

Studies in Base-Catalyzed Allenic Oxy-Cope Rearrangement: An Expedient Synthesis of Functionalized Bicyclo[4.3.0] and -[4.4.0] Systems and 3,5-Cycloundecadien-1-one

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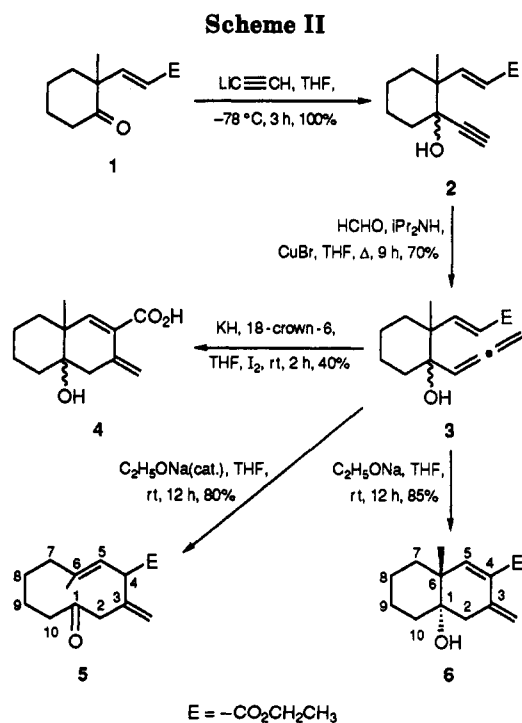
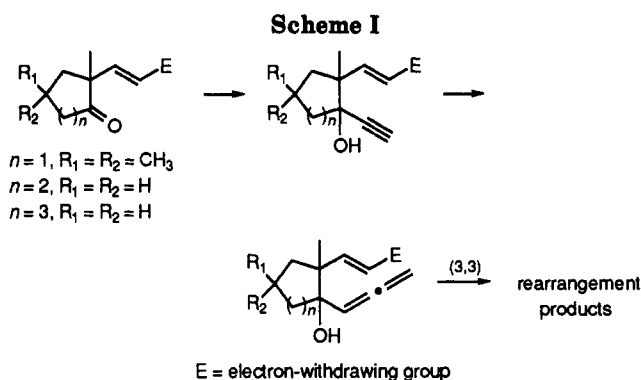
The base-catalyzed oxy-Cope rearrangement of systems incorporating an allenic π system was studied. The rearrangement incidentally leads to functionalized bicyclo[4.3.0]nonane 15, bicyclo[4.4.0]decanes 6 and 10, and 3,5-cycloundecadien-1-one 20. The effect of ring size and nature of the base on the rearrangement was also studied.

The utilization of the oxy-Cope rearrangement in the synthesis of the complex ring system present in a number of natural products has received considerable attention in recent years.¹ The tremendously enhanced rate of this rearrangement as demonstrated by Evans and Golob has added newer dimensions to the utility of this rearrangement in organic synthesis.² A number of variants of this reaction are known in which both the olefinic π systems are either unsubstituted, monosubstituted, disubstituted, or replaced by a ring with a π system, etc. A few examples of oxy-Cope rearrangements involving other substrates like aromatic π systems, acetylenic π systems, and hetero π systems are also known.³ Recently, there have been reports on studies in intramolecularly competitive anionic oxy-Cope rearrangement.⁴ Surprisingly, base-catalyzed rearrangement of an oxy-Cope system in which one of the π systems is replaced by an allenic moiety is hitherto unknown. With a proper structural assembly, such a process could provide considerable insight to what extent modest structural differences have an impact on the relative rate of the rearrangement and also its synthetic utility. Only a few examples of thermal oxy-Cope rearrangement involving an allenic π system were known⁵ from which no definitive conclusions could be drawn as to the rate.

Herein, we describe the preliminary results of our studies on base-catalyzed anionic oxy-Cope rearrangement on systems incorporating an allenic π system and also the effect of ring size on the mode of the rearrangement.

Our strategy for the synthesis of the allenic oxy-Cope systems is outlined in Scheme I.

Initial studies in this direction involved the synthesis of allenic alcohol 3, as detailed in Scheme II. Addition of lithium acetylide (3 equiv) to the known cyclohexanone derivative 1⁶ according to the literature procedure⁷ gave the known ethynyl alcohol 2 in 100% yield, but as a mixture (1.1:1) of diastereomers as evidenced⁸ from its 400-MHz ¹H NMR spectrum.



The ethynyl alcohol 2 was converted to the allenic alcohol 3 by a slight modification of the method of Crabbe et al.⁹ (1.6 equiv of paraformaldehyde, 1.2 equiv of diisopropylamine, 0.5 equiv of cuprous bromide, THF, reflux, 9 h,

(1) (a) Lutz, R. P. *Chem. Rev.* 1984, 84, 206. (b) Swaminathan, S. *Ind. J. Chem.* 1984, 99. (c) Paquette, L. A. *Angew. Chem., Int. Ed. Engl.* 1990, 29, 609. (d) Paquette, L. A. *Synlett.* 1990, 67. (e) Hill, R. K. In *Comprehensive Organic Synthesis*; Paquette, L. A., Ed.; Pergamon Press: Oxford, 1991; Vol. 5.

(2) Evans, D. A.; Golob, A. M. *J. Am. Chem. Soc.* 1975, 97, 4765.

(3) See ref 1c and pertinent references cited therein.

(4) (a) Paquette, L. A.; Guevel, R.; Sauer, D. R. *Tetrahedron Lett.* 1992, 923. (b) Balakumar, A.; Rajagopalan, K. Unpublished results.

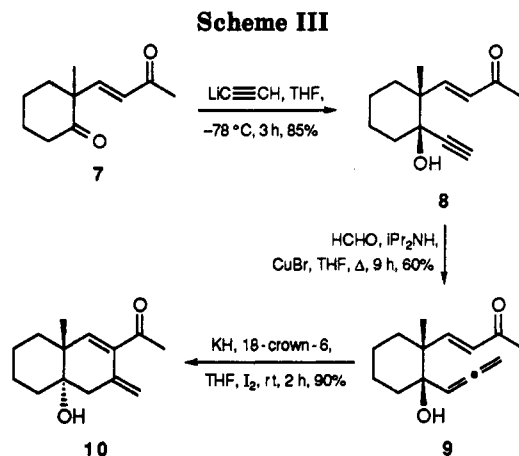
(5) (a) Cookson, R. C.; Singh, P. *J. Chem. Soc. C* 1971, 1477. (b) Douthean, A.; Balme, G.; Malacria, M.; Gore, J. *Tetrahedron Lett.* 1978, 1803.

(6) Thangaraj, K.; Srinivasan, P. C.; Swaminathan, S. *Synthesis* 1982, 855.

(7) Sathyamoorthy, G.; Thangaraj, K.; Srinivasan, P. C.; Swaminathan, S. *Tetrahedron* 1990, 46, 3559.

(8) For similar observations see: (a) Clive, D. L. J.; Russell, C. G.; Suri, S. C. *J. Org. Chem.* 1982, 47, 1632. (b) Kayo, T.; Kindo, H.; Nishimo, M.; Tanaka, M.; Hata, G.; Miyake, A. *Bull. Chem. Soc. Jpn.* 1980, 53, 2958. (c) Johnson, T. O.; Overmann, L. E. *Tetrahedron Lett.* 1991, 7361. (d) Ashby, E. C.; Laemmle, J. T. *Chem. Rev.* 1975, 75, 521. (e) Paquette, L. A.; Shi, Y. J. *J. Am. Chem. Soc.* 1986, 108, 8478. (f) Jisheng, L.; Gallardo, T.; White, J. B. *J. Org. Chem.* 1990, 55, 5426. (g) Reference 7 reports the formation of a single diastereomer from the addition of lithium acetylide.

(9) Crabbe, P.; Fillion, H.; Andre, D.; Luche, J. L. *J. Chem. Soc., Chem. Commun.* 1979, 859.



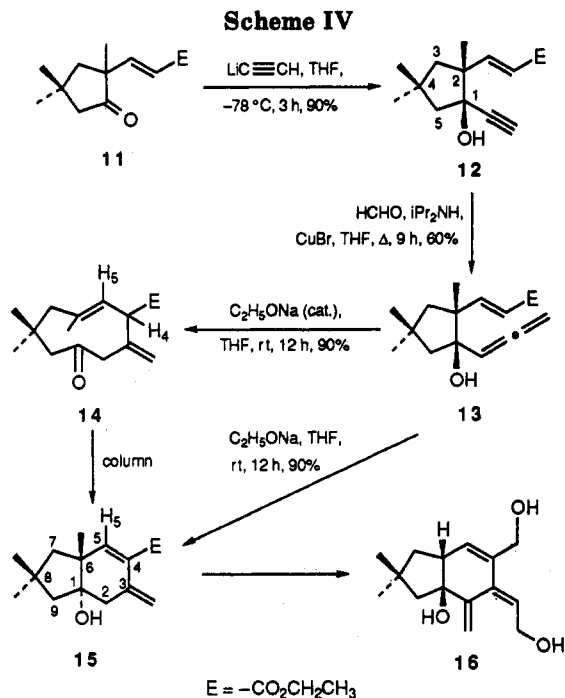
70%). The spectral data are consistent with the structural assignment.

Anionic oxy-Cope rearrangement of the allenic alcohol 3 under standard conditions¹⁰ (5 equiv of KH, 5 equiv of 18-crown-6, 0.15 equiv of I₂, THF, rt, 2 h, 40%) gave rise only to the carboxylic acid 4 (established by means of IR and ¹H NMR).¹¹ Attempts to purify the acid 4 by column chromatography over alumina resulted in the decomposition of the product. Treatment of allenic alcohol 3 with a catalytic amount of sodium ethoxide¹² as base (0.25 equiv of C₂H₅ONa, THF, rt, 12 h, 80%) gave rise to substituted cyclodecenone 5 in which the double bond has the *E* configuration. However, treatment of the allenic alcohol 3 with stoichiometric amounts of sodium ethoxide (1.1 equiv of C₂H₅ONa, THF, rt, 12 h, 85%) gave rise to the bicyclic system 6 via the ring enlargement compound 5 initially formed by allenic oxy-Cope rearrangement followed by transannular reaction. Compounds 5 and 6 showed satisfactory spectral data.

The susceptibility of the ester function (E = -CO₂C₂H₅) toward hydrolysis under KH/THF rearrangement conditions prompted the study of the allenic alcohol 9 (E = -COCH₃) which was prepared as shown in Scheme III.

Addition of lithium acetylide (2.2 equiv) to the keto derivative 7 furnished the known ethynyl alcohol 8⁷ in 85% yield as a single diastereomer as judged from its spectral data. Conversion of the ethynyl alcohol 8 to the allenic alcohol 9 was effected in 60% yield using the procedure described earlier for the conversion of ethynyl alcohol 2 to 3. Anionic oxy-Cope rearrangement of 9 (5 equiv of KH, 5 equiv of 18-crown-6, 0.15 equiv of I₂, THF, rt, 2 h, 90%) gave the bicyclic compound 10 via ring enlargement and subsequent transannular reaction. Thus, the allenic alcohols 3 and 9 after base-catalyzed rearrangement provide functionalized bicyclo[4.4.0] systems¹³ (octalins) 6 and 10, respectively.

This study was extended to the cyclopentanone derivative 11 (Scheme IV). The success of this methodology would lead to trans fused bicyclo[4.3.0]nonane (hydrindan)—a substitution pattern found in many naturally occurring compounds.¹⁴ Addition of lithium acetylide (3



equiv) to the ketone derivative 11 gave the ethynyl alcohol 12 in 90% yield as a single diastereomer as evidenced from its 400-MHz ¹H NMR spectrum and differential NOE studies. Irradiation of the angular methyl group at C-2 ($\delta = 1.21$) causes an enhancement of -OH proton at C-1 ($\delta = 2.27$), indicating the *cis* relationship between the two angular substituents.

Conversion of the ethynyl alcohol 12 to the allenic alcohol 13 according to the procedure described earlier (1.6 equiv of paraformaldehyde, 1.2 equiv of diisopropylamine, 0.5 equiv of cuprous bromide, THF, reflux, 9 h, 60%) gave the desired compound 13. Oxy-Cope rearrangement of allenic alcohol 13 with sodium ethoxide (0.25 equiv of C₂H₅ONa, THF, rt, 12 h, 90%) gave rise to ring-enlarged compound 14 (characterized by means of IR).

However, attempted purification by column chromatography over neutral alumina resulted in the quantitative formation of the transannular reaction¹⁵ product 15. Compound 15 was also obtained directly on treatment of the allenic alcohol 13 with stoichiometric amounts of sodium ethoxide (1.1 equiv of C₂H₅ONa, THF, rt, 12 h, 90%). The structure 15 was substantiated by spectral data, more specifically from differential NOE studies. Irradiation of the angular methyl group at C-6 ($\delta = 0.89$) causes an enhancement of 6.3% for the olefinic proton at C-5 ($\delta = 6.42$), 8.1% for one of the protons at C-7 ($\delta = 1.57$), 7.7% for one of the protons at C-9 ($\delta = 1.69$), and 6.7% for one of the methyl groups at C-8 ($\delta = 1.05$). No positive enhancement was observed for the -OH proton, thereby indicating that the angular methyl and the hydroxyl group are related *trans* to each other.

A significant aspect of the rearrangement is that the compound 15 obtained in this transformation can serve as a potential synthon for the recently isolated sesquiterpenoid metabolite candicansol 16, its epimer, and related compounds.¹⁶

(10) Macdonald, T. L.; Natalie, K. J., Jr.; Prasad, G.; Sawyer, J. S. *J. Org. Chem.* 1986, 51, 1124.

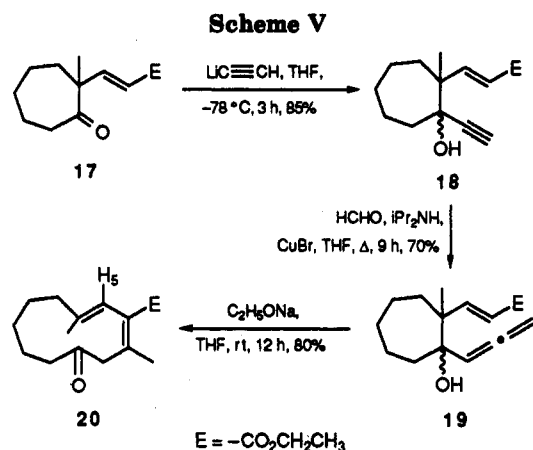
(11) Decreasing the equivalents of base from 5 to 1.5 gave the rearrangement product in which the ester group was not hydrolyzed but the yield is only 10%. This observation was confirmed by subjecting other systems containing ester groups to similar rearrangement conditions (unpublished observations of our group).

(12) Janardhanam, S.; Shanmugam, P.; Rajagopalan, K. *Synth. Commun.* 1993, 23, 311.

(13) Fischer, N. H.; Olivier, E. J.; Fischer, H. D. *Fortschr. Chem. Org. Naturst.* 1979, 38, 270, 272-274.

(14) (a) Porter, L. *Chem. Rev.* 1967, 67, 441. (b) Maclean, D. B. In *The Alkaloids*; Manske, R. H. F., Ed.; Academic Press: New York, 1968; Vol. 10, p 305. (c) Avent, A. G.; Hanson, J. R.; Hitchcock, P. B.; Yeoh, B. L. *J. Chem. Soc., Perkin Trans. 1* 1985, 2749. (d) Hirata, Y. *Bull. Chem. Soc. Jpn.* 1977, 50, 1813.

(15) Drieding model shows a small transannular distance between C₁ and C₆ atoms. For similar observations see ref 8e.



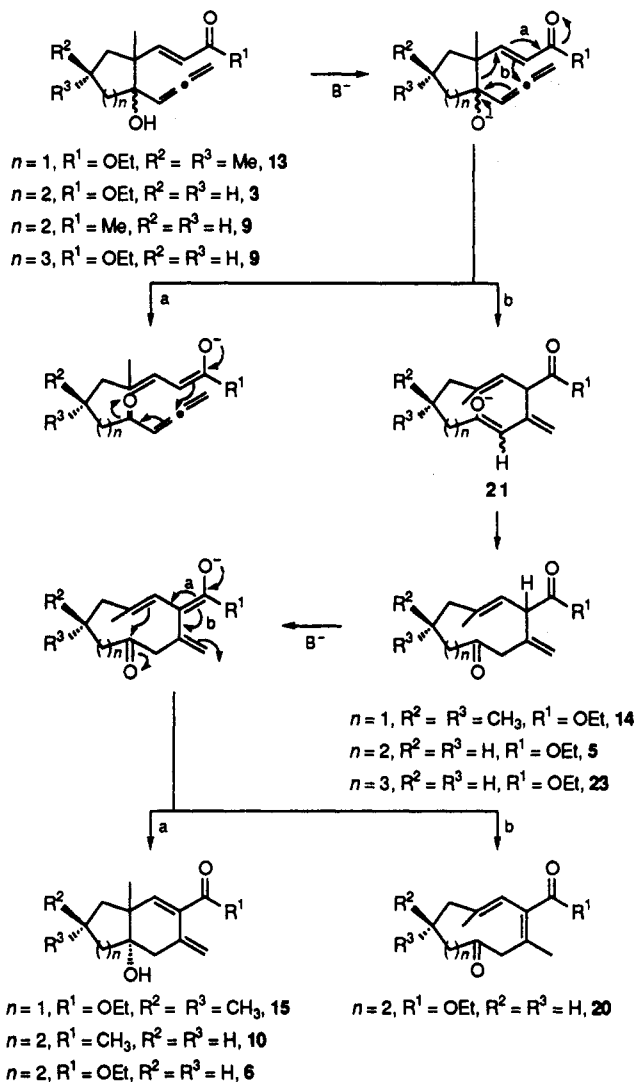
A further extension of this study was made to the cycloheptanone derivative 17 (Scheme V).

Addition of lithium acetylide (3 equiv) to the compound 17⁸ gave the ethynyl alcohol 18 in 85% yield as a mixture (1:2) of diastereomers as evidenced from its HPLC analysis.⁸ Treatment of this mixture of ethynyl alcohol 18 in a manner similar to that described for compound 2 (1.6 equiv of paraformaldehyde, 1.2 equiv of diisopropylamine, 0.5 equiv of cuprous bromide, THF, reflux, 9 h, 70%) gave the allenic alcohol 19 as a mixture (1:2) of diastereomers as evidenced from its ¹H NMR and ¹³C NMR data. Rearrangement of this mixture of allenic alcohol 19 with sodium ethoxide (1.1 equiv of C₂H₅ONa, THF, rt, 12 h, 80%) gave the ring-enlarged compound 20 where in isomerization of the exo double bond had occurred but failed to give the transannular reaction product.¹⁷

The trans nature of the ring junction as indicated in the rearrangement compounds was arrived at based on mechanistic consideration and differential NOE studies (irradiation of the angular CH₃ group in compounds 6, 10, and 15 showed no positive NOE enhancement of the -OH group indicating that they are trans to each other).

The formation of compounds 6, 10, 15, and 20 can be rationalized either by the fragmentation-recombination mechanism (path a) or a concerted oxy-Cope mechanism (path b).¹⁸ Path a involves a retro-aldol reaction followed by an intramolecular 1,4-addition of an intermediate dienolate to the resulting allenic ketone. Path b involves the concerted oxy-Cope process to give the enolate 21. Thus, the rearrangement carried out with sodium ethoxide (0.25 equiv) furnished compounds 5 and 14 after quenching, while with stoichiometric amounts, the second chemical event namely, the transannular reaction takes place to give the observed products 6, 10, and 15. But in the case of compound 22 only isomerization of the exo-double bond occurs to give compound 20. The failure to observe transannular reaction in the present instance could most probably be due to the unfavorable bond distance between C-1 and C-6 atoms.¹⁷

In conclusion, the participation of allenic π systems in a base-promoted oxy-Cope rearrangement has been demonstrated for the first time in an unequivocal manner. Our initial results indicate that the behavior of the allenic π systems will be similar to that of their vinyl counterpart,



but with enhanced reactivity. The strain which results from the cumulated π bonds present in 3, 9, 13, and 19 reduces the strength of π bonds relative to a vinyl group and may be partially responsible for the increased rate of reaction observed in the allenyl systems.¹⁹ More investigative details are needed to arrive at a meaningful conclusion in this regard. A singular advantage of this rearrangement is that it produces compounds with exo methylene moiety which will be of high synthetic utility.

Experimental Section

All boiling points and melting points are uncorrected. ¹H NMR spectra were recorded either at 400 MHz or at 90 MHz. ¹³C NMR spectra were either recorded at 100.6 MHz or at 22.5 MHz as indicated. Chemical shifts were reported in ppm (δ) using Me₄Si as standard, and coupling constants were expressed in Hz. Percent NOE enhancements were obtained by integrating the affected resonance relative to the irradiated resonance in the difference spectrum in each case. Elemental analyses were performed using a Perkin-Elmer 240 B elemental analyzer. Thin-layer chromatograms were developed on glass plates coated with silica gel-G (ACME) of 0.25 mm thickness and visualized with iodine. Column chromatography was either carried out with SiO₂ (silica gel, ACME, 100–200 mesh) or neutral Al₂O₃ (alumina, ACME, washed with ethyl acetate, and activated). Glassware used was thoroughly dried in an oven, cooled, and assembled

(16) Arnone, A.; Cardillo, R.; Di Modugno, V.; Nasini, G. *J. Chem. Soc., Perkin Trans. 1* 1989, 1995.

(17) Evaluation by means of MMX calculations using PC Model for 3-methylidene-*trans*-cyclohepta-5-en-1-one gave a transannular distance of 3.71 Å between C-1 and C-6 for potential cyclization.

(18) Uma, R.; Rajagopalan, K.; Swaminathan, S. *Tetrahedron* 1986, 42, 2757.

(19) For example, the observed standard heat of formation of 2,3-pentadiene (31.79 Kcal mol⁻¹) is 6.4 Kcal mol⁻¹ higher than that observed standard heat of formation of 1,4-pentadiene (25.41 Kcal mol⁻¹): Fraser, F. M.; Prosen, E. *J. Res. Natl. Bur.* 1955, 54, 143.

under a stream of nitrogen. The organic extracts of crude products were dried over anhydrous magnesium sulfate. Solvents were reagent grade and were purified and dried prior to use.

General Experimental Procedure for the Synthesis of Ketones 1, 11, and 17. To a solution of 2-formyl-2-methylcycloalkanone (0.062 mol) in 60 mL of dichloromethane along with carbethoxymethyltriphenylphosphonium bromide (0.08 mol) in 60 mL of water was added potassium carbonate (0.09 mol) in small portions over a period of 5 min. The resulting mixture was stirred for 2 h and the organic layer separated, washed with water, and dried. Removal of solvent gave a residue which solidified on cooling. Digestion of the solid with petroleum ether (40–60 °C), (10 × 25 mL) and evaporation of the solvent gave the residue which was either chromatographed (silica gel) or distilled under vacuum to give the ketone.

2-Methyl-2-(2'-carbethoxyvinyl)cyclohexanone (1). Following the general procedure, treatment of 2-formyl-2-methylcyclohexanone⁶ (8.68 g) gave the compound 1 in 60% yield (7.80 g) as a colorless liquid. $R_f = 0.78$ (1:10, AcOEt/hexane). IR (CCl₄): 1705–1710, 1640 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.13 (d, $J = 16.11$, 1H), 5.77 (d, $J = 16.11$, 1H), 4.19 (q, $J = 7.33$, 2H), 2.41–2.48 (m, 2H), 1.94–2.07 (m, 2H), 1.69–1.81 (m, methylenes, 4H), 1.30 (t, $J = 7.33$, 3H), 1.23 (s, 3H). Anal. Calcd for C₁₂H₁₈O₃: C, 68.55; H, 8.63. Found: C, 68.54; H, 8.63.

2,4,4-Trimethyl-2-(2'-carbethoxyvinyl)cyclopentanone (11). Following the general procedure, treatment of 2-formyl-2,4,4-trimethylcyclopentanone⁶ (9.55 g) gave the compound 11 in 65% yield (9.02 g) as a colorless liquid. $R_f = 0.6$ (1:20, AcOEt/hexane). IR (CCl₄): 1740, 1720, 1640 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.93 (d, $J = 16.11$, 1H), 5.84 (d, $J = 15.63$, 1H), 4.16 (q, $J = 7.33$, 2H), 2.23 (d, $J = 3.41$, 2H), 2.14 (d, $J = 13.67$, 1H), 1.82 (d, $J = 13.68$, 1H), 1.26 (t, $J = 7.33$, 3H), 1.25 (s, 3H), 1.14 (s, 3H), 1.06 (s, 3H). Anal. Calcd for C₁₃H₂₀O₃: C, 69.64; H, 8.92. Found: C, 69.59; H, 8.97.

2-Methyl-2-(2'-carbethoxyvinyl)cycloheptanone (17). Following the general procedure, treatment of 2-formyl-2-methylcycloheptanone⁷ (9.54 g) gave the compound 17 in 70% yield (9.73 g) as a colorless liquid. $R_f = 0.6$ (1:20, AcOEt/hexane). IR (CCl₄): 1705–15, 1640 cm⁻¹. ¹H NMR (90 MHz, CCl₄): δ 7.0 (d, $J = 17.24$, 1H), 5.8 (d, $J = 17.24$, 1H), 4.15 (q, $J = 7.30$, 2H), 1.5–2.2 (m, 10H), 1.2 (t, $J = 7.30$, 3H), 1.1 (s, 3H). Anal. Calcd for C₁₃H₂₀O₃: C, 69.64; H, 8.92. Found: C, 69.70; H, 8.92.

2-Methyl-2-(3'-oxo-1'-butenyl)cyclohexanone (7). A solution of 2-formyl-2-methylcyclohexanone⁶ (14 g, 0.1 mol) and Ph₃P=CHCOCH₃ (38.20 g, 0.12 mol) in 100 mL of dry benzene was refluxed for 10 h under nitrogen. The solvent was distilled off, the residue was extracted with petroleum ether (40–60 °C) (12 × 25 mL), and the solvent was evaporated to give a viscous liquid. It was distilled under reduced pressure to afford the compound 7 in 55% yield (9.90 g). Bp: 103–105 °C/0.5–0.8 mm (lit.⁷ bp 103–105 °C/0.5–0.8 mm). $R_f = 0.8$ (1:5, AcOEt/hexane). IR (CCl₄): 1700, 1670, 1620 cm⁻¹. ¹H NMR (90 MHz, CCl₄): δ 7.0 (d, $J = 17.11$, 1H), 6.0 (d, $J = 17.11$, 1H), 2.3 (s, 3H), 1.6–2.1 (m, 8H), 1.2 (s, 3H). Anal. Calcd for C₁₁H₁₆O₂: C, 72.33; H, 8.88. Found: C, 73.60; H, 9.04.

General Experimental Procedure for the Ethynylation⁷ of Substituted Cycloalkanones 1, 7, 11, and 17. A stream of acetylene was bubbled through 200 mL of THF for 2 h at –78 °C. Then *n*-butyllithium (0.06 mol) in 75 mL of dry ether was added dropwise over a period of 20 min. The resulting solution of lithium acetylide was stirred for 15 min, and a solution of ketone (0.02 mol) in 30 mL of THF was added over a period of 15 min. It was stirred at –78 °C for an additional 3 h, and then 20 mL of water was added followed by 10 g of potassium carbonate. The organic phase was decanted, and the aqueous layer was washed with ether (4 × 25 mL). The combined organic extracts were dried, and the solvent was distilled off to give the crude product which was chromatographed over a column of silica gel. Elution with ethyl acetate–hexane gave the ethynyl alcohol.

1-Ethynyl-2-(2'-carbethoxyvinyl)-2-methylcyclohexan-1-ol (2). Following the general procedure, treatment of ketone 1 (4.2 g) afforded compound 2 in 100% yield (4.7 g). $R_f = 0.6$ (1:10, AcOEt/hexane). IR (CCl₄): 3600, 3300, 1710, 1640 cm⁻¹. However, ¹H NMR (400 MHz, CDCl₃) shows the presence of a diastereomer in the ratio of 55:45. ¹H NMR (400 MHz, CDCl₃): δ 7.35 (d, $J = 16.12$, 2H), 5.88 (d, $J = 16.11$, 1H), [5.89 (d, $J =$

16.11, 1H)], 4.2 (q, $J = 7.33$, 4H), 2.55 (s, 1H), [2.56 (s, 1H)], 2.43 (br s, 2H), 1.45–2.04 (m, 16H), 1.29 (t, $J = 7.33$, 6H), 1.17 (s, 3H), [1.26 (s, 3H)]. MS: m/e 236 (M⁺). Anal. Calcd for C₁₄H₂₀O₃: C, 71.16; H, 8.53. Found: C, 71.02; H, 8.73.

1-Ethynyl-2-methyl-2-(3'-oxo-1'-butenyl)cyclohexan-1-ol (8). Following the general procedure, (only 2.2 equiv of *n*-BuLi was used instead of 3 equiv) ketone 7 (3.6 g) afforded the compound 8 in 85% yield (3.5 g). $R_f = 0.6$ (1:5, AcOEt/hexane). IR (CCl₄): 3600, 3300, 1670, 1620 cm⁻¹. ¹H NMR (90 MHz, CCl₄): δ 7.3 (d, $J = 17.12$, 1H), 6.2 (d, $J = 17.12$, 1H), 3.2 (br s, 1H), 2.55 (s, 1H), 2.3 (s, 3H), 1.5–1.8 (m, 8H), 1.2 (s, 3H). MS: m/e 206 (M⁺). Anal. Calcd for C₁₃H₁₈O₂: C, 75.72; H, 8.73. Found: C, 75.53; H, 8.68.

1-Ethynyl-2-(2'-carbethoxyvinyl)-2,4,4-trimethylcyclopentan-1-ol (12). Following the general procedure ketone 11 (4.48 g) afforded the compound 12 in 90% yield (4.34 g) as a colorless crystalline solid. Mp: 92–93 °C (ethyl acetate–hexane) (lit.⁷ mp 71–72 °C (CCl₄–hexane)). $R_f = 0.5$ (1:20, AcOEt/hexane). IR (CCl₄): 3600, 3300, 1720, 1650 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.29 (d, $J = 15.62$, 1H), 5.88 (d, $J = 16.11$, 1H), 4.2 (q, $J = 7.33$, 2H), 2.57 (s, 1H), 2.27 (br s, 1H), 2.08 (d, $J = 13.67$, 1H), 1.99 (d, $J = 13.67$, 1H), 1.86 (d, $J = 13.67$, 1H), 1.73 (d, $J = 13.67$, 1H), 1.29 (t, $J = 7.33$, 3H), 1.21 (s, 3H), 1.16 (s, 3H), 1.13 (s, 3H). 1D NOE (25 °C) irradiation of CH₃ at C-6 ($\delta = 1.13$) generated NOE (%) to OH (13.2%). MS: m/e 250 (M⁺). Anal. Calcd for C₁₅H₂₂O₃: C, 71.97; H, 8.85. Found: C, 71.94; H, 8.83.

1-Ethynyl-2-(2'-carbethoxyvinyl)-2-methylcycloheptan-1-ol (18). Following the general procedure ketone 17 (4.48 g) afforded the compound 18 in 85% yield (4.25 g). $R_f = 0.5$ (1:20, AcOEt/hexane). IR (CCl₄): 3600, 3300, 1720, 1640 cm⁻¹. However, ¹H NMR (400 MHz, CDCl₃) shows the presence of diastereomer in the ratio of 35:65. ¹H NMR (400 MHz, CDCl₃): δ 7.32 (d, $J = 16.11$, 1H), [7.22 (d, $J = 16.12$, 1H)], 6.04 (d, $J = 16.11$, 1H), [5.82 (d, $J = 16.11$, 1H)], 4.2 (q, $J = 7.33$, 4H), 2.52 (s, 1H), [2.50 (s, 1H)], 1.5–2.1 (m, 22H), 1.29 (t, $J = 7.33$, 6H), 1.09 (s, 3H), [1.06 (s, 3H)]. MS: m/e 250 (M⁺). Anal. Calcd for C₁₅H₂₂O₃: C, 71.96; H, 8.85. Found: C, 71.82; H, 8.81.

General Experimental Procedure for the Preparation of Allenic Alcohols 3, 9, 13, and 19. Following a slight modification of the procedure of Crabbe et al.,⁹ a 250-mL round-bottomed flask was charged with ethynyl alcohol (0.005 mol) diisopropylamine (0.00575 mol), cuprous bromide (0.0025 mol), paraformaldehyde (0.008 mol), and 100 mL of THF. The mixture was heated under reflux for 9 h. The solution was cooled, and the solvent was removed under reduced pressure. The residue was dissolved in dichloromethane, washed with water, dried, and concentrated under reduced pressure. The crude product was chromatographed over silica gel using hexane–ethyl acetate as eluent.

1-Allenyl-2-(2'-carbethoxyvinyl)-2-methylcyclohexan-1-ol (3). Following the general procedure, treatment of ethynyl alcohol 2 (1.18 g) gave the allenic alcohol 3 in 70% yield (0.88 g) as a pale yellow liquid. $R_f = 0.7$ (1:10, AcOEt/hexane). IR (CCl₄): 3580, 1950, 1715, 1640 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.28 (d, $J = 16.11$, 1H), 5.81 (d, $J = 16.12$, 1H), 5.36 (t, $J = 6.84$, 1H), 4.91 (d, $J = 6.34$, 2H), 4.19 (q, $J = 7.33$, 2H), 2.5 (s, OH, 1H), 1.44–1.79 (m, 8H), 1.28 (t, $J = 7.33$, 3H), 1.09 (s, 3H). ¹³C NMR (100.6 MHz, CDCl₃): δ 206.2 (s), 167.0 (s), 154.4 (d), 119.8 (d), 96.6 (d), 78.9 (t), 73.3 (s), 60.2 (t), 44.4 (s), 34.9 (t), 33.9 (t), 21.7 (t), 21.0 (t), 20.7 (q), 14.2 (q). MS: m/e 250 (M⁺). Anal. Calcd for C₁₅H₂₂O₃: C, 71.97; H, 8.86. Found: C, 71.90; H, 8.83.

1-Allenyl-2-methyl-2-(3'-oxo-1'-butenyl)cyclohexan-1-ol (9). Following the general procedure, treatment of ethynyl alcohol 8 (1.03 g) gave the allenic alcohol 9 in 60% yield (0.66 g) as a yellow liquid. $R_f = 0.7$ (1:5, AcOEt/hexane). IR (CCl₄): 3600, 1950, 1670, 1620 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.14 (d, $J = 16.21$, 1H), 6.08 (d, $J = 16.11$, 1H), 5.4 (t, $J = 6.83$, 1H), 4.92 (d, $J = 6.83$, 2H), 2.28 (d, $J = 0.94$, 3H), 2.12 (br s, 1H), 1.49–1.77 (m, 8H), 1.14 (s, 3H). ¹³C NMR (100.6 MHz, CDCl₃): δ 206.0 (s), 198.9 (s), 153.7 (d), 129.1 (d), 96.4 (d), 78.9 (t), 73.9 (s), 44.3 (s), 34.9 (t), 33.6 (t), 26.9 (q), 21.8 (t), 20.9 (t), 20.5 (q). MS: m/e 220 (M⁺). Anal. Calcd for C₁₄H₂₀O₂: C, 76.33; H, 9.15. Found: C, 76.23; H, 9.11.

1-Allenyl-2-(2'-carbethoxyvinyl)-2,4,4-trimethylcyclopentan-1-ol (13). Following the general procedure, treatment of ethynyl alcohol 12 (1.25 g) gave the allenic alcohol 13 in 60%

ylid (0.79 g) as a pale yellow liquid. $R_f = 0.5$ (1:20, AcOEt/hexane). IR (CCl₄): 3580, 1950, 1720, 1640 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 7.14 (d, $J = 15.62$, 1H), 5.81 (d, $J = 16.11$, 1H), 5.24 (t, $J = 6.84$, 1H), 4.93 (d, $J = 6.34$, 1H), 4.92 (d, $J = 4.89$, 1H), 4.19 (q, $J = 7.32$, 2H), 2.01 (d, $J = 13.67$, 1H), 1.72 (d, $J = 13.18$, 1H), 1.28 (t, $J = 7.33$, 3H), 1.21 (s, 3H), 1.14 (s, 6H). ¹³C NMR (100.6 MHz, CDCl₃): δ 206.1 (s), 166.9 (s), 154.6 (s), 119.0 (d), 95.3 (d), 82.9 (s), 79.1 (t), 60.2 (t), 54.1 (s), 52.8 (t), 35.3 (s), 33.2 (q), 32.6 (q), 18.5 (q), 14.2 (q). MS: m/e 246 (M⁺). Anal. Calcd for C₁₆H₂₄O₃: C, 72.69; H, 9.15. Found: C, 72.64; H, 9.15.

1-Allenyl-2-(2'-carbethoxyvinyl)-2-methylcycloheptan-1-ol (19). Following the general procedure, treatment of ethynyl alcohol 18 (1.25 g) gave the allenic alcohol 19 in 70% yield (0.92 g) as pale yellow liquid, but as a 1:2 mixture of diastereomers. $R_f = 0.54$ (1:20, AcOEt/hexane). ¹H NMR (400 MHz, CDCl₃): δ 7.20 (d, $J = 16.11$, 1H), [6.96 (d, $J = 16.11$, 1H)], 5.76 (d, $J = 16.11$, 1H), [5.72 (d, $J = 16.11$, 1H)], 5.33 (t, $J = 6.84$, 2H), 4.86 (d, $J = 6.84$, 4H), 4.13 (m, 4H), 2.5 (d (t), $J = 3.04$, 1H), [2.26 (d (t), $J = 2.44$, 1H)], 1.9–1.38 (m, 20 H), 1.21 (t, $J = 7.33$, 6H), 1.14 (s, 3H), [1.04 (s, 3H)]. ¹³C NMR (100.6 MHz, CDCl₃): δ 213.3 (d), [205.1], 166.8 (s) [166.3], 154.7 (d) [151.2], 120.2 (d) [119.1], 98.1 (d) [98.1], 78.4 (t), 75.6 (t), 60.4 (t) [60.3], 53.9 (s) [47.3], 40.8 (t) [38.7], 36.5 (t) [35.5], 26.3 (t) [26.3], 24.5 (t) [24.4], 23.1 (t) [22.0], 21.3 (q) [21.0], 14.2 (q) [14.1]. MS: m/e 264 (M⁺). Anal. Calcd for C₁₆H₂₄O₃: C, 72.69; H, 9.15. Found: C, 72.58; H, 9.12.

General Experimental Procedure for Anionic Oxy-Cope Rearrangement Using KH. Potassium hydride (35% mineral oil dispersion, 0.019 mol) was washed with hexane (3 × 15 mL) under N₂ atmosphere and suspended in dry THF. The magnetically stirred suspension was treated with a 10 mol % solution of iodine¹⁰ in THF until the brown orange color persisted for 5 min. Then it was cooled to 0 °C, and 18-crown-6 (0.019 mol) in 5 mL of THF was added followed by allenic alcohol (0.0038 mol) in 5 mL of THF. The mixture was stirred at 25 °C for 2 h. The reaction mixture was cooled to 0 °C and quenched with 15 mL of saturated ammonium chloride. At this point the pH of the solution was basic and was neutralized with dilute HCl and extracted with ether (8 × 25 mL). The combined organic layers were washed with brine, dried, and concentrated under reduced pressure. The residual liquid was chromatographed over neutral alumina using hexane-ethyl acetate as eluent.

1-Hydroxy-3-methylidene-6-methylbicyclo[4.4.0]dec-4-ene-4-carboxylic Acid (4). Following the general procedure, rearrangement of allenic alcohol 3 (0.95 g) gave the compound 4 in 40% yield. $R_f = 0.7$ (2:3, AcOEt/hexane). IR (CCl₄): 3600, 3060, 1700, 1630 cm⁻¹. ¹H NMR (90 MHz, CCl₄): δ 6.25 (br m, 1H), 6.1 (s, 1H), 5.2 (s, 1H), 4.4 (s, 1H), 1.9 (d, 1H), 1.7 (d, 1H), 0.9–1.2 (m, 9H), 0.8 (s, 3H). Attempts to purify compound 4 by chromatography resulted in decomposition.

4-Acetyl-1-hydroxy-3-methylidene-6-methylbicyclo[4.4.0]dec-4-ene (10). Following the general procedure, rearrangement of allenic alcohol 9 (0.84 g) gave compound 10 in 90% yield (0.75 g) as a brown liquid. $R_f = 0.6$ (1:5, AcOEt/hexane). IR (CCl₄): 3600, 3040, 1670, 1630 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.13 (s, 1H), 5.49 (s, 1H), 5.08 (t, $J = 1.46$, 1H), 2.39 (br s, 2H), 2.29 (d, $J = 0.97$, 3H), 1.34–1.58 (m, 8H), 1.06 (s, 3H). ¹³C NMR (100.6 MHz, CDCl₃): δ 200.7 (s), 147.9 (d), 136.9 (s), 116.8 (t), 71.5 (s), 43.0 (t), 41.7 (s), 36.5 (t), 34.3 (t), 28.7 (q), 22.3 (t), 22.1 (q). MS: m/e 220 (M⁺). Anal. Calcd for C₁₄H₂₀O₂: C, 76.32; H, 9.15. Found: C, 76.12; H, 9.13.

General Experimental Procedure for Anionic Oxy-Cope Rearrangement Using 0.25 Equiv of C₂H₅ONa. To a stirred suspension of freshly prepared sodium ethoxide (0.00125 mol) in 30 mL of dry THF was added slowly a solution of allenic alcohol (0.005 mol) in 10 mL of dry THF at room temperature under N₂ atmosphere. The reaction mixture was stirred for an additional 12–14 h, and then it was poured into water. The aqueous layer was neutralized with dilute HCl and extracted with ether (4 × 25 mL). The combined ether extracts were washed with brine, dried, and concentrated to give a viscous liquid which was chromatographed over a column of neutral alumina using hexane-ethyl acetate as eluent.

4-Carbethoxy-3-methylidene-6-methyl-(E)-cyclodec-5-en-1-one (5). Following the general procedure, allenic alcohol 3 (1.25 g) was subjected to rearrangement conditions to give the

compound 5 in 80% yield (1.00 g) as a pale yellow liquid. $R_f = 0.72$ (1:10, AcOEt/hexane). IR (CCl₄): 3080, 1740, 1710, 1640 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 5.37 (dd, $J = 9.28$, 1.43, 1H), 5.1 (d, $J = 5.86$, 2H), 4.12 (q, $J = 7.33$, 2H), 3.97 (d, $J = 9.28$, 1H), 3.24 (d, $J = 14.06$, 1H), 2.82 (d, $J = 14.06$, 1H), 2.43 (m, 2H), 1.47–2.17 (m, 6H), 1.60 (s, 3H), 1.28 (t, $J = 7.33$, 3H). ¹³C NMR (100.6 MHz, CDCl₃): δ 201.1 (s), 172.2 (s), 140.8 (s), 139.9 (s), 121.7 (d), 117.5 (t), 60.9 (t), 51.8 (d), 49.6 (t), 40.9 (t), 39.6 (t), 23.4 (t), 22.2 (t), 16.7 (q), 14.1 (q). MS: m/e 250 (M⁺). Anal. Calcd for C₁₅H₂₂O₃: C, 71.96; H, 8.86. Found: C, 71.95; H, 8.85.

4-Carbethoxy-3-methylidene-6,8,8-trimethyl-(E)-cyclonon-5-en-1-one (14). Following the general procedure, rearrangement of allenic alcohol 13 (1.32 g) gave the compound 14 in 90% yield (1.19 g) as a pale yellow liquid. $R_f = 0.5$ (1:20, AcOEt/hexane). IR (CCl₄): 3080, 1735, 1705, 1640 cm⁻¹.

Transannular Cyclization of 14. The compound 14 was transformed quantitatively into 15 by elution with hexane-ethyl acetate (20:1) through a column of alumina to give a pale yellow liquid.

4-Carbethoxy-1-hydroxy-3-methylidene-6,8,8-trimethylbicyclo[4.3.0]non-4-ene (15). $R_f = 0.4$ (1:20, AcOEt/hexane). IR (CCl₄): 3620, 3080, 1720, 1640 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.42 (s, 1H), 5.57 (s, 1H), 5.04 (s, 1H), 4.16 (m, 2H), 2.34 (d, $J = 14.16$, 1H), 2.26 (s, 1H), 2.24 (d, $J = 14.16$, 1H), 1.84 (d, $J = 13.18$, 1H), 1.69 (d, $J = 14.65$, 1H), 1.57 (d, $J = 13.19$, 1H), 1.50 (d, $J = 14.65$, 1H), 1.25 (d (t), 3H), 1.07 (s, 3H), 1.05 (s, 3H), 0.89 (s, 3H). ¹³C NMR (100.6 MHz, CDCl₃): δ 166.6 (s), 148.8 (d), 137.2 (s), 127.6 (s), 115.8 (t), 81.6 (s), 60.5 (t), 53.5 (t), 51.3 (t), 49.4 (s), 41.4 (t), 34.6 (t), 33.2 (q), 32.0 (q), 20.6 (q), 14.0 (q). 1D NOE (25 °C) irradiation of CH₃ at C-6 ($\delta = 0.89$) generated NOEs (%) to H-5 (6.3%), H_β-6 (8.1%), H_β-8 (7.7%), and β -methyl-7 (7.2%). MS: m/e 246 (M⁺). Anal. Calcd for C₁₅H₂₄O₃: C, 72.69; H, 9.15. Found: C, 72.63; H, 9.14.

Compound 15 was also obtained in 90% yield by treatment of compound 3 with 1.1 equiv of freshly prepared sodium ethoxide.

4-Carbethoxy-1-hydroxy-3-methylidene-6-methylbicyclo[4.4.0]dec-4-ene (6). Following the general procedure, treatment of compound 3 (1.25 g) with 1.1 equiv of freshly prepared sodium ethoxide gave the rearranged compound 6 in 85% yield (1.06 g). $R_f = 0.69$ (1:10, AcOEt/hexane). IR (CCl₄): 3600, 3060, 1720, 1630 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 6.37 (s, 1H), 5.75 (s, 1H), 5.09 (d, $J = 1.46$, 1H), 4.17 (q, $J = 7.32$, 2H), 2.68 (d (t), $J = 15.63$, 2.93, 1H), 2.16 (d, $J = 15.62$, 1H), 1.26 (t, $J = 7.32$, 3H), 1.16–1.20 (m, 9H), 1.07 (s, 3H). ¹³C NMR (100.6 MHz, CDCl₃): δ 166.7 (s), 147.7 (d), 134.9 (s), 128.5 (s), 117.8 (t), 71.7 (s), 60.6 (t), 42.2 (t), 40.8 (s), 31.8 (t), 31.4 (t), 23.3 (q), 20.5 (t), 20.4 (t), 14.1 (q). MS: m/e 250 (M⁺). Anal. Calcd for C₁₅H₂₂O₃: C, 71.97; H, 8.86. Found: C, 71.92; H, 8.84.

4-Carbethoxy-3,6-dimethyl-3(E),5(E)-cycloundecadien-1-one (20). Following the general procedure, the allenic alcohol 19 (1.32 g) was subjected to rearrangement conditions to give the compound 20 in 80% yield (1.06 g) as a pale yellow liquid. $R_f = 0.5$ (1:20, AcOEt/hexane). IR (CCl₄): 1710–20, 1640, 1630 cm⁻¹. ¹H NMR (400 MHz, CDCl₃): δ 5.68 (s, 1H), 4.12 (q, $J = 7.32$, 2H), 3.16 (s, 2H), 2.26 (dd, $J = 6.34$, 3.42, 2H), 2.22 (d, $J = 1.41$, 3H), 2.09 (d (t), $J = 6.89$, 2H), 1.43–1.62 (m, 6H), 1.40 (s, 3H), 1.21 (t, $J = 7.33$, 3H). ¹³C NMR (100.6 MHz, CDCl₃): δ 208.6 (s), 167.8 (s), 144.9 (s), 138.5 (s), 127.3 (s), 124.2 (d), 60.1 (t), 47.9 (t), 43.7 (t), 36.4 (t), 23.7 (q), 23.2 (t), 22.3 (t), 22.0 (t), 15.9 (q), 14.2 (q). MS: m/e 264 (M⁺). Anal. Calcd for C₁₆H₂₄O₃: C, 72.69; H, 9.15. Found: C, 72.67; H, 9.15.

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