with water and brine, dried, and concentrated. After silica gel chromatography with 4:1 petroleum ether–ethyl acetate as eluent and recrystallization from 95% ethanol, there was obtained 45 mg (12%) of **14** as white crystals, mp 223.5–225 °C; IR (KBr, cm^{-1}) 3010, 2895, 1545, 1465, 1370, 1355, 1330; ^1H NMR (300 MHz, $CDCl_3$) δ 3.68 (m, 4 H), 3.59–3.44 (m, 4 H), 2.64 (m, 2 H), 2.15 (td, J = 2.8, 18 Hz, 2 H); ^{13}C NMR (75 MHz, $CDCl_3$, ppm) 135.70, 102.59, 57.62, 52.83, 44.58, 44.49, 35.73; MS, m/z ($M^+ - 2NO_2$) calcd 281.0052, obsd 218.0083.

Reduction of 14. A solution of **14** (20 mg) in 60% aqueous ethanol (5 mL) was stirred for 1 h at room temperature with sodium borohydride (40 mg). Careful acidification with acetic acid was followed by ethanol removal in vacuo. The residue was extracted with dichloromethane (3 × 20 mL), and the combined organic layers were dried and evaporated. Trituration of the residue with ethyl acetate–petroleum ether afforded 5 mg (30%) of **5**.

2,2,6,6-Tetranitro[4]peristylane (7). To a refluxing suspension of **12** (160 mg, 0.575 mol) in dichloromethane (10 mL) was added under argon a solution of 100% nitric acid (2.0 mL), ammonium nitrate (15 mg, 0.19 mmol), and urea (15 mg, 0.25 mmol) in 5 mL of the same solvent. The solid dissolved immediately, and the solution turned orange. After 1 h at the reflux temperature, the reaction mixture was cooled and washed with ice water and brine. Following drying and solvent removal, the residue was subjected to MPLC on silica gel with dichloromethane as eluant. The first fraction afforded 25.2 mg (13%) of **7**: colorless crystals; mp 219–220 °C dec (from dichloromethane–hexanes); IR (KBr, cm^{-1}) 3010, 2885, 1575, 1565, 1465, 1375, 1330, 1300, 1205, 1120, 855, 835, 800, 790; ^1H NMR (300 MHz, acetone-d_6) δ 3.81 (m, 4 H), 3.58 (m, 4 H), 3.04 (dt, J = 17, 12 Hz, 2 H), 2.36 (dt, J = 17, 2.1 Hz, 2 H); ^{13}C NMR (75 MHz, CD_3COCD_3, ppm) 133.28, 53.64, 45.95, 35.97. Anal. Calcd for $C_{12}H_{12}N_4O_8$: C, 42.36; H, 3.55. Found: C, 42.42; H, 3.74.

Continued elution afforded a second fraction consisting of **5** (13.2 mg, 9.3%), the ^1H and ^{13}C NMR spectra of which were identical with those previously reported.

Finally, a last fraction contained 51.7 mg (34%) of **11**.

Acknowledgment. This research was made possible by the financial support of the U.S. Army Research and Development Command.

Cleavage of Carbon–Carbon Bonds with High Stereochemical Control. 4. Base-Induced Cleavage of Optically Active Nonenolizable Benzylic Ketones[1]

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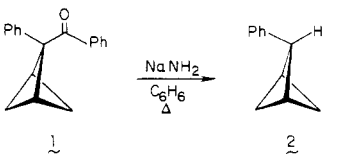
Treatment of the optically active tertiary α-phenyl ketones **9a** and **9b** with amide ion in anhydrous benzene, or with *tert*-butoxide ion in benzene or *tert*-butyl alcohol, results in C–C bond cleavage at the stereogenic center and protonation of the respective benzylic carbanions. These reactions proceed with 44–86% retention of configuration, maximal stereoselectivity materializing when *tert*-butoxide ion was employed. These observations signal that the reactive carbanion intermediates are efficiently captured from the front side as benzoyl is replaced by hydrogen. Use of *t*-BuOD leads to essentially complete d_1 incorporation. The stereoselectivity is reversed when recourse is made to $KOCH_2CH_2OH$ in ethylene glycol solution. Thus, retention is obtained in nonpolar media and inversion is observed in very polar protic media. The factors that underlie this dichotomy are discussed.

The Haller–Bauer reaction, that base-promoted process which results in C–C bond cleavage of nonenolizable ketones,[2] has not yet gained proper consideration as one of the more important degradative reactions in organic chemistry. The simplicity of the process is not at issue, since merely warming the substrate with an amide base[2] or with potassium *tert*-butoxide[3] delivers the product. Rather, the historical evolution of this transformation seems to have clouded its remarkable potential for highly stereocontrolled electrophilic capture. Originally, the Haller–Bauer reaction was designed to serve as a method for the synthesis of aryl amides.[2] More recently, the process has been expanded to constitute a tool for effecting the replacement of a benzoyl group by hydrogen as in the conversion of **1** to **2**.[4]



1 2

During the early development of this transformation, it was noted that C–C bond cleavage understandably holds particular effectiveness when the incipient carbanion is stabilized, e.g., in benzylic[4,5] and cyclopropyl examples.[1c,3b,6] Particularly relevant in this connection is Walborsky's elegant demonstration that anionic centers in three-membered rings generated by the Haller–Bauer method are protonated with retention of configuration.[6a–d] The *inherent mechanistic* significance of these studies was substantively lessened when independent studies revealed that

(1) (a) Paper 3 in this series: Paquette, L. A.; Gilday, J. P.; Ra, C. S.; Hoppe, M. *J. Org. Chem.* **1988**, *53*, 704. (b) Paper 2 in this series: Paquette, L. A.; Gilday, J. P.; Ra, C. S. *J. Am. Chem. Soc.* **1987**, *109*, 6858. (c) Paper 1 in this series: Paquette, L. A.; Uchida, T.; Gallucci, J. C. *Ibid.* **1984**, *106*, 335.

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

(3) (a) Swan, G. A. *J. Chem. Soc.* **1948**, 1408. (b) Gassman, P. G.; Lumb, J. T.; Zalar, F. V. *J. Am. Chem. Soc.* **1967**, *89*, 946. (c) Davies, D. G.; Derenberg, M.; Hedge, P. *J. Chem. Soc.* **1971**, 455.

(4) Alexander, E. C.; Tom, T. *Tetrahedron Lett.* **1978**, 1741.

(5) (a) Cram, D. J.; Langemann, A.; Allinger, J.; Kopecky, K. R. *J. Am. Chem. Soc.* **1959**, *81*, 5740. (b) Calas, M.; Calas, B.; Giral, L. *Bull. Soc. Chim. Fr.* **1976**, 857.

(6) (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. (e) Piehl, F. J.; Brown, W. G. *J. Am. Chem. Soc.* **1953**, *75*, 5023. (f) Hamlin, K. E.; Biermacher, U. *Ibid.* **1955**, *77*, 6376.

0022-3263/88/1953-4972$01.50/0

Table I. Haller–Bauer Cleavage of Optically Active 9b and 9c

expt no.	substr	base	solvent	yield,[a] %	ee, %	average net
1	**9b**[b]	* KO-*t*-Bu	*t*-BuOH, Δ	54–63	31.8–32.6	84% retention
2		** NaO-*t*-Bu	*t*-BuOH, Δ	24–32	34.1–36.4	88% retention
3		** LiO-*t*-Bu	*t*-BuOH, Δ	no cleavage after 80 h of reflux		
4		** KO-*t*-Bu	C_6H_6, Δ	35–45	34.1–34.9	86% retention
5		** KNH_2	C_6H_6, Δ	29–39	18.2–18.3	44% retention
6		* $NaNH_2$	C_6H_6, Δ	43	16.7–17.4	46% retention
7		* $LiNH_2$	C_6H_6, Δ	40–49	20.5–21.2	56% retention
8		** $KOCH_2CH_2OH$	$HOCH_2CH_2OH$, Δ	2–3	15.7–17.0[d]	40% inversion
9	**9c**[c]	$NaNH_2$	C_6H_6, Δ	35–36	21.6–22.0	44% retention
10		KO-*t*-Bu	*t*-BuOH, Δ	57–66	39.9–41.6	82% retention
11		KO-*t*-Bu	C_6H_6, Δ	51–56	28.9–30.5	60% retention
12		$KOCH_2CH_2OH$	$HOCH_2CH_2OH$, Δ	21–24	10.5–10.8[d]	22% inversion

[a] Duplicate experiments at a minimum. [b] Material of either 38% (*) or 40% ee (**). [c] Material of 50% ee. [d] Product of opposite $[\alpha]_D$.

the general inability of cyclopropyl anions to undergo inversion of configuration is intrinsic.[7] More amazing still is the fact that two reports briefly detailing stereochemical retention in open-chain benzylic ketones[5] have been largely ignored.

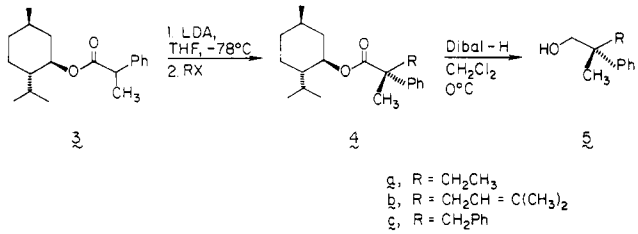
The synthetic advantages offered by any chemical reaction capable of delivering a product with high levels of stereochemical control in a predictable direction need no elaboration here. The preservation of configuration during cleavage of a bond to a stereogenic center under any circumstances holds particular fascination.[8] Motivated by such considerations, we have sought to clarify those stereochemical issues surrounding the classical Haller–Bauer reaction. The configurational consequences associated with acyclic chiral nonracemic ketones constitute the subject matter of this paper.[9] The structural ramifications introduced by five- and six-membered carbocyclic molecules are examined in the accompanying report.[10]

Results

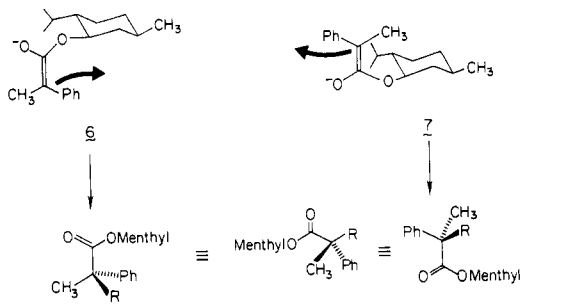
Preparation and Configuration of Starting Materials. Conclusions relating to the stereochemical course of any Haller–Bauer cleavage reaction are strictly dependent on reliable prior knowledge of the absolute configurations of both the starting ketone and hydrocarbon product. Although the phenmenthol controller group is recognized to deliver higher stereoselectivity than menthol,[11] the latter stereocontrol element was utilized here because of its ready availability and low cost and because the levels of stereoinduction realized proved to be adequately high for the present purposes.

Alkylation of the enolate anion of *l*-menthyl ester **3** in turn with ethyl iodide, prenyl bromide, and α-bromotoluene, followed by direct capillary GC analysis of the resulting mixtures showed one diastereomer to predominate in each case (Scheme I). The respective product

Scheme I



Scheme II



distributions were 63:37, 59:41, and 57:43. By means of medium pressure liquid chromatography, it proved possible in the latter two examples to increase the levels of diastereomeric excess to 38% and 50%. Ester **4a** was not processed analogously. Instead, its direct reduction with diisobutylaluminum hydride gave rise to **5a**, the pure *S* enantiomer of which has been earlier reported, $[\alpha]^{25}_D$ +6.80° (neat).[5a] The rotation of the alcohol produced by reduction, $[\alpha]^{25}_D$ −1.77° (neat), clearly showed it to be enriched in the *R* enantiomer as shown.

Since **4a–c** are formed from a common intermediate, the newly introduced stereogenic quaternary centers in all three esters are assumed to be configurationally related. The uniform *R* configuration of the major diastereomers receives convincing additional support from more rapid elution of the dominant ester during MPLC and GC in each series, as well as their consistent conversion to levorotatory alcohols, viz. **5a–c**.

The actual *E*/*Z* distribution within **3**⁻ (Scheme II) is not known. Simple first-order steric considerations favor placing the more bulky phenyl substituent trans to the solvated enolate oxyanion center and orienting the reactive enolate subunit as remote from the isopropyl group as possible. This pair of structural features comes together in **6**. However, the deprotonation may not be fully thermodynamically controlled and consideration need also be given to **7**.[11] Whatever the actual scenario, the predominance of the *R* configuration is consistent with preferential approach of the electrophilic alkylating agent to the less-hindered β surface of the two conformers shown.

(7) (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.; Mullen, K. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 243.

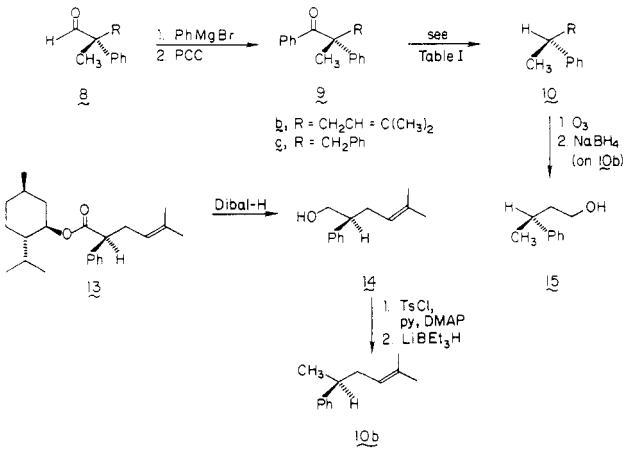
(8) Compare the extensive study by Cram and his co-workers relating to the stereochemistry of the base-catalyzed cleavage reactions of tertiary alcohols: Hoffman, T. D.; Cram, D. J. *J. Am. Chem. Soc.* **1969**, *91*, 1009 and earlier papers in this series.

(9) Reference 1b constitutes a preliminary communication of this investigation.

(10) Paquette, L. A.; Ra, C. S. *J. Org. Chem.*, following paper in this issue.

(11) (a) Meyers, A. I.; Reider, P. *J. Am. Chem. Soc.* **1979**, *101*, 2501. (b) Heathcock, C. H.; Buse, C. T.; Kelschick, W. A.; Pirrung, M. C.; Sohn, J. E.; Lampe, J. *J. Org. Chem.* **1980**, *45*, 1066. (c) Heathcock, C. H.; Pirrung, M. C.; Montgomery, S. H.; Lampe, J. *Tetrahedron* **1987**, *37*, 4087. (d) Evans, D. A.; McGee, L. R. *Tetrahedron Lett.* **1980**, *21*, 3975. (e) Ireland, R. E.; Muller, R. H.; Willard, A. K. *J. Am. Chem. Soc.* **1976**, *98*, 2868.

Scheme III



Ketone Preparation, Haller–Bauer Cleavages, and Product Stereochemistry. Aldehyde **8b**, obtained by pyridinium chlorochromate (PCC) oxidation of **5b**, had earlier been prepared in racemic form by an alternate route.[12] Since no loss of stereochemical integrity was possible in this step, **5c** was identically converted to **8c** and both aldehydes were then transformed into benzoyl compounds **9b** (38% ee) and **9c** (50% ee) by conventional means (Scheme III).

The first cleavage reactions on (*R*)-(−)-**9b** and (*R*)-(−)-**9c** were carried out in refluxing benzene as solvent with amide bases (Table I). These reactions were heterogeneous, circumstances that perhaps contribute in part to a slower reaction rate for lithium amide. Hydrocarbons **10b** and **10c**, ultimately isolated in yields just under 50%, were shown to be optically active. Since both enantiomers of 1,2-diphenylpropane (**10c**) are known,[13] it proved an easy matter to delineate the absolute configuration and enantiomeric excess directly in this instance. With due consideration of the optical purity of **9c** and the recorded $[\alpha]_D$ values for **10c**, the sodium amide promoted cleavage was determined to proceed with a stereochemical outcome of 44% net retention (Table I).

The enantiomeric excess for **10b** was established as follows. The *l*-menthyl ester **13**, available with a diastereomer distribution accurately assayable as 27% de by capillary GC analysis, was reduced to (−)-**14** with diisobutylaluminum hydride. Tosylation of (−)-**14** followed by reduction with lithium triethylborohydride in ether solution at −78 °C gave **10b**, $[\alpha]^{25}_D$ +3.58°, necessarily of 27% ee.

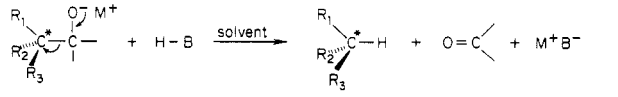
Absolute configurational assignment was subsequently achieved by sequential ozonolysis and sodium borohydride reduction of (+)-**10b** to give (*S*)-(+)-3-phenyl-1-butanol (**15**). The optically pure (*R*)-(−) enantiomer of **15** has been described previously.[14] Since the Haller–Bauer product was dextrorotatory, its configuration is necessarily *S*, indicating that stereochemical retention had once again prevailed.

A second series of cleavage reactions involved potassium *tert*-butoxide as the base in both *tert*-butyl alcohol and benzene as solvent. The first set of conditions gave rise to a homogeneous reaction mixture and delivered products with high (82–84%) retention of configuration. When the Haller–Bauer process was conducted in refluxing benzene solution, a dropoff in stereoselectivity on the order of 10% was seen in one example only. Notwithstanding, the level of retention observed in this instance still exceeded that seen for the amide bases under entirely comparable circumstances.

The last set of conditions examined involved refluxing ethylene glycol as solvent and its monopotassium salt as base. In the present examples, a *reversal in stereoselectivity* was now noted. While **9b** was cleaved to give predominantly *ent*-**10b** (Table I), **9c** was transformed into *ent*-**10c** at a level equivalent to 22% net inversion.

Discussion

The results summarized in Table I indicate that the particular conditions of reaction play a major role in controlling the stereochemical course of the Haller–Bauer cleavage. Cram and his co-workers have demonstrated that in the cleavage of alkoxides (typified by **16**) the specific solvent is important in determining whether retention, inversion, or racemization operates.[8] Poorly dissociating

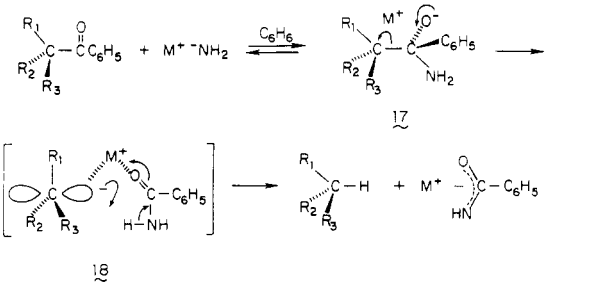


16

solvents such as benzene and *tert*-butyl alcohol are expected to favor intimate product pair formation, a phenomenon that fosters proton capture with retention of configuration. At the other extreme are the strongly dissociating solvents such as ethylene glycol where the intervention of solvent-separated product pairs and a heightened capacity for metal cation solvation combine to promote high levels of inversion.

A distinction unique to Haller–Bauer cleavages resides in the fact that a different leaving group materializes whenever the type of base is altered. While comparable solvent effects are highly likely to surface, the task at hand is to identify and characterize the direction of proton capture. Since fragmentation occurs only when a carbanion stabilizing group is attached to the stereogenic center,[1,2] the evidence is convincing that the carbon–carbon bond is broken and the carbon–hydrogen bond is made in separate steps. It follows, therefore, that discrete high energy intermediates carrying negative charge intervene in these reactions.

The use of amide bases in benzene solution provides opportunity for 1,2-addition to the carbonyl group and production of **17**. The process is very likely reversible,



17

18

but this option is of little, if any, consequence. In benzene, the ensuring *irreversible* bond cleavage is sheathed in solvent and the benzamide leaving group appears to have only a modest chance to escape from the intimate environment of the newly generated carbanion prior to proton transfer. It appears reasonable to assume that protonation as in **18**, a thermodynamically favorable event, is the source of configurationally retained product. Under these cir-

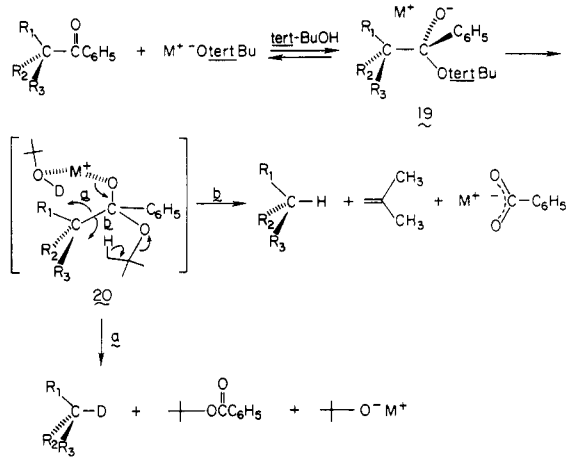
(12) Groenewegen, P.; Kallenberg, H.; Van den Gen, A. *Tetrahedron Lett.* **1978**, 491.

(13) The reported $[\alpha]^{25}_D$ values of this hydrocarbon are (*S*) = +76.7° (*c* 2.3, $CHCl_3$) and (*R*) = −76.3° (*c* 2.0, $CHCl_3$): Barnes, R. A.; Juliano, B. R. *J. Am. Chem. Soc.* **1959**, *81*, 6462.

(14) Cram, D. J. *J. Am. Chem. Soc.* **1952**, *74*, 2137.

cumstances, delivery of a proton via rotation of benzamide on the front face of the carbanion occurs more rapidly than leakage to solvent-separated species. The mechanism(s) underlying inversion and racemization clearly differs from the above, but the present data shed no light on the number of pathways involved and their distinctive characteristics at the molecular level.

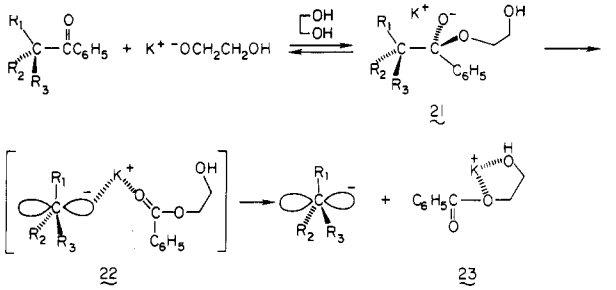
The uniformly highest retention levels are observed with *tert*-butyl alcohol solvent. These results correlate well with the fact that *tert*-butyl alcohol ($\epsilon = 11$) is only slightly more polar than benzene ($\epsilon = 2$). Moreover, the base happens to be soluble in this medium. The fragmentation of **19** to product with frontside protonation can proceed along the reaction channels labeled a and b in **20**. Significantly,



capture of the carbanion does not rest on kinetically accelerated intramolecular β-elimination within the *tert*-butoxy group (path b). Although in this instance two products, viz., the hydrocarbon and isobutylene, are nonpolar, the dissociation of **20** into three components appears to be a high energy process in this medium and represents at best only a very small segment of the total reaction profile. That path a is strongly favored was determined by performing the cleavage of ketone **9a** with KO-*t*-Bu in *t*-BuOD (99% d_1). Under these conditions, hydrocarbon **10a** incorporated 96% deuterium. The $[\alpha]_D$ values indicated the stereochemical course of deuteron transfer to be largely unaffected relative to its proton counterpart. Consequently, deuterium is transferred at the level of 84–86% selectivity with retention of configuration.

Our studies have indicated that potassium and sodium amides in benzene are significantly more reactive toward **9a** than is lithium amide. The reaction times necessary to consume **9a** totally were 12, 18, and 30 h, respectively. Since these particular reactions are heterogeneous, counterion influences under homogeneous conditions were also examined. The data recorded for the three alkali metal *tert*-butoxides in *tert*-butyl alcohol confirm that cations do indeed play an important kinetic role in Haller-Bauer reactions. The lack of cleavage with LiO-*t*-Bu again points to a reactivity order of $K^+ > Na^+ > Li^+$, as observed elsewhere in a different context.[15] Interestingly, the level of stereochemical retention reaches a maximum when Li^+ is present, suggesting that the small ionic radius of lithium and the low-level shielding of its positive charge combine to make the Li^+–O bond stronger than that between K^+–O or Na^+–O. As a result, benzamide is held somewhat more tightly in intimate product pair **18** and frontside protonation is enhanced.

In the dissociating solvent ethylene glycol ($\epsilon = 35$), the solvent-separated product pair **22** that results from bond rupture within **21** is redirected away from frontside protonation by the solvating power of the strategically positioned hydroxyl group.[16] In this instance, the metal ion is evidently complexed more tightly as in **23**. The effect



on the carbanion intermediate is net steric shielding of that surface that would lead to retention. Thus, inversion is the dominant pathway because protonation by solvent from the less-hindered surface of the carbanion is now kinetically favored.

The companion paper examines the sum of the effects discussed above as they operate in cyclic systems.[10] The consequences associated with the replacement of phenyl by other carbanion-stabilizing groups on the stereochemistry of Haller–Bauer reactions will be reported elsewhere in the near future.

Experimental Section

***l*-Menthyl 2-Phenylpropanoate (3).** Racemic 2-phenylpropanoic acid (Aldrich, 10.0 g, 66.6 mmol) was dissolved in benzene (10 mL) containing thionyl chloride (13.0 g, 110 mmol). The mixture was stirred at room temperature for 30 min and then warmed slowly to reflux for 2 h. The benzene and excess thionyl chloride were removed by distillation to leave a dark red oil. Distillation gave the acid chloride as a pale pink liquid, bp 118–121 °C at 23 Torr (9.89 g, 88%).

l-Menthol (9.07 g, 58.0 mmol), pyridine (5.0 mL, 62 mmol), and 4-(dimethylamino)pyridine (50 mg) were dissolved in dichloromethane (100 mL) and cooled to 0 °C. 2-Phenylpropanoyl chloride (9.89 g, 58.7 mmol) in dichloromethane (30 mL) was introduced dropwise over 10 min and the magnetically stirred solution was allowed to warm to room temperature during 4 h. The mixture was poured into water (50 mL), and the separated organic phase was washed with water and brine, dried, and evaporated. Filtration of the residue through silica gel (elution with 3% ethyl acetate in petroleum ether) gave **3** as a colorless oil (15.83 g, 95%): IR (neat, cm^{-1}) 3090, 3070, 2960, 2930, 2870, 1725, 1490, 1455, 1205, 1170; ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.20 (m, 5 H), 4.75–4.55 (9 lines, 1 H), 3.75–3.65 (overlapping q, $J = 7.2$ Hz, 2 × 0.5 H), 2.05–1.95 (m, 0.5 H), 1.47 (d, $J = 7.2$ Hz, 1.5 H), 1.46 (d, $J = 7.2$ Hz, 1.5 H), 1.9–1.15 (m, 5.5 H), 1.15–0.9 (m, 3), 0.87, 0.86, 0.85, 0.70, 0.67, 0.50 (series of d, 1.5 H); MS, m/z (M^+ – methene) calcd 150.0681, obsd 150.0749; $[\alpha]^{23}_D$ −70.2° (*c* 12.3, $CHCl_3$).

***l*-Menthyl 2,5-Dimethyl-2-phenyl-4-hexenoate (4b).** Ester **3** (6.0 g, 20.8 mmol) was added dropwise to a magnetically stirred solution of lithium diisopropylamide (25 mmol) in anhydrous tetrahydrofuran (30 mL) cooled to −78 °C. The mixture was stirred at this temperature for 30 min before prenyl bromide (3.28 g, 22 mmol) was introduced, allowed to warm to room temperature overnight, and poured into saturated ammonium chloride solution (100 mL). The product was extracted into ether (150 mL) and the organic phase was washed with ammonium chloride solution, water, and brine. The combined aqueous washings were further extracted with ether (30 mL). The combined ether solutions were dried and evaporated to leave an orange oil, chromatography of which on silica gel (elution with 2% ethyl acetate in petroleum

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

(16) Cram, D. J.; Hauck, F.; Kopecky, K. R.; Nielsen, W. D. *J. Am. Chem. Soc.* **1959**, *81*, 5767.

ether) gave a 59:41 mixture of diastereomers of **4b** (5.96 g, 80%): IR (film, cm^{-1}) 2960, 2930, 2870, 1722, 1455, 1230.

For the major isomer: ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.18 (m, 5 H), 4.97 (t, J = 6.9 Hz, 1 H), 4.62 (m, 1 H), 2.75 (dd, J = 15.0, 6.8 Hz, 1 H), 2.62 (dd, J = 15.0, 6.9 Hz, 1 H), 1.95 (d, J = 6.1 Hz, 1 H), 1.67–1.45 (m, 4 H), 1.65 (s, 3 H), 1.57 (s, 3 H), 1.49 (s, 3 H), 1.26 (t, J = 10.8 Hz, 1 H), 0.86 (d, J = 6.5 Hz, 3 H), 0.72 (d, J = 6.9 Hz, 3 H), 0.61 (d, J = 6.9 Hz, 3 H), 1.1–0.6 (m, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.56, 143.92, 134.12, 128.04, 126.39, 126.12, 119.99, 74.56, 50.45, 46.99, 40.50, 37.49, 34.31, 31.37, 25.88, 25.60, 23.11, 22.48, 22.01, 20.71, 17.97, 15.54.

For the minor isomer: ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.18 (m, 5 H), 5.02 (t, J = 6.8 Hz, 1 H), 4.64 (m, 1 H), 2.80 (dd, J = 15.0, 6.8 Hz, 1 H), 2.55 (dd, J = 15.0, 6.8 Hz, 1 H), 1.95 (d, J = 6.1 Hz, 1 H), 1.67 (s, 3 H), 1.67–1.45 (m, 4 H), 1.59 (s, 3 H), 1.49 (s, 3 H), 1.26 (t, J = 10.8 Hz, 1 H), 1.1–0.6 (m, 3 H), 0.86 (d, J = 6.5 Hz, 3 H), 0.73 (d, J = 6.0 Hz, 3 H), 0.62 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.36, 144.15, 134.28, 127.97, 126.29, 126.04, 119.91, 74.51, 50.57, 47.03, 40.42, 37.20, 34.31, 31.37, 25.93, 25.72, 23.16, 22.99, 22.01, 20.71, 18.06, 15.89.

For the mixture: MS, m/z (M^+) calcd 356.2715, obsd 356.2758; $[\alpha]^{23}_D$ −59.80° (c 7.2, $CHCl_3$).

Anal. Calcd for $C_{24}H_{36}O$: C, 80.85; H, 10.18. Found: C, 80.41; H, 10.14.

***l*-Menthyl 2-Methyl-2-phenylbutanoate (4a).** In the same way, the enolate generated from **3** (0.95 g, 3.3 mmol) was treated with ethyl iodide to yield **4a** as a 63:37 mixture of diastereomers (1.04 g, 98%).

For the major diastereomer: ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.18 (m, 5 H), 4.60 (td, J = 10.8, 4.6 Hz, 1 H), 2.17–1.20 (m, 8 H), 1.51 (s, 3 H), 1.1–0.5 (m, 6 H), 0.86 (d, J = 6.4 Hz, 3 H), 0.73 (d, J = 7.0 Hz, 3 H), 0.61 (d, J = 6.9 Hz, 3 H).

For the minor diastereomer: ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.18 (m, 5 H), 4.62 (m, 1 H), 2.17–1.20 (series of m, 8 H), 1.51 (s, 3 H), 1.1–0.5 (m, 6 H), 0.84 (d, J = 6.5 Hz, 3 H), 0.73 (d, J = 7.0 Hz, 3 H), 0.61 (d, J = 6.9 Hz, 3 H).

For the mixture: $[\alpha]^{23}_D$ −59.2° (c 6.4, $CHCl_3$).

***l*-Menthyl 2,3-Diphenyl-2-methylpropanoate (4c).** In the manner described above, the enolate of **3** (6.0 g, 20.8 mmol) was quenched with benzyl bromide (3.76 g, 22 mmol) and worked up to give **4c** as a 57:43 mixture of diastereomers (7.07 g, 90%).

For the major isomer: ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.15 (m, 8 H), 6.88–6.82 (m, 2 H), 4.63 (td, J = 10.8, 6.4 Hz, 1 H), 3.34 (d, J = 13.4 Hz, 1 H), 3.23 (d, J = 13.4 Hz, 1 H), 2.0–1.95 (m, 1 H), 1.45 (s, 3 H), 1.7–1.2 (m, 5 H), 1.1–0.7 (m, 3 H), 0.88 (d, J = 6.5 Hz, 3 H), 0.67 (d, J = 7.0 Hz, 3 H), 0.58 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.58, 142.91, 137.58, 130.61, 127.99, 127.55, 126.64, 126.51, 126.17, 74.83, 51.02, 47.06, 45.57, 40.64, 34.30, 31.39, 25.63, 23.23, 22.00, 21.23, 20.59, 15.94; MS, m/z (M^+) calcd 378.2559, obsd 378.2591.

For the minor isomer: ^1H NMR (300 MHz, $CDCl_3$) δ 7.34–7.15 (m, 8 H), 6.95–6.90 (m, 2 H), 4.65 (m, 1 H), 3.49 (d, J = 13.6 Hz, 1 H), 3.12 (d, J = 13.6 Hz, 1 H), 2.0–1.95 (m, 1 H), 1.7–1.2 (m, 5 H), 1.46 (s, 3 H), 1.1–0.7 (m, 3 H), 0.87 (d, J = 6.5 Hz, 3 H), 0.74 (d, J = 7.0 Hz, 3 H), 0.62 (d, J = 6.9 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 175.23, 143.54, 137.58, 130.61, 128.11, 127.64, 126.64, 126.51, 126.30, 74.83, 51.25, 46.97, 45.23, 40.35, 34.30, 31.39, 25.63, 23.11, 22.00, 21.23, 20.78, 15.94.

(*R*)-(−)-2-Methyl-2-phenyl-1-butanol (5a). A cold (0 °C), magnetically stirred solution of **4a** (545 mg, 1.7 mmol) in dichloromethane (10 mL) was treated with diisobutylaluminum hydride (5 mL of 1 M in hexane, 5.0 mmol) and stirred at 0 °C for 1 h. Ether (20 mL) was added and the excess Dibal-H was quenched with methanol (1 mL) and sodium potassium tartrate solution at room temperature for 1 h. The organic layer was separated, washed with brine (2 × 20 mL), dried, and evaporated. Purification of the residue by MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether) gave **5a** as a colorless oil (251 mg, 89%): ^1H NMR (300 MHz, $CDCl_3$) δ 7.31–7.11 (m, 5 H), 3.64 (d, J = 10.8 Hz, 1 H), 3.46 (d, J = 10.8 Hz, 1 H), 1.74 (sextet, J = 7.5 Hz, 1 H), 1.50 (sextet, J = 7.5 Hz, 1 H), 1.28 (s, 1 H), 1.26 (s, 3 H), 0.66 (t, J = 7.4 Hz, 3 H); MS, m/z calcd 164.1201, obsd 164.1203; $[\alpha]^{25}_D$ −1.77° (neat).

(*R*)-(−)-2,5-Dimethyl-2-phenyl-4-hexen-1-ol (5b). A 2.04-g (5.72 mmol, 38% de) sample of **4b** was reduced with Dibal-H (14 mmol) in dichloromethane (20 mL) as described above to provide 1.03 g (88%) of **5b** as a colorless oil: IR (film, cm^{-1}) 3490, 2970, 2920, 1495, 1445, 1380; ^1H NMR (300 MHz, $CDCl_3$) δ 7.38–7.19 (m, 5 H), 4.95 (ddq, J = 6.9, 6.9, 0.5 Hz, 1 H), 3.74 (d, J = 11.0 Hz, 1 H), 3.59 (d, J = 11.0 Hz, 1 H), 2.39 (dd, J = 13.2, 6.9 Hz, 1 H), 2.33 (dd, J = 13.2, 6.9 Hz, 1 H), 1.63 (d, J = 0.5 Hz, 3 H), 1.58 (s, 3 H), 1.35 (s, 1 H), 1.32 (s, 3 H); MS, m/z (M^+) calcd 204.1514, obsd 204.1526; $[\alpha]^{24}_D$ −7.48° (c 6.4, $CHCl_3$), $[\alpha]_{578}$ −7.65°, $[\alpha]_{546}$ −8.7°, $[\alpha]_{436}$ −15.4°, $[\alpha]_{365}$ −25.6°.

(*R*)-(−)-2,3-Diphenyl-2-methylpropanol (5c). Treatment of **4c** (1.71 g, 4.52 mmol, 50% de) with Dibal-H (12.0 mmol) as above afforded **5c** (822 mg, 80%) as a colorless oil after MPLC on silica gel (elution with 15% ethyl acetate in petroleum ether): IR (CH_2Cl_2, cm^{-1}) 3610, 2970, 2940, 2880, 1495; ^1H NMR (300 MHz, $CDCl_3$) δ 7.50–7.25 (m, 8 H), 7.01–6.98 (m, 2 H), 3.84 (d, J = 11.1 Hz, 1 H), 3.64 (d, J = 11.1 Hz, 1 H), 2.96 (s, 2 H), 1.37 (s, 1 H), 1.28 (s, 3 H); MS, m/z calcd 226.1358, obsd 226.1363; $[\alpha]^{25}_D$ −32.6° (c 1.7, $CHCl_3$), $[\alpha]_{578}$ −34.1°, $[\alpha]_{546}$ −39.2°, $[\alpha]_{436}$ −72.7°, $[\alpha]_{365}$ −128.5°.

(*R*)-(−)-2,5-Dimethyl-2-phenyl-4-hexenal (8b). Pyridinium chlorochromate (2.85 g, 13.3 mmol) was slurried in dichloromethane (10 mL) and cooled to 0 °C during the addition of **5b** (102 mg, 5.0 mmol). The reaction mixture was stirred at 0 °C for 45 min, filtered through Celite and silica gel, and evaporated. Purification of the residue by silica gel chromatography (elution with 3% ethyl acetate in petroleum ether) gave **8b** as a colorless oil (736 mg, 73%): IR (film, cm^{-1}) 2980, 2925, 2915, 1725, 1495, 1445, 1375; ^1H NMR (300 HMz, $CDCl_3$) δ 9.53 (d, J = 2.2 Hz, 1 H), 7.40–7.25 (m, 5 H), 4.97–4.92 (m, 1 H), 2.70–2.55 (m, 2 H), 1.65 (s, 3 H), 1.56 (s, 3 H), 1.42 (d, J = 2.2 Hz, 3 H); MS, m/z calcd 202.1358, obsd 202.1322; $[\alpha]^{23}_D$ −15.3° (c 7.3, $CHCl_3$), $[\alpha]_{578}$ −16.0°, $[\alpha]_{546}$ −18.3°, $[\alpha]_{436}$ −32.9°, $[\alpha]_{365}$ −54.5°.

(*R*)-(−)-2,3-Diphenyl-2-methylpropanal (8c). An 820-mg (3.63 mmol) sample of **5c** was treated with PCC (1.51 g) in the predescribed manner to furnish 672 mg (83%) of **8c** as a colorless oil: IR (film, cm^{-1}) 3060, 2975, 2910, 2800, 2705, 1720, 1600, 1495, 1455, 1445; ^1H NMR (300 MHz, $CDCl_3$) δ 9.62 (s, 1 H), 7.39–7.30 (m, 3 H), 7.19–7.10 (m, 5 H), 6.80–6.77 (m, 2 H), 3.22 (d, J = 13.6 Hz, 1 H), 3.16 (d, J = 13.6 Hz, 1 H), 1.37 (s, 3 H); MS, m/z (M^+) calcd 224.1201, obsd 224.1203; $[\alpha]^{25}_D$ −74.3° (c 4.1, $CHCl_3$), $[\alpha]_{578}$ −78.0°, $[\alpha]_{546}$ −90.3°, $[\alpha]_{436}$ −175.3°, $[\alpha]_{365}$ −347.8°.

Anal. Calcd for $C_{16}H_{16}O$: C, 85.68; H, 7.19. Found: C, 85.35; H, 7.22.

(*R*)-(−)-2,5-Dimethyl-1,2-diphenyl-4-hexen-1-one (9b). A solution of (−)-**8b** (736 mg, 3.64 mmol) in ether (25 mL) was cooled to −78 °C, treated dropwise with ethereal phenylmagnesium bromide solution (2.8 M, 5.0 mmol), and stirred at −78 °C for 1 h. Saturated ammonium chloride solution was added and the reaction mixture was allowed to warm to room temperature during 2 h and diluted with ether and saturated ammonium chloride solution. The separated organic layer was washed with ammonium chloride solution, water, and brine prior to drying. Solvent evaporation left the alcohol as a yellow oil which was directly oxidized with PCC in the manner described above. Silica gel chromatography (elution with 2% ethyl acetate in petroleum ether) gave **9b** as a colorless oil (659 mg, 65% overall): IR (film, cm^{-1}) 3030, 2985, 2925, 2850, 1675, 1600, 1495, 1375, 1245; ^1H NMR (300 MHz, $CDCl_3$) δ 7.44–7.18 (m, 10 H), 4.89 (m, 1 H), 2.84 (dd, J = 14.2, 7.8 Hz, 1 H), 2.68 (dd, J = 14.2, 7.0 Hz, 1 H), 1.61 (d, J = 0.6 Hz, 3 H), 1.55 (s, 3 H), 1.37 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 203.16, 144.04, 137.10, 134.34, 131.20, 129.31, 128.69, 127.70, 126.64, 126.22, 119.39, 55.02, 38.16, 25.78, 24.06, 17.55; MS, m/z (M^+) calcd 278.1671, obsd 278.1669; $[\alpha]^{23}_D$ −33.3° (c 1.7, $CHCl_3$), $[\alpha]_{578}$ −35.1°, $[\alpha]_{546}$ −40.9°, $[\alpha]_{436}$ −82.6°.

Anal. Calcd for $C_{20}H_{22}O$: C, 86.28; H, 7.97. Found: C, 86.04; H, 7.94.

(*R*)-(−)-2-Methyl-1,2,3-triphenyl-1-propanone (9c). A 670-mg (3.0 mmol) sample of **8c** was treated with phenyllithium (1.4 M in cyclohexane/ether, 4.2 mmol) in a manner paralleling that described above. The resulting pale yellow oil (902 mg, 2.98 mmol) was directly oxidized with PCC (1.65 g) according to the established procedure to yield after silica gel chromatography (elution with 2.5% ethyl acetate in petroleum ether) 666 mg (75%) of **9c** of 50% ee as a colorless oil that solidified on standing, mp 66.5–69 °C. The racemic ketone exhibits mp 99.5–100 °C (from dichloromethane–petroleum ether): IR (CH_2Cl_2, cm^{-1}) 3045, 3030, 3015, 1675, 1600, 1580, 1495, 1445, 1245; ^1H NMR (300 MHz,

Table II. Yield and Optical Rotation Data

expt no.[a]	run no.	yield, %	optical rotation
1	A	63	$[\alpha]^{25}_D$ +4.2° (*c* 1.2, $CHCl_3$)
	B	54	$[\alpha]^{25}_D$ +4.3° (*c* 0.8, $CHCl_3$)
2	A	24	$[\alpha]^{25}_D$ +4.5° (*c* 0.9, $CHCl_3$)
	B	32	$[\alpha]^{25}_D$ +4.8° (*c* 1.0, $CHCl_3$)
3	no cleavage		
4	A	45	$[\alpha]^{25}_D$ +4.6° (*c* 1.3, $CHCl_3$)
	B	35	$[\alpha]^{25}_D$ +4.5° (*c* 1.0, $CHCl_3$)
5	A	39	$[\alpha]^{25}_D$ +2.4° (*c* 1.0, $CHCl_3$)
	B	29	$[\alpha]^{25}_D$ +2.4° (*c* 0.8, $CHCl_3$)
6	A	42	$[\alpha]^{25}_D$ +2.2° (*c* 1.0, $CHCl_3$)
	B	42	$[\alpha]^{25}_D$ +2.3° (*c* 0.4, $CHCl_3$)
7	A	49	$[\alpha]^{25}_D$ +2.8° (*c* 1.6, $CHCl_3$)
	B	40	$[\alpha]^{25}_D$ +2.7° (*c* 0.8, $CHCl_3$)
8	A	2	$[\alpha]^{23}_{365}$ −8.2° (*c* 0.1, $CHCl_3$)
	B	2	$[\alpha]^{23}_{365}$ −8.8° (*c* 0.1, $CHCl_3$)
9	A	35	$[\alpha]^{25}_D$ +16.6° (*c* 1,2, $CHCl_3$)
	B	36	$[\alpha]^{25}_D$ +16.9° (*c* 1.0, $CHCl_3$)
10	A	66	$[\alpha]^{25}_D$ +31.9° (*c* 2.7, $CHCl_3$)
	B	57	$[\alpha]^{25}_D$ +30.6° (*c* 2.1, $CHCl_3$)
11	A	56	$[\alpha]^{25}_D$ +22.2° (*c* 1.7, $CHCl_3$)
	B	51	$[\alpha]^{25}_D$ +23.3° (*c* 1.3, $CHCl_3$)
12	A	24	$[\alpha]^{25}_D$ −8.0° (*c* 0.3, $CHCl_3$)
	B	21	$[\alpha]^{25}_D$ −8.3° (*c* 0.7, $CHCl_3$)
13[b]	A	48	$[\alpha]^{25}_D$ +4.6° (*c* 2.0, $CHCl_3$)
	B	41	$[\alpha]^{25}_D$ +4.6° (*c* 2.1, $CHCl_3$)

[a] The numbers correspond to those in Table I. [b] Experiment involving KO-*t*-Bu/*t*-BuOD.

$CDCl_3$) δ 7.46–7.05 (m, 13 H), 6.62–6.59 (dd, *J* = 7.4, 1.5 Hz, 2 H), 3.32 (s, 2 H), 1.52 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 202.83, 142.78, 137.31, 136.84, 131.32, 130.73, 129.48, 128.55, 127.77, 127.31, 126.81, (2C), 125.99, 55.34, 46.38, 22.48; MS, *m/z* (M^+) calcd 300.1514, obsd 300.1490.

Anal. Calcd for $C_{22}H_{20}O$: C, 87.96; H, 6.71. Found: C, 87.64; H, 6.64.

Haller–Bauer Cleavages. Ketone **9b** or **9c** (40–70 mg) was dissolved in the reaction solvent (benzene or *tert*-butyl alcohol, 4 mL) and the base (potassium amide, sodium amide, lithium amide, or potassium *tert*-butoxide, 10–15 equiv) was introduced. The mixture was heated at the reflux temperature under nitrogen for 12–30 h, allowed to cool, and diluted with pentane (20 mL). The organic solution was washed with brine, dried, and evaporated at 0 °C to leave ca. 2 mL of solution. The product was isolated by preparative gas chromatography in the yields and optical purities described in Table II.

A solution of potassium ethylene glycolate in ethylene glycol (0.49 M) was prepared from ethylene glycol (freshly distilled from sodium) and potassium *tert*-butoxide according to the method of Cram.[17] All products were at least 99.5% pure by capillary GC and/or packed GC analysis. For the capillary work, a Carlo Erba Model 4130 instrument equipped with a 30 m × 0.25 mm Durabond DB5 (J and W Co.) column was employed (13:1 split injection, helium flow rate of 2 mL/min, 100 °C, FID detector). The packed GC work was performed on a Varian 3000 instrument equipped with a 1.7 m × 3 mm column of 3% OV-101 on 100/120-mesh Gaschrom and FID detector (He flow rate of 30 mL/min).

For **10b**: packed column, inject at 200 °C; column at 130 °C for 5 min → 220 °C at 10 °C/min; t_R 1.9 min (ketone **9b** has t_R 13.4 min). Capillary column: inject at 170 °C; column at 130 °C, t_R 4.4 min.

For **10c**: packed column, inject at 220 °C; column at 150 °C for 5 min → 250 °C at 10 °C/min; t_R 2.8 min (ketone **9c** has t_R 14.2 min).

Capillary column: inject at 200 °C; column at 150 °C; retention time 7.1 min.

A. 2-Methyl-5-phenyl-2-hexene (10b): ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.14 (m, 5 H), 5.08 (t, *J* = 7.1 Hz, 1 H), 2.78–2.65 (sextet, 1 H), 2.32–2.19 (m, 2 H), 1.66 (s, 3 H), 1.55 (s, 3 H), 1.23 (d, *J* = 7.0 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 147.61, 132.37, 128.19, 126.99, 125.76, 122.94, 40.34, 36.90, 25.73, 21.37, 17.78; MS, *m/z* (M^+) calcd 174.1408, obsd 174.1417.

B. 1,2-Diphenylpropane (10c): ^1H NMR (300 MHz, $CDCl_3$) δ 7.29–7.06 (m, 10 H), 3.03–2.91 (m, 2 H), 2.76 (dd, *J* = 12.6, 7.7 Hz, 1 H), 1.23 (d, *J* = 6.8 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) ppm 146.98, 140.81, 129.14, 128.27, 128.07, 127.03, 125.98, 125.81, 45.08, 41.86, 21.16; MS, *m/z* (M^+) calcd 196.1252, obsd 196.1249.

***l*-Menthyl 2-Phenyl-5-methyl-4-hexenoate (13).** *l*-Menthyl phenylacetate (2.30 g, 8.4 mmol) dissolved in anhydrous tetrahydrofuran (3 mL) was added dropwise to a magnetically stirred solution of lithium diisopropylamide (10.0 mmol) in the same solvent (10 mL) at −78 °C. After 30 min, prenyl bromide (1.2 mL, 11 mmol) was introduced. Ten minutes later, the cooling bath was removed and the solution allowed to warm to room temperature over 1 h. The reaction mixture was diluted with petroleum ether (100 mL) and saturated ammonium chloride solution (50 mL). The separated organic phase was washed with ammonium chloride solution (50 mL) and brine (3 × 50 mL), dried, and evaporated. Column chromatography of the residual yellow oil (silica gel, elution with 1% ethyl acetate in petroleum ether) gave **13** (2.45 g, 85%) as a 46:54 mixture of diastereomers (capillary GC analysis). HPLC with peak shaving gave material having a 63.5:36.5 (27% de) proportion of isomers (1.02 g, 36%) as a colorless oil: IR (film, cm^{-1}) 3060, 2950, 2920, 2865, 1723, 1450; ^1H NMR (300 MHz, C_6D_6) δ peaks characteristic of the major isomer 1.61 (d, *J* = 0.6 Hz, 1 H), 1.53 (s, 3 H), 0.87 (d, *J* = 7.0 Hz, 3 H), 0.84 (d, *J* = 7.0 Hz, 3 H), 0.63 (d, *J* = 6.5 Hz, 3 H); for the minor isomer 1.57 (d, *J* = 0.7 Hz, 3 H), 1.50 (s, 3 H), 0.73 (d, *J* = 6.5 Hz, 3 H), 0.69 (d, *J* = 7.0 Hz, 3 H), 0.63 (d, *J* = 7.0 Hz, 3 H); MS, *m/z* (M^+ − menthene) calcd 204.1150, obsd 204.1132; $[\alpha]^{25}_D$ −45.3° (*c* 3.5, C_6H_6).

(*S*)-(+)-2-Phenyl-5-methyl-4-hexenol (14). Ester **13** (460 mg, 1.33 mmol, 27% de) was dissolved in dichloromethane (10 mL) and cooled to 0 °C. Diisobutylaluminum hydride (1.0 M in hexanes, 5 mmol) was introduced and the mixture was stirred at 0 °C for 1 h. Methanol (1 mL), ether (50 mL), and saturated sodium potassium tartrate solution (10 mL) were added and the resulting two-phase mixture was stirred until clear (3 h at room temperature). The ether layer was separated, washed with brine, dried, and evaporated to leave a colorless oil. Purification by MPLC on silica gel (elution with 10% ethyl acetate in petroleum ether) gave **14** as a colorless oil (221 mg, 87%): IR (film, cm^{-1}) 3480, 3080, 3060, 3020, 2960, 2915, 1490, 1450, 1375; ^1H NMR (300 MHz, $CDCl_3$) δ 7.35–7.21 (m, 5 H), 5.08 (t, *J* = 7 Hz, 1 H), 3.78 (m, 2 H), 2.82 (m, 1 H), 2.43 (m, 1 H), 2.27 (m, 1 H), 1.65 (s, 3 H), 1.58 (s, 3 H), 1.43 (s, 1 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 142.60, 132.77, 128.35, 127.93, 126.43, 122.01, 66.74, 48.77, 30.95, 25.54, 17.64; MS, *m/z* (M^+) calcd 190.1357, obsd 190.1369; $[\alpha]^{25}_D$ +4.2° (*c* 4.8, $CHCl_3$).

(*S*)-(+)-2-Methyl-5-phenyl-2-hexene (10b). Alcohol **14** (124 mg, 0.65 mmol), *p*-toluenesulfonyl chloride (153 mg, 0.8 mmol), 4-(dimethylamino)pyridine (10 mg), and pyridine (0.5 mL) were dissolved in dichloromethane (5 mL) and stirred at room temperature for 16 h. The mixture was extracted with ether, washed with brine, dried, and evaporated. purification of the residue by MPLC on silica gel (elution with 15% ethyl acetate in petroleum ether) afforded the tosylate as a colorless viscous oil (169 mg, 75%): IR (film, cm^{-1}) 3030, 2960, 2910, 2850, 1600, 1495, 1455, 1360; ^1H NMR (300 MHz, $CDCl_3$) δ 7.63 (d, *J* = 8.3 Hz, 2 H), 7.27–7.18 (m, 5 H), 7.06 (dd, *J* = 7.5, 1.5 Hz, 2 H), 4.93 (t, *J* = 7.7 Hz, 1 H), 4.14 (m, 2 H), 2.92 (m, 1 H), 2.43 (s, 3 H on top of a m, 1 H), 2.26 (m, 1 H), 1.61 (s, 3 H), 1.51 (s, 3 H); ^{13}C NMR (20 MHz, $CDCl_3$) ppm 144.36, 140.58, 133.71, 133.22, 130.13, 129.58, 128.31, 127.70, 126.75, 120.71, 73.14, 45.28, 30.60, 25.48, 21.43, 17.65; MS, *m/z* (M^+ − TsOH) calcd 172, obsd 172; $[\alpha]^{24}_D$ +1.0° (*c* 3.8, $CHCl_3$).

The above tosylate (169 mg, 0.49 mmol) was dissolved in anhydrous tetrahydrofuran (25 mL) and cooled to −78 °C. Super-Hydride (Aldrich, 3.0 mL of 1.0 M in THF, 3.0 mmol) was introduced and the stirred solution was allowed to warm to room temperature overnight. The mixture was extracted with pentane, washed with water and brine, dried, and evaporated at 0 °C to leave ca. 2 mL of solution. Preparative GC gave **10b** (44.3 mg, 52%) having the identical spectral properties as **10b**: $[\alpha]^{25}_D$ +3.58° (*c* 2.3, $CHCl_3$).

Degradation of (*S*)-(+)-10a to (*S*)-(+)-3-Phenyl-1-butanol (15). A solution of (*S*)-(+)-**10b** (10 mg, 0.06 mmol) in methanol (2 mL) was cooled to −78 °C and ozonolyzed until a blue color

(17) Cram, D. J.; Langemann, A.; Hauck, F. *J. Am. Chem. Soc.* **1959**, *81*, 5750.

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, $CDCl_3$).

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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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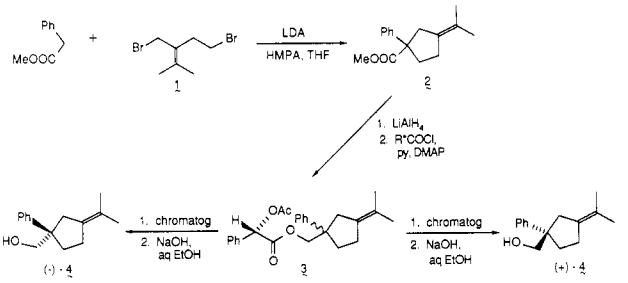
The Haller–Bauer cleavages of three ketones, (*R*)-(+)-3-benzoyl-3-phenyl-1-isopropylidinecyclopentane (**9**) and the *cis*- and *trans*-1-benzoyl-1-phenyl-4-*tert*-butylcyclohexanes (**16** and **25**), have been studied with different base and solvent systems. Whereas the fragmentation profile of **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.

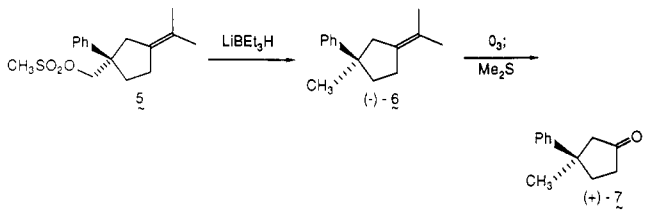
In the preceding paper,[1] the stereochemical course of the Haller–Bauer cleavage of a pair of representative chiral (nonracemic), nonenolizable, *open-chain* benzylic ketones was systemically studied. Moderate levels of retention were observed when the dissociating power of the solvent was low as in 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.

0022-3263/88/1953-4978$01.50/0