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Conservation of the Planar Chiral Information in the Tandem Oxy-Cope/Ene Reaction

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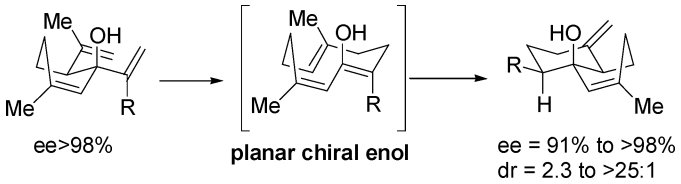

We report the stereoselective synthesis of a Decalin unit using a tandem oxy-Cope/ene reaction. [3,3]-Shift of 1,2-divinylcyclohexenol **18** generates (1*E*, 3*Z*, 7*E*) cyclodecatrien-2-ol **23** which tautomerizes to ketone **21** (Figure 3). The chiral information embedded in **23** is transferred into the newly formed stereogenic carbon C6 in **21**. The efficiency of the chirality transfer is a reflection of the difference in the rates of ring inversion versus tautomerization of **23**. Ketone **21** undergoes a carbonyl-ene reaction to give Decalin **20**. Assuming a rapid equilibrium between macrocyclic diastereomers, the diastereomeric ratio of the transannular ene reaction is governed by the Curtin−Hammett principle. Analysis of the conservation of the planar chiral information in the tandem oxy-Cope/ene reaction is presented.

Introduction

The limited freedom incurred by the presence of an *E* olefin on a cyclic structure may introduce atropisomerism to a ring.[2] When the transannular portion of the methylene chain on a *trans*-cycloalkene is short enough, the structures may exist as enantiomers even though the molecule is devoid of stereogenic centers on the backbone of the macrocycle. In 1962, Cope and co-workers reported the first examples of atropisomerism in cycloalkenes with the isolation of (+)-*cis*-*trans*-1,5-cyclooctadiene **2** from the Hofmann elimination of (−)-methiodide **1** (eq 1) and the resolution of (±)-*trans*-cyclooctene **3** with platinum dichloride and (+)-1-phenyl-2-amino propane (eq 2) (Scheme 1).[3,4] The chirality observed in these compounds was explained by the high rigidity of these structures in addition to the interaction of transannular hydrogens which prevent the rotation of the *E* olefin.

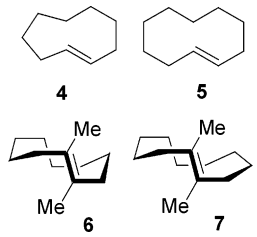

FIGURE 1. Structure of optically active cycloalkenes.

Applying the resolution presented above to larger cycloalkenes such as (±)-*trans*-cyclononene **4** and (±)-*trans*-cycodecene **5** did not produce the corresponding enantiopure macrocycles owing to their flexibility allowing a rapid interchange between enantiomers (ring inversion), thus preventing their isolation at room temperature (Figure 1).[5,6] In (±)-**4**, however, it was possible to observe optical activities at 0 °C after a rapid resolution of the racemic mixture followed by immediate cooling to −80 °C.

(1) Current address: Merck-Frosst Canada, Pointe-Claire, Canada.

(2) For discussion on planar chirality in macrocycles, see (a) Eliel, E. L.; Wilen, S. H. *Stereochemistry of Organic Compounds*; Wiley-Interscience: New York, 1994. (b) Schlögl, K. *Top. Curr. Chem.* **1984**, *125*, 27.

(3) (a) Cope, A. C.; Howell, C. F.; Knowles, A. *J. Am. Chem. Soc.* **1962**, *84*, 3190. (b) Cope, A. C.; Ganelin, C. R.; Johnson, H. W. *J. Am. Chem. Soc.* **1962**, *84*, 3191. (c) Manor, P. C.; Shoemaker, D. P.; Parkes, A. S. *J. Am. Chem. Soc.* **1970**, *92*, 5260.

(4) For the preparation of optically active (*E*)-cycloheptene and (*E*)-cyclooctene from the corresponding (*Z*)-cycloalkenes in the presence of a chiral sensitizer, see (a) Hoffmann, R.; Inoue, Y. *J. Am. Chem. Soc.* **1999**, *121*, 10702. (b) Inoue, Y.; Matsushima, E.; Wada, T. *J. Am. Chem. Soc.* **1998**, *120*, 10687. (c) Inoue, Y.; Yamasaki, N.; Yokoyama, T.; Tai, A. *J. Org. Chem.* **1993**, *58*, 1011. (d) Inoue, Y.; Yamasaki, N.; Yokoyama, T.; Tai, A. *J. Org. Chem.* **1992**, *57*, 1332.

(5) Cope, A. C.; Banholzer, K.; Keller, H.; Pawson, B. A.; Whang, J. J.; Winkler, H. J. S. *J. Am. Chem. Soc.* **1965**, *87*, 3644.

(6) For transfer of planar chiral information in nine-membered lactam rings, see (a) Nubbmeyer, U. Sudau, A.; Münich, W. *Chem. Eur. J.* **2001**, *7*, 611. (b) Nubbmeyer, U. Sudau, A. *Angew. Chem., Int. Ed.* **1998**, *37*, 1140. (c) Nubbmeyer, U. Sudau, A.; Münich, W.; Bats, J. W. *J. Org. Chem.* **2000**, *65*, 1710.

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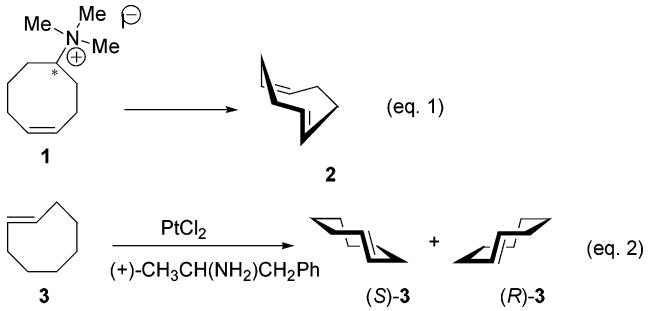

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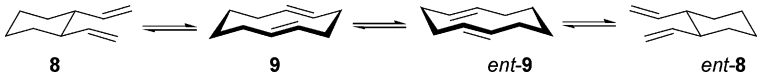


From this, the energy barriers for rotation and the half-lives of the optical activity at room temperature for **3**,[7] **4**,[3] and **5**[8] were measured and reported as 35.6 kcal/mol ($t_{1/2} \sim 10^5$ years), 20.0 kcal/mol ($t_{1/2} \sim 10$ s), and 10.7 kcal/mol ($t_{1/2} \sim 10^{-4}$ s), respectively. The superior flexibility of **5** which accounts for its inability to be resolved was of particular interest. In 1980, Marshall and co-workers successfully isolated optically stable *trans*-1,2-dimethylcyclodecene **6** and *trans*-1,2-dimethylcycloundecene **7**.[9] They demonstrated that the presence of the methyl substituents on the double bond raised the activation energy for racemization by increasing steric interactions during double-bond rotation. Marshall reported that **7** showed no loss of optical activity after heating for 3 days at 100 °C and two distillations at 190−205 °C. Wharton and Johnson measured the rate constant for the conversion of *trans*-1,2-divinylcyclohexane **8** to *ent*-**8** on the basis of its racemization (Scheme 2).[10] Cope reaction of **8** followed by ring inversion of **9** and the reverse [3,3] resulted in the loss of chirality of **8**. Despite their high rigidity, the *trans-trans*-1,5-cyclodecadiene **9** or *ent*-**9** proved to be enantiomerically unstable.

In 2001, Barriault and Deon accomplished the first total synthesis of (+)-arteannium M (**10**)[11] using the tandem oxy-Cope/ene reaction[12] as the key step to create the Decalin core **15**.

The tandem process is triggered by an oxy-Cope reaction of **11** (ee > 98%) to furnish enol **12** which tautomerizes to enone **13**. The latter is poised to undergo a transannular ene reaction giving the desired Decalin **15**. A close inspection of macrocyclic enol **12** reveals that the backbone of the ring is devoid of sp^3 stereogenic centers. In this case, the molecular chirality of **12** is due to all of the sp^2 carbons embedded in the macrocyclic backbone. We suggested that the chirality transfer observed during the oxy-Cope rearrangement can be explained on the basis of an energy barrier for inversion of **12** to *ent*-**12** and preferential stereofacial protonation (Figure 2). The macrocycle **12** possesses a conjugated

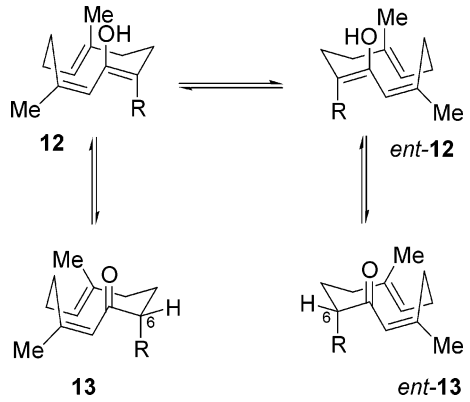


FIGURE 2. Preferential stereofacial protonation of macrocyclic enols **12** and *ent*-**12**.

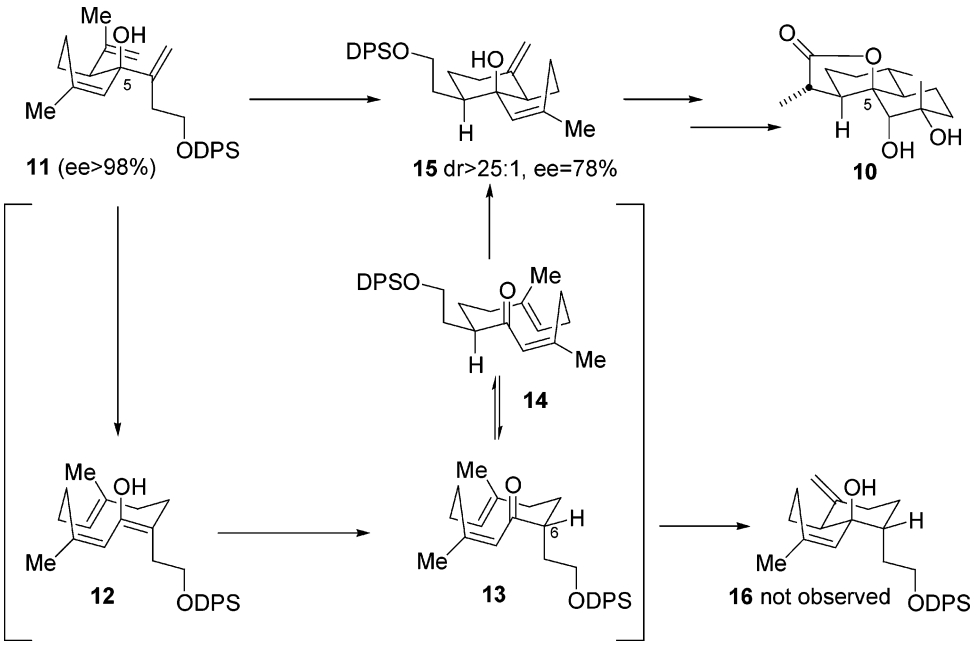
dienol (*E*, *Z*) and a second *E* double bond (ene donor) which creates a strained and rigid macrocyclic ring. As a result, the conversion of **12** into *ent*-**12** requires that the enol moiety rotates inside the macrocycle, which is an energetically demanding process.[7] At the same time, protonation of enol **12** occurs from the β-face to yield ketone **13**. Complete transfer of chirality, however, was not observed and a 20% loss of enantiopurity occurred which suggests that a partial protonation from the α face of **12** gave *ent*-**13** directly. This represents a rare case of the use of planar chirality in macrocycles in the total synthesis of natural products. To explain the enantioselectivity of the tandem process in greater detail, a series of 1,2-divinylcyclohexenols was prepared and irradiated with microwaves under various conditions.[13]

Results and Discussion

1,2-Divinylcycohexenols **18a**−**f** (ee > 98%) were readily obtained by a halogen−metal exchange of the corresponding haloalkene using *tert*-butyllithium, followed by the addition of *S*-isopiperitenone **17** (Scheme 4).[14] Sub-

(7) Cope, A. C.; Pawson, B. A. *J. Am. Chem. Soc.* **1965**, *87*, 3649.
(8) Binsh, G.; Roberts, J. D. *J. Am. Chem. Soc.* **1965**, *87*, 5157.
(9) Marshall, J. A.; Konicek, T. R.; Flynn, K. E. *J. Am. Chem. Soc.* **1980**, *102*, 3287.
(10) Wharton, P. S.; Johnson, D. W. *J. Org. Chem.* **1973**, *38*, 4117.
(11) Barriault, L.; Deon, D. H. *Org. Lett.* **2001**, *3*, 1925.
(12) (a) Barriault, L.; Warrington, J. M.; Yap, G. P. A. *Org. Lett.* **2000**, *2*, 663. For other examples see (b) Paquette, L. A.; Nakatani, S.; Zydowsky, T. M.; Edmondson, S. D.; Sun, Q.-L.; Skerlj, R. *J. Org. Chem.* **1999**, *64*, 3244. (c) Rajagopalan, K.; Srinivasan, R. *Tetrahedron Lett.* **1998**, *39*, 4133. (d) Shanmugan, P.; Devan, B.; Srinivasan, R.; Rajagopalan, K. *Tetrahedron* **1997**, *53*, 12637. (e) Rajagopalan, K.; Shanmugam, P. *Tetrahedron* **1996**, *52*, 7737. (f) Rajagopalan, K.; Janardhanam, S.; Devan, B. *Tetrahedron Lett.* **1993**, *34*, 6761. (g) Rajagopalan, K.; Janardhanam, S.; Balakumar, A. *J. Org. Chem.* **1993**, *58*, 5482. (h) Chorlton, A. P.; Morris, G. A.; Sutherland, J. K. *J. Chem. Soc, Perkin Trans. 1* **1991**, 1205.

SCHEME 3



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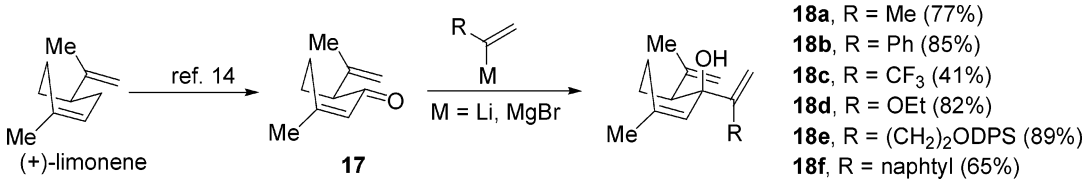
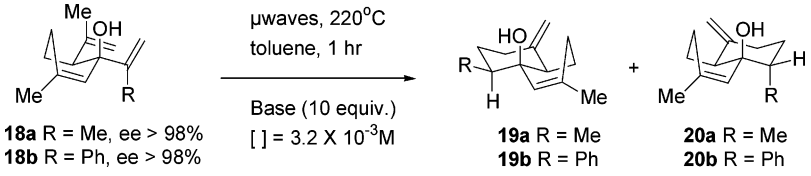


TABLE 1. Tandem Oxy-Cope/Ene Reaction of 18a and 18b with Various Bases



entry	base	yield[a], (ee),[c] **19a** R = Me	yield[b], (ee),[c] **19b** R = Ph
1	DBU	60%, (93%)	93%, (35%)
2	TMEDA	48%, (>98%)	86%, (>98%)
3	Et_3N	36%, (96%)	76%, (>98%)
4	pyridine	39%, (>98%)	36%, (>98%)
5	2,6-di-*tert*-butylpyridine	decomp.	65%, (>98%)
6	DMAP	28%, (97%)	75%, (>98%)
7	sparteine	57%, (>98%)	91%, (>98%)
8	2-*t*-Bu-1,1,3,3-tetramethylguanidine	46%, (96%)	98%, (>98%)

[a] Ratio (**19a/20a**) = 15:1. [b] Ratio (**19b/20b**) > 25:1. [c] Enantiomeric excesses were determined using HPLC with a ChiralPak AS column, eluent: hexanes/*i*-PrOH.

strates **18a** and **18b** were irradiated at 600 W for 1 h (T = 220 °C)[15] in toluene ([ ] = 3.2 × 10^{-3} M) in the presence of various bases (10 equiv) (Table 1).

Chemical yields obtained for the transformation of **18a** and **18b** to **19a** and **19b** ranged from 28% to 98% with diastereomeric ratios of 15:1 and greater that 25:1, respectively. We noticed small differences in the transfer of chirality in **18a** (entries 3, 6, and 8). However, a significant drop in the enantiopurity was observed when DBU was used as a base (entry 1). This was most evident in the transformation of **18b** to **19b** (R = Ph, ee = 35%). Good chemical yields and enantiomeric excesses were obtained when TMEDA and sparteine were used (entries 2 and 7).

(13) For review on Microwaves in Organic Synthesis, see (a) Loupy, A.; Petit, A.; Hamelin, J.; Texier-Boullet, F.; Jacquault, P.; Mathé, D. *Synthesis* **1998**, 1213. (b) Majetich, G.; Hichs, R. J. *J. Microwave Power Electromagnetic Energy* **1995**, *30*, 27. (c) Loupy, A.; Perreux, L. *Tetrahedron* **2001**, *57*, 9199. (d) Lidström, P.; Tierny, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225.

(14) Dauben, W. G.; Lorber, M.; Fullerton, D. S. *J. Org. Chem.* **1969**, *34*, 3587.

(15) We found that 220 °C is the minimal temperature to trigger the tandem process.

SCHEME 5

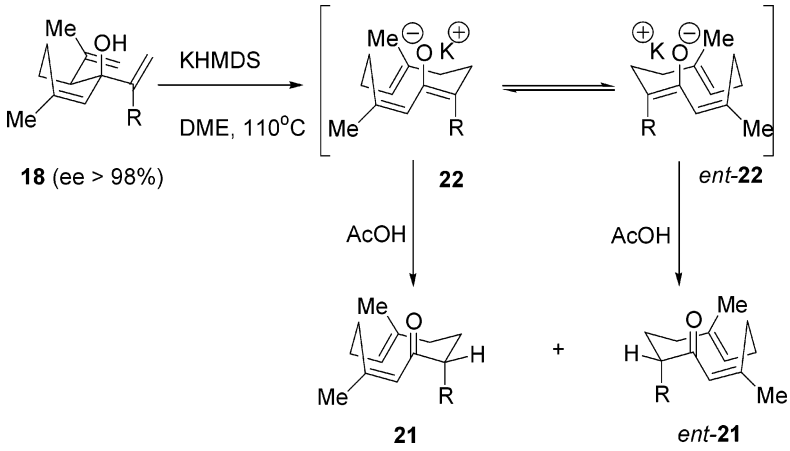
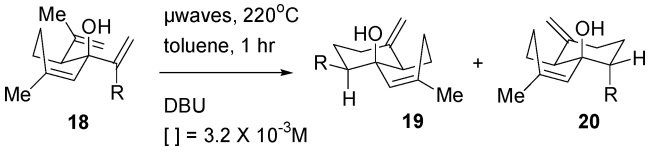


TABLE 2. Tandem Oxy-Cope/Ene Reaction of 18a and 18b with Various Amount of DBU



entry	equiv of DBU	yield[a], (ee)[c] **19a**, R = Me	yield[b], (ee)[c] **19b**, R = Ph
1	0	49%, (97%)	74%, (>98%)
2	0.5	47%, (>98%)	87%, (83%)
3	1	72%, (>98%)	99%, (77%)
4	5	65%, (95%)	86%, (51%)
5	10	60%, (93%)	93%, (35%)

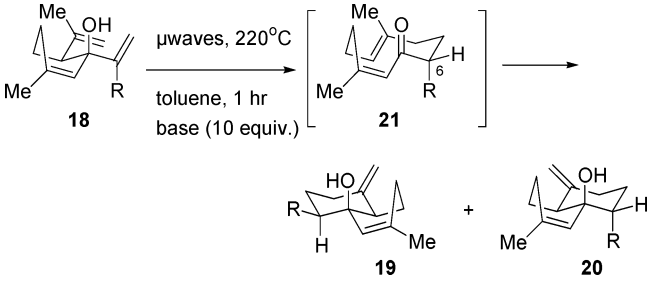
[a] Ratio **19a/20a** = 15:1. [b] Ratio **19b/20b** > 25:1. [c] Enantiomeric excesses were determined using HPLC with a ChiralPak AS column, eluent: hexanes/*i*-PrOH.

Owing to the noticeable decrease of enantiomeric excess when DBU was used, the tandem reaction was performed with various equivalents of DBU ([ ] = 3.2×10^{-3} M in toluene) (Table 2). When the reaction was performed without base, almost no loss of chirality was observed in either case (entry 1). In the conversion of **18a** to **19a**, the increase in DBU equivalents did not affect drastically the enantiomeric excess (entries 2−4). Despite the beneficial effect of DBU on the chemical yield, a significant erosion of enantioselectivity was noted when **18b** was irradiated in the presence of various amounts of DBU (entries 1−5).

To explore the electronic influence of the vinylic substituents on the enantioselectivity erosion, various 1,2-divinylcyclohexanols were irradiated in toluene with either DBU, TMEDA, or without base (Table 3). Irradiation of 1,2-divinylcyclohexenols **18c** and **18d** in the absence of base (entries 3 and 6) gave the corresponding Decalins **19c** and **19d** in 76% and 11% yields, respectively, with minimal loss of optical activity.[16] However, the enantiomeric excesses of these reactions were significally diminished in the presence of base (entries 1, 2, 4, and 5). This effect became more pronounced when the tandem reaction was performed with DBU (entries 1 and 4). Heating of 1,2-divinylcyclohexenols **18e** and **18f** in the presence of TMEDA furnished Decalins **19e** and **19f** in 37% and 59% yield, respectively, without loss of chirality (entries 8 and 10). The results reported in Tables 1−3 strongly suggest that the pK_a of the proton at C6 in **21**, combined with the strength of the base used, are directly responsible for the loss of chirality transfer.

(16) Tandem reaction precursor **18d** is highly unstable and low yields were consequently observed.

TABLE 3. Tandem Oxy-Cope/Ene Reactions of 1, 2-Divinylcyclohexenols 18c−f



entry	substrate	base	yield (%)[a]	Ee (%)[b]	ratio (**19/20**)
1	**18c**, R = CF_3	DBU	17	70	8.5:1
2	**18c**, R = CF_3	TMEDA	72	83	8.5:1
3	**18c**, R = CF_3	no base	76	>98	8.5:1
4	**18d**, R = OEt	DBU	26	74[c]	1:2.3
5	**18d**, R = OEt	TMEDA	15	82[c]	1:2.3
6	**18d**, R = OEt	no base	11	91[c]	1:2.3
7	**18e**, R = $(CH_2)_2$ODPS	DBU	66	82	>25:1
8	**18e**, R = $(CH_2)_2$ODPS	TMEDA	37	>98	>25:1
9	**18f**, R = naphthyl	DBU	76	84	>25:1
10	**18f**, R = naphthyl	TMEDA	59	>98	>25:1

[a] In all cases, the starting material was completely consumed. [b] Enantiomeric excesses were determined using HPLC with a ChiralPak AS column, eluent: hexanes/*i*-PrOH. [c] The enantiomeric excess was measured on Decalin **20d**.

In light of these results, one might propose that the enol ring inversion competes with the tautomerization process when strong bases are used. To verify this hypothesis, 1,2-divinylcyclohexenols **18a** and **18b** were treated with KHMDS (5 equiv) in DME at 110 °C (Scheme 5). After 1 h, the reaction mixture was cooled to −78 °C and a solution of acetic acid (1 M) in THF was added to give macrocycles **21a** (R = Me) and **21b** (R = Ph) in 75% and 78% yield, respectively. Both macrocycles were isolated in their racemic form.

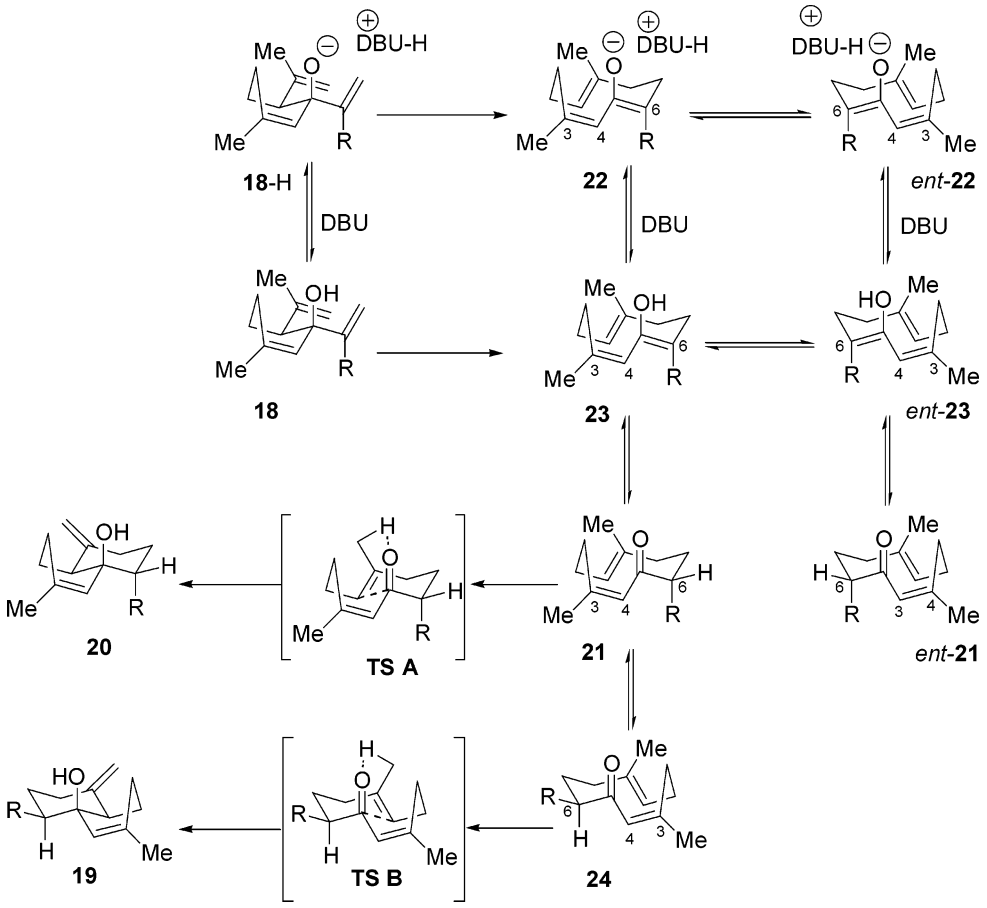


FIGURE 3. Proposed mechanism to explain the stereospecificity of the tandem oxy-Cope/ene reaction.

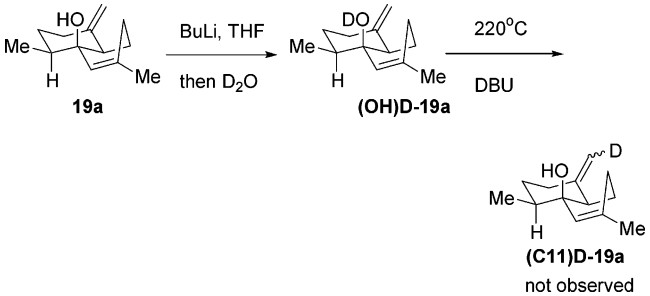
This observation can be rationalized as follows. Assuming that the inversion is a fast process,[17] this allows a rapid conversion between **22** and *ent*-**22** which after protonation gives macrocycles **21** and *ent*-**21** as an equal mixture (ee = 0%). Therefore, the previously suggested hypothesis[11] of an elevated inversion barrier can be ruled out since its existence would predict a complete conservation of the stereochemical information during the anionic oxy-Cope reaction.

On the basis of the results obtained above, the high enantio- and diastereoselectivity of the tandem oxy-Cope/ene can be explained as follows. After the sigmatropic rearrangement of **18**, macrocyclic enol **23** can invert to give its mirror image *ent*-**23** or tautomerize to afford ketone **21** (Figure 3) assuming complete enantioselectivity in the protonation. If one assumes that the ring inversion is a relatively slow process compared to tautomerization, macrocycle **21** should be produced as a single enantiomer when no base or weak bases are used. On the other hand, when DBU is utilized as a base, a partial deprotonation of **18** gives **18-**H which rearranges to enolate **22**. The latter can be also obtained from a deprotonation of **23**. As a result, the protonation of enolate **22** with the conjugate acid of DBU competes with the ring inversion process thereby producing a mixture of **21** and *ent*-**21**.

Macrocycle **21** is poised to undergo an irreversible transannular ene reaction.[18] Assuming a rapid equilibrium takes place between ketone **21** and its diastereomer **24**, the diastereomeric ratio of the transannular carbonyl-ene reaction (**19/20**) should correspond to the energy difference between **TS A** and **TS B**.[19] A close examination of **TS A** reveals destabilizing steric interactions between

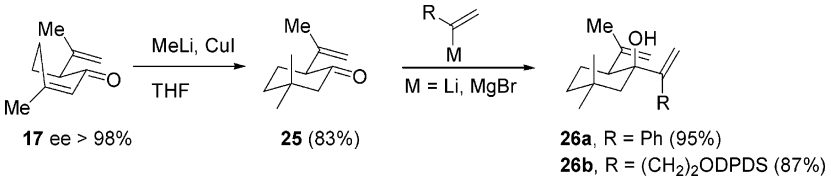
(17) This is in concordance with similar ring systems. The barriers for swiveling the trans double bond through the unsaturated 10-membered ring in *E,E*-1,6-cyclodecadiene and *Z,E*-1,6-cyclodecadiene were calculated to be 14.8 and 24.5 kcal/mol, respectively, see Yavari, I.; Hosseini-Tabatabaei, M. R.; Nori-Shargh, D.; Jabbari, A. *J. Mol. Struct. (THEOCHEM)* **2001**, *574*, 9.

(18) **(OH)D-19a** was heated in toluene at 220 °C for 2 h in the presence of 10 equiv of DBU. No incorporation of deuterium in the exocyclic double bond, i.e., formation of **(C11)D-19a**, was not observed. Only **(OH)D-19a** was isolated thereby proving that the ene reaction is an irreversible process.



(19) (a) Curtin, D. Y. *Rec. Chem. Prog.* **1954**, *15*, 111. (b) Winstein, S.; Holness, N. J. *J. Am. Chem. Soc.* **1955**, *77*, 5562. (c) Eliel, E. L. *Stereochemistry of Carbon Compounds*; McGraw-Hill: New York, 1962. (d) Hammett, L. P. *Physical Organic Chemistry*; McGraw-Hill: New York, 1970; Chapter 5. (e) Seeman, J. I *Chem. Rev.* **1983**, *83*, 83. (f) Seeman, J. I. *J. Chem. Educ.* **1986**, *63*, 42.

SCHEME 6



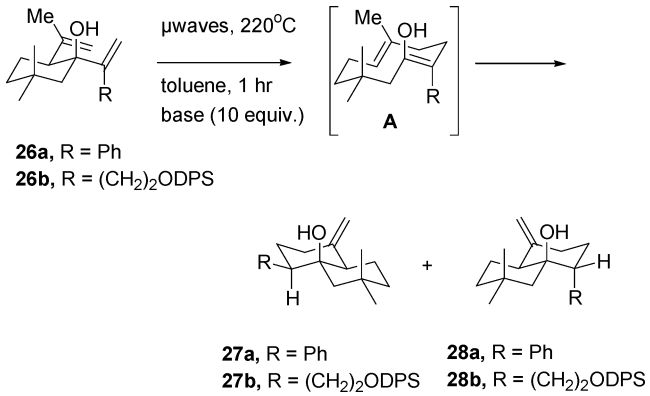
the axial R group and the ring thereby favoring **TS B** over **TS A** to provide **19**. This readily explains the high enantio- and diastereoselectivity obtained when various 1,2-divinylcyclohexenol **18** were irradiated with or without the presence of weak bases.

However, lower diastereomeric ratios were observed when R = CF_3 and OEt (Table 3, entries 1−6). It seems unlikely, in these cases, that the ene reaction is governed by the Curtin−Hammett principle. Alternatively, one might propose that after the oxy-Cope/tautomerization process, the ring inversion (**21**→**24**) competes with the ene reaction since the latter reaction is accelerated by electron-withdrawing groups such as R = CF_3 and OEt adjacent to the carbonyl in **21**.[20] This effect is most dramatic when R = OEt, as the diastereoselectivity was inverted and Decalin **20d**, having an axial R group, was isolated as the major isomer.[21] Alternatively, one might consider that the observed diastereoselectivity results from the minimization of the carbonyl and ethoxy dipoles at the transition state of the ene reaction. We previously demonstrated that the dipoles have only a minor role, if any, in governing the outcome of this tandem reaction.[22]

As discussed above, the presence of the trisubstituted *Z* olefin C3−C4 in enol **23** introduces rigidity in the macrocycle. Its importance in conserving the chiral information during the cascade process was investigated. The reduction of this olefin without creating a chiral center was achieved by a 1,4-addition of lithium dimethylcuprate on **17** to afford ketone **25** (Scheme 6). The latter was treated with 2-lithiopropene and α-lithiostyrene vinyllithium to produce 5,5-dimethyl-1,2-divinylcyclohexenols **26a** and **26b** in 95% and 87% yield, respectively.

Irradiation of **26a** and **26b** at 220 °C for 1 h with and without base gave the desired Decalins **27** in yields ranging from 40% to 99% (Table 4). The conservation of the enantiopurity was noticed in all cases even in the presence of DBU. It is believed that the replacement of the olefin by a gem-dimethyl group may lower the ground-state energy of the enol **A** or ketone intermediate thus preventing its racemization by increasing the required energy of activation for ring inversion. The basicity of the gem-dimethyl enol intermediate **A** constitutes another possibility to rationalize the high transfer of chirality. Assuming a greater basicity of the nonconjugated enol **A**, the tautomerization process is likely to occur faster with this substrate independent of the base used. This demonstrates that this olefin is not crucial to maintaining the chirality during the tandem process.

TABLE 4



entry	substrate	base	yield (%)[a]	Ee (%)[b]
1	**26a**	DBU	93	95
2	**26a**	TMEDA	99	98
3	**26b**	DBU	92	96[c]
4	**26b**	TMEDA	58	91[c]
5	**26b**	no base	40	98[c]

[a] All products were obtained with dr > 25:1 (**27**/**28**). [b] Enantiomeric excesses were determined using HPLC with a ChiralPak AS column, eluent: hexanes/*i*-PrOH. [c] Ee was measured after treatment with TBAF.

Conclusion

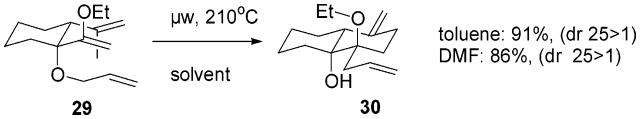
An analysis of the reaction mechanism reveals that the chiral information embedded in the 1,2-divinylcyclohexenols **18** was conserved through the cascade process owing to the rate of tautomerization which is much larger than the rate of inversion of macrocycle **23**. The enantiomeric excess is dependent on the base used in the cascade process and the electronic nature of the vinylic substituent on **18**. On the other hand, the diastereoselectivity of the process is controlled by the conformational preferences of macrocycles at the transition state for the ene reactions. In summary, the planar chiral information generated in the tandem oxy-Cope/ene reaction was transferred into new stereogenic centers in a highly efficient manner at high temperature (220 °C). This proves to be a powerful and simple method to produce Decalin frameworks in high enantiomeric excesses.

Acknowledgment. We thank the Natural Science and Engineering Research Council of Canada (NSERC), Merck-Frosst Canada, Boehringer Ingelheim, Bristol Myers Squibb, AstraZeneca, Canada Foundation for

(20) (a) Snider, B. B. In *Comprehensive Organic Synthesis, Combining C−C π bond*; Paquette, L. A., Ed.; Pergamon Press: Oxford, 1991; Vol. 5, Chapter 1.1. (b) Snider, B. B. In *Comprehensive Organic Synthesis, addition to C−X π bond*; Heathcock, C. H., Ed.; Pergamon Press: Oxford, 1991; Vol. 2, Chapter 2.1.

(21) The relative stereochemistry of **20d** was established without ambiguity by 1-D NOE experiments.

(22) Tandem oxy-Cope/Claisen/ene reaction of **29** gave **30** (dr > 1) in toluene. Repeating the experiment in a more polar solvent, such as DMF, gave no change in the product ratio (25 > 1). Barriault, L.; Sauer, E. L. O. *J. Am. Chem. Soc.* **2004**, *126*, 8569.



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Supporting Information Available: Experimental procedures, spectroscopic data and copies of ^{1}H and ^{13}C NMR for compounds **18a**−**f**, **19a**−**f**, **21a, 21b, 25**, **26a**, **26b**, **27a**, and **27b**. This material is available free of charge via the Internet at http://pubs.acs.org.

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