Hz, 3 H), 0.70–0.60 (m, 1 H), –0.03 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) 131.06, 125.25, 30.31, 25.77, 20.80, 17.75, 14.18, –3.12 ppm; MS m/z (M^+) calcd 170.1491, obsd 170.1502.

Experiment 1 ($NaNH_2$): 9% yield, $[\alpha]^{25}_{365}$ +9.6° (*c* 0.3, CH_2Cl_2). Experiment 2 ($NaNH_2$): 8% yield, $[\alpha]^{25}_{365}$ +9.6° (*c* 0.2, CH_2Cl_2). Experiment 3 (KNH_2): 14% yield, $[\alpha]^{25}_{365}$ +8.5° (*c* 0.9, CH_2Cl_2). Experiment 4 (KNH_2): 14% yield, $[\alpha]^{25}_{365}$ +8.6° (*c* 0.6, CH_2Cl_2).

C. (*R*)-(+)-1-Phenyl-3-(trimethylsilyl)butane (21c): IR (C_6H_6, cm^{-1}) 2850, 1245, 840; ^1H NMR (300 MHz, C_6D_6) δ 7.21–7.07 (m, 5 H), 2.74 (ddd, *J* = 13.5, 10.1, 4.9 Hz, 1 H), 2.44 (ddd, *J* = 13.5, 10.0, 6.9 Hz, 1 H), 1.78 (dddd, *J* = 13.6, 10.1, 6.9, 3.8 Hz, 1 H), 1.37 (dddd, *J* = 13.6, 10.7, 10.0, 4.9 Hz, 1 H), 0.95 (d, *J* = 7.3 Hz, 3 H), 0.59 (ddq, *J* = 10.7, 3.8, 7.3 Hz, 1 H), –0.07 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 143.12, 128.72, 128.62, 125.95, 35.30, 34.25, 19.47, 14.00, –3.24 ppm; MS m/z ($M^+ - CH_3$) calcd 191.1256, obsd 191.1303.

Experiment 1 ($NaNH_2$): 7% yield, $[\alpha]^{21}_D$ +12.1° (*c* 0.3, C_6H_6). Experiment 2 ($NaNH_2$): 16% yield, $[\alpha]^{21}_D$ +12.7° (*c* 0.7, C_6H_6). Experiment 3 (KNH_2): 18% yield, $[\alpha]^{22}_D$ +11.2° (*c* 0.8, C_6H_6). Experiment 4 (KNH_2): 26% yield, $[\alpha]^{21}_D$ +11.8° (*c* 1.2 C_6H_6).

D. (*R*)-(+)-2-(Trimethylsilyl)heptane (21d): IR ($CHCl_3$, cm^{-1}) 2950, 2922, 2850, 1465, 1245, 838; ^1H NMR (300 MHz, C_6D_6) δ 1.55–1.41 (m, 2 H), 1.37–1.08 (series of m, 6 H), 0.94 (dd, *J* = 7.4 Hz, 3 H), 0.89 (t, *J* = 6.9 Hz, 3 H), 0.63–0.53 (m, 1 H), –0.01 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 32.40, 32.16, 28.74, 23.08, 19.89, 14.36, 14.24, –3.09 ppm; MS m/z (M^+) 172.1648, obsd 172.1646.

Experiment 1 ($NaNH_2$): 32% yield, $[\alpha]^{22}_D$ +28.4° (*c* 1.3, C_6H_6). Experiment 2 ($NaNH_2$): 33% yield, $[\alpha]^{22}_D$ +29.2° (*c* 1.3, C_6H_6). Experiment 3 (KNH_2): 16% yield, $[\alpha]^{24}_D$ +27.6° (*c* 0.7, C_6H_6). Experiment 4 (KNH_2): 8% yield, $[\alpha]^{23}_D$ +27.3° (*c* 0.3, C_6H_6).

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

Supplementary Material Available: Tables V and VI of final bond lengths and angles and VII and VIII of final positional and thermal parameters, as well as the numbering scheme (Figure 2), for **12a** (6 pages). Ordering information is given on any current masthead page.

Cleavage of Carbon–Carbon Bonds with High Stereochemical Control. 7. Chiral α-Silyl Benzoylcycloalkanes Undergo Base-Catalyzed Cleavage with Retention of Configuration When Not Sterically Congested[1]

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Received August 19, 1988

The cyclic phenyl ketone (–)-1 has been prepared in a manner that allows definition of its absolute configuration. On being heated with sodium and potassium amide in benzene, (–)-1 undergoes C–C bond cleavage with outstanding (96–98%) levels of configurational retention. This conclusion required interconversion of (–)-1-(trimethylsilyl)-3-isopropylidenecyclopentane (**2**) with (*S*)-(–)-3-(trimethylsilyl)cyclopentene (**3**). The racemic ketones **21**, **22**, **36**, and **37** have also been synthesized and subjected to the Haller–Bauer process. In each case, the resultant cyclic silanes were demonstrated to arise by virtually exclusive stereochemical retention. In the case of **28**, an example where the benzoyl carbonyl group is sterically shielded, desilylation was the kinetically dominant reaction with these bases. These results are interpreted on the basis of initial α-silyl carbanion formation within a solvent shell that also encases benzamide. The benefits derived from these special solvational features are predicted not to be useful for extending stereocontrol to targets requiring the operation of intermediate energy-demanding steps.

The ability of optically active tertiary phenyl ketones bearing an α-silyl substituent to undergo Haller–Bauer deacylation with high levels of stereochemical retention has been documented.[1,2] In these acyclic cases, the additional α substitution has consisted of methyl and an alkyl, alkenyl, or aralkyl group. A ready and general synthetic entry to chiral, nonracemic C-centered organosilanes[3,4] has thereby been made available. As useful as this advance has been, it remained to address the crucial question of its adaptability to cyclic systems. We have therefore proceeded to examine the response of several judiciously chosen five- and six-membered α-silyl benzoylcycloalkanes to cleavage with amide bases. The special emphasis given to stereochemistry has been rewarded by confirmation that this process ranks as perhaps the most stereospecific carbon–carbon bond cleavage yet uncovered.[5]

Results

An Optically Active Cyclopentyl Substrate. A structural property especially suited to assessing the stereochemical course of cleavage reactions is optical activity. Implementation of this probe does require, however, that the absolute configurations of the starting material and product be known without question. Beyond that, we wished not to introduce steric compression near the reaction site as a possible source of complication this early

(1) Part 6: Gilday, J. P.; Gallucci, J. C.; Paquette, L. A., preceding paper in this issue.

(2) Paquette, L. A.; Gilday, J. P.; Ra, C. S.; Hoppe, M. *J. Org. Chem.* **1988**, *53*, 704.

(3) Hathaway, S. J.; Paquette, L. A. *J. Org. Chem.* **1983**, *48*, 3351.

(4) For alternative entries into this class of compounds, consult: (a) Hayashi, T.; Konishi, M.; Ito, H.; Kumada, M. *J. Am. Chem. Soc.* **1982**, *104*, 4962. (b) Hayashi, T.; Kabeta, K.; Yamamoto, T.; Tameo, K.; Kumada, M. *Tetrahedron Lett.* **1983**, 5661. (c) Hayashi, T.; Yamamoto, A.; Iwata, T.; Ito, Y. *J. Chem. Soc., Chem. Commun.* **1987**, 398. (d) Coppi, L.; Ricci, A.; Taddei, M. *Tetrahedron Lett.* **1987**, 965.

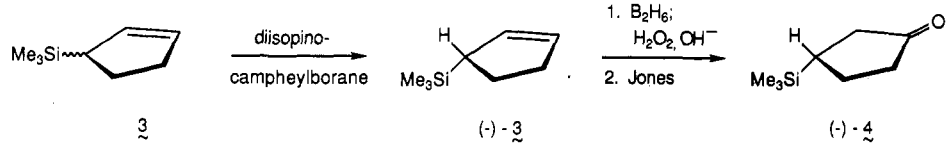
(5) Comparison is made particularly with the structurally related α-phenyl analogues[6] as well as with Cram's very extensive and systematic study of the base-catalyzed cleavage of tertiary alcohols.[7]

(6) (a) Paquette, L. A.; Gilday, J. P.; Ra, C. S. *J. Am. Chem. Soc.* **1987**, *109*, 6558. (b) Paquette, L. A.; Gilday, J. P. *J. Org. Chem.* **1988**, *53*, 4972. (c) Paquette, L. A.; Ra, C. S. *Ibid.* **1988**, *53*, 4978.

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

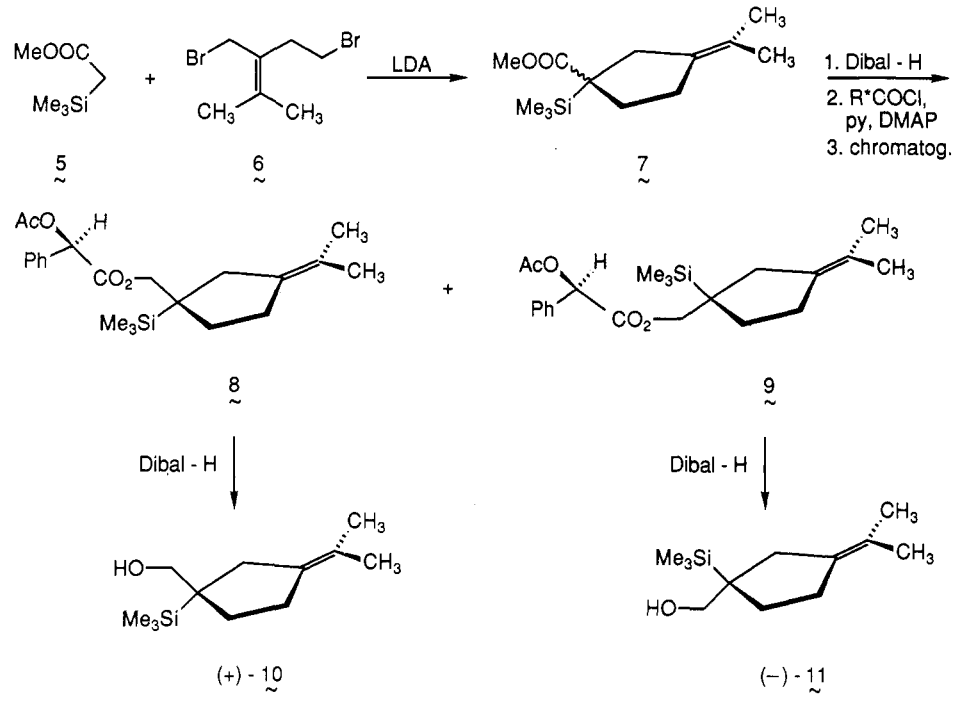
0022-3263/89/1954-1408$01.50/0

Scheme I



3 (-) - 3 (-) - 4

Scheme II



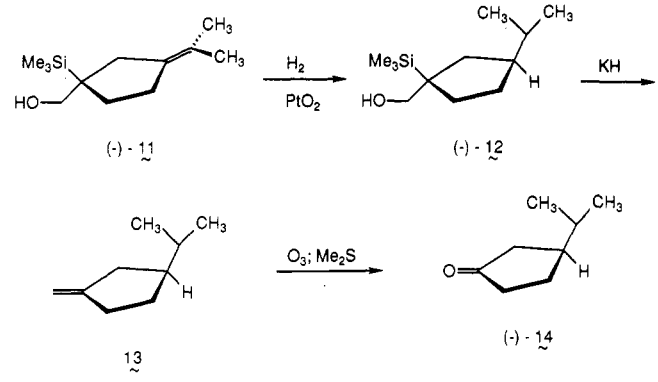
5 6 7 8 9 (+) - 10 (−) - 11

in the investigation. Accordingly, β-keto silane **1** was targeted and the extent to which **1** would give rise stereospecifically to silane **2** was made the issue of synthetic and mechanistic significance.

1 2

Racemic 3-(trimethylsilyl)cyclopentene (**3**) has previously been described,[8,9] and it proved an easy matter to accomplish its kinetic resolution by Brown's method[10] (Scheme I). Larson and co-workers had previously examined the hydroboration–oxidation of (±)-**3** with diborane under kinetic and thermodynamic conditions and demonstrated that only *trans*-3-(trimethylsilyl)cyclopentanol results.[8] In the present instance, recourse was made to 0.5 molar equiv of diisopinocampheylborane in tetrahydrofuran solution at −25 °C for 4 h. These conditions made possible the isolation of levorotatory **3** by preparative VPC in 40% yield. The $[\alpha]_D$ of −70.7° recorded for this material showed it to be of the *S* configuration and 34% enantiomerically pure. These conclusions are based on Hayashi's data for (*S*)-(−)-**3** prepared via an alternative procedure.[4b] Subsequent hydroboration–oxidation of this material according to Larson[8] gave (*S*)-(−)-3-(trimethylsilyl)cyclopentanone (**4**). This ketone was destined to serve later as the key relay link to **2**.

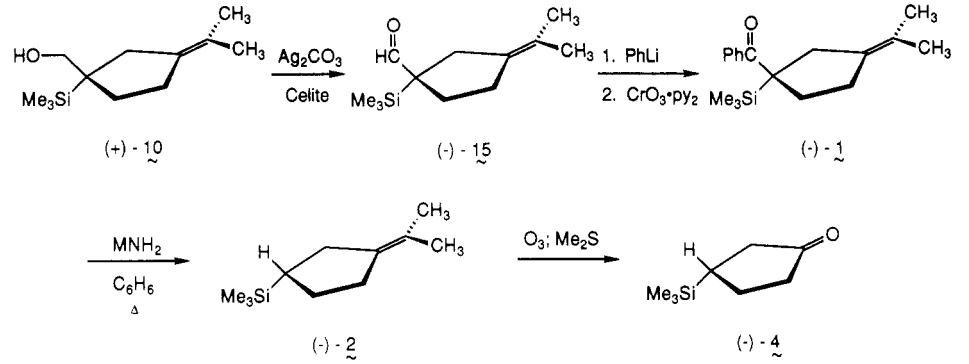
Scheme III



Ester **7** was prepared by spiroalkylation of methyl (trimethylsilyl)acetate (**5**) with dibromide **6**[11] (Scheme II). Following reduction to the primary carbinol with diisobutylaluminum hydride, the diastereomeric *O*-acetylmandelate esters **8** and **9** were prepared and partially separated by chromatography.[12] The purification proved more difficult than anticipated; however, the respective 40% and 30% de values were entirely adequate. Once enriched **8** and **9** were individually reduced, it became

(8) DeJesus, M.; Rosario, O.; Larson, G. L. *J. Organomet. Chem.* **1977**, *132*, 301.
(9) Reuter, J. M.; Sinha, A.; Salomon, R. G. *J. Org. Chem.* **1978**, *43*, 2438.
(10) Brown, H. C.; Desai, M. C.; Jadhav, P. K. *J. Org. Chem.* **1982**, *47*, 5065.
(11) Paquette, L. A.; Charmumilind, P.; Kravetz, T. M.; Böhm, M. C.; Gleiter, R. *J. Am. Chem. Soc.* **1983**, *105*, 3126.
(12) The use of *O*-acetylmandelate esters for resolution was first reported by Whitesell: Whitesell, J. K.; Reynolds, D. *J. Org. Chem.* **1983**, *48*, 3548.

Scheme IV



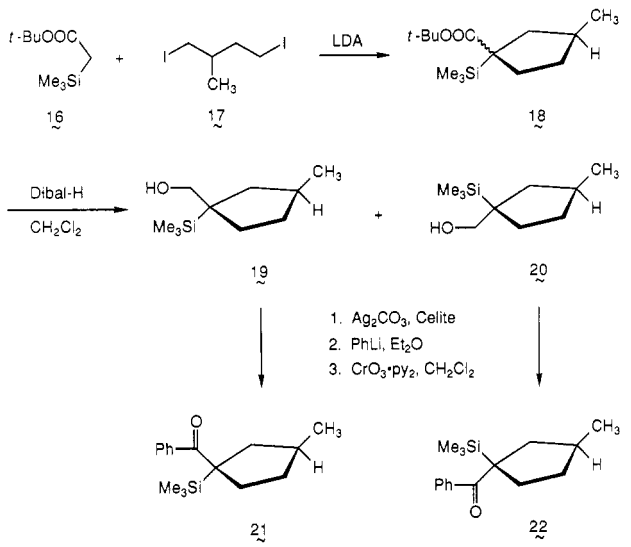
necessary to assign absolute stereochemistry to alcohols (+)-**10** and (−)-**11**.

After several vain attempts to modify these structures in a manner that would retain the silicon substituent, the route outlined in Scheme III was ultimately pursued. Hydroxyl-directed hydrogenation of the extraannular double bond[13] in (−)-**11** made possible the acquisition of (−)-**12**. The configurational assignment to the seat of isopropyl substitution was confirmed by a difference NOE experiment. Double irradiation of the Me_3Si singlet at 500 MHz had no effect on the CH_2OH absorption, but enhanced the integration of the isopropyl peak by 7.8%. With the structure of (−)-**12** secure, chirality transfer had been accomplished successfully to generate a new stereogenic center of *S* configuration. The original asymmetric carbon was then put out of existence by application of the Peterson olefination reaction. Once **13** had been obtained, it was directly degraded by ozonolysis. Realization that the end product was the known (*S*)-(−)-3-isopropylcyclopentanone (**14**)[14] made clear the absolute configurations of all compounds in the series **8**–**13**.

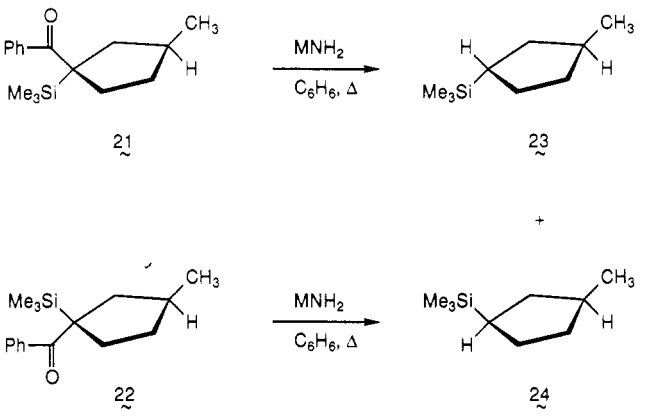
In a companion series of reactions, (+)-**10** was oxidized with Fetizon reagent[15] to give (−)-**15**, which was directly condensed with phenyllithium and oxidized under Collins conditions[16] to give (−)-**1** (Scheme IV). Haller–Bauer cleavage of this ketone (40% ee) was found to proceed with outstanding levels of configurational retention, sodium amide being slightly better in this regard (98%) than the potassium base (96%). Direct evidence bearing on the optical purity of (−)-**2** was gained by ozonolytic cleavage to (−)-**4** and direct comparison with material prepared via Scheme I.

Alternative Configurational Probing of α-Silyl Carbanion Generation and Capture in the Cyclopentane Series. In view of the excellent stereochemical retention exhibited by (−)-**1**, other cyclopentane systems were examined where relative rather than absolute configuration was the stereochemical probe. Racemic ketones **21** and **22** were selected next. These isomers were prepared as outlined in Scheme V. Two-step spiroalkylation of *tert*-butyl (trimethylsilyl)acetate (**16**)[17] with 2-methyl-1,4-diiodobutane (**17**)[18] in the presence of lithium diiso-

Scheme V



Scheme VI



propylamide provided **18**, reduction of which as before made available the chromatographically separable primary alcohols **19** and **20**. Appropriate distinction between the diastereomers was achieved by means of nuclear Overhauser studies. Whereas **20** is characterized by two key NOE effects, $CH_3/Si(CH_3)_3$ (2.4%) and methine CH/CH_2OH (2.7%), **19** gives evidence of nonbonded steric

(13) For leading references, consult: (a) Howard, T. J.; Morley, B. *Chem. Ind. (London)* **1967**, 73. (b) Sekio, M.; Yasuhisa, S.; Hideyo, S. *Bull. Chem. Soc. Jpn.* **1966**, 694.

(14) The *R*-(+) enantiomer of **4** has been reported to exhibit $[\alpha]^{20}_D$ +186° ($CHCl_3$): Posner, G. H.; Frye, L. L.; Hulce, M. *Tetrahedron* **1984**, *40*, 1401. (b) Nakazaki, M. *Bull. Chem. Soc. Jpn.* **1962**, *35*, 1904. (c) Naves, Y.-R. *Bull. Soc. Chim. Fr.* **1958**, 1372.

(15) (a) Baloph, V.; Fêtizon, M.; Golfier, M. *J. Org. Chem.* **1971**, *36*, 1339. (b) Fetizon, M.; Golfier, M. *C. R. Seances Acad. Sci., Ser. C* **1968**, *267*, 900. (c) McKillop, A.; Young, D. W. *Synthesis* **1979**, 401.

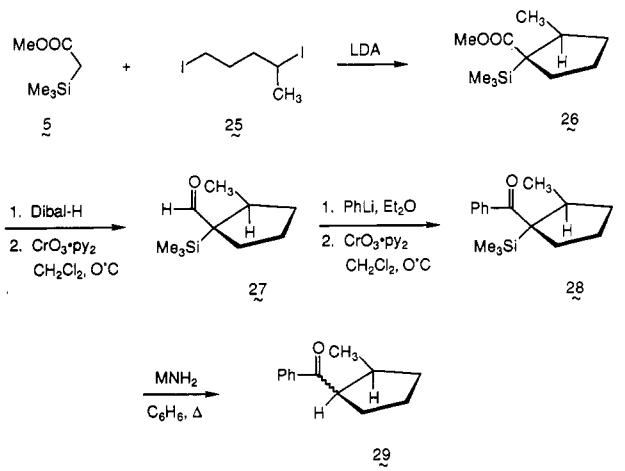
(16) Collins, J. C.; Hess, W. W.; Frank, F. J. *Tetrahedron Lett.* **1968**, 3363.

(17) Rathke, M. W.; Sullivan, D. F. *Synth. Commun.* **1973**, *3*, 67.

(18) The dibromide precursor of **16** has been used elsewhere without specification of its source[19a] and produced in a Russian laboratory via a route initially involving the condensation of propene with chloromethyl methyl ether in the presence of zinc chloride.[19b] For our purposes, dimethyl itaconate was hydrogenated, reduced with lithium aluminum hydrie, and transformed into the dibromide by reaction of the bis(tetrahydropyranyl ether) with triphenylphosphine dibromide.

(19) (a) Riddell, F. G.; Williams, D. A. R. *Tetrahedron* **1974**, *30*, 1083. (b) Volynskii, N. P.; Schherbakova, L. P. *Izv. Akad. Nauk SSSR, Ser. Khim.* **1979**, 1080.

Scheme VII



interaction only between its methine C*H* and Si(CH_3)$_3$ (2.7%). Evidently, the distance between the CH_3 and CH_2OH groups in the latter falls outside the range capable of giving rise to a detectable effect despite their cis orientation.

Subsequently, each alcohol was converted to the respective α-(trimethylsilyl)benzoylcyclopentane. With pure **21** and **22** in hand, their response to Haller–Bauer cleavage as promoted by sodium and potassium amides in refluxing benzene was studied (Scheme VI). With $NaNH_2$, the cleavage of **21** was complete in 2 h. The product composition was determined by capillary GC to be 98:2, and the major product was shown (following isolation) to be **23**. This silane exhibited a pair of intense NOE effects: CH_3/α-silyl C*H* (11.2%) and α-methyl C*H*/Si(CH_3)$_3$ (19.4%). With KNH_2 as the coreagent, the cleavage took somewhat longer (5 h) and the product composition fell reproducibly to 96:4. However, **23** remained the dominant component of the reaction mixture.

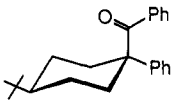
Presumably because of prevailing 1,3 steric effects, the Haller–Bauer cleavages of **22** proceeded somewhat more slowly than those involving **21**. The respective reaction times required to realize complete consumption to ketone were 3.5 h ($NaNH_2$) and 10 h (KNH_2). Both processes gave rise to an identical 95:5 product distribution. That cis silane **24** had now been produced predominantly was evident from the α-silyl C*H*/α-methyl C*H* NOE effect generated within the molecule (1.4%) and the anticipated (in light of the behavior of **19**) undetectability of a related CH_3/Si(CH_3)$_3$ contribution.

Thus, **21** and **22** share with (–)-**1** the ability to undergo benzoyl cleavage with remarkably high levels of configurational retention at the site of the transient α-trimethylsilyl carbanions.

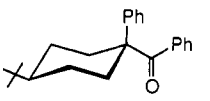
Consequences of Steric Blockage in an α-Silyl Benzoylcyclopentane. The three ketones examined to this point were designed to carry the stereochemical marker at a locus reasonably remote from the reaction center. Accordingly, steric congestion close to the seat of carbanion generation had not yet surfaced as a potentially perturbing factor. Concern over this question caused attention to be turned next to preparation of the fourth silylated benzoylcyclopentane **28** (Scheme VII). In this instance, the spiroalkylation of **5** as before with 1,4-diiodopentane (**25**)[20] at –78 to –30 °C provided a single cyclized diastereomer in 45% yield. Assignment of a trans relationship between the methyl and trimethylsilyl substituents in **26**, originally based on steric considerations alone, was later given credence by virtue of the chemical reactivity of **28** (see below). This stereoselectivity appears to be a general feature of diiodide **25** in its reactions with dianions. For example, the supplantation of **5** by (trimethylsilyl)acetonitrile resulted in formation of a 30:1 diastereomeric mixture rich in the nitrile analogue of **26**.[21]

The stereochemical integrity of **26** allowed for ready conversion of **28** without need for extensive chromatographic purification. Once the benzoyl derivative was reached, it too was treated with $NaNH_2$ and KNH_2 in refluxing benzene. In this instance, however, no Haller–Bauer cleavage was seen. Rather, **28** preferentially undergoes desilylation to give **29**. Evidently, the increased steric congestion in the vicinity of the carbonyl group in **28** is adequate to deter nucleophilic addition of amide ion across the C–O double bond. This kinetic retardation then allows direct nucleophilic attack at silicon to become kinetically dominant. Consequently, steric compression as found in **28** is indeed deleterious to generation of an α-silyl carbanion via fragmentation.

Analysis of the Effect of Axial/Equatorial Leaving-Group Orientation in a Conformationally Fixed Cyclohexane Setting. In earlier work,[6c] we demonstrated that the stereochemically well defined ketones **30** and **31** respond quite differently to Haller–Bauer cleavage. When



30



31

the benzoyl group is axial as in **30**, the course of protonation varies widely as progression is made from $LiNH_2$ (10% inversion) to $NaNH_2$ (40% retention), and ultimately to KNH_2 (78% retention). In contrast, retention falls off rapidly for diastereomer **31** across the same series of reagents (70%, 42%, and 20% retention, respectively). These trends have been concisely accounted for in terms of tight and loose product pairs and their ultimate dissociation by solvent molecules.

As a direct consequence of the strikingly divergent behavior of **30** and **31**, we have deemed it important to investigate the sensitivity of the α-trimethylsilyl analogues **36** and **37** to the action of amide bases. To this end, **16** was first spiroalkylated with diiodide **32** (Scheme VIII). Attempted separation of the cyclohexyl esters so produced (**33**) by means of high-pressure liquid chromatography was partially successful on a preparative scale. Subsequent hydride reduction of the individually enriched fractions facilitated isolation of pure samples of the two diastereomeric alcohols. Whereas the carbinol protons of the axial-CH_2OH epimer (the trans series) appear at δ 3.50, those of the equatorial stereoisomer are considerably more shielded (δ 3.17), in line with a well-established trend.[22]

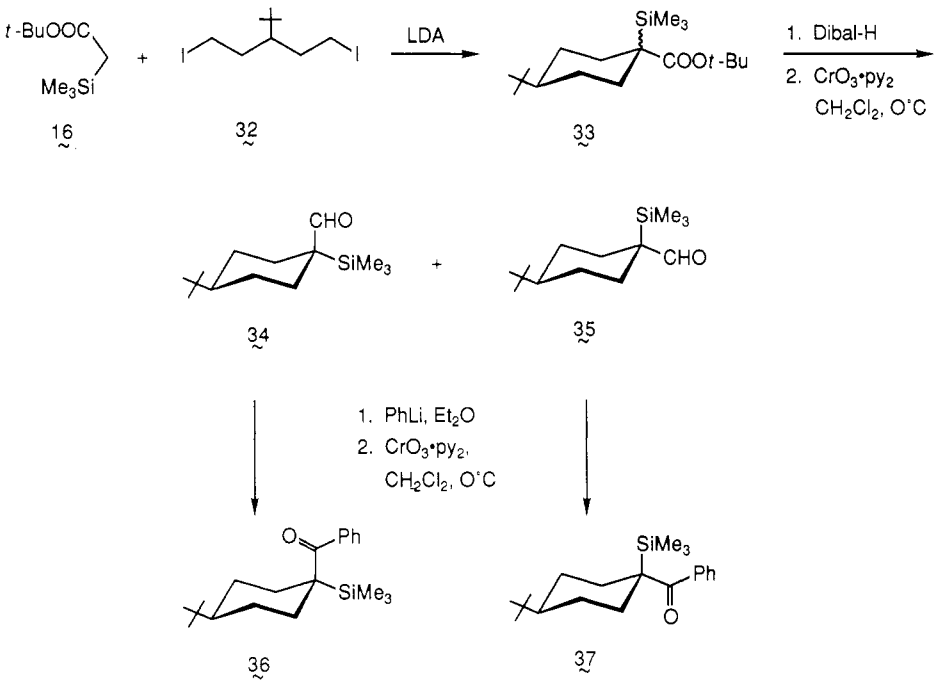
Once **36** and **37** were elaborated as described above, serial experiments were conducted in hot, anhydrous benzene solution in order to assess possible differences between sodium and potassium amides, on the one hand, and spatial orientation of the reaction center on the other (Scheme IX). Cis ketone **36** underwent Haller–Bauer cleavage with considerable difficulty when heated with

(20) Prepared by application of the Finkelstein reaction to the commercially available (Aldrich) dibromide. For an earlier alternative preparation of **24**, consult: Liu, H. J.; Schewchuk, L. M.; Llinas-Brunet, M. *Heterocycles* **1986**, *24*, 3043.

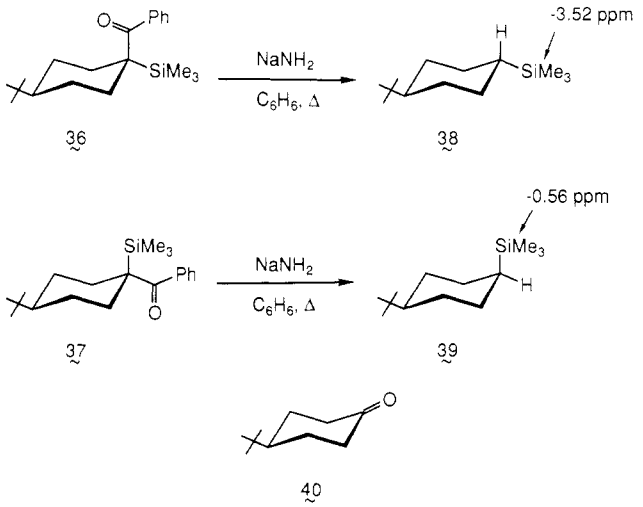
(21) Maynard, G. D., unpublished results.

(22) Walton, J. C.; Ingold, K. U. *J. Chem. Soc., Perkin Trans. 2* **1986**, 1337.

Scheme VIII



Scheme IX



either amide base. In the runs involving $NaNH_2$, reaction times of approximately 135 h were necessary to consume the majority of the starting material. According to capillary GC analysis, these reactions resulted uniquely in loss of the benzoyl group. However, the relative levels of silanes **38** and **39** could not be established by this analytical technique since the isomers were shown not to be separable under a wide variety of temperature and flow-rate conditions. When recourse was made instead to 300-MHz ^1H NMR, only trans isomer **38** could be detected within confidence limits of ±5%. Accordingly, cleavage occurs in this instance with at least 95% retention of configuration.

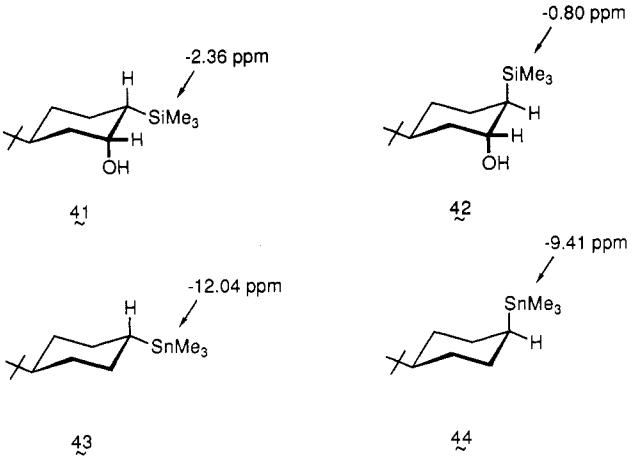
With KNH_2 as base, reaction was complete in 100 h. However, only a trace of **38** was formed; the major product was 4-*tert*-butylcyclohexanone (**40**). In our view, ketone formation originates by initial desilylation with generation of the potassium enolate. As a consequence of the long reaction time, the latter intermediate finds it possible to react with adventitious oxygen present in the reaction vessel.[23] To test this premise, **36** was purposefully desilylated with tetra-*n*-butylammonium fluoride in tetrahydrofuran and the unpurified 4-*tert*-butylcyclohexyl phenyl ketone was heated with KNH_2 in benzene. After 36 h, conversion to **40** had materialized to a substantial extent, although some minor unidentified compounds were produced concomitantly.

The unreactivity of **36** can be attributed to massive steric screening. Its benzoyl carbonyl center not only resides in an axial environment but is also flanked by a geminal trimethylsilyl group. When the location of the two substituents is reversed as in **37**, the congestion is somewhat alleviated because benzoyl is now situated equatorially. As a consequence, **37** was expected to be more reactive than **36**, and it is. Heating **37** with $NaNH_2$ in benzene for only 3 h resulted in smooth conversion to **39**. Stereochemical purity within ±5% limits was established by ^1H NMR analysis. Recourse to KNH_2 required 16 h to consume all of **37**. The resulting two-component product mixture consisted of **39** (14%) and **40** (86%). Thus, desilylation remains kinetically important where KNH_2 is concerned. The loss of trimethylsilyl in **37** may stem from its axial nature, the steric acceleration attending its departure from the molecule likely being substantial. Notwithstanding, **37** also responds to the desired cleavage by experiencing protonation predominantly, if not exclusively, with retention.

The structural assignments to **38** and **39** follow convincingly from comparison of select ^1H and ^{13}C NMR shifts with those established by others for closely related molecules.[24] As seen in Scheme IX, the equatorial trimethylsilyl group in **38** is more shielded than its axial counterpart in **39** ($\Delta\delta$ = 2.96). This relative ordering has been recognized before. The **41**/**42** ($\Delta\delta$ = 1.56) and **43**/**44** stereoisomeric pairs ($\Delta\delta$ = 2.63) are exemplary of the trend.

(23) For example: (a) Bailey, E. J.; Barton, D. H. R.; Elks, J.; Templeton, J. F. *J. Chem. Soc.* **1962**, 1578. (b) Gardner, J. N.; Carlon, F. E.; Gnoj, O. *J. Org. Chem.* **1968**, *33*, 3294. (c) Gardner, J. N.; Poppen, T. L.; Carlon, F. E.; Gnoj, O.; Herzog, H. L. *Ibid.* **1968**, *33*, 3695.

(24) (a) Lambert, J. B.; Wang, G.; Finzel, R. B.; Teramura, D. H. *J. Am. Chem. Soc.* **1987**, *109*, 7838. (b) Kitching, W.; Adcock, W.; Doddrell, D.; Wiseman, P. A. *J. Org. Chem.* **1976**, *41*, 3036. (c) Kitching, W.; Olszowy, H.; Waugh, J. *Ibid.* **1978**, *43*, 898.



Additionally, the relative configuration of **38** is indicated by the appearance of its cyclohexyl α-silyl proton as a clean triplet of triplets with coupling constants of 12.3 and 3.0 Hz, as would be predicted from the torsional angles this C–H bond defines in the adjacent methylene protons.

Finally, the stability of **38** and **39** to the reaction conditions under which they are produced was ascertained by heating each with KNH_2 in benzene at reflux for 100 h. No significant decomposition of either silane was detected by capillary GC. Because of the volatility of these compounds, losses were incurred during such treatment. This factor almost certainly contributes in a major way to the modest yields realized for the Haller–Bauer cleavages of α-trimethylsilyl ketones.

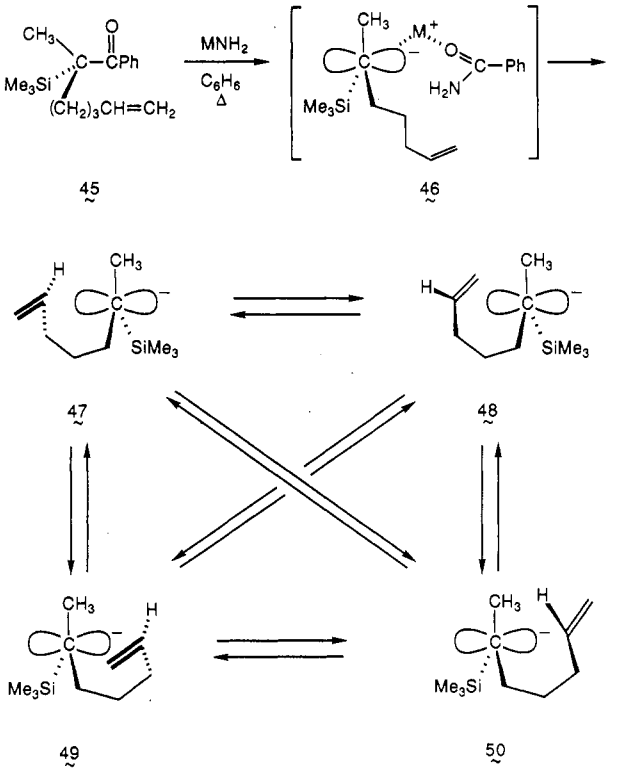
Discussion

Our companion investigation of the Haller–Bauer cleavage of chiral, acyclic α-trimethylsilyl phenyl ketones[1] with $NaNH_2$ and KNH_2 in hot benzene disclosed that high levels of asymmetric protonation[25] are the norm. Stereochemical retention in excess of 88% is routinely attainable because loss of the benzoyl group is accompanied by departure of benzamide from the front side of the α-silyl carbanion. Although these silicon-containing anionic intermediates are not normally capable of configurational stability, their mode of formation under these conditions uniquely preserves their global chirality. Thus, the carbanions are formed within a benzene solvent cage, such that subsequent protonation is performed almost exclusively by the departing benzamide molecule prior to any mutual rotation.

Entirely comparable control of the stereochemical course of protonation is herein shown to occur when cyclic α-silyl carbanions are involved. The implications for synthesis are clear. If the substrate molecule is capable of supporting optical activity and, like (–)-**1**, is available in optically active condition, then stereochemical control can be exercised to gain access to optically active silanes (e.g., (–)-**2**), a class of molecules still highly restricted in their total number.[1,2,4] Moreover, knowledge of the absolute configuration of the benzoyl precursor permits confident assignment of the silane's stereochemistry because of the overwhelming preference for retention in these reactions.

These mechanistic consequences can be equally well exploited in racemic systems where relative topological selectivity is at issue. Here, a variety of structural options can be envisioned, and some (e.g., **21**, **22**, **36**, and **37**) have presently been tested with uniform results. In essence, the carbon atom commonly bonded to the trimethylsilyl and benzoyl groups can be used as a template for the construction of a whole range of cyclic silanes of defined stereochemistry. Limitations seemingly arise only when the benzoyl group is made sufficiently hindered by neighboring substituents that nucleophilic attack by amide ion is kinetically retarded. Desilylation occurs preferably under these circumstances.

In contemplating extension of the useful characteristics of the Haller–Bauer reaction to the construction of multiply chiral ensembles via anionic cyclization,[26] several additional factors must be given serious consideration. Although a system such as **45** will give rise initially to the product pair depicted by **46**,[1,6] ensuing intramolecular capture of the tethered double bond requires proper orbital alignment with the carbanionic center. The activation barriers associated with achieving collinearity and σ-bond formation can be expected to be adequately high to permit full disengagement of the benzamide molecule from the near vicinity. This event should result not only in loss of stereocontrol during generation of the new stereogenic center (compare **47** and **48**) but in indiscriminate capture of the carbanion from either of its surfaces as well (as in **47**/**48** versus **49**/**50**).



Although these issues remain to be tested, mention is made here to emphasize the very special interplay of forces that lend very useful character to the Haller–Bauer process. A substituent such as silicon needs to be present at the set of reaction to stabilize the incipient carbanion. Importantly, formation of this intermediate occurs within a solvent shell that also encases benzamide such that protonation occurs with very high stereochemical retention. However, we predict that any attempt to utilize these features for the purpose of extending stereocontrol to targets requiring intermediate energy-demanding steps are not likely to benefit from the special solvational features

(25) Duhamel, L.; Duhamel, P.; Launay, J.-C.; Plaquevent, J.-C. *Bull. Soc. Chem. Fr.* **1984**, 422.

(26) (a) Chamberlin, A. R.; Bloom, S. H.; Cervini, L. A.; Fotsch, C. H. *J. Am. Chem. Soc.* **1988**, *110*, 4788 and relevant references cited therein. (b) Gilday, J. P., unpublished observations in this laboratory.

available at the time of initial bond heterolysis.[27]

Experimental Section

(*S*)-(−)-3-(Trimethylsilyl)cyclopentene (3). To a cold (0 °C), magnetically stirred solution of the borane–dimethyl sulfide complex (1.01 mL, 10.0 mmol) in anhydrous tetrahydrofuran (3 mL) was added dropwise 3.18 mL (20 mmol) of α-pinene ($[\alpha]^{25}_D$ +43.6° (neat); 85% ee). After 50 min, an initially formed white solid had disappeared and stirring was maintained for an additional 3 h at 0 °C. The dimethyl sulfide and tetrahydrofuran were removed in vacuo (0 °C/30 Torr). To the residue were added 3.6 mL of tetrahydrofuran and 0.48 mL (3.0 mmol) of (+)-α-pinene, and the resulting mixture was stored at 0 °C for 3 days to permit equilibration.

This suspension was cooled to −25 °C under nitrogen, and 2.81 g (20.0 mmol) of racemic **3** was introduced dropwise. During 4 h of stirring at this temperature, dissolution occurred and a pale green color developed. Water (10 mL) was added, stirring was continued at 0 °C for 2 h, and the α-pinene and **3** were codistilled. The optically active silane was isolated from this mixture by preparative GC (15 ft × 0.25 in. 5% Se-30): 560 mg (40%); $[\alpha]^{25}_D$ −70.7° (*c* 0.60, benzene) corresponding to 34% ee.[4b]

(*S*)-(−)-3-(Trimethylsilyl)cyclopentanone (4). To a cold (0 °C), magnetically stirred solution of (−)-**3** (300 mg, 2.14 mmol) in anhydrous tetrahydrofuran (2 mL) under nitrogen was added 2.5 mL (2.5 mmol) of borane–tetrahydrofuran complex. After 2 h, this mixture was oxidized by careful addition of 3 N sodium hydroxide solution (0.7 mL) and then dropwise addition of 30% hydrogen peroxide (0.7 mL). After 3 h at room temperature, sodium chloride was introduced and the organic phase was separated. The aqueous layer was extracted with ether (2 × 10 mL), and the combined organic solutions were dried and carefully concentrated under reduced pressure.

The alcohol was taken up in acetone (3 mL), treated dropwise at 0 °C with Jones reagent until a brown color persisted, and finally quenched with a small amount of isopropyl alcohol. The usual workup followed by MPLC on silica gel (elution with 7% ethyl acetate in petroleum ether) gave **4** (130 mg, 38% overall) as a colorless oil. Final purification by preparative GC (15 ft × 0.25 in. 10% SE-30, 150 °C) gave material exhibiting $[\alpha]^{26}_D$ −6.23° (*c* 0.75, $CHCl_3$). The spectral properties corresponded closely to those reported for the racemic material.[8]

Methyl 1-(Trimethylsilyl)-3-isopropylidenecyclopentanecarboxylate (7). To a cold (−78 °C), magnetically stirred solution of lithium diisopropylamide (1.25 mmol) in anhydrous tetrahydrofuran (2.5 mL) was added neat **5** (1.08 g, 6.50 mmol) dropwise. After 20 min of stirring at this temperature, a solution of **6** (1.54 g, 6.00 mmol) in HMPA (1.08 g, 6.00 mmol) was introduced via syringe. Twenty minutes later, an additional 1.25 mmol of LDA in 2.5 mL of tetrahydrofuran was added. After 45 min, the stirred reaction mixture was allowed to warm to room temperature during 1 h. Saturated ammonium chloride solution (20 mL) was added, and the mixture was diluted with ether (30 mL). The separated aqueous phase was extracted with ether (2 × 30 mL), and the combined organic layers were washed with brine (2 × 15 mL), dried, and evaporated. The residual oil was purified by flash chromatography on silica gel (elution with 2% ethyl acetate in petroleum ether) to give 1.15 g (80%) of **7** as a colorless oil: IR ($CDCl_3$, cm^{-1}) 2960, 1695, 1250, 840; ^1H NMR (300 MHz, $CDCl_3$) δ 3.63 (s, 3 H), 2.93–1.58 (series of m, 6 H), 1.63 (s, 3 H), 1.59 (s, 3 H), 0.04 (s, 9 H); ^{13}C NMR (20 MHz, $CDCl_3$) 174.7, 134.3, 121.7, 51.4, 45.8, 35.7, 31.5, 21.3, 20.1, −3.3 ppm; MS *m/z* (M^+) calcd 240.1545, obsd 240.1554.

Anal. Calcd for $C_{13}H_{24}O_2Si$: C, 64.94; H, 10.06. Found: C, 64.96; H, 10.06.

1-(Hydroxymethyl)-1-(trimethylsilyl)-3-isopropylidenecyclopentane. A solution of **7** (1.5 g, 6.25 mmol) in dry ether (100 mL) was cooled in ice and treated slowly via syringe with diisobutylaluminum hydride (1 N in hexanes, 15 mmol). After 2 h, the mixture was quenched with potassium sodium tartrate solution and the product was extracted into ether. The combined organic layers were dried and evaporated to give 1.08 g (81%) of alcohol as a colorless oil: IR (neat, cm^{-1}) 3400, 2980–2860, 1250, 840; ^1H NMR (300 MHz, $CDCl_3$) δ 3.53 (s, 2 H), 2.4–1.7 (series of m, 6 H), 1.63 (s, 3 H), 1.61 (s, 3 H), 1.43 (br s, 1 H), 0.02 (s, 9 H); ^{13}C NMR (20 MHz, $CDCl_3$) 135.5, 121.7, 68.7, 35.4, 30.4, 29.4, 21.3, 21.2, −2.8 ppm; MS *m/z* ($M^+ - H_2O$) calcd 194.1491, obsd 194.1516.

***O*-Acetylmandelic Acid Esters 8 and 9.** (*S*)-(+)-*O*-Acetylmandelic acid chloride was prepared from *S*-(+) acid (195 mg, 1.00 mmol, $[\alpha]^{19}_D$ +147.5° (*c* 2, acetone)) in 5 mL of benzene by heating with thionyl chloride (1.1 mL, 15 mmol) for 30 min. The excess reagent was removed in vacuo, and the residue was dissolved in cold (0 °C) dichloromethane (2 mL). To this solution were added sequentially and dropwise 4-(dimethylamino)pyridine (6.1 mg) dissolved in pyridine (0.74 mL) and the above alcohol (212 mg, 1.0 mmol) dissolved in dichloromethane (3 mL). After 30 min, water and ether were added, and the organic phase was dried and evaporated. MPLC purification (silica gel, elution with 5% ethyl acetate in petroleum ether) gave the diastereomeric mixture as a colorless oil (270 mg, 70%): IR (neat, cm^{-1}) 3030, 2960, 1750, 845; ^1H NMR (300 MHz, $CDCl_3$) δ 7.46–7.36 (m, 5 H), 5.89 (s, 1 H), 4.09 (d, *J* = 10.8 Hz, 0.5 H), 4.03 (d, *J* = 10.8 Hz, 0.5 H), 3.96 (d, *J* = 10.8 Hz, 0.5 H), 3.88 (d, *J* = 10.8 Hz, 0.5 H), 2.19 (s, 3 H), 2.19–1.49 (m, 6 H), 1.58 (s, 6 H), −0.06 (s, 9 H); MS(CI) *m/z* (M + 1) calcd 389, obsd 389.

Diastereomeric enrichment was realized on a Waters Prep 500 instrument on silica gel using recycling and peak-shaving techniques. The mixed fractions were recycled 10–14 times. This effort produced 4.3 g of a combined fraction, $[\alpha]^{21}_D$ −48.7° (*c* 7.25, CH_3OH), that consisted of a 70:30 mixture of the isomers. In addition, a second fraction could be obtained (6.2 g), which was enriched in the opposite direction to the extent 35:65.

Reduction of the Enriched *O*-Acetylmandelate Esters. A. Diisobutylaluminum hydride reduction of the 40% de material (4.3 g) gave (+)-**10** (1.73 g, 74%), $[\alpha]^{22}_D$ +3.97° (*c* 0.76, CH_3OH).

B. Comparable treatment of the 30% de material (2.40 g) made available (−)-**11** (0.93 g, 70%), $[\alpha]^{25}_D$ −3.20° (*c* 2.66, CH_3OH).

Hydrogenation of (−)-11. A 155-mg (0.73 mmol) sample of (−)-**11** was dissolved in ethyl acetate (4 mL) and hydrogenated over Adams catalyst at 80 psi for 16 h. The catalyst was separated by filtration, and the product was purified by MPLC on silica gel (elution with 9% ethyl acetate in petroleum ether). There was isolated 70 mg (44%) of **12** as a colorless oil: IR (neat, cm^{-1}) 3450, 2950, 2868, 1470, 1255, 845; ^1H NMR (300 MHz, $CDCl_3$) δ 3.52 (s, 2 H), 1.89–1.01 (series of m, 9 H), 0.90 (d, *J* = 6.6 Hz, 6 H), 0.009 (s, 9 H); ^{13}C NMR (20 MHz, $CDCl_3$) 69.72, 47.76, 36.22, 34.28, 33.65, 32.04, 30.45, 21.79, −3.21 ppm; MS *m/z* ($M^+ - H_2$) calcd 212.1596, obsd 212.1575; $[\alpha]^{25}_D$ −9.71° (*c*, 1.38, $CHCl_3$).

Anal. Calcd for $C_{12}H_{26}OSi$: C, 67.22; H, 12.22. Found: C, 67.12; H, 12.22.

(*S*)-(−)-3-Isopropylcyclopentanone (14). Potassium hydride (154 mg of 26% suspension in oil) was washed with pentane (2 × 2 mL) and tetrahydrofuran (2 × 2 mL). Following the addition of dry tetrahydrofuran (0.7 mL), a solution of (−)-**12** (70 mg, 0.33 mmol) in the same solvent (1.5 mL) was introduced dropwise, and the mixture was stirred at room temperature for 1 h. The insolubles were separated by filtration, and the filtrate was carefully concentrated to leave ca. 35 mg of **13**, which was not purified further.

The methylenecyclopentane was dissolved in methanol (1.5 mL) containing a drop of pyridine, cooled to −78 °C, and ozonolyzed for 2 min. Dimethyl sulfide (50 μL) was added, and the solution was allowed to warm slowly to room temperature. Brine was added, and the product was extracted into ether. Drying and solvent evaporation was followed by MPLC on silica gel and finally preparative GC (15 ft × 0.25 in. 10% SE-30, 150 °C). There was isolated 2.8 mg (7.8%) of **14**: $[\alpha]^{23}_D$ −87.5° (*c* 0.28, $CHCl_3$); IR (neat, cm^{-1}) 2960, 2870, 1747, 1165; ^1H NMR (300 MHz, $CDCl_3$)

(27) In subsequent work, this prediction has been verified to be factual. We mention this in connection with the suggestion by a reviewer that the observed cleavage with retention of configuration might be better explained by an S_Ei pathway in which the intervention of true carbanions is bypassed. This cannot be, since we now recognize that once the reactive species leaves the solvent shell, it experiences rapid racemization. Furthermore, potassium *tert*-butoxide serves as a highly effective Haller–Bauer cleavage reagent in other contexts,[1] yet does not serve as a proton donor.[2,6] Its use in the present series is precluded because of its proclivity for inducing more rapid desilylation. Nonetheless, it seems unlikely that closely allied substrates would select different operational reaction channels, and these must be predominantly anionic in character.

δ 2.40–1.44 (series of m, 8 H), 0.95 (dd, J = 8.3, 6.7 Hz, 6 H); ^{13}C NMR (75 MHz, $CDCl_3$) 219.60, 44.61, 43.61, 39.07, 33.48, 27.70, 21.18, 20.29 ppm; MS m/z (M^+) calcd 126.1044, obsd 126.1044.

(*S*)-(−)-1-(Trimethylsilyl)-3-isopropylidenecyclopentanecarboxaldehyde (15). Freshly prepared Fetizon reagent[15] (25 g, ca. 44 mmol) that had been dried on a rotary evaporator for 5 h was heated with benzene for 1 h to remove the remaining water. Concentration of the solvent volume to 50 mL was followed by the addition of (+)-**10** (569 mg, 2.68 mmol) and heating at the reflux temperature in the dark for 1.5 h. The reaction mixture was filtered through Celite and concentrated to give **15** as a pale yellow oil (500 mg, 88%): IR ($CDCl_3$, cm^{-1}) 1705, 1262, 845; ^1H NMR (300 MHz, $CDCl_3$) δ 9.53 (s, 1 H), 2.9–1.4 (series of m, 6 H), 1.64 (s, 3 H), 1.57 (s, 3 H), 0.07 (s, 9 H); ^{13}C NMR (20 MHz, $CDCl_3$) 206.7, 133.5, 121.8, 55.6, 32.7, 30.2, 29.7, 21.3, 21.2 ppm; $[\alpha]^{22}_D$ −21.4° (c 1.05, CH_3OH).

(*S*)-(−)-1-Benzoyl-1-(trimethylsilyl)-3-isopropylidenecyclopentane (1). To a cold (−78 °C) solution of (−)-**15** (500 mg, 2.38 mmol) in dry tetrahydrofuran (10 mL) was added a hexane solution of phenyllithium (3.1 mmol) dropwise. The reaction mixture was stored for 30 min before quenching of the excess reagent with 10% acetic acid in tetrahydrofuran (5 mL). The usual workup afforded 880 mg of carbinol, which was directly oxidized by the Collins procedure.

The reagent was prepared by adding chromium trioxide (2.4 g, 24 mmol) to 3.8 mL of pyridine (48 mmol) in dichloromethane (40 mL). Three-fourths of this reagent mixture was cannulated into a solution of the carbinol in dichloromethane (10 mL), and this mixture was stirred for 15 min, then diluted with ether (50 mL), filtered through 5 g of silica gel (2.5% ethyl acetate in petroleum ether), and concentrated MPLC purification of the residue on silica gel (elution with 2% ethyl acetate in petroleum ether) gave 301 mg (44% overall) of **1** as a colorless oil: IR 2960, 2900, 1680, 1485, 1255, 845; ^1H NMR (300 MHz, $CDCl_3$) δ 7.61–7.34 (m, 5 H), 3.05–1.98 (series of m, 6 H), 1.63 (s, 3 H), 1.60 (s, 3 H), 0.87 (s, 9 H); ^{13}C NMR (20 MHz, $CDCl_3$) 208.5, 140.2, 134.0, 130.7, 127.9, 121.9, 54.7, 37.4, 33.3, 30.1, 21.1 (2 C), −2.06 ppm (1 C not observed); MS m/z (M^+) calcd 286.1777, obsd 286.1765; $[\alpha]^{22}_D$ −12.3° (c 1.3, CH_3OH).

Haller–Bauer Cleavages of (−)-1. (*S*)-(−)-1-(Trimethylsilyl)-3-isopropylidenecyclopentane (2). A mixture of (−)-**1** (85 mg, 0.293 mmol) and freshly prepared sodium amide (140 mg, 3.59 mmol) in dry benzene (5 mL) was heated at the reflux temperature for 15 h, cooled, and poured slowly into a mixture of water (10 mL) and pentane (10 mL). The organic phase was dried and carefully concentrated to ca. 100 μL. Preparative GC purification (15 ft × 0.25 in. 5% SE-30, 120 °C) gave **2** (17.5 mg, 32%) as a colorless liquid: IR ($CDCl_3$, cm^{-1}) 2960, 2925, 2860, 1250, 865, 840; ^1H NMR (300 MHz, $CDCl_3$) δ 2.39–0.97 (series of m, 7 H), 1.63 (s, 6 H), −0.02 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) 137.17, 120.35, 32.43, 32.35, 28.73, 27.70, 21.36, 21.08, −2.99 ppm; MS m/z (M^+) calcd 182.1490, obsd 182.1474; $[\alpha]^{25}_D$ −7.7° (c 1.13, CH_3CN).

Anal. Calcd for $C_{11}H_{22}Si$: C, 72.44; H, 12.16. Found: C, 72.13; H, 12.04.

Comparable reaction of 65 mg (0.227 mmol) of (−)-**1** with 125 mg (2.27 mmol) of freshly prepared potassium amide in benzene (7 mL) for 2 h furnished 13.2 mg (32%) of **2** after GC purification; $[\alpha]^{26}_D$ −7.39° (c 0.88, CH_3CN).

Ozonolysis of (−)-2. A cold (−78 °C) solution of (−)-**2** (9 mg, 0.049 mmol) and 2 equiv of pyridine in 1 mL of chloroform was ozonolyzed until a blue color developed. Dimethyl sulfide (50 μL), powdered zinc (30 mg), and acetic acid (1 drop) were added, and warming to room temperature was allowed to occur slowly. After the predescribed workup including preparative GC purification, there was isolated 4.5 mg (58%) of (−)-**4**, $[\alpha]^{28}_D$ −68.4° (c 0.45, $CHCl_3$), having spectral properties identical with those recorded above.

2-Methyl-1,4-diiodobutane (17). A mixture of sodium iodide (18.0 g, 120 mmol), dry acetone (40 mL), and 2-methyl-1,4-dibromobutane (7.00 g, 30 mmol)[18] was stirred overnight at room temperature under argon. The reaction mixture was filtered, concentrated under reduced pressure, diluted with pentane, and filtered through Celite. The pentane was evaporated in vacuo to provide **16** as a pale yellow liquid (9.67 g, 99%): ^1H NMR (80 MHz, $CDCl_3$) δ 3.4–3.0 (m, 4 H), 2.05–1.35 (series of m, 3 H), 0.99 (d, J = 6.0 Hz, 3 H).

***tert*-Butyl 1-(Trimethylsilyl)-3-methylcyclopentanecarboxylate (18).** To a solution of lithium diisopropylamide (70.1 mmol, from 53.9 mL of 1.30 M n-butyllithium and 11.2 mL (80.0 mmol) of diisopropylamine) in anhydrous tetrahydrofuran (200 mL) at −78 °C was added **16** (11.0 g, 58.4 mmol) dropwise. After 15 min at −78 °C, the reaction mixture was warmed to −30 °C, at which point **17** (20.8 g, 64.2 mmol) was added in one portion. Reaction was allowed to proceed at this temperature for 3 h before another 70.1 mmol of lithium diisopropylamide was introduced dropwise. After overnight stirring at 20 °C, the solution was treated with saturated ammonium chloride solution and diluted with ether (200 mL). The separated organic phase was washed with saturated sodium bicarbonate and sodium chloride solutions, dried, and concentrated. Flash chromatography of the residue afforded **18** (10.78 g, 72%) as a pale yellow oil, which was a 60:40 mixture of diastereomers (GC analysis): IR (neat, cm^{-1}) 2950, 2860, 1700, 1363, 1245, 1150, 840; ^1H NMR (300 MHz, C_6D_6) δ 2.70–2.40 (m, 1 H), 2.20–1.45 (m, 4 H), 1.37 (2 s, 9 H), 1.30–0.95 (m, 2 H), 0.98 and 0.92 (2 d, J = 6.48 and 6.45 Hz, 3 H), 0.07 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 177.55, 177.11, 79.27, 46.00, 44.77 41.07, 39.57, 35.46, 35.38, 34.51, 31.97, 30.78, 28.25, 20.25, 19.82, −3.18, −3.25 ppm; MS the molecular-ion peak was observed, but was too transient for high-resolution measurement.

Anal. Calcd for $C_{14}H_{28}O_2Si$: C, 65.57; H, 11.00. Found: C, 65.51; H, 11.14.

***cis*- and *trans*-1-(Trimethylsilyl)-3-methylcyclopentanemethanol (19 and 20).** To a cold (−10 °C), magnetically stirred solution of **18** (10.78 g, 42.0 mmol) in anhydrous dichloromethane (500 mL) under argon was added diisobutylaluminum hydride (127 mL of 1.0 M in hexane, 127 mmol) dropwise over 40 min. The reaction mixture was stirred for 4 h at −10 to 0 °C, cautiously quenched with methanol (50 mL), diluted with ether (1 L), and stirred with saturated Rochelle salt solution for 1 h. The separated organic phase was washed with brine, dried, and evaporated to leave an oil, which was purified by bulb-to-bulb distillation in a Kugelrohr apparatus. There was isolated 7.62 g (97%) of a mixture of **19** and **20** as a clear, colorless liquid. These diastereomers were separated by HPLC on silica gel to give 1.40 g of pure **19**, 1.29 g of pure **20**, and 1.58 g of residual mixture.

For **19**: IR (neat, cm^{-1}) 3340, 2940, 1245, 1040, 835; ^1H NMR (300 MHz, C_6D_6) δ 3.27 (s, 2 H), 1.80–1.35 (m, 5 H), 1.20–1.00 (m, 1 H), 0.98 (d, J = 5.9 Hz, 3 H), 0.90–0.70 (m, 2 H), 0.04 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 70.02, 40.25, 36.68, 35.42, 34.99, 31.67, 20.26, −2.96 ppm.

Anal. Calcd for $C_{10}H_{22}OSi$: C, 64.45; H, 11.90. Found: C, 64.24; H, 11.91.

For **20**: IR (neat, cm^{-1}) 3340, 2940, 1245, 1040, 835; ^1H NMR (300 MHz, C_6D_6) δ 3.27 (s, 2 H), 1.95–1.80 (m, 1 H), 1.80–1.66 (m, 1 H), 1.66–1.57 (m, 3 H), 1.35–1.20 (m, 1 H), 1.05–0.80 (m, 2 H), 0.96 (d, J = 6.3 Hz, 3 H), 0.05 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 69.52, 40.39, 36.19, 35.26, 34.57, 31.05, 19.99, −2.97 ppm; MS m/z ($M^+ - Me_3SiOH$) calcd 96.0813, obsd 96.0953.

Anal. Calcd for $C_{10}H_{22}OSi$: C, 64.45; H, 11.90. Found: C, 64.13; H, 11.81.

***trans*-1-Benzoyl-1-(trimethylsilyl)-3-methylcyclopentane (21).** A solution of **19** (1.52 g, 8.16 mmol) in benzene (100 mL) was treated with Fetizon's reagent (25 g, ~5.4 equiv),[15] and the mixture was heated at reflux while vigorously being stirred under a Dean–Stark trap for 7 h. After cooling, the mixture was filtered through a Celite pad, which was then rinsed with ether (50 mL). Evaporation of solvent provided the aldehyde as a clear liquid (1.28 g, 85%): IR (neat, cm^{-1}) 2960, 2870, 2810, 2690, 1745, 1695, 1455, 1255, 1160, 1120, 845, 755; ^1H NMR (300 MHz, C_6D_6) δ 9.52 (s, 1 H), 2.29–2.21 (m, 1 H), 1.79–1.28 (m, 6 H), 0.83 (d, J = 6.1 Hz, 3 H), −0.11 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 204.71, 54.48, 36.83, 35.68, 35.54, 29.70, 19.88, −3.81 ppm; MS m/z (M^+) calcd 184.1283, obsd 184.1299.

To a cold (−78 °C), magnetically stirred solution of the aldehyde in anhydrous ether (125 mL) was added phenyllithium (14.9 mL of 2 M, 29.8 mmol) dropwise during 10 min. After an additional 20 min, water was added and the mixture was allowed to warm to room temperature. The separated organic phase was washed with water (2 × 100 mL) and brine (100 mL), dried, and concentrated to leave 2.10 g of the carbinol, which was directly oxidized.

Table I. Haller–Bauer Cleavage of 21 and 22 (C_6H_6 Solution at the Reflux Temperature)[a]

reactant	base	time, h	isolated yield, mg	major product	diastereomeric ratio[b]
21	$NaNH_2$	2	13.1	23	98:2
		2	12.8	23	98:2
	KNH_2	5	14.4	23	96:4
		5	14.7	23	95:5
22	$NaNH_2$	3.5	16.1	24	95:5
		3.5	15.6	24	95:5
	KNH_2	10	16.0	24	94:6
		10	15.2	24	95:5

[a] The scale is as indicated in the Experimental Section (60 mg for $NaNH_2$ and 80 mg for KNH_2). [b] Determined by capillary GC.

To a stirred suspension of dry chromium trioxide (6.90 g, 6.90 mmol) in dichloromethane (150 mL) at 0 °C under argon was added pyridine (11.05 g, 14.0 mmol) dropwise via syringe. After 20 min, the above carbinol was introduced dropwise as a solution in dichloromethane (5 mL). Forty minutes later, the reaction mixture was filtered through Celite. The filter pad was rinsed with ether, and the combined filtrates were concentrated to provide 2.39 g of yellow liquid. MPLC on silica gel (elution with 0.4% ethyl acetate in petroleum ether) furnished **21** (1.40 g, 78% from the aldehyde) as a colorless solid, mp 45–47 °C (from pentane): IR (KBr, cm^{-1}) 3070, 2970, 2895, 1645, 1595, 1575, 1445, 1365, 1255, 1230, 1050, 1025, 845, 750, 700; ^1H NMR (300 MHz, C_6D_6) δ 7.89–7.86 (m, 2 H), 7.11–7.09 (m, 3 H), 2.94–2.86 (m, 1 H), 2.18–2.15 (m, 2 H), 1.83–1.73 (m, 2 H), 1.50–1.46 (m, 1 H), 0.98–0.78 (m, 1 H), 0.77 (d, J = 6.5 Hz, 3 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 205.18, 138.96, 131.10, 129.73, 128.31, 53.35, 42.72, 36.25, 35.59, 33.94, 19.74, −2.17 ppm; MS m/z (M^+) calcd 260.1597, obsd 260.1587.

Anal. Calcd for $C_{16}H_{24}OSi$: C, 73.79; H, 9.29. Found: C, 73.87; H, 9.28.

***cis*-1-Benzoyl-1-(trimethylsilyl)-3-methylcyclopentane (22).** Oxidation of 1.40 g (7.51 mmol) of **20** in benzene (100 mL) with 25 g (6.0 equiv) of Fetizon's reagent[15] as described above afforded 1.15 g (83%) of the aldehyde as a clear liquid: IR (neat, cm^{-1}) 2930, 2870, 2690, 1745, 1695, 1455, 1255, 1160, 1120, 845, 755; ^1H NMR (300 MHz, C_6D_6) δ 9.46 (s, 1 H), 2.61–2.35 (m, 1 H), 1.85–1.15 (m, 6 H), 0.84 (d, J = 6.4 Hz, 3 H), 0.04 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 204.65, 55.18, 38.41, 35.32, 34.99, 28.07, 19.58, −3.73 ppm.

This aldehyde was reacted with phenyllithium in the predescribed manner to furnish the carbinol as a yellowish liquid (1.89 g). Next, oxidation with the chromium trioxide–dipyridine complex was repeated. MPLC on silica gel afforded 1.07 g (66% from the aldehyde) of **22** as colorless crystals, mp 65–67 °C (from pentane): IR (KBr, cm^{-1}) 3060, 2950, 2880, 1630, 1595, 1445, 1250, 1060, 845, 750, 700; ^1H NMR (300 MHz, C_6D_6) δ 7.83–7.79 (m, 2 H), 7.11–7.07 (m, 3 H), 3.11–3.04 (m, 1 H), 2.49–2.39 (m, 1 H), 2.01–1.93 (m, 1 H), 1.63–1.49 (m, 2 H), 1.30–1.22 (m, 1 H), 0.95–0.83 (m, 1 H), 0.86 (d, J = 6.1 Hz, 3 H), 0.02 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 205.41, 139.28, 130.96, 129.43, 128.33, 54.15, 43.03, 36.30, 35.24, 33.79, 19.46, −2.08 ppm.

Anal. Calcd for $C_{16}H_{24}OSi$: C, 73.79; H, 9.29. Found: C, 73.81; H, 9.29.

Haller–Bauer Cleavages of 21 and 22. For those runs involving sodium amide as base, 60 mg of ketone was combined with 390 mg of sodium amide in 4 mL of dry benzene and heated at reflux. For those runs involving potassium amide, 80 mg of ketone was combined with 600 mg of the base in 4 mL of benzene and heated at reflux. The results are compiled in Table I.

For **23**: IR (neat, cm^{-1}) 2955, 2870, 1450, 1250, 900, 838, 750; ^1H NMR (300 MHz, C_6D_6) δ 1.90–1.86 (m, 1 H), 1.85–1.68 (m, 2 H), 1.58–1.48 (m, 1 H), 1.32–1.19 (m, 2 H), 1.14–0.60 (m, 2 H), 0.97 (d, J = 6.7 Hz, 3 H), −0.01 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 35.88, 34.93, 34.26, 27.43, 23.57, 20.12, −3.92 ppm; MS m/z (M^+) calcd 156.1334, obsd 156.1348.

For **24**: IR (neat, cm^{-1}) 2960, 2870, 1455, 1252, 900, 840, 750; ^1H NMR (300 MHz, $CDCl_3$) δ 1.80–1.56 (m, 4 H), 1.35–1.25 (m, 1 H), 1.05–0.78 (m, 2 H), 0.88 (d, J = 6.2 Hz, 3 H), 0.76–0.63 (m, 1 H), −0.15 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) 37.62, 36.46, 35.52, 26.85, 26.73, 20.36, 12.13 ppm.

Methyl *trans*-1-(Trimethylsilyl)-2-methylcyclopentanecarboxylate (26). To a cold (−78 °C), magnetically stirred solution of lithium diisopropylamide (26.3 mmol) in anhydrous tetrahydrofuran (150 mL) was introduced 3.21 g (21.9 mmol) of **5**. After 20 min, the reaction mixture was warmed to −30 °C and 7.45 g (23.0 mmol) of **25** was added in one portion. After 3 h, another 26.3 mmol of amide base was dripped in slowly. The resulting solution was allowed to warm to −10 °C during 3 h, quenched with saturated ammonium chloride solution (50 mL), and diluted with ether (100 mL). The separated organic phase was processed as described earlier to give 6.21 g of yellow liquid. Flash chromatography of this material on silica gel provided 2.10 g (45%) of **26** as a colorless oil: IR (neat, cm^{-1}) 2950, 2875, 1715, 1450, 1252, 1220, 842, 760; ^1H NMR (300 MHz, C_6D_6) δ 3.37 (s, 3 H), 2.58–2.56 (m, 1 H), 2.20–2.05 (m, 1 H), 1.95–1.75 (m, 1 H), 1.74–1.61 (m, 2 H), 1.45–1.38 (m, 2 H), 1.13 (d, J = 6.8 Hz, 3 H), 0.11 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 176.30, 50.47, 47.25, 40.67, 35.40, 31.59, 24.28, 17.76, −2.52 ppm; MS m/z (M^+) calcd 214.1389, obsd 214.1368.

Anal. Calcd for $C_{11}H_{22}O_2Si$: C, 61.63; H, 10.34. Found: C, 61.81; H, 10.41.

***trans*-1-(Trimethylsilyl)-2-methylcyclopentanecarboxaldehyde (27).** To a cold (−10 °C), magnetically stirred solution of **26** (2.93 g, 13.7 mmol) in anhydrous dichloromethane (250 mL) was added under a nitrogen atmosphere diisobutylaluminum hydride (41.0 mL of 1.0 M in hexane, 41.0 mmol) dropwise over 20 min. After 4 h at −10 to 0 °C, the reaction mixture was cautiously quenched with methanol (10 mL), diluted with ether (1 L), and stirred with saturated Rochelle salt solution for 1 h. The usual workup followed by Kugelrohr distillation gave 2.52 g (82%) of the primary alcohol as a colorless liquid: IR (neat, cm^{-1}) 3400, 2950, 1450, 1248, 1025, 835, 687; ^1H NMR (300 MHz, C_6D_6) δ 3.36 (q, J = 5.6 Hz, 2 H), 1.90–1.75 (m, 1 H), 1.75–1.60 (m, 2 H), 1.60–1.50 (m, 2 H), 1.45–1.20 (m, 3 H), 1.01 (d, J = 6.9 Hz, 3 H), 0.06 (s, 9 H); MS the molecular-ion peak was observed, but was too transient for high-resolution measurement.

To a suspension of anhydrous chromium trioxide (4.29 g, 42.9 mmol) in dichloromethane (100 mL) at 0 °C was added pyridine (6.79 g, 85.8 mmol) dropwise. After 20 min, the above alcohol (800 mg, 4.29 mmol) as a solution in dichloromethane (5 mL) was introduced dropwise with vigorous stirring, and the mixture was stirred at 0 °C for 1.5 h. The usual workup delivered 720 mg of **27** as a clear liquid, which was utilized without further manipulation: IR (neat, cm^{-1}) 2950, 2860, 2720, 1680, 1455, 1375, 1250, 840, 752; ^1H NMR (80 MHz, C_6D_6) δ 9.77 (s, 1 H), 2.30–0.75 (series of m, 7 H), 1.06 (d, J = 6.8 Hz, 3 H), −0.03 (s, 9 H).

***trans*-1-Benzoyl-1-(trimethylsilyl)-2-methylcyclopentane (28).** The preceding aldehyde (1.95 mmol) in anhydrous ether (100 mL) at −78 °C under nitrogen was treated with phenyllithium (12 mmol) as described earlier. After 30 min, the predescribed workup was applied to provide 1.60 g of the carbinol as a yellowish liquid.

Oxidation of this material as a solution in dichloromethane (5 mL) with the Collins reagent in a manner paralleling that detailed above, followed by MPLC on silica gel (elution with 1.5% ethyl acetate in petroleum ether), gave pure **28** (395 mg, 35% from the alcohol) as a colorless oil: IR (neat, cm^{-1}) 2950, 2870, 1640, 1250, 1235, 840, 750, 700; ^1H NMR (300 MHz, C_6D_6) δ 7.85–7.75 (m, 2 H), 7.12–7.05 (m, 3 H), 2.90–2.65 (m, 1 H), 2.50–2.30 (m, 2 H), 2.05–0.80 (series of m, 4 H), 1.02 (d, J = 6.7 Hz, 3 H), 0.10 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 206.40, 141.29, 130.81, 128.45, 127.80, 57.41, 41.26, 35.00, 30.73, 22.57, 18.44, −1.52 ppm; MS m/z (M^+) calcd 260.1594, obsd 260.1620.

Anal. Calcd for $C_{16}H_{24}OSi$: C, 73.79; H, 9.29. Found: C, 73.77; H, 9.35.

Attempted Haller–Bauer Cleavage of 28. Heating of **28** (60 mg, 0.23 mmol) with either sodium amide (390 mg, 10 mmol) or potassium amide (600 mg, 11 mmol) in dry benzene (4 mL) under nitrogen was continued until starting material was consumed, as indicated by gas chromatography. The cooled reaction mixture was quenched with saturated ammonium chloride solution and diluted with pentane (10 mL). The separated organic phase was washed with brine, dried, and concentrated to leave **29** as a pale yellow oil. For the purified (GC) major diastereomer: IR (neat, cm^{-1}) 3070, 2965, 2880, 1677, 1597, 1582, 1450, 1375, 1220, 700; ^1H NMR (300 MHz, $CDCl_3$) δ 7.97–7.93 (m, 2 H), 7.56–7.25 (m,

3 H), 3.33–3.24 (m, 1 H), 2.45–2.34 (m, 1 H), 2.10–1.40 (series of m, 5 H), 1.37–1.23 (m, 1 H), 1.03 (d, J = 6.7 Hz, 3 H); ^{13}C NMR (75 MHz, $CDCl_3$) 203.04, 137.46, 132.66, 128.44, 128.30, 54.23, 38.08, 34.88, 31.21, 24.83, 19.77 ppm; MS m/z (M^+) calcd 188.1201, obsd 188.1192.

***tert*-Butyl 1-(Trimethylsilyl)-4-*tert*-butylcyclohexanecarboxylate (33).** To a cold (−78 °C), magnetically stirred solution of lithium diisopropylamide (70 mmol) in dry tetrahydrofuran (350 mL) was added dropwise under argon a solution of **16** (11.30 g, 60 mmol) in the same solvent (30 mL). The reaction mixture was maintained at −78 °C for 10 min, allowed to warm to −30 °C, and treated dropwise with a solution of **32** (22.80 g, 60 mmol)[28] in tetrahydrofuran (30 mL). Approximately 3 h later, the solution was returned to −78 °C, treated with an additional 70 mmol of the base via cannula, and allowed to reach ambient temperature slowly during 3 h. The usual workup gave rise to 21.7 g of a dark oil consisting of a 60:40 diastereomeric mixture (GC analysis). Chromatography on silica gel (elution with 0.5% ethyl acetate in petroleum ether) provided 12.78 g (71%) of **33** as a light yellow liquid. Analytical samples of each isomer were obtained by preparative GC.

For *trans*-**33**: IR (neat, cm^{-1}) 2950, 2855, 1705, 1480, 1445, 1390, 1365, 1250, 1165, 1140, 1040, 905, 850, 755; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.22–2.18 (m, 2 H), 1.63–1.59 (m, 2 H), 1.44 (s, 9 H), 1.24–0.82 (series of m, 5 H), 0.80 (s, 9 H), 0.01 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) 175.29, 79.17, 47.80, 39.69, 32.53, 29.59, 28.29, 27.26, 24.70, −3.97 ppm; MS the molecular-ion peak was observed, but was too transient for high-resolution measurement.

Anal. Calcd for $C_{18}H_{36}O_2Si$: C, 69.17; H, 11.61. Found: C, 69.05; H, 11.61.

For *cis*-**33**: IR (neat, cm^{-1}) 2950, 2855, 1705, 1475, 1445, 1390, 1365, 1250, 1155, 840, 755; ^{1}H NMR (300 MHz, $CDCl_3$) δ 2.06–1.99 (m, 2 H), 1.71–1.61 (m, 4 H), 1.42 (s, 9 H), 1.21–0.80 (m, 3 H), 0.83 (s, 9 H), 0.10 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) 177.32, 79.32, 46.29, 38.07, 32.58, 29.90, 28.25, 27.54, 24.09, −1.32 ppm; MS the molecular-ion peak was observed, but was too transient for high-resolution measurement.

Anal. Calcd for $C_{18}H_{36}O_2Si$: C, 69.17; H, 11.61. Found: C, 69.41; H, 11.49.

***trans*- and *cis*-1-(Trimethylsilyl)-4-*tert*-butylcyclohexanecarboxaldehyde (34 and 35).** Partially enriched fractions of the diastereomeric esters **33** as derived from HPLC purification of the mixture were reduced separately. A total of 7.66 g (25.5 mmol) of **33** was treated with diisobutylaluminum hydride as described earlier, and the resulting primary alcohols were purified by HPLC on silica gel (elution with 3% ethyl acetate in petroleum ether). In the end, there was obtained 1.23 g of pure trans alcohol, 1.40 g of pure cis alcohol, 1.40 g of cis-enriched mixture, and 1.06 g of trans-enriched mixture. The combined weight of 5.19 g represents an 84% yield.

For the trans alcohol: IR (neat, cm^{-1}) 3380, 2950, 2865, 1480, 1450, 1395, 1370, 1250, 1030, 860, 755; ^{1}H NMR (300 MHz, C_6D_6) δ 3.51 (s, 2 H), 1.64–1.59 (m, 2 H), 1.41–1.31 (m, 2 H), 1.30–1.20 (m, 2 H), 1.13–0.85 (m, 4 H), 0.86 (s, 9 H), 0.10 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 64.80, 48.67, 32.61, 28.59, 27.61, 26.44, 21.79, −2.98 ppm.

For the cis alcohol: colorless crystals, mp 89–90 °C (from pentane); IR (KBr, cm^{-1}) 3370, 2960, 2860, 1480, 1450, 1390, 1370, 1255, 1030, 860, 840, 755; ^{1}H NMR (300 MHz, C_6D_6) δ 3.17 (s, 2 H), 1.87–1.81 (m, 2 H), 1.61–1.55 (m, 3 H), 1.20–0.80 (m, 5 H), 0.85 (s, 9 H), 0.15 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 73.78, 48.48, 32.58, 31.97, 29.29, 27.70, 24.68, −0.08 ppm; MS the molecular-ion peak was observed, but was too transient for high-resolution measurement.

Anal. Calcd for $C_{14}H_{30}OSi$: C, 69.35; H, 12.47. Found: C, 69.38; H, 12.39.

Oxidation of the trans alcohol (960 mg, 3.96 mmol) with anhydrous chromium trioxide (4.12 g, 41.2 mmol) and pyridine (6.52 g, 82.4 mmol) in dichloromethane (100 mL) as before afforded 890 mg of **34** as a tan solid, which was used immediately without further purification: IR (film, cm^{-1}) 2960, 2860, 1710, 1455, 1365, 1250, 1175, 1145, 1095, 850, 760, 695; ^{1}H NMR (300 MHz, C_6D_6) δ 9.49 (s, 1 H), 2.45–1.95 (m, 2 H), 1.90–1.05 (series of m, 4 H), 1.00–0.60 (m, 3 H), 0.77 (s, 9 H), 0.06 (s, 9 H).

Comparable treatment of the cis alcohol (1.00 g, 4.12 mmol) furnished **35** (920 mg) as a tan solid: IR (film, cm^{-1}) 2960, 2865, 1670, 1450, 1365, 1255, 845, 760, 690; ^{1}H NMR (300 MHz, C_6D_6) δ 9.47 (s, 1 H), 2.30–1.70 (m, 2 H), 1.60–1.45 (m, 4 H), 1.10–0.70 (m, 3 H), 0.77 (s, 9 H), −0.04 (s, 9 H).

***trans*-1-Benzoyl-1-(trimethylsilyl)-4-*tert*-butylcyclohexane (36).** Reaction of **34** (890 mg, 3.7 mmol) in cold (−78 °C) ether (80 mL) under argon with phenyllithium (14.8 mmol) as earlier described provided 1.40 g of the carbinol, which was oxidized directly as obtained under Collins conditions (4.12 g (41.2 mmol) of CrO_3, 6.52 g (82.4 mmol) of pyridine, 100 mL of dichloromethane, −10 °C). The usual workup followed by MPLC purification on silica gel (elution with 0.5% ethyl acetate in petroleum ether) gave **36** (780 mg, 62% overall) as a colorless crystalline solid, mp 109.5–110.5 °C (from pentane): IR (KBr, cm^{-1}) 3050, 2950, 2870, 1635, 1385, 1370, 1260, 980, 870, 770, 750, 705; ^{1}H NMR (300 MHz, C_6D_6) δ 7.69–7.65 (m, 2 H), 7.11–7.05 (m, 3 H), 2.79–2.73 (m, 2 H), 1.57–1.52 (m, 2 H), 1.35–1.07 (series of m, 4 H), 0.98–0.89 (m, 1 H), 0.75 (s, 9 H), 0.00 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 206.67, 142.85, 130.20, 128.32, 127.68, 49.57, 48.49, 32.52, 31.43, 27.45, 25.64, −2.74 ppm; MS m/z (M^+) calcd 316.2223, obsd 316.2205.

Anal. Calcd for $C_{20}H_{32}OSi$: C, 75.89; H, 10.19. Found: C, 75.83; H, 10.14.

***cis*-1-Benzoyl-1-(trimethylsilyl)-4-*tert*-butylcyclohexane (37).** The preceding two reactions were performed identically on **35** (920 mg, 3.8 mmol). Chromatographic purification of the residue on silica gel afforded pure **37** (785 mg, 60% from the alcohol) as a colorless solid, mp 89–90 °C (from pentane): IR (KBr, cm^{-1}) 3060, 2970, 2860, 1645, 1450, 1365, 1255, 1320, 1070, 990, 860, 845, 705; ^{1}H NMR (300 MHz, C_6D_6) δ 7.61–7.58 (m, 2 H), 7.11–7.07 (m, 3 H), 2.38–2.31 (m, 3 H), 1.85–1.75 (m, 2 H), 1.55–1.48 (m, 2 H), 1.18–1.06 (m, 2 H), 0.90–0.70 (m, 1 H), 0.78 (s, 9 H), 0.14 (s, 9 H); ^{13}C NMR (75 MHz, C_6D_6) 209.09, 141.76, 130.09, 127.91, 127.68, 46.59, 46.30, 32.56, 32.20, 27.50, 24.76, −0.26 ppm; MS m/z (M^+) calcd 316.2223, obsd 316.2216.

Anal. Calcd for $C_{20}H_{32}OSi$: C, 75.89; H, 10.19. Found: C, 75.67; H, 10.16.

Haller–Bauer Cleavages of 36 and 37. These reactions were performed as described earlier for **21** and **22**. The results are compiled in Table II.

For **38**: IR (neat, cm^{-1}) 2960, 2848, 1477, 1450, 1364, 1250, 883, 834, 750, 686; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.85–1.70 (m, 4 H), 1.15–0.7 (series of m, 5 H), 0.83 (s, 9 H), 0.44 (tt, J = 12.3, 3.0 Hz, 1 H), −0.07 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) 48.45, 32.52, 28.88, 27.89, 27.49, 25.99, −3.52 ppm; MS m/z (M^+) calcd 212.1961, obsd 212.1950.

For **39**: IR (neat, cm^{-1}) 2960, 2845, 1477, 1450, 1364, 1250, 883, 834, 750, 686; ^{1}H NMR (300 MHz, $CDCl_3$) δ 1.95–1.83 (m, 2 H), 1.65–1.44 (m, 4 H), 1.1–0.9 (m, 3 H), 0.9–0.75 (m, 1 H), 0.86 (s, 9 H), 0.06 (s, 9 H); ^{13}C NMR (75 MHz, $CDCl_3$) 48.22, 32.64, 27.70, 27.56, 25.42, 23.69, −0.56 ppm; MS m/z (M^+) calcd 212.1961, obsd 212.1968.

Anal. Calcd for $C_{13}H_{28}Si$: C, 73.50; H, 13.28. Found: C, 73.92; H, 13.29.

Desilylation–Oxidation of 36. A solution of **36** (173 mg, 0.55 mmol) in tetrahydrofuran (5 mL) was treated with tetra-*n*-bu-

Table II. Haller–Bauer Cleavage of 36 and 37 (C_6H_6 Solution at the Reflux Temperature)[a]

reactant	base	time, h	isolated yield, mg	products	product ratio[b]
36	$NaNH_2$	135	6.5	**38**; **(39)**[c]	≥95:5
			8.2	**38**; **(39)**[c]	≥95:5
	KNH_2	100	9.6	**40**	*d*
			11.7	**40**	*d*
37	$NaNH_2$	3	17.0	**39**; **(38)**[c]	≥95:5
			19.7	**39**; **(38)**[c]	≥95:5
	KNH_2	16	15.5	**40**; **39**	86:14
			18.7	**40**; **39**	86:14

[a] Same as for footnote *a* of Table I. [b] Determined by 300-MHz ^{1}H NMR (see text). [c] No direct evidence exists for the actual presence of the minor component. [d] A trace of **38** could be detected in these products (capillary GC analysis).

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tylammonium fluoride (1.0 mL of 1.0 M in tetrahydrofuran, 1.0 mmol) dropwise with stirring. The reaction mixture was stirred at room temperature for 1 h, diluted with water (10 mL), and extracted with ether (15 mL). The organic phase was washed with water (2 × 10 mL), dried, evaporated, and placed under vacuum (0.3 Torr) overnight.

The resulting desilylated ketone (167 mg) was heated with potassium amide (800 mg) and benzene (5 mL) at reflux under argon for 36 h. The reaction mixture was quenched with saturated ammonium chloride solution (10 mL) and diluted with pentane (10 mL). The organic phase was washed with water (2 × 10 mL) and dried. The solvent was carefully removed, and the residue was distilled in a Kugelrohr apparatus (35 °C/0.3 Torr). There was isolated 5.1 mg of clear colorless liquid shown by capillary GC and ^{1}H NMR to contain >80% 4-*tert*-butylcyclohexanone.

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

^{17}O NMR Studies on Alkylindanones: Steric Effects

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Received October 13, 1988

Natural abundance ^{17}O NMR spectroscopic data, in acetonitrile at 75 °C, were obtained for 32 alkyl-substituted 1-indanones (**2–33**). Excellent additivity of substituent effects was observed for the ^{17}O chemical shifts of the substituted compounds. Introduction of alkyl groups proximate to the carbonyl group (7-position) produces large (21–36 ppm) downfield shifts. These downfield shifts were correlated with repulsive van der Waals energies estimated from molecular mechanics calculations. In multisubstituted indanones substituent effects are also additive, and the downfield shifts caused by alkyl groups proximate to the carbonyl are large enough to be used to distinguish between positional isomers. Examples of the combined use of ^{1}H, ^{13}C, and ^{17}O NMR chemical shifts to make structural assignments are given.

The use of ^{17}O NMR spectroscopy as a probe for a variety of structural questions is growing at a rapid pace.[1] Recent studies have shown that quantitative relationships can be developed between downfield shifts of ^{17}O NMR data and torsion angles for aromatic nitro compounds,[2] acetophenones,[3] aromatic carboxylic acids and derivatives,[4] and aryl ketones.[5] Large downfield shifts for ^{17}O NMR data of carbonyl groups on introduction of alkyl groups promixate to the carbonyl function in a variety of systems have also been reported.[3-7] Correlations between ^{17}O NMR data and in-plane bond angle distortions for hindered 3-substituted phthalic anhydrides[6] and multisubstituted phthalimides[7] have been found. Recent reports have suggested that local van der Waals interactions are responsible for deshielding shifts for several nucleii in sterically hindered systems.[8,9] More recently it has been shown that ^{17}O chemical shifts for certain rigid, planar amides, anhydrides, and quinones are correlated with their repulsive van der Waals energies.[10] Consequently, we have clearly demonstrated that downfield chemical shift changes in the ^{17}O NMR data for hindered carbonyl systems can result from two distinctly different phenomena: torsion angle rotation and, when such rotation is not possible, from repulsive van der Waals interaction.[11] Alkylindanones are rigid, planar systems, which can be studied to further assess the importance of repulsive van der Waals interactions on ^{17}O chemical shifts. Earlier, studies[12-14] in our laboratories on the chemical and physical properties of alkylindanones provided further impetus to investigate the influence of alkyl substitution on the ^{17}O chemical shifts of hindered indanones.

Results and Discussion

The 1-indanones used in this study were purchased (1 and 18) or synthesized as described below. Polyphosphoric acid (PPA) catalyzed cyclization of 2-methyl-3-phenyl-

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