Ph); mass spectrum M^+ 204.1509 ($C_{14}H_{20}O$ requires 204.1514).

A solution of **17** (0.68 g, 3.1 mmol in 5 mL of THF) was added to 6.2 mmol of KH in 10 mL of THF at 25 °C and the solution refluxed for 30 min and filtered into a flask containing Me_3SiCl (0.93 g, 9 mmol) and Et_3N (0.6 g, 6 mmol) in 5 mL of THF at 25 °C. After stirring overnight wet THF and pentane were added and the solution was extracted with cold $NaHCO_3$ solution, dried over $CaSO_4$, and distilled at 140 °C (3 torr) to give a mixture of **12** and **18** (0.73 g, 81%) in the ratio of 55/45 as estimated from the relative intensities of the CMe_2 and the Me_3Si ^1H NMR resonances of the two isomers.

A solution of **17** (0.56 g, 2.6 mmol) in 2 mL of THF was added dropwise to a solution prepared from *i*-Pr_2NH (0.26 g, 2.6 mmol) in 20 mL of THF and 3.5 mmol of *n*-BuLi in 2 mL of hexane at 0 °C and then cooled to −78 °C. After 30 min of stirring Me_3SiCl (0.38 g, 3.5 mmol) was added and the solution allowed to warm to room temperature overnight. The solvent was evaporated to give crude **18** (0.72 g) which was separated by VPC (OV-101, 150 °C): IR (CCl_4) 1581 cm^{-1} (weak, C=C); UV λ_{max} ($CHCl_3$) 230 nm (ϵ 4500, sh, greater absorption at shorter λ); ^1H NMR (CCl_4) δ 0.22 (s, 9 $SiMe_3$), 0.85 (s, 6, CMe_2), 1.0–1.4 (m, 6, $(CH_2)_3$), 1.6–2.2 (m, 2, $C{=}CCH_2$), 7.25 (s, 5, Ph); mass spectrum $(M + 1)^+$ 289.1996 ($C_{18}H_{29}OSi$ requires 289.1980).

2-Phenyl-3-heptanone (**21**, 0.72 g, 3.8 mmol) in 3 mL of THF was added dropwise to a solution prepared from addition of *n*-BuLi (4 mmol in 2.5 mL of hexane) to *i*-Pr_2NH (0.404 g, 4.0 mmol) in 20 mL of THF at −78 °C. The solution was stirred for 1 h and Me_3SiCl (0.864 g, 8.0 mmol) was added in one portion. The solution was stirred for 2 h while warming to 25 °C, evaporated, and triturated with 20 mL of pentane which was filtered and evaporated again to give 0.77 g of an oil analyzed by VPC (3% OV-101, 150 °C) to contain **23**, **25**, and **27** in 15, 35, and 50% relative yields, respectively. These were separated on an OV-101 column. (*E*)-2-Phenyl-3-trimethylsilyloxy-2-heptene (**23**): ^1H NMR (CCl_4) δ 0.25 (s, 9, $SiMe_3$), 0.8–1.6 (m, 7, *n*-Pr), 1.87 (s, 3, $C{=}CCH_3$), 2.0–2.2 (m, 2, $C{=}CCH_2$), and 7.18 (s, 5, Ph). (*E*)-2-Phenyl-3-trimethylsilyloxy-3-heptene (**25**): ^1H NMR (CCl_4) δ 0.03 (s, 9, $OSiMe_3$), 1.06 (t, 3, J = 6 Hz, CH_3CH_2), 1.2–1.6 (m, 4, CH_2CH_2), 1.35 (d, 3, J = 7 Hz, CH_3CH), 3.40 (q, 1, J = 7 Hz, PhC*H*), 4.60 (t, 1, J = 7.5 Hz, C=CH), 7.20 (s, 5, Ph). (*Z*)-2-Phenyl-3-trimethylsilyloxy-3-heptene (**27**): ^1H NMR (CCl_4) δ 0.03 (s, 9, $OSiMe_3$), 1.06 (t, 3, J = 6 Hz, CH_3CH_2), 1.2–1.6 (m, 4, CH_2CH_2), 1.40 (d, 3, J = 7 Hz, CH_3CH), 3.90 (q, 1, J = 7 Hz) PhC*H*), 4.47 (t, 1, J = 7.5 Hz, C=CH), 7.20 (s, 5, Ph).

2-Phenyl-3-heptanone (**21**, 0.5 g, 2.6 mmol) in 3 mL of THF was added dropwise to a stirred suspension of KH (0.12 g, 3 mmol) in 10 mL of THF at 25 °C. After 30 min of stirring Me_3SiCl (0.59 g, 5.5 mmol) was added in one portion and after 1 h of stirring the solution was filtered through a filter stick, evaporated, diluted with 20 mL of pentane, filtered again, and concentrated to 0.80 g of an oil analyzed by VPC (3% OV-101, 150 °C) to show only one peak but which by ^1H NMR contained **13** and **23** in a ratio of 60 to 40.

3-Phenyl-4-octanone (**22**, 1.05 g, 5.0 mmol) was reacted with *i*-Pr_2NLi and Me_3SiCl as for **21** to give 1.04 g of an oil analyzed with the OV-101 column to contain **24**, **26**, and **28** in relative yields of 25, 30, and 45%, respectively. These were separated to give (*E*)-3-phenyl-4-trimethylsilyloxy-3-octene (**24**): ^1H NMR (CCl_4) δ 0.12 (s, 9, $SiMe_3$), 0.5–0.85 (m, 6, 2 CH_3), 1.0–1.5 (m, 4, CH_2CH_2), 1.9–2.4 (m, 4, $CH_2C{=}CCH_2$), 7.23 (s, 5, Ph); ^{13}C NMR ($CDCl_3$) 0.50, 13.75 (2 C), 22.18, 24.56, 29.67, 32.77, 122.94, 125.80, 127.79, 129.49, 141.70, 146.78. (*E*)-3-Phenyl-4-trimethylsilyloxy-4-octene (**26**): ^1H NMR (CCl_4) δ 0.02 (s, 9, $SiMe_3$), 0.8–1.1 (m, 6, 2 CH_3), 1.1–2.2 (m, 6, 3 CH_2), 3.04 (t, 1, J = 8 Hz, PhC*H*), 4.61 (t, 1, J = 7 Hz, C=CH), 7.22 (s, 5, Ph). (*Z*)-3-Phenyl-4-trimethylsilyloxy-4-octene (**28**): ^1H NMR (CCl_4) δ −0.01 (s, 9, $SiMe_3$), 0.66–1.05 (m, 6, 2 CH_3), 1.2–2.2 (m, 6, 3 CH_2), 3.53 (t, 1, J = 8 Hz, PhC*H*), 4.50 (t, 1, J = 7 Hz, C=CH), 7.18 (s, 5, Ph).

3-Phenyl-4-octanone (**22**) was reacted with KH followed by Me_3SiCl in a manner analogous to that for **21** to give the isomeric silyl vinyl ethers **14** and **24** in relative yields of 85 and 15%, respectively.

To a solution of **15** (1.0 g, 3.6 mmol) in 5 mL of pentane was added 1 mL of 1.5 N HCl, and the mixture was stirred 1 h at 25 °C. The pentane layer was separated, dried with $MgSO_4$, and evaporated to give 0.62 g (3.1 mmol, 86%) of crude 3-trimethylsilyl-4-octanone (**29**): IR ($CDCl_3$) 1681 cm^{-1} (C=O); ^1H NMR ($CDCl_3$) δ 0.10 (s, 9, SiMe), 0.8–1.9 (m, 12, Et and *n*-Pr), and 2.2–2.5 (m, 3, $CHCOCH_2$); mass spectrum M^+ 200.1592 ($C_{11}H_{24}OSi$ requires 200.1590). This material rearranged on distillation to give isomeric trimethylsilyl vinyl ethers.

Acknowledgment is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the Natural Sciences and Engineering Research Council of Canada for support of this work.

Registry No. 4, 97234-76-9; **4** (anilide derivative), 97234-95-2; **5**, 1193-47-1; **6**, 13155-56-1; **7**, 97234-77-0; **8**, 3156-07-8; **9**, 20452-67-9; **10**, 97234-78-1; **11**, 59005-31-1; **12**, 97234-79-2; **13**, 97234-80-5; **14**, 97234-81-6; **15**, 97234-82-7; **16**, 77078-58-1; **17**, 97234-83-8; **18**, 97234-79-2; **21**, 7661-44-1; **22**, 97234-84-9; **23**, 97234-85-0; **24**, 97234-86-1; **25**, 97234-87-2; **26**, 97234-88-3; **27**, 97234-89-4; **28**, 97234-90-7; **29**, 97234-91-8; **30**, 97234-92-9; **31**, 97234-93-0; Me_3SiCH_2OMe, 14704-14-4; PhEtCHCOCl, 36854-57-6; PhMeCHCOCl, 22414-26-2; $Me_3SiEtCHCOCl$, 97234-94-1; $PhNH_2$, 62-53-3; *t*-$BuCH_2COCl$, 7065-46-5; PhBr, 108-86-1; $CdCl_2$, 10108-64-2; 2-methylcyclohexanone, 583-60-8; 2,2-dimethylcyclohexanecarboxylic acid, 62581-18-4; 2-bromo-3,3-dimethylbutanoyl bromide, 74702-95-7; 2,2-dimethylcyclohexanecarbonyl chloride, 97234-96-3; diphenylcadmium, 2674-04-6.

Supplementary Material Available: Comparative NMR spectra of compounds **15**, **30**, and **31** with model compounds (1 page). Ordering information is given on any current masthead page.

Regio- and Diastereoselective Preparation of Aldols from α-Branched Ketone Enolates Generated from BHT Ester Enolates and Organolithium Reagents—In Situ Generation and Trapping of Ketenes from Ester Enolates[1]

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Contribution from the Laboratorium für Organische Chemie der Eidgenössischen Technischen Hochschule, ETH-Zentrum, CH-8092 Zürich, Switzerland. *Received November 27, 1984. Revised Manuscript Received April 2, 1985*

Abstract: The thermally induced cleavage of the lithium enolates derived from α-branched 2,6-di-*tert*-butyl-4-methylphenyl (BHT) alkanoates and 3- to 6-membered ring carboxylates to ketenes and LiO–BHT in the presence of alkyllithium compounds, benzyllithium or phenyllithium, allows the generation of thermodynamically unstable tetrasubstituted ketone enolates. These enolates give, under the conditions chosen (no amide bases, dilute solution), the corresponding silyl enol ethers with trimethylchlorosilane and aldols with aldehydes. The aldols are produced regioselectively and, in the case of unsymmetrical ketenes, diastereoselectively. Almost two dozen examples are described, illustrating the use of BHT ester enolates as **nucleophilic** ketene precursors.

From X-ray crystal structure data of ester lithium enolates we could predict the trajectory of the incipient elimination of a leaving group from an sp^2-center with formation of a ketene[3-5] (see the black arrows in formula A of Figure 1). We could also make

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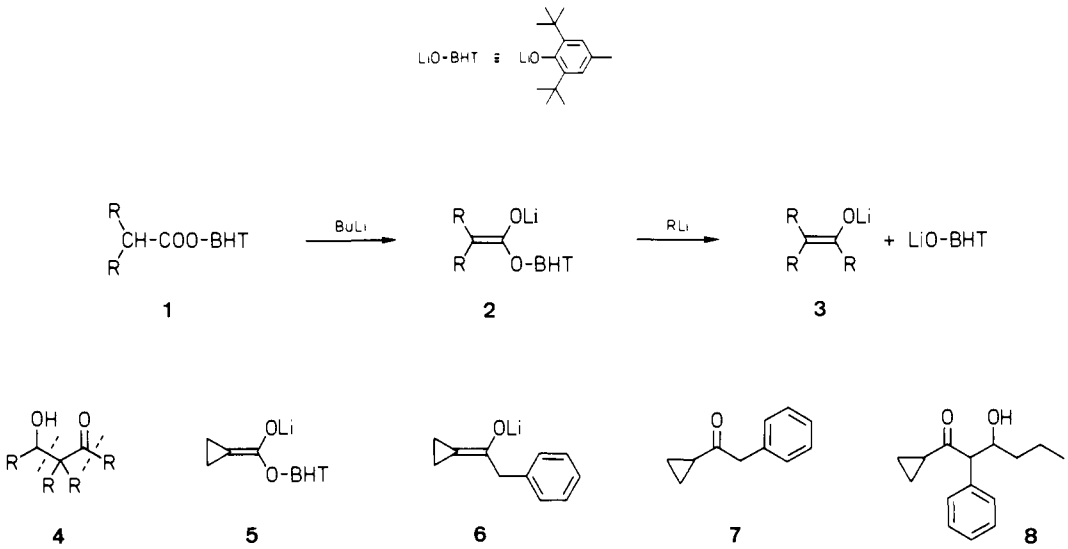
Scheme I



predictions about the reverse reaction, the addition of a nucleophile to a ketene (see the white arrows in formula B). The new structural information not only shed new light upon known properties of ester enolates[6] such as their instability compared with ketone and amide enolates and the fact that acetic ester enolates are less stable than those of higher acids but also suggested that additions of carbon nucleophiles to ketenes[7] might be very sensitive to steric hindrance. The additions should occur slowly with bulky nucleophiles, or stereoselectively with unsymmetrical ketenes (R smaller than R′ in B).[8,9] We therefore investigated a suitable type of carboxylic acid derivative, the enolate of which would serve as a nucleophilic in situ source of ketenes.[10]

BHT Ester Enolates as Ketenoids

We found[11] that the enolates **2** of 2,6-di(tert-butyl)-4-methylphenyl or BHT[12] esters **1**, when slowly warmed above ca. −20 °C in THF, in the presence of organolithium reagents, are converted to the corresponding ketone enolates **3**. These have been trapped with trimethylchlorosilane[3,5] and with aldehydes to give silyl enol ethers and the aldols, **4**, respectively (Scheme I). The scope is evident from the examples listed in Table I; the method can be successfully applied to α-branched carboxylic acid derivatives, including the BHT cycloalkane carboxylates from three- to six-membered rings. As representative nucleophiles, we employed methyl-, butyl-, benzyl-, phenyl-, and an alkynyllithium, as well as lithium diethylamide; *sec*- and *tert*-butyllithium and ethylmagnesium bromide did not work. It is remarkable that the aldols (**4**) derived from the ketone enolates (**3**) with tetrasubstituted double bonds are formed even under the most unfavorable conditions; the enolate **5** of cyclopropane carboxylate[13] furnishes

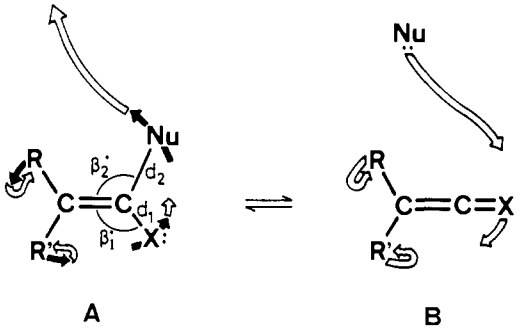


Figure 1. Sketch of the suggested reaction path for the cleavage of a molecule with a trigonal center into a molecule with a diagonal center and a leaving group Nu^-, or, equivalently, for the reverse reaction, i.e., nucleophilic attack on a diagonal center (in the case of ester enolates: X = O^-, Nu = OR″). The experimentally observed[5] differences d_2–d_1 (up to 0.11 Å) and $\beta_1' - \beta_2'$ (up to 13°) and the displacements of R and R′ from the expected positions in A were interpreted in terms of an incipient fragmentation. Similar distortions of tetrahedral centers were observed several years ago and led to the formulation of the Bürgi–Dunitz rule (see the discussions in ref 3–5).

(1) First reported in a lecture presented on the international symposium Chemistry of Carbanions at the University of Durham, Durham, England, July 17th, 1984.

(2) Part of the projected Ph.D. thesis of R. H., ETH, Zürich.

(3) Part of the Dissertation No. 7649, Th.L., ETH, Zürich, 1984.

(4) Seebach, D. "Crystal Structures and Stereoselective Reactions of Organic Lithium Derivatives", Proceedings of the Robert A. Welch Foundation, Conferences on Chemical Research, XXVII. Stereospecificity in Chemistry and Biochemistry, November 7–9, 1983, Houston, Texas, 1984, p 93.

(5) Seebach, D.; Amstutz, R.; Laube, Th.; Schweizer, W. B.; Dunitz, J. D. *J. Am. Chem. Soc.*, in press.

(6) The decomposition of ester enolates to ketenes is considered as a mechanism for the so-called self-condensation of such enolates. Bis(trimethylsilyl)ketene was isolated as the product of decomposition of the corresponding enolate; see the work of Rathke et al.: Woodbury, R. P. *Diss. Abstr. Int., B* **1977**, *37* (*12, Pt 1*), 6144. Sullivan, D. F.; Woodbury, R. P.; Rathke, M. W. *J. Org. Chem.* **1977**, *42*, 2038. Woodbury, R. I.; Lang, N. R.; Rathke, M. W. *Ibid.* **1978**, *43*, 376.

(7) The addition of polar organometallic reagents to independently prepared ketenes (mostly sterically or conjugatively stabilized ones) is well documented: Schaumann, E.; Walter, W. *Chem. Ber.* **1974**, *107*, 3562. Tidwell, Th. T. *Tetrahedron Lett.* **1979**, 4615. Friedrich, E. Dissertation, Universität Giessen, BRD, 1979. Lenoir, D.; Seikaly, H. R.; Tidwell, Th. T. *Tetrahedron Lett.* **1982**, 4987.

(8) Ketenes have often been used for N-, O-, and S-acylations. These reactions may be highly diastereoselective with unsymmetrical ketenes. Thus, addition of *tert*-butyl dibutylthioborinate to methylketene gives the vinyloxyborane of *E* configuration: Hirama, M.; Masamune, S. *Tetrahedron Lett.* **1979**, 2225. See also: Inomata, K.; Muraki, M.; Mukaijama, T. *Bull. Chem. Soc. Jpn.* **1973**, *46*, 1807.

(9) For additions to ketenes catalyzed by bases see: Pracejus, H. *Liebigs Ann. Chem.* **1960**, *634*, 9. Wynberg, H.; Staring, E. G. J. *J. Am. Chem. Soc.* **1982**, *104*, 166. Salz, U.; Rüchardt, C. *Tetrahedron Lett.* **1982**, 4017. Wynberg, H.; Staring, E. G. J. *J. Chem. Soc., Chem. Commun.* **1984**, 1181.

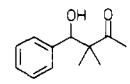
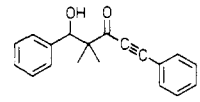
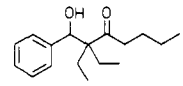
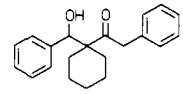
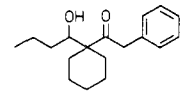
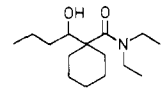
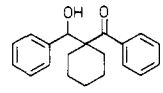
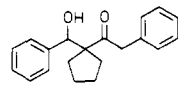
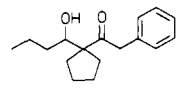
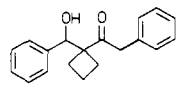
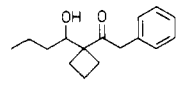
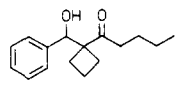
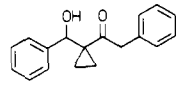
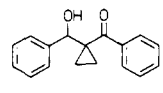
(10) Cf. also in situ generation and trapping of ketene imines: Meyers, A. I.; Knaus, G.; Kamata, K.; Ford, M. E. *J. Am. Chem. Soc.* **1976**, *98*, 567. Meyers, A. I.; Mihelich, E. D. *Angew. Chem.* **1976**, *88*, 321; *Angew. Chem., Int. Ed. Engl.* **1976**, *15*, 270.

(11) Unsuccessful attempts were made with: R_2CH–COOMe, R_2CH–COO-t-Bu, and $R_2CHCOOCO$-*t*-Bu.

(12) See the use of esters of this type (a) for providing sterically protected, but electronically effective carbonyl groups [Hassel, T.; Seebach, D. *Helv. Chim. Acta* **1978**, *61*, 2237] and (b) for the stereoselective generation of ester enolates derived from nonbranched carboxylic acids [Heathcock, C. H.; Pirrung, M. C.; Montgomery, St. H.; Lampe, J. *Tetrahedron* **1981**, 4087]; in the latter paper lithium ester *Z* enolates are specified as trans enolates, and the same species are referred to as *E* enolates in Heathcock's review article (see ref 19b).

(13) In this case, it is advantageous to use *tert*- instead of *n*-butyllithium for rapid and quantitative deprotonation of the ester. So far, only thiolesters and esters of α-(trimethylsilyl)cyclopropane carboxylic acid could be used for alkylations: Knochel, P.; Seebach, D. *Nouv. J. Chim.* **1981**, *5*, 75. Seebach, D.; Knochel, P. *Helv. Chim. Acta* **1984**, *67*, 261. Paquette, L. A.; Blankenship, C.; Wells, J. G. *J. Am. Chem. Soc.* **1984**, *106*, 6442. The reactions of **5** with various electrophiles will be reported elsewhere.

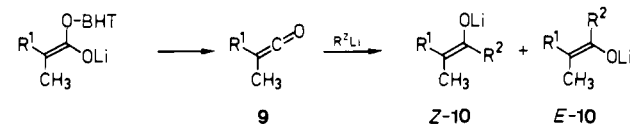
Table I. β-Hydroxy Ketones (**4a–e,g–n**) and an Amide (**4f**) Obtained from BHT Ester Li Enolates, Organolithium Reagents (10–20% excess), and Aldehydes (The Yields Are Those of Purified Products (see Experimental Section))

2,6-Di-t-butyl-4-methyl-phenyl (BHT) esters, lithium nucleophiles and aldehydes employed as starting materials	Products of type **4**	% Yield
2-methyl-propanoate methyllithium benzaldehyde	**a** 	79
2-methyl-propanoate lithio-phenyl-acetylene benzaldehyde	**b** 	56
2-ethyl-butanoate butyllithium benzaldehyde	**c** 	72
cyclohexane carboxylate benzyllithium benzaldehyde	**d** 	85
cyclohexane carboxylate benzyllithium butanal	**e** 	74
cyclohexane carboxylate lithium diethylamide butanal	**f** 	66
cyclohexane carboxylate phenyllithium benzaldehyde	**g** 	88
cyclopentane carboxylate benzyllithium benzaldehyde	**h** 	62
cyclopentane carboxylate benzyllithium butanal	**i** 	81
cyclobutane carboxylate benzyllithium benzaldehyde	**j** 	76
cyclobutane carboxylate benzyllithium butanal	**k** 	72
cyclobutane carboxylate butyllithium benzaldehyde	**l** 	60
cyclopropane carboxylate benzyllithium benzaldehyde	**m** 	44
cyclopropane carboxylate phenyllithium benzaldehyde	**n** 	29

the enolate **6** of benzyl cyclopropyl ketone regioselectively, which in turn can be trapped in reasonable yields with non-enolizable aldehydes (cf. Scheme I and the example in Table I). With the enolizable butanal a mixture of the product **7** of protonation and of the aldol **8** derived from the regioisomeric enolate is formed.

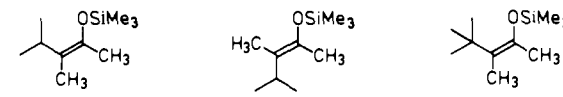
Obviously, the transformations described here crucially depend upon several factors: (i) due to steric protection of the carbonyl group, the BHT esters can be deprotonated by butyllithium, providing amine-free enolate solutions; (ii) the bulkiness of the BHT ester enolates also prevents "self-condensation", during enolate generation and/or under the conditions of substitution (**2** → **3**) of the OBHT group;[14] (iii) obedience of the stoichiometry is required, so that no proton source is present for equilibration of the enolates with their thermodynamically more stable regioisomers; (iv) only "fast" electrophiles, such as aldehydes and trimethylchlorosilane (but not alkyl halides), can be used for trapping most of these enolates; (v) BHT ester enolates stabilized by C_6H_5 or RO substituents do not undergo the reaction under the conditions tested by us; (vi) finally, the BHT esters of non-branched carboxylic acids could not be employed, maybe because the intermediate monosubstituted ketenes are deprotonated to inolates[15] by the RLi reagents present.

Scheme II



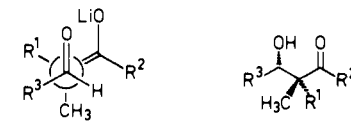
9 **Z-10** **E-10**

R^1	C_2H_5	$CH(CH_3)_2$	$C(CH_3)_3$
Z/*E* with R^2=CH_3	17:1	70:1	>99:1



11 (*Z*) **12** (*E*) **13** (*Z*)

$^5J_{CH_3CH_3}$ = 1.01 Hz 1.44 Hz 1.00 Hz



C (rel. topicity *ul*) **14** (*u*-configuration)

(specification of *like* and *unlike* for the examples in Table 2)

Generation of Ketone *Z* Enolates with Tetrasubstituted Double Bonds

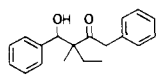
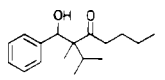
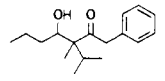
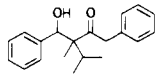
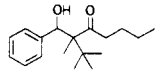
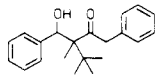
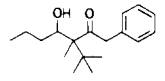
In order to examine the stereoselectivity of attack[8,9,16] of unsymmetrical ketenes **9** by organolithium reagents, we used suitably substituted BHT ester enolates (Scheme II). The ketone enolates **10** obtained by trapping with methyllithium (R^2 = CH_3) were formed diastereoselectively. The lithium enolates were O-silylated, and the configuration of the silyl enol ethers **11–13** was assigned by measuring the ^5J-coupling constants between the methyl hydrogens on the double bond, by high-field ^1H NMR spectroscopy; typical values of ca. 1 Hz in the cases of cis position and 1.5 Hz in the cases of trans position of the methyl groups were observed.[17]

(14) An S_N2- or A/E-type substitution of the OBHT group cannot be excluded by our experiments, but it is considered less likely than the mechanism involving ketenes.

(15) Cf. the generation of inolates from 5-lithio-3,4-diphenylisoxazol [Schöllkopf, U.; Hoppe, J. *Angew. Chem.* **1975**, *87*, 814; *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 765] and from (trimethylsilyl)ketene [Woodbury, R. P.; Long N. R.; Rathke, M. W. *J. Org. Chem.* **1978**, *43*, 376].

(16) Cf. the reactions of ketene groups which are part of orthoquiodimethanes: Schiess, P.; Eberle, M.; Huys-Francotte, H.; Wirz, J. *Tetrahedron Lett.* **1984**, 2201.

Table II. Aldols **14** from α-Methyl-Branched BHT Ester Li Enolates, Alkyllithium Reagents, and Aldehydes[a]

2,6-Di-t-butyl-4-methyl-phenyl (BHT) esters, lithium nucleophiles and aldehydes employed as starting materials	Products of type **14**	% Yield	% ds
2-methyl-butanoate benzyllithium benzaldehyde	**a** 	77	60
2,3-dimethyl-butanoate butyllithium benzaldehyde	**b** 	78	84
2,3-dimethyl-butanoate benzyllithium butanal	**c** 	54	83
2,3-dimethyl-butanoate benzyllithium benzaldehyde	**d** 	65	>97
2,3,3-trimethyl-butanoate butyllithium benzaldehyde	**e** 	60	>99
2,3,3-trimethyl-butanoate benzyllithium benzaldehyde	**f** 	52	>99
2,3,3-trimethyl-butanoate benzyllithium butanal	**g** 	27	84

[a] Since the deprotonation of the most hindered ester (2,3,3-trimethylbutanoate) is very slow, it is advantageous to do the lithiation and the subsequent trapping of the ketene with the same lithium compound (see Experimental Section). The diastereoselectivities are given as % ds (fraction of the major diastereomer × 100).[21] The major diastereomers **14** were separated chromatographically (except **a** and **g**) and fully characterized (see Experimental Section).

According to this assignment, the *Z*/*E* ratio rises with increasing difference in size between the two substituents on the intermediate ketene, with the methyllithium attacking the ketene from the less hindered side. If the BHT ester enolates have the *Z* configuration[12b] (Scheme II), the substitution of OBHT by CH_3 would formally take place with inversion of configuration.[14,18] Without proof, we tentatively assign the *Z* configuration also to the major isomers **10** formed with lithium derivatives other than methyllithium.

Diasteroselective Aldol Additions of Ketone Enolates with Tetrasubstituted Double Bonds to Aldehydes

The enolates from trapping unsymmetrical ketenes were used for aldol additions. The examples with yields and diastereoselectivities (% ds of major isomers) are given in Table II. We assume that the α,α-disubstituted aldols **14** are formed by the same steric course as previously shown for less substituted analogues[19] (see **C** in Scheme II), i.e., by combination of the two trigonal centers with relative topicity[20] ul.

The method outlined here provides lithium ketone enolates with a tetrasubstituted double bond, and thus the corresponding α,α-disubstituted aldols, regio- and diastereoselectively. The present work constitutes a case in which the idea to search for a synthetic method actually occurred to us while doing a systematic X-ray crystal structure analysis with quite a different goal.[3-5]

Experimental Section

General. All reactions were carried out under argon atmosphere. Tetrahydrofuran (THF) and toluene were freshly distilled over potassium and sodium, respectively, before use. *N,N,N',N'*-Tetramethylethylenediamine (TMEDA) was distilled over CaH_2 and stored under argon. Commercially available solutions of butyllithium (BuLi, ca. 1.6 M in hexane), *tert*-butyllithium (*t*-BuLi, ca. 1.6 M in pentane), and methyllithium (MeLi, ca. 1.6 M in diethyl ether) were standardized by the diphenylacetic acid method.[22] Benzyllithium (BzLi) was always freshly prepared following the procedure (with TMEDA) described in the literature.[23] Phenyllithium (PhLi) was prepared as described in the literature.[24] Flash chromatography[25] involved silica gel 60 (E. M. Merck, Darmstadt, particle size 0.040–0.063 mm, 230–400 mesh, ASTM). Diastereomeric ratios of crude products were determined by ^{13}C NMR spectroscopy.

General Procedure: Generation of BHT Ester Enolates. A solution of the BHT ester (2.5 to 10 mmol) in 2.5 to 10 mL of THF is added dropwise to a solution of BuLi (1.05 equiv) in 25 to 100 mL of THF at −78 °C. The solution is stirred at −78 °C for 30 to 60 min.

General Procedure: Workup. The reaction is quenched with 5 mL of saturated aqueous NH_4Cl, and the reaction mixture is warmed to room temperature, diluted with 40 mL of ether, washed with 1% aqueous HCl and brine, dried over Na_2SO_4, and concentrated.

Lithiophenylacetylene was prepared by treating a solution of a slight excess of phenylacetylene (10.5 mmol) in 20 mL of THF with BuLi (10.0 mmol) at −78 °C. The slightly yellow solution was stirred for 1 h before use.

Inverse Addition Procedure. The solution of the enolate was pressed through a Teflon brand tube to a solution of the aldehyde.[26]

Illustrative Procedure for the Preparation of BHT Esters.[12b] **2,6-Bis(1,1-dimethylethyl)-4-methylphenyl Cyclohexanecarboxylate (BHT Cyclohexanecarboxylate (1c)).** BuLi (187 mmol) was added to an ice-cooled solution of BHT (41.3 g, 187 mmol) in 200 mL of THF. After a period of 15 min, cyclohexanecarbonyl chloride (29.0, g, 198 mmol) was added and the mixture stirred at room temperature for 24 h and poured onto 100 mL of saturated NH_4Cl. After separation of the layers, the aqueous layer was extracted with 200 mL of ether, and the organic phases were combined and washed with saturated $NaHCO_3$ and brine, dried over Na_2SO_4, and concentrated. Recrystallization from methanol gave 52.0 g (85%) of **1c**: mp (pentane) 88.8–89.2 °C; ^1H NMR ($CDCl_3$) δ 1.30 (s, 18 H, *t*-Bu), 1.30–2.00 (m, 8 H), 2.00–2.25 (m, 2 H), 2.25 (s, 3 H, $ArCH_3$), 2.30–2.70 (m, 1 H, CHCO), 7.10 (s, 2 H, ArH). Anal. Calcd for $C_{22}H_{34}O_2$: 79.95; H, 10.37. Found: C, 80.09; H, 10.31.

2,6-Bis(1,1-dimethylethyl)-4-methylphenyl 2-Methylpropanoate (BHT 2-Methylpropanoate (1a)). Treatment of isobutyryl chloride as described above yielded 82% of **1a** after recrystallization from methanol: mp (pentane) 50.2–51.0 °C; ^1H NMR ($CDCl_3$) δ 1.30 (s, 18 H, *t*-Bu), 1.30–1.40 (d, 6 H, $CH_3(CH)CH_3$), 2.30 (s, 3 H, $ArCH_3$), 2.83 (h, J = 7 Hz, 1 H, $CH(CH_3)_2$), 7.13 (s, 2 H, ArH). Anal. Calcd for $C_{19}H_{30}O_2$: C, 78.57; H, 10.41. Found: C, 78.74; H, 10.46.

2,6-Bis(1,1-dimethylethyl)-4-methylphenyl Cyclopentanecarboxylate (BHT Cyclopentanecarboxylate (1d)). Treatment of cyclopentanecarbonyl chloride as described above yielded 76% of **1d** after recrystallization from methanol: mp (pentane) 80.2–81.6 °C; ^1H NMR ($CDCl_3$) δ 1.30 (s, 18 H, *t*-Bu), 1.55–2.20 (m, 8 H), 2.30 (s, 3 H, $ArCH_3$), 2.80–3.20 (m, 1 H, CHCO), 7.10 (s, 2 H, ArH). Anal. Calcd for $C_{21}H_{32}O_2$: C, 79.70; H, 10.19. Found: C, 79.67; H, 10.22.

2,6-Bis(1,1-dimethylethyl)-4-methylphenyl Cyclobutanecarboxylate (BHT cyclobutanecarboxylate (1e)). Treatment of cyclobutanecarbonyl chloride as described above yielded 74% of **1e** after recrystallization from methanol: mp (pentane) 52.0–53.6 °C; ^1H NMR ($CDCl_3$) δ 1.25 (s, 18 H, *t*-Bu), 1.75–2.73 (m, 6 H), 2.27 (s, 3 H, $ArCH_3$), 3.15–3.65 (m, 1 H, CHCO), 7.10 (s, 2 H, ArH). Anal. Calcd for $C_{20}H_{30}O_2$: C, 79.42; H, 10.00. Found: C, 79.29; H, 10.12.

2,6-Bis(1,1-dimethylethyl)-4-methylphenyl Cyclopropanecarboxylate (BHT Cyclopropanecarboxylate (1f)). Treatment of cyclopropanecarbonyl chloride as described above yielded 92% of **1f** after recrystallization from methanol: mp (pentane) 66.8–67.6 °C; ^1H NMR ($CDCl_3$)

(17) Sternhell, S. *Q. Rev.* **1969**, *23*, 236 and references cited therein.
(18) For in situ trapping of the thermodynamically less stable regioisomeric ketone enolates with di- or trisubstituted double bond by deprotonation see: Corey, E. J.; Gross, A. W. *Tetrahedron Lett.* **1984**, *25*, 495.
(19) Reviews: (a) Seebach, D.; Goliński, J. *Helv. Chim. Acta* **1981**, *64*, 1413. (b) Heathcock, C. H. "The Aldol Addition Reaction" In "Asymmetric Synthesis"; Morrison, J. D., Ed.; Academic Press: Orlando, 1984; Vol. 3, p 111.
(20) Seebach, D.; Prelog, V. *Angew. Chem.* **1982**, *94*, 696; *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 654.
(21) Seebach, D.; Naef, R. *Helv. Chim. Acta* **1981**, *64*, 2704. Thaisrivongs, S.; Seebach, D. *J. Am. Chem. Soc.* **1983**, *105*, 7407.
(22) Kofron, W. G.; Baclawski, L. M. *J. Org. Chem.* **1976**, *41*, 1879.
(23) Eberhardt, G. G.; Butte, W. A. *J. Org. Chem.* **1964**, *29*, 2928.
(24) Seebach, D.; Neumann, H. *Chem. Ber.* **1974**, *101*, 847.
(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.
(26) Seebach, D.; Weller, Th.; Protschuk, G.; Beck, A. K.; Hoekstra, M. S. *Helv. Chim. Acta* **1981**, *64*, 716. Seebach, D.; Hidber, A. *Chimia* **1983**, *37*, 449.

δ 0.90–1.20 (m, 4 H), 1.35 (s, 18 H, *t*-Bu), 1.75–2.05 (m, 1 H, CHCO), 2.27 (s, 3 H, $ArCH_3$), 7.15 (s, 2 H, ArH). Anal. Calcd for $C_{19}H_{28}O_2$: C, 79.12, H, 9.79. Found: C, 79.39; H, 9.81.

2,6-Bis(1,1-dimethylethyl)-4-methylphenyl 2-Methylbutanoate (BHT 2-Methylbutanoate (1g)). Treatment of 2-methylbutyryl chloride as described above yielded 63% of **1g** as a colorless liquid after bulb-to-bulb distillation: bp (air temperature) 110 °C (0.05 torr); ^1H NMR ($CDCl_3$) δ 1.00 (t, J = 7 Hz, $CH_3(CH_2)$), 1.30 (s, 18 H, *t*-Bu), 1.30–1.45 (d, 3 H, $CH_3(CH)$), 1.80–2.25 (m, 2 H, $CH_2(CH_3)$), 2.30 (s, 3 H, $ArCH_3$), 2.40–2.80 (m, 1 H, $CH(CH_3)$), 7.15 (s, 2 H, ArH). Anal. Calcd for $C_{20}H_{32}O_2$: C, 78.90; H, 10.59. Found: C, 79.06%; H, 10.41.

2,6-Bis(1,1-dimethylethyl)-4-methylphenyl 2,3-Dimethylbutanoate (BHT 2,3-Dimethylbutanoate (1h)). Treatment of 2,3-dimethylbutyryl chloride[27] as described above yielded 62% of **1h** after recrystallization from methanol: mp (pentane) 75.8–77.4 °C; ^1H NMR ($CDCl_3$) δ 0.97 (d, J = 7 Hz, 3 H, $CH_3(CHCH_3)$), 1.07 (d, J = 7 Hz, 3 H, $CH_3(CHCH_3)$), 1.25–1.35 (d, 3 H, $CH_3(CH)$), 1.30 (s, 18 H, *t*-Bu), 2.23–2.53 (m, 1 H), 2.30 (s, 3 H, $ArCH_3$), 2.53–2.85 (m, 1 H), 7.10 (s, 2 H, ArH). Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.07; H, 10.57.

2,6-Bis(1,1-dimethylethyl)-4-methylphenyl 2-Ethylbutanoate (BHT 2-Ethylbutanoate (1b)). To a cooled (ice bath) solution of BHT (8.80 g, 40 mmol) in 50 mL of THF was added BuLi (40 mmol), followed by 2-ethylbutyryl chloride (5.92 g, 44 mmol). After stirring at room temperature overnight, the solution was refluxed for 6 h for completion of the reaction, cooled to room temperature, and worked up as described above. The crude product was purified by bulb-to-bulb distillation (120 °C (0.05 torr)) to give 11.2 g (88%) of **1b** as a colorless visous liquid which solidified upon cooling: mp (pentane) 45.0–45.8 °C; ^1H NMR ($CDCl_3$) δ 1.05 (t, J = 7 Hz, 6 H, $CH_3(CH_2)$), 1.33 (s, 18 H, *t*-Bu), 1.65–2.15 (m, 4 H), 2.30 (s, 3 H, $ArCH_3$), 2.40–2.70 (m, 1 H, CHCO), 7.10 (s, 2 H, ArH). Anal. Calcd for $C_{21}H_{34}O_2$: C, 79.19; H, 10.76. Found: C, 79.07; H, 10.91.

2,6-Bis(1,1-dimethylethyl)-4-methylphenyl 2,3,3-Trimethylbutanoate (BHT 2,3,3-Trimethylbutanoate (1i)). To a cooled (ice bath) solution of BHT (16.5 g, 75 mmol) in 80 mL of THF was added BuLi (75 mmol), followed by 2,3,3-trimethylbutyryl chloride[28] (11.6 g, 78 mmol). The mixture was refluxed for 36 h, cooled to room temperature, and poured onto 50 mL of saturated NH_4Cl and the layers were separated. The aqueous phase was extracted with 200 mL of pentane, and the organic phases were combined, washed with saturated $NaHCO_3$ and brine, dried over $MgSO_4$, and concentrated. Recrystallization from methanol gave 10.9 g (44%) of **1i**: mp (pentane) 88.2–89.0 °C; ^1H NMR ($CDCl_3$) δ 1.10 (s, 9 H, *t*-Bu), 1.30 (s, 9 H, Ar-*t*-Bu), 1.33 (s, 9 H, Ar-*t*-Bu), 1.50 (d, J = 7 Hz, 3 H, $CH_3(CH)$), 2.30 (s, 3 H, $ArCH_3$), 2.57 (q, J = 7 Hz, 1 H, $CH(CH_3)$), 7.15 (s, 2 H, ArH). Anal. Calcd for $C_{22}H_{36}O_2$: C, 79.25; H, 11.01. Found: C, 79.46; H, 10.91.

3,3-Dimethyl-4-hydroxy-4-phenylbutan-2-one (4a). MeLi (8.0 mmol) was added to a solution of the enolate of BHT ester **1a** (8.0 mmol). The solution was warmed to room temperature overnight and again cooled to −78 °C. A solution of benzaldehyde (0.896 g, 8.4 mmol) in 5 mL of THF was added dropwise. The solution was stirred for 5 min and worked up to give 3.047 g of a white solid of which 0.728 g was purified by flash chromatography (pentane:ether = 40:60) to yield 0.288 g (79%) of **4a** as a white solid: mp (pentane) 75.0–76.2 °C; ^1H NMR ($CDCl_3$ δ 1.05 (s, 3 H, $CH_3C(CH_3)$), 1.15 (s, 3 H, $CH_3C(CH_3)$), 2.20 (s, 3 H, CH_3CO), 2.90 (d, J = 4 Hz, 1 H, OH), 4.90 (d, J = 4 Hz, 1 H, ArCH), 7.30 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 18.35 (q), 22.84 (q), 26.70 (q), 52.24 (s), 78.53 (d), 127.67 (d), 127.77 (d), 140.37 (s), 215.31 (s); MS, m/e 86 (M^+ − 106, 100). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.91; H, 8.20.

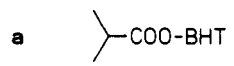
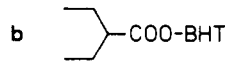
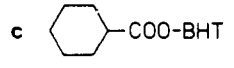
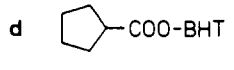
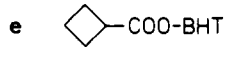
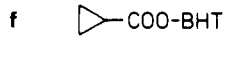
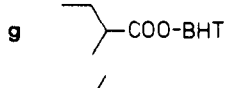
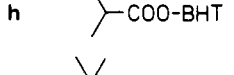
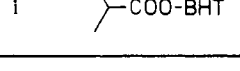
4,4-Dimethyl-1,5-diphenyl-5-hydroxy-1-pentyn-3-one (4b). Lithiophenylacetylene (3.3 mmol) was added to a solution of the enolate of BHT ester **1a** (3.0 mmol). The solution was warmed to room temperature overnight. After cooling to −78 °C a solution of benzaldehyde (0.417 g, 4.0 mmol) in 4 mL of THF was added dropwise. The solution was stirred for 5 min and worked up to give 1.484 g of an oil of which 0.792 g was purified by flash chromatography (pentane:ether = 85:15) to yield 0.248 g (56%) of solid **4b**: mp (pentane/ether) 74.4–75.0 °C; ^1H NMR ($CDCl_3$) δ 1.10 (s, 3 H, CH_3), 1.23 (s, 3 H, CH_3), 2.70 (s br, 1 H, OH), 5.13 (s, 1 H, ArCH), 7.20–7.67 (m, 5 H, ArH), 7.30 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 17.97 (q), 22.70 (q), 53.36 (s), 77.86 (d), 86.44 (s), 93.25 (s), 120.19 (s), 127.85 (d), 128.67 (d), 130.81 (d), 133.12 (d), 140.06 (s); MS, m/e 278 (M^+), 172 (M^+ − 106, 100). Anal. Calcd for $C_{19}H_{18}O_2$: C, 81.99; H, 6.52. Found: C, 82.11; H, 6.41.

2,2-Diethyl-1-hydroxy-1-phenylheptan-3-one (4c). A solution of BHT ester **1b** (0.837 g, 2.6 mmol) in 3 mL of THF was added to a solution of BuLi (5.3 mmol) in 40 mL of THF at −78 °C. The solution was warmed to room temperature overnight and cooled to −78 °C again. Benzaldehyde (0.320 g, 3.0 mmol) was dissolved in 2 mL of THF and added slowly. Stirring for 5 min and workup gave 1.252 g of a yellow oil of which 1.165 g was purified by flash chromatography (pentane:ether = 92:8) to yield 0.456 g (72%) of **4c** as a colorless liquid: ^1H NMR ($CDCl_3$) δ 0.87 (t, J = 8 Hz, 3 H, CH_3), 0.90 (t, J = 8 Hz, 3 H, CH_3), 0.95 (t, J = 8 Hz, 3 H, CH_3), 1.10–1.90 (m, 8 H), 2.20–2.50 (m, 2 H, CH_2CO), 3.57 (d, J = 5 Hz, 1 H, OH), 4.93 (d, J = 5 Hz, 1 H, ArCH), 7.27 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 8.85 (q), 9.45 (q), 13.91 (q), 22.33 (t), 23.92 (t), 25.44 (t), 26.30 (t), 39.85 (t), 58.95 (s), 76.97 (d), 127.31 (d), 127.61 (d), 127.92 (d), 140.98 (s), 218.32 (s); MS, m/e 71 (100). Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.52; H, 10.06.

1,4-Diphenyl-4-hydroxy-3,3-pentamethylenebutan-2-one (4d). BzLi (10.4 mmol) was added to a solution of the enolate of BHT ester **1c** (9.1 mmol). The solution was warmed to room temperature overnight and added dropwise by the inverse addition procedure to a solution of benzaldehyde (1.20 g, 11.3 mmol) in 30 mL of THF at −78 °C. After completion of addition the solution was stirred for another 5 min. Workup gave 4.70 g of a white solid of which 1.519 g was purified by flash chromatography (pentane:ether = 9:1 to 1:1) to give 0.766 g (85%) of white solid **4d**: mp (pentane/ether) 106.8–108.0 °C; ^1H NMR ($CDCl_3$) δ 0.97–1.75 (m, 8 H), 2.03–2.37 (m, 2 H), 2.60 (d, J = 5 Hz, 1 H, OH), 3.75 (AB, J = 17 Hz, 2 H, $ArCH_2$), 4.77 (d, J = 5 Hz, 1 H, ArCH), 7.03–7.40 (m, 10 H, ArH); ^{13}C NMR ($CDCl_3$) δ 22.88 (t), 23.25 (t), 25.75 (t), 28.56 (t), 31.61 (t), 46.14 (t), 57.06 (s), 79.70 (d), 126.51, 127.63, 127.85, 128.23, 129.94 (d), 134.76 (s), 140.55 (s), 212.69 (s); MS, m/e 83 (100). Anal. Calcd for $C_{21}H_{24}O_2$: C, 81.78; H, 7.84. Found: C, 81.73; H, 7.82.

4-Hydroxy-3,3-pentamethylene-1-phenylheptan-3-one (4e). BzLi (3.25

Table III. BHT Esters **1** Prepared from the Corresponding Acid Chlorides

2,6-Di-t-butyl-4-methyl-phenyl (BHT) ester **1**	Yield (%)	Mp (°C) (pentane)
a 	82	50.2-51.0
b 	88	45.0-45.8
c 	85	88.8-89.2
d 	76	80.2-81.6
e 	74	52.0-53.6
f 	92	66.8-67.6
g 	63	110/0.05 Torr[a]
h 	62	75.8-77.4
i 	44	88.2-89.0

[a] Bp (bulb-to-bulb distillation; air temperature)

(27) 2,3-Dimethylbutanoic acid was prepared as described in the literature; see: Hommelen, M. *Bull. Soc. Chim. Belg.* **1933**, *42*, 243.

(28) 2,3,3-Trimethylbutanoic acid was prepared by hydrolysis (refluxing for 20 h in 25% KOH in ethanol:water = 2:1) of the corresponding ethyl ester; cf. the following: Mac Phee, J. A.; Dubois, J.-E. *J. Chem. Soc., Perkin Trans. 1* **1977**, 694.

mmol) was added to a solution of the enolate of BHT ester **1c** (3.0 mmol). The solution was warmed to room temperature overnight and added dropwise by the inverse addition procedure to a solution of butanal (0.301 g, 4.2 mmol) in 10 mL of THF at −78 °C. After completion of addition the solution was stirred for another 5 min. Workup gave 1.536 g of a yellow oil of which 0.726 g was purified by flash chromatography (pentane:ether = 70:30) to give 0.287 g (74%) of the desired aldol **4e**: mp (pentane) 64.0–65.0 °C; ^{1}H NMR ($CDCl_3$) δ 0.87 (t, J = 6 Hz, 3 H, CH_3), 1.03–1.75 (m, 12 H), 2.00–2.30 (m, 2 H, CH_2(CHOH)), 2.23 (d, J = 6 Hz, 1 H, OH), 3.40–3.67 (m, 1 H, CH(OH)), 3.85 (AB, J_{AB} = 16 Hz, 2 H, $ArCH_2$), 7.07–7.43 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 13.92 (q), 20.08 (t), 22.86 (t), 23.13 (t), 26.07 (t), 29.96 (t), 30.46 (t), 34.40 (t), 45.99 (t), 57.09 (s), 76.77 (d), 126.67 (d), 128.35 (d), 130.02 (d), 134.96 (s), 212.59 (s); MS, m/e 202 (M^+ − 72, 15). Anal. Calcd for $C_{18}H_{26}O_2$: C, 78.79; H, 9.55. Found: C, 78.91; H, 9.76.

***N,N*-Diethyl-3-hydroxy-2,2-pentamethylenehexanamide (4f).** A solution of BHT ester **1c** (2.633 g, 8.0 mmol) in 8 mL of THF was added to a solution of BuLi (16.0 mmol) in 50 mL of THF at −78 °C. After stirring for 30 min diethylamine (0.701 g, 9.5 mmol) was added. The solution was warmed to room temperature overnight and again cooled to −78 °C. A solution of butanal (0.605 g, 8.3 mmol) in 4 mL of THF was added. After warming to room temperature the reaction was quenched with 5 mL of saturated NH_4Cl. The reaction mixture was diluted with 100 mL of CH_2Cl_2, washed with 40 mL of 1% HCl, and separated. The aqueous phase was twice extracted with 50 mL of CH_2Cl_2, and the organic phases were combined and dried over Na_2SO_4. Removal of the solvent gave 3.64 g of an oil of which 0.838 g was purified by flash chromatography (pentane:ether = 1:1) to give 0.313 g (66%) of the desired amide **4f**: mp (pentane/ether) 89.4–90.4 °C; ^{1}H NMR ($CDCl_3$) δ 0.80–1.05 (m, 3 H, CH_3), 1.15 (t, J = 7 Hz, 6 H, 2 CH_3-[CH_2N]), 1.20–1.80 (m, 12 H), 1.90–2.30 (m, 2 H), 2.37 (d, J = 6 Hz, 1 H, OH), 3.30–3.80 (m, 5 H, N(CH_2)$_2$, CHO); ^{13}C NMR ($CDCl_3$) δ 13.28 (q), 14.01 (q), 20.16 (t), 23.58 (t), 23.68 (t), 26.36 (t), 31.00 (t), 32.85 (t), 34.66 (t), 42.22 (t), 53.71 (s), 75.58 (d), 173.87 (s); MS, m/e 255 (M^+, 0.9). Anal. Calcd for $C_{15}H_{29}O_2N$: C, 70.54; H, 11.45; N, 5.48. Found: C, 70.66, H, 11.28; N, 5.36.

1,3-Diphenyl-3-hydroxy-2,2-pentamethylenepropan-1-one (4g). PhLi (3.4 mmol) was added to a solution of the enolate of BHT ester **1c** (3.0 mmol). The solution was warmed to room temperature overnight and cooled to −78 °C. Benzaldehyde (0.420 g, 4.0 mmol) was dissolved in 4 mL of THF and added slowly. The solution was stirred for 5 min and worked up to give 1.727 g of an oil of which 0.820 g was purified by flash chromatography (pentane:ether = 80:20) and recrystallized from pentane/ether to give 0.367 g (88%) of **4g**: mp 121.8–122.4 °C; ^{1}H NMR ($CDCl_3$) δ 0.90–1.60 (m, 8 H), 2.20–2.55 (m, 2 H), 2.83 (d, J = 5 Hz, 1 H, OH), 4.90 (d, J = 5 Hz, 1 H, ArCH), 7.30 (s, 5 H, ArH), 7.35 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 22.51 (t), 23.12 (t), 25.70 (t), 29.96 (t), 33.45 (t), 57.60 (s), 80.25 (d), 127.07 (d), 127.92 (d), 130.3 (d), 141.10 (s), 141.66 (s), 211.89 (s); MS, m/e 188 (M^+ − 106, 38). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.58; H, 7.58.

1,4-Diphenyl-4-hydroxy-3,3-tetramethylenebutan-2-one (4h). BzLi (2.55 mmol) was added to a solution of the enolate of BHT ester **1d** (2.45 mmol). The solution was warmed to room temperature overnight and added dropwise by the inverse addition procedure to a solution of benzaldehyde (0.297 g, 28 mmol) in 10 mL of THF at −78 °C. After completion of addition the solution was stirred for another 5 min. Workup gave 1.178 g of a yellow oil of which 1.125 g was purified by flash chromatography (pentane:ether = 70:30) to yield 0.429 g (62%) of the aldol **4h**: mp (pentane/ether) 91.0–91.8 °C; ^{1}H NMR ($CDCl_3$) δ 1.30–1.73 (m, 4 H), 1.80–2.25 (m, 4 H), 3.13 (d, J = 5 Hz, 1 H, OH), 3.70 (s, 2 H, $ArCH_2$), 4.90 (d, J = 5 Hz, 1 H, ArCH), 7.0–7.4 (m, 5 H, ArH), 7.30 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 24.87 (t), 25.35 (t), 30.48 (t), 33.32 (t), 46.10 (t), 65.33 (s), 78.26 (d), 126.78, 127.48, 127.87, 128.13, 128.37, 129.66, 134.54 (s), 141.12 (s), 213.19 (s); MS, m/e 188 (M^+ − 106, 33), 91 (100). Anal. Calcd for $C_{20}H_{22}O_2$: C, 81.60; H, 7.53. Found: C, 81.75; H, 7.60.

4-Hydroxy-1-phenyl-3,3-tetramethyleneheptan-2-one (4i). BzLi (3.1 mmol) was added to a solution of the enolate of BHT ester **1d** (3.0 mmol). The solution was warmed to room temperature overnight and added dropwise by the inverse addition procedure to the solution of butanal (0.307 g, 4.2 mmol) in 10 mL of THF at −78 °C. After completion of addition the solution was stirred for another 5 min. Workup gave 1.445 g of an oil of which 0.733 g was purified by flash chromatography (pentane:ether = 70:30) to yield 0.321 g (81 %) of **4i** as a colorless, viscous liquid: ^{1}H NMR ($CDCl_3$) δ 0.90 (t, J = 6 Hz, 3 H, CH_3), 1.10–1.47 (m, 4 H), 1.47–1.80 (m, 5 H), 1.80–2.25 (m, 3 H), 2.45 (d, J = 7 Hz, 1 H, OH), 3.55–3.85 (m, 1 H, CH(OH)), 3.85 (s, 2 H, $ArCH_2$), 7.10–7.40 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 13.96 (q), 20.04 (t), 25.84 (t), 26.34 (t), 31.67 (t), 32.18 (t), 35.47 (t), 45.80 (t), 65.11 (s), 76.27 (d), 126.78 (d), 128.46 (d), 129.67 (d), 134.89 (s), 212.48 (s); MS, m/e 69 (100). Anal. Calcd for $C_{17}H_{24}O_2$: C, 78.42; H, 9.29. Found: C, 78.25; H, 9.43.

1,4-Diphenyl-4-hydroxy-3,3-trimethylenebutan-2-one (4j). BzLi (5.2 mmol) was added to a solution of the enolate of BHT ester **1e** (5.0 mmol). The solution was warmed to room temperature overnight and added dropwise by the inverse addition procedure to a solution of benzaldehyde (0.583 g, 5.5 mmol) in 10 mL of THF at −78 °C. After completion of addition the solution was stirred for another 5 min. Workup gave 2.525 g of an oil of which 1.219 g was purified by flash chromatography (pentane:ether = 70:30) to yield 0.515 g (76 %) of **4j** as a colorless, viscous liquid: ^{1}H NMR ($CDCl_3$) δ 1.45–1.80 (m, 2 H, (CH_2)CH_2(CH_2)), 2.20–2.47 (m, 4 H, CH_2(CH_2)CH_2), 3.00 (d, J = 5 Hz, 1 H, OH), 3.67 (AB, J = 16 Hz, 2 H, $ArCH_2$), 4.93 (d, J = 5 Hz, 1 H, ArCH), 6.97–7.33 (m, 5 H, ArH), 7.27 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 15.32 (t), 26.06 (t), 27.46 (t), 45.95 (t), 58.83 (s), 77.14 (d), 126.70, 126.88, 127.98, 128.31, 129.67, 134.33 (s), 140.80 (s), 212.25; MS, m/e 280 (M^+). Anal. Calcd for $C_{19}H_{20}O_2$: C, 81.40; H, 7.19. Found: C, 81.20; H, 7.17.

4-Hydroxy-1-phenyl-3,3-trimethyleneheptan-2-one (4k). BzLi (5.4 mmol) was added to a solution of the enolate of BHT ester **1e** (5.1 mmol). The solution was allowed to warm to room temperature overnight and was added dropwise by the inverse addition procedure to a solution of butanal (0.433 g, 6.0 mmol) in 10 mL of THF. After completion of addition the solution was stirred for another 5 min. Workup gave 2.221 g of colorless crude product, of which 0.778 g was purified by flash chromatography (pentane:ether = 70:30) to give 0.315 g (72%) of **4k** as a colorless, viscous liquid: ^{1}H NMR ($CDCl_3$) δ 0.93 (t, J = 6 Hz, 3 H, CH_3), 1.15–1.55 (m, 4 H), 1.67–2.53 (m, 7 H), 3.73–4.00 (m, 1 H, CH(OH)), 3.85 (s, 2 H, $ArCH_2$), 7.10–7.45 (5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 13.95 (q), 15.17 (t), 19.79 (t), 26.39 (t), 34.47 (t), 45.53 (t), 58.73 (s), 75.11 (d), 126.75 (d), 128.45 (d), 129.71 (d), 134.66 (s), 211.73 (s); MS, m/e 174 (M^+ − 72, 5), 55 (100). Anal. Calcd for $C_{16}H_{22}O_2$: C, 78.01; H, 9.00. Found: C, 78.12; H, 9.14.

1-Hydroxy-1-phenyl-2,2-trimethyleneheptan-3-one (4l). A solution of BHT ester **1e** (1.515 g, 5.0 mmol) in 3 mL of THF was added to a solution of BuLi (10.0 mmol) in 40 mL of THF at −78 °C. After warming to room temperature overnight the solution was cooled to −78 °C and a solution of benzaldehyde (0.550 g, 5.2 mmol) in 2 mL of THF was added dropwise. The solution was stirred for 5 min. Workup gave 2.27 g of a colorless oil, of which 0.742 g was purified by flash chromatography (pentane:ether = 70:30) to give 0.240 g (60%) of **4l** as a colorless liquid: ^{1}H NMR ($CDCl_3$) δ 0.70–0.95 (m, 3 H, CH_3), 1.05–1.85 (m, 6 H), 2.15–2.50 (m, 6 H), 3.00 (d, J = 5 Hz, 1 H, OH), 4.90 (d, J = 5 Hz, 1 H, ArCH), 7.30 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 13.86 (q), 15.45 (t), 22.29 (t), 25.58 (t), 26.13 (t), 27.47 (t), 39.01 (t) 58.35 (s), 77.33 (d), 126.80, 127.33, 127.90, 132.01, 144.76 (s), 213.99 (s); MS, m/e 140 (M^+ − 106, 95). Anal. Calcd for $C_{16}H_{22}O_2$: C 78.01; H, 9.00. Found: C, 78.06; H, 9.23.

1,4-Diphenyl-3,3-ethylene-4-hydroxybutan-2-one (4m). A solution of BHT ester **1f** (0.870 g, 3.0 mmol) in 3 mL of THF was added to a solution of *t*-BuLi (3.1 mmol) in 30 mL of THF at −78 °C. After the mixture was stirred for 30 min, BzLi (3.3 mmol) was added and the solution allowed to warm to room temperature (6 h). This solution was added dropwise by the inverse addition procedure to a solution of benzaldehyde (0.380 g, 3.6 mmol) in 10 mL of THF at −78 °C and after completion of addition stirred for another 5 min. Workup gave 1.400 g of an oil of which 0.574 g was purified by flash chromatography (pentane:ether = 60:40) to yield 0.144 g (44%) of **4m** as a colorless, viscous liquid: ^{1}H NMR ($CDCl_3$) δ 0.75–1.50 (m, 4 H, CH_2CH_2), 3.47 (d, J = 5 Hz, 1 H, OH), 3.50 (s, 2 H, $ArCH_2$), 5.03 (d, J = 5 Hz, 1 H, ArCH), 7.0–7.33 (m, 5 H, ArH), 7.27 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 11.65 (t), 13.85 (t), 37.05 (s), 43.62 (t), 74.39 (d), 126.83, 127.57, 128.10, 128.53, 129.32, 134.15 (s), 140.85 (s); MS, m/e 266 (M^+, 22). Anal. Calcd for $C_{18}H_{18}O_2$: C, 81.17; H, 6.81. Found: C, 80.97; H, 6.77.

1,3-Diphenyl-2,2-ethylene-3-hydroxypropan-1-one (4n). A solution of BHT ester **1f** (0.864 g, 3.0 mmol) in 3 mL of THF was added to a solution of *t*-BuLi (3.1 mmol) in 30 mL of THF at −78 °C. After the mixture was stirred for 30 min PhLi (3.4 mmol) was added and the solution allowed to warm to room temperature overnight. After cooling to −78 °C benzaldehyde (0.430 g, 4.0 mmol), dissolved in 4 mL of THF, was added slowly. The solution was stirred for 5 min and worked up to give 1.592 g of a brown oil of which 0.850 g was purified by flash chromatography (pentane:ether = 60:40) and recrystallized from pentane/ether to yield 0.101 g (29%) of **4n**: mp 113.2–114.4 °C; ^{1}H NMR ($CDCl_3$) δ 0.83–1.13 (m, 4 H, CH_2CH_2), 2.85 (d, J = 5 Hz, 1 H, OH), 5.13 (d, J = 5 Hz, 1 H, ArCH), 7.20 (s, 5 H, ArH), 7.28–7.75 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 9.62 (t), 10.50 (t), 36.18 (s), 74.73 (d), 126.69 (d), 127.90 (d), 128.27 (d), 131.81 (d), 137.63 (s), 141.32 (s), 203.68 (s); MS, m/e 252 (M^+, 24). Anal. Calcd for $C_{17}H_{16}O_2$: C, 80.93; H, 6.39. Found: C, 80.76; H, 6.61.

Benzyl Cyclopropyl Ketone (7). The solution of the enolate **6**, generated as described for the preparation of **4m** and **4n**, was quenched with saturated NH_4Cl. Workup gave 1.761 g of an oil of which 0.616 g was purified by flash chromatography (pentane:ether = 70:30) and then bulb-to-bulb distilled to give 0.120 g (71%) of **7** as a colorless liquid: bp (air temperature) 90 °C (0.06 torr); ^1H NMR ($CDCl_3$) δ 0.70–1.13 (m, 4 H, CH_2CH_2), 1.80–2.10 (m, 1 H, CHCO), 3.83 (s, 2 H, $ArCH_2$), 7.15–7.40 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 11.16 (t), 20.06 (d), 50.66 (t), 126.89 (d), 128.66 (d), 129.52 (d), 134.53 (s), 208.12 (s); MS, *m/e* 160 (M^+, 9). Anal. Calcd for $C_{11}H_{12}O$: C, 82.46; H, 7.55. Found: C, 82.41; H, 7.50.

1-Cyclopropyl-3-hydroxy-2-phenylhexan-1-one (8). The solution of the enolate **6** was added dropwise by the inverse addition procedure to a solution of butanal (0.250 g, 3.5 mmol) in 10 mL of THF at −78 °C. Workup gave 1.412 g of an oil, of which 0.598 g was purified by flash chromatography (pentane:ether = 60:40) to yield 0.118 g (40%) of **8**: mp (pentane) 74.6–75.0 °C; ^1H NMR ($CDCl_3$) δ 0.65–0.90 (m, 4 H), 0.90–1.07 (m, 2 H), 1.07–1.50 (m, 5 H), 1.65–1.93 (m, 1 H, $(CH_2)_2CHCO$), 3.20 (d, J = 4 Hz, 1 H, OH), 3.77 (d, J = 9 Hz, 1 H, ArCH), 4.00–4.30 (m, 1 H, CH(OH)), 7.20–7.37 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 11.54 (t), 11.87 (t), 13.85 (q), 18.58 (t), 21.33 (d), 35.79 (t), 66.32 (d), 72.47 (d), 127.63 (d), 129.06 (d), 129.17 (d), 136.26 (s), 212.14 (s); MS, *m/e* 69 (100). Anal. Calcd for $C_{15}H_{20}O_2$: C, 77.55; H, 8.68. Found: C, 77.69; H, 8.69.

(*Z*/*E*)-3,4-Dimethyl-2-trimethylsilyloxy-2-pentene (11/12). MeLi (10.6 mmol) was added to a solution of the enolate of BHT ester **1h** (9.7 mmol). The solution was allowed to warm to room temperature overnight and cooled to −78 °C, and a solution of trimethylsilyl chloride (3.25 g, 30.0 mmol) in 10 mL of THF was added. After warming to room temperature, the solution was concentrated to a total volume of 5 mL, separated from the solid material by filtration, and distilled in a microdistillation apparatus to give 0.979 g (53%) of **11/12** as a colorless liquid: bp 49–51 °C (12 torr); ^1H NMR (250 MHz, $CDCl_3$) δ 0.114 and 0.119 (two s, 9 H, $Si(CH_3)_3$), 0.856 and 0.902 (two d, J = 7.0 and 7.0 Hz, 6 H, CH_3CCH_3), 1.406 and 1.430 (two q, ^5J = 1.00 ± 0.02 and 1.45 ± 0.02 Hz, 3 H, ratio = 7.0:1, CH_3C=), 1.709 and 1.744 (two q, ^5J = 1.02 ± 0.02 and 1.43 ± 0.02 Hz, 3 H, ratio = 7.0:1, CH_3C=), 2.568 and 3.034 (two h, J = 6.9 and 6.9 Hz, 1 H, ratio = 1:7.0, $CH(CH_3)_2$).

(*Z*)-2,2,3-Trimethyl-4-trimethylsilyloxy-3-pentene (13). MeLi (16.2 mmol) was added to a solution of BHT ester **1i** (2.329 g, 7.0 mmol) in 70 mL of THF at −78 °C. After warming to room temperature overnight, the solution was cooled to −78 °C and a solution of trimethylsilyl chloride (2.17 g, 20 mmol) in 5 mL of THF was added. The resulting solution was treated as described above to yield 0.795 g (57%) of **13** as a colorless liquid: bp 73–74 °C (13 torr); ^1H NMR (250 MHz, $CDCl_3$) δ 0.220 (s, 9 H, $Si(CH_3)_3$), 1.135 (s, 9 H, (*t*-Bu), 1.555 (q, ^5J = 0.99 ± 0.02 Hz, 3 H, CH_3C=), 1.844 (q, ^5J = 1.00 ± 0.02 Hz, 3 H, CH_3C=).

1,4-Diphenyl-3-ethyl-4-hydroxy-3-methylbutan-2-one (14a). BzLi (3.3 mmol) was added to a solution of the enolate of BHT ester **1g** (2.9 mmol). The solution was warmed to room temperature overnight and added dropwise by the inverse addition procedure to a solution of benzaldehyde (0.410 g, 3.9 mmol) in 10 mL of THF at −78 °C. After completion of addition the solution was stirred for another 5 min. Workup gave 1.770 g of an oil of which 0.737 g was purified by flash chromatography (pentane:ether = 85:15 to 65:35) to yield 0.263 g (77%) of solid **14a**: mp (pentane) 72.8–73.6 °C; ^1H NMR ($CDCl_3$) mixture of diastereomers, δ 0.80 and 0.90 (two t, J = 7 Hz, 3 H, $CH_3(CH_2)$), 1.17 and 1.23 (two s, 3 H, CH_3C), 1.33–2.07 (m, 2 H), 2.80 (d, J = 6 Hz, 1 H, OH), 3.65 and 3.80 (AB and s, respectively, J = 16 Hz, 2 H, $ArCH_2$), 4.95 (d, J = 6 Hz, 1 H, ArCH), 7.00–7.50 (m, 5 H, ArH), 7.30 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) mixture of diastereomers, δ 8.63 (q) and 9.29 (q), 15.28 (q) and 17.48 (q), 27.71 (t) and 29.79 (t), 46.35 (t) and 46.79 (t), 56.64 (s), 78.68 (d), 126.75 (d), 127.82 (d), 128.34 (d), 129.87 (d), 134.44 (s), 140.67 (s), 213.85 (s), ratio of diastereomers ds = 60% (integration); MS, *m/e* 176 (M^+ − 106, 86). Anal. Calcd for $C_{19}H_{22}O_2$: C, 80.82; H, 7.85. Found: C, 80.65; H, 7.94.

1-Hydroxy-2-methyl-2-(1-methylethyl)-1-phenylheptan-3-one (14b). A solution of BHT ester **1h** (0.955 g, 3.0 mmol) in 3 mL of THF was added to a solution of BuLi (6.4 mmol) in 30 mL of THF at −78 °C. The solution was warmed to room temperature overnight and cooled to −78 °C. Benzaldehyde (0.420 g, 4.0 mmol) was dissolved in 2 mL of THF and added slowly. Stirring for 5 min and workup gave 1.597 g of an oil of which 0.864 g was purified by flash chromatography (pentane:ether = 95:5 to 50:50) to give 0.330 g (78%) of **14b** as a colorless, viscous liquid: ^1H NMR ($CDCl_3$) δ 0.70–1.00 (m, 3 H, $CH_3(CH_2)$), 0.83 (d, J = 7 Hz, 3 H, $CH_3(CH)$), 1.03 (d, J = 7 Hz, 3 H, $CH_3(CH)$), 1.03 (s, 3 H, CH_3C), 1.15–1.55 (m, 4 H, $CH_2CH_2(CH_3)$), 1.85–2.25 (m, 2 H, CH_2CO), 1.80 (h, J = 7 Hz, 1 H, $CH(CH_3)_2$), 4.35 and 4.55 (AB, J = 9 Hz, OH and ArCH; D_2O exchange: 4.55 (s, 1 H)), 7.05–7.35 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$), major diastereomer, δ 13.24 (q), 13.87 (q), 16.70 (q), 18.47 (q), 22.04 (t), 24.79 (t), 32.16 (d), 42.57 (t), 57.51 (s), 78.29 (d), 127.51 (d), 127.89 (d), 141.64 (s), 220.85 (s); MS, *m/e* 156 (M^+ − 106, 23). Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 77.79; H, 9.96.

4-Hydroxy-3-methyl-3-(1-methylethyl)-1-phenylheptan-2-one (14c). BzLi (3.3 mmol) was added to a solution of the enolate of BHT ester **1h** (3.0 mmol). The solution was warmed to room temperature overnight and added dropwise by the inverse addition procedure to a solution of butanal (0.310 g, 4.3 mmol) in 10 mL of THF at −78 °C. After completion of addition the solution was stirred for another 5 min. Workup gave 1.369 g of an oil of which 0.844 g was purified by flash chromatography (pentane:ether = 78:22) to yield 0.261 g (54 %) of **14c** as a colorless, viscous liquid: ^1H NMR ($CDCl_3$) δ 0.85 (d, J = 7 Hz, 3 H, $CH_3(CH)$), 0.95 (d, J = 7 Hz, 3 H, $CH_3(CH)$), 0.8–1.0 (m, 3 H, $CH_3(CH_2)$), 1.13 (s, 3 H, CH_3C), 1.13–1.73 (m, 4 H, $CH_2CH_2(CH_3)$), 2.53 (h, J = 7 Hz, 1 H, $CH(CH_3)_2$, 2.65 (d br, J = 7 Hz, 1 H, OH), 3.55 (t br, J = 8 Hz, 1 H, CH(OH)), 3.80 (s, 2 H, $ArCH_2$), 7.07–7.40 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) major diastereomer, δ 13.64 (q), 13.98 (q), 17.15 (q), 18.13 (q), 20.09 (t), 31.89 (d), 35.18 (t), 48.59 (t), 58.03 (s), 75.54 (d), 126.78 (d), 128.34 (d), 129.95 (d), 134.16 (s), 216.23 (s); MS, *m/e* 71 (100). Anal. Calcd for $C_{17}H_{26}O_2$: C, 77.82; H, 9.99. Found: C, 78.00; H, 10.26.

1,4-Diphenyl-4-hydroxy-3-methyl-3-(1-methylethyl)butan-2-one (14d). The solution of the enolate generated as in the preceding procedure was added dropwise by the inverse addition procedure to a solution of benzaldehyde (0.420 g, 4.0 mmol) in 10 mL of THF at −78 °C. Workup gave 1.512 g of an oil of which 0.709 g was purified by flash chromatography (pentane:ether = 85:15) to yield 0.269 g (65 %) of **14d** as a colorless viscous liquid: ^1H NMR ($CDCl_3$) 1.83 (d, J = 7 Hz, 3 H, $CH_3(CH)$), 1.00 (d, J = 7 Hz, 3 H, $CH_3(CH)$), 1.08 (s, 3 H, CH_3C), 2.67 (h, J = 7 Hz, 1 H, $CH(CH_3)_2$), 3.35 (AB, J = 18 Hz, 2 H, $ArCH_2$), 4.17 and 4.57 (AB, J = 9 Hz, 2 H, OH and ArCH; D_2O exchange: 4.57 (s, 1 H)), 6.80–7.40 (m, 10 H, ArH); ^{13}C NMR ($CDCl_3$) δ 13.42 (q), 16.70 (q), 18.54 (q), 32.24 (d), 49.34 (t), 58.08 (s), 78.25 (d), 126.90, 127.64, 127.76, 128.00, 128.34, 129.89, 133.50 (s), 141.41 (s), 217.17 (s); MS, *m/e* 106 (42), 71 (100). Anal. Calcd for $C_{20}H_{24}O_2$: C, 81.04; H, 8.16. Found: C, 80.74; H, 8.16.

1-Hydroxy-2-methyl-2-(1-methylethyl)-1-phenylheptan-3-one (14e). A solution of BHT ester **1i** (0.895 g, 2.7 mmol) in 3 mL of THF was added to a solution of (5.8 mmol) in 30 mL of THF at −78 °C. The solution was warmed to room temperature overnight and cooled to −78 °C. Benzaldehyde (0.335 g, 3.2 mmol) was dissolved in 3 mL of THF and added slowly. Stirring for 5 min and workup gave 1.220 g of a yellow oil of which 0.768 g was purified by flash chromatography (pentane:ether = 95:5 to 50:50) to give 0.283 g (60%) of **14e** as a colorless, viscous liquid: ^1H NMR ($CDCl_3$) δ 0.75–0.95 (m, 3 H, $CH_3(CH_2)$), 1.07 (s, 9 H, *t*-Bu), 1.13 (s, 3 H, CH_3C), 1.13–1.70 (m, 4 H), 2.20–2.65 (m, 2 H, CH_2CO), 4.40 (d, J = 7 Hz, 1 H, OH), 4.90 (d, J = 7 Hz, 1 H, ArCH), 7.23 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 13.92 (q), 16.84 (q), 22.21 (t), 25.45 (t), 27.46 (q), 37.29 (s), 43.09 (t), 58.53 (s), 78.67 (d), 127.50 (d), 127.99 (d), 128.09 (d), 143.49 (s), 219.71 (s); MS *m/e* 106 (41), 85 (100). Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.20; H, 10.13.

3-(1,1-Dimethylethyl)-1,4-diphenyl-4-hydroxy-3-methylbutan-2-one (14f). BzLi (5.5 mmol) was added to a solution of BHT ester **1i** (0.833 g, 2.5 mmol) in 30 mL of THF at −78 °C. The solution was warmed to room temperature overnight and added dropwise by the inverse addition procedure to a solution of benzaldehyde (0.430 g, 4.1 mmol) in 10 mL of THF at −78 °C. After completion of addition the solution was stirred for 5 min. Workup gave 1.415 g of an oil of which 0.887 g was purified by flash chromatography (pentane:ether = 85:15) to yield 0.248 g (52%) of **14f**: mp (pentane) 92.8–93.2 °C; ^1H NMR ($CDCl_3$) δ 1.00 (s, 9 H, *t*-Bu), 1.20 (s, 3 H, CH_3C), 3.65 (AB, J = 17 Hz, 2 H, $ArCH_2$), 4.07 (d, J = 7 Hz, 1 H, OH), 4.93 (d, J = 7 Hz, 1 H, ArCH), 7.00–7.40 (m, 5 H, ArH), 7.20 (s, 5 H, ArH); ^{13}C NMR ($CDCl_3$) δ 16.73 (q), 27.45 (q), 37.47 (s), 49.80 (t), 59.22 (s), 78.55 (d), 126.85 (d), 127.62, 128.05, 128.16, 128.35, 130.00, 134.14 (s), 143.12 (s), 216.34 (s); MS, *m/e* 204 (M^+ − 106, 18), 85 (100). Anal. Calcd for $C_{21}H_{26}O_2$: C, 81.25; H, 8.44. Found: C, 81.07; H, 8.25.

3-(1,1-Dimethylethyl)-4-hydroxy-3-methyl-1-phenylheptan-2-one (14g). Substituting benzaldehyde by butanal (0.285 g, 41.0 mmol in 10 mL of THF at −78 °C) in the preceding procedure and working up gave 1.244 g of an oil of which 0.698 g was purified by flash chromatotraphy (pentane:ether = 80:20 to 50:50) to yield 0.103 g (27%) of **14g**: mp (pentane) 84.8–85.4 °C; ^1H NMR ($CDCl_3$) δ 0.75–0.97 (m, 3 H, $CH_3(CH_2)$), 1.05 (s, 9 H, *t*-Bu), 1.05–1.63 (m, 4 H, $CH_2CH_2(CH_3)$), 1.27 (s, 3 H, CH_3C), 2.55 (d, J = 8 Hz, 1 H, OH), 3.73 (s, 2 H, $ArCH_2$), 3.85–4.15 (m, 1 H, CH(OH)), 7.05–7.45 (m, 5 H, ArH); ^{13}C NMR ($CDCl_3$) major diastereomer, δ 14.03 (q), 14.70 (q), 19.68 (t), 27.89 (q), 35.71 (t), 36.43 (s), 49.19 (t), 59.56 (s), 75.86 (d), 126.76 (d), 128.35

(d), 129.94 (d), 134.51 (s), 215.81 (s); MS *m/e* 85 (100). Anal. Calcd for $C_{18}H_{28}O_2$: C, 78.21; H, 10.21. Found: C, 78.23; H, 10.19.

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Structures of Three Lithium Ester Enolates by X-ray Diffraction: Derivation of Reaction Path for Cleavage into Ketene and Alcoholate[1]

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Abstract: Crystal structure analyses have been carried out for lithium enolates of the following three esters: *tert*-butyl propionate ((*Z*)-**1**), *tert*-butyl 2-methylpropionate (**2**), and methyl 3,3-dimethylbutanoate ((*Z*)-**3**). Enolates (*Z*)-**1** and **2** are dimeric (with one TMEDA per Li atom), whereas (*Z*)-**3** is tetrameric (with one THF per Li atom). The *Z* configuration of **1** and **3** established by X-ray analysis is in agreement with that assigned by Ireland. From a detailed analysis of the geometry of the ester enolate grouping, the reaction path trajectory for the breakdown of this type of molecule can be derived. The implication of ketenes as intermediates, suggested by this analysis, could be confirmed chemically.

In spite of the central importance of ester enolates as reactive intermediates in synthetic organic chemistry, very little is known about the actual structures of the metallated species involved. This lack of information is largely attributable to the low stability of ester enolates in general. In fact, the structures of only two metal derivatives of esters have been established by X-ray analysis: one is the Reformatksy reagent derived from *tert*-butyl bromoacetate,[2] and the other is a lithium derivative of the highly acidic pentakis(methoxycarbonyl)cyclopentadiene.[3] Neverthless, it has been more than 10 years since the Lochmann[4] and Rathke[5] groups described the isolation of pure lithium derivatives of esters as solid substances. The analysis of these compounds was at that time limited to what could be achieved by IR and NMR spectroscopy; the deduction was that they are to be formulated as enolates. Deprotonation of esters of the type RR'CH–COOR'' with LDA (lithium diisopropylamide) gives in principle (*E*)- or (*Z*)-configurated enolates, shown as (*E*)-**1** and (*Z*)-**1** for the example of *tert*-butyl propionate (Scheme I).

Ireland and his co-workers[6] have shown that these are obtainable as distinct species by deprotonation in different media and were able to assign their configurations by identification of the Claisen rearrangement products of all four crotyl propionate enolates under the assumption that the [3.3]-sigmatropic shift proceeds via a chair-like transition state.

Scheme I

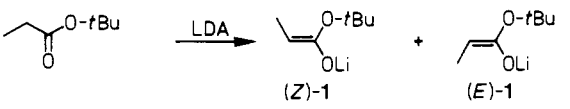

Table I. Crystallographic Data for (*Z*)-**1**·TMEDA, **2**·TMEDA, and (*Z*)-**3**·THF

	(*Z*)-**1**·TMEDA	**2**·TMEDA	(*Z*)-**3**·THF
formula	$C_{13}H_{29}N_2O_2Li$	$C_{14}H_{31}N_2O_2Li$	$C_{11}H_{21}O_3Li$
formula wt	252.33	266.35	208.23
space group	*C*2/*c*	*C*2/*c*	*P*$\bar{1}$
temp, °C	−130	−140	−170
a, Å	20.050 (9)	19.91 (1)	10.454 (2)
b, Å	8.773 (4)	9.172 (3)	10.679 (2)
c, Å	18.75 (1)	18.94 (1)	24.959 (4)
α, °	90	90	77.04 (1)
β, °	103.66 (4)	95.35 (5)	78.60 (2)
γ, °	90	90	67.94 (2)
V, Å^3	3205.6	3442.9	2496.6
Z	8	8	8
sin θ_{max}/λ, Å^{-1}	0.724	0.504	0.538
d_{calcd}, g/cm^3	1.05	1.03	1.11
no. of unique data			
total	5090	1843	6524
with $I > 3\sigma_I$	2522	1125	3482
R, %	4.2	4.7	4.1
R_w, %	4.9	4.7	4.2

(1) Based in part on the dissertation of T.L., ETH Zürich Nr. 7649, 1984; discussed in part in: Seebach, D. Proceedings of the Robert A. Welch Foundation, Conferences on Chemical Research, XXVII, Stereospecificity in Chemistry and Biochemistry, Houston, Texas, 1984, p 93.

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