Intramolecular Nucleophilic Addition to Unsaturated Carbon. Dependence of Cyclization Efficiency on the Method of Carbon–Carbon Bond Cleavage Utilized To Generate the Reactive Species

Leo A. Paquette,* John P. Gilday, and George D. Maynard

Evans Chemical Laboratories, The Ohio State University, Columbus, Ohio 43210

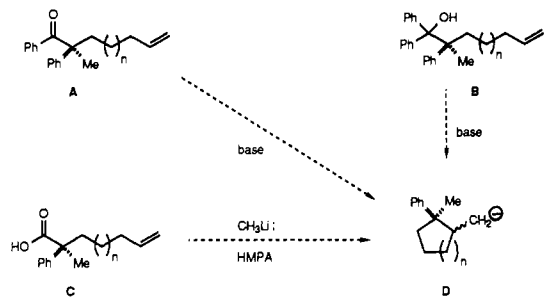
Received April 19, 1989

The following three reactions have been studied for the purpose of comparing their intrinsic ability to generate carbanionic intermediates capable of intramolecular cyclization: (a) the Haller–Bauer cleavage of ketones **15a** and **15b**, as well as the (*S*)-(+)-antipode of **15a** (viz. **47**); (b) the base-promoted cleavage of 1,1-diarylcarbinols **16a** and **16b**; (c) decarboxylative elimination within the methyllithium adducts of carboxylic acids **17a** and **17b**. The Haller–Bauer process proceeds predominantly via carbanion intermediates, which most often experience protonation to give **18** and **21**. Cyclization becomes possible, however, under certain circumstances and reaches a maximum of 33% with $NaNH_2$ in benzene. Using (+)-**47** as a probe, it has been possible to ascertain that 56% of the reactive intermediate molecules racemize and that only the racemic species generates cyclic product. On the other hand, the Cram-type cleavages of **16a** and **16b** proceed mainly by homolytic cleavage to generate the benzophenone radical anion and free-radical intermediate. The latter dimerize, capture solvent, and abstract hydrogen to varying degrees depending upon counterion and solvent. Finally, reactions of type c are the most efficient at effecting intramolecular ring closure.

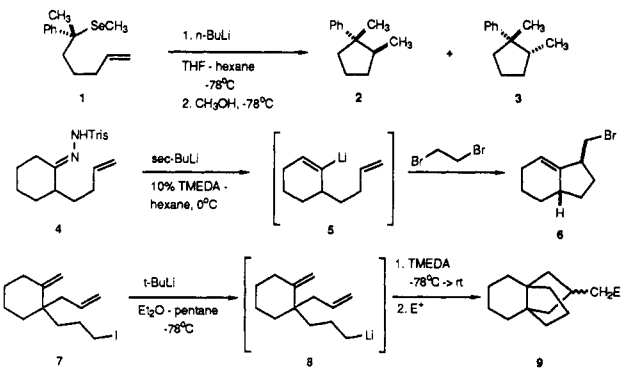
Although ring-forming reactions mediated by the attack of cationic[1] and radical centers[2] on tethered double bonds have played an increasingly dominant role in synthetic methodology, the utilization of carbanions in comparable circumstances has languished despite several important potential advantages. Interesting intramolecular cyclizations of organometallic reagents (M = Li, Mg, Al) have been reported.[3a] However, concern over mechanistic detail[4] has often beclouded the latent synthetic capability of these processes. The finding that alkyllithium intermediates rarely undergo cyclization onto 1,2-disubstituted alkenes (contrast the ease of organomagnesium ring closures under these circumstances[3b]) could be regarded as mitigating against serviceability. On the other hand, carbanionic cyclizations make possible the direct functionalization of initially formed cyclic products by ensuing reaction with suitable electrophiles,[5] a feat not generally found feasible when radical intermediates are involved.[6]

Three recent developments are considered by us to demonstrate the inherent desirability of exploring further

Scheme I



the area of anionic cyclization. Krief and Barbeaux have shown that treatment of the methylseleno compound **1**



with *n*-butyllithium in a tetrahydrofuran–hexane solvent system at −78 °C results in rapid transmetalation and ring closure.[7] Quenching with cold methanol after 30 min provided in 85% yield a mixture of **2** and **3** in which the cis isomer predominates heavily (98:2). Chamberlin and co-workers uncovered at about the same time that the Shapiro degradation of trisylhydrazones typified by **4** gives rise to vinyllithium intermediates, e.g., **5**, which undergo intramolecular addition to the double bond with formation of lithiated alkylidenecyclopentanes that can be trapped with electrophiles.[5] Notably, this reaction is also highly cis stereoselective, the production of **6** (81%) being representative. More recently, Bailey and Rossi have dem-

(1) (a) Johnson, W. S. *Bioorg. Chem.* **1976**, *5*, 51. (b) Sutherland, J. K. *Chem. Soc. Rev.* **1980**, 265. (c) van Tamelen, E. E. *Acc. Chem. Res.* **1975**, *8*, 152. (d) Speckamp, N. *Recl.: J. R. Neth. Chem. Soc.* **1981**, *100*, 345.

(2) (a) Julia, M. *Rec. Chem. Progr.* **1964**, *25*, 3. (b) Nonhebel, D. C.; Walton, J. *Free Radical Chemistry*; Cambridge University Press: Cambridge, 1974; Chapter 14. (c) Hart, D. J. *Science* **1984**, *223*, 883. (d) Giese, B. *Radicals in Organic Synthesis*; Pergamon: New York, 1986. (e) Neumann, W. P. *Synthesis* **1987**, 665. (f) Curran, D. P. *Ibid.* **1988**, 417, 489.

(3) (a) For an extensive compilation of literature citations, consult: Hill, E. A. *J. Organomet. Chem.* **1975**, *91*, 123, and ref 5. (b) For example: Kossa, W. G.; Rees, T. C., Jr.; Richey, H. G., Jr. *Tetrahedron Lett.* **1971**, 3455. Hill, E. A.; Thiessen, R. J.; Doughty, A.; Miller, R. *J. Org. Chem.* **1969**, *34*, 3681.

(4) For example: (a) Last, L. A.; Fretz, E. R.; Coates, R. M. *J. Org. Chem.* **1982**, *47*, 3211. (b) Bailey, W. F.; Patricia, J. J.; Delgobbo, V. C.; Jarret, R. M.; Okarma, P. J. *Ibid.* **1985**, *50*, 1999. (c) Ross, G. A.; Koppang, M. D.; Bartak, D. E.; Woolsey, N. F. *J. Am. Chem. Soc.* **1985**, *107*, 6742. (d) Bailey, W. F.; Nurmi, T. T.; Patricia, J. J.; Wang, W. *Ibid.* **1987**, *109*, 2442. (e) Ashby, E. C.; Phem, T. N.; Park, B. *Tetrahedron Lett.* **1985**, *26*, 4691. (f) Ashby, E. C.; Phem, T. N. *J. Org. Chem.* **1987**, *52*, 1291. (g) Newcomb, M.; Kaplan, J. *Tetrahedron Lett.* **1988**, *29*, 3449.

(5) (a) Chamberlin, A. R.; Bloom, S. H. *Tetrahedron Lett.* **1986**, *27*, 551. (b) Chamberlin, A. R.; Bloom, S. H.; Cervini, L. A.; Fotsch, C. H. *J. Am. Chem. Soc.* **1988**, *110*, 4788.

(6) A major expection is atom-transfer cycloaddition: (a) Curran, D. P.; Kim, D. *Tetrahedron Lett.* **1986**, *27*, 5821. (b) Curran, D. P.; Chen, M.-H.; Kim, D. *J. Am. Chem. Soc.* **1986**, *108*, 2489. (c) Curran, D. P.; Chen, M.-H. *Ibid.* **1987**, *109*, 6558.

(7) Krief, A.; Barbeaux, P. *J. Chem. Soc., Chem. Commun.* **1987**, 1214.

0022-3263/89/1954-5044$01.50/0

Table I. Haller–Bauer Results Involving 15a

base	solvent	rel yield by GC analysis,[a] % 18	2	3	19	20	combined yield, %
KO-*t*-Bu	*t*-BuOH, Δ	>99.5					94[b]
KO-*t*-Bu	C_6H_6, Δ	>99.5					82[b]
NaO-*t*-Bu	*t*-BuOH, Δ	>99.5					89[b]
KNH_2	C_6H_6, Δ	59	4	0.5	36.5		89[b]
$NaNH_2$	C_6H_6, Δ	62	15	18		5[a]	47[c]
$LiNH_2$	C_6H_6, Δ	99	(1% combined)				51[c]
$NaNH_2$	THF, Δ	41	10	1	48		91[b]

[a] Based on use of *n*-undecane as internal standard. [b] As determined by GC analysis. [c] An isolated by preparative GC.

onstrated the feasibility of extending this chemistry to sequential polyolefinic cyclization.[8] Thus, the generation of 8 provides for 2-fold anionic ring closure and subsequent electrophilic capture to give functionalized tricyclic compounds such as **9**.

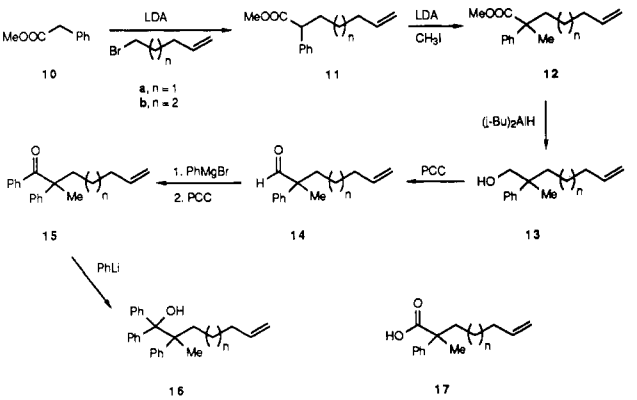
Definition of the Approach. The studies that have been made of anionic cyclization have raised questions concerning possible interrelationships between C–C bond-forming efficiency, the method of carbanion generation, and the nature of the metal involved. Since the phenomenon of carbanion generation has not been examined systematically, we have undertaken a survey of three methods for heterolytic carbon–carbon bond cleavage with regard to their intrinsic ability to produce reactive anionic intermediates capable of intramolecular nucleophilic addition across a tethered olefinic center (Scheme I).

The first of these involves Haller–Bauer cleavage[9] of non-enolizable ketones A (Scheme I). Our extensive investigation of this fascinating reaction involving optically active substrates has disclosed that high levels of asymmetric protonation (with retention of configuration) are the norm.[10] Global chirality is preserved because the carbanion intermediates are produced within a solvent cage such that proton delivery from the departing byproduct molecule takes place on the front face prior to any mutual rotation. How strict are these limitations? May carbanions generated in this manner engage in anionic cyclization and do so with preservation of the absolute configuration of the original seat of reaction?

The stereochemistry of the base-promoted cleavage of 1,1-diphenylcarbinols has been investigated by Cram.[11] The steric course of this particular reaction was found to correlate with solvent dielectric constant[11a] as does the Haller–Bauer process. However, higher temperatures are usually required, and transient color formation often develops, suggesting that homolytic cleavage may compete effectively with carbanion generation or at the extreme be the dominant pathway.[11d] Of course, radical cleavage would lead only to racemic products. Some distinctions between A and B as starting materials are therefore already apparent.

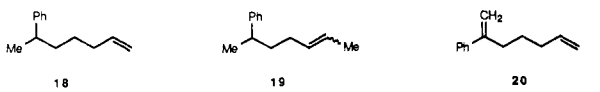
We have recently demonstrated that methyllithium addition to carboxylic acids carrying stabilizing substituents at the α position can, if performed in highly coordinating solvents, result in ready fragmentation of the intermediate dialkoxide with carbanion generation.[12] The process is particularly efficient if the initial 1,2-addition is performed in ethereal solution, with subsequent introduction of HMPA to effect ion-pair dissociation and substantial enhancement of oxyanionic reactivity. The conditions utilized for advancing to the requisite carbanion from C (Scheme I) are therefore adequately different from those associated with the cleavage reactions of A and B as to warrant direct comparison of their capacity for cyclizing to D.

Scheme II



Preparation of Racemic Starting Materials. Condensation of the lithium enolate of methyl phenylacetate (**10**) with 4-bromo-1-pentene in tetrahydrofuran solution containing HMPA produced ester **11a** in 80% yield. The alkylative route to **11b** involving 6-iodo-1-hexene[13] could be achieved with equivalent efficiency in the absence of polar aprotic solvation (Scheme II). Methylation of both ester enolates under standard conditions introduced the required quaternary center (88–94%). It proved more expedient to transform **12a** and **12b** into their alcohols and then to oxidize **13a,b** with PCC than to proceed directly to aldehydes **14a,b** by controlled reduction of these esters. Conversion to the benzoyl compounds **15a,b** and the tertiary carbinols **16a,b** was realized by conventional means. Carboxylic acids **17a,b** were prepared by saponification of esters **12a,b**.

Haller–Bauer Reactions. Ketone **15a** was heated at the reflux temperature with a series of base/solvent combinations as summarized in Table I. The reactions performed with potassium or sodium *tert*-butoxide in *tert*-butyl alcohol or benzene were found to afford the cleavage product **18** exclusively and in high yield. In those instances



(8) Bailey, W. F.; Rossi, K. *J. Am. Chem. Soc.* **1989**, *111*, 765.
(9) Hamlin, K. E.; Weston, A. A. *Org. React.* **1957**, *9*, 1. (b) Kaiser, E. M.; Warner, C. D. *Synthesis* **1975**, 395.
(10) (a) Paquette, L. A.; Uchida, T.; Gallucci, J. C. *J. Am. Chem. Soc.* **1984**, *106*, 335. (b) Paquette, L. A.; Gilday, J. P.; Ra, C. S. *Ibid.* **1987**, *109*, 6858. (c) Paquette, L. A.; Gilday, J. P.; Ra, C. S.; Hoppe, M. *J. Org. Chem.* **1988**, *53*, 704. (d) Paquette, L. A.; Gilday, J. P. *Ibid.* **1988**, *53*, 4972. (e) Paquette, L. A.; Ra, C. S. *Ibid.* **1988**, *53*, 4978. (f) Gilday, J. P.; Gallucci, J. C.; Paquette, L. A. *Ibid.* **1989**, *54*, 1399. (g) Paquette, L. A.; Maynard, G. D.; Ra, C. S.; Hoppe, M. *Ibid.* **1989**, *54*, 1408.
(11) (a) Cram, D. J.; Langemann, A.; Allinger, J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 5740. (b) Cram, D. J.; Langemann, A.; Hauck, F. *Ibid.* **1959**, *81*, 5750. (c) Cram, D. J.; Kopecky, K. R.; Hauck, F.; Langemann, A. *Ibid.* **1959**, *81*, 5754. (d) Cram, D. J.; Langemann, A.; Lwowski, W.; Kopecky, K. R. *Ibid.* **1959**, *81*, 5760, and later papers in this series.
(12) Gilday, J. P.; Paquette, L. A. *Tetrahedron Lett.* **1988**, *29*, 4505.
(13) Ashby, E. C.; Oswald, J. *J. Org. Chem.* **1988**, *53*, 6068.

Table II. Haller–Bauer Results Involving 15b

base	solvent	rel yield by GC analysis, % 21	22	23	other[a]	combined yield, %
KO-*t*-Bu	C_6H_6, Δ	>99.5				35[b]
KO-*t*-Bu	*t*-BuOH, Δ	>99.5				64,[b] 95[c]
NaO-*t*-Bu	C_6H_6, Δ	>99.5				89[c]
NaO-*t*-Bu	*t*-BuOH, Δ	>99.5				92[c]
KNH_2	C_6H_6, Δ	90	10			88[c]
$NaNH_2$	C_6H_6, Δ	85	6	3	6	85[c]
$LiNH_2$	C_6H_6, Δ	>99.5				76[c]
$NaNH_2$	THF, Δ	80	18		2	89[c]

[a] Combination of several minor unidentified products. [b] Isolated by preparative GC. [c] Yield calculated by GC based on use of *n*-undecane as internal standard.

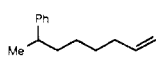
where preparative GC isolation was undertaken, actual product yields in the 50–55% range were realized on small scale. When the same ketone was treated with the amide bases in hot benzene or tetrahydrofuran, the formation of more than one product could be detected by GC analysis.

These heterogeneous reactions, in fact, offered quite a diversity of product compositions. In the case of lithium amide/benzene, **18** continued to dominate heavily (99%), although trace amounts of the cyclopentanes **2** and **3** were now clearly in evidence. The structures of these minor components were assigned on the strength of suitable ^1H NMR and GC/MS comparisons relative to those of authentic samples provided by Professor Krief.[7]

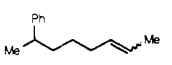
Cleavage of **15a** with potassium amide/benzene produced **18** (59%), **2** (4%), and **3** (0.5%), as well as a fourth hydrocarbon (36.5%) that was isomeric to the other three. Relevantly, resubmission of **18** to the original reaction conditions resulted in >90% conversion to this compound after 90 h, thereby allowing for its convenient isolation and complete characterization. In actuality, **19** is a mixture of geometric isomers resulting from internalization of the double bond in **18**. Presumably, the KNH_2 is capable of effecting deprotonation of the terminal olefin with generation of the allylic anion, the latter subsequently undergoing protonation with thermodynamically more favorable positioning of the π bond.

The reactions with sodium amide provided equally complex mixtures. When this Haller–Bauer cleavage was carried out in benzene, cyclopentanes **2** and **3** were formed in significant amounts (15% and 18%, respectively) alongside **18** (62%). Although **19** was now not seen, the "dehydro" product **20** was detected to the extent of 5%. It proved an easy matter to establish the structure of **20** by ^1H NMR and GC/MS analysis, as well as by direct analogy to **23** as derived from the octenone series (see below). The change in solvent from benzene to tetrahydrofuran had several consequences. Not only was the consumption of **15a** notably accelerated, but the amount of cyclized product was reduced approximately 4-fold (Table I). Furthermore, the isomerization from **18** to **19** resurfaced, to the greatest extent noted at any time. The actual scenario is therefore one where 89% of the cleavage of **15a** occurs without intramolecular cyclization.

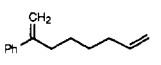
A second series of Haller–Bauer reactions involving ketone **15b** was implemented analogously. A similar reactivity pattern was noted with **21** and **22** arising as the



21



22



23

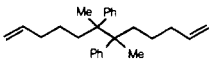
major products (Table II). As expected, cyclization was now severely curtailed because of the kinetically less attractive ring-size requirements. Also, the "dehydro" product **23** was observed in only one experiment. This exocyclic methylene compound was independently prepared by alkylation[14a] of the anion of acetophenone dimethylhydrazone[14b] with 5-bromo-1-pentene, followed by periodate oxidation[14a] and methylenation with the Lombardo reagent.[14c]

Table III. Volatile Products from the Base-Promoted Cleavage of 16a[a]

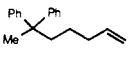
base	solvent	yield by GC analysis,[b] % 18	20	25
KO-*t*-Bu	C_6H_6, Δ	27	2	1
KNH_2	C_6H_6, Δ	28	1	3
$NaNH_2$	C_6H_6, Δ	2	3	1
$LiNH_2$	C_6H_6, Δ	2	8	
KO-*t*-Bu	*t*-BuOH, Δ	16		
$NaNH_2$	*t*-BuOH, Δ	3	8	
$LiNH_2$	*t*-BuOH, Δ	2	6	

[a] Yields of dimer **24** ranged from 50–75% isolated after chromatography. [b] Based on use of *n*-undecane as internal standard.

Cram-Type Cleavages. In the first series of experiments, **16a** was heated as its sodium, lithium, or potassium salt in refluxing benzene or *tert*-butyl alcohol (Table III). Although **18** and **20** did make their appearance, these hydrocarbons were invariably isolated only in quite low yields. This is because of the concomitant formation of dimer **24** to the extent of 50–75% depending on the precise



24



25

reaction conditions. This dimer was not conveniently observed by gas chromatography and shows no significant molecular ion under FABMS conditions due to ready fragmentation. Once separated by standard column chromatographic techniques, however, its ^1H NMR spectrum compares closely to that of **18** except for the absence of a benzylic proton absorption and the appearance of the methyl peaks as a pair of singlets instead of a doublet. These spectral features support the expectation that **24** be obtained as a meso/*dl* diastereomeric mixture.

Two particularly significant observations remain to be addressed. First, no evidence was found under any set of circumstances for cyclization leading to either **2** or **3**. Second, when these cleavages were performed with KNH_2 in benzene under the standard conditions, hydrocarbon **25**, the result of solvent capture, was formed in modest amounts. An increase in the relative amount of KNH_2 from 15 to 46 equiv induced a substantial enhancement in the level of phenylation products (7% of **25** and 11%

(14) (a) Corey, E. J.; Enders, D.; Bock, M. G. *Tetrahedron Lett.* **1976**, 7. (b) Newkome, G. R.; Fishel, D. L. *J. Org. Chem.* **1966**, *31*, 677. (c) Lombardo, L. *Tetrahedron Lett.* **1982**, *23*, 4293.

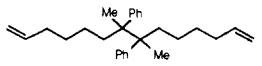
Table IV. Volatile Products from the Base-Promoted Cleavage of 16b[a]

base	solvent	yield by GC analysis,[b] % 21	23	27
KO-*t*-Bu	C_6H_6, Δ	29		2
KNH_2	C_6H_6, Δ	31		16
$NaNH_2$	C_6H_6, Δ	9	2	1
$LiNH_2$	C_6H_6, Δ	<1	<1	
KO-*t*-Bu	*t*-BuOH, Δ	24		
$NaNH_2$	*t*-BuOH, Δ	9	2	
$LiNH_2$	*t*-BuOH, Δ	<1	<1	

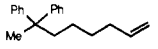
[a] Yields of dimer **26** ranged from 50 to 85% isolated after chromatography. [b] Based on use of *n*-undecane as internal standard.

of its internal double-bond isomers) within the total reaction mixture.

Entirely similar trends were realized with **16b** (Table IV). As before, cyclization was not observed, dimerization to give **26** was rampant, and the phenylated product **27** arose when recourse was made to KNH_2 in benzene. In the latter experiment, an impressive 18% yield of **27** was realized.



26



27

Decarboxylative Anion Generation. In a first series of experiments, carboxylic acids **17a** and **17b** were individually treated with 5 equiv of methyllithium in ether and directly hydrolyzed. In line with expectation,[12] ketones **29a** and **29b** were formed exclusively (Schemes III and IV). Repetition of these reactions, but with addition of HMPA preceding the aqueous quench, caused the solutions to become deep red in color and yielded no methyl ketones. Instead, **17a** was converted predominantly into the stereoisomeric cyclopentanes **2** and **3** (ratio 1:3, 71% combined yield) and 6-phenyl-1-heptene (**18**, 22%).

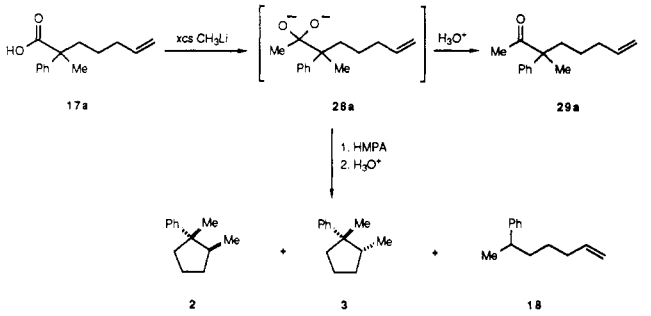
The presence of an additional methylene carbon as in **17b** did not deter the strong tendency for cyclization. Thus, the breakdown of intermediate **28b** under the same conditions gave rise to **30** and **31** (79%, 2.8:1 mixture, relative stereochemistry unknown) and to **21** (13%).

Accordingly, the decarboxylative route to carbanion generation is particularly well suited to the realization of intramolecular cyclization.

Synthesis of Optically Active 15a. The results of our studies involving racemic **15a** were considered of sufficient interest to warrant the preparation of this ketone in an optically active condition. In this way, information would be gained about the global asymmetry of various intermediates as they proceed down diverse reaction channels to the products. As always, conclusions relating to the stereochemical course of the Haller–Bauer cleavage are strictly dependent on the reliable prior determination of absolute configuration in both the starting material and end products.

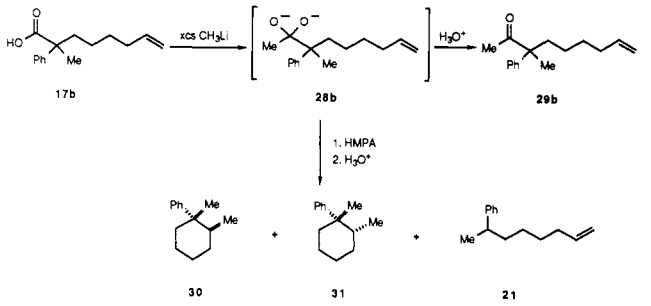
Initial efforts focused on achieving suitable levels of diastereocontrol in the alkylation of menthyl ester **32** with 5-iodo-1-pentene,[10d,f] as well as accomplishing chromatographic separation of oxazolidinone diastereomers **35** and **36**.[15] While the formation of esters **33** and **34** proceeds in reasonable yield (83%), only 8% de could be realized under the best kinetically controlled conditions developed. Furthermore, attempts to accomplish MPLC enrichment of the less polar diastereomer beyond the 32% de level were unsuccessful. This less than optimal situation caused us to look at **35** and **36**.[15] Here again, however, the two

Scheme III



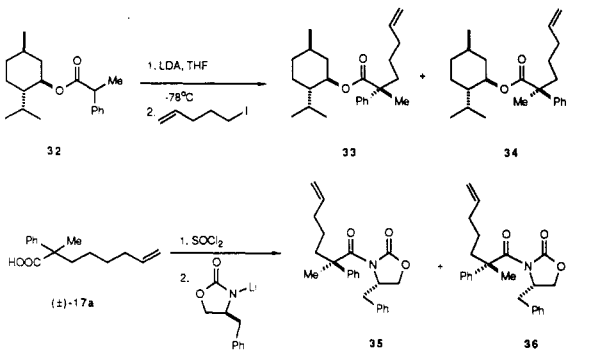
17a 28a 29a 2 3 18

Scheme IV



17b 28b 29b 30 31 21

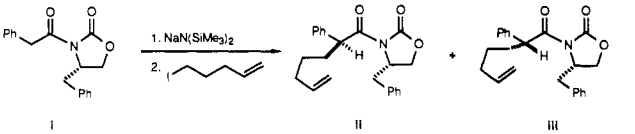
diastereomers are not readily separated, the desired diastereomer enrichment never exceeding 20%. The combination of a quaternary center and relatively long flexible side chain are seemingly contributory to precluding synthetic routes that require diastereomer separation.



32 33 34 35 36

The chiral ketone **38**[18] was consequently examined as a potential alternative source of **15a** (Scheme V). Racemic 2-phenylcyclohexanone (**37**) was prepared in two steps according to Newman and Farbman.[19] The presence of the α-phenyl substituent was not per se sufficient to guarantee enolate anion formation in the desired direction

(15) Alkylation of oxazolidinone i with 5-iodo-1-pentene in the presence of sodium hexamethyldisilazide gives product (ii and iii) with quite



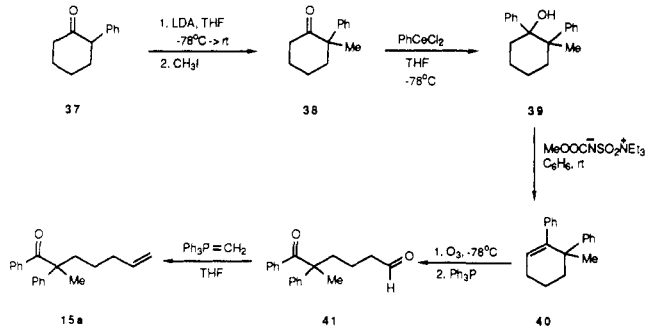
i ii iii

good diastereoselectivity (89:11 ratio, 78% de),[16] although in modest yield. Furthermore, it proved an easy matter to completely separate these diastereomers by MPLC. Subsequent attempts to methylate ii and iii resulted largely in production of the free oxazolidinone as a consequence of enolate fragmentation with ketene formation. It has been noted previously that alkylation of such enolates does not occur below 0 °C.[17]

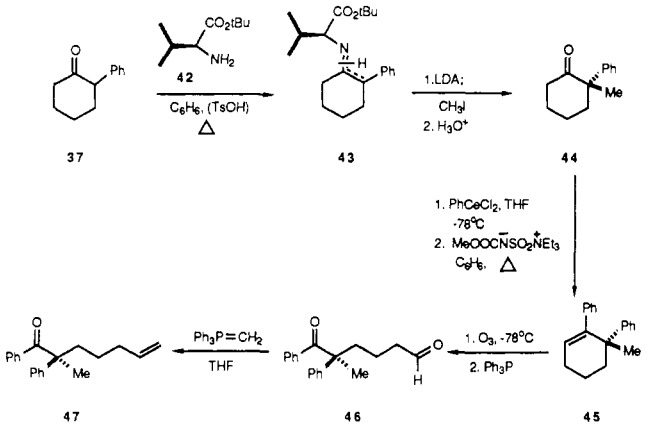
(16) Evans, D. A.; Britton, T. C.; Dorow, R. L.; Dellaria, J. F. *J. Am. Chem. Soc.* **1986**, *106*, 6395.

(17) Evans, D. A. *Aldrichimica Acta* **1982**, *15*, 23.

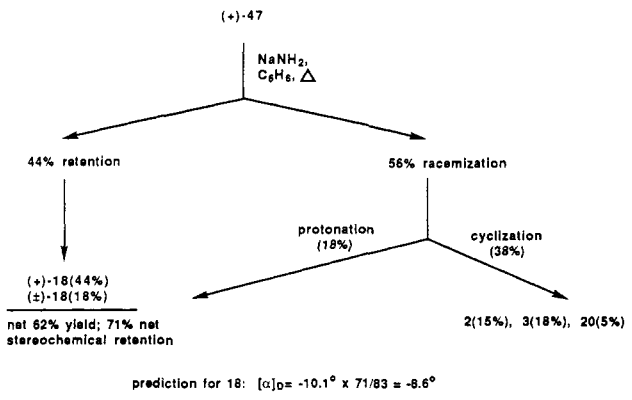
Scheme V



Scheme VI



Scheme VII



under standard conditions (LDA or KHMDS, THF, −78 °C). Instead, quenching with methyl iodide produced 2-methyl-6-phenylcyclohexanone in >85% yield. However, the proper regioselectivity was realized by treating **37** with lithium diisopropylamide in tetrahydrofuran at −78 °C and then allowing the solution to warm to room temperature during 3 h prior to methyl iodide addition (87% of **38**).

Several possible routes to **15a** from **38** were next given attention. The most efficient pathway involved the conversion of **38** to tertiary carbinol **39** by reaction with dichlorophenylcerium(III) and dehydration to styrene **40** with Burgess reagent[20] (91% overall). Ozonolysis of **40** with a triphenylphosphine workup gave keto aldehyde **41** in variable yields (58–87%). Wittig methylenation of **41** provided **15a**, spectroscopically identical in every detail with material prepared earlier.

Armed with these results, we next proceeded to condense *tert*-butyl-L-valine (**42**) with **37** according to Hashimoto and Koga[18] (Scheme VI). Condensation of the lithium salt of **43** with iodomethane and subsequent citric acid hydrolysis produced (*S*)-(−)-ketone **44**. The extensive chromatographic purification demanded by this reaction is reflected in the 40% yield. More attractive was its optical purity, which varied from 87 to 90% ee in three runs.[21] Substitution of *tert*-butyl-*tert*-leucine enhanced the level of stereoinduction to 96%. Optically active **44** was found to be unstable to prolonged storage, even at 0 °C. It was therefore directly transformed into (*S*)-(+)-**47** as before.

Haller–Bauer Studies Involving (*S*)-(+)-47. The first cleavage reactions of (*S*)-(+)-**47** were carried out with potassium *tert*-butoxide in benzene and in *tert*-butyl alcohol. The $[\alpha]^{22}_D$ values for (−)-**18** isolated in 50–55% yield under these circumstances were determined to be −11.6° and −10.1°, respectively. These values were highly consistent over several runs. If the stereochemical profile so universally observed for the latter base–solvent system, i.e., 83% net retention,[10b-g] is applied to the present example, the resulting prediction would be that the levorotatory hydrocarbon product should possess the *R* configuration and, when optically pure, exhibit an $[\alpha]_D$ value in chloroform closely approximating −13.9° (±1°).

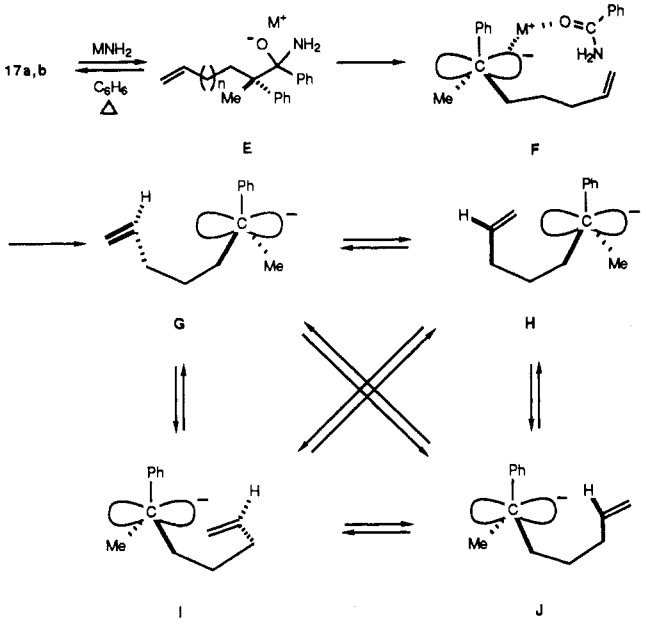
Acyclic optically active benzylic ketones are comparably cleaved by sodium amide in hot benzene with 44% net retention.[10b-g] If the preceding extrapolation is reliable, we would anticipate the cleavage of (+)-**47** under these conditions to provide samples of **18** that exhibit an $[\alpha]_D$ value closely approaching −10.1° × 0.44/0.83 or −5.4°. In actuality, the $NaNH_2$-promoted cleavages gave GC-purified samples of **18** showing $[\alpha]^{22}_D$ −8.4°, clearly indicating them to be more optically enriched than predicted according to existing guidelines. In actuality, this most salient finding signals the onset of mechanistic behavior that convincingly distinguishes (+)-**47** from the norm.

It is first important to recognize specifically that sodium amide–benzene routinely promotes cleavage such that 44% retention and 56% racemization materializes in the debenzoylated product.[10b-g] If we now assume that the cyclized products, **2**, **3**, and **20** (see Table I) all derive from that reactive species that would otherwise lead to racemic **18**, the accountability tree shown in Scheme VII can be constructed. The net *predicted* consequences of this bifurcation are that **18** cannot be formed in relative amounts exceeding 62% and that a heightened proportion (44/62 × 100 or 71%) of this hydrocarbon rather than the customary 44% would result from the stereochemical retention pathway. Stated differently, competitive cyclization by way of only one (the racemic option) and not both of two reactive intermediates raises the expected $[\alpha]_D$ of **18** to −8.6°, a value very close to the experimentally determined optical rotation (average of three runs).

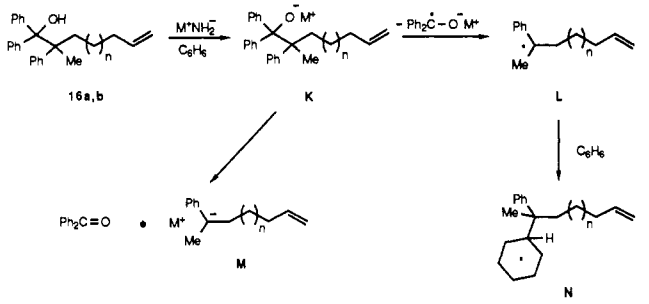
Additional support for the operation of independent pathways comes from two additional sources. In the Haller–Bauer cleavages of (+)-**47** conducted with $LiNH_2$ in benzene, the $[\alpha]_D$ of the isolated samples of **18** was −7.9°, within reasonable proximity of the −7.1° value based on the anticipated 56–60% net retention customarily noted in such cleavages.[10b-g] Also, mixtures of cyclopentanes **2** and **3** isolated from selected $NaNH_2$-promoted reactions showed virtually no capability for rotating plane-polarized light. The observed values fall in the range bracketed by 0–0.2°. Since the $[\alpha]_D$'s reported for pure (*S*)-(+)-**2** and (*S*)-(+)-**3** are +26.4 (*n*-hexane) and 79.2° (*n*-hexane), re-

(18) Hashimoto, S.; Koga, K. *Tetrahedron Lett.* **1978**, 573.
(19) Newman, M. S.; Farbman, M. D. *J. Am. Chem. Soc.* **1944**, *66*, 1550.
(20) Burgess, E. M.; Penton, H. R.; Taylor, E. A. *J. Org. Chem.* **1973**, *38*, 26.
(21) These values were arrived at simply by comparing the $[\alpha]_D$ values in cyclohexane solvent to literature values. The estimated $[\alpha]_D$ for optically pure **38** is −163°.

Scheme VIII



Scheme IX



spectively,[22] residual optical activity, if present at all, must indeed be quite minimal.

Discussion

Reactive intermediates at tertiary benzylic centers have been generated by C–C bond cleavage under three different sets of conditions, and the outcome in each instance is distinctive and mechanistically diagnostic. For example, the Haller–Bauer cleavage of ketones **15a** and **15b** serves as the most efficient means for arriving at **18** and **21**, respectively. This is particularly true when recourse is made to KO-*t*-Bu in *t*-BuOH, which conditions deliver the acyclic hydrocarbon in good yield and a high state of purity. Although the point has not been proven experimentally, it is reasonable to assume that optical retention is followed with (*R*)-(−)-**18** stemming from (*S*)-(+)-**47**.[10] Cleavage with KO-*t*-Bu in benzene also occurs efficiently. The proton source for this reaction is presumably provided by more than one constituent of the mixture, as was demonstrated elsewhere.[10e]

Performing the reaction with amide bases in benzene provides for more intricate developments. Consistent with all available facts is initial 1,2-addition by amide ion to give E, which presumably fragments to provide the coordinated benzylic carbanion F (Scheme VIII).[10] Most often, F experiences protonation. When the proton transfer is mediated by the departing benzamide molecule prior to any mutual rotation, retention of configuration is seen since the global environment in which F finds itself is chiral and still related to **15** in absolute configuration.[10] Conditions particularly conducive to providing added lifetime to the carbanion center in F should allow for intramolecular cyclization. This end result is seen to be most highly favored when M^+ is the sodium counterion. The potassium species, in contrast, is too highly reactive and short-lived, with the result that solvent molecules are unable to move rapidly enough out of the reaction zone required to realize C–C bonding. Conversely, the lithium species may be too highly coordinated to oxygen as in F to engage in interaction with the double bond. Central between these extremes, the sodium ion has a reactivity level appropriate to allow cyclization to **2** and **3** in moderate yield. However, the activation barriers most cerntainly associated with this intramolecular capture of the tethered double bond should be adequately high to require full disengagement of the benzamide molecule from the carbanion vicinity as in G.[10g] This event will surely be accompanied by loss of stereocontrol during generation of the new stereogenic center (compare G and H), as well as indiscriminate capture of the carbanion from either of its surfaces (viz., G–J). The expectation, therefore, is that the rapid interconversion of these intermediates should guarantee that any ensuing products will be racemic. This conclusion is fully supported by the experimental observations.

The sodium amide reaction, when performed in tetrahydrofuran rather than benzene, shows appreciably less tendency to proceed into ring closure. This phenomenon can be attributed to several causes. The sodium benzyl is more reactive in tetrahydrofuran due to enhanced coordination of the metal ion by solvent. Consequently, protonation becomes more favorable and increasingly prevalent. Tetrahydrofuran is also a more acidic solvent, such that there is a higher concentration of proton source. Furthermore, its ethereal nature should act to loosen the level of coordination in E and F (Scheme VIII).

The response of (*S*)-(+)-**47** indicates that the special solvational features of the Haller–Bauer reaction as represented in F are shed approximately 56% of the time when M^+ is sodium. Once this happens, ring formation ensues twice as fast as direct capture of the racemic acyclic intermediate. Cyclopentanes **2** and **3** are the anticipated products of either carbanionic or free radical closure reactions. Given the chemical genesis of G–J, it is likely that the anionic pathway dominates. However, it is not totally exclusive since low levels of **20** are formed concomitantly. This diene presumably arises by disproportionation of the free-radical precursor. Analogous arguments can be formulated to account for the small amount of **23** that stems from **15b** when it is heated with sodium amide in benzene.

The results of the Cram-type cleavages involving **16a** and **16b** strongly suggest that thermolysis of oxyanions K produces largely the benzophenone radical anion and the unpaired electron species L. These intermediates could arise either by electron transfer from M to the proximal benzophenone in the solvent cage or by direct homolytic cleavage (Scheme IX). When M^+ is potassium, greater amounts of **18** and **21** are seen since the higher reactivity (lower association) of this counterion allows for greater "leakage" into the carbanion manifold where M is formed and subsequently protonated. Noteworthily, radical L generated by this means dimerizes exclusively at its benzylic position, such that no cyclic hydrocarbons are produced. When generated in benzene, L is sufficiently reactive to capture solvent as in N. These observations constitute added evidence that cyclization during the Haller–Bauer reaction occurs predominantly via an anionic pathway.

(22) Brugidou, J.; Christol, H.; Fabre, J. M.; Giral, L.; Sales, R. *Bull. Chim. Soc. Fr.* **1974**, *12*, 2906.

Finally, decarboxylative anion generation involving **17a** and **17b** provides the most efficient means for realizing cyclization. Therefore, intermediate lithium anions M ($M^+ = Li^+$) generated by this process appear to possess the appropriate lifetime and reactivity to facilitate cyclization. Although HMPA is known to enhance electron transfer where feasible,[23] no acceptor molecules are present in these solutions, and the capture of electrophiles when introduced[12] proceeds smoothly and efficiently.

Experimental Section[24]

Methyl 2-Phenyl-6-heptenoate (11a). Methyl phenylacetate (6.76 g, 45.0 mmol) in dry tetrahydrofuran (20 mL) was added dropwise to a solution of lithium diisopropylamide (50.0 mmol) in the same solvent (100 mL) at −78 °C. After 45 min at this temperature, 1-bromo-4-pentene (6.5 mL) in tetrahydrofuran (10 mL) was added dropwise, followed by HMPA (5 mL). The reaction mixture was allowed to warm to room temperature overnight, diluted with 1:1 ether–petroleum ether (300 mL), washed with ammonium chloride solution and brine, and dried. Solvent evaporation left a yellow oil, chromatography of which on silica gel (elution with 2% ethyl acetate in petroleum ether) gave an almost colorless oil that was further purified by Kugelrohr distillation. There was obtained 7.86 g (80%) of **11a** as a colorless oil: bp 135–140 °C (0.8 Torr); IR (neat, cm^{-1}) 3060, 3030, 2950, 2855, 1732, 1635, 1490, 1450, 1430; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.22 (m, 5 H), 5.82–5.69 (m, 1 H), 5.02–4.91 (m, 2 H), 3.65 (s, 3 H), 3.54 (t, J = 7.7 Hz, 1 H), 2.12–2.03 (m, 3 H), 1.82–1.72 (m, 1 H), 1.41–1.28 (m, 2 H); MS, m/z (M^+) calcd 218.1307, obsd 218.1323.

Methyl 2-Methyl-2-phenyl-6-heptenoate (12a). A solution of **11a** (7.81 g, 35.8 mmol) in dry tetrahydrofuran (20 mL) was added dropwise to a cold (−78 °C), magnetically stirred solution of lithium diisopropylamide (44.8 mmol) in the same solvent (100 mL) during 10 min. After 1 h at this temperature, methyl iodide (11.4 g, 80 mmol) in tetrahydrofuran (10 mL) was introduced dropwise. The reaction mixture was allowed to warm to room temperature during 2 h, diluted with 1:1 ether–petroleum ether (300 mL), and washed with ammonium chloride solution and brine prior to drying. Solvent evaporation was followed by filtration through silica gel (elution with 5% ethyl acetate in petroleum ether) and Kugelrohr distillation (135 °C (0.5 Torr)). There was obtained 7.32 g (88%) of **12b** as a colorless oil: IR (neat, cm^{-1}) 3060, 2970, 2945, 2860, 1726, 1635, 1495, 1455, 1445, 1435; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.20 (m, 5 H), 5.81–5.69 (m, 1 H), 5.02–4.92 (m, 2 H), 3.65 (s, 3 H), 2.09–1.86 (m, 4 H), 1.55 (s, 3 H), 1.33–1.21 (m, 2 H); MS, m/z (M^+) calcd 232.1463, obsd 232.1472. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.70; H, 8.81.

2-Methyl-2-phenylhept-6-en-1-ol (13a). A cold (0 °C), magnetically stirred solution of **12a** (6.72 g, 28.9 mmol) in dichloromethane (50 mL) was treated dropwise with DIBAL-H (65 mL of 1 M in hexanes, 65 mmol) over 30 min. After an additional 2 h at 0 °C, methanol (5 mL) was introduced followed by ether (50 mL) and saturated sodium potassium tartrate solution (50 mL), and the mixture was allowed to warm to room temperature overnight. The ethereal layer was separated, washed with ammonium chloride solution (2 × 50 mL) and brine (2 × 50 mL), dried, and filtered through silica gel. Evaporation of the solvent and Kugelrohr distillation of the residue (140–145 °C (0.3 Torr)) gave **13a** as a viscous colorless oil (5.61 g, 95%): IR (neat, cm^{-1}) 3400, 3060, 2970, 2930, 2865, 1638, 1495, 1455; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.18 (m, 5 H), 5.79–5.66 (m, 1 H), 4.98–4.89 (m, 2 H), 3.70 (dd, J = 10.8, 5.4 Hz, 1 H), 3.53 (dd, J = 10.8, 7.8 Hz, 1 H), 2.02–1.05 (m, 2 H) (hydroxyl proton not observed); MS, m/z (M^+) calcd 204.1514, obsd 204.1527.

2-Methyl-2-phenyl-6-heptenal (14a). To a solution of **13a** (2.15 g, 10.5 mmol) in cold (0 °C) dichloromethane (50 mL) were added pyridinium chlorochromate (3.5 g, 16.2 mmol) and ground 3-Å molecular sieves (3.5 g). The dark brown slurry was stirred at 0 °C for 40 min, diluted with ether (100 mL), filtered through Celite, and concentrated to a volume of approximately 20 mL. Filtration of this solution through silica gel (elution with 5% ethyl acetate in petroleum ether) gave a colorless oil that was further purified by chromatography on silica gel (elution with 3% ethyl acetate in petroleum ether) and Kugelrohr distillation (125 °C (0.5 Torr)). There was isolated 1.69 g (80%) of **14a** as a colorless liquid: IR (neat, cm^{-1}) 2975, 2960, 2865, 1720, 1635, 1492, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 9.50 (s, 1 H), 7.35 (t, J = 7.2 Hz, 2 H), 7.31–7.19 (m, 3 H), 5.80–5.66 (m, 1 H), 5.00–4.91 (m, 2 H), 2.07–1.54 (m, 4 H), 1.45 (s, 3 H), 1.31–1.14 (m, 2 H); MS, m/z (M^+ − CHO) calcd 173.1330, obsd 173.1330. Anal. Calcd for $C_{14}H_{18}O$: C, 83.12; H, 8.96. Found: C, 83.03; H, 9.11.

1,2-Diphenyl-2-methyl-6-hepten-1-one (15a). A cold (−78 °C) solution of **14a** (1.32 g, 6.5 mmol) in anhydrous ether (60 mL) was treated with phenylmagnesium bromide (3.0 mL of 3.0 M in ether, 9.0 mmol), and stirring was continued for 10 min. Ammonium chloride solution (3 mL) was added, and the reaction mixture was allowed to warm to room temperature. The ethereal layer was separated, washed with brine, dried, and evaporated. The resulting yellow oil was dissolved in dichloromethane (80 mL), cooled to 0 °C, and treated with pyridinium chlorochromate (3.5 g, 16.2 mmol) and ground 3-Å molecular sieves (3.5 g). The mixture was stirred at 0 °C for 1.5 h, filtered through silica gel, and evaporated. Silica gel chromatography of the yellow oil (elution with 2% ethyl acetate in petroleum ether) followed by Kugelrohr distillation (195–200 °C (0.2 Torr)) gave **15a** as a colorless oil (1.13 g, 62%): IR (neat, cm^{-1}) 3060, 2970, 2940, 2860, 1673, 1596, 1495, 1460, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.17 (m, 10 H), 5.72–5.69 (m, 1 H), 4.94–4.85 (m, 2 H), 2.16–1.94 (m, 4 H), 1.57 (s, 3 H), 1.28–1.14 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) 203.12, 144.23, 138.07, 136.82, 131.21, 129.18, 128.68, 127.66, 126.56, 126.02, 114.43, 54.44, 39.01, 33.94, 24.10, 23.40 ppm; MS, m/z (M^+) calcd 278.1670, obsd 278.1661. Anal. Calcd for $C_{20}H_{22}O$: C, 86.29, H, 7.97. Found: C, 85.90; H, 8.14.

2-Methyl-1,1,2-triphenyl-6-hepten-1-ol (16a). A cold (−78 °C), magnetically stirred solution of **15a** (341 mg, 1.22 mmol) in anhydrous ether (20 mL) was treated with phenyllithium (1.5 mL of 2.0 M in cyclohexane–ether, 3.0 mmol) and stirred at this temperature for 1 h. Aqueous citric acid (5%, 10 mL) was added, and the mixture was allowed to warm to room temperature during 1 h. The organic phase was separated, washed with sodium bicarbonate and brine solutions, and dried prior to evaporation. The residue was chromatographed on silica gel (elution with 2% ethyl acetate in petroleum ether) to give **16a** (410 mg, 94%) as an extremely viscous colorless oil: IR (neat, cm^{-1}) 3540, 3040, 3010, 2940, 1635, 1600, 1490, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42–7.39 (m, 4 H), 7.23–7.16 (m, 9 H), 6.98–6.95 (m, 2 H), 5.70–5.59 (m, 1 H), 4.92–4.84 (series of m, 2 H), 2.47 (s, 1 H), 2.28–2.18 (m, 1 H), 1.99–1.90 (m, 3 H), 1.49 (s, 3 H), 1.26–1.13 (m, 1 H), 0.88–0.77 (m, 1 H); MS, the molecular ion was too transient for high-resolution measurement.

2-Methyl-2-phenyl-6-heptenoic Acid (17a). A solution of **12a** (22.01 g, 94.7 mmol) in methanol (150 mL) was treated with potassium hydroxide pellets (16.3 g, 0.29 mol) and heated at reflux for 6 h. Approximately 65% of the methanol was removed on a rotary evaporator. Water (500 mL) was added, and the aqueous solution was extracted with ether, acidified with hydrochloric acid, and reextracted with dichloromethane (3 × 25 mL). The latter extracts were combined, dried, and evaporated to give **17a** (19.46 g, 94%) as a colorless solid, mp 49 °C (from petroleum ether); ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.21 (m, 5 H), 5.75 (ddt, J = 16.9, 10.3, 6.7 Hz, 1 H), 5.02–4.91 (m, 2 H), 2.09–1.89 (m, 4 H), 1.57 (s, 3 H), 1.41–1.20 (m, 2 H) (hydroxyl proton not seen); ^{13}C NMR (75 MHz, $CDCl_3$) 182.39, 142.91, 138.33, 128.39, 126.88, 126.17, 114.75, 49.99, 38.55, 34.06, 23.98, 22.36 ppm; MS, m/z (M^+) calcd 218.1306, obsd 218.1312. Anal. Calcd for $C_{14}H_{18}O_2$: C, 77.03; H, 8.31. Found: C, 76.96; H, 8.34.

Methyl 2-Phenyl-7-octenoate (11b). Methyl phenylacetate (6.01 g, 40.0 mmol) was alkylated with 6-iodo-1-hexene (9.24 g, 44.0 mmol) in the manner described for **10a** with the exception that the HMPA was omitted. The crude yellow oil was purified by sequential silica gel chromatography (elution with 2% ethyl acetate in petroleum ether) and Kugelrohr distillation (160–165 °C (0.7 Torr)). There was isolated 7.6 g (82%) of **11b** as a colorless

(23) Panek, E. J. *J. Am. Chem. Soc.* **1975**, *97*, 2341.

(24) The purity of all title compounds was judged to be ≥95% by GC, TLC, and $^1H/^{13}C$ NMR spectral determinations.

oil: IR (neat, cm^{-1}) 3065, 3030, 2930, 2860, 1734, 1640, 1495, 1455, 1435; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.22 (m, 5 H), 5.83–5.69 (m, 1 H), 5.00–4.89 (m, 2 H), 3.64 (s, 3 H), 3.53 (t, J = 7.7 Hz, 1 H), 2.24–1.97 (m, 3 H), 1.83–1.71 (m, 1 H), 1.45–1.22 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) 174.44, 139.26, 138.65, 128.54, 127.87, 127.13, 114.37, 51.82, 51.63, 33.45, 33.40, 28.63, 27.03 ppm; MS, m/z (M^+) calcd 232.1463, obsd 232.1450.

Methyl 2-Methyl-2-phenyl-7-octenoate (12b). Methylation of **11b** (7.28 g, 31.3 mmol) with methyl iodide (8.0 g, 56 mmol) as described for **12a** afforded 7.26 g (94%) of **12b** as a colorless oil after silica gel chromatography (elution with 1.5% ethyl acetate in petroleum ether) and bulb-to-bulb distillation (135–140 °C (0.3 Torr)): IR (neat, cm^{-1}) 3060, 2970, 2940, 2860, 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.19 (m, 5 H), 5.76 (ddt, J = 17.0, 10.2, 6.6 Hz, 1 H), 5.00–4.90 (m, 2 H), 3.64 (s, 3 H), 2.10–1.99 (m, 3 H), 1.96–1.85 (m, 1 H), 1.54 (s, 3 H), 1.44–1.32 (m, 2 H), 1.27–1.14 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 176.69, 144.02, 138.71, 128.30, 126.57, 125.91, 114.31, 51.96, 50.32, 39.08, 33.48, 29.35, 24.19, 22.83 ppm; MS, m/z (M^+) calcd 246.1620, obsd 246.1622. Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.09; H, 9.06.

2-Methyl-2-phenyl-7-octen-1-ol (13b). A 3.81 g (15.5 mmol) sample of **12b** was reduced with DIBAL-H (36 mmol) as before to give 3.26 g (96%) of **13b** as a colorless oil after Kugelrohr distillation (155–160 °C (0.8 Torr)): IR (neat, cm^{-1}) 3620–3140 (br), 2980, 2935, 2865, 1495, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.29 (m, 4 H), 7.25–7.16 (m, 1 H), 5.74 (ddt, J = 17.0, 10.2, 6.6 Hz, 1 H), 4.98–4.87 (series of m, 2 H), 3.70 (d, J = 10.8 Hz, 1 H), 3.52 (d, J = 10.8 Hz, 1 H), 1.98 (q, J = 7 Hz, 2 H), 1.76 (td, J = 13, 4.5 Hz, 1 H), 1.52 (td, J = 13, 4.5 Hz, 1 H), 1.34 (s, 3 H) (hydroxyl proton not seen); ^{13}C NMR (75 MHz, $CDCl_3$) 144.84, 138.84, 128.34, 126.64, 126.02, 114.18, 72.53, 43.38, 38.31, 33.54, 29.58, 23.25, 21.49 ppm; MS, m/z (M^+) calcd 218.1670, obsd 218.1694.

2-Methyl-2-phenyl-7-octenal (14b). Alcohol **13b** (3.13 g, 14.3 mmol) was oxidized with pyridinium chlorochromate (4.6 g, 21.3 mmol) in the presence of powdered 3-Å molecular sieves (4.5 g) in the manner reported for **14a**. The identical workup provided 2.20 g (71%) of **14b** as a colorless oil: bp 155–165 °C (0.9 Torr); IR (neat, cm^{-1}) 2980, 2940, 2865, 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 9.49 (s, 1 H), 7.40–7.22 (m, 5 H), 5.74 (ddt, J = 17.0, 10.3, 6.7 Hz, 1 H), 4.99–4.88 (series of m, 2 H), 2.04–1.79 (m, 4 H), 1.44 (s, 3 H), 1.40–1.30 (m, 2 H), 1.27–1.04 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) 202.22, 140.33, 138.52, 128.74, 127.03 (2C), 114.39, 53.87, 35.84, 33.40, 29.38, 23.44, 18.94 ppm; MS, m/z (M^+) calcd 216.1514, obsd 216.1497. Anal. Calcd for $C_{15}H_{20}O$: C, 83.29; H, 9.32. Found: C, 83.16; H, 9.38.

1,2-Diphenyl-2-methyl-7-octen-1-one (15b). Aldehyde **14b** (2.04 g, 9.4 mmol) was dissolved in anhydrous ether (50 mL), cooled to −78 °C, and treated with 15 mmol of phenyllithium as before. Direct oxidation of the alcohol so produced with pyridinium chlorochromate (2.7 g, 12.5 mmol) in the presence of pulverized 3-Å molecular sieves (4.5 g) in the predescribed manner delivered 2.07 g (75%) of **15b** after silica gel chromatography (elution with 1.5% ethyl acetate in petroleum ether) and Kugelrohr distillation (200–210 °C (0.7 Torr)): IR (neat, cm^{-1}) 3065, 2980, 2940, 2765, 1675, 1600, 1448; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.17 (m, 10 H), 5.70 (ddt, J = 17.0, 10.3, 6.7 Hz, 1 H), 4.93–4.84 (series of m, 2 H), 2.16–1.90 (m, 4 H), 1.56 (s, 3 H), 1.36–1.05 (m, 4 H); ^{13}C NMR (20 MHz, $CDCl_3$) 203.63, 144.50, 138.68, 137.10, 131.38, 129.34, 128.84, 127.83, 126.71, 126.24, 114.25, 54.74, 39.40, 33.35, 29.43, 24.32, 23.64 ppm; MS, m/z ($M^+ - C_6H_5CO$) calcd 187.1487, obsd 187.1482. Anal. Calcd for $C_{21}H_{24}O$: C, 86.26; H, 8.27. Found: C, 86.18; H, 8.30.

2-Methyl-1,1,2-triphenyl-7-octen-1-ol (16b). In the same way as above, ketone **15b** (641 mg, 2.19 mmol) was treated with phenyllithium (5.0 mmol) to give **16b** as a very viscous colorless oil (782 mg, 96%) following purification by silica gel chromatography (elution with 1.5% ethyl acetate in petroleum ether): IR (neat, cm^{-1}) 3550, 3050, 3010, 2940, 2920, 1640, 1600, 1495, 1455; ^1H NMR (300 MHz, $CDCl_3$) δ 7.42–7.39 (m, 4 H), 7.26–7.12 (m, 9 H), 6.99–6.96 (m, 2 H), 5.69 (ddt, J = 17.0, 10.2, 6.6 Hz, 1 H), 4.92–4.82 (series of m, 2 H), 2.47 (s, 1 H), 2.21 (td, J = 12.9, 3.5 Hz, 1 H), 1.97–1.87 (m, 3 H), 1.49 (s, 3 H), 1.34–1.23 (m, 2 H), 1.18–1.05 (m, 1 H), 0.76–0.70 (m, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) 145.15, 144.68, 143.30, 138.95, 129.70, 128.65, 128.24, 127.08 (2 C), 127.00, 126.66, 126.54, 126.16, 114.07, 82.75, 51.15, 36.72, 33.62, 29.77, 23.93, 21.92 ppm; MS, the molecular ion was too transient for high-resolution measurement.

2-Methyl-2-phenyl-7-octenoic Acid (17b). Ester **12b** (460 mg, 1.87 mmol) was heated with potassium hydroxide (2.12 g, 24 mmol) in methanol (25 mL) in the predescribed manner. Following the identical workup, **17b** was purified by bulb-to-bulb distillation (220–225 °C (0.7 Torr)) and isolated as a colorless oil (380 mg, 88%): IR (neat, cm^{-1}) 3500–2300 (br), 1690, 1635; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.30 (m, 4 H), 7.27–7.22 (m, 1 H), 5.76 (ddt, J = 17.0, 10.2, 6.7 Hz, 1 H), 5.00–4.88 (m, 2 H), 2.09–1.88 (m, 4 H), 1.57 (s, 3 H), 1.46–1.13 (m, 4 H) (hydroxyl proton not seen); MS, m/z (M^+) calcd 232.1463, obsd 232.1470. Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.25; H, 8.76.

General Procedure for the Cleavage Reactions of Ketones 15 and Carbinols 16. The substrate (0.06–0.2 mmol) was dissolved in the appropriate dry solvent (3–6 mL). An accurately weighed amount (ca. 10 mg) of *n*-undecane, the internal standard, was added to those reaction mixtures that were to be monitored by capillary GC. The base (~15 equiv for potassium bases, 30 equiv for sodium bases, and 45 equiv for lithium bases) was next introduced, and the mixture was heated to reflux.

For analytical runs, the progress of reaction was monitored periodically by means of GC. A small portion was removed and quenched with saturated ammonium chloride solution. Several drops of pentane were added, the mixture was shaken, and a sample of the organic phase was subjected to capillary GC analysis.

For preparative runs, the reaction was allowed to proceed until the starting material had been consumed (TLC analysis). The excess residual base was quenched with saturated ammonium chloride solution, and the products were extracted into pentane. The combined organic phases were washed with brine, dried, and concentrated by careful distillation of the solvent through a Vigreux column at atmospheric pressure. The residual oils were purified by preparative GC (100–120 °C, 12 ft × 0.25 in. 5% SE-30 on Chromosorb W) to yield the product hydrocarbons (see below for spectral properties).

For the cleavage of **15a** with sodium amide, the preceding procedure was followed except that the residue after concentration was purified by MPLC on silica gel (elution with petroleum ether) to separate the cyclopentanes **2** and **3** (first eluted) from **18**. The acyclic hydrocarbon was purified by preparative GC as before. The **2**/**3** mixture was partially separated under analogous conditions, and their spectra were identical with those of authentic samples.[7]

6-Phenyl-1-heptene (18): IR ($CHCl_3$, cm^{-1}) 3070, 3000, 2960, 2925, 2855, 1635, 1602, 1493, 1450; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.14 (m, 5 H), 5.82–5.71 (m, 1 H), 4.99–4.88 (series of m, 2 H), 2.67 (sextet, J = 7.0 Hz, 1 H), 2.05–1.97 (m, 2 H), 1.67–1.18 (m, 4 H), 1.23 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 147.70, 138.91, 128.25, 126.95, 125.77, 114.28, 39.86, 37.87, 33.84, 27.03, 22.29 ppm; MS, m/z (M^+) calcd 174.1408, obsd 174.1423.

***cis*-1,2-Dimethyl-1-phenylcyclopentane (2):** ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.35 (m, 2 H), 7.31–7.22 (m, 2 H), 7.18–7.13 (m, 1 H), 2.22–2.16 (m, 1 H), 2.00–1.91 (m, 2 H), 1.76–1.68 (m, 3 H), 1.46–1.41 (m, 1 H), 1.16 (s, 3 H), 0.87 (d, J = 6.7 Hz, 3 H); GC MS, m/z (M^+) calcd 174, obsd 174.

***trans*-1,2-Dimethyl-1-phenylcyclopentane (3):** ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.21 (m, 4 H), 7.18–7.12 (m, 1 H), 2.23–2.16 (m, 1 H), 2.05–1.95 (m, 2 H), 1.88–1.70 (m, 3 H), 1.52–1.33 (m, 1 H), 1.28 (s, 3 H), 0.57 (d, J = 6.9 Hz, 3 H); GC MS, m/z (M^+) calcd 174, obsd 174.

6,6-Diphenyl-1-heptene (25): ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.06 (m, 10 H), 5.83–5.68 (m, 1 H), 504–4.87 (m, 2 H), 2.25–1.97 (series of m, 4 H), 1.66 (s, 3 H), 1.30–1.11 (m, 2 H); MS, m/z (M^+) calcd 250.1722, obsd 250.1701.

7-Phenyl-1-octene (21): IR (neat, cm^{-1}) 3080, 3060, 3030, 2960, 2915, 2850, 1640, 1490, 1455; ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.14 (m, 5 H), 5.77 (ddt, J = 17.0, 10.2, 6.7 Hz, 1 H), 4.99–4.88 (series of m, 2 H), 2.67 (hextuplet, J = 7.0 Hz, 1 H), 2.03–1.96 (m, 2 H), 1.64–1.50 (m, 2 H), 1.43–1.12 (m, 4 H), 1.23 (d, J = 7.0 Hz, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 147.91, 139.02, 128.29, 126.97, 125.79, 114.13, 39.93, 38.28, 33.68, 29.07, 27.22, 22.29 ppm; MS, m/z (M^+) calcd 188.1565, obsd 188.1596. Anal. Calcd for $C_{14}H_{20}$: C, 89.29; H, 10.71. Found: C, 89.37; H, 10.69.

2-Phenyl-1,6-heptadiene (20): ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.10 (m, 5 H), 5.91–5.72 (m, 1 H), 5.27 (br s, 1 H), 5.07 (br

s, 1 H), 5.05–4.90 (m, 2 H), 2.45–2.30 (m, 4 H), 1.75–1.27 (m, 2 H); MS, m/z (M^+) calcd 172.1252, obsd 172.1249.

2-Methyl-2-phenylmethylenecyclohexane: IR (neat, cm^{-1}) 3080, 3065, 3020, 2930, 2855, 1638, 1600, 1490, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.33–7.28 (m, 4 H), 7.22–7.13 (m, 1 H), 4.98 (br s, 1 H), 4.91 (br s, 1 H), 2.48–2.43 (m, 1 H), 2.22–2.17 (m, 1 H), 2.00–1.91 (m, 1 H), 1.70–1.30 (series of m, 5 H), 1.27 (s, 3 H); MS, m/z (M^+) calcd 186.1408, obsd 186.1412.

7,7-Diphenyl-1-octene (27): ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.09 (m, 10 H), 5.85–5.67 (m, 1 H), 5.05–4.84 (m, 2 H), 2.19–1.93 (series of m, 4 H), 1.63 (s, 3 H), 1.49–1.03 (series of m, 4 H); MS, m/z (M^+) calcd 264.1878, obsd 264.1922.

Isolation of the Dimers. A. 6,7-Dimethyl-6,7-diphenyldodeca-1,11-diene (24). Alcohol **16a** (38.3 mg, 0.107 mmol) was treated with lithium amide (0.05 g, ca. 20 equiv) in *tert*-butyl alcohol (5 mL) as before. The mixture was heated at reflux for 12 h, allowed to cool, and quenched with ammonium chloride solution. The products were extracted into pentane, and the combined organic layers were washed with water and brine prior to drying. Following solvent evaporation, the residue was subjected to silica gel chromatography (elution with 0.5% ether in petroleum ether) gave 13.9 mg of a colorless oil enriched in **24**. The ^1H NMR spectrum (300 MHz, $CDCl_3$) displayed the following peaks consistent with the structural assignment: δ 7.37–7.10 (m, 4 H), 6.95–6.88 (m, 1 H), 5.73–5.67 (m, 1 H), 4.94–4.84 (series of m, 2 H), 2.11–1.95 (m, 2 H), 1.72–0.86 (series of m), 1.27 (s), 1.23 (s); many other minor peaks were also present. MS (FAB), m/z 327 (1.5%).

B. 7,8-Dimethyl-7,8-diphenyltetradeca-1,13-diene (26). Similar treatment of **16b** (64.2 mg, 0.173 mmol) with lithium amide (0.12 g, 5.2 mmol) in *tert*-butyl alcohol (6 mL) gave, after chromatography, a mixture of hydrocarbons (24.8 mg) enriched in **26**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–6.89 (series of m, 5 H), 5.78–5.65 (m, 1 H), 5.98–4.84 (m, 2 H), 2.15–1.90 (m, 3 H), 1.68–0.81 (series of m, 5 H), and singlets at 1.32, 1.30, 1.26, and 1.22 (total area, 6 H).

Base-Promoted Isomerizations of Terminal Olefins. A small quantity (~20 mg) of hydrocarbon **18** or **20** was subjected to the conditions of the Haller–Bauer reaction with potassium amide. After the usual workup, the isolated material exhibited those spectral properties anticipated for **19** and **22**, respectively. The purity levels were 80–85%.

19: ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.12 (m, 5 H), 5.45–5.32 (m, 2 H), 2.78–2.65 (m, 1 H), 2.06–1.82 (m, 2 H), 1.70–1.51 (m, 5 H), 1.34–1.21 (series of m); GC MS, m/z calcd 174, obsd 174.

22: ^1H NMR (300 MHz, $CDCl_3$) δ 7.30–7.14 (m, 5 H), 5.40–5.35 (m, 5 H), 1.38–1.18 (m, 5 H); GC MS, m/z calcd 188, obsd 188.

Independent Preparation of 2-Phenyl-1,7-octadiene (23). A solution of acetophenone *N,N*-dimethylhydrazone (2.00 g, 12.3 mmol) in dry tetrahydrofuran (3 mL) was added dropwise under argon to cold (−78 °C), magnetically stirred *n*-butyllithium in hexanes (9.75 mL of 1.4 M solution, 13.6 mmol). After 30 min, the anion solution was warmed to −40 °C and treated dropwise with 5-bromo-1-pentene (2.03 g, 13.6 mmol) dissolved in tetrahydrofuran (3 mL). The reaction mixture was allowed to warm slowly to room temperature during 3.5 h and poured into a 3:1 water/dichloromethane mixture. The organic phase was washed twice with water, dried, and evaporated. Bulb-to-bulb distillation at 125–150 °C (0.1 Torr) gave the alkylation product as a pale yellow oil (2.79 g, 98%): IR (neat, cm^{-1}) 3080, 3060, 2980, 2945, 2930, 2850, 2820, 2775, 1640, 1600, 1468, 1445, 1320, 1025, 965, 915, 768, 700; ^1H NMR (300 MHz, $CDCl_3$) δ 7.70–7.21 (series of m, 5 H), 5.87–5.70 (m, 1 H), 5.05–4.82 (m, 2 H), 3.00–2.79 (m, 2 H), 2.55 (s, 6 H), 2.15–1.92 (m, 2 H), 1.59–1.32 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) 168.65, 138.54, 137.99, 129.13, 128.27, 126.97, 114.46, 47.80, 33.31, 28.92, 28.41, 26.57 ppm; MS, m/z (M^+) calcd 230.1783, obsd 230.1759.

To a stirred solution of the alkylation product (2.74 g, 11.9 mmol) in methanol (180 mL) and pH 7 phosphate buffer (36 mL) was added a solution of sodium periodate (5.60 g, 26.2 mmol) in water (60 mL). After 19 h, an additional 4 equiv of sodium periodate was introduced, and the solution was warmed to 40 °C for 3 h. The mixture was filtered, diluted with water, and extracted twice with dichloromethane. The combined organic phases were washed with water (2×), dried, and concentrated. Purification of the residue was achieved by bulb-to-bulb distillation at 140–160 °C (0.1 Torr) to give 1.91 g (85%) of the ketone: IR (neat, cm^{-1}) 3080, 3065, 2940, 2860, 1640, 1600, 1450, 1225, 993, 912, 755, 695; ^1H NMR (300 MHz, $CDCl_3$) δ 8.01–7.90 (m, 2 H), 7.62–7.35 (m, 3 H), 5.89–5.67 (m, 1 H), 5.07–4.87 (m, 2 H), 3.02–2.91 (m, 2 H), 2.17–2.04 (m, 2 H), 1.85–1.70 (m, 2 H), 1.60–1.42 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 200.21, 138.47, 137.03, 132.83, 128.50, 127.98, 114.59, 38.37, 33.56, 28.57, 23.80 ppm; MS, m/z (M^+) calcd 188.1201, obsd 188.1203.

A magnetically stirred solution of the preceding ketone (500 mg, 2.66 mmol) in dichloromethane (25 mL) was blanketed with argon, treated with Lombardo's reagent (ca. 3 equiv), and stirred for 3 h at room temperature. The mixture was poured into dichloromethane (100 mL) and saturated sodium bicarbonate solution (200 mL) and stirred for 1 h. The separated organic phase was washed with water (2 × 50 mL), dried, and carefully evaporated in the cold to give 447 mg (90%) of diene, which was pure by TLC and capillary GC. A sample for combustion analysis was prepared by preparative GC (1.5 m × 0.25 in. 5% SE-30 on Chromosorb W, 135 °C); IR (neat, cm^{-1}) 3080, 3060, 3020, 2940, 2860, 1640, 1600, 1595, 1447, 1065, 992, 906, 780, 705; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.16 (m, 5 H), 5.88–5.67 (m, 1 H), 5.25 (d, J = 1.5 Hz, 1 H), 5.04 (d, J = 1.4 Hz, 1 H), 5.07–4.89 (m, 2 H), 2.55–2.43 (m, 2 H), 2.10–1.95 (m, 2 H), 1.61–1.30 (m, 4 H); ^{13}C NMR (75 MHz, $CDCl_3$) 149.54, 141.38, 138.88, 128.19, 127.22, 126.08, 114.28, 112.10, 35.19, 33.56, 28.59, 27.73 ppm; MS, m/z ($M^+ - C_2H_4$) calcd 158.1095, obsd 158.1094. Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 89.86; H, 9.68.

3-Methyl-3-phenyl-7-octen-2-one (29a). Carboxylic acid **17a** (131 mg, 0.60 mmol) was dissolved in anhydrous ether (6 mL), cooled to −5 °C, treated with the methyllithium–lithium bromide complex (2.5 mL of 1.5 M in ether, 3.75 mmol), and allowed to warm to room temperature during 1.5 h. The reaction mixture was cooled to 0 °C, quenched with dilute hydrochloric acid, and extracted with pentane. The combined organic phases were washed with sodium bicarbonate solution, water, and brine before drying and solvent evaporation. Chromatography of the residue on silica gel (elution with 1.5% ethyl acetate in petroleum ether gave **29a** as a colorless oil (72 mg, 55%): IR (neat, cm^{-1}) 3070, 2985, 2950, 2870, 1709, 1640, 1495, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.20 (m, 5 H), 5.74 (ddt, J = 17.0, 10.3, 6.7 Hz, 3 H), 5.01–4.91 (series of m, 2 H), 2.10–1.85 (m, 4 H), 1.89 (s, 3 H), 1.47 (s, 3 H), 1.27–1.10 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) 210.40, 143.17, 138.29, 128.62, 126.78, 126.31, 114.66, 55.83, 36.90, 34.13, 25.71, 23.73, 21.36 ppm; MS, m/z (M^+) calcd 216.1514, obsd 216.1538.

3-Methyl-3-phenyl-8-nonen-2-one (29b). Acid **17b** (140 mg, 0.603 mmol) was treated with methyllithium (3.75 mmol) as described above to give **29b** as a colorless oil (79 mg, 57%): IR (neat, cm^{-1}) 3060, 2970, 2935, 2860, 1705, 1640, 1495, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.36–7.13 (m, 5 H), 5.75 (ddt, J = 17.0, 10.2, 6.7 Hz, 1 H), 4.98–4.88 (series of m, 2 H), 2.10–1.84 (m, 4 H), 1.89 (s, 3 H), 1.46 (s, 3 H), 1.43–1.33 (m, 2 H), 1.14–1.06 (m, 2 H); ^{13}C NMR (20 MHz, $CDCl_3$) 210.50, 143.26, 138.64, 128.64, 126.73, 126.33, 114.33, 55.92, 37.25, 33.43, 29.52, 25.72, 23.81, 21.42 ppm; MS, m/z (M^+) calcd 230.1671, obsd 230.1690.

Decarboxylative Anion Generation. A. Cleavage of 17a. Acid **17a** (157 mg, 0.719 mmol) was dissolved in ether (20 mL), treated with methyllithium (7 mL of 1.5 M solution, 10.5 mmol), and stirred at room temperature for 12 h. HMPA (6 mL) was added, and the red solution was maintained at room temperature for 4 h, quenched with 5% citric acid, and extracted with pentane. The combined organic layers were washed with water and brine, dried, and evaporated to leave a yellow oil. Purification by MPLC (silica gel, elution with petroleum ether) gave the cyclopentanes **2** and **3** as a 1:3 mixture of isomers (88.7 mg, 71%) and the straight-chain alkene **18** (27.5 mg, 22%).

B. Cleavage of 17b. Similar treatment of **17b** (48.1 mg, 0.207 mmol) provided a 2.8:1 mixture of **30/31** (30.9 mg, 79%) as well as **21** (5.1 mg, 13%).

30/31: ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.13 (m, 5 H), 2.06–1.92 (m, 2 H), 1.79–1.25 (series of m, 7 H), 1.33 (s, minor isomer, 0.25 × 3 H), 1.25 (s, major isomer, 0.75 × 3 H), 0.61 (d, J = 7.1 Hz, minor isomer, 0.25 × 3 H), 0.58 (d, J = 6.7 Hz, major isomer, 0.75 × 3 H); MS, m/z (M^+) calcd 188.1564, obsd 188.1557.

2-Methyl-2-phenylcyclohexanone (38).[19] A solution of **37** (3.00 g, 17.2 mmol) in dry tetrahydrofuran (5 mL) was added to

a cold (−78 °C) solution of lithium diisopropylamide (16.3 mmol) in the same solvent (60 mL) at −78 °C. The mixture was stirred magnetically for 10 min before being allowed to warm to room temperature where agitation was continued for 3 h. The pale yellow solution was returned to −78 °C, treated with methyl iodide (2 mL, ~32 mmol), and allowed to warm to room temperature overnight. The mixture was diluted with petroleum ether and washed with saturated ammonium chloride solution and brine prior to drying. Solvent evaporation left a yellow oil, column chromatography of which on silica gel (elution with 2% ethyl acetate in petroleum ether) followed by Kugelrohr distillation (135–145 °C (0.8 Torr)) gave **38** as a colorless oil (2.67 g, 82%): IR (neat, cm^{-1}) 2930, 2860, 1700, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.34 (t, J = 7.1 Hz, 2 H), 7.32–7.16 (m, 3 H), 2.71–2.66 (m, 1 H), 2.39–2.26 (m, 2 H), 1.98–1.92 (m, 1 H), 1.81–1.66 (m, 4 H), 1.27 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) 212.90, 143.11, 128.68, 126.25, 125.80, 54.04, 39.60, 37.96, 28.11 (2 C), 21.66 ppm.

(*S*)-(−)-2-Methyl-2-phenylcyclohexanone (44). L-Valine *tert*-butyl ester (9.62 g, 55.5 mmol), 2-phenylcyclohexanone (8.56 g, 49.0 mmol), and *p*-toluenesulfonic acid monohydrate (10 mg) were dissolved in benzene (170 mL), and the mixture was heated to reflux under a Dean–Stark trap for 36 h. The benzene was removed on a rotary evaporator, and the residue purified by bulb-to-bulb distillation (145–160 °C (0.5 Torr)) to give **43** as a viscous pale yellow oil (15.81 g, 98%).

A solution of **43** (18.65 g, 56.6 mmol) in tetrahydrofuran (25 mL) was added dropwise to a cold (−78 °C) solution of lithium diisopropylamide (59.7 mmol) in the same solvent (120 mL). After 45 min at this temperature, methyl iodide (18.2 g, 125 mmol) was introduced, and the solution was allowed to warm to 0 °C cover 4 h. A 5% citric acid solution (100 mL) was added, and the two-phase mixture was stirred at 0 °C for 3 h. The product was extracted into 1:1 ether–petroleum ether, and the combined organic layers were washed with sodium bicarbonate solution and brine prior to drying and solvent evaporation. The residual yellow oil, a 5:1 mixture of **44** and **37** was chromatographed on a Waters Prep 500 HPLC instrument (silica gel, elution with 2.2% ethyl acetate in petroleum ether with five recycles). There was isolated 4.26 g (40%) of **44** as a colorless oil, $[\alpha]^{22}_D$ −145° (*c* 2.0, cyclohexane).

(*S*)-(−)-1,6-Diphenyl-6-methylcyclohexene (45). Cerium trichloride heptahydrate (9.02 g, 24.2 mmol) was placed in a 500-mL three-necked flask and heated at 145 °C (0.5 Torr) for 4.5 h. The off-white powdery solid was allowed to cool to room temperature under nitrogen and slurried in dry tetrahydrofuran (250 mL). After 1 h, the mixture was cooled to −78 °C, phenyllithium (11.0 mL of 2.0 M in 7:3 ether–cyclohexane, 22.0 mmol) was added, and the buff-colored slurry was stirred at −78 °C for 1 h. A solution of **44** (3.18 g, 16.9 mmol) in dry tetrahydrofuran (30 mL) was introduced via syringe, and the slurry was stirred at −78 °C to room temperature overnight. The reaction mixture was diluted with saturated ammonium chloride solution and filtered through Celite (ether wash). The organic phase was separated, washed with brine, dried, and evaporated. The resulting yellow solid was chromatographed on silica gel (elution with 3% ethyl acetate in petroleum ether) to give optically active 1,2-diphenyl-2-methylcyclohexanol (4.39 g, 98%) as a white solid, mp 77–78 °C (from petroleum ether): IR ($CHCl_3$, cm^{-1}) 3600–3560, 3010, 2960, 2935, 2885, 1495, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.19–7.10 (m, 6 H), 7.04–6.99 (m, 2 H), 6.90–6.87 (m, 2 H), 2.81 (td, J = 12.3, 5.1 Hz, 1 H), 2.58 (td, J = 13.5, 4.2 Hz, 1 H), 2.01–1.67 (m, 4 H), 1.53–1.46 (m, 1 H), 1.38 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 145.55, 144.43, 128.53, 126.93 (2C), 126.66, 126.47, 126.17, 77.31, 45.52, 34.46, 33.43, 21.73, 21.45, 21.34 ppm; MS, m/z (M^+) calcd 266.1671, 266.1661.

The racemic alcohol exhibited mp 78–79 °C after recrystallization from petroleum ether (lit.[25] bp 154–156 °C (0.35 Torr)).

The above alcohol (4.39 g) was dissolved in benzene (60 mL), and Burgess reagent (6.5 g, 1.5 equiv) added. The reaction mixture was stirred at room temperature for 16 h, filtered through silica gel with 10% ethyl acetate in petroleum ether, and evaporated. The resulting oil was subjected to silica gel chromatography (elution with petroleum ether) and bulb-to-bulb distillation (180–185 °C (0.8 Torr)) to give **45** as a colorless oil (3.83 g, 91% from **44**): IR (neat, cm^{-1}) 3070, 3050, 3020, 2930, 2860, 2820, 1600, 1485, 1440; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47 (d, J = 7.9 Hz, 2 H), 7.33 (t, J = 7.9 Hz, 2 H), 7.22 (t, J = 7.9 Hz, 1 H), 7.12–7.10 (m, 3 H), 7.07–6.98 (m, 2 H), 6.11 (t, J = 3.8 Hz, 1 H), 2.39–2.16 (m, 2 H), 1.84–1.76 (m, 2 H), 1.60–1.45 (m, 2 H), 1.39 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 148.33, 143.54, 142.51, 128.76, 128.02, 127.82, 127.49 (2C), 126.11, 125.65, 42.40, 42.24, 27.57, 26.11, 17.91 ppm; MS, m/z (M^+) calcd 248.1565, obsd 248.1539; $[\alpha]^{22}_D$ −36.3° (*c* 2.1, cyclohexane), $[\alpha]^{22}_{578}$ −38.8°, $[\alpha]^{22}_{546}$ −46.8°, $[\alpha]^{22}_{436}$ −110.3°, $[\alpha]^{22}_{365}$ −252.3°.

The racemic hydrocarbon has been described previously.[23]

Ozonolysis of 45. Ozone was bubbled through a cold (−78 °C), magnetically stirred solution of (*S*)-(−)-**45** (3.74 g, 15.1 mmol) in dichloromethane (300 mL) until a blue color persisted. The solution was purged with oxygen for 15 min and then nitrogen. A solution of triphenylphosphine (6.25 g, 24 mmol) in the same solvent (60 mL) was added dropwise during 10 min, and the reaction mixture was allowed to warm to room temperature during 9 h, filtered through silica gel (ether elution), and evaporated. Chromatography of the residue on silica gel (elution with 6–15% ethyl acetate in petroleum ether) gave **46** as a viscous colorless oil (3.02 g, 72%): IR (neat, cm^{-1}) 2950, 1720, 1672, 1598; ^1H NMR (300 MHz, $CDCl_3$) δ 9.64 (t, J = 1.5 Hz, 1 H), 7.44–7.18 (m, 10 H), 2.36 (t, J = 7.2 Hz, 2 H), 2.08–1.97 (m, 2 H), 1.63 (s, 3 H), 1.54–1.39 (m, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$) 203.29, 202.11, 143.54, 136.61, 131.63, 129.39, 128.97, 127.92, 126.96, 126.17, 54.50, 44.16, 39.66, 23.46, 17.10 ppm; MS, m/z (M^+) calcd 280.1463, obsd 280.1478; $[\alpha]^{23}_D$ +77.4° (*c* 1.1, $CHCl_3$), $[\alpha]^{23}_{578}$ +81.4°, $[\alpha]^{23}_{546}$ +95.6°, $[\alpha]^{23}_{436}$ +206.6°.

(*S*)-(+)-1,2-Diphenyl-2-methyl-6-hepten-1-one (47). Keto aldehyde **46** (2.84 g, 10.1 mmol) was dissolved in dry tetrahydrofuran (100 mL) and cooled to −78 °C. Triphenylphosphonium bromide (4.5 g, 12.6 mmol) was slurried in dry tetrahydrofuran (100 mL) at −78 °C, *n*-butyllithium (7.0 mL of 1.6 M in hexanes, 11.2 mmol) was added, and the mixture was allowed to warm to 0 °C for 30 min. The yellow suspension was cooled to −78 °C and transferred to the solution of **46** until a yellow color persisted. The mixture was allowed to warm to room temperature and then filtered through silica gel. The residue after evaporation was chromatographed on silica gel (elution with 2% ethyl acetate in petroleum ether) to give **47** (1.90 g, 67%), having spectral properties identical with those of its racemic counterpart **17a**; $[\alpha]^{22}_D$ +41.8° (*c* 1.3, $CHCl_3$), $[\alpha]^{22}_{578}$ +43.7°, $[\alpha]^{22}_{546}$ +51.4°, $[\alpha]^{22}_{436}$ +109.9°.

Acknowledgment. The financial support for this research was provided by the National Science Foundation. G.D.M. is the recipient of a Department of Education sponsored National Need Fellowship.

(25) Garbisch, E. W., Jr. *J. Org. Chem.* **1962**, *27*, 4243.