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ON POSSIBLE REDIRECTION OF THE COURSE OF ANIONIC OXY-COPE REARRANGEMENTS†

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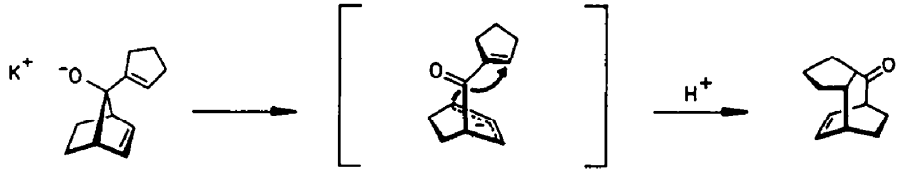
Abstract: The β,γ-unsaturated ketones bicyclo[2.2.1]hept-2-en-7-one (10) and 7,7-dimethoxybicyclo[2.2.1]hept-2-en-5-one (15) have been condensed with 1-metalated *trans*-1-methoxybutadienes (7a or 7b) and 2-isopropenylcyclopentenes (8b or 8c). Oxyanion formation within the resulting alcohols is followed by skeletal rearrangement at room temperature. Careful product analysis has revealed the [3,3] sigmatropic reaction manifold to be followed almost exclusively. Only in the case of 13 is a modest amount (4%) of formal antarafacial-retention [1,3] sigmatropic bridgehead carbon migration in evidence. Consequently, the structural features inherent to these alcohols are not conducive to redirecting electronic reorganization to an alternative isomerization process.

That oxy-Cope rearrangements can be strikingly accelerated by prior alkoxide formation[1] is now well recognized. A number of theoretical studies which attempt to correlate this substituent effect with mechanism have made their appearance.[2] The orbital symmetry control available to [3,3] sigmatropic processes[3] constitutes the underlying working hypothesis common to all of these investigations. Notwithstanding, examples are known where concertedness is clearly by-passed in favor of a kinetically controlled cleavage-recombination alternative. For example, potassium alkoxide 1 is recognized to fragment to 2, which subsequently experiences an intramolecular Michael ring closure.[4] This rearrangement is accelerated as usual, but complications stemming from the relatively large distance between the π-bond termini and less than ideal π-orbital overlap apparently contribute to non-operation of synchronous six-electron reorganization.



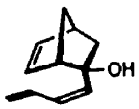
1 2 3

The non-concerted nature of the 1 → 3 conversion has led us to consider the possibility of redirecting the course of this and allied rearrangements. In particular, we have considered studying cases where the bicyclic framework is maintained intact while the olefinic sidechain is extended as in 4 and 5. MODEL calculations[5] reveal the terminal vinyl

†Dedicated to Professor Edward C. Taylor on the occasion of his 65th birthday.

carbon in *unconstrained* 6 to be capable of approaching the proper norbornene sp^2-center to the extent of only 3.547 Å (see A). In 5, homologation with full planarity along the diene

4



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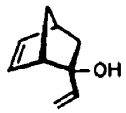

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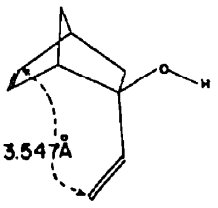
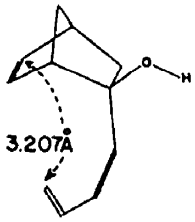
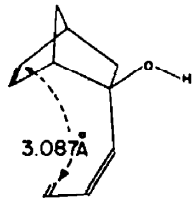
subunit reduces the distance between the relevant reaction sites to 3.207 Å (see b). If rotation is allowed in the diene component as depicted in C, still closer proximity (3.087 Å) can be achieved at the expense of some resonance energy.



A



B



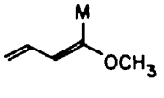
C

Adherence by 4 and 5 to a concerted isomerization pathway was not anticipated because symmetry-disfavored [3,5] sigmatropy would be forced upon these systems. Instead, the test being proposed was whether the availability of an extended π system as in 4 and 5 could, by virtue of a greater potential for proximity, divert the rearrangement pathway otherwise followed by their lower homologues.[6] The alkoxide of 6 most certainly experiences substantive structural distortion in the transition state associated with its oxy-Cope rearrangement. Attempts to simulate this state of affairs by calculation were not made. However, the potential importance of this phenomenon in enhancing proximity and proper orbital overlap should not be, and was not, underestimated from the outset.

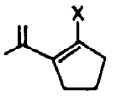
Results and Discussion

The two nucleophiles selected for this study were 7 and 8. Metalation of *trans*-1-methoxybutadiene[7] with *tert*-butyllithium is recognized to proceed with retention of configuration at C-1 to give 7a.[8] Conversion of 7a to the dichlorocerium reagent 7b, necessary to curtail enolization in the ketonic reaction partner when operative,[6e-g,9] was achieved simply by transferring 7a into a dry tetrahydrofuran slurry of anhydrous cerium trichloride.

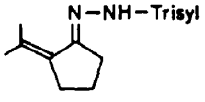
To arrive at vinyl bromide 8a, the previously reported trisylhydrazone 9[10] was subjected to the Shapiro reaction.[11] The vinyllithium reagent so formed was subsequently treated with 1,2-dibromotetrafluoroethane.[4,12] The eventual formation of 8b and 8c was accomplished as before.



7g, M=Li
b, M=$CeCl_2$

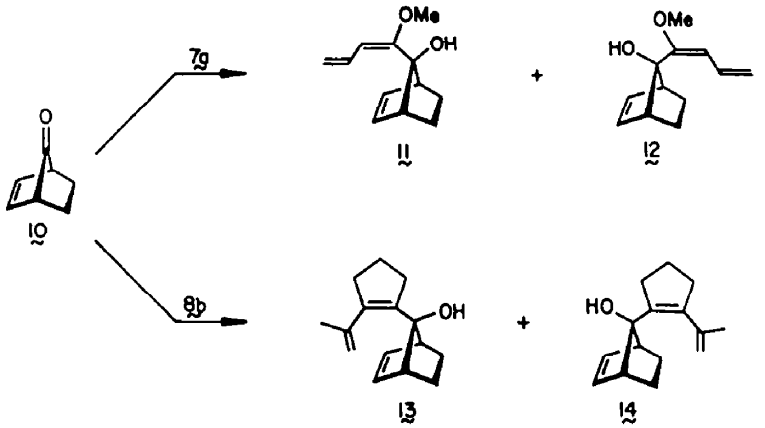


8g, X=Br
b, X=Li
c, X=$CeCl_2$



9

The reaction of 7a with bicyclo[2.2.1]hept-2-en-7-one (10) in anhydrous tetrahydrofuran provided alcohols 11 and 12 in isolated yields of 64% and 5%, respectively. The relative stereochemistry of these isomers was deduced by multiple chemical shift comparison with related molecules.[4] For instance, the exo protons of the ethano bridge in 11 (δ 2.13-2.07) appear downfield of those in 12 (δ 1.89-1.86), which are shielded by virtue of their proximity to the unsaturated sidechain. Additionally, the -(MeO)C=C<u>H</u>- proton of the dienyl



substituent is subject to the reciprocal effect. That is, shielding by the norbornene double bond in 11 (δ 5.21) causes the proton in question to appear upfield of the corresponding signal in 12 (δ 5.26).

In the condensation of 8b with 10, anti alcohol 13 was isolated in 64% yield. No attempt was made to obtain minor component 14 in pure condition. Unequivocal identification of 13 was realized by X-ray crystallographic analysis (Figure 1, Tables I and II).

The dominant syn attack on 10 by 7a and 8b compares closely to the stereochemical course followed by methyllithium (60% syn).[13] However, 1-cyclopentenyllithium reagents show a modest preference for attack from the anti direction.[4] In the case of (pentafluoroethyl)lithium, nucleophilic capture occurs exclusively from the anti direction.[14] Grignard reagents also vary widely in their stereoselective approach to 10.[4,14,15] The origin of this phenomenon is very likely electronic in nature,[16] and appears to be especially dependent on the character of the attacking anion.

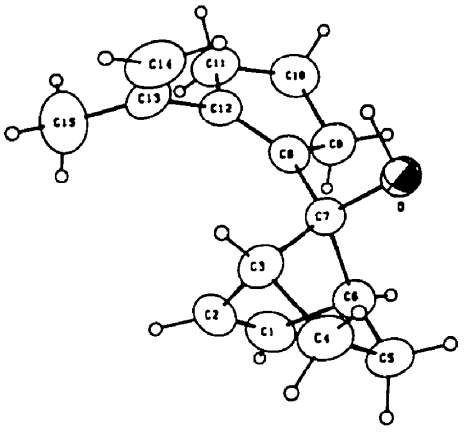
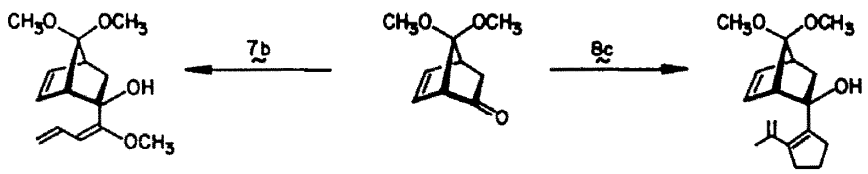


Figure 1. Computer-generated perspective drawing of 13 as determined by X-ray crystallography. The atom numbering is arbitrary.

In order to realize good yields of alcohols 16 and 17, recourse was made to the dichlorocerium reagents 7b and 8c as recommended by Learn and Romine for this system.[6a-g] Despite the striking sensitivity of these alcohols to acid, it proved possible to achieve their purification by medium pressure liquid chromatography (MPLC) on silica gel.



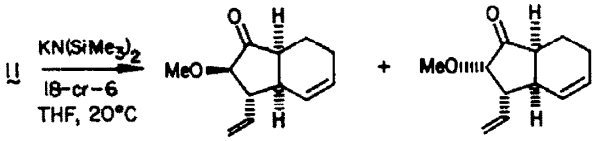
16 15 17

Table I. Crystal Data and Summary of Intensity Data Collection and Structure Refinement for 13.

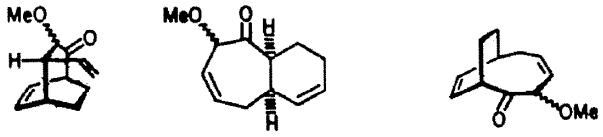
Compd	$C_{15}H_{20}O$
Color/Shape	clear/fragment
Mol wt.	216.3
Space group	$I4_1/a$
Temp., °C	20
Cell constants[a]	
a, Å	22.949(5)
c, Å	9.498(1)
Cell vol, Å^3	5002
Formula units/unit cell	16
D_{calc}, g cm^{-3}	1.15
μ(calc), cm^{-1}	0.37
Diffractometer/Scan	Enraf-Nonius CAD4/θ-2θ
Radiation, graphite monochromator	MoKα (λ = 0.71073)
Max crystal dimensions, mm	0.80 x 0.30 x 0.40
Scan width	0.80 + 0.35tan θ
Standard reflections	(800), (080), (004)
Decay of standards	-30%
Reflections measured	2564
2θ range, deg	$2 \leq 2\theta \leq 50$
Range of h,k,l	$\pm$27, +27, +11 (except $\|h\|>\|k\|$ and h+k+l = 2n)
Reflections observed [$F_o \geq 5\sigma(F_o)$][b]	1288
Computer programs[c]	SHELX[17]
Structure solution	MULTAN[18]
No. of parameters varied	145
Weights	$[\sigma(F_o)^2 + 0.0001\ F_o^2]^{-1}$
GOF	1.82
R int	0.080
$R = \geq\|\|F_o\| - \|F_c\|\|/\geq\|F_o\|$	0.064
R_w	0.066
Largest feature final diff. map	0.3 e$^-$/Å

[a]Least-squares refinement of (sinθ/λ)^2 values for 23 reflections $\theta > 20°$. [b]Corrections: Lorentz, polarization and absorption (empirical, psi scan). [c]Neutral atom scattering factors and anomalous dispersion corrections from ref. 19.

When 11 was exposed to excess potassium hexamethyldisilazide in anhydrous tetrahydrofuran containing greater than 1 equiv of 18-crown-6, rearrangement was complete within 30 min at room temperature. Careful chromatography of the mixture revealed the presence of only two products. Of the two resulting ketones, the major constituent (50% isolated) was identified as 18 and the minor (4%) as 19. The high volatility of both substances contributed to material losses during their isolation. A revealing spectral property of both 18 and 19 was their infrared carbonyl absorption at 1745 cm^{-1} characteristic of cyclopentanone character. In addition, five vinylic protons are clearly visible in their ^1H NMR spectra which show no evidence for a signal at *ca* 3 ppm that is diagnostic of the bridgehead α-carbonyl proton in molecules related to 25.[4] In fact, no evidence whatsoever was found for the formation of 20 (the end product of a [1,3] shift), 21 (the [3,5] sigmatropic option), of 22 (the [1,5] carbon migrated isomer).



11 18 19



20 21 22

It is clear that 18 results from kinetically controlled protonation of the initially formed enolate anion from the sterically more accessible α surface. That 19 is epimeric

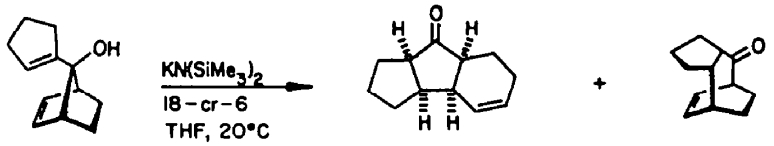
Table II. Bond Distances (Å) and Angles (deg) for 13.

Atoms	Distance	Atoms	Distance
O -- C(7)	1.447(4)	C(1) -- C(2)	1.318(6)
C(1) -- C(6)	1.509(5)	C(2) -- C(3)	1.499(5)
C(3) -- C(4)	1.544(5)	C(3) -- C(7)	1.550(5)
C(4) -- C(5)	1.540(5)	C(5) -- C(6)	1.537(5)
C(6) -- C(7)	1.550(5)	C(7) -- C(8)	1.514(5)
C(8) -- C(9)	1.513(5)	C(8) -- C(12)	1.337(5)
C(9) -- C(10)	1.526(5)	C(10) -- C(11)	1.520(5)
C(11) -- C(12)	1.521(5)	C(12) -- C(13)	1.469(5)
C(13) -- C(14)	1.314(6)	C(13) -- C(15)	1.503(6)

Atoms	Angle	Atoms	Angle
C(2) -- C(1) -- C(6)	107.4(3)	C(1) -- C(2) -- C(3)	108.2(3)
C(2) -- C(3) -- C(4)	106.4(3)	C(2) -- C(3) -- C(7)	98.7(3)
C(4) -- C(3) -- C(4)	101.8(3)	C(3) -- C(4) -- C(5)	103.2(3)
C(4) -- C(5) -- C(6)	103.0(3)	C(1) -- C(6) -- C(5)	106.3(3)
C(1) -- C(6) -- C(7)	98.7(3)	C(5) -- C(6) -- C(7)	102.3(3)
O -- C(7) -- C(3)	113.1(3)	O -- C(7) -- C(6)	108.7(3)
C(3) -- C(7) -- C(6)	92.4(3)	O -- C(7) -- C(8)	109.3(3)
C(3) -- C(7) -- C(8)	118.2(3)	C(6) -- C(7) -- C(8)	114.0(3)
C(7) -- C(8) -- C(9)	118.0(3)	C(7) -- C(8) -- C(12)	130.8(3)
C(9) -- C(8) -- C(12)	111.2(3)	C(8) -- C(9) -- C(10)	103.9(3)
C(9) -- C(10) -- C(11)	105.5(3)	C(10) -- C(11) -- C(12)	103.9(3)
C(8) -- C(12) -- C(11)	110.8(3)	C(8) -- C(12) -- C(13)	130.4(3)
C(11) -- C(12) -- C(13)	118.8(3)	C(12) -- C(13) -- C(14)	122.5(4)
C(12) -- C(13) -- C(15)	116.0(4)	C(14) -- C(13) -- C(15)	121.5(4)

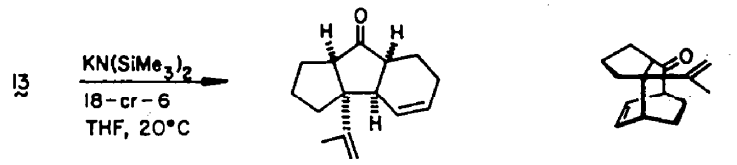
with 18 at the methoxyl substituted carbon was established by decoupling and difference NOE studies performed at the 300 MHz level (Table III). Perhaps the most pertinent evidence is the 6% enhancement observed in the H_B signal when H_C was irradiated.

The complete adherence of 11 to [3,3] sigmatropy came as somewhat of a surprise, since alcohol 23 in the presence of potassium hydride is known to deliver 24 and 25 in a 3:1 ratio.[4] Repetition of the rearrangement of 23 with potassium hexamethyldisilazide as base and 18-crown-6 as promoter, in order to simulate the reaction conditions employed for 11, enhanced the level of 25 (38% isolated) relative to 24 (16%)!



23 24 25

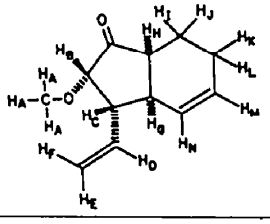
Treatment of 13 in an entirely analogous manner gave rise to 26 (82%) and 27 (4%). The ^1H NMR spectrum of 26 compares closely to that of 24 with the exception of the effects introduced by the isopropenyl substituent. In line with precedence,[4] the carbonyl absorption of 26 at 1736 cm^{-1} differs intrinsically from that observed for 27 (1679 cm^{-1}). The



26 27

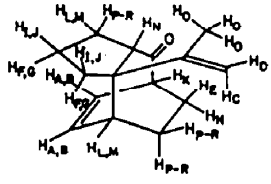
stereochemistry of the isopropenyl group in 27 was ascertained by COSY and difference NOE studies at 500 MHz. The results, summarized in Table IV, reveal in particular the proximity of H_C to H_{P-R}.

Table III. Selected Difference NOE Data for 19 (300 MHz, C_6D_6 solution).



Proton irradiated	NOE (% enhancement)
H	D (2.5)
	G (8.4)
	I-L (7.1)[a]
G	D (6.1)
	M,N (6.9)[a]
	H (10.6)
C	D (3.0)
	M,N (3.0)[a]
	F (3.0)
	B (6.0)

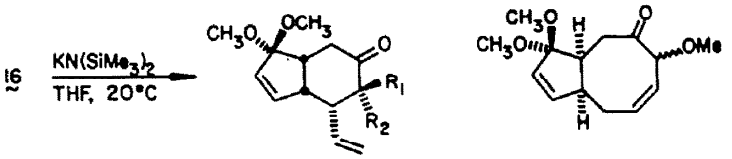
Table IV. Selected Difference NOE Data for 27 (500 MHz, C_6D_6 solution).



Proton irradiated	NOE (% enhancement)
O	D (4.2)
D	C (14.1)
	O (2.8)
C	D (10.0)
	I,J (1.9)
	N (0.3)
	O (1.0)
	P-R (2.1)

[a]The multiplet involved incorporates the protons listed.

The potassium salts of 16 and 17 did not require the presence of 18-crown-6 in order to rearrange rapidly at room temperature. Stirring 16 with hexamethyldisilazide in tetrahydrofuran at room temperature for 45 min gave a mixture of the two epimeric ketones 28a and 28b in nearly equal amounts. Although a sensitivity on the part of these α-methoxycyclohexanones to silica gel was noted, their separation could be effected by chromatography on Florisil. The less polar constituent is tentatively formulated as 28a since its

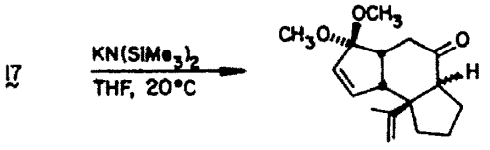


28a, R_1=H, R_2=OMe
b, R_1=OMe, R_2=H

29

methoxy substituent is situated on the concave surface and is further sterically shielded by the vinyl group. In line with their cyclohexanone character, the infrared carbonyl absorptions of 28a and 28b appear at 1725 cm^{-1}. Their ^1H NMR spectra feature five olefinic protons and are otherwise particularly distinctive. These data happen not to be compatible with 29, the possible end product of [3,5] sigmatropy. In actuality, no evidence was obtained for the formation of 29.

In similar fashion, the potassium alkoxide derived from 17 isomerized exclusively via the [3,3] sigmatropic manifold to deliver a 2:1 mixture of the epimeric ketones 30. The spectral properties of 30 proved consistent only with the presence of the 5-6-5 tricyclic framework.



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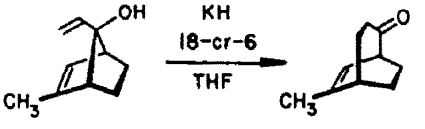
Thus, alcohols 11, 13, 16, and 17 have shown little tendency to undergo any rearrangement other than the oxyanionic Cope process. In actuality, the presence of a dienic sidechain in the first two examples has actually served to induce stricter adherence to the [3,3] sigmatropic pathway than witnessed normally. Whereas 11 isomerizes exclusively to give 18 and 19, 13 delivers 26 and 27 in an 18:1 ratio. This response can be compared to that of 23 (2.4:1) and 31 (only 32 results!).[4] This may be a reflection of the high



31 32

electron density that normally resides at C-3 in a pentadienyl anion or radical.

Since the four substrates described herein show a heightened tendency for oxy-Cope isomerization, their structural features are clearly not conducive to redirecting electronic reorganization away from this particular reaction channel.

Experimental Section

1-Bromo-2-isopropenylcyclopentene (8a). A cold (-78 °C), mechanically stirred, and nitrogen-blanketed solution of 9 (20.00 g, 49.5 mmol) in N,N,N',N'-tetramethylethylenediamine (108 mL) and anhydrous tetrahydrofuran (90 mL) was treated dropwise during 30 min with *sec*-butyllithium in cyclohexane (104 mmol). After 45 min, the reaction mixture was warmed to 0 °C for 45 min and recooled to -78 °C. 1,2-Dibromo-1,1,2,2-tetrahydrofluoroethane (27.01 g, 104 mmol) was introduced rather rapidly, stirring at -78 °C was continued for another hour, and water (200 mL) was added. The mixture was partitioned between petroleum ether and brine, the aqueous phase was extracted with petroleum ether (3 x 200 mL), and the combined organic layers were washed with water (3 x 250 mL), 10% hydrochloric acid (3 x 150 ml), saturated sodium bicarbonate solution (3 x 150 mL), and brine (3 x 150 mL) prior to drying. This solution was filtered through neutral alumina on Celite and evaporated. The crude product was passed through neutral alumina (elution with petroleum ether) and distilled to give 1.82 g (20%) of 8a as a pale yellow liquid, bp 84-86 °C/5 torr; ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.07-5.05 (m, 2 H), 2.78-2.71 (m, 2 H), 2.55-2.48 (m, 2 H), 2.05 (d, J = 1.0 Hz, 3 H), 2.01-1.59 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 139.87, 139.46, 116.16, 115.81, 42.65, 35.20, 22.13, 21.63; MS m/z (M^+) calcd 188.0023, obsd 188.0032.

Alcohols 11 and 12. A magnetically stirred solution of *trans*-1-methoxy-1,3-butadiene (202 mg, 2.40 mmol) in anhydrous tetrahydrofuran (8 mL) was blanketed with nitrogen, cooled to -78 °C, and treated dropwise with *tert*-butyllithium in pentane (2.40 mmol). The reaction mixture was slowly warmed to -20 °C over 30 min and recooled to -78 °C. Ketone 10 (216 mg, 2.00 mmol) dissolved in anhydrous tetrahydrofuran (3.1 mL) was added dropwise during 10 min. After 2 h, saturated ammonium chloride solution (5 mL) was added and this mixture was partitioned between ether and brine. The aqueous phase was extracted with ether (3x) and the combined organic layers were washed with brine (2x), dried, and evaporated. The residue was subjected to MPLC on silica gel. Elution with 10% ether in petroleum ether gave 244 mg (64%) of 11 as a pale yellow, unstable oil while flushing with 40% ether in petroleum ether afforded 20 mg (5%) of 12 as a colorless oil.

For 11: IR (neat, cm^{-1}) 3460, 3066, 2994, 2974, 2945, 2906, 2868, 2834, 1631, 1590, 1463, 1453; ^{1}H NMR (300 MHz, C_6D_6) δ 6.98 (ddd, J = 16.8, 11.0, 10.6 Hz, 1 H), 5.87 (t, J = 2.2 Hz, 2 H), 5.21 (d, J = 11.0 Hz, 1 H), 5.02 (dd, J = 16.5, 2.1 Hz, 1 H), 4.91 (dd, J = 10.6, 2.2 Hz, 1 H), 3.08 (s, 3 H), 2.94-2.92 (m, 1 H), 2.13-2.07 (m, 2 H), 1.73 (s, 1 H), 1.08-0.98 (m, 3 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 161.52, 134.09 (2C), 133.12, 112.08, 103.52, 92.58, 54.41, 48.91 (2C), 23.14 (2C); MS m/z (M^+) calcd 192.1150, obsd 192.1155.

For 12: IR (neat, cm^{-1}) 3546, 3087, 3066, 3000, 2930, 2913, 2878, 2839, 1638, 1463; ^{1}H NMR (300 MHz, C_6D_6) δ 7.02 (ddd, J = 16.9, 10.9, 10.5 Hz, 1 H), 5.81 (d, J = 2.0 Hz, 1 H), 5.80 (d, J = 1.9 Hz, 1 H), 5.26 (d, J = 10.9 Hz, 1 H), 5.06 (dd, J = 17.0, 2.1 Hz, 1 H), 4.96 (dd, J = 10.2, 2.1 Hz, 1 H), 3.08 (s, 3 H), 3.08-3.05 (m, 2 H), 2.46 (s, 1 H), 1.89-1.86 (m, 2 H), 0.86-0.77 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 158.83, 133.89 (2C), 132.93, 112.37, 103.26, 94.31, 54.51, 50.37 (2C), 22.70 (2C); MS m/z (M^+) calcd 192.1150, obsd 192.1162.

Alcohol 13. A magnetically stirred solution of 8a (449 mg, 2.4 mmol) in 8 mL of anhydrous tetrahydrofuran was blanketed with nitrogen, cooled to -78 °C, and treated dropwise with *tert*-butyllithium (4.8 mmol) in pentane. After 30 min, ketone 10 (216 mg, 2.0 mmol) dissolved in dry tetrahydrofuran (3.1 mL) was slowly added during 10 min and stirring was maintained at -78 °C for 2 h. Quenching and workup in the predescribed manner gave a residue, purification of which by MPLC on silica gel (elution with 10% ether in petroleum ether) afforded 276 mg of 13 as a colorless solid, mp 85.5-86 °C (from petroleum ether); IR ($CDCl_3$, cm^{-1}) 2982, 2950, 2873, 2849, 1624, 1443; ^{1}H NMR (300 MHz, C_6D_6) δ 5.83 (d, J = 2.2 Hz, 1 H), 5.83 (d, J = 2.2 Hz, 1 H), 4.85 (dd, J = 2.3, 1.4 Hz, 1 H), 4.80 (dd, J = 2.0, 1.3 Hz, 1 H), 2.85-2.82 (m, 2 H), 2.41-2.30 (m, 4 H), 2.20-2.16 (m, 2 H), 1.74 (t, J = 1.11 Hz, 3 H), 1.69-1.59 (m, 2 H), 1.38 (s, 1 H), 1.04 (d, J = 3.5 Hz, 1 H), 1.00 (d, J = 3.6 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 144.78, 141.64, 138.36, 134.97, 127.92, 113.30, 89.73, 48.79, 38.55, 38.06, 23.49, 22.46, 22.30; MS m/z (M^+) calcd 216.1514, obsd 216.1517.

Anal. Calcd for $C_{15}H_{20}O$: C, 83.28, H, 9.32. Found: C, 83.42; H, 9.41.

X-Ray Data Collection, Structure Determination, and Refinement for 13. A transparent single crystal fragment of 13 was mounted on a pin and transferred to the goniometer. The space group was determined to be the centric $I4_1/a$ from the systematic absences. A linear decay of -30% was noted for the standard during data collection. A correction was applied to the data. A summary of the data collection parameters is given in Table I.

The geometrically constrained hydrogen atoms were placed in calculated positions 0.95 Å from the bonded carbon atom and allowed to ride on that atom with B fixed at 5.5 Å^2. The C(14) and C(15) hydrogen atoms were located from a difference Fourier map and included with fixed contributions (B = 5.5 Å^2). Refinement of the nonhydrogen atoms with anisotropic temperature factors led to final values of R = 0.064 and R_w = 0.066. The final values of the positional parameters are given in Table II.

Alcohol 16. A 651 mg sample (2.64 mmol) of anhydrous cerium trichloride was heated under high vacuum at 140 °C for 1.5 h. The flask was flushed with nitrogen and cooled to room temperature, at which point 8 mL of dry tetrahydrofuran was added. The resultant slurry was stirred for 2 h. During this time, *trans*-1-methoxy-1,3-butadiene (202 mg, 2.40 mmol) in 5 mL of tetrahydrofuran was being lithiated with *tert*-butyllithium (2.40 mmol) as described earlier. This solution was transferred via cannula to the cerium chloride slurry at -78 °C. This mixture was stirred for 30 min before dropwise addition of 7,7-dimethoxynorbornenone (336 mg, 2.00 mmol) in tetrahydrofuran (1.67 mL). After 2.5 h at -78 °C, saturated ammonium chloride solution (5 mL) was added and the mixture was partitioned between ether and brine. The usual workup and MPLC on silica gel (elution with 30% ether in petroleum ether) furnished 239 mg (47%) of 16 and 98 mg of recovered 15. The yield

based on reisolated starting material is 76%.

For 16: colorless oil; IR (neat, cm^{-1}) 3486, 3086, 2984, 2940, 2837, 1635, 1450; ^1H NMR (300 MHz, C_6D_6) δ 7.36 (ddd, J = 16.9, 10.4, 10.4 Hz, 1 H), 6.00-5.92 (m, 2 h), 5.29 (d, J = 10.8 Hz, 1 H), 5.11 (ddd, J = 16.8, 2.1, 0.7 Hz, 1 H), 5.03 (ddd, J = 10.7, 2.2, 0.6 Hz, 1 H), 4.44 (s, 1 H), 3.18-3.16 (m, 1 H), 3.12 (s, 3 H), 2.93 (s, 3 H), 2.90 (s, 3 H), 2.63-2.61 (m, 1 H), 2.42 (d, J = 12.7 Hz, 1 H), 1.81 (dd, J = 9.0, 3.7 Hz, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 161.91, 136.51, 134.13, 130.87, 120.11, 111.60, 102.75, 82.32, 55.12, 54.51, 52.10, 49.07, 45.47, 41.71; MS m/z (M^+) calcd 252.1361, obsd 252.1148.

Anal. Calcd for $C_{14}H_{20}O_4$: C, 66.64; H, 7.99. Found: C, 66.48; H, 8.04.

Alcohol 17. Cerium chloride (542 mg, 2.20 mmol) was dried as above and slurried for 2 h in 8 mL of anhydrous tetrahydrofuran. In the meantime, 8a (374 mg, 2.00 mmol) was metalated with *tert*-butyllithium (4.00 mmol) as before. The resulting solution of 8b was transferred via cannula to the magnetically stirred cerium chloride slurry cooled to -78 °C, stirred for 30 min, and treated dropwise with a solutin of 15 (280 mg, 1.67 mmol) in 1.39 mL of dry tetrahydrofuran. This mixture was stirred at -78 °C for 30 min, quenched and processed as above, and purified by MPLC on silica gel (elution with 20% ethyl acetate in petroleum ether). There was isolated 96 mg (21%) of 17 and 183 mg of recovered 15. The yield based on unconsumed starting material is 86%.

For 17: IR (neat, cm^{-1}) 3503, 3083, 2950, 2849, 1626, 1454; ^1H NMR (300 MHz, C_6D_6) δ 5.98 (ddd, J = 6.2, 3.2, 0.9 Hz, 1 H), 5.86 (dd, J = 6.1, 3.5 Hz, 1 H), 5.36 (d, J = 2.9 Hz, 1 H), 5.01-4.99 (m, 1 H), 4.36 (s, 1 H), 3.01-2.85 (m, 1 H), 2.96 (s, 3 H), 2.92 (s, 3 H), 2.80-2.68 (m, 1 H), 2.65-2.63 (m, 1 H), 2.56-2.33 (m, 3 H), 2.21 (d, J = 12.9 Hz, 1 H), 1.86-1.63 (m, 3 H), 1.85 (t, J = 1.0 Hz, 3 H); ^{13}C NMR (20 MHz, C_6D_6) ppm 144.14, 140.74, 139.45, 136.81, 130.97, 120.43, 114.36, 79.30, 55.03, 52.02, 49.00, 45.78, 40.76, 38.95, 36.83, 22.65, 22.49; MS m/z (M^+) calcd 276.1725, obsd 276.1724.

Anal. Calcd for $C_{17}H_{24}O$: C, 73.88; H, 8.75. Found: C, 73.79; H, 8.84.

Anionic Rearrangement of 11. A solution of 11 (178 mg, 0.927 mmol) and 18-crown-6 (294 mg, 1.11 mmol) in 5 mL of anhydrous tetrahydrofuran was treated dropwise with a solution of potassium hexamethyldisilazide (1.11 mmol) in the same solvent. The reaction mixture was stirred under nitrogen at room temperature for 30 min, cooled to -78 °C, and treated with 1 mL of saturated ammonium chloride solution. The solution was transferred to a separatory funnel and partitioned between petroleum ether and brine. The organic phase was separated and washed twice with brine before being dried and concentrated. Purification of the residue by MPLC on silica gel (elution with 20% ether in petroleum ether) gave 7 mg (4%) of 19 and 89 mg (50%) of 18.

For 18: colorless solid, mp 50.0 °C (from petroleum ether); IR (C_6D_6, cm^{-1}) 1745; ^1H NMR (300 MHz, C_6D_6) δ 5.67-5.51 (m, 3 H), 5.10-5.03 (m, 2 H), 3.43 (s, 3 H), 3.20 (dd, J = 11.0, 1.5 Hz, 1 H), 2.37 (ddd, J = 11.0, 8.0, 3.0 Hz, 1 H), 2.07-1.90 (m, 2 H), 1.83-1.74 (m, 1 H), 1.69-1.62 (m, 2 H), 1.24-1.10 (m, 1 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 214.65, 138.47, 128.11, 125.99, 117.14, 87.58, 58.43, 51.50, 43.07, 35.96, 23.79, 21.39; MS m/z (M^+) calcd 192.1150, obsd 192.1147.

Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.93; H, 8.42.

For 19: colorless oil; IR (C_6D_6, cm^{-1}) 1744; ^1H NMR (300 MHz, C_6D_6) δ 5.92 (ddd, J = 16.7, 10.8, 8.4 Hz, 1 H), 5.58 (d, J = 12.4 Hz, 1 H), 5.53 (dd, J = 12.3, 1.8 Hz, 1 H), 5.07 (dd, J = 9.1, 1.6 Hz, 1 H), 5.05 (d, J = 17.3 Hz, 1 H), 3.38 (d, J = 6.1 Hz, 1 H), 3.26 (s, 3 H), 2.63-2.58 (m, 1 H), 2.41 (q, J = 6.5 Hz, 1 H), 2.27 (q, J = 7.3 Hz, 1 H), 1.73-1.59 (m, 2 H), 1.57-1.47 (m, 2 H) - see also Table III; ^{13}C NMR (75 MHz, $CDCl_3$) ppm 216.33, 134.71, 128.79, 128.34, 117.58, 84.06, 58.12, 48.47, 42.92, 37.82, 22.04, 21.49; MS m/z (M^+) calcd 192.1150, obsd 192.1152.

Anionic Rearrangement of 13. A solution of 13 (202 mg, 0.935 mmol) and 18-crown-6 (296 mg, 1.12 mmol) in anhydrous tetrahydrofuran was treated as above with potassium hexamethyldisilazide (1.12 mmol) and stirred under nitrogen at room temperature for 20 min. Workup in the predescribed manner and purification by MPLC on silica gel (elution with 4% ether in petroleum ether) afforded 8 mg (4%) of 27 and 165 mg (82%) of 26.

For 26: colorless oil; IR (neat, cm^{-1}) 3084, 3026, 2946, 2876, 1736, 1724, 1633, 1444; ^1H NMR (300 MHz, C_6D_6) δ 5.68-5.59 (m, 2 H), 4.71 (d, J = 0.6 Hz, 1 H), 4.64 (s, 1 H), 2.63-2.53 (m, 2 H), 2.40-2.33 (m, 1 H), 2.19-2.09 (m, 1 H), 1.93-1.86 (m, 1 H), 1.73-1.55 (m, 4 H), 1.58 (s, 3 H), 1.52-1.33 (m, 4 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 218.81, 149.23, 128.78, 127.26, 109.65, 59.43, 56.59, 45.62, 40.25, 33.81, 27.06, 24.55, 22.41, 21.88, 20.44; MS m/z (M^+) calcd 216.1514, obsd 216.1499.

For 27: pale yellow oil; Ir (C_6D_6, cm^{-1}) 1679; ^1H NMR (300 MHz, C_6D_6) δ 5.71-5.58 (m, 2 H), 4.86 (s, 1 H), 4.81-4.80 (m, 1 H), 3.25-2.88 (m, 1 H), 2.67-2.39 (m, 3 H), 2.37-2.27 (m, 2 H), 2.11-1.80 (series of m, 4 H), 1.71 (s, 3 H), 1.68-1.50 (m, 3 H) - see also Table IV; MS m/z (M^+) calcd 216.1514, obsd 216.1469.

Anionic Rearrangement of 16. A solution of 16 (170 mg, 0.675 mmol) in 3 mL of anhydrous tetrahydrofuran was blanketed with nitrogen, treated dropwise with potassium hexamethyldisilazide (0.81 mmol) in the same solvent, and stirred at room temperature for 45 min. Workup in the predescribed manner was followed by MPLC on Florisil (elution with 20% ethyl acetate in petroleum ether). There was isolated 61 mg (36%) of 28b and 69 mg (40%) of 28a. Both compounds proved to be very unstable to storage. The stereochemical assignments are tentative.

For the minor, less polar component: IR (neat, cm^{-1}) 2988, 2943, 2908, 2832, 1726, 1638, 1463; ^1H NMR (300 MHz, C_6D_6) δ 5.89 (ddd, J = 17.4, 10.6, 7.6 Hz, 1 H), 5.79 (d, J =

6.3 Hz, 1 H), 5.77 (d, J = 7.5 Hz, 1 H), 4.97 (dd, J = 10.1, 0.7 Hz, 1 H), 4.96 (dd, J = 17.3, 0.7 Hz, 1 H), 3.37 (d, J = 3.2 Hz, 1 H), 3.21 (s, 3 H), 3.06-2.96 (m, 1 H), 2.99 (s, 3 H), 2.96 (s, 3 H), 2.65-2.58 (m, 2 H), 2.48-2.34 (m, 2 H); ^{13}C NMR (75 MHz, C_6D_6) ppm 207.20, 138.50, 137.52, 131.35, 116.51, 112.14, 83.79, 58.12, 49.49, 49.44, 48.50, 44.37, 44.24, 36.50; MS m/z (M^+) calcd 252.1362, obsd 252.1373.

For the major, more polar component: IR (neat, cm^{-1}) 2976, 2944, 2834, 1724, 1640, 1460; ^{1}H NMR (300 MHz, C_6D_6) δ 5.84 (dd, J = 6.1, 1.4 Hz, 1 H), 5.77 (d, J = 6.2 Hz, 1 H), 5.49 (ddd, J = 17.3, 10.4, 7.0 Hz, 1 H), 5.01 (dd, J = 10.7, 1.6 Hz, 1 H), 4.96 (dd, J = 17.3, 1.5 Hz, 1 H), 3.36 (s, 3 H), 3.09-2.83 (m, 2 H), 2.98 (s, 3 H), 2.97 (s, 3 H), 2.42-2.38 (m, 3 H), 2.18 (dd, J = 15.3, 6.5 Hz, 1 H); ^{13}C NMR (20 MHz, C_6D_6) ppm 207.42, 138.25, 137.72, 131.05, 116.74, 111.89, 83.64, 58.40, 49.59, 49.47 (2C), 46.49, 44.10, 37.40; MS m/z (M^+) calcd 252.1362, obsd 252.1359.

Anionic Rearrangement of 17. Exposure of 17 (91 mg, 0.330 mmol) with potassium hexamethyldisilazide (0.396 mmol) in anhydrous tetrahydrofuran under nitrogen for 30 min at room temperature was followed by the usual processing to give an oil. Purification by MPLC on Florisil (elution with 10% ethyl acetate in petroleum ether) gave 55 mg (60%) of 30 as a 2:1 mixture of isomers. The unstable pale yellow oil partially solidified on standing in the freezer: IR (neat, cm^{-1}) 3074, 2944, 2834, 1704, 1635, 1454; ^{1}H NMR (300 MHz, C_6D_6) δ 5.94-5.65 (m, 2 H), 4.83-4.73 (m, 2 H), 3.20-2.95 (m, 6 H), 2.88-2.39 (series of m, 3 H), 2.32-2.19 (m, 1 H), 1.95-1.86 (m, 1 H), 1.78-1.27 (series of m, 9 H); MS m/z calcd 276.1726, obsd 276.1714.

Supplementary Material. Tables of fractional coordinates, thermal parameters, and observed and calculated structure factors for 13 (6 pages). These crystallographic data have been deposited at the Cambridge Crystallographic Data Centre.

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