it is the mind of man free to invent, free to experiment, free to dream, that is our most precious resource. The value of silicon chip does not lie in the sand from which it comes, but it lies in the microscopic architecture engraved upon it by ingenious human mind. The most promising superconductors are made from ceramics— their value does not come from their material, but from the brilliant inspiration of a few scientists. It is human imagination that is going to build the 21st century out of sand and clay. Let our scientists, science administrators and policy makers ponder whether we will be able to compete with the rest of the nations of the world in the 21st century with the help of policies we had been following during the last 45 years completely neglecting the education of science the way it has been done.


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REVIEW ARTICLE

Complex cyclic ketones via oxy-Cope rearrangement – Studies relevant to stereocontrolled synthesis

K. Durairaj

Department of Chemistry, Sri Venkateswara College of Engineering, Pennalur 602 105, India

Oxy-Cope rearrangement is one of the suitable reactions in organic synthesis that is accompanied by high levels of chirality and regiocontrol. Condensation of β,γ-unsaturated ketones with a vinyl organometallic and subsequent [3,3] sigmatropic shift is the benefit of substantive enhancement in structural complexity with the complementary regeneration of the carbonyl group in a new structural context of polycyclic frameworks. As the carbonyl functionality in synthetic transformations plays a pivotal role, reacquisition of such a reaction site translates into heightened chemical versatility. The trajectories followed by vinyl organometallics as they engage in 1,2 addition to ketones are being understood. Diastereoselective control of this bond-making process when coupled with the chair or boat conformation adopted during the oxy-Cope process is discussed. The synthesis of stereocontrolled elaborate carbocycles and other complex molecules via oxy-Cope rearrangement, and the developments in the area of oxy-Cope rearrangement and its application to the elaboration of cyclic and polycyclic ketones are compiled in the present paper.
**Diastereoselectivity in the initial coupling reaction**

The 1,2 addition generates another stereogenic centre if both reaction partners are chiral, and consequently give rise to at least eight diastereomeric products. However, the problem can be conveniently dealt with and high levels of molecular recognition attained if the following criteria are accorded proper consideration: (a) Nucleophilic capture by the carbonyl should be relegated exclusively to one prochiral face by suitable steric control. If this stereoselectivity is strictly governed, only a maximum of four diastereomeric alcohols can result. (b) If respectable levels of diastereoselectivity are to operate under these circumstances, then the number of possible products will again be halved. At this point, the use of either reagent in optically pure form can result in net kinetic resolution (single product formation). The extent and direction of diastereoselection in such reactions is still found in a limited number of cases. For example, bicyclic ketone (1)-2 adds nucleophiles only from its exo surface. However, the conformational mobility of its vinyl group lessens the overall capacity of the molecule for steric discrimination. Consequently, the potential for diastereocontrol falls off rapidly (3:4 = 1.65:1, Scheme 2). The cyclobutoxide character of the first-formed intermediate results in spontaneous sigmatropy above −78°C and leads (via boat transition states) to products carrying six stereogenic centres.

Comparative analysis of the response of racemic ketones 5 and 6 to capture by chiral organocerates revealed that the additional σ bond in 6 does not appreciably enhance key intermolecular interaction of steric origin (Figure 1), and for the series 7 to 11 (Figure 1), the extent of diastereoselection reaches a maximum at 11. These data have allowed the formulation of a transition-state model consistent with the greater discriminatory power of substituents positioned in the vicinity of the four-membered ring.
review article

When chiral racemic reaction partners are brought into condensation, 1:1 stoichiometry can be used because double diastereoselection operates. The two enantiomers of both reagents are consumed with equal rapidity. However, if either reagent is optically pure, the (R) and (S) forms of racemic coreactant will necessarily be consumed at different rates. Studies involving (R)-(−)-isopiperitenone have ascertained that the maximum yields of homochiral 1,2-addends can be most efficiently and economically realized with an RLi-to-ketone ratio of 3:1 (ref. 9). Face selection during theoxy-Cope reaction has also been accorded. For example, (RR, SS)- and (RS, SR)-fluoroadamantane alcohols 12 and 13 have given 16 and 17 through a pair of chair transition states available to each diastereomer (Scheme 3). The transition states 14 and 15 have the phenyl group axial and equatorial respectively. Consequently, steric factors would favour the reaction via 14 in both instances. In contrast, the hyperconjugative effect of the electronegative fluorine atom would prefer to induce bond formation 'Syn' to the halogen. The (RR, SS)-fluoroadamantane alcohol 12 gives rise to an 81:19 ratio of diastereomeric acetophenones 16 and 17 respectively, because the effects operate in the same direction, and the product distribution from the alcohol 13 is 36:64. Thus, syn approach is favouried by a factor of 1.4 due to hyperconjugation.

**Expansion of six-membered ring**

**Expansion of cyclohexanones**

The thermal oxy-Cope rearrangement of trans-1,2-divinylcyclohexanol constitutes an excellent example for ring enlargement by four carbon atoms. The formation of trans-5-cyclodecen-1-one shows that isomerization proceeds by way of chair transition state. This pathway requires that the transient enol double bond have a Z geometry. Later, a stereochemical feature that has established via trapping experiments conducted under anionic conditions. Heating of cis-1,2-divinylcyclohexanol at 220°C does not give an equally stereo- selective product, but a 97 and 3% mixture of trans- and cis-5-cyclodecen-1-one results respectively. It is found that 18 is kinetically preferable to undergo conformational inversion to 21 prior to isomerization via 22 to 23 (97%), because the alkoxy oxygen is axial in 21 and equatorial in 18. The axial alkoxy oxygen (electron-rich substituent) 21 is more preferable than equatorial alkoxy oxygen 18, yielding 97% of 23 via 22 and a 3% of 20 via 19 (Scheme 4). The cis product

![Scheme 3](image)

![Scheme 4](image)
Expansion of 2-cyclohexenones

Acoragermacrone (26) and preisocalamendiol (27) are synthesized by addition of 2-lithio-3-methyl-1-butene to isopiperitenone (24) followed by anionic oxy-Cope rearrangement of the resultant alcohol (25) (Scheme 5). An elegant addition-elimination sequence is next utilized to isomerize the conjugated double bond and arrive directly at 26. Alternatively, simple deconjugation of 25 delivers 27.

![Scheme 5.](image)

Kuwahara and Morie have prepared (-)-periplanone B, the cockroach sex pheromone, in eighteen steps from (S)-3-cyclohexene-1-carboxylic acid by means of a very similar oxy-Cope ring expansion. The significance in the present context is the tolerance of various carbonyl substituents to oxy-Cope sigmatropy. A classic example is the addition of vinylmagnesium bromide to 28 and subsequent refluxing in tetrahydrofuran results in conversion to 29 (Scheme 6). The structural features of 29 are recognized to be conducive to transannular cyclization under mildly basic conditions.

![Scheme 6.](image)

The oxy-Cope system in conversion of 30 to 31 is undoubtedly rationalized by a fragmentation-recombination pathway. The process is viewed as capable of operating as well in the concerted sigmatropic mode depending on conditions. These deductions are made possible chiefly on the strength of studies conducted more recently on optically active substrates. The (1R, 8aS) alcohol 30 gives 31 in optically active form, when 30 is isomerized with potassium hydride in tetrahydrofuran. The use of potassium hydroxide in methanol affords racemic product. These findings at the mechanistic level are outlined in Scheme 7.

![Scheme 7.](image)

Expansion of 2-vinylcyclobutanones and 2-vinylcyclopentanones

Extension of the oxy-Cope rearrangement to 2-vinylcyclobutanones allows cyclooctene and cyclooctadiene formation. Gadwood and Lett reported that both cis- and trans-1,2-dialkenylocyclobutanols undergo [3, 3] sigmatropic ring enlargement on treatment with potassium hydride. Salaun et al. pointed out that the reactivity of these isomers is clearly distinguished on the basis of their stereochemical features. Cyclooctanoid terpenes can also be formed via ring expansion of the bicyclicvinylcyclobutanone. For example, the sesquiterpene alcohols, poitediol and dactylol have been reported by ring expansion of the bicyclicvinylcyclobutanone and good overall yields realized if lithium acetylide adduct isomerized under neutral conditions. Reduction of poitediol with sodium in liquid ammonia gave dactylol. Divinylation of 2-chlorocyclopentanone provides the formation of an 81:19 mixture of isomers 32 and 33. Thermal activation of the composite sample of 32 and 33 results in exclusive formation of E,5-cyclononene-1-one (34). This stereochemical result confirms that chair-like transition-state geometries are involved in the thermal activation process (Scheme 8).

![Scheme 8.](image)

Expansion of medium-ring systems

The trans- and cis-1,2-divinylcyclooctadecanols have been subjected to thermal rearrangement with interesting results. For example, trans-1,2-divinylcyclooctanol (35) gives 37 as the single product, whereas cis-1,2-divinyl-
cyclooctanol (38) gives a 24:76 mixture of 37 and 41 under the same conditions (Scheme 9). The reactions are found to be stereospecific, and the trans-isomer 35 probably passes entirely through chair transition state 36. The cis arrangement in 38 fosters competition between the involvement of 39 and 40. Of these, the pathway leading to Z enone 41 clearly dominates, in contrast to the partitioning exhibited by the six-ring lower homologue 18, which favours formation of the E isomer by a small margin. When one of the double bonds is endocyclic, the alcohols exhibit a greatly reduced capability for oxy-Cope behaviour. Identical behaviour has been reported in trans-1,2-divinylcyclohexanol.

Expansion of spirocyclic $\beta, \gamma$-unsaturated ketones

Spirocyclic compounds offer two alternatives as oxy-Cope templates. As a general rule, the allylic alcohols isomerize too rapidly to permit their isolation, the rigid S-cis boat orientation of the double bonds further reducing the activation energy of the rearrangement step. The Syn capture of vinyl organometallics by such ketones provides vinyl alcohols, oxynionic Cope rearrangement of which gives bicyclic bridgehead olefins having a carbonyl group in the largest bridge. For example, octahydrobenzocyclooctenones are isolated from the spirocyclic compounds 42 and 43 which have the $\beta, \gamma$ double bond in the form of methylene group (Scheme 10).

Dianionic oxy-Cope rearrangements

Divinyl alcohols are quite susceptible to thermal [3,3] sigmatropy. In the few examples, it has been found that large ring dienolates result and these intermediates undergo transannular aldolization. The trans-diol 44, available from 9,10-phenanthraquinone, is isomerized initially to 45 on heating with potassium hydride in tetrahydrofuran, and finally dibenzotropone (46) is formed (Scheme 11). The trans-stereochemistry is a necessary prerequisite for this rearrangement since the vinyl groups must both be equatorially disposed to be with bonding distance.
RESEARCH ARTICLE

A study of seismicity of Northeast India and adjoining areas based on statistical analyses

V. P. Singh, D. Shanker and K. Hamada*

Department of Geophysics, Banaras Hindu University, Varanasi 221 005, India
*National Research Centre for Disaster Prevention, Tennodai, 3-1, Tsukuba-shi, Ibaraki-ken 305, Japan

Seismicity data from 1912 to 1977 of northeast India (18°N to 32°N and 84°E to 100°E) for large earthquakes with magnitude M ≥ 6.0 have been used to discuss seismicity variation by stationary model of seismicity rates and seismic energy released during three-year intervals. Seismicity rates vary from 0.73 to 2.15 events/year. Seismicity data of 66 years show that earthquake occurrence follows Poisson distribution. The time series of considered events for different range of magnitude consists of random (6.0 ≤ M ≤ 7.0) and non-random (7.9 ≤ M ≤ 8.7) shocks.

Seismicity data have been statistically analysed by several earlier researchers to study seismic quiescence, seismic rates and seismicity fluctuations before the occurrences of medium to large earthquakes1-6. Based on statistical calculation of seismicity data, the Mexico earthquake of Central America was predicted7,8. These studies had used the seismicity data of small regions to study the seismic behaviours. If long duration of seismicity data for large areas is considered, it may reveal the temporal behaviour of seismic activity of the region. Seismicity data of strong earthquakes in large areas have revealed the possibility of seismic cycles for the regions9-11.

The north-east region of India is seismically active as two large earthquakes of magnitude M ≥ 8.4 occurred in this zone since 1912. Besides, the area shows widespread distribution of seismic activity where a large number of earthquakes of M ≥ 6.0 occurred during the past hundred years. Seismicity data has also been analysed to draw conclusions12. Deviation of seismicity rates from the normal before and after large earthquakes has been reported by Khattri and Wyss13 who also stated that all earthquakes of M ≥ 6.6 were preceded by

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