **5e**, and **6e**, whose dioxiranes do not undergo chair–chair ring inversion, have thus been envisaged to check the role of ring inversion and of fluorine orientation on the efficiency and enantioselectivity of epoxidation reactions.



We herein report the synthesis of ketones **4a**, **5e**, and **6e** from commercially available (and 90% enantioenriched) (−)-(*R*)-4,4a,5,6,7,8-hexahydro-4a-methyl-2(3*H*)-naphthalenone **7** (Scheme 2), their structures (X-ray, NMR) and their use as catalysts for the epoxidation of *trans*-stilbene, *trans*-β-methylstyrene and *trans*-methyl *p*-methoxycinnamate. The *trans*-decalones **5e** and **6e** have been envisaged because we did not succeed in the synthesis of isomer **4e**.

2. Results and discussion

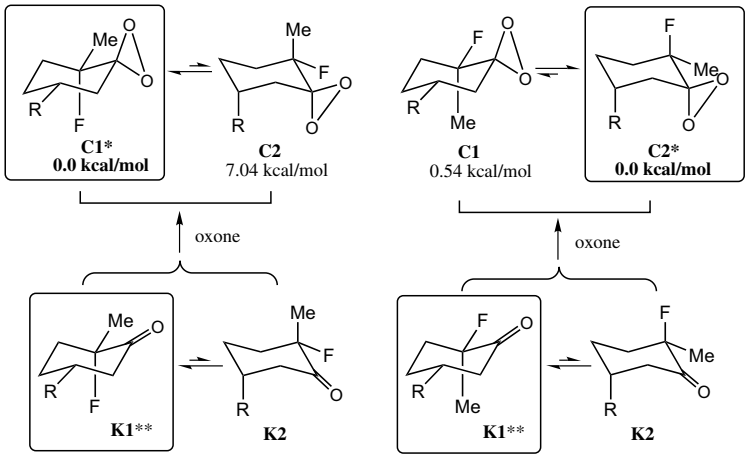
2.1. Synthesis

As shown in Scheme 2, the desired ketone **4a** was obtained in seven steps as a single diastereomer from commercially available (−)-(*R*)-4,4a,5,6,7,8-hexahydro-4a-methyl-2(3*H*)-naphthalenone **7**. The starting compound **7** was assigned an enantiomeric excess of 90% based on the measured specific rotation $\{[\alpha]_D = -198$ (*c* 1.1, MeOH)} compared with the maximum specific rotation $\{[\alpha]_D Max = -219$ (*c* 1.1, MeOH)} obtained by Toda and Tanaka[11] after resolution with TADDOL.

Li/NH_3 reduction[12] of enone **7** provided 95% of a mixture of **8** (90%) and of the corresponding decalol (10%), which are separated by chromatography. ^1H and ^{13}C NMR of **8** were consistent with Vecchi et al.'s results[13] and with a *trans* relationship between the rings.

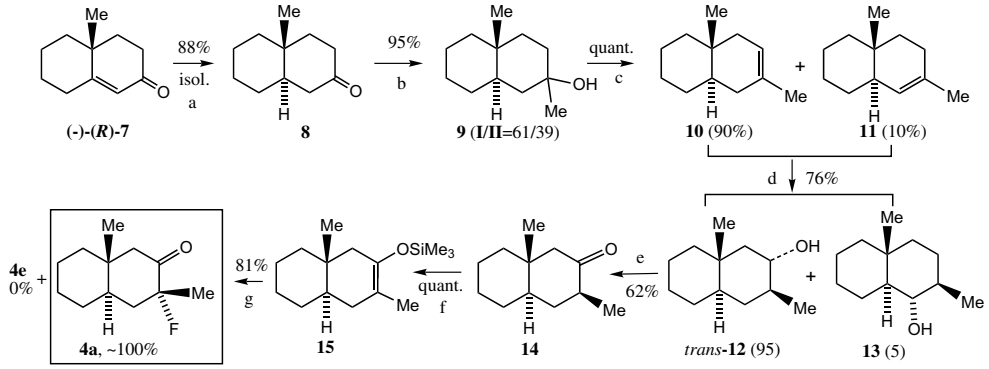
Upon addition of MeLi,[14] the two expected diastereomers **9I** + **9II** were obtained as a 61/39 mixture, in 95% yield. The mixture was used as such for the next dehydration step[14] leading, in quantitative yield, to a mixture of **10** (90%) and **11** (10%). Hydroboration of the **10** and **11** mixture provided a 95/5 mixture of *trans*-**12** (95%) and *trans*-**13** (5%) in 76% yield.

The desired methyl decalone **14** was then obtained through PCC oxidation in 62% isolated yield as a single diastereomer and without traces of the ketone corresponding to **13**. The thermodynamic silylenolate **15** was obtained in quantitative yield after modification of

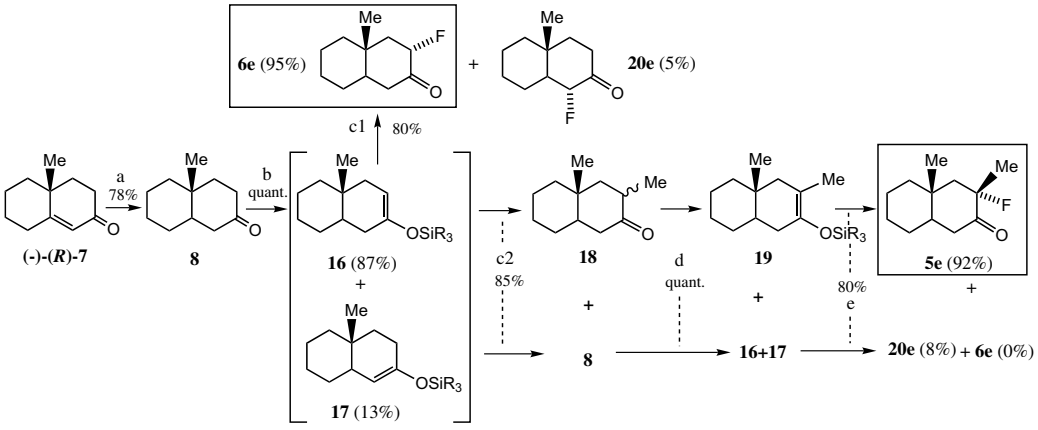


* most populated according to modelization, *cf.* ref 6. ** most populated according to ^1H NMR in C_6D_6.

Scheme 1.



Scheme 2. Reagents and conditions: (a) Li/NH_3, Et_2O, −78 °C, EtOH, from −78 ° C to rt, NH_4Cl (cf. Ref. 13); (b) MeLi/THF, reflux; (c) pTsOH (0.02 equiv)/benzene, reflux (cf. Ref. 14); (d) BH_3: THF, from 0 °C to rt, NaOH, H_2O_2; (e) PCC (2 equiv), CH_2Cl_2, from 0 °C to rt; (f) TMSCl/NaI (2 equiv), Et_3N (2 equiv), MeCN/pentane, rt (cf. Ref. 15); (g) Selectfluor (1.4 equiv)/DMF, 0 °C.



Scheme 3. Reagents and conditions: (a) Li/NH_3, Et_2O, −78 °C, EtOH, from −78 °C to rt, NH_4Cl (cf. Ref. 13); (b) TMSCl/NaI (2 equiv), NEt_3 (2 equiv), MeCN/pentane, rt (cf. Ref. 15); (c1) Selectfluor (1.4 equiv)/DMF, 0 °C; (c2) MeI/TBAF/THF; (d) TMSCl/NaI (2 equiv), NEt_3 (2 equiv), MeCN/pentane, rt (cf. Ref. 15); (e) Selectfluor (1.4 equiv)/DMF, 0 °C.

the literature work-up[15] while the fluorination was performed with Selectfluor in 81% yield providing a single diastereomer identified (cf. below) as **4a** (no traces of **4e** were detected by NMR). The high diastereoselectivity of this step could be due to the better availability of the face of the double bond *trans* to the methyl group in the twist conformation of the ring. Diastereomer **4a** was thus obtained in 32% overall yield.

Ketone **5e** was synthesized in five steps from (−)-(*R*)-**7** (Scheme 3) and obtained as a single diastereomer (isomer **5a** has not been detected) although traces (8%) of ketone **20e** was obtained simultaneously because of the formation of silylenolate **17**, which seemingly did not undergo methylation during step 3.

Ketone **6e** was synthesized in three steps from (−)-(*R*)-**7** (Scheme 3) and obtained as a 95/5 mixture of **6e** (major, 95%) and ketone **20e** (5%), due again to the presence of silylenolate **17**.

After chromatographic purification, ketone **5e** was obtained pure in 48% overall yield, while **6e** was obtained as a 95/5 mixture of **6e** and **20e** (both having the fluorine equatorial) in 56% overall yield.

2.2. Structural determination of 4a, 5e, and 6e

The *trans*-structure, chair conformation and axial orientation of the fluorine in ketone **4a** were determined by X-ray analysis of a single crystal (Fig. 1).

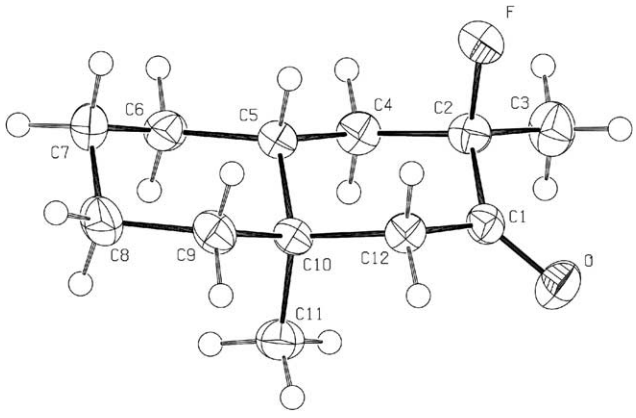
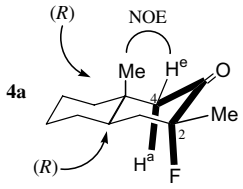


Figure 1. ORTEP plot of one molecule of **4a**: F–C2–C1–O = −117.5°; F–C2–C1–C12 = 64.2°. Configuration (2*R*,5*R*,10*R*) from the known (*R*)-configuration at ClO.

Therefore, α-fluoro decalone **4a** was assigned the (2*R*,5*R*,10*R*)-configuration (according to the X-ray numbering of atoms shown in Fig. 1) on the basis of the known (*R*)-configuration at C10 of the starting decalenone **7** (Fig. 1). NOESY (Fig. 2) and the 6.5 Hz value for $^4J_{HF}$[16] corroborated the *trans*-(*R*,*R*)-structure of the decalone **4a** and the axial orientation of the fluorine atom.



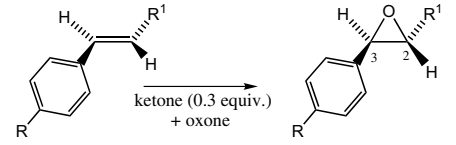
H4e = doublet, $^2J_{(H4e\text{-}H4a)}$= 12.5 Hz and NOE with Me
H4a = double doublet, $^2J_{(H4a\text{-}H4e)}$ = 12.5 Hz and $^4J_{HF}$ = 6.5 Hz

Figure 2.

α-Fluoro decalones **5e** and **6e** were assigned the (3*S*,*R*,*R*)-configuration (according to Fig. 3 numbering) with an equatorial fluorine (Fig. 3) using NOESY and ^{1}H NMR patterns.

2.3. Epoxidation of *trans*-olefins

The results of the asymmetric epoxidation of stilbene **21**, β-methylstyrene **22** and methyl *p*-methoxy cinnamate **23** (Scheme 4) with these ketones are shown in Table 1. The conversions have been determined by combining weights and ^{1}H NMR (300 and/or 400 MHz) of solvent-free crude products. Epoxides were then isolated by flash chromatography on silica gel. The ees of the epoxides were determined by ^{1}H NMR using Eu(hfc)$_3$ in $CDCl_3$ and absolute configurations determined by comparing the measured specific rotation with the literature values.[17] The ees (Table 1, columns 7 and 9) have been corrected considering that all ketones used were 90% ee.



21: R=H; R^1=Ph ⟶ **24** (+)-(*R*,*R*)
22: R=H; R^1=Me ⟶ **25**: (+)-(*R*,*R*)
23: R=MeO; R^1=CO_2Me ⟶ **26**: (+)-(2*S*,3*R*)

Scheme 4.

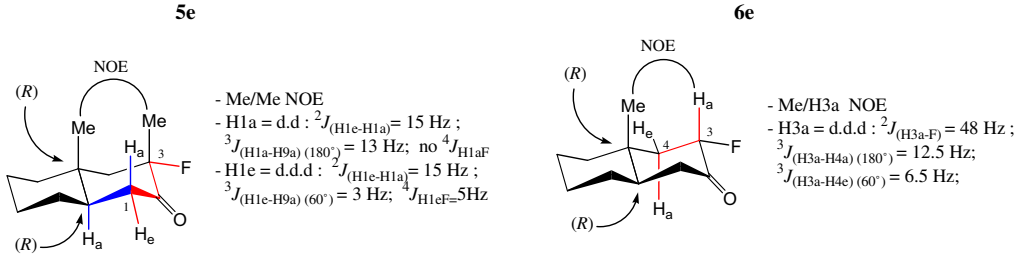
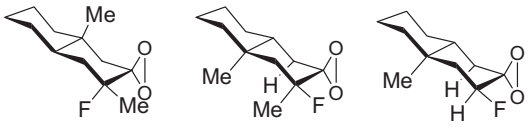


Figure 3.

Table 1. Epoxidations of stilbene **21**, β-methylstyrene **22** and methyl *p*-methoxy cinnamate **23**



Dioxiranes from : **4a** **5e** **6e**

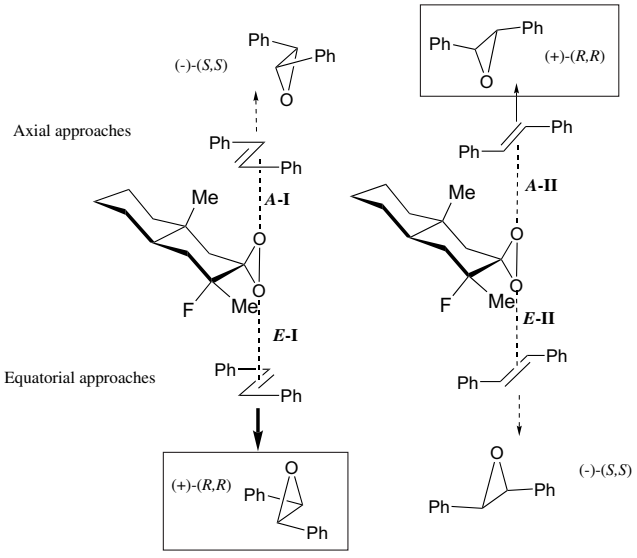
Olefin	Ketone	Solvent[a]	Temp. (°C)	React. time (h)	Conv. (%)[b]	Er (%)[c]	Absol. Conf.[d]	Ee (%)
PhCH = CHMe	**4a**	Diox/H_2O	25	6	100	85/15	(+)-(*R*,*R*)	70
	5e	Diox/H_2O	25	6	88	61/39	(+)-(*R*,*R*)	22
	6e	Diox/H_2O	25	6	100	50/50	—	0
PhCH = CHPh	**4a**	Diox/H_2O	25	6	100	93/7	(+)-(*R*,*R*)	86
	5e	Diox/H_2O	25	6	0	—	—	—
	6e	Diox/H_2O	25	6	0	—	—	—
Cinnamate	**4a**	Diox/H_2O	25	6	75	73/27	(+)-(2*S*,*R*)	46
	5e	Diox/H_2O	25	6	0	—	—	—
	6e	Diox/H_2O	25	6	0	—	—	—

[a] Diox/H_2O: 2/1 (3 equiv of oxone), rt.
[b] Determined by ^{1}H NMR (300 and/or 400 MHz) on the crude products of the reactions.
[c] Enantiomeric ratios have been determined by ^{1}H NMR (400 MHz) using Eu(hfc)$_3$ in $CDCl_3$: the precision is ±2%.
[d] Absolute configurations have been determined from the sign of the specific rotation as compared with literature results (cf. Ref. 17).

From previous results[5] and theoretical calculation by Armstrong et al.,[18] decalones **5e** and **6e** with the fluorine equatorial were expected to be weaker catalysts, than ketone **4a** with the fluorine axial and, as expected, did not catalyze the epoxidation of stilbene **21** and cinnamate **23** but did catalyze the epoxidation of β-methyl styrene **22**.[3,5,8]

Considering the configurations of **4a** and **5e**, using the well-accepted *spiro*-model[19] and both equatorial[20–22] and axial[9] approaches (Fig. 4 and Fig. 5 with R = Me) one could expect the enantiomers (+)-(*R*,*R*)-**24**, (+)-(*R*,*R*)-**25** and (+)-(2*S*,3*R*)-**26** to be obtained, which is indeed observed (Table 1, lines 1, 2, 4, and 8). Equatorial ***E*-I** approach with no n·π repulsion (between F and the phenyl) involved was expected to be favored over the ***E*-II** approach, which involves such a n·π repulsion. Similarly, in the case of *axial* approaches ***A*-II**, which involves no steric Me·Ph repulsive interaction, is favored over ***A*-I**. Both ***E*-I** and ***A*-II** provide the same enantiomer of the epoxide.

Furthermore ketone **6e** (95%) as well as ketone **20e** (5%) provide almost racemic epoxides (Fig. 5 with R = H) again as observed (Table 1, line 3). In this case all approaches (***E*-I**, ***E*-II**, ***A*-I**, and ***A*-II**) involve H·Ph interactions.



***E*-I >> *E*-II**
F/Ph n.π repulsion in ***E*-II**

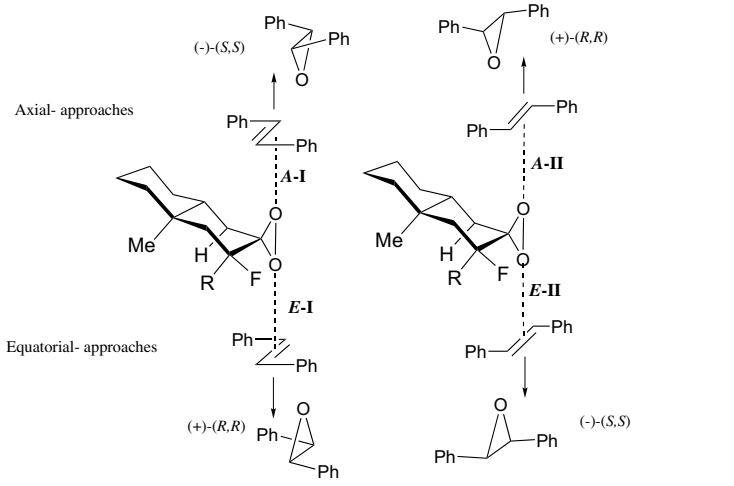
***A*-II > *A*-I**
Me/Ph repulsion in ***A*-I**

Figure 4. Model epoxidation of *trans*-stilbene by the dioxirane derived from **4a**.

3. Conclusion

Although direct epoxidation of β-methyl styrene by oxone is a competitive reaction responsible for the lower ee observed with this olefin,[23] the observation of ee's by using **4a** (70%: Table 1, line 1) and **5e** (22%: Table 1, line 2) indicates that these ketones play the expected role of a catalyst (the corresponding dioxiranes ?tul?> providing at least part of the epoxidation reaction). It can be suggested that this is also true for ketone **6e**, which provides part of the epoxidation but toward a racemic mixture as expected from the model.

In summary, as predicted from the model and consistent with Armstrong and Houk's theoretical calculations:[18]



***E*-I~*E*-II** when R=H
H/Ph interaction in both cases
[(-)-epoxide] ~[(+)-epoxide] expected

***E*-I >*E*-II** when R=Me
Me/Ph repulsion in *E*-**II**
[(+)-epoxide] > [(-)-epoxide] expected

***A*-I ~ *A*-II** when R=H or Me
H/Ph interaction in both cases
[(-)-epoxide] ~[(+)-epoxide] expected

Figure 5. Model epoxidation of *trans*-stilbene by the dioxirane derived from **5e** (R = Me) and **6e** (R = H).

- Dioxiranes with an axial α-fluorine (and an equatorial methyl) are more reactive and provide higher ees than dioxiranes with an axial methyl (and an equatorial fluorine): Table 1, compare line 1 with line 2 and lines 4 and 7 with lines 5 and 8.
- An axial methyl group (ketone **5e**) is less efficient than an axial fluorine (ketone **4a**) providing lower yields and lower ees (considering, of course, that the extent of direct epoxidation is identical/similar in both cases): Table 1, compare line 1 with line 2.
- An axial proton even with an α-fluorine *equatorial* has no effect on the enantioselectivity: Table 1, compare line 1 with line 3.

It thus appears that our very first hypothesis[6] to rationalize the inverted enantioselectivities and high yields obtained during epoxidation of stilbene and/or cinnamate using (2*R*,5*R*)-cyclohexanones (F-equatorial) is satisfactory.

1. The Curtin–Hammett principle holds true because of rapid exchange between the dioxirane ring conformations **C1** (with an equatorial fluorine) and **C2** (with an axial fluorine).
2. Inversion of the ring is equivalent to an inversion of configuration. Therefore, if **C1** provides the (−)-enantiomer, **C2** will provide (+)-enantiomer.
3. **C2**, in which the fluorine is axial, has a higher reactivity[18] than **C1** and could/will contribute to the reaction even if less populated than **C1**, which will increase the apparent reactivity and decrease the enantioselectivity.
4. Calculation and modeling show that conformation **C2** with an F-axial is significantly populated, which makes its contribution larger.
5. The enantioselectivity observed is the result of three rate constants [rate of exchange, reactivity of **C1** providing the (−)-enantiomer and of **C2** providing the (+)-enantiomer].
6. If the contribution of **C2** to the reaction is large enough, the (+)-enantiomer will dominate and an inversion of enantioselectivity will be observed.

4. Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker AC 300 (300 MHz) or a Bruker Avance (400 MHz) spectrometer with $CDCl_3$ or C_6D_6 as solvent. Chemical shifts (δ) are given in ppm downfield from TMS. Optical rotations were determined with a Perkin–Elmer 341 polarimeter. Rotations were determined in EtOH ($c = 1$) for stilbene oxide {lit.[17]; (*S*,*S*): $[\alpha]_D^{20} = -299$, ~100% ee}, in MeOH ($c = 0.5$) for the methyl *p*-methoxy cinnamate epoxide {lit.[17]; (2*R*,3*S*): $[\alpha]_D^{20} = -212$, ~100% ee} and neat for phenylpropileneoxide {lit.[17]; (*R*,*R*): $[\alpha]_D^{20} = +110$}. (−)-(*R*)-4,4a,5,6,7,8-Hexahydro-4a-methyl-2(3*H*)-naphthalenone (90% ee) was purchased from Aldrich. Stilbene oxide and styrene oxide exhibit identical NMR spectra with the racemic compounds purchased from Aldrich. Methyl *p*-methoxy cinnamate epoxide exhibits identical NMR spectra with the racemic compound provided to us by Sylachim–Finorga. Reactions were monitored by TLC using Merck's glass plates with silica gel 60 F_{254}. Silica gel Si 60 (40–60 μm) from Merck was used for the chromatographic purifications.

4.1. Silylenol ether: general procedure

To a solution of the desired ketone (1 equiv) in dry pentane (7 mL for 9 mmol) were added, under argon, Et_3N (2 equiv) and TMSCl (2 equiv) followed by a solution of anhydrous NaI (2 equiv) in dry CH_3CN (20 mL).[12] After 3 or 4 h at room temperature, stirring was stopped and the upper organic layer (pentane) transferred into a dry flask. The remaining mixture was extracted with dry pentane until no trace of silylenol ether was detected on TLC in the acetonitrile layer.[15] The pentane phases were gathered and evaporated to give a colorless oil, pure by NMR analysis.

4.2. Fluoration: general procedure

To a solution of the desired silylenol ether (1 equiv) in dry DMF (25 mL for 7 mmol) was added dropwise, under argon, a solution of Selecfluor (1.4 equiv) in DMF (40 mL). The mixture was stirred at 0 °C for 2 h. Then water (50 mL) was poured into the reaction mixture, the different phases were separated and the aqueous phase was extracted with ether (3 × 100 mL). The organic phases dried over $MgSO_4$. After filtration and evaporation, the residue (containing DMF) was directly purified by column chromatography with an appropriate pentane/ether gradient.

4.3. Epoxidation: general procedure

Distilled water (6 mL) and a solution (4 mL) of acetic acid (0.5 mL) and 0.1 M aqueous K_2CO_3 (100 mL) were added under stirring to a solution of 1 mmol of the desired olefin and 0.1 or 0.3 mmol of ketone (0.1 or 0.3 equiv) in DME (16 mL). The mixture was maintained at the desired temperature and a solution of oxone (1.850 g, 3 mmol, 6 equiv of oxidant) in distilled water (7 mL) added dropwise over 6 h. During the addition of oxone, the pH was controlled and regulated (~8.5–9) by the addition of a solution of K_2CO_3 1 M. The reaction was immediately quenched by the addition of CH_2Cl_2 (30 mL) and water (10 mL). The mixture was extracted with CH_2Cl_2 (3 × 20 mL), dried over Na_2SO_4 and analyzed by NMR. After chromatographic purification, the ketone was recovered and the isolated epoxide analyzed (NMR, optical rotation and/or chiral HPLC).

4.4. *trans*-10-Methyl decal-2-one, 8

For ^{1}H and ^{13}C NMR of **8** see Ref. 13.

4.5. *trans*-1,10-Dimethyl decal-1-ol, 9

2 Diastereomers **I/II** = 61/39. ^{1}H NMR ($CDCl_3$) 0.79 (s; 3H, Me, **I**); 0.84 (s, 3H, Me, **II**); 1.21 (s, 3H, Me, **I**); 1.26 (s, 3H, Me, **II**) and all ring protons between 1.1 and 1.5 ppm. ^{13}C NMR ($CDCl_3$) **I**: 14.7; 22.0; 26.9; 28.6; 31.8; 33.2; 34.8; 37.3; 39.8; 41.3; 42.0; 70.4. **II**: 15.3;

21.9; 26.8; 26.9; 28.8; 33.7; 36.4; 39.6; 41.2; 42.7; 43.5; 71.9.

4.6. Decalene 10 (90%)

^{1}H NMR ($CDCl_3$) 0.77 (s, 3H, Me); 1.62 (s, 3H, Me); ring signals 1.1–1.62; 5.27 (bm, 1H, olefinic). ^{13}C NMR ($CDCl_3$) 16.8; 22.4; 23.5; 27.1; 29.0; 32.1; 35.3; 40.5; 41.3; 119.9; 133.1.

4.7. Decalene 11 (10%)

^{1}H NMR ($CDCl_3$): all signals overlapped with those of **10** but 0.76 (s, 3H, Me) and 5.02 (br, 1H).

4.8. Dimethyl decalol 12 (95%)

^{1}H NMR ($CDCl_3$) 0.83 (s, 3H, Me); 0.93 (d, $^3J = 6$ Hz, 3H, Me); 0.9–1.7 (m, 15H); 3.39 (ddd br, $^3J_{gauche} = 4.5$ Hz, $^3J_{trans} = 9.5$ and 11 Hz, 1H, 95%). ^{13}C NMR ($CDCl_3$) 16.8; 18.6; 21.4; 26.9; 28.0; 35.3; 36.9; 41.3; 41.4; 45.0; 50.9; 73.3.

4.9. Dimethyl decalol 13 (5%)

All signals overlapped with those of **12** but 3.41 (t, $^3J_{trans} = 11$ Hz, 1H).

4.10. Dimethyl decalone 14

$[\alpha]_D^{25} = -38$ (*c* 1.17, $CHCl_3$) (90% ee). ^{1}H NMR ($CDCl_3$) 0.74 (s, 3H; Me); 0.99 (d, $^3J = 6$ Hz, 3H, Me); 1.1–1.9 (m, 11H); 2.08 (d, $^2J = 12.5$ Hz, 1H); 2.18 (d, $^2J = 12.5$ Hz, 1H); 2.38 (qdd, $^3J = 6.5$ Hz three times, $^3J_{trans} = 9$ Hz, $^3J_{gauche} = 2$ Hz, 1H). ^{13}C NMR ($CDCl_3$) 14.4; 16.5; 21.2; 26.6; 27.9; 38.6; 38.8; 41.2; 44.3; 45.4; 56.9; 212.9.

4.11. Trimethylsilyl derivative 15

^{1}H NMR ($CDCl_3$) 0.18 (s, 9H); 0.82 (s, 3H, Me); 1.55 (s, 3H, Me); 1.15–1.6 (m, 12H); 1.93 (d, $^2J = 20$ Hz, 1H). ^{13}C NMR ($CDCl_3$) 1.15, 16.3; 16.8; 22.3; 27.1; 28.7; 34.2; 35.6; 40.9; 41.5; 47.4; 111.0; 142.0.

4.12. Decalone 4a

$[\alpha]_D^{25} = -101$ (*c* 1.0, $CHCl_3$) (90% ee). IR ($CHCl_3$) 1730 cm^{-1}. Anal. Calcd for $C_{12}H_{19}FO$: C, 72.68; H, 9.65. Found: C, 72.32; H, 9.14. ^{1}H NMR (C_6D_6) 0.49 (s, 3H, Me); 0.68 (q br, 1H); 0.90–1.20 (m, 6H); 1.23 (m, 1H); 1.32 (d, 3H, $^3J_{HF} = 22$ Hz, Me); 1.52 (m, 1H); 1.62 (ddd, 1H, $^2J_{HH} = 12.5$ Hz, $^3J_{HH\,trans} = 13$ Hz, $^3J_{HF} = 4$ Hz); 1.79 (tt, 1H, $^3J_{trans} = {}^3J_{trans} = 13$ Hz, $^3J_{cis} = {}^3J_{cis} = 3.5$ Hz); 1.95 (d, 1H, $^2J = 12.5$ Hz, $^4J_{HF} = 6.5$ Hz). ^{13}C NMR (C_6D_6) 15.7; 20.5 (d, $^2J_{CF} = 24$ Hz); 21.2; 26.6; 27.4; 38.5; 39.2; 40.9; 42.6 (d, $^2J_{CF} = 22$ Hz); 53.2 (d, $^3J_{CF} = 2$ Hz); 96.5 (d, $^1J_{CF} = 169$ Hz); 204.7 (d, $^2 J_{CF} = 25$ Hz).

4.13. Trimethylsilyl derivatives 16 and 17 = 87/13

^{1}H NMR ($CDCl_3$), **16**: 0.20 (s, 9H, Me); 0.85 (s, 3H, Me); 1.15 (m, 4H); 1.50 (m, 5H); 1.70 (br d, 2H); 1.85 (br dt, 2H); 4.70 (m, 1H). ^{1}H NMR ($CDCl_3$), **17**: all signals overlapped with those of **16** but 4.50 (br, 1H).

^{13}C NMR ($CDCl_3$), **16**: 0.7; 16.5; 22.6, 26.9; 29.2; 32.4; 35.1; 40.9; 41.1; 41.2; 103.4; 149.0.

^{13}C NMR ($CDCl_3$), **17**: 0.7; 15.3; 22.2; 27.1; 28.2; 28.4; 33.0; 38.7; 39.8; 43.7, 109.3, 149.0.

4.14. Decalone 18

^{1}H NMR ($CDCl_3$) 0.95 (d, 3H, 3JHH = Hz, Me); 1.0 (s, 3H, Me); 1.1–1.2 (m, 3H); 1.45 (m, 5H); 1.65 (m, 2H); 2.16 (AB part of an ABX, 2H, $^2J_{HH} = 14$ Hz, $^3J_{AX} \sim 4$ Hz, $^3J_{BX} \sim 14$ Hz); 2.50 (d.pint = 7 lines, $^3J_{MeH} = {}^3J_{gauche} = 6.5$ Hz, $^3J_{trans} = 13$ Hz, 1H). ^{13}C NMR ($CDCl_3$) 14.5; 15.8; 21.4; 26.0; 28.8; 34.0; 40.2; 41.3; 45.1; 45.9; 51.5; 212.8.

4.15. Decalone 5e

$[\alpha]_D^{25} = +84$ (*c* 1.03, $CHCl_3$) (90% ee). IR ($CHCl_3$) 1730 cm^{-1}. Anal. Calcd for $C_{12}H_{19}FO$: C, 72.68; H, 9.65. Found: C, 72.24; H, 9.11. ^{1}H NMR (C_6D_6) 0.50 (s, 3H, Me); 0.65–1.25 (m, 8H); 1.30 (d, 3H, $^3J_{HF} = 22$ Hz, Me); 1.40 (m, 1H); 1.52 (t, 1H, $^2J_{HH} = {}^3J_{HF} = 14$ Hz); 1.71 (dd, 1H, $^2J_{HH} = 14$ Hz, $^3J_{HF} = 26$ Hz); 1.83 (dd, 1Haxial, $^2J_{HH} = 14.5$ Hz, $^3J_{HHtrans} = 13$ Hz); 2.25 (ddd, 1Hequatorial, $^2J_{HH} = 14.5$ Hz, $^3J_{HHcis} = 3$ Hz, $^4J_{HF} = 5$ Hz). ^{13}C NMR ($CDCl_3$) 17.1; 20.8; 24.4 (d, $^2J_{CF} = 27$ Hz); 225.7; 28.2, 40.8, 42.3; 43.7; 54.4 (d, $^2J_{CF} = 21$ Hz).

4.16. Decalone 6e

$[\alpha]_D^{25} = +66$ (*c* 1.10, $CHCl_3$) (containing 5% of **20e**, both being 90% ee). IR ($CHCl_3$) 1730 cm^{-1}. Anal. Calcd for $C_{11}H_{17}FO$: C, 71.70; H, 9.29. Found: C, 71.22; H, 9.01. ^{1}H NMR ($CDCl_3$) 1.10 (s, 3H, Me); 1.15–1.35 (m, 3H); 1.45–1.55 (m, 6H); 1.75 (m, 1H); 2.22 (m, 3H); 5.05 (ddd, 1Haxial, $^2J_{HF} = 48$ Hz, $^3J_{HHtrans} = 13$ Hz, $^3J_{HHgauche} = 7$ Hz). ^{13}C NMR (C_6D_6) 15.7; 20.5; 25.5; 27.9; 34.1; 39.6; 43.5; 47.8 (d, $^2J_{CF} = 17$ Hz); 90.4 (d, $^1J_{CF} = 188$ Hz); 202.6 (d, $^2J_{CF} = 12$ Hz).

4.17. Decalone 20e

^{1}H NMR ($CDCl_3$) signals overlapped with those of **6e** but 4.62 (dd, 1Haxial, $^2J_{HF} = 49$ Hz, $^3J_{HHtrans} = 12$ Hz). ^{13}C NMR (C_6D_6) 15.7; 21.0; 23.7; 25.0; 36.7; 40.2; 40.3; 50.0; 93.3 (d, $^1J_{CF} = 189$ Hz).

4.18. X-ray structure analysis of 4a

The selected crystal was mounted on a Nonius Kappa-CCD area detector diffractometer (Mo Kα, $\lambda = 0.71073$ Å). The complete conditions of data collection (Denzo software) and structure refinements are given below. The cell parameters were determined from reflections taken from one set of ten frames (1.0° steps in phi angle), each at 20 s exposure. The structures were solved using direct methods (SIR97) and refined against F^2 using the SHELXL97 software. All non-hydrogen

atoms were refined anisotropically. Hydrogen atoms were generated according to stereochemistry and refined using a riding model in SHELXL97.

Crystallographic data (excluding structure factors) have been deposited in the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 249289. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK (fax: (+44)1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Crystal data and structure refinement details: Colorless crystal; crystal dimension: $0.22 \times 0.17 \times 0.10\,mm^3$; $C_{12}H_{19}FO$, $M = 198.27\,g\,mol^{-1}$; orthorhombic; space group $P2_12_12_1$; $a = 7.479(5)$ Å; $b = 7.578(5)$ Å; $c = 19.197(5)$ Å; $Z = 4$; $Dc = 1.21\,g\,cm^{-3}$; μ(Mo Kα) = $0.086\,mm^{-1}$; a total of 1310 reflections; $2.89° < \theta < 26.967°$, 1310 independent reflections with 1279 having $I > 2\sigma(I)$; 127 parameters; Final results: $R1 = 0.0256$; $wR2 = 0.0614$, Goof = 1.040, maximum residual electronic density = $0.097\,e\,Å^{-3}$.

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