Stereochemistry of the Baker's Yeast Mediated Reduction of the C=C Bond of (*Z*)- and (*E*)-5-Benzoyloxyhex-3-en-2-one

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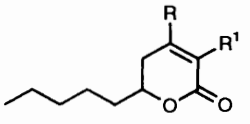
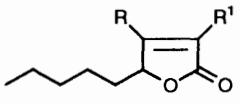
Baker's yeast reduction of the *Z* and *E* enones **5** and **6** to the methyl ketone **7** proceeds with kinetic preference for the *R* and *S* enantiomers, respectively. However, irrespective of the double-bond stereochemistry and of the absolute configuration of the oxygen-bearing carbon atom at position 5, the C=C bond reduction occurs by formal *anti* addition of hydrogen, with delivery of the hydrogen atom at position 4 from the *re*-face of the molecule, as shown by ^{2}H NMR studies onto lactones **17** and **18** obtained in experiments with deuteriated precursors.

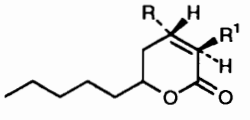
Recently,[1-3] we have been studying the sterochemical aspects of the baker's yeast (BY) mediated reduction of the unsaturated δ- and γ-lactones **1** and **2** to **3** and **4**. By means of experiments with both enantiomerically pure and racemic substrates it has been shown that the reduction proceeds in the δ and γ series with kinetic preference for the *R* and *S* enantiomers, respectively. Moreover, experiments with a set of racemic structural analogues of **2** indicate that, at similar conversions, the ee values slightly increase with the length of the alkyl side-chain. However, deuterium labelling experiments and ^{2}H NMR studies on the educts isolated from the BY incubation showed that reduction of the double bond takes place in both series by formal *anti* addition of hydrogen, with delivery of the hydrogen atom β to the carbonyl from the *re* face of the molecule. Accordingly, the materials obtained by BY reduction of α,β-dideuteriated (*R*) **1a** and (*S*) **2a** are presented by the structural formulae **3a** and **4a**, respectively.



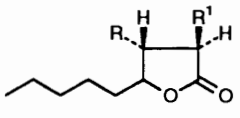
1 R = R^1 = H
1a R = R^1 = ^{2}H



2 R = R^1 = H
2a R = R^1 = ^{2}H



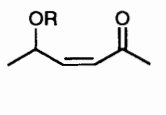
3 R = R^1 = H
3a R = R^1 = ^{2}H



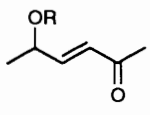
4 R = R^1 = H
4a R = R^1 = ^{2}H

The above observed inversion of the enantiomeric preference in the reduction of **1** and **2** with a shift in the stereogenic centre from the γ to the δ position with respect to the carbonyl which activates the double bond, induced us to study further the structural features influencing the mode of BY transformation of substrates possessing this kind of functionality. The stereochemical course of the enzymic saturation of carbonyl-activated C=C bonds, which are present in a variety of biologically active compounds,[4-7] is of continuing interest, and here we report our results for the stereochemical reduction of the *Z* and *E* unsaturated methyl ketones **5** and **6** to **7**.

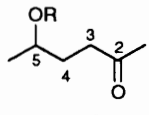
Compounds **5** and **6** on BY reduction afford, solely, the saturated methyl ketone **7**, a transformation which is of comparable rapidity for the two substrates requiring only a modest amount of yeast. Such features suggested that this system, formally mediated by an enone reductase, would be a suitable one for a detailed study of the stereochemical differences of the transformation. The starting materials **5** and **6** are easily prepared from hydroxy ketone **8**[8] by the sequence of Scheme 1, which allows, when required, the synthesis of products in regiospecifically deuteriated forms.



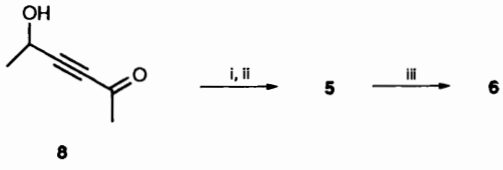
5 R = Bz



6 R = Bz



7 R = Bz



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Scheme 1 *Reagents and conditions:* i, PhCOCl/Et$_3$N; ii, H_2, Lindlar catalyst; iii, I_2 in toluene

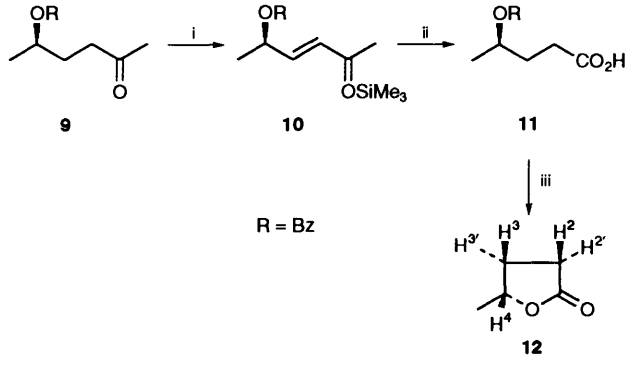
Initially, it appeared that the BY reduction of the double bond in compounds **5** and **6** proceeded with kinetic resolution, samples of **7** obtained at partial conversion being enriched in a single enantiomer as evidenced from the ^{1}H spectra in the presence of chiral shift reagents. However, these samples were shown to possess the opposite absolute configuration. The saturated materials obtained from (*Z*) **5** and (*E*) **6** at 22 and 18% conversions show 0.62 and 0.48 ee, respectively. The major enantiomers present in **7** obtained from the *Z* and *E* isomers **5** and **6** under these incubation conditions were assigned *R* and *S* absolute configurations, respectively, on the basis of the following evidence. The methyl ketone **7**, formed by BY reduction from (*Z*) **5**, was converted into γ-valerolactone (Scheme 2), *via* the silyl enol ether **10**[9] and the acid **11**. The latter, upon hydrolysis of its benzoate ester, provides γ-valerolactone which was shown to contain an excess of the *R* enantiomer of **12** by optical rotation measurements, multidimensional GLC analysis and comparison with an authentic sample.[10,11] These results thus allow assignment of *S* and *R* absolute configuration, respectively, to the enantiomeric forms of (*Z*) **5** and (*E*) **6** which, reduced by BY at a lower rate, were present in excess in the final incubation mixtures.

The observed inversion of the enantiomeric preference in the C=C bond reduction on going from (*Z*) **5** to (*E*) **6** allowed us to verify the existence of a correlation with the mode of hydrogen

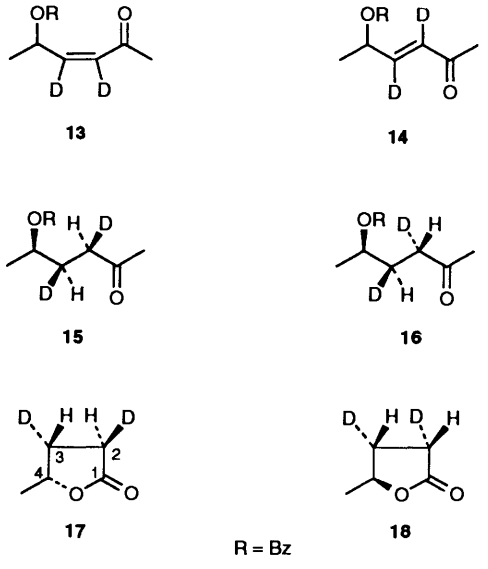
Table 1 NMR data for γ-lactones **12**,[a] **17**[b] and **18**[b]

	12							
Proton	δ	Coupling	J Hz	Deuterium	(*R*) **17**[c] δ	(*S*) **17**[d] δ	(*R*) **18**[d] δ	(*S*) **18**[c] δ
2	1.78	*J*(2,2')	−17.5	2	1.77			1.79
2'	1.89	*J*(3,3')	−12.5	2'		1.88	1.89	
3	1.29	*J*(2,3)	9.5	3		1.28		1.29
3'	0.84	*J*(2,3')	9.5	3'	0.84		0.85	
4	3.80	*J*(2',3)	4.4					
Me	0.83	*J*(2',3')	9.3					
		J(3,4)	6.5					
		J(3',4)	7.8					
		J(Me,4)	6.0					

[a] Solvent C_6D_6; chemical shifts referred to internal $SiMe_4$. [b] Solvent C_6H_6; chemical shifts measured from the natural abundance ^2H signal of the solvent taken at 7.16 ppm. [c] Major isomer. [d] Minor isomer.



Scheme 2 *Reagents and conditions:* i, LDA, Me_3SiCl, −78 °C; ii, O_3 in CH_2Cl_2 −78 °C; iii, 10% aqueous NaOH, H_3O^+



addition onto the double bond of the two substrates during the biohydrogenation to **7**. The required information was achieved by means of deuterium labelling experiments and ^2H NMR studies as indicated below.

Thus, dideuteriated compounds (*Z*) **13** and (*E*) **14** obtained from **8** (Scheme 1) by using deuterium gas in the reduction step, were submitted to the yeast reduction, to give, as above, at low conversion, (*R*) **15** and (*S*) **16**. The stereochemistry of the hydrogen addition was determined by ^2H NMR studies on the valerolactones **17** and **18** obtained from **15** and **16**, respectively, through the degradative sequence used to obtain **12**. Indeed, attempts to deduce from the ^2H NMR spectra of the dideuteriated lactones **17** and **18** the stereochemistry of the deuterium atoms depend on the assignment of the proton spectrum of the full protonated compound **12** (Table 1). The

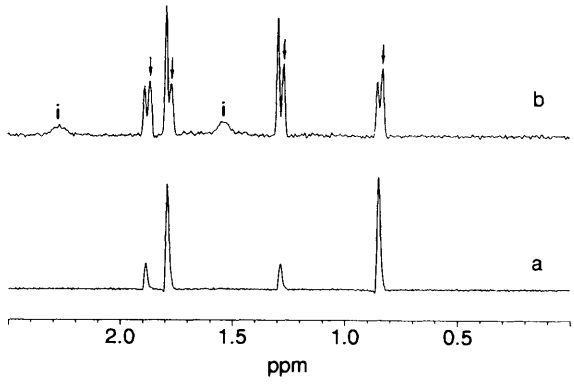


Fig. 1 Expanded region of the ^2H NMR spectra (solvent C_6H_6) of (a) (*R*) **17** obtained from **5** and (b) (*S*) **18** obtained from **6**. The arrows indicate the resonances of the tetradeuteriated species; i denotes deuteriated impurities present in the sample.

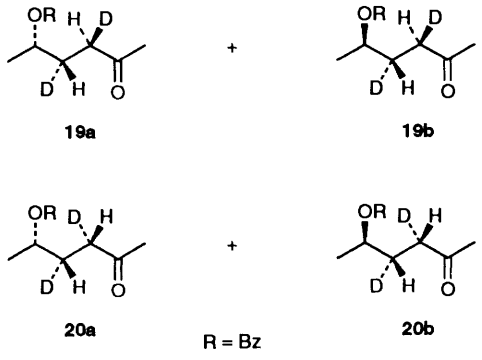
distinction between the hydrogens 2-H *vs.* 2-H' and 3-H *vs.* 3-H' for **12** is based on the following observations: (i) γ-valerolactone is present in solution mainly in the envelope conformation (*ca.* 70%) with a pseudoequatorial methyl group;[12] thus the value of the vicinal coupling constant *J*(2',3) of 4.4 Hz indicates that protons 2-H' and 3-H are *trans* and pseudoequatorially orientated; (ii) 3-H' is expected to resonate at higher field with respect to 3-H due to the upfield β effect exerted by the *syn* vicinal methyl group[13] (observed effect −0.45 ppm); (iii) 2-H' is expected to resonate at lower field with respect to 2-H due to the downfield effect of the *syn* methyl group in position[13] (observed effect +0.19 ppm). Once assigned the chemical shift of the ring hydrogens of **12** the position of the deuterium atoms in **17** and **18** can be determined from the chemical shifts measured on the ^2H spectra.

Multidimensional GLC analysis of **17** and **18** indicated 0.62 and 0.22 ee, respectively. Thus the ^2H NMR spectrum of **17** [Fig. 1(a)] exhibits two main signals belonging to (*R*) **17** (1.77 and 0.84 ppm) and two minor signals corresponding to the diastereoisomer (*S*) **17** (1.88 and 1.28 ppm) (Table 1). The ^2H NMR spectrum of **18** [Fig. 1(b)] is complicated by the presence in the sample of *ca.* 25% tetradeuteriated racemic species. This is due to the presence in the initial *E* ketone **14** of some fully saturated tetradeuterio species, formed at an earlier stage in the Lindlar-catalysed deuteriation of the benzoate of **8**. The content of tetradeuteriated species, *i.e.*, of racemic tetradeuteriated **7** into **14**, was *ca.* 12% (from NMR studies). However, since only part of unsaturated **14** is reduced, the amount of tetradeuteriated species actually present in the material converted into **18** was raised to 25%. Accordingly, γ-valerolactone obtained by degradation of **16** isolated in the bioreduction of **14** is composed of dideuteriated (*S*) **18** (signals at 1.79 and 1.29 ppm), of the diastereoisomer (*R*) **18** (signals at 1.89 and 0.85 ppm), and,

Table 2 ^{1}H NMR data for compounds **15**, **16**, **19a**, **19b**, **20a** and **20b**[a,b]

Proton (δ) coupling (Hz)	**15**	**16**	**19a**	**19b**	**20a**	**20b**
3-H	1.95	1.95	1.99	1.99	1.95	1.99
4-H	1.71	1.78	1.71	1.78	1.71	1.78
5-H	5.12	5.12	5.12	5.12	5.12	5.12
J(3,4)	6.4	8.6	8.6	8.6	6.4	5.6
J(4,5)	4.2	8.6	4.2	8.6	4.2	8.6

[a] Solvent C_6D_6; chemical shifts referred to internal $SiMe_4$; spectra acquired with deuterium decoupling. [b] Other resonances: δ 1.10 (3 H, d, J 6.0, 5-Me), 1.59 (3 H, s, 1-Me) and 7.0–7.15 (5 H, m, C_6H_5).



finally, by *ca.* 25% of the tetradeuteriated racemic species, whose origin has been just explained above (signals at 1.87, 1.77, 1.27 and 0.83 ppm). The resonances of the tetradeuteriated compound can be recognized with respect to that of the dideuteriated species since they are shifted *ca.* 0.02 ppm upfield because of the mutual deuterium isotope effect through two bonds.[14]

The stereochemistry of the deuterium atoms in lactones **17** and **18** thus suggest that the enzymic saturation of the double bond in **5** and **6** leading to **7** occurs in an *anti* fashion with a formal hydrogen delivery at position β to the carbonyl group from the *re*-face of the molecule.

Confirmation of the different deuterium stereochemistry in the dideuteriated saturated ketones obtained in the above experiments arises also from the analysis of the ^{1}H spectra of **15** and **16**. In these spectra the hydrogens 3-H, 4-H and 5-H show broad signals due to the large number of the proton–deuterium coupling constants through two and three bonds. Thus, the spectra have been acquired with deuterium decoupling to obtain clean proton signals. The ^{1}H NMR data of **15** and **16** together with those of the racemic mixtures **19** and **20** obtained from **5** and **6** by reduction with deuterium gas in the presence of Lindlar catalyst are collected in Table 2. The *syn* catalytic reduction of **5** and **6** gives rise to an equimolar proportion of the four racemic diastereoisomers **19a**, **19b** and **20a**, **20b**, two of which (**20a** and **19b**) are identical with **15** and **16**. The ^{1}H spectra of these dideuteriated species are of first order and allow the determination of the chemical shifts and the vicinal coupling constants of the C-3 and C-4 methylene hydrogens which, in contrast, for the strongly coupled spectrum of **7** are difficult to obtain. Moreover, molecular mechanics calculations performed on **7** showed that the molecule is *ca.* 0.4 kcal mol^{-1} more stable in the conformation bearing substituents at C-3 and C-4 [Ac and CH(Me)OBz] *anti* orientated to each other compared with the conformations in which they were in a *gauche* relationship. Thus, reasonably it can be assumed that the vicinal coupling constants of 8.6 Hz in the C(3)–C(4) ethane fragment occur between hydrogens predominantly *anti* (**16**, **19a** and **19b**), while that of 5.6 and 6.4 Hz occur between protons which are predominantly *gauche* (**15**, **20a** and **20b**). Such considerations immediately allow us to establish that formally the addition of hydrogen to **5** and **6** to give **15** and **16** is *anti* but, owing to ambiguity in the assignment of the geminal protons, it is not possible to determine from which face the reduction occurs; this can be deduced only through correlation with the cyclic lactones **17** and **18**.

Seen together, the above studies thus indicate the BY reduction of **5** and **6** to give **7** has the following stereochemical features. Reduction of the C=C bond of racemic γ-benzoyloxy substituted *Z* and *E* α,β-unsaturated methyl ketones occurs with kinetic resolution. The enantiomeric preference varies from the *R* to the *S* form on going from the *Z* to the *E* stereoisomer and is more marked in the case of the *Z* stereoisomer **5**. However, irrespective of the absolute configuration of the oxygen-bearing carbon atom adjacent to the double bond in the γ position with respect to the carbonyl carbon, and of the double bond geometry, the enzyme-mediated reduction of the α,β C=C bond takes place in all cases by formal *anti* hydrogen addition, with delivery of the hydrogen atom from the β *re*-face of the molecule.

The observed ee values of the products present in the incubation mixtures are quite low, thus rendering this transformation unattractive from a preparative point of view. However, the accessibility by these means of the enantiomeric forms **17** and **18** of asymmetrically labelled γ-valerolactone may have synthetic potential in the context of the current biosynthetic studies on mould metabolites.[11] The present studies indicate a mode of BY C=C bond reduction of acyclic unsaturated *Z* and *E* ketones **5** and **6** identical with that recently demonstrated as operating in the α,β-unsaturated lactones **1** and **2**,[1,3] in which the *Z* double bond is activated by the lactone carbonyl, and of cinnamaldehyde.[4] However, *si*-face, *anti* addition is observed in the *Penicillum decumbens*-mediated reduction of the carbonyl activated double bond of testosterone,[5] whereas in the case of the saturation of the *Z* hindered double bond of verbenone leading to verbanone, which occurs in cultured cells of *Nicotiana tabacum*, *re-re*-face, *syn* addition was observed.[7]

Studies on the mode of BY reduction of a set of racemic substrates structurally related to **5** and **6**, designed to establish the factors dictating the degree of enantiodifferentiation during the C=C bond saturation, are in progress.

Experimental

All NMR spectra were acquired on a Bruker ARX 400 spectrometer. The ^{2}H spectra were run in the gated ^{1}H broad-band decoupling mode and the proton spectra of deuteriated compounds were obtained under gated deuterium decoupling to eliminate all proton–deuterium coupling constants which cause a substantial broadening of the signals; J values in Hz. Molecular modelling was done with the CVFF force field as implemented in Bioym's INSIGHT/DISCOVER software (Biosym technologies, 9685 Scranton Road, San Diego, CA 92121-2777) on a Silicon Graphics IRIS 4D-35 personal workstation. Values of $[\alpha]_D$ are given as 10^{-1} deg cm^2 g^{-1}.

General Procedure for the Baker's Yeast Reduction of Unsaturated Methyl Ketones and Separation of the Transformation Products.—To a stirred mixture of baker's yeast (150 g) and glucose (75 g) in tap water (1.5 dm^3), the substrate (3 g) in ethanol (10 cm^3) was added at 35–38 °C. After 1 h, the reaction mixture was diluted with AcOEt (1 dm^3), stirred for 10 min and filtered on a large Buchner funnel through a Celite pad. This was washed twice with AcOEt (1 dm^3) and the combined organic phases were used to extract the filtrate. The washed and dried organic phase was evaporated to give the crude product mixture (70–80% yield). Product **7** was separated from unchanged **5** by SiO_2 column chromatography with increasing

amounts of AcOEt in hexane. Product **6** was co-eluted with **7**. Accordingly a chemical separation of **7** from **6** was achieved by submitting the mixture to ozonolysis. To this end, the crude product mixture was dissolved in CH_2Cl_2–MeOH (9:1) (typically, 10 g in 200 cm^3) and treated with ozonized oxygen at −78 °C until the ozone absorption was complete. Nitrogen was passed through the solution for 10 min after which PPh_3 was added to it; an equimolar amount of PPh_3 was used, based on the amount of **6** present in the mixture. Product **7** was recovered by SiO_2 column chromatography of the evaporated crude material, from which Ph_3PO was removed by precipitation with ether–hexane. Product **7**, obtained from **5** (22% conversion), was obtained as an oil, $[\alpha]_D^{20}$ −20 (*c* 0.8, $CHCl_3$) (Found: C, 70.8; H, 7.3. $C_{13}H_{16}O_3$ requires C, 70.89; H, 7.32%); $\delta_H(CDCl_3)$ 1.36 (3 H, d, *J* 6.4, 5-Me), 1.98 (2 H, q, *J* 7, 4-H), 2.14 (3 H, s, 1-Me), 2.55 (2 H, t, *J* 7, 3-H), 5.16 (1 H, m, 5-H) and 7.4–8.0 (5 H, m, C_6H_5). Its ee value was measured by NMR studies in the presence of tris[3-heptafluoropropylhydroxymethylene)-(+)-camphorato]europium(III) (two signals of the acetyl group at δ 2.70 and 2.72 were observed for 1:1 mixture by weight) and was 0.62. Similarly, product **7**, obtained from **6** (18% conversion), an oil, $[\alpha]_D^{20}$ +11.2 (*c* 0.75, $CHCl_3$) showed 0.48 ee, measured as above.

(Z)- *and* (E)-5-*Benzoyloxyhex*-3-*en*-2-*ones* **5** *and* **6** *and the* [3,4-$^2H_2$]*Analogues* **13** *and* **14**.—To a stirred solution of **8**[8] (14 g, 125 mmol) in CH_2Cl_2 (150 cm^3) and Et_3N (19 cm^3, 136 mmol) benzoyl chloride (16 cm^3, 137 mmol) was added at 0 °C. After 16 h at room temperature, the reaction mixture was poured into ice–water; the organic phase was separated and washed with dil. HCl, 3% aqueous $NaHCO_3$ and water. The oily residue obtained upon evaporation of the dried solution was chromatographed over a short SiO_2 path with hexane–AcOEt (9:1) to give the benzoate ester of **8**, an oil (22 g, 81%) (Found: C, 72.3; H, 5.6. $C_{13}H_{12}O_3$ requires C, 72.21; H, 5.59%); $\delta_H(CDCl_3)$ 1.68 (3 H, d, *J* 6.8, 5-Me), 2.34 (3 H, s, 1-Me), 5.53 (1 H, q, *J* 6.8, 5-H) and 7.4–8.1 (5 H, m, C_6H_5). The latter material (10.8 g, 50 mmol) in AcOEt (60 cm^3) was hydrogenated at room conditions in the presence of 10% (w/w) of Lindlar catalyst (Fluka) until 1 mol equiv. of hydrogen had been adsorbed. The filtered solution was evaporated to give an oil, which was chromatographed on a short SiO_2 path (hexane–AcOEt, 9:1) to give **5**, an oil (9.7 g, 89%) (Found: C, 71.6; H, 6.4. $C_{13}H_{14}O_3$ requires C, 71.54; H, 6.47%); $\delta_H(CDCl_3)$ 1.52 (3 H, d, *J* 6.5. 5-Me), 2.27 (3 H, s, 1-Me), 6.09 (1 H, dd, *J* 11.5 and 7.4, 4-H), 6.24 (1 H, dd, *J* 1.0 and 11.5, 3-H), 6.33 (1 H, m, 5-H) and 7.40–8.06 (H, m, C_6H_5). Product **5** was converted into **6** quantitatively upon being heated under reflux for 1 h in toluene with a few crystals of I_2. The cooled solution was washed with dil. aqueous $NaHSO_3$ and evaporated. Product **6**, an oil, was purified by chromatography on a short SiO_2 path (hexane–AcOEt, 9:1) (Found: C, 71.6; H, 6.5. $C_{13}H_{14}O_3$ requires C, 71.54; H, 6.47%); $\delta_H(CDCl_3)$ 1.52 (3 H, d, *J* 6.5, 5-Me), 2.29 (3 H, s, 1-Me), 5.77 (1 H, m, 5-H), 6.29 (1 H, dd, *J* 16.1 and 1.4, 3-H), 6.82 (1 H, dd, *J* 16.1 and 4.8, 4-H) and 7.44–8.10 (5 H, m, C_6H_5). By substitution of deuterium gas for hydrogen in the preparation of **5**, we similarly obtained **13**; $\delta_H(CDCl_3)$ 1.52 (3 H, d, *J* 6.5, 5-Me), 2.28 (3 H, s, 1-Me), 6.35 (1 H, q, 5-H), 7.4–8.0 (5 H, m, C_6H_5); δ_D(61.4 MHz, $CHCl_3$) 6.11 (4-D), 6.25 (3-D) and **14**; $\delta_H(CDCl_3)$ 1.52 (3 H, d, *J* 6.5, 5-Me), 2.29 (3 H, s, 1-Me), 5.77 (1 H, q, 5-H) and 7.42–8.13 (5 H, m, C_6H_5); δ_D(61.4 MHz, $CHCl_3$) 6.31 (3-D) and 6.84 (4-D).

(R)- *and* (S)-γ-*Valerolactone from Compounds* **7**, **15** *and* **16**.—Product **7** (2.2 g, 10 mmol) in dry THF (4 cm^3) was added under a N_2 atmosphere at −78 °C to a stirred solution of LDA, previously prepared by adding 1.6 mol dm^{-3} BuLi (6.6 cm^3) to diisopropylamine (1.7 cm^3, 12 mmol) in THF (80 cm^3). The solution was stirred for 1 h and then Me_3SiCl (2.1 cm^3, 17 mmol) was added to it. The reaction mixture was brought to room temperature, diluted with light petroleum (20 cm^3), filtered and evaporated to dryness to give **10** which was used immediately without further purification for the next step; $\delta_H(CDCl_3)$ 0.2 [9 H, s, $Si(Me)_3$], 1.35 (3 H, d, *J* 6.9, Me), 1.7–1.22 (4 H, m, 2-H and 3-H), 4.02 (2 H, s, $=CH_2$), 5.15 (1 H, m, 5-H) and 7.4–8.1 (5 H, m, C_6H_5). The latter material (*ca.* 2.7 g) was submitted to ozonolysis at −78 °C in CH_2Cl_2 (40 cm^3). At the end of the process the reaction mixture was carefully evaporated and the residue partioned between 3% $NaHCO_3$ and AcOEt (100 cm^3). Acidification of the aqueous phase with 2 mol dm^{-3} HCl and extraction with CH_2Cl_2 (2 × 50 cm^3) afforded the acid **11**, a thick oil, $[\alpha]_D^{20}$ −23 (*c* 0.53, $CHCl_3$); $\delta_H(CDCl_3)$ 1.37 (3 H, d, *J* 6.9, 4-Me), 2.03 (2 H, q, *J* 7, 2-H), 2.48 (2 H, t, *J* 7, 2-H), 5.20 (1 H, m, 4-H), 7.4–8.1 (5 H, m, C_6H_5) and 9.5 (1 H, s br, CO_2H). The latter material was refluxed for 1 h in 10% aqueous NaOH (5 cm^3). The cooled solution was acidified to pH 3 and benzoic acid filtered off. The aqueous phase was concentrated almost to dryness when it was extracted several times with AcOEt (*ca.* 50 cm^3). The combined extracts were dried and evaporated and the oily residue was distilled (bulb-to-bulb, oven temp. 100 °C) at 0.1 mmHg to give the lactone **12**, an oil (*ca.* 110 mg, 10% overall from **7**), $[\alpha]_D^{20}$ +14.8 (*c* 1.3, CH_2Cl_2) (lit.[10] for the *S* enantiomer, −29.6°). GLC conditions: DANI 8610 apparatus equipped with Megadex 5 column (modified β-cyclodextrin-coated fused silica gel column); He carrier gas, 0.75 bar. Temperature program: 40 °C (1 min), then 1.5 °C min^{-1}; t_R 28.3, t_S 28.8. This sequence, repeated on a sample of the ketone **7** possessing *ca.* 0.2 ee by NMR studies, obtained from **6** by a BY reduction, afforded (*S*)-valerolactone, 0.22 ee. The lactones **17** and **18** were similarly obtained from the methyl ketones **15** and **16**.

[3,4-$^2H_2$]*Ketones* **19** *and* **20**.—The unsaturated ketones **5** and **6** were quantitatively converted into compounds **19** and **20** upon treatment in AcOEt with deuterium gas in the presence of 10% (w/w) of Lindlar catalyst. At the end of the reaction, the oily residue obtained upon evaporation of the filtered solution, was chromatographed on a short SiO_2 path with hexane–AcOEt, for NMR results see Table 2.

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Paper 4/03476G
Received 9th *June* 1994
Accepted 22nd *June* 1994