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Regio- and Stereoselective Ring Opening of 2,3-Diaryl Oxiranes by LiBr/Amberlyst 15: A New Stereocontrolled Access to 1,2-Diaryl-2-bromo Alcohols

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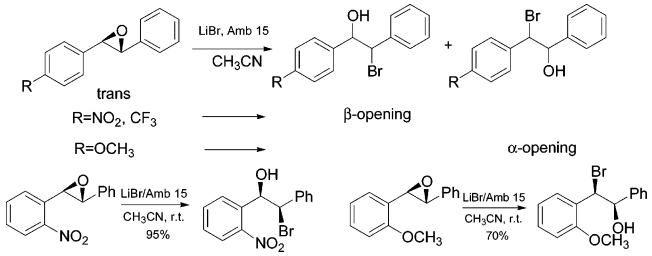

Both symmetrical and nonsymmetrical *trans*-2,3-diaryloxiranes are regio- and stereoselectively opened by the LiBr/Amberlyst 15 system. In the case of symmetrical *trans*-stilbene oxide, the *syn*- versus *anti*-bromohydrins ratio ranged between 88/12 and 30/70, by varying the reaction temperature from 20 to −30 °C. In the case of nonsymmetrical *para*-substituted *trans*-2,3-diaryloxiranes, the regioselectivity is determined by electronic effects. If one phenyl bears a strong electron-withdrawing group (as NO_2 or CF_3), the nucleophilic attack is totally on the β-carbon with respect to the substituted phenyl ring. With one phenyl bearing a strong electron-releasing group (OCH_3), the regioselectivity is reversed. Ab initio calculation at the DFT/B3LYP/6-31G* level, run on protonated epoxide structures, supports the formation of a cationic acyclic intermediate. Application of the method on *ortho*-methoxy and *ortho*-nitro 2,3-diaryloxiranes afforded the *syn*-bromohydrins in excellent yield, via regio- and stereoselective opening at either α- or β-carbon, respectively.

Introduction

Vicinal halo alcohols have attracted the interest of organic chemists both for their usefulness as versatile building blocks, as well as key intermediates in the synthesis of halogenated marine natural products. Although a variety of new procedures have been reported, most of them have some limitations, in terms of either harsh reaction conditions or low regioselectivity in the opening of unsymmetrical epoxides.[1] The most common method for the synthesis of 1,2-halohydrines from 1,2-epoxides is their ring opening either with hydrogen halides or with hydrohalogenic acid. These procedures are generally associated with byproducts such as *vic*-dihalides and 1,2-diols. In the past few years, new and milder procedures have been proposed, which used silyl halides in the presence of different promoters,[2] elemental halogen with various catalysts,[3] borane halogenides,[4] and metal halides with Lewis acid systems.[5] Among these

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TABLE 1. LiBr/Amb 15 Promoted Ring Opening of *trans*-Stilbene Oxide in Different Reaction Conditions

entry	LiBr/substrate	Amb/substrate mg/mmol	T	time	conv (%)[a]	yield (%)[b]	syn/anti[a]
1	2/1	440	rt	1 h	100	95	88/12
2	2/1	220	rt	6 h	81	80	83/17
3	4/1	440	rt	50 min	100	95	75/25
4	4/1	220	−15 °C	6 h	80	80	47/53
5	4/1	220	−25 °C	18 h	70	70	50/50
6	4/1	440	−30 °C	2 h 30 min	100	95	30/70
7	4/1	0	rt	4 h		no reaction	

[a] Calculated by ^{1}H NMR analysis of the crude mixture. [b] Isolated.

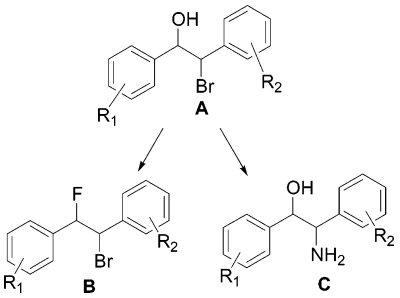
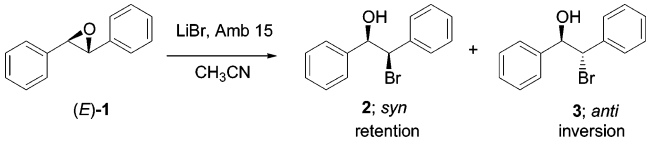


FIGURE 1. 2-Halo-1,2-diaryl alcohols as versatile intermediates.

methods, the use of elemental halogens suffers from low conversions, prolonged reaction times, and poor regioselectivity.[6] Lithium halides have been shown to be versatile reagents because of their availability at low cost. They also facilitate ring opening under mild conditions. Nevertheless, the use of strong Lewis acids often results in low yield of halohydrins when applied to acid sensitive substrates. Recently, the use of ionic liquids has broadened the application of such procedures.[7] Although there are many methods, very few are suitable to regioselective opening of nonsymmetrical 2,3-disubstituted oxiranes, and, in such cases, regio- and stereoselective openings are usually performed on substrates bearing chelating groups.[8]

In this context, 2,3-diaryloxiranes are challenging substrates in terms of regio- and stereoselectivity of the ring opening, due to the small (if any) differences of benzylic carbons reactivity. From a synthetic point of view, they represent useful starting materials, because the corresponding 2-halo-1,2-diaryl alcohols **A** are versatile intermediates for the synthesis of functionalized diaryl compounds, as, for instance, β-fluorobromides **B**,[9] and β-amino alcohols **C** (Figure 1). These latter compounds have recently received great attention, due to their use, in optically active form, as chiral auxiliaries in asymmetric synthesis,[10] chiral stationary phases for HPLC,[11] and chiral ligands in asymmetric catalysis.[12]

SCHEME 1



During our study on metal halides-promoted oxiranyl ring opening of (*E*)-2,3-diaryloxiranes, we found interesting results in terms of regio- and stereoselectivity, using either $MgBr_2$ or the NaBr/Amberlyst 15 system on either (*E*)-3-phenyl-2-(2-pyridyl)oxirane or (*E*)-2-(2-fluorophenyl)-3-phenyloxirane.[13]

The subsequent study on (*E*)-stilbene oxide using different metal bromides with or without Amberlyst 15 has led to a new straightforward stereodivergent synthesis to chiral *syn*- and *anti*-2-amino-1,2-diphenylethanols.[14]

These preliminary results prompted us to study, more deeply, both the influence of reaction conditions on the stereoselectivity in the opening of the model (*E*)-stilbene oxide and the regioselectivity in the opening of nonsymmetrical substituted 2,3-diaryloxiranes.

Results and Discussion

Among the different metal halides, LiBr was the reagent of choice for its high solubility in the reaction medium (acetonitrile) and its high reactivity, even at low temperatures. We considered also the optimum match between thermodynamic stability and chemical reactivity of the produced bromohydrins, if compared with the corresponding chlorohydrins or iodohydrins.

At the beginning, we analyzed the influence of different parameters (substrate/bromide ratio, substrate/Amberlyst 15 ratio, temperature, reagents concentration) on the stereoselectivity in the opening of (*E*)-stilbene oxide **4** with the LiBr/Amberlyst 15 system (Scheme 1). The most significant results are collected in Table 1.

As shown, different substrate/LiBr or substrate/Amberlyst ratios have usually little, if any, effect on the overall reaction rate, conversion, and/or stereoselectivity (compare entries 1−3).[15] On the other hand, by changing the reaction temperature, we noted a dramatic effect on

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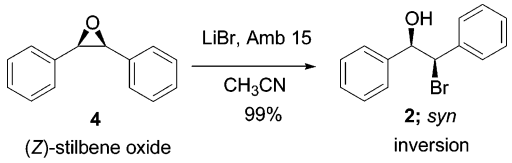
(15) Changes in reagent concentration had no apparent effect on the reaction.

SCHEME 2



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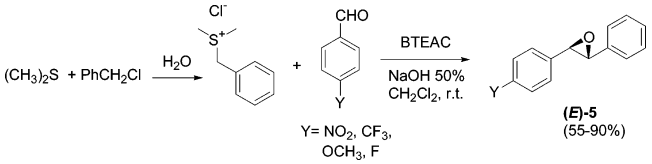

the stereoselectivity of the ring opening. At room temperature, the corresponding bromohydrins were obtained in high yield, with a syn/anti ratio ranging between 75/25 and 88/12 (entries 1−3). By lowering the temperature, the anti-bromohydrin increased, until becoming the major reaction product below −25 °C (entries 4−6).[16] A similar stereoselective opening "with retention of configuration" at the oxiranyl carbon atom had been already observed using different metal halides ($MgBr_2$, NaBr, KBr) and Amberlyst 15 at room temperature.[14] These more recent results could be explained assuming the formation of an acyclic cationic-type intermediate, which competes with a classical S_N2 opening. Moreover, the *syn*-bromohydrin resulted more favorably in these conditions. By lowering the temperature, the formation of the acyclic intermediate becomes slower, an S_N2 opening with inversion of configuration becomes competitive, and the syn/anti ratio of the products decreases. The hypothesis of a *syn*-bromohydrin favored by the formation of an acyclic intermediate was supported by the reaction of (*Z*)-stilbene epoxide **4**, which, in the presence of the LiBr/Amb 15 system at room temperature, also led quantitatively to *syn*-bromohydrin **2**, via nucleophilic opening with inversion of configuration (Scheme 2).

The existence of a possible thermodynamic equilibration between the two bromohydrins was excluded by the complete unreactivity of the *anti*-bromohydrin in the same reaction conditions (LiBr/substrate 4/1, Amb 15/substrate 440 mg/mmol, rt 24 h).

With these results in hands, we then studied the behavior of nonsymmetrical *para*-substituted 2,3-diaryloxiranes, because it still lacks an efficient regioselective opening method for such substrates. Thus, we prepared different *p*-substituted (*E*)-2,3-diaryloxiranes **5** in good to excellent yields, by the reaction of benzylidensulfur ylide, generated from the corresponding sulfonium salts under phase-transfer conditions, with the appropriate aryl aldehyde (Scheme 3).[17]

The results of the opening reactions with the LiBr/Amberlyst 15 system, at room temperature (Scheme 4), are collected in Table 2.

The relative (anti vs syn) stereochemistry was determined by alkaline ring closure of the bromohydrins mixture and determination of the trans or cis structure of the epoxides obtained using ^{1}H NMR. The regiochemistry was determined either after GC−MS analysis of the crude mixtures by identification of characteristic fragments or by NOESY experiments on the mixtures.

Characterization of Bromohydrins 6aI and 6aII. The structure **6a** was assigned to both the major **II** and the minor **I** isomers by NOESY experiments, which identified a correlation between the aryl protons at C2 and the proton at C5, assigned to CH(OH) (Figure 2).

Characterization of Bromohydrins 6bI and 6bII. The structure **6b** was assigned to both the major **II** and the minor **I** isomers after GC−MS analysis of the crude mixture, by identification of the characteristic fragments (peaks *m/z* =175 and *m/z* = 170 (^{79}Br), 172 (^{81}Br)) (Figure 3).

The mixture of **6c**, **7c**, and **7e** was characterized in a similar manner.

As it can be seen in Table 2, regioselectivity is affected by substituents electronic properties. In the oxiranes with one phenyl ring bearing a strong electron-withdrawing group (NO_2, CF_3: entries 1 and 2), only the regioisomer **6** was detected in the reaction mixture, in which the attack of the nucleophile is totally on the *β*-carbon with respect to the substituted phenyl ring.

On the other hand, fluorine substitution (entry 3) gave rise to both α and *β* openings with a low regioselectivity toward regioisomer **7c** (**6/7** = 40/60). In the presence of OCH_3 (electron-releasing group) on the phenyl ring, the regioisomer **7d** (α-opening) was the only one observed. In this case, the reaction was performed at −30 °C, obtaining bromohydrins **7d** in quantitative yield. Due to the lability of the products, they were characterized as acetates, by ^{1}H NMR and GC−MS analysis, after being quenched in situ by addition of a 1/1 Ac_2O/Pyr mixture. In these reaction conditions, we obtained also 25% of **8** (Figure 4), as byproduct, which was the only product when the reaction was performed at room temperature.

In the case of *trans*-*β*-methyl styrene epoxide (entry 5), the reaction was completely regioselective toward **7**, via an attack of the bromide on the most electrophilic benzylic carbon. All of these results match a general model in which the regioselectivity of the bromide attack is determined by the relative electrophilicity of the oxiranyl carbons.

To theoretically support the observed high regioselectivity, we considered the protonated epoxides **5a**($\mathbf{H}^+$) and **5d**($\mathbf{H}^+$) (Figure 5) as model structures for the reactive intermediate.

SCHEME 4

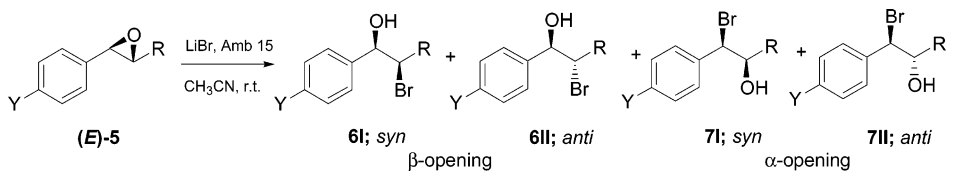

TABLE 2. LiBr/Amb 15 Promoted Ring Opening of Nonsymmetrical 2,3-Substituted Oxiranes, at Room Temperature (Except Entry 4)

					β-opening		α-opening	
entry[a]	epoxide	R	Y	reaction time	**6I**[b]	**6II**[b]	**7I**[b]	**7II**[b]
1	5a	Ph	NO_2	1 h	31	69		
2	5b	Ph	CF_3	45 min	38	57		5
3	5c	Ph	F	40 min	18[c]	22[c]	38[c]	22[c]
4	5d	Ph	OCH_3	2 h ($T = -30$ °C)			95 (dr = 3/2)[d]	
5	5e	CH_3	H	1 h			19[c]	81[c]

[a] All reactions were performed at rt, with LiBr/substrate = 4/1, Amb 15/substrate = 440 mg/mmol. The conversions were all higher than 99% and were determined by ^{1}H NMR spectroscopy of the crude product. [b] Determined by ^{1}H NMR spectroscopy of the crude product. [c] Determined by GC/MS analysis of the crude together with GC/MS and ^{1}H NMR analysis of the alkaline ring closure of the bromohydrins mixture. [d] The bromohydrins were characterized as acetates, after quenching the reaction in situ by adding a 1:1 Ac_2O/Pyr mixture at low temperature (see Experimental Section).

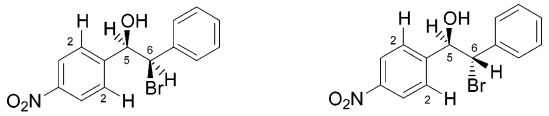

FIGURE 2. Bromohydrins **6aI** and **6aII**.

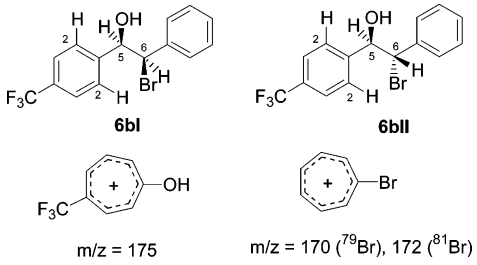

FIGURE 3. Bromohydrins **6bI** and **6bII** and characteristic fragments.

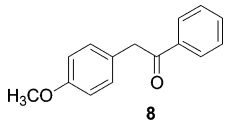

FIGURE 4. Structure of the byproduct **8**.

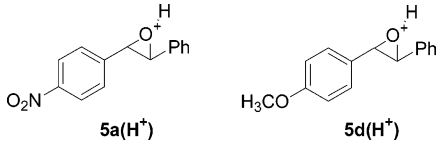

FIGURE 5. Model structures for the reactive intermediate.

We first noted that these structures invariably converged to acyclic cationic structures, if submitted to semiempirical calculations at the PM3 level. Thus, we first carried out a conformational search on the two couples of opened cationic structures by this level of calculation, using a SPARTAN 02 package. Each conformer found was then submitted to ab initio calculations at the DFT/B3LYP/6-31G* level using a GAUSSIAN 03 package.[18] Comparing the predicted free energies of the two opened *p*-NO_2 cationic structures **5a**(**H**$^+$)**A** and **5a**(**H**$^+$)**B**,[19] which would give products **6** and **7**, respectively, we calculated a difference in stability of 4.1 kcal/mol in favor of structure **5a**(**H**$^+$)**A** (Figure 6). Such a value would give rise to a complete regioselective ring opening, which was indeed observed.

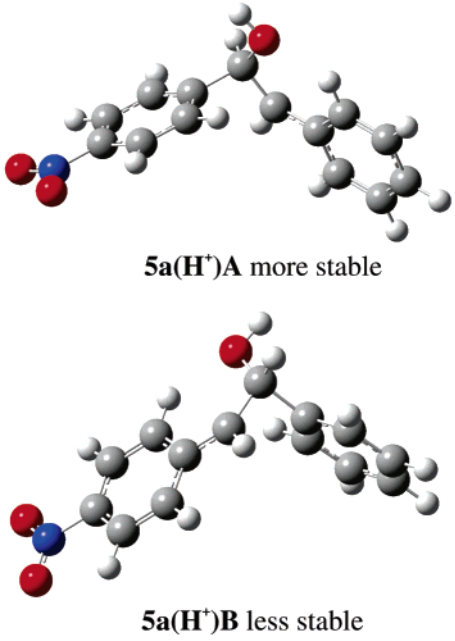

FIGURE 6. Minimized structures for **5a**(**H**$^+$)**A** and **5a**(**H**$^+$)**B**.

On the other hand, the same comparison between the free energies of *p*-OCH_3 cationic structures **5d**(**H**$^+$)**A** and **5d**(**H**$^+$)**B** provided a difference in stability of 7.6 kcal/

(16) At −30 °C with LiBr/substr. 4/1 and Amb 15/substr. 220 mg/mmol, we had syn/anti = 20/80; see ref 14.

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(19) Each structure was confirmed as a real minimum by noting the absence of imaginary values in the list of length frequencies.

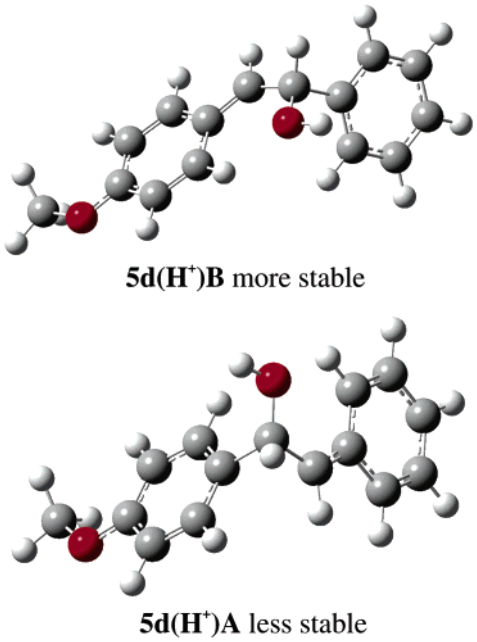
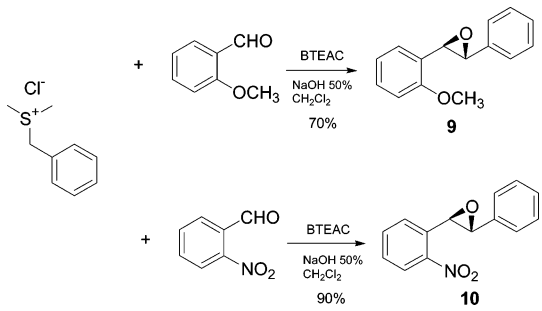


FIGURE 7. Minimized structures for **5d(H⁺)A** and **5d(H⁺)-B**.

SCHEME 5



mol in favor of **5d(H⁺)B** (Figure 7), which accounts for the total opposite regioselectivity (only **7** was observed) found in the experimental data.

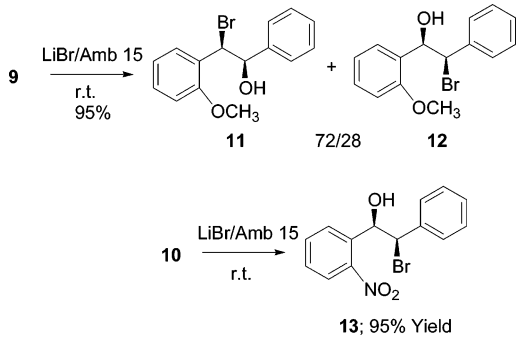
Concerning the stereoselectivity of the ring opening, there was a general trend in favoring *anti*-bromohydrins, whatever the *para*-substituent on the phenyl ring. This indicates a reliance between the stereoselectivity of ring opening and electronic effects of substituents, even if it is much less effective than in the regioselectivity.

Such interesting results, together with the previous ones[13] on substituent-induced regioselectivity, prompted us to investigate *ortho*-substituted nonsymmetric 2,3-diaryloxiranes, as trans **9** and **10**, which were prepared, in high yield, from benzyliden-dimethylsulfur ylide and either *o*-anisaldheyde or 2-nitrobenzaldehyde, respectively (Scheme 5).

Both epoxides were treated with the Li/Br Amb 15 system, in acetonitrile at room temperature (Scheme 6). *ortho*-Methoxy epoxide **9** afforded the *syn*-bromohydrin **11** in excellent yield, via a regio- and stereoselective opening at the α-carbon, with retention of configuration. On the other hand, *ortho*-nitro epoxide **10** showed a complete inversion of regioselectivity, leading to *syn*-bromohydrin **13**, almost quantitatively.

In these cases, the effects of the substituents on regio- and stereoselectivity match. Again, the regioselectivity

SCHEME 6



can be explained by a pure electronic effect. The extremely high stereoselectivity toward *syn* product, if compared with that observed for *para*-substituted compounds, indicates a likely stereoorienting effect of the *ortho* substituent on the cationic intermediate, which leads to the product with retention of configuration.

Conclusions

Symmetrical and nonsymmetrical *trans*-2,3-diaryloxiranes represent useful substrates in the regio- and stereoselective ring opening with the LiBr/Amberlyst 15 system. The high *syn* stereoselectivity observed in the case of *trans*-stilbene oxide, together with the electronic effect of substituents on the regioselectivity in the case of nonsymmetrical substrates,[20] allowed us to prepare, in high yield, *ortho*-methoxyaryl and *ortho*-nitroaryl bromohydrins, as key intermediates in the synthesis of new polydentate ligands.

Experimental Section

(*E*)-Stilbene oxide 1, **(*Z*)-stilbene oxide 4, and (*E*)-1-phenylpropylene oxide 5e** were prepared by oxidation of commercial *trans*-stilbene, *cis*-stilbene, and *trans*-*β*-methyl styrene with *m*CPBA, in CH_2Cl_2 at room temperature. The ^1H NMR spectra were consistent with those of commercially available compounds.

(*E*)-2-(4-Nitrophenyl)-3-phenyloxirane 5a was obtained in 80% yield after chromatographic purification (*n*-hexane/Et_2O = 7/3). The ^1H and ^{13}C NMR spectra were consistent with literature data.[21]

(*Z*)-2-(4-Nitrophenyl)-3-phenyloxirane was detected in the crude of alkaline ring closure of a 31/69 **6aI/6aII** mixture. ^1H NMR (300 MHz, $CDCl_3$), in mixture with **5a**: overlapping signals but $\delta = 4.42$ (A part of AB system, $^3J_{AB} = 7.0$ Hz, 1H), 4.49 (B part of AB system, $^3J_{AB} = 7.0$ Hz, 1H).

(*E*)-3-Phenyl-2-(4-trifluoromethylphenyl)oxirane 5b was obtained in 80% yield after chromatographic purification (*n*-hexane/CH_2Cl_2/benzene = 8/1/1). ^1H NMR (500 MHz, $CDCl_3$): $\delta = 3.88$ (d, $^3J = 1.4$ Hz, 1H), 3.97 (d, $^3J = 1.4$ Hz, 1H), 7.40−7.43 (m, 5H), 7.50 (d, $^3J = 8.1$ Hz, 2H), 7.67 (d, $^3J = 8.1$ Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): $\delta = 62.0$, 63.1, 124.0 (q, $^1J_{CF} = 273$ Hz), 125.5, 125.8, 128.3, 128.6, 128.7, 130.4 (q, $^2J_{CF} = 32$ Hz), 136.5, 141.1. MS (*m*/*z*, %): 264 [M⁺] (100), 246 (46), 235 (97). Anal. Calcd for $C_{15}H_{11}F_3O$: C, 68.18; H, 4.20. Found: C, 68.3; H, 4.2.

10% of (*Z*) epoxide was also detected in the crude. ^1H NMR (300 MHz, $CDCl_3$), in mixture with **5b**: overlapping signals but $\delta = 4.64$ (A part of AB system, $^3J_{AB} = 7.0$ Hz, 1H), 4.67 (B

(20) For a recent study on the electronic effect on the regioselectivity in the opening of aryloxiranes with acetylides, see: Shindo, M.; Sugioka, T.; Shishido, K. *Tetrahedron Lett.* **2004**, 9265−9268.

(21) Imuta, M.; Ziffer, H. *J. Org. Chem.* **1979**, *44*, 2505−2509.

part of AB system, $^3J_{AB}$ = 7.0 Hz, 1H). MS (*m/z*, %): 264 [M$^+$] (100), 246 (45), 235 (99).

(*E*)-2-(4-Fluorophenyl)-3-phenyl-oxirane 5c was obtained in 67% yield after chromatographic purification (petroleum ether/Et_2O = 9/1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.86 (brs, 1H), 3.89 (brs, 1H), 7.09 (d, ^3J = 10 Hz, 1H), 7.11 (d, ^3J = 10 Hz, 1H), 7.32−7.42 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 62.2, 62.7, 115.5 (d, $^2J_{CF}$ = 22 Hz), 125.4, 127.1 (d, $^3J_{CF}$ = 14 Hz), 128.4, 128.5, 132.8 (d, $^4J_{CF}$ = 3 Hz), 136.8, 162.7 (d, $^1J_{CF}$ = 245 Hz). MS (*m/z*, %): 214 [M$^+$] (46), 213 (40), 196 (24), 185 (100). Anal. Calcd for $C_{14}H_{11}FO$: C, 78.49; H, 5.18. Found: C, 49.2; H, 4.90.

29% of (*Z*) epoxide was also isolated. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 4.35 (brs, 1H), 4.37 (brs, 1H), 6.88 (d, ^3J = 10 Hz, 1H), 6.90 (d, ^3J = 10 Hz, 1H), 7.14−7.23 (m, 7H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 59.1, 59.6, 114.8 (d, $^2J_{CF}$ = 22 Hz), 126.8, 127.6, 127.8, 128.5 (d, $^3J_{CF}$ = 14 Hz), 130.1, 134.1, 163.7 (d, $^1J_{CF}$ = 245 Hz). MS (*m/z*,%): 214 [M$^+$] (44), 213 (40), 196 (23), 185 (100).

(*E*)-2-(4-Methoxyphenyl)-3-phenyl-oxirane 5d was obtained in 70% yield after recrystallization in petroleum ether. The ^{1}H NMR and MS spectra were consistent with literature data.[22]

(*Z*)-1-Phenylpropylene oxide was detected in the crude of alkaline ring closure of a 19/81 **7eI/7eII** mixture. ^{1}H NMR (300 MHz, $CDCl_3$), in mixture with **5e**: overlapping signals but δ = 1.10 (d, ^3J = 6.0 Hz), 3.37 (dd, $^3J_1$ = 6.0 Hz, $^3J_2$ = 4.0 Hz), 4.09 (d, ^3J = 4.0 Hz).

(*E*)-2-(2-Methoxyphenyl)-3-phenyloxirane 9 was obtained in 65% yield after chromatographic purification (petroleum ether/Et_2O = 9/1). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.85 (s, 3H), 3.86 (d, ^3J = 1.8 Hz, 1H), 4.34 (d, ^3J = 1.8 Hz, 1H), 6.94 (d, ^3J = 8.8 Hz, 1H), 7.06 (dd, $^3J_1$ = 7.5 Hz, $^3J_2$ = 7.5 Hz, 1H), 7.33−7.45 (m, 7H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.2, 58.2, 62.2, 110.1, 120.6, 124.9, 125.6, 128.0, 128.3, 128.8, 137.4, 158.0. MS (*m/z*,%): 226 [M$^+$] (20), 209 (22), 197 (41), 91 (100). Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.8; H, 6.3.

34% of (*Z*) epoxide was also isolated. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.72 (s, 3H), 4.42 (A part of AB system, $^3J_{AB}$ = 4.4 Hz, 1H), 4.46 (B part of AB system, $^3J_{AB}$ = 4.4 Hz, 1H), 6.70 (d, ^3J = 8.2 Hz, 1H), 6.84 (dd, $^3J_1$ = 7.5 Hz, $^3J_2$ = 7.5 Hz, 1H), 7.12−7.21 (m, 6H), 7.28 (dd, $^3J_1$ = 7.5 Hz, $^3J_2$ = 1.6 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 55.1, 57.3, 59.2, 109.7, 119.7, 126.5, 127.1, 127.3, 128.0, 128.4, 134.9, 157.5. MS (*m/z*, %): 226 [M$^+$] (20), 209 (22), 197 (41), 91 (100). Anal. Calcd for $C_{15}H_{14}O_2$: C, 79.62; H, 6.24. Found: C, 79.7; H, 6.2.

(*E*)-2-(2-Nitrophenyl)-3-phenyloxirane 10 was obtained in 90% yield after chromatographic purification (petroleum ether/Et_2O = 4/1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.83 (d, ^3J = 3.0 Hz, 1H), 4.54 (d, ^3J = 3.0 Hz, 1H), 7.40−7.45 (m, 5H), 7.54 (m, 1H), 7.75 (m, 2H), 8.20 (d, ^3J = 11 Hz, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 59.9, 62.1, 124.7, 125.8, 126.0, 127.0, 128.5, 128.6, 128.6, 133.9, 134.3, 136.1. MS (*m/z*, %): 225 [M − 16]$^+$ (1), 135 (100). Anal. Calcd for $C_{14}H_{11}NO_3$: C, 69.70; H, 4.70. Found: C, 69.5; H, 4.6.

(*Z*)-2-(2-Nitrophenyl)-3-phenyloxirane was detected in the crude of alkaline ring closure of **13**. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 4.59 (d, $^3J_1$ = 4.5 Hz, 1H), 4.81 (d, ^3J = 4.5 Hz, 1H), 7.20 (m, 5H), 7.76 (m, 1H), 7.57 (d, ^3J = 10 Hz, 1H), 7.96 (d, ^3J = 10 Hz, 1H).

Spectra of *syn*- and *anti*-2-bromo-1,2-diphenylethanols **2** and **3** were compared with known data.[14]

The *syn*- and *anti*-2-Bromo-1-(4-nitrophenyl)-2-phenylethanols 6aI and 6aII. Characterization by ^{1}H NMR of the mixture **6aI/6aII** = 31/69. ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.80 (brs, 1H, OH, **6II**, 69%), 3.30 (brs, 1H, OH, **6aI**, 31%), 5.06 (d, ^3J = 8.5 Hz, 1H, C*H*Br, **6aI**, 31%), 5.07 (d, ^3J = 6.4 Hz, 1H, C*H*Br, **6aII**, 69%), 5.15 (d, ^3J = 8.5 Hz, 1H, C*H*OH, **6aI**, 31%), 5.29 (d, ^3J = 6.4 Hz, 1H, C*H*OH, **6aII**, 69%), 7.20−7.40 (m, C*H* arom., **6aI**+**6aII**), 7.47 (d, ^3J = 8.6 Hz, 2H, C*H* arom., **6aII**, 69%), 8.04 (d, ^3J = 8.6 Hz, 2H, **6aI**, 31%), 8.15 (d, ^3J = 8.6 Hz, 2H, **6aII**, 69%). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 58.2 (*C*HBr, **6aI**), 63.1 (*C*HBr, **6aII**), 77.1 (*C*HOH, **6aII**), 77.5 (*C*HOH, **6aI**), 123.2, 126.5, 127.8, 128.0, 128.2, 128.4, 128.6, 128.7, 128.8, 129.1, 130.1, 136.6, 137.4, 145.9, 146.6.

***syn*-2-Bromo-2-phenyl-1-(4-trifluoromethylphenyl) ethanol 6bI** was obtained in 35% yield after chromatographic purification (*n*-hex/Et_2O/benzene = 8/2/1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.17 (brs, 1H), 5.10 (brs, 2H), 7.25−7.40 (m, 6H), 7.46 (d, ^3J = 8.1 Hz, 2H), 7.58 (m, 1H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 63.7, 77.7, 123.9 (q, $^1J_{CF}$ = 271 Hz), 125.1 (q, $^3J_{CF}$ = 3.8 Hz), 126.7, 127.2, 127.5, 128.3, 128.6, 128.9, 130.2 (q, $^2J_{CF}$ = 32 Hz), 137.6, 142.6. MS (*m/z*, %): 327 [M + 2]$^+$ (2), 325 [M$^+$] (2), 175 (100), 172 (26), 170 (26). Anal. Calcd for $C_{15}H_{12}BrF_3O$: C, 52.20; H, 3.50. Found: C, 53.3; H, 3.6.

***anti*-2-Bromo-2-phenyl-1-(4-trifluoromethylphenyl) ethanol 6bII** was obtained in 55% yield after chromatographic purification (*n*-hex/Et_2O/benzene = 8/2/1). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.55 (brs, 1H), 5.07 (d, ^3J = 6.4 Hz), 5.25 (brd, ^3J = 6.4 Hz), 7.25 (m, 2H), 7.33−7.44 (m, 5H), 7.58 (d, ^3J = 8.1 Hz, 2H). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 58.4, 77.5, 125.1, 126.1 (q, $^1J_{CF}$ = 271 Hz), 127.5, 128.3, 128.4. MS (*m/z*, %): 327 [M + 2]$^+$ (2), 325 [M$^+$] (2), 175 (100), 172 (26), 170 (26). Anal. Calcd for $C_{15}H_{12}BrF_3O$: C, 52.20; H, 3.50. Found: C, 53.4; H, 3.7.

The *syn*- and *anti*-2-bromo-2-(4-methoxyphenyl)-1-phenyl-ethanols 7dI and 7dII were obtained as the only reaction products in the crude and were analyzed by ^{1}H NMR. ^{1}H NMR (500 MHz, $CDCl_3$), 63/37 mixture of two diastereoisomers: δ = 3.78 (s, 3H, OCH_3, 63%), 3.82 (s, 3H, OCH_3, 37%), 4.66 (A part of AB system, J_{AB} = 6.5 Hz, 1H, 63%), 4.69 (B part of AB system, J_{AB} = 6.5 Hz, 1H, 63%), 4.78 (A part of AB system, J_{AB} = 5.5 Hz, 1H, 37%), 4.82 (B part of AB system, J_{AB} = 5.5 Hz, 1H, 37%), 6.77 (d, ^3J = 8.0 Hz, 2H, 63%), 6.86 (d, ^3J = 8.5 Hz, 2H, 37%), 7.05 (d, ^3J = 8.0 Hz, 2H, 63%), 7.13 (m, 1H), 7.19 (d, ^3J = 8.5 Hz, 2H, 37%), 7.24−7.34 (m, 4H).

The *syn*- and *anti*-2-bromo-2-(4-methoxyphenyl)-1-phenyl-ethanol acetates were obtained by quenching the reaction mixture with 1 mL of a Ac_2O/pyridine 1/1 mixture, at −30 °C and usual workup. ^{1}H NMR (300 MHz, $CDCl_3$) in mixture (76/24) with ketone **8**: δ = 3.74 (s, 3H, OCH_3, 48%), 3.80 (s, 3H, OCH_3, **8**, 24%), 3.82 (s, 3H, OCH_3, 28%), 4.24 (s, 2H, **8**, 24%), 5.18 (d, ^3J = 8.5 Hz, 1H, 28%), 5.19 (d, ^3J = 9.5 Hz, 1H, 48%), 6.23 (d, ^3J = 9.5 Hz, 1H, 48%), 6.29 (d, ^3J = 8.5 Hz, 1H, 28%), 6.70−7.60 (m), 8.03 (d, ^3J = 6.6 Hz, 2H, **8**, 24%). MS (for both the acetates) (*m/z*, %): 350 [M + 2]$^+$ (1), 348 [M$^+$] (1), 290 (4), 288 (4), 201 (17), 199 (17), 137 (100).

MS (for **8**) (*m/z*, %): 226 [M]$^+$ (26), 121 (100), 105 (83).

The *syn*- and *anti*-3-bromo-3-phenyl-2-propanols 7eI and **7eII** were obtained quantitatively after the workup. ^{1}H NMR (500 MHz, $CDCl_3$), 81/19 mixture of **7eII/7eI**: δ = 1.13 (d, ^3J = 6.5 Hz, 3H, CH_3, **7eI**, 19%), 1.37 (d, ^3J = 5.5 Hz, 3H, CH_3, **7eII**, 81%), 2.26 (brs, 1H, OH, **7eI** and **7eII**), 4.24 (m, 1H, **7eI** and **7eII**), 4.88 (d, ^3J = 7.0 Hz, 1H, **7eI**, 19%), 4.90 (d, ^3J = 6.0 Hz, 1H, **7eII**, 81%), 7.33−7.49 (m, 5H, **7eI** and **7eII**). MS (for both **7eI** and **7eII**) (*m/z*, %): 216 [M + 2]$^+$ (1), 214 [M$^+$] (1), 172 (32), 170 (32), 91 (100).

***syn*-2-Bromo-2-(2-methoxyphenyl)-1-phenyl-ethanol 11 and *syn*-2-Bromo-1-(2-methoxyphenyl)-2-phenyl ethanol 12** were obtained quantitatively after the workup. ^{1}H NMR (300 MHz, $CDCl_3$), 72/28 mixture of **11/12**: δ = 2.83 (brs, 1H), 3.66 (s, 3H, OCH_3, **11**, 72%), 3.73 (s, 3H, OCH_3, **12**, 28%), 5.14 (d, ^3J = 8.0 Hz, 1H, **11**, 72%), 5.28 (d, ^3J = 6.8 Hz, 1H, **12**, 28%), 5.75 (d, ^3J = 8.0 Hz, 1H, **11**, 72%), 5.76 (d, ^3J = 6.8 Hz, 1H, **12**, 28%), 6.71 (d, ^3J = 8.4 Hz, 1H, **11**, 72%), 6.83 (d, ^3J = 8.4 Hz, 1H, **12**, 28%), 6.92 (dd, $^3J_1$ = 7.6 Hz, $^3J_2$ = 7.5 Hz, 1H, **11**, 72%), 7.00 (dd, $^3J_1$ = 7.6 Hz, $^3J_2$ = 7.5 Hz, 1H, **12**, 28%), 7.17−7.22 (m, 6H), 7.53 (dd, ^3J = 7.5 Hz, ^4J = 1.3 Hz, 1H, **11**, 72%), 7.60 (d, ^3J = 7.5 Hz, 1H, **12**, 28%).

(22) Majima, T.; Tojo, S.; Ispida, A.; Takamuko, S. *J. Org. Chem.* **1996**, *61*, 7793−7800.

The crude was acetylated by a 1/1 Ac_2O/pyridine mixture at room temperature. After usual workup, the reaction mixture was analyzed via ^1H NMR and GC−MS.

***syn*-2-Bromo-2-(2-methoxyphenyl)-1-phenyl-ethanol and *syn*-2-Bromo-1-(2-methoxyphenyl)-2-phenyl-ethanol Acetates.** ^1H NMR (300 MHz, $CDCl_3$), 72/28 mixture of acetates: δ = 2.20 (s, 3H, CH_3COO), 3.70 (s, 3H, OCH_3, 72%), 3.72 (s, 3H, OCH_3, 28%), 5.79 (d, ^3J = 9.0 Hz, 1H, CHBr, 72%), 5.81 (d, ^3J = 9.0 Hz, 1H, CHBr, 28%), 6.33 (d, ^3J = 9.0 Hz, 1H, C*H*OAc, 72%), 6.35 (d, ^3J = 9.0 Hz, 1H, C*H*OAc, 28%), 6.68 (brd, ^3J = 8.3 Hz, 1H), 6.88 (m, 2H), 7.17−7.33 (m, 5H), 7.44 (m, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 52.2, 55.4, 55.6, 58.1, 77.3, 110.9, 120.7, 120.8, 126.8, 126.9, 127.0, 127.3, 127.4, 127.7, 128.1, 128.3, 128.4, 129.8, 130.0, 130.3, 139.2, 140.0, 155.9, 156.6. MS (for both the acetylated products) (*m*/*z*, %): 350 $[M + 2]^+$ (1), 348 $[M^+]$ (1), 290 (7), 288 (7), 269 (73), 107 (100).

***syn*-2-Bromo-1-(2-nitrophenyl)-2-phenyl ethanol 13** was obtained in 95% yield after chromatographic purification. ^1H NMR (300 MHz, $CDCl_3$): δ = 5.41 (d, ^3J = 4.8 Hz, 1H), 5.70 (d, ^3J = 4.8 Hz, 1H), 7.31 (m, 3H), 7.43 (m, 3H), 7.65 (m, 1H), 7.85 (d, ^3J = 11.4 Hz, 1H). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 62.1, 72.6, 124.6, 128.2, 128.3, 128.7, 128.8, 128.9, 129.4, 129.6, 129.9, 133.1, 135.5, 138.2. Anal. Calcd for $C_{14}H_{12}BrNO_3$: C, 52.20; H, 3.75. Found: C, 52.1; H, 3.6.

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Supporting Information Available: Spectral data of compounds **5b**−**d**, **6a**,**b**, **7d**,**e**, **8**, **9**, **10**, **11**, **12**, **13**. ^1H and ^{13}C NMR spectra of key compounds. Energies and Cartesian coordinates for structures **5a**(**H**$^+$)**A**, **5a**(**H**$^+$)**B**, **5d**(**H**$^+$)**A**, and **5d**(**H**$^+$)**B**. This material is available free of charge via the Internet at http://pubs.acs.org.

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