persisted. The excess ozone was purged with oxygen, sodium borohydride (10 mg) was added, and the reaction mixture was allowed to warm to room temperature over 3 h. Ether (5 mL) was introduced and the resulting solution was washed with water (10 mL). The aqueous phase was extracted with ether (4 × 5 mL) and the combined organic layers were washed with brine, dried, and concentrated at 0 °C until 1 mL remained. Preparative gas chromatography gave 3.7 mg (43%) of **15** as a colorless oil: IR ($CHCl_3$, cm^{-1}) 3610, 2960, 1490, 1450; ^1H NMR (80 MHz, $CDCl_3$) δ 7.34–7.15 (m, 5 H), 3.57 (t, J = 6.6 Hz, 2 H), 2.88 (m, 1 H), 1.86 (m, 2 H), 1.45 (s, 1 H), 1.28 (d, J = 6.9 Hz, 3 H); $[\alpha]^{25}_D$ +7.32° (c 0.4, $CDCl_3$).

Acknowledgment is made to the National Science Foundation for financial support and to the Fulbright Commission for a travel grant (to J.P.G.).

Cleavage of Carbon–Carbon Bonds with High Stereochemical Control. 5. Course of the Haller–Bauer Reaction of Cyclic α-Phenyl Ketones[1]

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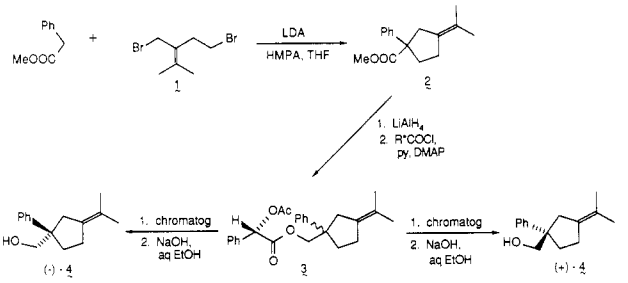
Received June 29, 1988

The Haller–Bauer cleavages of three ketones, (*R*)-(+)-3-benzoyl-3-phenyl-1-isopropylidinecyclopentane (**9**) and the *cis*- and *trans*-1-benzoyl-1-phenyl-4-*tert*-butylcyclohexanes (**16** and **25**), have been studied with different base and solvent systems. Whereas the fragmentation profile of **9** very closely mirrors that of a sterically unconstrained acyclic analogue, the stereochemically well-defined **16** and **25** respond quite differently and in opposite directions. The percent stereochemical retention rises steeply for **16** as progression is made from $LiNH_2$ to $NaNH_2$ and ultimately to KNH_2. In contrast, retention falls off rapidly for **25** across the same series. These trends are satisfactorily accounted for in terms of tight and loose product pairs and their ultimate dissociation by solvent molecules. Exceptionally high stereochemical retention was encountered in all three examples when recourse was made to potassium *tert*-butoxide in benzene. Appropriate deuterium labeling experiments shed light on the fate of those reactive intermediates formed under these conditions. In line with precedent, the use of the strongly dissociative solvent ethylene glycol gave rise to appreciable levels of inversion of configuration.

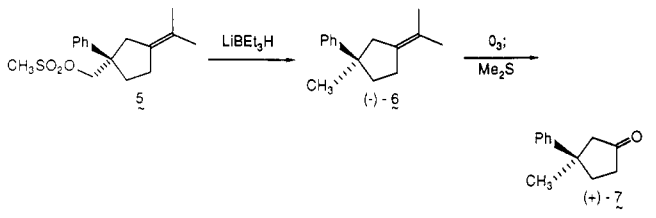
In the preceding paper,[1] the stereochemical course of the Haller–Bauer cleavage of a pair of representative chiral (nonracemic), nonenolizable, *open-chain* benzylic ketones was systemically studied. Moderate levels of retention were observed when the dissociating power of the solvent was low as in benzene or *tert*-butyl alcohol. While the nature of the cation played a secondary role in dictating configurational control, the progression from potassium to lithium ion was accompanied by rate retardation.

The present investigation was concerned with the consequences of incorporating the incipient benzylic carbanion in common ring systems.[2] Walborsky has made particularly elegant use of the Haller–Bauer process[3] in demonstrating that cyclopropyl anions are configurationally stable.[4-6] Comparable hybridization effects do not apply to larger cyclic systems. Moreover, conformationally biased cyclohexane rings offer the attractive possibility of assessing the behavior of leaving groups when initially projected in either axial or equatorial environments.

Scheme I



Scheme II



Results

A Cyclopentyl Example. Carbocyclic rings larger than cyclopropane allow for positioning of the reaction site relatively more distant from elements of steric compression. Principally for this reason, recourse was made to a remote in-plane isopropylidene group as in **2** to reduce symmetry. With optical activity as the stereochemical probe, the absolute configurations and optical purities of both the starting material and product had first to be established unequivocally.

To this end, ester **2** was prepared by spiroalkylation of methyl phenylacetate with dibromide **1**[7] (Scheme I).

(1) Part 4: Paquette, L. A.; Gilday, J. P. *J. Org. Chem.*, preceding paper in this issue.

(2) For a preliminary report dealing with a portion of this work, see: Paquette, L. A.; Gilday, J. P.; Ra, C. S. *J. Am. Chem. Soc.* **1987**, *109*, 6858.

(3) (a) Hamlin, K. E.; Weston, A. W. *Org. React. (N.Y.)* **1957**, *9*, 1. (b) Kaiser, E. M.; Warner, C. D. *Synthesis* **1975**, 395.

(4) (a) Walborsky, H. M.; Impastato, F. J. *Chem. Ind. (London)* **1958**, 1690. (b) Walborsky, H. M. *Rec. Chem. Prog.* **1962**, *23*, 75. (c) Impastato, F. J.; Walborsky, H. M. *J. Am. Chem. Soc.* **1962**, *84*, 4838. (d) Walborsky, H. M.; Allen, L. E.; Traenckner, H.-J.; Powers, E. J. *J. Org. Chem.* **1971**, *36*, 2937.

(5) See also: (a) Piehl, F. J.; Brown, W. G. *J. Am. Chem. Soc.* **1953**, *75*, 5023. (b) Hamlin, K. E.; Biermacher, U. *Ibid.* **1955**, *77*, 6376. (c) Paquette, L. A.; Uchida, T.; Gallucci, J. C. *Ibid.* **1984**, *106*, 335.

(6) (a) Walborsky, H. M.; Impastato, F. J. *J. Am. Chem. Soc.* **1959**, *81*, 5835. (b) Walborsky, H. M.; Young, A. E. *Ibid.* **1961**, *83*, 2595; **1964**, *86*, 3288. (c) Pierce, J. B.; Walborsky, H. M. *J. Org. Chem.* **1968**, *33*, 1962. (d) Walborsky, H. M.; Johnson, F. P.; Pierce, J. B. *J. Am. Chem. Soc.* **1968**, *90*, 5222. (e) Webb, J. L.; Mann, C. K.; Perisamy, M. P. *Ibid.* **1974**, *96*, 3711. (f) Hoell, D.; Schnieders, C.; Müllen, K. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 243.

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Table I. Haller–Bauer Cleavages of (+)-9 or (−)-9

base	solvent	reactn time, h	starting material[a]	yield,[b,c]	optical rotation	% ee	normalized % ee[d]	average net optical course
			(+)-9	32	+2.14° (*c* 1.45, $CHCl_3$)	15.4	15.4	
$NaNH_2$	C_6H_6, Δ	16						44% retention
			(+)-9 (30% ee)	26	+2.24° (*c* 0.76, $CHCl_3$)	16.2	16.2	
			(+)-9	35	+4.22° (*c* 0.45, $CHCl_3$)	30.4	30.4	
$NaNH_2$	*n*-$BuNH_2$, Δ	16						82% retention
			(−)-9	18	−3.24° (*c* 0.70, $CHCl_3$)	24.3	29.2	
			(+)-9	53	+2.93° (*c* 1.40, $CHCl_3$)	21.1	21.1	
$LiNH_2$	C_6H_6, Δ	24						80% retention
			(−)-9	35	−2.44° (*c* 1.05, $CHCl_3$)	17.6	21.1	
KNH_2	C_6H_6, Δ	2	(+)-9	68	+2.75° (*c* 1.44, $CHCl_3$)	19.8	19.8	58% retention
			(+)-9	30	+3.98° (*c* 1.03, $CHCl_3$)	28.7	28.7	
KO-*t*-Bu	*t*-BuOH, Δ[e]	24						80% retention
			(−)-9	30	−3.43° (*c* 1.03, $CHCl_3$)	24.7	29.6	
			(+)-9	45	+4.90° (*c* 1.06, $CHCl_3$)	35.4	35.4	
KO-*t*-Bu	C_6H_6, Δ	15						98% retention
			(−)-9	38	−4.13° (*c* 1.09, $CHCl_3$)	29.8	35.8	

[a] Starting (+)-9 was of 36% ee, except where noted; (−)-9 was of 30% ee. [b] Duplicate experiments at a minimum; error bars of ±5%. [c] The yields cited are for hydrocarbon actually isolated following preparative GC purification. [d] Normalized to account for differences in optical purity of the starting ketones. [e] 30% starting material was recovered; yield has been adjusted to reflect this fact.

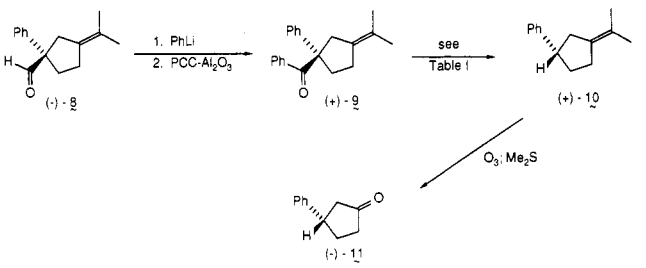
Reduction to the alcohol with $LiAlH_4$ was followed by conversion to *O*-acetylmandelate esters **3**.[8] After partial separation of the diastereomers of **3** by chromatography, the purity of the individual esters was quantified by repeated integration of their 300-MHz ^1H NMR spectra. Subsequent saponification provided (−)-**4** (30% ee) and (+)-**4** (36% ee).

The absolute configurations of these enantiomeric alcohols were arrived at by conversion of (−)-**4** to its mesylate and reduction of **5** with lithium triethylborohydride to give (−)-**6** (Scheme II). The acquisition of this hydrocarbon allowed for ready ozonolytic cleavage of its double bond to give **7**, $[\alpha]^{26}_D$ +4.8° (30% ee). Although this ketone has not been previously prepared in optically active form, its (*R*)-(+)-*p*-tolyl homologue (90% ee) is known to exhibit $[\alpha]^{25}_D$ +9.8°.[9] The assignment of *R* configuration to (+)-**7** rests on the rotatory relationship of the two ketones.

To set the stage for the Haller–Bauer studies, (+)-**4** was oxidized to carboxaldehyde (−)-**8** with pyridinium chlorochromate on alumina.[10] Sequential addition of phenyllithium to (−)-**8** and oxidation of the benzylic carbinol as before gave (+)-**9** (Scheme III). Direct evidence bearing on the *S* configuration and enantiomeric purity of (+)-**10**, obtained from the benzoyl derivative as described below, was gained by its ozonolytic degradation to (−)-**11**. The resulting levorotatory cyclopentanone has been amply described by Posner and co-workers.[11]

In the first series of cleavage experiments, (+)-**9** was heated in anhydrous benzene solution with sodium, potassium, and lithium amides. The rate of ketone consumption was monitored qualitatively by TLC analysis at regular time intervals. The reaction times needed for total dissappearance of (+)-**9** were 2, 16, and 24 h, respectively. Thus, the reactivity order $K^+ > Na^+ > Li^+$ was again

Scheme III



observed.[1] Retention of configuration at a quite respectable level (44–60% net) was seen in all three instances (Table I).

Where sodium amide is concerned, a solvent change from hot benzene to refluxing *n*-butylamine did not speed up the Haller–Bauer cleavage (16 h to completion). However, the latter conditions gave rise to considerably improved selectivity (82% net). Control experiments conducted in both solvent systems showed that the product hydrocarbon did not racemize once formed.

When recourse was made to potassium *tert*-butoxide in *tert*-butyl alcohol, 30% of (+)-**9** remained after 2 days at reflux. However, the level of net retention in samples of **10** produced in this manner was very good (80%). Substitution of benzene for *tert*-butyl alcohol had an accelerating effect on the cleavage rate (complete in 15 h). Moreover, this reagent combination proved particularly conducive to providing the maximum levels of stereochemical control (98% retention)!

No useful results could be obtained with potassium ethyleneglycolate in refluxing ethylene glycol. Because of the extreme slowness of the Haller–Bauer cleavage, degradation of (+)-**9** along other ill-defined reaction channels predominated.

Conformationally Rigid Cyclohexyl Stereoisomers. The purpose of the independent line of investigation pursued in the cyclohexane series was to focus on the possible differences in the stereochemical response of axial and equatorial benzoyl groups. The axial substrate was prepared as shown in Scheme IV. Addition of dichlorophenylcerium[12] to 4-*tert*-butylcyclohexanone (**12**) afforded a 52:48 mixture of alcohols **13** and **14** in 78% yield. When

(7) Paquette, L. A.; Charumilind, P.; Kravetz, T. M.; Böhm, M. C.; Gleiter, R. *J. Am. Chem. Soc.* **1983**, *105*, 3126.

(8) The use of *O*-acetylmandelate esters for resolution was first reported by Whitesell [Whitesell, J. K.; Reynolds, D. *J. Org. Chem.* **1983**, *48*, 3548].

(9) $[\alpha]^{25}_D$ +9.8° ($CHCl_3$), 90% ee. Posner, G., private communication. Consult: Posner, G. H.; Kogan, T. P.; Hulce, M. *Tetrahedron Lett.* **1984**, *25*, 383.

(10) Cheng, Y.-S.; Lin, W.-L.; Chen, S.-L. *Synth. Commun.* **1980**, *10*, 223.

(11) For the optically pure ketone, $[\alpha]^{25}_D$ −84.9° (*c* 0.72, $CHCl_3$). Posner, G., private communication. Compare: Taber, D. F.; Raman, K.; Gaul, M. D. *J. Org. Chem.* **1987**, *52*, 28 footnote 14. Posner, G. H.; Hulce, M. *Tetrahedron Lett.* **1984**, *25*, 379.

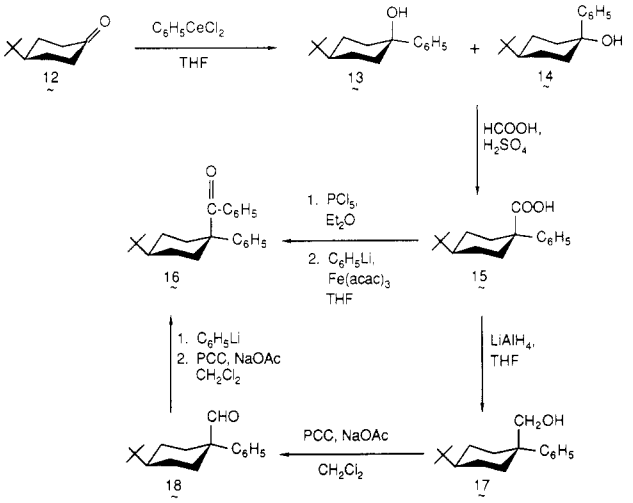
(12) Imamoto, T.; Sugiura, Y.; Takiyama, N. *Tetrahedron Lett.* **1984**, *25*, 4233.

Table II. Haller-Bauer Cleavages of 16 and 25

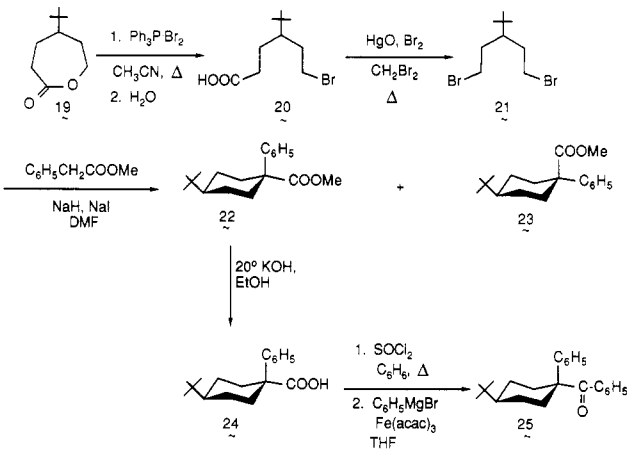
reactant	base (equiv)	solvent	reflux time, h	yield,[a] %	26:27	net stereochemical course
16	$LiNH_2$ (100)	C_6H_6	120	7.3[b]	45:55	10% inversion
	$NaNH_2$ (18)	C_6H_6	91	73	70:30	40% retention
	KNH_2 (12)	C_6H_6	16.5	87	89:11	78% retention
	KO-*t*-Bu (20)	C_6H_6	64	79	92:8	84% retention
	KO-*t*-Bu (20)	*t*-BuOH	86	36[b]	90:10	80% retention
	$KOCH_2CH_2OH$ (24)	$HOCH_2CH_2OH$	105	2.3[b]	28:72	44% inversion
25	$LiNH_2$ (100)	C_6H_6	120	24[b]	15:85	70% retention
	$NaNH_2$ (18)	C_6H_6	16	64	29:71	42% retention
	KNH_2 (12)	C_6H_6	16.5	79	40:60	20% retention
	KO-*t*-Bu (20)	C_6H_6	2	86	7:93	86% retention
	KO-*t*-Bu (20)	*t*-BuOH	86	90	15:85	70% retention
	$KOCH_2CH_2OH$ (24)	$HOCH_2CH_2OH$	105	3.2[b]	84:16	68% inversion

[a] All yields were calculated by capillary GC analysis using *n*-$C_{15}H_{32}$ as internal standard. [b] Considerable amounts of the starting material remained at the end of these experiments.

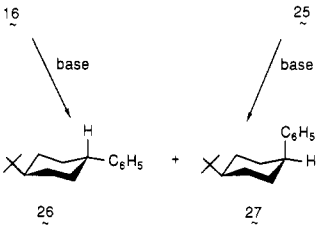
Scheme IV



Scheme V



Scheme VI



phenyllithium was used, the addition proceeded with significantly reduced efficiency (below 50%) because of competing enolization.[13] Koch–Haaf carbonylation of the **13**/**14** mixture[14] gave rise to the lone carboxylic acid **15**, structural assignment to which rests unequivocally on an X-ray crystallographic analysis.[15]

Following activation of **15** by formation of the acid chloride, condensation with various phenylating agents was undertaken. Lithium diphenylcuprate gave irreproducible yields of **16** in the 0–30% range. Phenylmagnesium bromide, with or without $Fe(acac)_3$ as catalyst,[16] did not deliver **16**. Phenyllithium, in combination with $Fe(acac)_3$ provided **16**, but yields were typically only 30–40%. For this reason, an alternative route via **17** and **18** was developed. Although four steps were now involved, laboratory execution was straightforward and the unoptimized overall yield (66%) proved acceptable.

The Koch–Haaf process gave no indication of giving rise to the stereoisomeric carboxylic acid (300-MHz ^1H NMR analysis). Recourse to other starting materials such as 1-phenyl-4-*tert*-butylcyclohexene did not alter the overwhelming preference for axial carbonylation. Accordingly, the development of a totally different approach was required and the successful route to **25** is outlined in Scheme V.

The synthetic protocol began by Baeyer–Villiger ring expansion of **12**[17] and conversion of **19** to bromo carboxylic acid **20** by the Sakurai procedure.[17,18] Following Hunsdiecker degradation of **20** to the symmetrical dibromide **21**,[17] spiroalkylation of methyl phenylacetate was implemented. Our expectations of stereoselectivity were exceeded when chromatographic separation of esters **22** (41% isolated) and **23** (16%) showed the former to predominate. Once acid **24** was in hand, its conversion to **25** was effected more readily than in the axial series, likely the direct consequences of reduced nonbonded steric interactions.

The stereoisomeric 4-*tert*-butyl-1-phenylcyclohexanes **26** and **27** have already been characterized by Garbisch and Patterson.[13] The results of the cleavage reactions of pure **16** and **25** (Scheme VI) were assessed in terms of authentic samples of these hydrocarbons and their calibrated responses to capillary GC analysis. The findings are recorded in Table II.

The first series of experiments, conducted in anhydrous benzene solution, was geared to assessing the differences

(13) Phenylmagnesium bromide behaves analogously: Garbisch, E. W., Jr.; Patterson, D. B. *J. Am. Chem. Soc.* **1963**, *85*, 3228.
(14) Malissard, M.; Sicsic, S.; Welvart, Z.; Chiaroni, A.; Riche, C.; Pascard-Billy, C. *Bull. Soc. Chim. Fr.* **1974**, 1459.
(15) Chiaroni, A.; Riche, C.; Pascard-Billy, C. *Acta Crystallogr.* **1974**, *B30*, 1914.
(16) Fiandanese, V.; Marchese, G.; Martina, V.; Ronzini, L. *Tetrahedron Lett.* **1984**, *25*, 4805.
(17) Sakurai, H.; Murakami, M. *Org. Prep. Proc. Int.* **1973**, *5*, 1.
(18) Smissman, E. E.; Alkaysi, H. N.; Creese, M. W. *J. Org. Chem.* **1975**, *40*, 1640.

between lithium, sodium, and potassium amides. Although the usual gradation in reactivity was observed to operate in common ($LiNH_2$ reacting the slowest), some striking reproducible differences were noted between **16** and **25**. With equatorial orientation of the benzoyl group, a regular dropoff in retention was seen as the cation was changed from Li^+ (70%) to Na^+ (42%) to K^+ (20%). The stereochemical response of the axial epimer was reversed, the greatest level of net retention being realized with KNH_2 (78%). In fact, the use of $LiNH_2$ caused inversion to be marginally favored (10%). Neither **26** nor **27** epimerized under these conditions.

In those runs where potassium *tert*-butoxide in benzene was employed, the highest level of stereochemical retention (84–86%) was evidenced by both substrates. Here, the heightened reactivity of **25** was particularly evident. Only a 2-h reaction time was necessary for complete consumption of the equatorial derivative. In contrast, a total of 64 h was necessary to complete the cleavage of **16**.

Substitution of benzene solvent by *tert*-butyl alcohol was accompanied both by kinetic retardation and modest lowering of the stereoselectivity of proton transfer. When both compounds were heated with potassium ethyleneglycolate in ethylene glycol, the Haller–Bauer process occurred very slowly. GC analysis of the small amounts of hydrocarbon so obtained revealed that rather high levels (44–68%) of net inversion had materialized. This departure from the norm signaled that a substantive change in mechanism was not especially conducive to forming the C–H bond from the backside of the carbanion intermediate.

Discussion

The concept that effectively planar benzylic carbanions can be generated under conditions such that their stereoselective protonation can be engineered holds fascination. The vast body of information concerning such reactive species clearly indicates that the specific nature of the *metallic* counterion is apt to play at most a minor role in holding the configuration of these reactive species.[19,20] On the other hand, solvent composition can make possible by virtue of solvation capacity the proper orientation of one or more closely neighboring molecules such that a source of protons is available at the front face of the site of carbanion generation. Cram's extensive scrutiny of SE_1 reactions involving the base-catalyzed cleavage of tertiary alcohols[21] has made evident the fact that media of low dielectric constant can foster heightened levels of stereochemical retention in the protonated product. The UCLA group also found the concentration of proton donors to be unimportant in relation to the retention mechanism,[22] although a change to quaternary ammonium counterions did eventuate in almost complete racemization.[23]

The salient facts associated with the Haller–Bauer reaction correlate well with the intervention of carbanion intermediates, at least in open-chain compounds and cyclopropyl systems.[1-5] Furthermore, the very nature of this cleavage reaction requires that a neutral leaving group depart from the seat of reaction with liberation of a carbanion in close syn-facial proximity. As a consequence, the replacement of benzoyl by hydrogen with excellent stereochemical control has been realized in optically active acyclic systems.[1]

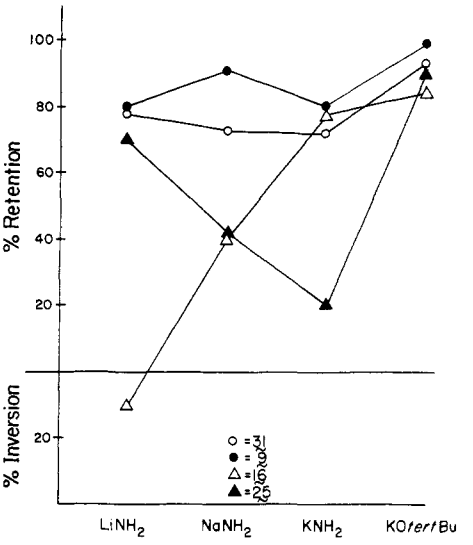
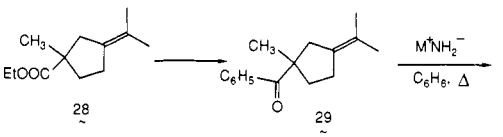
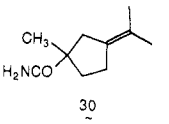


Figure 1. Sterochemical course of the Haller–Bauer cleavage of four representative α-phenyl ketones in refluxing benzene as a function of base.

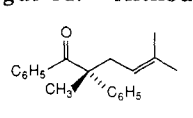
We have deemed it important to demonstrate that the success of the Haller–Bauer reaction in *cyclic* systems is indeed sensitive to the gross structure of the leaving group. For this purpose, ester **28** was prepared in a manner





paralleling the acquisition of **2** and converted analogously to **29**.[24] Heating of **29** with amide bases in benzene resulted in cleavage only of the bond to phenyl. The conclusion that satisfactorily explains this observation is that the carbanion enjoying the greater level of stability is generated more rapidly.

When the alternative cleavage mode operates as it does when the leaving group is resonance stabilized, appreciable structural variation is of course possible. The many special effects associated with the exact structure of the transient carbanion render analysis of Haller–Bauer stereochemistry interesting. Figure 1 summarizes how the cyclopentyl example (**9**) compares to the responses of the pair of epimeric six-membered ring compounds **16** and **25**, as well as the acyclic analogue **31**.[1] Although retention of configuration is almost always seen with the amide bases or



(19) Consult, for example: Fraenkel G.; Hsu, H.; Su, B. M. "The Structure and Dynamic Behavior of Organolithium Compounds in Solution. ^{13}C, ^{6}Li, and ^{7}Li NMR" In *Lithium: Current Applications in Science, Medicine, and Technology*; Bach, R., Ed.; Wiley: New York, 1985; p 273 ff.

(20) Gilday, J. P.; Paquette, L. A., submitted for publication.

(21) Cram, D. J. *The Fundamentals of Carbanion Chemistry*; Academic Press: New York, 1965; Chapter IV.

(22) Cram, D. J.; Kopecky, K. R.; Hauck, F.; Langemann, A. *J. Am. Chem. Soc.* **1959**, *81*, 5754.

(23) Cram, D. J.; Hauck, F.; Kopecky, K. R.; Nielsen, W. D. *J. Am. Chem. Soc.* **1959**, *81*, 5767. (b) Cram, D. J.; Mateos, J. L.; Hauck, F.; Langemann, A.; Kopecky, K. R.; Nielsen, W. D.; Allinger, J. *Ibid.* **1959**, *81*, 5774.

(24) Ra, C. S., unpublished observations.

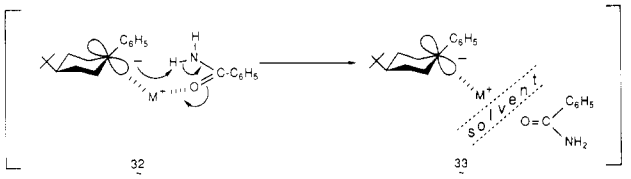
Table III. Experiments Involving Deuterium Incorporation[a]

ketone	reflux time, h	isolated yield, prepn GC, %	deuterium incorprtn (%)	isomer ratio	normal ratio
16	65	72	26 (53)	72	93
			27 (54)	28	7
25	2	71	26 (5)	19	8
			27 (33)	81	92

[a] Performed in benzene with 20 equiv of $KOC(CD_3)_3$.

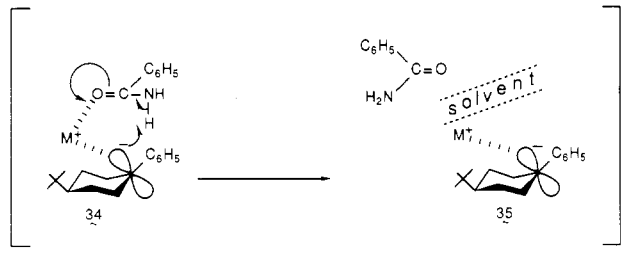
potassium *tert*-butoxide in hot benzene solvent, certain striking differences are clearly apparent. The especially close correspondence between substrate **31** and cyclopentane **9** suggests that the levels of stereochemical retention observed in these examples correspond to a norm. As steric factors of one type or another gain relative importance, these levels of retention should be perturbed accordingly. The entirely opposite directions taken by **16** and **25** can be explained in these terms.

When the benzoyl group is equatorially disposed as it is in **25**, attack by amide ion gives rise to the product-separated species **32**. As C–C bond cleavage is initiated, the 1,3-diaxial steric compression exerted on the phenyl substituent can reasonably be expected to seek relief. The data show that when M^+ in **32** is lithium, the small ionic radius of this metal ion and its characteristic penchant for tight coordination do not allow for significant extranormal leakage of the system away from **32**. The increase in backside protonation relative to **9** amounts to only 8–10%. With progressive loosening of the coordinative binding, as operates when M^+ becomes sodium and ultimately potassium ion, it is reasonable to expect that the conversion of **32** to **33** becomes increasingly competitive with proton



transfer within the original coordination sphere. The progressive dropoff in stereochemical retention (70% → 42% → 20%) can be plausibly accounted for in these terms. It would appear that benzamide is not completely disloged from the frontside of the carbanion even in the most extreme situation ($M^+ = K^+$) since a modicum of retention persists.

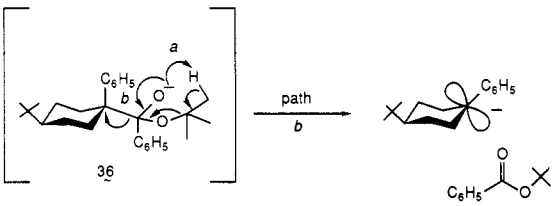
The behavior of **16** is quite the opposite, the level of stereochemical control *increasing* substantially as one progresses from lithium to potassium amide (Figure 1). It must be recognized that fission of the C–C bond in the axial epimer gives rise to product pair **34**. Under these



circumstances, the customarily tight complexation of Li^+ to both the carbanionic center and benzamide is now quite sterically demanding. As decompression occurs, the axial surface of the carbanion likely remains temporarily blocked (see **35**), such that proton delivery from the equatorial direction competes effectively. Increased stereochemical retention is expressed when lithium is replaced by sodium and potassium for at least three reasons. The product-separated pairs represented by **34** become increasingly loose and less sterically congested. Simutlaneously, the reactivity of the carbanion increases and reaches a maximum when K^+ is involved. Also, the strongly favored axial protonation in this example stems from the conventional reluctance on the part of the phenyl substituent to be thrust into an axial orientation.

In this connection, it is noteworthy that the **26**/**27** product ratios stemming from **16** and **25** are equal and opposite when $NaNH_2$ serves as base. On the other hand, the distributions of **26** and **27** derived from the KNH_2-promoted cleavages reflect in all likelihood the customarily greater kinetic preference for axial capture of the proton.[20]

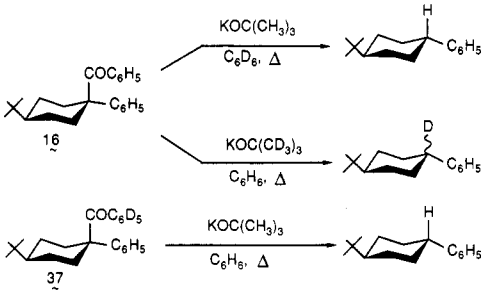
When potassium *tert*-butoxide and benzene serve as the reagent and reaction medium, the highest levels of retention are observed in all four systems. At the mechanistic level, addition of *tert*-butoxide ion leads to **36**, the frag-



mentation of which does not give rise to as good a proton donor as benzamide. To what might the strikingly enhanced stereoselectivity be attributed? Several options exist. The collapse of **36** may occur intramolecularly with abstraction of a *tert*-butyl proton via a six-centered transition state and elimination of isobutylene together with benzoate ion. It will be recalled that this scheme is bypassed completely when the solvent is *tert*-butyl alcohol.[1]

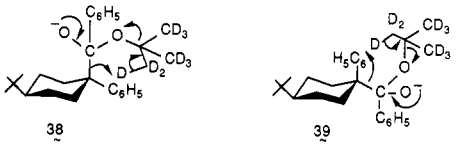
Isobutylene may also be lost prior to a decarboxylative event (path a). Alternatively, proton transfer from interstitial benzene solvent might operate to provide the net retention observed. Yet a fourth possibility resides in cleavage of **36** along path b. The *tert*-butyl benzoate released on the front face of the carbanion could protonate the reactive intermediate with retention before it found it necessary to disrupt the surrounding solvent structure. From an a priori standpoint, the latter mechanism might be viewed as most appealing since the ortho and para protons of the benzoate ester are the most acidic of those immediately available.

A triad of experiments was performed to clarify the actual state of affairs. First, ketone **16** was heated with potassium *tert*-butoxide in benzene-d_6. Secondly, the base was fully labeled isotopically and allowed to react with **16** in C_6H_6. Finally, **37** was prepared and subjected to the usual Haller–Bauer conditions. The results are summarized in the equation below and Table III. Not only was deuterium not incorporated when **16** and **37** were heated with potassium *tert*-butoxide in C_6D_6 and C_6H_6, respectively, but the cis/trans product isomer ratio (93:7±1) was not different from that observed earlier. On the other hand, recourse to $KOC(CD_3)_3$ in hot benzene proceeded with only 44% retention, the Haller–Bauer cleavage not



responding clearly to a deuterium isotope effect of reasonable proportions. The level of D incorporation in **26** and **27** was comparable (53–54% d_1). These measurements derive from integration of the benzylic protons due to **26** (δ 2.44, m, 1 H) and **27** (δ 3.03, s, 1 H), relative to their respective *tert*-butyl singlet absorptions (δ 0.89; δ 0.80).

When **25** was analogously treated, the level of retention was comparably reduced (to 62%), as was the level of deuterium incorporation in both 4-*tert*-1-phenylcyclohexanes (Table II). Thus, the mechanistic concepts expressed in **36** are too simplistic. Some intramolecular collapse such as illustrated in **38** and **39** likely operates. However, the lower level of deuterium incorporation from **39** suggests in particular that alternative fragmentation



modes which take advantage of the presence of adventitious proton donors can also materialize when an isotope effect must be overcome.

Finally, the high levels of inversion arising from use of ethylene glycol as solvent follow precedent[1] and arise unquestionably from its high dielectric constant and strongly dissociative nature.[22,23]

Experimental Section

Methyl 1-Phenyl-3-isopropylidene-1-cyclopentanecarboxylate (2). A cold (−78 °C) magnetically stirred solution of lithium diisopropylamide (125 mmol) in anhydrous tetrahydrofuran (75 mL) was treated dropwise via syringe with neat methyl phenylacetate (15.0 g, 100 mmol). After 20 min, dibromide **1** (21.6 g, 100 mmol) in HMPA (17.9 g, 100 mmol) was also added dropwise. Twenty minutes later, the second 125 mmol of LDA in tetrahydrofuran (75 mL) was introduced. Following a final 40 min at −78 °C, the reaction mixture was allowed to warm to room temperature where stirring was maintained for 30 min. The product was partitioned between saturated ammonium chloride solution (50 mL) and ether (100 mL). The aqueous phase was extracted with ether (3 × 50 mL) and the combined ethereal solutions were washed with brine (2 × 25 mL), dried, and evaporated. HPLC purification (silica gel, elution with 3% ethyl acetate in petroleum ether) gave 16.5 g (68%) of **2**: IR (neat, cm^{-1}) 2995, 2915, 1735, 1604, 1507, 1453; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39–7.19 (m, 5 H), 3.61 (s, 3 H), 2.75–1.54 (series of m, 6 H), 1.71 (s, 3 H), 1.61 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 176.00, 142.79, 132.04, 128.27, 126.79, 126.63, 122.89, 58.11, 52.27, 40.61, 35.89, 28.66, 21.04, 20.86; MS, m/z (M^+) calcd 244.1463, obsd 244.1445.

Anal. Calcd for $C_{16}H_{20}O_2$: C, 78.65; H, 8.25. Found: C, 78.51; H, 8.25.

1-Phenyl-3-isopropylidene-1-cyclopentanecarbinol. A solution of **2** (14.6 g, 59.8 mmol) in anhydrous tetrahydrofuran (20 mL) was added dropwise to a stirred suspension of lithium aluminum hydride (2.27 g, 59.8 mmol) in the same solvent (130 mL) at 0 °C. After being stirred for 1 h at room temperature, the reaction mixture was quenched by dropwise addition of ethyl acetate (3 mL) followed by a 2 N sodium hydroxide solution (30 mL). The product was extracted into ether (2 × 250 mL) and the ethereal solution was dried and concentrated to give the alcohol as a white solid (10.6 g, 82.2%). Additional purification was effected by MPLC on silica gel (elution with 9% ethyl acetate in petroleum ether): IR (neat, cm^{-1}) 3400, 3020, 2913, 1604, 1599, 1450; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.21 (m, 5 H), 3.58–3.47 (AB, 2 H), 2.75–1.83 (m, 6 H), 1.69 (s, 3 H), 1.62 (s, 3 H), 1.21 (br s, 1 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 146.18, 133.07, 128.30, 127.03, 126.23, 122.86, 69.61, 52.40, 39.22, 33.19, 28.29, 21.12, 20.84; MS, m/z (M^+) calcd 216.1514, obsd 216.1520.

Esterification of the Alcohol with (*R*)-(−)-*O*-Acetylmandelic Acid Chloride. (*R*)-(−)-*O*-Acetylmandelic acid chloride, prepared by refluxing the acid (19.4 g, 100 mmol), $[\alpha]^{23}_D$ −153.5° (*c* 2.20, acetone) in benzene (50 mL) with oxalyl chloride (25.4 g, 200 mmol) for 2 h and removing the excess reagents in vacuo, was dissolved in dry dichloromethane (50 mL) at 0 °C. Next to be introduced were the alcohol (10.6 g, 49.0 mmol), 4-(dimethylamino)pyridine (733 mg, 6 mmol), and pyridine (15.1 g, 180 mmol). The mixture was stirred for 1 h at room temperature. After the usual workup, the product was purified by flash chromatography on silica gel. Elution with 9% ethyl acetate in petroleum ether furnished **3** (15.9 g, 83%) as a colorless, oily 1:1 mixture of diastereomers: IR (neat, cm^{-1}) 3025, 2900, 1743; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.09 (m, 10 H), 5.83 (s, 1 H), 4.29–3.95 (m, 2 H), 2.66–1.78 (series of m, 6 H), 2.13 (s, 3 H), 1.64 (s, 3 H), 1.59 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 170.02 (168.61, 168.53), 145.42, 133.88, (132.23, 132.16), 128.97, 128.59, 127.93, 127.46, 126.72, 126.07, 123.28, 74.38, 70.09 (50.05, 50.01), (33.74, 33.64), 28.07, (21.05, 21.00), 20.83, 20.60; MS (CI), m/z ($M^+ + 1$) calcd 393, obsd 393.

Diastereomer enrichment was achieved on a preparative scale by use of peak shaving techniques in tandem with recycling on a Waters Prep 500 system (dual silica gel cartridges; 9% ethyl acetate in petroleum ether). Differentiation of the diastereomers was easily accomplished by quantitation of the areas of their AB signals due to the -CH_2O- protons. In one case, these absorptions were centered at δ 4.27 and 3.97 (J = 10.7 Hz). In the other, the doublets appeared at δ 4.13 and 4.08 (J = 10.7 Hz).

Saponification of Diastereomerically Enriched 3. General Procedure. The diastereomerically enriched ester (36% de) (4.52 g, 11.5 mmol) was dissolved in ethanol (40 mL), treated with a solution of sodium hydroxide (920 mg, 23 mmol) in water (10 mL), and heated at the reflux temperature for 30 min. The cooled reaction mixture was acidified to pH 2 with concentrated hydrochloric acid and extracted with ether (2 × 50 mL). The combined ethereal phases were washed with brine, dried, and concentrated. The residue was purified by MPLC on silica gel (elution with 12% ethyl acetate in petroleum ether) to deliver 1.85 g (74%) of the carbinol as a white solid, $[\alpha]^{22}_D$ +13.5° (*c* 1.09, CH_3OH).

Analogous treatment of the second diastereomeric ester (30% de) furnished crystalline carbinol, $[\alpha]^{22}_D$ −11.4° (*c* 0.985, CH_3OH).

(*R*)-(+)-3-Methyl-3-phenylcyclopentanone (7). A cold (0 °C), magnetically stirred solution of (*S*)-(−)-**4** (100 mg, 0.46 mmol, $[\alpha]^{22}_D$ −11.4°) and dry pyridine (44 μL, 0.55 mmol) in dichloromethane (1 mL) was treated with freshly distilled methanesulfonyl chloride (43 μL, 0.55 mmol), warmed to room temperature, and stirred for 20 min. Saturated sodium bicarbonate solution (0.5 mL) was introduced, the product was taken up in ether, and the ether phase was washed with cold dilute hydrochloric acid and brine prior to drying. Evaporation left the oily mesylate **5**, which was directly taken up in tetrahydrofuran (3 mL), cooled to 0 °C, treated with lithium triethylborohydride (2.5 mL of 1 M, 2.5 mmol), and stirred overnight. The reaction mixture was quenched by cautious addition of water (0.2 mL), 3 N sodium hydroxide solution (0.6 mL), and 30% hydrogen peroxide (0.5 mL). The hydrocarbon product was taken up in ether, washed with water, dried, and carefully concentrated. Preparative GC on the oily residue (15 ft × 0.25 in. 10% SE-30, 230 °C) furnished 40 mg (43%) of (*R*)-(−)-**6**: $[\alpha]^{26}_D$ −9.06° (*c* 0.96, $CHCl_3$); IR (neat, cm^{-1}) 3084, 3056, 3014, 2925, 1604, 1506, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.14 (m, 5 H), 2.51–1.89 (series of m, 6 H), 1.68 (s, 3 H), 1.64 (s, 3 H), 1.23 (s, 3 H); MS, m/z (M^+) calcd 200.1567, obsd 200.1567.

Ozonolysis of (−)-**6** (40 mg, 0.20 mmol) was performed at −78 °C in dichloromethane solution (2 mL) containing pyridine (35

μL, 0.4 mmol). When a blue color developed after approximately 1 min, dimethyl sulfide (50 μL), zinc (50 mg), and a drop of acetic acid were added and the mixture was allowed to warm to room temperature with stirring during 1 h. The product was partitioned between saturated sodium bicarbonate solution (2 mL) and ether (2 × 5 mL). The combined ethereal layers were washed with brine and dried. Solvent evaporation and subsequent preparative GC purification (15 ft × 0.25 in. 10% SE-30, 220 °C) provided 10.2 mg (29%) of (*R*)-(+)-**7** as a colorless liquid: $[a]^{26}_D$ +4.8° (*c* 1.02, $CHCl_3$); IR (neat, cm^{-1}) 3088, 3058, 3028, 2968, 1746, 1604, 1499, 1447, 1407, 1064; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.23 (m, 5 H), 2.69–2.27 (m, 6 H), 1.39 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 218.29, 148.45, 128.55, 126.30, 125.42, 52.26, 43.81, 36.72, 35.85, 29.41; MS, *m/z* (M^+) calcd 175.1081, obsd 175.1081.

(*R*)-(+)-3-Benzoyl-3-phenyl-1-isopropylidenecyclopentane (9). A solution of (+)-**4** (1.00 g, 4.62 mmol, $[\alpha]^{22}_D$ +13.5°) in benzene (12 mL) was treated with freshly prepared pyridinium chlorochromate on alumina (dried overnight in vacuo, 11 g, 13.6 mmol). The reaction mixture was stirred at room temperature for 2 h, filtered through Celite, and concentrated to give 750 mg (76%) of **8** as a pale yellow oil (750 mg). This aldehyde was usually used directly, but material purified by MPLC on silica gel slowly crystallized on standing in a refrigerator, mp 57 °C: IR (neat, cm^{-1}) 3040, 3020, 2910, 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 9.43 (s, 1 H), 7.40–7.28 (m, 5 H), 3.21–1.91 (series of m, 6 H), 1.71 (s, 3 H), 1.61 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 200.68, 139.62, 131.55, 128.74, 127.45, 127.24, 123.43, 62.81, 36.92, 32.25, 28.69, 21.13, 20.87; MS, *m/z* (M^+) calcd 214.1358, obsd 214.1346; $[\alpha]^{22}_D$ −7.48° (*c* 0.615, $CHCl_3$).

A magnetically stirred solution of the aldehyde (95 mg, 0.44 mmol) in cold (−78 °C) ether was treated dropwise with phenyllithium (0.47 mL of 1.4 M, 0.66 mmol) and stirred for 30 min. Water and ether were added and the organic phase was dried prior to solvent evaporation. MPLC purification (silica gel) afforded 68 mg (53%) of a diastereomeric mixture of alcohols: IR (neat, cm^{-1}) 3500, 2910, 1602, 1498, 1452; ^1H NMR (300 MHz, $CDCl_3$) δ (diastereomer A) 7.28–6.75 (m, 10 H), 4.71 (s, 1 H), 3.28–1.85 (series of m, 6 H), 1.72 (s, 3 H), 1.60 (s, 3 H); (diastereomer B) 7.30–6.75 (m, 10 H), 4.71 (s, 1 H), 2.67–1.96 (series of m, 6 H), 1.87 (s, 3 H), 1.85 (s, 3 H); MS, *m/z* ($M^+ - H_2O$) calcd 274.1722, obsd 274.1724.

A solution of the diastereomeric alcohols (41 mg, 0.14 mmol) in benzene (3 mL) was treated as described above with freshly prepared pyridinium chlorochromate on alumina (0.7 g, 0.28 mmol). After being stirred for 2 h at room temperature, the reaction mixture was filtered through Celite and concentrated. MPLC of the residue on silica gel afforded 21 mg (53%) of **9** as a colorless oil that crystallized on standing in the cold: IR (neat, cm^{-1}) 2915, 1729, 1677, 1601, 1500, 1450; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60–7.22 (m, 10 H), 2.92–2.06 (m, 6 H), 1.65 (s, 3 H), 1.63 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 202.09, 143.24, 136.60 132.43, 131.60, 129.40, 128.80, 127.86, 126.69, 126.13, 122.81, 62.65, 40.99, 37.01, 28.01, 21.01, 20.93; MS, *m/z* (M^+) calcd 290.1671, obsd 290.1699; $[\alpha]^{22}_D$ −23.9° (*c* 1.03, CH_3CN) (30% ee). For the (*R*)-(+) enantiomer: $[\alpha]^{22}_D$ +29.0° (*c* 1.33, CH_3CN) (36% ee).

Anal. Calcd for $C_{21}H_{22}O$: C, 86.85; H, 7.64. Found: C, 86.56; H, 7.69.

Haller–Bauer Cleavages. The analytical GC conditions were the same as those utilized elsewhere.[1] A mixture of (+)-**9** (50–80 mg, 0.17–0.28 mmol) and base (ca. 15 molar equiv) in dry solvent (3 mL) was heated at the reflux temperature for an appropriate time period. The cooled reaction mixture was treated with water (5 mL) and the aqueous phase was extracted with petroleum ether (2 × 5 mL). The combined organic layers were dried and evaporated, and the residue was purified by filtration through a small column of silica gel (1 g, elution with 3% ethyl acetate in petroleum ether). Preparative GC of the concentrate afforded **10** as a colorless oil: IR (neat, cm^{-1}) 3030, 2930, 1605, 1498, 1459; ^1H NMR (300 MHz, $CDCl_3$) δ 7.32–7.15 (m, 5 H), 3.14–1.68 (series of m, 7 H), 1.65 (s, 3 H), 1.64 (s, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 145.41, 134.71, 128.23, 126.99, 125.88, 121.67, 45.85, 38.88, 34.50, 30.46, 21.10, 20.81; MS, *m/z* (M^+) calcd 186.1408, obsd 186.1390.

Anal. Calcd for $C_{14}H_{18}$: C, 90.26; H, 9.74. Found: C, 90.25; H, 9.72.

(*S*)-(−)-3-Phenylcyclopentanone (11). A solution of **10** [$[\alpha]^{25}_D$ +2.19° (*c* 1.45, $CHCl_3$), 23 mg, 0.12 mmol] in dichloromethane (5 mL) was cooled to −78 °C and ozonolyzed for 2 min when a blue color developed. Dimethyl sulfide (50 μL) was introduced and the temperature was slowly increased to 25 °C during 1.5 h. Following the usual workup, the residual oil was purified by MPLC on silica gel (elution with 5% in ethyl acetate in hexane) and subsequent preparative GC (15 ft × 0.25 in. 5% SE-30, 190 °C). There was isolated 10.8 mg (55%) of **11**: IR (neat, cm^{-1}) 3032, 3015, 2960, 1740, 1013; ^1H NMR (300 MHz, $CDCl_3$) δ 7.37–7.22 (m, 5 H), 3.48–3.36 (m, 1 H), 2.71–2.63 (m, 1 H), 2.51–2.24 (m, 1 H), 2.06–1.92 (m, 1 H); MS, *m/z* (M^+) calcd 160.0888, obsd 160.0901; $[\alpha]^{25}_D$ −13.4° (*c* 0.73, $CHCl_3$).[11]

***cis*- and *trans*-1-Phenyl-4-*tert*-butylcyclohexanol (13 and 14).** Cerium trichloride heptahydrate (365 mg, 0.98 mmol) was stirred magnetically and heated at 150 °C and 0.1 Torr for 2 h. After cooling, anhydrous tetrahydrofuran (1 mL) was introduced and the mixture was stirred for 2 h under nitrogen before being cooled to −78 °C. To the resultant slurry was added phenyllithium (0.98 mmol) followed 30 min later with 4-*tert*-butylcyclohexanone (136 mg, 0.88 mmol) in 1 mL of tetrahydrofuran. The reaction mixture was allowed to warm slowly to room temperature overnight, at which point saturated ammonium chloride solution was added. Insoluble material was removed by filtration through a small pad of Celite and the filtrate was extracted with ether. The combined organic layers were washed with brine, dried, and concentrated, MPLC of the residue on silica gel (elution with 45% ethyl acetate in petroleum ether) furnished 82 mg (40%) of **13** and 77 mg (38%) of **14**.

For **13**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.53–7.24 (m, 5 H), 1.86–1.10 (series of m, 10 H), 0.92 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 149.55, 128.12, 126.58, 124.45, 72.71, 47.56, 39.42, 32.46, 27.60, 22.92, (1 C not observed).

For **14**: ^1H NMR (300 MHz, $CDCl_3$) δ 7.57–7.28 (m, 5 H), 2.57–2.52 (m, 2 H), 1.80–0.98 (series of m, 8 H), 0.77 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 144.43, 128.45, 127.28, 126.35, 73.36, 47.78, 38.87, 32.21, 27.58, 24.99.

***cis*-1-Phenyl-4-*tert*-butylcyclohexanecarboxylic Acid (15).** A 1-L three-necked flask fitted with a mechanical stirrer was charged with 1.7 mol of concentrated sulfuric acid. A solution of the **13**/**14** mixture (24.7 g, 0.106 mol) in 140 mL of carbon tetrachloride was placed in one of a pair separatory funnels and 0.32 mol of formic acid in the other. Addition was performed concomitantly during 2 h with gentle stirring. The reaction mixture was poured into ice water (400 mL) and extracted with ether (3 × 250 mL). The combined extracts were treated with 20% potassium hydroxide solution and then hot tetrahydrofuran until all organic materials dissolved. This solution was acidified while hot with 6 N hydrochloride acid to pH 2 and concentrated on a rotary evaporator. The residual yellow powder was dissolved in ether, washed twice with brine, dried, and evaporated to give 11.2 g (40%) of **15** as colorless needles, mp 235–239 °C (from 7:3 hexane–methanol) (lit.[14] mp 224–227 °C): IR (KBr, cm^{-1}) 1690; ^1H NMr (80 MHz, $CDCl_3$) δ 7.45–7.21 (m, 5 H), 2.73–2.69 (d, *J* = 11.4 Hz, 2 H), 1.86–1.02 (series of m, 7 H), 0.86 (s, 9 H); ^{13}C NMR (75 MHz, DMSO-d_6) ppm 175.54, 144.65, 128.38, 125.25, 50.06, 46.40, 34.74, 31.96, 27.22, 24.33; MS, *m/z* (M^+) calcd 260.1776, obsd 260.1768.

***cis*-1-Benzoyl-1-phenyl-4-*tert*-butylcyclohexane (16). A. Phenylation of the Acid Chloride.** An ether (2 mL) suspension of **15** (40 mg, 0.15 mmol) was treated with phosphorus pentachloride (100 mg, 0.48 mmol) and stirred overnight at room temperature. The resulting clear solution was treated with cold water (2 mL) and extracted with ether (2 × 3 mL). The combined organic layers were dried and evaporated to leave the acid chloride as a colorless crystalline mass (40 mg).

The above material was dissolved in dry tetrahydrofuran (1 mL) and treated sequentially with $Fe(acac)_3$ (3 mg) and phenyllithium (0.20 mmol) dropwise. The reaction mixture was stirred for 2 h, treated with 1 N hydrochloric acid, and extracted with ether (3 × 5 mL). After concentration, the residue was purified by MPLC on silica gel (elution with 2% ethyl acetate in petroleum ether) to give **16** (18 mg, 37%) as a colorless crystalline solid, mp 156–157 °C (from 4:1 methanol–ether): IR ($CHCl_3$, cm^{-1}) 3040, 2960, 1875, 1601, 1455; ^1H NMR (300 MHz, $CDCl_3$) δ 7.43–7.19 (m, 10 H), 2.68–1.05 (series of m, 9 H), 0.82 (s, 9 H); ^{13}C NMR

(75 MHz, $CDCl_3$) ppm 204.89, 144.39, 138.59, 131.00, 128.98, 128.57, 127.82, 126.93, 126.00, 55.33, 47.63, 36.43, 32.34, 27.47, 24.37; MS, m/z ($M^+ - COC_6H_5$) calcd 215.1800, obsd 215.1772.

Anal. Calcd for $C_{23}H_{28}O$: C, 86.20; H, 8.81. Found: C, 85.88; H, 8.87.

B. Via Alcohol 17 and Aldehyde 18. A stirred, cold (0 °C) suspension of lithium aluminum hydride (570 mg, 15.0 mmol) in anhydrous tetrahydrofuran (50 mL) was treated dropwise with a solution of **15** (3.02 g, 11.6 mmol) in 20 mL of the same solvent. The reaction mixture was heated at reflux for 2.5 h, cooled, and treated carefully with ethyl acetate (2 mL) and then 3 N sodium hydroxide solution. After being stirred for 1 h at room temperature, the customary workup furnished 2.50 g (87%) of **17** as a white powder.

A mixture of **17** (120 mg, 0.49 mmol), pyridinium chlorochromate (157 mg, 0.73 mmol), sodium acetate (12 mg, 0.146 mmol), and 3-Å molecular sieves (0.5 g) in dichloromethane (2 mL) was stirred for 20 min. Ether (25 mL) was added and the mixture was filtered through a short silica gel column (2 g, elution with 2% ethyl acetate in petroleum ether). Evaporation of the eluate gave **18** (119 mg, quantitative) as a colorless solid.

The aldehyde (119 mg, 0.487 mmol) was dissolved in ether (2 mL) and tetrahydrofuran (3 mL), cooled to −78 °C, and treated slowly with phenyllithium (365 μL of 2 M, 0.73 mmol). After 30 min and the usual workup, purification was performed by MPLC on silica gel (elution with 5.5% ethyl acetate in petroleum ether). There was isolated 132 mg (84%) of the carbinol as a colorless solid.

The above alcohol (120 mg, 0.372 mmol) was oxidized with pyridinium chlorochromate (120 mg, 0.558 mmol), sodium acetate (10 mg, 0.124 mmol), and 3-Å molecular sieves (0.5 g) in the predescribed manner. MPLC on silica gel afforded 107 mg (90%) of **16** as a colorless solid, identical in all respects with the compound prepared in part A.

***cis*- and *trans*-Methyl 1-Phenyl-4-*tert*-butylcyclohexanecarboxylate (22 and 23).** To a mixture of sodium iodide (2.6 g, 17.5 mmol), sodium hydride (3.5 g of 60% oil dispersion, 87.4 mmol), and hexamethylphosphoramide (3.13 g, 7.5 mmol) in 45 mL of cold (0 °C), anhydrous dimethylformamide was added dropwise a solution of dibromide **21** (5.0 g, 17.5 mmol) and methyl phenylacetate (3.94 g, 26.2 mmol) in 30 mL of the same solvent. After 2 h at 0 °C, saturated ammonium chloride solution (20 mL) was introduced and the product was extracted into ether. The dried concentrate was subjected to MPLC (silica gel, elution with 35% ethyl acetate in petroleum ether) to give 1.97 g (41%) of **22** and 0.75 g (16%) of **23**.

For **22**: IR ($CHCl_3$, cm^{-1}) 3030, 2950, 1723 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47–7.20 (m, 5 H), 3.55 (s, 3 H), 2.77–2.72 (d, J = 14.5 Hz, 2 H), 1.86–0.85 (series of m, 7 H), 0.73 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 176.86, 139.66, 128.40, 127.68, 126.44, 52.02, 49.15, 48.01, 33.23, 32.27, 27.40, 22.76; MS, m/z (M^+) calcd 274.1933, obsd 274.1959.

Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.63; H, 9.59.

For **23**: IR ($CHCl_3$, cm^{-1}) 3030, 2950, 1725; ^1H NMR (300 MHz, $CDCl_3$) δ 7.40–7.23 (m, 5 H), 3.65 (s, 3 H), 2.72–2.68 (d, J = 11.8 Hz, 2 H), 1.84–1.02 (series of m, 7 H), 0.86 (s, 9 H): ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.40, 144.51, 128.38, 126.73, 125.52, 51.91, 51.05, 47.34, 35.40, 32.35, 27.50, 25.07; MS, m/z (M^+) calcd 274.1933, obsd 274.1939.

***trans*-1-Phenyl-4-*tert*-butylcyclohexanecarboxylic Acid (24).** A mixture of **22** (250 mg, 0.91 mmol), potassium hydroxide (140 mg of 88% purity, 2.2 mmol), ethanol (2 mL), and water (5 mL) was heated at reflux for 3 h and acidified with 6 N hydrochloric acid. Ether extraction (3 × 10 mL), washing of the combined organic layers with brine, drying, and solvent evaporation furnished 237 mg (100%) of **24** as a white solid, mp 224–226 °C dec; IR ($CHCl_3$, cm^{-1}) 1696; ^1H NMR (300 MHz, $CDCl_3$) δ 7.47–7.20 (m, 5 H), 2.74–2.70 (d, J = 14.3 Hz, 2 H), 1.86–0.81 (series of m, 7 H), 0.72 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 181.86, 138.93, 128.53, 127.81, 126.75, 48.94, 47.93, 32.89, 32.27, 27.39, 22.67; MS, m/z (M^+) calcd 260.1776, obsd 260.1798.

***trans*-1-Benzoyl-1-phenyl-4-*tert*-butylcyclohexane (25).** A mixture of **24** (99 mg, 0.38 mmol) and thionyl chloride (139 μL, 1.9 mmol) in 2 mL of benzene was heated at reflux for 2 h and evaporated under reduced pressure to leave the acid chloride as a pale yellow oil. To a cold (0 °C) solution of this material in anhydrous ether (2 mL) was added $Fe(acac)_3$ (11 mg, 0.03 mmol) and then phenyllithium (2 M in cyclohexane–ether, 0.38 mmol) dropwise. After 30 min, the reaction mixture was processed as detailed above the crude product was purified by MPLC on silica gel. There was isolated 59 mg (48%) of **25** as a colorless solid, mp 97–98 °C (from 1:7 ether–hexane): IR ($CHCl_3$, cm^{-1}) 3040, 2950, 1672, 1602, 1452; ^1H NMR (300 MHz, $CDCl_3$) δ 7.41–7.08 (m, 10 H), 2.55–1.01 (series of m, 9 H), 0.71 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 205.26, 140.59, 138.66, 130.62, 128.72, 128.49, 128.41, 127.72, 126.64, 54.62, 47.82, 34.78, 32.35, 27.43, 23.11; MS, m/z (M^+) calcd 320.2140, obsd 320.2159.

Anal. Calcd for $C_{23}H_{28}O$: C, 86.20; H, 8.81. Found: C, 85.93; H, 8.90.

Cleavage Reactions of 16 and 25. Accurately weighed amounts of the appropriate ketone, specific base, and internal standard (n-$C_{15}H_{32}$) were heated to reflux in the solvent indicated in Table II. At appropriate time intervals, an aliquot (ca. 300 μL) was removed, treated with water, and extracted with pentane. The pentane layer was analyzed by capillary GC. The product distributions are based on the calibrated response factors of **26** and **27** as determined separately with authentic samples. In several instances, yields derived in this manner were checked with actual isolated yields.

Acknowledgment. The financial support for this research was provided by the National Science Foundation.

Registry No. **1**, 85221-99-4; (±)-**2**, 110458-32-7; (±)-**2** (alcohol), 116404-31-0; (*R*,*R*)-**3**, 116350-10-8; (*R*,*S*)-**3**, 116350-09-5; (+)-**4**, 110458-35-0; (−)-**4**, 110458-34-9; (−)-**6**, 110458-36-1; (+)-**7**, 110508-59-3; (−)-**8**, 116350-11-9; (+)-**9**, 110458-37-2; (−)-**9**, 116350-14-2; (*R*)-**9** (*R*-alcohol), 116350-13-1; (*R*)-**9** (*S*-alcohol), 116350-12-0; (+)-**10**, 110458-38-3; (−)-**10**, 116350-15-3; (−)-**11**, 86505-50-2; **12**, 98-53-3; **13**, 17807-26-0; **14**, 21024-55-5; **15**, 53400-31-0; **16**, 116350-16-4; (±)-**16** (alcohol), 116350-18-6; **17**, 77691-47-5; **18**, 116350-17-5; **21**, 758-75-8; **22**, 52866-66-7; **23**, 52866-65-6; **24**, 53517-40-1; **25**, 116350-19-7; **28**, 36359-47-4; **27**, 36359-46-3; $PhCH_2COOMe$, 101-41-7; (*R*)-PhCH(OAc)CB_2H, 51019-43-3; (*R*)-PhCH(OAc)COCl, 49845-69-4.