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STEREOCHEMISTRY OF [3.3]-SIGMATROPIC REARRANGEMENTS IN THE OXAZOLE SERIES

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Abstract- The transfer of chirality from optically active propargyl and cinnamyl N-acyl-C-phenylglycinates to α-branched ketones may be achieved by sigmatropic rearrangements of oxazole intermediates followed by catalytic hydrogenation of the resulting 3-oxazolinones and subsequent reductive ring cleavage. From (R)-4-phenyl-3-buten-1-ol both enantiomers of 1,4-diphenyl-2-methylbutan-1-one (6) could be obtained by starting either from the (E)- or (Z)-diastereomer of the alcohol.

Recently a mild and efficient method for the chain elongation of carboxylic acids has been described which makes use of [3.3]-sigmatropic rearrangements in the oxazole series.[1,2] In this publication we report on the stereochemistry of these rearrangements and describe the possibility of using this method for the preparation of optically active α-branched ketones by chirality transfer from optically active unsaturated alcohols.

A. Propargyl Derivatives

On treatment with $COCl_2/NEt_3$ in acetonitrile at 0°C propargyl N-acyl-C-phenylglycinates 1 are smoothly converted into 4-allenyl-2-oxazolin-5-ones 3 (Table 1).[3] The reaction proceeds via the non-isolable oxazoles 2 which undergo Claisen rearrangement under the cyclization conditions. The oxazolinones 3 can be obtained from the crude reaction mixture by careful crystallization from methanol. Recently this method has been used for the synthesis of 2-allenylamino acids.[4]

Cyclization of the chiral propargyl esters 1d-1f results in the formation of mixtures of diastereomers. The ratio is dependent on the size of R^1 and changes

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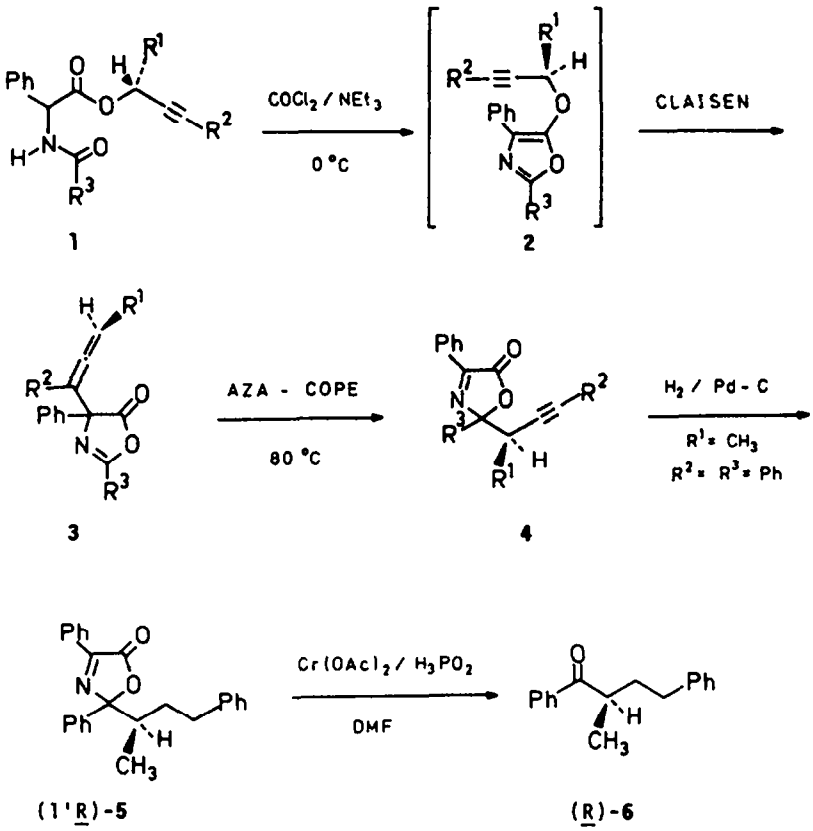


Table 1. Claisen and aza-Cope rearrangement products 3 and 4

	R^1	R^2	R^3	Claisen step (ratio of diastereomers 3)	aza-Cope step (equilibrium of compounds 3:4)	aza-Cope step (reaction time) [h]
a	H	H	p-Cl-Ph	-	100 : 0	-
b	H	Me	p-Cl-Ph	-	70 : 30	112
c	H	Ph	p-Cl-Ph	-	0 : 100	18
d	Me	Ph	p-Cl-Ph	60 : 40	0 : 100	8
d'	Me	Ph	Ph	60 : 40	0 : 100	8
e	iPr	Ph	p-Cl-Ph	65 : 35	40 : 60	15
f	tBu	Ph	p-Cl-Ph	70 : 30	100 : 0	-

from 60:40 to 70:30 in going from **3d** to **3f**. In the case of **3d** both diastereomers could be separated by HPLC.

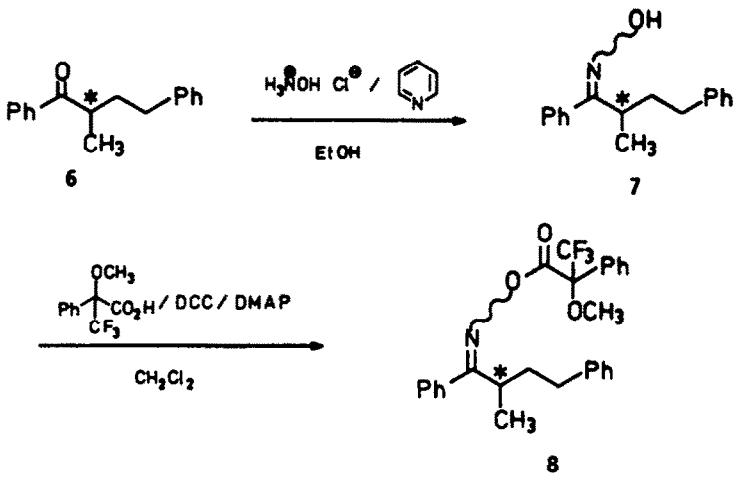
On heating the 2-oxazolinones **3** in refluxing benzene for 10-18 h an aza-Cope rearrangement with the formation of 2-propargyl-3-oxazolin-5-ones **4** may be observed. The ease of the aza-Cope rearrangement depends strongly on the presence and size of substituents R^1 and R^2 (Table 1). In the case of **3c** and **3d** the rearranged products **4c** and **4d**, respectively, were formed without any side products. In these cases the steric interactions between the 4-phenyl group at the oxazolinone ring and the neighbouring phenyl substituent at the allenyl side chain render the 2-oxazolinones thermodynamically less stable. This situation is reversed, however, in the case of compounds **3e** and **3f**. Here considerable steric interactions are present in the 3-oxazolinones **4**, which lead to the formation of a 40:60 equilibrium mixture of **3e** and **4e** in the case of the isopropyl derivative and prohibit the formation of **4f** completely if a tert-butyl group is present in the side chain. The simple allenyl derivative **3a** is so stable that even at reflux temperature in p-xylene no rearrangement into **4a** takes place. The methyl derivative yields a 70:30 equilibrium mixture of the 2- and 3-oxazolinones **3b** and **4b** which reflects the decrease in steric interactions in comparison to **3c**.

In the aza-Cope rearrangement of compounds **3** with $R^1 \neq H$ each of the two diastereomers undergoes the aza-Cope rearrangement with virtually complete stereoselectivity. In the case of **3d** the initial 58.7:41.3-mixture of diastereomers yielded a 57.8:42.2-mixture of the **4d** diastereomers as indicated by HPLC analysis.

The efficient rearrangement of **3d** into **4d** suggested the possibility of using this method for a chirality transfer from (R)-4-phenyl-3-butyn-2-ol to α-methyl branched ketones. To test this idea the (R)-alcohol was prepared in 66% ee by Midland's[5] procedure from the corresponding alkynone. Conversion of the alcohol into the optically active ester (1'R)-**1d'** was achieved by DCC/DMAP mediated esterification[7] with N-Boc-C-phenylglycine, followed by removal of the N-protecting group with trifluoroacetic acid and reacylation with benzoylchloride. Cyclization of (1'R)-**1d'** and thermal rearrangement of (2'R)-**3d'** into the 3-oxazolinone (1'R)-**4d'** was carried out as described above. To determine the effectiveness of the chirality transfer to the C-1' position, the chiral centre at C-2 of the oxazolinone ring had to be removed. Because reductive cleavage of (1'R)-**4d'** with chromium(II) acetate and hypophosphorous acid[8] could not be effected due to the sensitivity of the triple bond, this step had to be performed after catalytic hydrogenation of (1'R)-**4d'** to (1'R)-**5**. The resulting (R)-1,4-diphenyl-2-methylbutan-1-one (R-**6**)[9] had an optical rotation $[\alpha]_D^{20} = -18.2°$. Comparison of our ketone with a sample of the (S)-compound ($[\alpha]_D^{20} = +26.1°$) synthesized by Ender's method[10] from the corresponding SAMP-hydrazone indicated that our product had the (R)-configuration.

Due to insufficient signal separation the optical purity of (R)-**6** could not

be determined by ^{1}H NMR shift experiments with Eu(hfc)$_3$. However, the determination of the optical purity could be easily carried out with ester 8, which was obtained by acylation of the E/Z-mixture of oxime 7 with Mosher's reagent.[11] At 400 MHz



the ^{1}H NMR spectrum of 8 (1:1 E/Z mixture) gives rise to four methyl doublets, two of which being totally separated (Figure 1). In the case of (2R,2'S),(E/Z)-8 the integration of the signals yields a 82:18 ratio of diastereomers [64% ee of (R)-6].

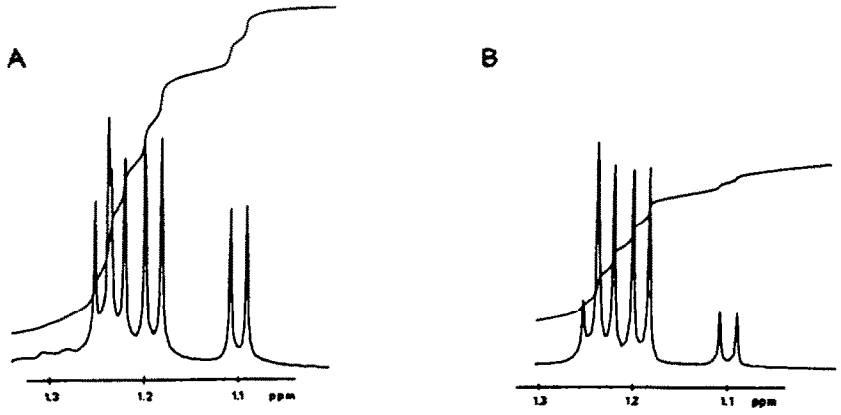
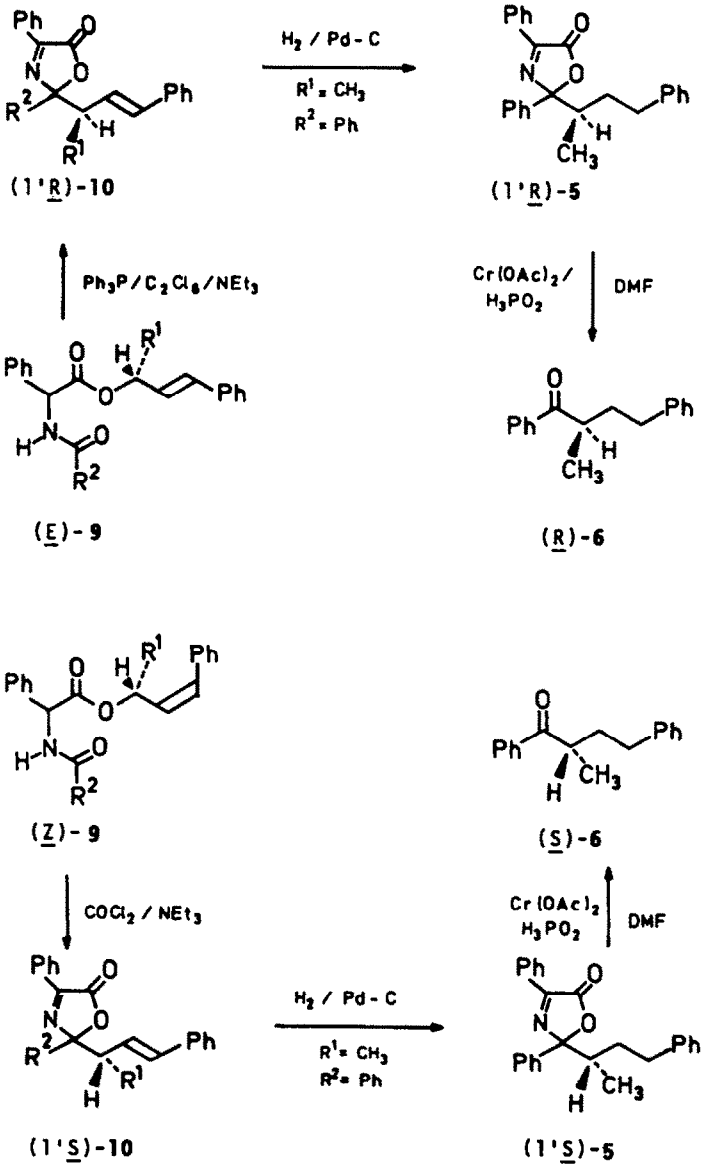


Figure 1. Determination of the enantiomeric excess from the ^{1}H NMR spectra (400 MHz, $CDCl_3$) of the diastereomeric oxime derivatives 8 (A: 60:40 mixture; B: 82:18 mixture).

This leads to the conclusion that the configuration of the starting propargyl alcohol remained nearly unchanged after the two consecutive [3.3]-sigmatropic rearrangements and the reductive cleavage of the oxazolinone ring.

B. Cinnamyl Derivatives

The cyclization of the two stereoisomeric cinnamyl N-acyl-C-phenylglycinates (E)-9a and (Z)-9a leads to a remarkable result. Both stereoisomers yield at room temperature on dehydration by the usual procedures[1,2] the same (E)-2-cinnamyl-3-oxazolinone 10a.[2] This may be explained by assuming chair-like transition states for both sigmatropic rearrangements of (E)-9a, whereas with (Z)-9a the aza-Cope rearrangement proceeds via a boat-like transition state. This is in accord with the complete stereoselectivity of the Claisen rearrangement of crotyl (Z)-N-acyl-C-phenylglycinates[12] and the corresponding cycloalkenyl esters.[12,13]



	R^1	R^2
a	H	p-Cl-Ph
b	Me	Ph

These results suggested the use of these rearrangements for the transfer of chirality from (E)- and (Z)-4-phenyl-3-buten-2-ol to an α-methylbranched ketone **6** with either retention or inversion of configuration.

To prove this possibility the optically active ester (1'R),(E)-**9b** (66% ee) was prepared by base catalyzed transesterification[14] of methyl N-benzoyl-C-phenylglycinate with (R)-(E)-4-phenyl-3-buten-2-ol.[15] Cyclization led to a mixture of diastereomers of (1'R)-**10b** with different configuration at C-2 of the oxazolinone ring, which on reductive cleavage after catalytic hydrogenation of the double bond afforded the ketone (R)-**6** ($[\alpha]_D^{20}$ = -18.2°). The value of the optical rotation is the same as in the case of the propargyl ester (1'R)-**1d'** and indicates a transfer of chirality without loss of optical information.

The corresponding ester (1'R),(Z)-**9b** was obtained by hydrogenation of (1'R)-**1d'** with Lindlar catalyst. Cyclization leads to formation of the diastereomeric (E)-oxazolinone (1'S)-**10b**, which was transformed into (S)-**6** as described before. The product exhibited an optical rotation $[\alpha]_D^{20}$ = +16.1°. The ketone (S)-**6** was derived in the same manner as (R)-**6** to give (2S,2'S),(E/Z)-**8**. A 77:23 ratio of diastereomers was found which corresponds to a 54% ee of (S)-**6**. The loss of optical purity may be due to a contamination of (1'R),(Z)-**9b** with (1'R),(E)-**9b**, the latter having been formed during the catalytic reduction of the triple bond.[16] Because the (Z)-isomer of **10** could not be detected within the limits of the ^{1}H NMR spectral analysis, a loss of stereospecificity during the aza-Cope rearrangement appears unlikely.

These results demonstrate the value of our method for the chain elongation of acids with transfer of chirality to the resulting ketones from the starting unsaturated alcohols. By changing the geometry of the double bond both enantiomers may be obtained from the same starting material.[17]

EXPERIMENTAL

Melting points were determined with a Büchi melting-point apparatus and are uncorrected. Infrared spectra were recorded on a Pye Unicam SP 1100 instrument and a Perkin Elmer 1420 spectrophotometer. The proton magnetic resonance spectra were recorded with Varian EM 390 and Bruker WM 400 instruments (solutions in deuteriochloroform, tetramethylsilane as internal reference). Optical rotations were measured with a Perkin Elmer 241 polarimeter. TLC separations were carried out on silica gel TLC plates Merck 60 F_{254}. Flash chromatography was carried out according to lit.[18] on Merck silica gel (article no. 9385). Organic solutions were dried over anhydrous magnesium sulphate and solvent evaporation was carried out at reduced pressure using a rotatory evaporator. Deoxygenation of reagents and solvents used for the Cr(II)-reduction was carried out on the evacuated solvents with ultrasound. Microanalyses were performed at the Institut für Organische Chemie und Biochemie der Universität Bonn and by Mikroanalytisches Labor Pascher, Bonn.

Materials

The propargyl N-(4-chlorobenzoyl)-C-phenylglycinates **1a-1c** were prepared by direct esterifica-

tion of N-(4-chlorobenzoyl)-C-phenylglycine with the corresponding alcohols in refluxing benzene using p-toluenesulfonic acid as a catalyst and a water separator (method A).

In the case of esters **1d-1f**, N-tert-butyloxycarbonyl-C-phenylglycine was esterified with the corresponding alcohols in dry dichloromethane using the DCC/DMAP procedure.[8] After removal of the protecting group with trifluoroacetic acid at 0°C the resulting trifluoroacetates were acylated in dry dichloromethane at 0°C with benzoyl chloride or 4-chlorobenzoyl chloride using two equivalents of triethylamine (method B). Yields, melting points and analytical data of compounds **1** are given in Table 2.

Table 2. Yields, melting points and analytical data of compounds **1**

No	method of preparation	yield [%]	mp [°C]	molecular formula		elemental analysis C	H	N
1a	A	85	120-122	$C_{18}H_{14}ClNO_3$ (327.8)	calcd	65.96	4.30	4.27
					found	66.43	4.28	4.35
1b	A	60	135-136	$C_{19}H_{16}ClNO_3$ (341.8)	calcd	66.76	4.72	4.10
					found	66.62	4.62	4.26
1c	A	76	141-142	$C_{24}H_{18}ClNO_3$ (403.9)	calcd	71.38	4.49	3.47
					found	71.33	4.39	3.48
1d	B	95[a]	73-130[b]	$C_{25}H_{20}ClNO_3$ (417.9)	calcd	71.85	4.82	3.35
					found	71.76	4.91	3.35
(1'R)-**1d'**	B	50	156-157[c]	$C_{25}H_{21}NO_3$ (383.5)	calcd	78.31	5.52	3.65
					found	78.36	5.56	3.76
1e	B	95[b]	85-126[b]	$C_{27}H_{24}ClNO_3$ (446.0)	calcd	72.71	5.41	3.14
					found	72.60	5.76	2.83
1f	B	95[a]	80-110[b]	$C_{28}H_{26}ClNO_3$ (460.0)	calcd	73.11	5.70	3.05
					found	73.20	5.66	2.79

a) Yield of the acylation step.

b) The crude products were oils. After treating with petrol ether 40/60 they solidified to give amorphous mixtures of the two diastereomers.

c) Recrystallized from acetonitrile.

(R)-4-Phenyl-3-butyn-2-ol was prepared from 4-phenyl-3-butyn-2-one according to lit.[5]: $[\alpha]_D^{20}$ = 51.5° (neat, corresponds to 66% ee).

(R),(E)-4-Phenyl-3-buten-2-ol was obtained from (R)-4-phenyl-3-butyn-2-ol by reduction with lithium aluminium hydride (1 eq.) in dry tetrahydrofuran under argon.[15]

The reference ketone (S)-1,4-diphenyl-2-methylbutan-1-one [(S)-**6**] was prepared according to lit.[10]: colourless oil, $[\alpha]_D$ = +26.0° (c = 1.00, EtOAc).

General procedure for the cyclization of N-acyl-C-phenylglycinates **1**, (Z)-**9** and (E)-**9**

Method A: To a cooled and stirred solution of ester **1** or **9** (2 mmol) and triethylamine (6.5 ml) in acetonitrile (6.5 ml) was added at 0°C a 5% solution of phosgene (commercial 20% solution in toluene diluted with acetonitrile). After 20-30 min (TLC control) the dark reaction mixture was evaporated, taken up in dichloromethane, extracted with 2% hydrochloric acid (50 ml) and stirred with a saturated aqueous solution of $NaHCO_3$ (50 ml) for 10-12 h at room temperature. Evaporation of the dried organic phase yielded the crude allenes **3** as dark oils which crystallized after addition of some methanol. The yields and physical data are summarized in Table 3.

Method B: To a solution of **9b** (3.9 g, 10 mmol), triphenylphosphine (3.93 g, 15 mmol) and triethylamine (4.8 ml, 33 mmol) in dry acetonitrile (30 ml) a solution of hexachloroethane (3.6 g,

15 mmol) in acetonitrile (30 ml) was added dropwise at 0°C under an argon atmosphere. The mixture was stirred overnight at 25°C. After evaporation of the solvent the dark oily residue was treated with dry tetrahydrofuran and the crystalline triethylamine hydrochloride was removed by filtration. Evaporation of the filtrate yielded an oily product which was purified by flash chromatography (eluent CCl_4/acetone 40:1).

Table 3. Physical, analytical and spectroscopic data of allenes 3

No	yield [%]	mp[a] [°C]	molecular formula	elemental analysis	C	H	N	IR (KBr) [cm^{-1}]	^1H NMR ($CDCl_3$)
3a	80	108-110	$C_{18}H_{12}ClNO_2$ (309.8)	calcd	69.80	3.91	4.52	1960, 1833, 1660	5.00-5.10 (m, 2H), 5.62 and 5.72 (t, J 7 Hz, total 1H), 7.21-8.17 (m, 9H).
				found	69.58	3.89	4.52		
3b	65	88-90	$C_{19}H_{14}ClNO_2$ (323.8)	calcd	70.48	4.36	4.33	1963, 1825, 1654	1.71 (t, J 5 Hz, 3H), 4.73-5.06 (m, 2H), 7.24-7.80 (m, 7H), 7.93-8.23 (m, 2H).
				found	70.40	4.41	4.39		
3c	50	129-130	$C_{24}H_{16}ClNO_2$ (385.9)	calcd	74.71	4.18	3.63	1945, 1840, 1660	5.13, 5.40 (AB-system, J 18 Hz, 2H), 7.10-7.67 (m, 12H), 7.90-8.13 (m, 2H).
				found	74.97	4.23	3.66		
3d	83	124-126	$C_{25}H_{18}ClNO_2$ (399.9)	calcd	75.09	4.54	3.50	1955, 1828, 1652	1.67, 1.90 (each d, J 7 Hz, total 3H), 5.50-5.83 (m, 1H), 7.03-7.63 (m, 12H), 7.97-8.17 (m, 2H).
				found	75.20	4.69	3.57		
(1'R)-3d'	56	131-136	$C_{25}H_{19}NO_2$ (365.4)	calcd	82.17	5.24	3.83	1950, 1822, 1652	1.67, 1.90 (each d, J 7 Hz, total 3H), 5.43-5.80 (m, 1H), 7.03-7.67 (m, 13H), 7.97-8.20 (m, 2H).
				found	81.99	5.36	3.88		
3e	60	98-102	$C_{27}H_{23}ClNO_2$ (427.9)	calcd	75.78	5.18	3.27	1843, 1656	0.97, 1.17 (each d, J 7 Hz, total 6H), 2.39 (heptet, J 7 Hz, 1H), 5.63, 5.76 (each d, J 7 Hz, 1H), 7.00-8.13 (m, 14H).
				found	75.87	5.28	3.36		
3f	53	95-102	$C_{28}H_{24}ClNO_2$ (442.0)	calcd	76.09	5.47	3.17	1957, 1842, 1655	1.00 (s, 6H), 1.18 (s, 3H), 5.56, 5.70 (each s, total 1H), 7.00-7.67 (m, 12H), 7.93-8.10 (m, 2H).
				found	76.20	5.52	3.26		

a) 3a and 3b were recrystallized from petroleum ether (40/60 and 60/90, respectively), 3c-3f from MeOH.

General procedure for the preparation of 2-propargyl-3-oxazolin-5-ones 4

A solution of 3 (2.5 mmol) in benzene or tetrachloromethane (25 ml) was heated under reflux (reaction times see Table 1). Because we were unable to find a TLC system for separating 3 and 4, the progress of the reaction had to be monitored by ^1H NMR. In the case of 3c, 3d and 3d' the solvent was evaporated after completion of the reaction. 3c could be recrystallized from methanol, whereas the other compounds gave oily mixtures of diastereomers (Table 1). The properties of compounds 4 are given in Table 4.

(2'R,4R/4S)-2-(4-chlorophenyl)-4-(3'-methyl-1'-phenylallenyl)-4-phenyl-2-oxazolin-5-one [(2'R)-3d']:

The compound was prepared in 40% yield from (1'R)-1d' by method A. The mixture of diastereomers showed $[\alpha]_D^{22}$ = +27.7 (c = 2, EtOAc). The ratio of the diastereomers was determined as 58.7:41.3 by HPLC using a Lichrosorb Si 60 column with CH_2Cl_2/CCl_4 (1:9) as eluent and UV-detection at 270 nm.

(1'R,2R/2S)-2-(4-chlorophenyl)-2-(1'-methyl-3'-phenyl-2'-propyn-1'-yl)-4-phenyl-3-oxazolin-5-one [(1'R)-4d']

The compound was obtained in quantitative yield by refluxing (2'R)-3d' in benzene for 8 h. Oil, $[\alpha]_D^{22}$ = +42.5° (c = 1.0, EtOAc). The ratio of diastereomers (57.8:42.2) was determined by HPLC as described with (2'R)-3d', but with CH_2Cl_2/CCl_4 (1:4) as eluent.

1'-Methyl-3'-phenyl-2'-propen-1'-yl (1'R,2R/2S)-(E)-N-benzoyl-C-phenylglycinate [(1'R),(E)-9b]

Methyl N-benzoyl-C-phenylglycinate (8.1 g, 30 mmol) and (R)-4-phenyl-3-buten-2-ol (35 mmol) were shaken in dry tetrahydrofuran (80 ml) with molecular sieve (60 g; Merck, 4 A, 2 mm) and 50 mg of an 80% sodium hydride suspension in paraffin-oil for 48 h. The reaction mixture was filtered and the filtrate was evaporated. The crude product was purified by flash-chromatography (eluent: CCl_4/acetone 30:1). White solid (6.25g, 54%); m.p. 108-115°C ($MeOH/H_2O$).- IR (KBr): 3325, 1746, 1642, 1530 cm^{-1}. - ^1H NMR: δ = 1.27 and 1.43 (each d, J 7 Hz, total 3H), 5.53 (pentet, J 7 Hz, 1H), 5.80 (d, J 8 Hz, 1H), 5.97-6.73 (m, 2H), 6.93-7.50 (m, 14H), 7.63-7.87 (m, 2H). - Anal. Calcd. for $C_{25}H_{23}NO_3$ (387.9): C, 78.04; H, 5.87; N, 3.61; Found: C, 77.87; H, 6.16; N, 3.95.

1'-Methyl-3'-phenyl-2'-propen-1'-yl (1'R,2R/2S)-(Z)-N-benzoyl-C-phenylglycinate [(1'R),(Z)-9b]

The ester (1'R)-1d' (2.31 g, 6 mmol) was hydrogenated with Lindlar catalyst (1.0 g, 5% Pd/$CaCO_3$ poisoned with lead, Aldrich) in ethyl acetate (100 ml). The reaction was stopped after the uptake of 165 ml (7.4 mmol) hydrogen. The mixture was filtered over celite and evaporated to yield a yellow oil (2.3 g, 95%), which was used for the next step without further purification. - IR (KBr): 1743, 1645, 1530 cm^{-1}. - ^1H NMR ($CDCl_3$): δ = 1.30 and 1.38 (each d, J 7 Hz, total 3H), 5.60-5.87 (m, 2H), 6.47 (d, J 11 Hz, 1H), 6.77-6.92 (m, 1H), 6.94-7.53 (m, 13H), 7.70-7.87 (m, 2H).

(1'S,2R/2S)-(E)-2,4-Diphenyl-2-(1'-methyl-3'phenyl-2'-propen-1'-yl)-3-oxazolin-5-one [(1'S)-10b]

Prepared from (1'S),(E)-9b by cyclization method A in 40% yield. Yellow oil, $[\alpha]_D^{20}$ = -36.2° (c = 1.11, EtOAc). - ^1H NMR: δ = 1.15 (d, J 7 Hz, 3H), 3.16 (pentet, J 7 Hz, 1H), 5.93 (dd, J 16 and 7 Hz, 1H), 6.34 (d, J 16 Hz, 1H), 7.07-7.67 (m, 13H), 8.30-8.47 (m, 2H).

(1'R,2R/2S)-(E)-2,4-Diphenyl-2-(1'-methyl-3'-phenyl-2'-propen-1'-yl)-3-oxazolin-5-one [(1'R)-10b]

Prepared by cyclization of (1'R),(Z)-9b (method B) in 45% yield. Yellow oil, $[\alpha]_D^{20}$ = +46.05° (c = 1.06, EtOAc). - IR (film): 1782, 1623, 1493, 1450, 1187 cm^{-1}. - ^1H NMR: same as for (1'S)-10b. - Anal. Calcd. for $C_{25}H_{21}NO_2$ (367.5): C, 81.72; H, 5.76; N, 3.81; Found: C, 82.08; H, 5.92; N, 3.99.

Table 4. Selected spectroscopic data of 3-oxazolin-5-ones 4

No	IR (film) [cm^{-1}]	^1H NMR ($CDCl_3$)
4b[a]	1825, 1654	4.73-5.06 (m, 2H), 2.95-3.10 (m, 2H).
4c	1780, 1628	3.30 (s, 2H), 7.00-7.67 (m, 12H), 8.30-8.47 (m, 2H).
4d	1790, 1625	1.27 (d, J 7 Hz, 3H), 3.51, 3.57 (each q, J 7 Hz, total 1H), 7.10-7.77 (m, 12 H), 8.33-8.53 (m, 2H).
(1'R)-4d'		1.30 (d, J 7 Hz, 3H), 3.57, 3.60 (each q, J 7 Hz, total 1H), 7.10-7.67 (m, 13 H), 8.30-8.53 (m, 2H).
4e[b]		3.55 (d, J 7 Hz).

a) In admixture with 3b; ratio 3b:4b = 70:30.
b) In admixture with 3e; ratio 3e:4e = 60:40.

General procedure for the hydrogenation of oxazolinones 4 and 10

The 3-oxazolinones (1'R)-4, (1'R)-10b or (1'S)-10b (3 mmol) were hydrogenated in ethyl acetate in the presence of a palladium catalyst (0.4 g, 10% Pd/C, Aldrich). After 3 h the catalyst was removed and the solvent was evaporated.

(1'R,2R/2S)-2,4-Diphenyl-2-(1'-methyl-3'-phenyl-1'-propyl)-3-oxazolin-5-one [(1'R)-5]

Yield 97% from (1'R)-4 or (1'R)-10b; colourless oil. - IR (film): 1780, 1622, 1493, 1450, 1187 cm^{-1}. - ^1H NMR: δ = 1.00 (d, J 7 Hz, 3H), 1.16- 2.90 (m, 5H), 6.93-7.67 (m, 13H), 8.30-8.58 (m, 2H). - Anal. Calcd. for $C_{25}H_{23}NO_2$ (369.5): C, 81.27; H, 6.27; N, 3.79; Found: C, 80.98; H, 6.30; N, 3.69.

(1'S,2R/2S)-2,4-Diphenyl-2-(1'-methyl-3'-phenyl-1'-propyl)-3-oxazolin-5-one [(1'S)-5]

Yield 94% from (1'S)-10b; colourless oil. - Spectroscopic data identical with those for (1'R)-5.

General procedure for the preparation of ketones 6

To a solution of (1'R)-5 or (1'S)-5 (2 mmol) and 50% hypophosphorous acid (20 mmol, oxygen-free) in dimethylformamide (20 ml, oxygen-free) chromium(II) acetate (10 mmol) was added under an argon atmosphere. After 1-2 min the colour of the reaction mixture changed from red to green and after 15 min the reaction was complete (TLC control). 2 N HCl (100 ml) was added and the mixture was shaken 5 times with ether. The combined ether phases were washed with water, dried and evaporated. The crude product was purified by flash chromatography (eluent: dichloromethane) or by distillation in a kugelrohr oven.

(R)-1,4-Diphenyl-2-methylbutan-1-one [(R)-6]

1) From (1'R)-5 [derived from (1'R)-4] in 94% yield. Colourless liquid, $[\alpha]_D^{22}$ = -18.2° (c = 1.10, EtOAc). - IR (film): 1685, 1535, 1452, 1225, 1198 cm^{-1}. - ^1H NMR: δ = 1.20 (d, J 7 Hz, 3H), 1.50-2.37 (m, 2H), 2.60 (t, J 8 Hz, 2H), 3.43 (heptet, J 8 Hz, 1H), 7.00-7.57 (m, 8H), 7.77-7.93 (m, 2H). - Anal. Calcd. for $C_{17}H_{18}O$ (238.3): C, 85.74; H, 7.61; Found: C, 85.67; H, 7.61.

2) From (1'R)-5 [derived from 10b] in 94% yield. $[\alpha]_D^{22}$ = -18.2° (c = 1.10, in EtOAc).

(S)-1,4-Diphenyl-2-methylbutan-1-one [(R)-6]

From (1'S)-5 in 50% yield; colourless liquid, b.p. 150°C/0.15 Torr, $[\alpha]_D^{22}$ = +16.1° (c = 1.15, EtOAc).

General procedure for the preparation of the (E/Z)-oximes 7

A solution of hydroxylamine hydrochloride (1 mmol), freshly distilled pyridine (1 mmol) and ketone 6 (0.5 mmol) in dry ethanol (20 ml) is refluxed for 12 h. The reaction mixture is evaporated and the residue is purified by filtration of its dichloromethane solution over silica gel.

(2R),(E/Z)-1,4-Diphenyl-2-methylbutan-1-one oxime [(2R),(E/Z)-7]

Yield 83%, colourless oil. - IR ($CHCl_3$): 3280, 3080, 3060, 3030, 3010, 2970, 2930, 1600, 1495, 1450, 700 cm^{-1}. - ^1H NMR: δ = 1.17, 1.28 (each d, J 7 Hz, total 3H), 1.43-2.30 (m, 2H), 2.43-2.87 (m, 2.5H), 3.47 (q, J 7 Hz, 0.5H), 6.93-7.53 (m, 10H), 9.20 (br.s, 1H). - Anal. Calcd. for $C_{17}H_{19}NO$ (253.4): C, 80.60; H, 7.56; N, 5.53; Found: C, 80.40; H, 7.83; N, 5.30.

(2S),(E/Z)-1,4-Diphenyl-2-methylbutan-1-one oxime [(2S),(E/Z)-7]

Yield 80%, colourless oil. - Spectroscopic data identical with those of the stereoisomer.

General procedure for the preparation of the O-acyloximes 8

The oximes 7 were acylated by the DCC/DMAP method as described in lit.[7]

(2R,2'S),(E/Z)-O-[2'-Methoxy-2'-(trifluoromethyl)phenylacetyl]-1,4-diphenyl-2-methylbutan-1-one oxime [(2R,2'S),(E/Z)-8]

Yield 82%, pale yellow oil. - IR ($CHCl_3$): 3065, 3040, 2980, 2950, 2850, 1750, 1490, 1450, 1445, 690 cm^{-1}. - ^1H NMR (400 MHz): δ = 1.10, 1.19, 1.23, 1.24 (each d, J 7 Hz, total 3H, integration ratio: d [δ = 1.10] : d [δ = 1.19] = 18:82), 1.64-2.02 (m, 2H), 2.36-2.81 (m, 2H), 2.93, 3.21 (each q, J 7 Hz), 3.25, 3.59 (each s; q and s total 4H), 6.90-7.63 (m, 15H). - Anal. Calcd. for $C_{27}H_{26}F_3NO_3$ (469.5): C, 69.07; H, 5.58; N, 2.98; Found: C, 68.98; H, 5.55; N, 3.02.

(2S,2'S),(E/Z)-O-[2'-Methoxy-2'-(trifluoromethyl)phenylacetyl]-1,4-diphenyl-2-methylbutan-1-one

oxime [(2S,2'S),(E/Z)-8]

Yield 86%, pale yellow oil. - The spectroscopic data were identical with those of the stereoisomer. - ^{1}H NMR (400 MHz): integration ratio of d [δ = 1.10] : d [δ = 1.19] = 77:23.

(2S,1'R)-(1'-Methyl-3'-phenyl-2'-propyn-1'-yl)-2-methoxy-2-(trifluoromethyl)phenylacetate

From (R)-4-phenyl-3-butyn-2-ol and (-)-2-methoxy-2-(trifluoromethyl)phenylacetic acid by the DCC/DMAP method[7] (reaction time: 15 h). Yield 95%, colourless oil. - IR ($CHCl_3$): 3620, 3020, 2400, 1750 cm^{-1}. - ^{1}H NMR (400 MHz): δ = 1.61, 1.67 (each d, J 7 Hz, total 3H; integration ratio: d [δ = 1.61] : d [δ = 1.67] = 17:83), 3.57 (s, 3H), 5.87, 5.89 (each q, J 7 Hz, total 1H), 7.28-7.45 (m, 8H), 7.53-7.62 (m, 2H). - Anal. Calcd. for $C_{20}H_{17}F_3O_3$ (362.4): C, 66.30; H, 4.73; Found: C, 66.25; H, 4.73.

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