Chiral α-Sulphinyl Hydrazones as Effective Reagents for Stereoselective Aldol-type Condensation

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The stereoselective aldol-type synthesis of optically active β-hydroxy hydrazones and β-hydroxy ketones mediated by chiral α-sulphinyl hydrazones is described. In some cases a good degree of enantioselectivity (up to 88%) is achieved. The factors affecting the stereochemical outcome of the process, *i.e.* the nature and stoicheiometry of the base and the structures and steric requirements of the α-sulphinyl hydrazones are discussed.

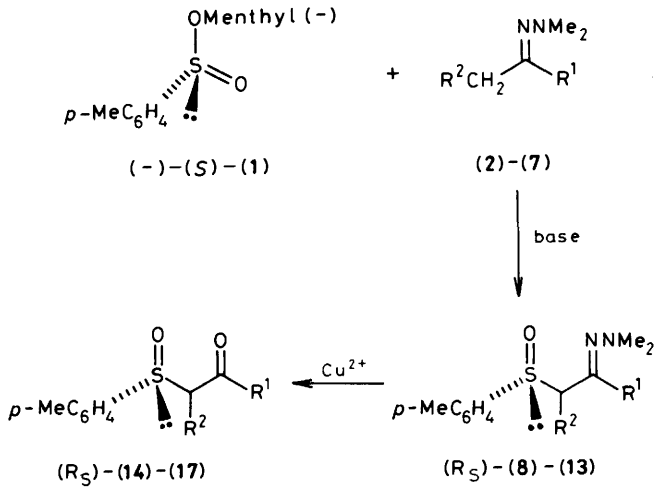
A major challenge in organic chemistry is the stereoselective formation of C–C bonds,[1] an area in which a dominant role is played by aldol and related reactions.[1] One possible approach is represented by the use of easily accessible optically pure functionalized sulphoxides, various classes of which have been employed[2] in aldol-type reactions.

We here report the enantioselective condensation[3] of α-sulphinyl hydrazones[4] with aldehydes which yield, after desulphurization of the adducts, β-hydroxy hydrazones and β-hydroxy ketones of good enantiomeric purity.

Synthesis and Stereochemistry of α-Sulphinyl Hydrazones.—Facile access[4] to the title compounds is constituted by metallation of *N,N*-disubstituted hydrazones (**2**)—(**7**) and subsequent reaction with (−)-(*S*)-menthyl toluene-*p*-sulphinate (**1**). By this route compounds (**8**)—(**13**) were prepared in excellent yields (see Experimental section). ^{1}H N.m.r. spectroscopy in the presence of chiral shift reagents as well as, in a few instances, copper ion catalysed conversion[4] into the corresponding β-sulphinyl ketones (**14**)—(**15**) established that compounds (**8**)—(**13**) are optically pure at the sulphur atom and that, as expected,[4] reaction of the sulphinate ester proceeds with inversion of chirality at the sulphur atom. Thus the (R_S) absolute configuration can be assigned to α-sulphinyl hydrazones. These are usually obtained as mixtures of *Z*:*E* isomers (see Experimental Section) in ratios determined[4] through ^{1}H n.m.r. and ^{13}C n.m.r. spectroscopy.

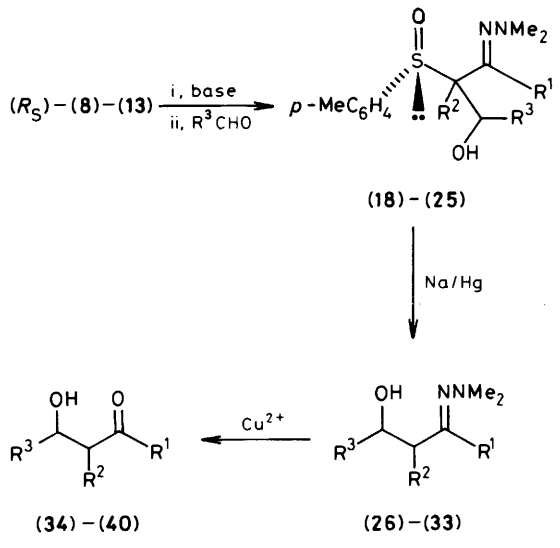
In the case of compounds (**12**) and (**13**) the presence of an asymmetrically substituted carbon atom results in the formation of epimers at carbon, the ratio of which can be determined by n.m.r. spectroscopy directly or after conversion into the corresponding β-keto sulphoxides (**16**) and (**17**); no separation of these was attempted. It should be noted that for the hydrazone (**13**) the stereochemical integrity at the carbon α to the sulphoxide group is not retained along the route to the aldol products (see below).

Aldol-type Condensations.—Metallation of α-sulphinyl hydrazones with a suitable base and subsequent reaction with aldehydes leads to the adducts (**18**)—(**25**) (as a mixture of diastereoisomers) which upon reductive desulphurization affords the β-hydroxy hydrazones (**26**)—(**33**). The stereo-



(**2**), (**8**)	$R^1 = R^2 = H$
(**3**), (**9**), (**14**)	R^1 = Me; R^2 = H
(**4**), (**10**), (**15**)	R^1 = Ph; R^2 = H
(**5**), (**11**)	R^1 = Bu^t; R^2 = H
(**6**), (**12**), (**16**)	R^1 = Bu^s; R^2 = H
(**7**), (**13**), (**17**)	R^1 = Et, R^2 = Me

Scheme 1.



(**18**), (**26**)	$R^1 = H$ $R^2 = H$ $R^3 = Ph$
(**19**), (**27**), (**34**)	R^1 = Me $R^2 = H$ $R^3 = Ph$
(**20**), (**28**), (**35**)	R^1 = Me $R^2 = H$ R^3 = Pr^i
(**21**), (**29**), (**36**)	R^1 = Ph $R^2 = H$ R^3 = Pr^i
(**22**), (**30**), (**37**)	R^1 = Bu^s $R^2 = H$ $R^3 = Ph$
(**23**), (**31**), (**38**)	R^1 = Bu^s $R^2 = H$ R^3 = Et
(**24**), (**32**), (**39**)	R^1 = Et R^2 = Me $R^3 = Ph$
(**25**), (**33**), (**40**)	R^1 = Et R^2 = Me R^3 = Et

Scheme 2.

Table 1. Enantioselective synthesis of (**26**) from (**8**) and benzaldehyde

Entry	Base	*a* t_1(min)	*b* T_1 (°C)	*c* t_2 (min)	*d* T_2 (°C)	*e* Yield (%)	*f* e.e (%)
A	Bu^tMgBr [g]	30	−78	1500	20	42	35 [h]
B	Bu^tMgBr [g]	30	0	1500	−78	47	23 [h]
C	LDA [i]	60	−78	60	−78	29	19 [h]
D	LDA [i]	60	0	60	−78	48	29 [h]
E	LDA [i]	60	20	60	20	50	30 [j]
F	Bu^nLi [k]	5	−90	2	−90	28	21 [h,l]
G	Bu^nLi [k,m]	5	−90	2	−90	40	34 [h,l]

[a] Metallation time. [b] Metallation temperature. [c] Condensation time. [d] Condensation temperature. [e] Overall yield of (**26**). [f] By ^1H n.m.r. spectroscopy (see text). [g] 15 Mol equiv. of base. [h] Laevorotatory. [i] 2 Mol equiv. of base. [j] Dextrorotatory. [k] 1 Mol equiv. of base. [l] See ref. 3. [m] In the presence of 2 mol equiv. of HMPA.

chemical outcome of the process strongly depends on the experimental conditions. The latter were established by working with the sulphoxide (**8**) (see Table 1), the enantiomeric excesses (e.e.) of the β-hydroxy hydrazone (**26**) being determined by ^1H n.m.r. spectroscopy in the presence of the chiral shift reagent tris[3-(heptafluoropropylhydroxymethylene)](+)-camphoratoeuropium(III) [$Eu(hfc)_3$] (see Table 1).

Variations of the nature of the base and of metallation and condensation times and temperatures definitely affect both the chemical and optical yields. t-Butylmagnesium bromide, although satisfactory from the point of view of enantioselectivity, must be used in large excess and requires long condensation times. Comparable results were achieved with n-butyl-lithium in the presence of hexamethylphosphoric triamide (HMPA) at −90 °C with much shorter reaction times. Therefore the latter conditions were generally used throughout this work.*

The β-hydroxy hydrazone (**26**) was not converted into the corresponding β-hydroxy aldehyde because of the intrinsic instability of the latter. Since (**26**) is obtained as a mixture of *E* and *Z* isomers in different ratios (the *E* isomer however being largely predominant) a linear correlation between e.e. and optical rotation values for this compound was not observed. On the other hand β-hydroxy hydrazones (**27**)—(**33**) could be cleanly unmasked [3] to give the corresponding ketols (**34**)—(**40**). Table 2 summarizes the results of a series of aldol-type condensations carried out on the sulphinyl derivatives (**9**), (**10**), (**12**), and (**13**) with different aldehydes.

From the reported data it appears that good degrees of enantioselectivity are generally achieved only by carefully selecting the condensation conditions, with particular emphasis on base nature and stoicheiometry; in a few instances a reversal of enantioselectivity was observed (entries D and E, and entries H, J, and K).

In the latter cases both enantiometers of the β-hydroxy hydrazone (**26**) and of the β-ketol (**34**) were obtained from a single chiral precursor, (**8**) and (**9**) respectively.† Therefore, in further discussing the factors affecting the stereoselectivity, only comparisons within homogeneous sets of condensation are, in our opinion, reliable.

Let us consider first those hydrazones in which the sulphoxide group represents the only asymmetric stereocentre, *i.e.* (**8**), (**9**), and (**10**). As already pointed out,[3] an increase in the bulk of the aldehyde residue R^3 is reflected in an increase in the enantioselectivity of the reaction. With sterically comparable aldehydes such as benzaldehyde and isobutyraldehyde (entries H and I) the steric requirements of R^1 group are of major importance (entries G, H, and L, and J and M). As far as the structures of the hydrazones (**8**), (**9**), and (**10**) are concerned, the presence of a bulky R^1 group gives rise to a larger presence of the *Z* isomer, the *E*:*Z* ratios being 100:0, 75:25, and 15:85 for (**8**), (**9**), and (**10**) respectively.[4] It seems likely that in the derived aza-allyl anion, the C=N isomer *E*:*Z* ratio should reflect to some extent the situation met with in the starting material,‡ thus leading to a more crowded transition state capable of higher enantiofacial differentiation.

To further substantiate this hypothesis, aldol condensations on the sulphoxide (**11**), which exists only as the *Z* isomer, were attempted but, unfortunately, resulted in extremely poor yields. In the case of the sulphoxide (**13**). however, a different enantioselectivity between the *E* and *Z* isomers was observed (see below).

The sulphinyl hydrazones (**12**) and (**13**) both contain two asymmetric stereocentres, and their aldol condensations generate mixtures of diastereoisomeric ketols (**37**)—(**40**). The sulphoxide (**12**) is a mixture (*ca.* 45:55) of epimers at the carbon as determined by conversion into the β-keto sulphoxide (**16**) and by inspection of the ^1H n.m.r. spectrum of the latter. No epimer separation was attempted on (**12**) and the ketols (**37**) and (**38**) obtained from it, reflect the original diastereoisomeric ratio.

The extent of aldehyde enantiofacial differentiation is, not unexpectedly, different for the two epimers (50 and 33% respectively) and is lower than those obtained by working with the hydrazone (**10**) under comparable conditions. This fact is not a consequence of a different *E*:*Z* isomer ratio at the C=N bond since the sulphoxides (**10**) and (**12**) are comparable from this point of view (see Experimental Section), but most likely depends on the combination of the effects of the two asymmetric stereocenters in (**12**).

Finally, in the case of the sulphoxide (**13**) column chromatography allowed separation of the *Z* and *E* isomers at the C=N bond, each consisting of a *ca.* 1:1 mixture of epimers at carbon (see Experimental section). Indeed hydrolysis of both fractions afforded the same β-keto sulphoxide (**17**) as a *ca.* 1:1 mixture of diastereoisomers.

Reaction of (**3**) as a 2:1 *E*:*Z* mixture with benzaldehyde or propanal gave eventually the adducts (**39**) or (**40**) as 3:1 or 4:1 mixtures of diastereoisomers, respectively. The enantiomeric excesses could be determined as 10 and 30%, respectively, only for the prevailing *erythro* [7] stereoisomers. When the condens-

* Anyway, these conditions did not secure top enantioselectivities in the case of the total synthesis of both enantiomers of gingerol, higher stereoselections being achieved with a condensation temperature of −10 °C.[5]

† This fact finds some analogies in the aldol condensation involving sulphinyl amides.[2b]

‡ In related hydrazone lithio-anions the *E*:*Z* ratio has been shown to be strongly dependent on the nature of the hydrazone and on the metallation conditions.[6]

Table 2. Enantioselective synthesis of the ketols (**34**)—(**40**) from the hydrazones (**9**), (**10**), (**12**), and (**13**).

Entry	Hydrazone[a]	Ketols	Yield[b] (%)	$[\alpha]_D^{23}$[c]	e.e.[d] (%)	Diastereoisomeric ratio[e]
H	(**9**)[f]	(**34**)	22	−37.7	50	
I	(**9**)[f]	(**35**)	20	−22.6	50	
J	(**9**)	(**34**)	20	+7.6	10	
K	(**9**)[g]	(**34**)	25	+37.8	50	
L	(**10**)[f]	(**36**)	25	−33.1	56	
M	(**10**)	(**36**)	25	−51.9	88	
N	(**12**)[h]	(**37**)	27	+20.7[i]	48, 33[j]	1:1
O	(**12**)[h]	(**38**)	10	−4.2[i]	50, 33[j]	1:1
P	(**13**)[k]	(**39**)	30	−2.0[i]	10[l]	3:1
Q	(**13**)[k]	(**40**)	30	−6.6[i]	30[l]	4:1

[a] Condensations carried out at −90 °C with 1.5 mol equiv. of Bu^{n}Li and 3.0 mol equiv. of HMPA and with metallation and condensation times of 1 and 3 h respectively, unless otherwise stated. [b] Overall yield from sulphinyl hydrazones. [c] *c* 1, in $CHCl_3$. [d] As determined by ^{1}H n.m.r. spectroscopy in the presence of Eu(hfc)$_3$. [e] As determined by ^{1}H n.m.r. spectroscopy. [f] Condensation carried out at −90 °C with 1.0 mol equiv. of Bu^{n}Li and 2.0 mol equiv. of HMPA and with metallation and condensation times of 3 min. [g] Under the conditions described in footnote *f* but with Bu^{t}Li as base. [h] The starting material is a mixture of epimers at the carbon γ to the sulphur moiety. [i] Optical rotation of the diastereoisomeric mixture of ketols. [j] Enantiomeric excesses of the two diastereoisomeric ketols, respectively. [k] The starting material is a *ca.* 1:1 mixture of epimers at the carbon α to the sulphur moiety. [l] E.e. of the major diastereoisomer, *i.e. erythro*.[14,15]

ation with benzaldehyde was repeated starting from pure *E*-(**13**), the e.e. dropped to ≤2%, thus clearly showing the importance of the geometry at the C=N bond in the starting hydrazone in affecting the stereochemical outcome of the aldol-type condensation.

Experimental

^{1}H and ^{13}C n.m.r. spectra were recorded on Varian XL 200 or a Bruker WP-80 instrument, using tetramethylsilane as internal standard and $CDCl_3$ as solvent. I.r. spectra were recorded with a Perkin-Elmer 457 spectrometer. Optical rotations were measured on a Perkin-Elmer 241 spectrometer. Elemental analyses were performed with a Perkin-Elmer 240 instrument. Silica gel was used for analytical, preparative, and column chromatography. H.p.l.c. analyses were performed on a Varian 5000 Liquid chromatograph with a Lichrosorb SI 100 10 μm column using a Hewlett-Packard 3390 A integrator. Organic extracts were dried over Na_2SO_4 and filtered before removal of the solvent under reduced pressure. 'Dry' solvents were distilled under dry N_2 atmosphere before use: tetrahydrofuran (THF) was distilled from sodium (in the presence of benzophenone ketide as indicator), hexamethylphosphoric triamide (HMPA) and di-isopropylamine from CaH_2, methanol from Mg turnings. All reactions employing 'dry' solvents were run under an inert atmosphere. Enantiomeric excesses (e.e.) were evaluated by ^{1}H n.m.r. spectroscopy in $CDCl_3$ with the aid of the chiral shift reagent tris[3-(heptafluoropropylhydroxymethylene)(+)-camphorato]europium(III) [Eu(hfc)$_3$] under conditions pre-established on the corresponding racemic samples. *N,N*-Dimethylhydrazones were prepared accordingly to described procedures.[8,9] Aldehydes were distilled immediately before the condensation reactions.

Synthesis of α-Sulphinyl Hydrazones.—α-Sulphinyl hydrazones were synthesized accordingly to the method described,[4] from *N,N*-dimethylhydrazones and (−)-menthyl toluene-*p*-sulphinate $[\alpha]_D^{23} = -204.1$ (*c* 1, acetone).[2a]

Compound (**11**): white crystals (77%), m.p. 70—71 °C (from di-isopropyl ether); δ_H 7.23—7.73 (4 H, m, C_6H_4), 3.59—3.86 (2 H, AB system, CH_2), 2.45, (9 H, s, Me_2N and MeC_6H_4), and 1.13 (9 H, s, Bu^t); δ_C 171.4 (C=N), 143.5, 141.2, 129.7, and 124.1 (aromatic C), 58.7 (CH_2), 46.2 (Me_2N), 37.9 (*C*Bu^t), 27.7 (C*Bu*^{t}), and 21.3 (*Me*C_6H_4); $[\alpha]_D^{23} = +164°$ (*c* 1 acetone) (Found: C, 64.2; H, 8.65, N, 10.0 $C_{15}H_{24}N_2OS$ requires C, 64.2; H, 8.6; N, 10.0%).

Compound (**12**): thick oil (81%), $[\alpha]_D^{23} = +80.5$ (*c* 1, $CHCl_3$); n_D^{22} 1.5390 (Found: C, 64.15; H, 8.6; N, 9.95. $C_{15}H_{24}N_2OS$ requires C, 64.24; H, 8.63; N, 10.0%). This product comprised a 45:55 mixture of epimers at carbon and a 1:4 *E*:*Z* isomer ratio at the C=N bond, as evaluated by both ^{1}H and ^{13}C n.m.r. spectroscopy: δ_H 7.15—7.70 (4 H, m, C_6H_4), 3.50—3.95 (2 H, AB system, CH_2; 1 H, m, C*H*Me), 2.40 (9 H, s, Me_2N and MeC_6H_4), 1.18—1.80 (2 H, m, CH_2Me), 0.95—1.15 (3 H, 2 d, *Me*CH), and 0.68—0.90 (3 H, t, *Me*CH_2); δ_C 168.2, 167.9 (*Z* and *E* isomers, C=N), 60.3, 60.0 (*E* isomer of both carbon epimers, CH_2SO), 58.9, 58.7 (*Z* isomer for both carbon epimers, CH_2SO), and 47.7, 46.8 (*E* and *Z* isomers, NMe_2).

Compound (**13**): oil (85% yield); *Z isomer:* n_D^{22} 1.5418; $[\alpha]_D^{23} = +17.0°$ (*c* 1, $CHCl_3$) is constituted by a 1:1 mixture of epimers at carbon, as determined by n.m.r. spectroscopy (Found: C, 63.1; H, 8.4; N, 10.3 $C_{14}H_{22}N_2OS$ requires C, 63.1; H, 8.3; N, 10.5%); δ_H 7.15—7.65 (4 H, m, C_6H_4), 4.54—4.99 (1 H, 2 q, CH), 2.44 (3 H, s, MeC_6H_4), 2.32 and 2.35 (6 H, 2 s, Me_2N), 0.82—1.62 (8 H, m, CH*Me* and CH_2*Me*); δ_C 169.7, 168.8, (C=N), 59.5, 57.9 (CH_2), 47.15, 47.05 (NMe_2); E *isomer*: $[\alpha]_D^{23} = +66.8°$ (*c* 1, $CHCl_3$); n_D^{22} 1.5421 (Found: C, 63.25; H, 8.4; N, 10.65. $C_{14}H_{22}N_2OS$ requires C, 63.1; H, 8.3; N, 10.5%). This product comprised a 6:4 mixture of epimers at carbon; δ_H 7.15—7.62 (4 H, m, C_6H_4), 3.35—3.78 (1 H, 2q, CH), 2.18—2.83 (2 H, m, CH_2), 2.42 (9 H, s, Me_2N and MeC_6H_4), and 0.73—1.32 (6 H, m, CH*Me* and CH_2*Me*); δ_C 168.15, 167.50 (C=N), 66.1, 64.7 (CHSO), and 47.35, 47.30 (NMe_2).

General Procedure for the Preparation of the Adducts (**18**)—(**25**).—To a stirred solution of the hydrazone (1 mmol) in dry THF (20 ml) or, if necessary, in THF–HMPA, was added dropwise the appropriate base (for metallation conditions see Tables 1 and 2). Subsequently 2 mol equiv. of aldehydes were added as such (for condensation conditions see Tables 1 and 2). The reaction was quenched with saturated aqueous ammonium chloride and the aqueous layer extracted with ether (3 × 40 ml). The organic layers were combined, dried, and evaporated under reduced pressure, to give the adducts (**18**)—(**25**) which were used as such for subsequent reaction.

General Procedure for the Preparation of β-Hydroxy Hydrazones (**26**)—(**33**).—The crude adducts (1 mmol) were dissolved in dry methanol (15 ml) and cooled to −20 °C under a nitrogen atmosphere. Anhydrous NaH_2PO_4 (1.2 g) and then freshly ground 10% sodium amalgam (1.5 g) were added with

vigorous stirring. The reaction was monitored by t.l.c. After a 2—4 h period saturated aqueous ammonium chloride (30 ml) was added and the suspension allowed to warm to room temperature; it was then filtered through Celite. The organic solvents were evaporated and the aqueous layer was extracted twice with dichloromethane, dried, and concentrated to give crude products. This could be purified by column chromatography (silica gel, with n-hexane–ethyl acetate–triethylamine as eluant) or directly converted into the corresponding ketols (see text). The β-hydroxy hydrazone (**26**) was a colourless oil (Found: C, 68.65; H, 8.5; N, 14.6. $C_{11}H_{16}N_2O$ requires C, 68.7; H, 8.4; N, 14.6%); δ_H 7.22—7.42 (5 H, m, C_6H_5), 6.72 (1 H, t, CH=N, *J* 4.5 Hz), 4.96 (1 H, t, C*H*OH, *J* 6.3 Hz), 3.50 (1 H, br s, OH), 2.73 (6 H, s, Me_2N), and 2.50—2.70 (2 H, m, CH_2).

General Procedure for the Preparation of the β-Hydroxy Ketones (**34**)—(**40**).—The crude β-hydroxy hydrazones (**27**)—(**33**) (1 mmol) dissolved in THF (15 ml) were added to a stirred solution of copper(II) chloride (2.2 mmol) in water (5 ml) and pH 7 phosphate buffer (3 ml). After being stirred overnight, the mixture was treated with aqueous ammonium chloride–ammonium hydroxide (pH = 8; 10 ml), extracted with methylene chloride (3 × 7 ml), and the extracts dried and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel, with n-hexane–diethyl ether as eluant). Yields and optical rotations are reported in Table 2. 4-Hydroxy-4-phenylbutan-2-one (**34**),[10] 4-hydroxy-5-methylhexan-2-one (**35**),[11] 3-hydroxy-4-methyl-1-phenylpentan-1-one (**36**),[12] 1-hydroxy-4-methyl-1-phenylhexan-3-one (**37**),[13] 1-hydroxy-2-methyl-1-phenylpentan-3-one (**39**),[14] 5-hydroxy-4-methylheptan-3-one (**40**),[15] and 6-hydroxy-3-methyloctan-4-one (**38**)[13] had physical and spectral properties in agreement with the literature.

Synthesis of β-Keto Sulphoxides (**16**) and (**17**).—These compounds were prepared following the described procedure.[4] Compound (**16**), a waxy material, was obtained as a 45:55 mixture of epimers at carbon in 89% yield from the hydrazone (**12**); $[\alpha]_D^{23}$ = +133.8° (*c* 1, $CHCl_3$); δ_H 7.25—7.60 (4 H, m, C_6H_4), 3.71—4.05 (2 H, m, CH_2CN), 2.44 (1 H, q, CH), 2.40 (3 H, s, *Me*C_6H_4), 1.20—1.80 (1 H, 2 m, C*H*Me), 0.92—1.08 (3 H, 2 d, *Me*CH), and 0.73—0.88 (3 H, 2t, *Me*CH_2) (Found: C, 65.4; H, 7.65. $C_{13}H_{18}O_2S$ requires C, 65.5; H, 7.6%).

Compound (**17**) was obtained from the *Z* isomer of the hydrazone (**13**) in 82% yield, as a 1:1 mixture of epimers at carbon; n_D^{22} 1.5489; $[\alpha]_D^{23}$ = +90.8° (*c* 1, $CHCl_3$). Starting from the *E* isomer of (**13**), (**17**) was obtained as a 6:4 mixture of epimers at carbon; n_D^{22} = 1.5498, $[\alpha]_D^{23}$ = +80.3 (*c* 1, $CHCl_3$); δ_H 7.13—7.50 (4 H, m, C_6H_4), 3.60—3.90 (1 H, m, C*H*Me), 2.22—2.68 (2 H, m, CH_2), 2.40 (3 H, s, *Me*C_6H_4), 1.18—1.41 (3 H, 2 d, CH*Me*), and 0.85—1.08 (3 H, q, *Me*CH_2) (Found: C, 64.35; H, 7.15. $C_{12}H_{16}O_2S$ requires C, 64.25; H, 7.2%).

References

1 D. A. Evans, J. V. Nelson, and T. R. Taber, *Top. Stereochem.*, 1982, **13**, 1; T. Mukaiyama, *Org. React.*, 1981, 203; C. H. Heathcock, *Science*, 1981, **214**, 395; S. Masamune, in 'Organic Synthesis Today and Tomorrow', B. M. Trost and C. R. Hutchinson, eds. Pergamon, London, 1981, p. 197; R. W. Hoffmann, *Angew. Chem., Int. Ed. Engl.*, 1982, **21**, 555.

2 (*a*) G. Solladié, F. Matloubi-Moghadam, C. Luttmann, and C. Mioskowski, *Helv. Chim. Acta.*, 1982, **65**, 1602, and references therein; (*b*) R. Annunziata, M. Cinquini, F. Cozzi, F. Montanari, and A. Restelli, *J. Chem. Soc., Chem. Commun.*, 1983, 1138; (*c*) R. Annunziata, M. Cinquini, F. Cozzi, and A. Gilardi, *Synthesis*, 1983, 1016.

3 L. Colombo, C. Gennari, G. Poli, C. Scolastico, R. Annunziata, M. Cinquini, and F. Cozzi, *J. Chem. Soc., Chem. Commun.*, 1983, 403.

4 R. Annunziata, L. Banfi, L. Colombo, F. Cozzi, and C. Gennari, *Synthesis*, 1982, 829.

5 R. Annunziata, S. Cardani, C. Gennari, and G. Poli, *Synthesis*, 1984, 702.

6 K. G. Davenport, H. Eichenauer, D. Enders, M. Newcomb, and D. E. Bergbreiter, *J. Am. Chem. Soc.*, 1979, **101**, 5654.

7 C. H. Heathcock, M. C. Pirrung, J. Lampe, C. T. Buse, and S. D. Young, *J. Org. Chem.*, 1981, **46**, 2290.

8 E. J. Corey, D. Enders, *Chem. Ber.*, 1978, **111**, 1362, and references therein.

9 G. J. Karabatsos, R. A. Teller, *Tetrahedron*, 1968, **24**, 3923.

10 D. P. Curran, *J. Am. Chem. Soc.*, 1982, **104**, 4024.

11 H. Eichenauer, E. Friedrich, W. Lutz, and D. Enders, *Angew., Chem. Int., Ed. Engl.*, 1978, **17**, 206.

12 T. Mukaiyama, K. Banno, and K. Narasaka, *J. Am. Chem. Soc.*, 1974, **96**, 7503.

13 D. Seebach, V. Ehrig, and M. Teschner, *Liebigs Ann., Chem.*, 1976, 1357.

14 C. H. Heathcock, C. T. Buse, W. E. Kleschick, M. C. Pirrung, J. E. Sohn, and J. Lampe, *J. Org. Chem.*, 1980, **45**, 1066.

15 C. H. Heathcock, M. C. Pirrung, and J. E. Sohn, *J. Org. Chem.*, 1979, **44**, 4294.

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