Applications of the Chiral Auxiliaries DIOZ and TRIOZ for Conjugate Additions and Comparison with Other Auxiliaries

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and

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A number of *N*-acryloyl-, *N*-crotonoyl-, *N*-(3,3,3-trifluorocrotonoyl)-, *N*-cinnamoyl-, and *N*-(3-nitroacryloyl)-4-isopropyl- or -4-phenyl-oxazolidin-2-ones with *geminal* diphenyl substitution, *i.e.*, **7**–**15**, have been prepared and used for conjugate additions of organocuprate reagents (Me, ^{i}Pr, Ph, 4-MeOPh) in the β-carbonyl (*Table 2*) and in the α-carbonyl position (NO_2-derivative **11** in *Scheme 3*). The yields and diastereoselectivities are compared with previously tested enoyl-oxazolidinones (*Table 2*). Highest diastereoselectivities (> 90%) are always observed with the 4-Ph derivatives (*Hruby* effect). Nitro-acryloyl-oxazolidinones and a corresponding phenylmenthol ester undergo less diastereoselective additions (*Scheme 3*). A 3-(1-methylethyl)-5,5-diphenyloxazolidin-2-one (DIOZ)-derived Li_2-enolate-nitronate was also tested for α-carbonyl alkylation (*Scheme 4*). The X-ray crystal structures of three acryloyl-oxazolidinones and of four adducts are described (*Tables 1* and *3*), and they serve for configurational assignments and description of the stereochemical courses of the additions and alkylation. Possible applications of the nitro compounds for the preparation of β^2-amino acids are discussed (*Scheme 2*).

1. Introduction. – Overall enantioselective *Michael* additions using a chiral auxiliary group (now rivaled by organocatalytic methods [1]) have been achieved by acylating chiral heterocycles with an α,β-unsaturated carboxylic acid derivative, performing a diastereoselective conjugate addition and cleaving off the auxiliary (preferably with

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[1]) Bachelor Theses of *H. S.* (2006), *S. P.* (2007), and *M. M.* (2008), Zürcher Hochschule für Angewandte Wissenschaften (ZHAW); the experimental work was carried out in the Laboratorium für Organische Chemie of ETH-Zürich in all three cases.

[2]) New address: Ecole d'Ingénieurs et d'Architectes de Fribourg, Département des Technologies Industrielles, Filière de Chimie, Bd de Pérolles 80, CH-1705 Fribourg (phone: +41-26-4296703; fax: +41-26-4296600; e-mail: roger.marti@hefr.ch).

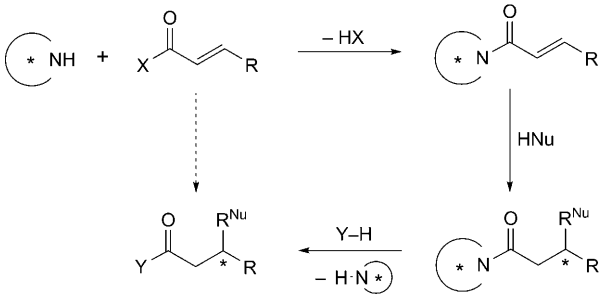
[3]) Part of the Ph.D. Thesis of *C. G.*, ETH-Zürich Dissertation No. 14516, 2002.

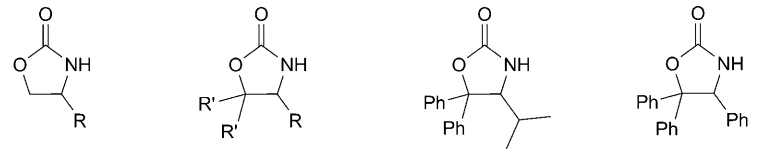
[4]) Postdoctoral co-worker at ETH-Zürich (2008/09), financed by *Swiss National Science Foundation* (SNF-Project No. 200020-117586). We thank *Novartis AG* for continuing financial support.

[5]) Postdoctoral co-worker at ETH-Zürich (2002), we thank *Novartis AG* for financial support.

recovery!) (*Scheme 1*). The most commonly used auxiliaries are the oxazolidinones popularized by *D. Evans* [2]. It turned out that, as compared to the simple valine- or phenylalanine-derived oxazolidinones **1**, the geminally disubstituted derivatives **2** [3] and **3** [4][6]) have certain general advantages (amply discussed in the literature [3–5]). In the *Michael* addition outlined in *Scheme 1*, it turned out that the phenylglycine-derived auxiliaries **1** and **2**, R = Ph, give highest diastereoselectivities (R^{Nu}MgBr/CuBr as nucleophiles) [3a][6][7]); the 4,5,5-triphenyloxazolidin-2-one (**4**; TRIOZ) had, so far, not been used for this purpose.

Scheme 1. *Principle of Enantioselective* Michael *Additions Using a Chiral Auxiliary Group*





(*R*)- or (*S*)-**1** (*Evans* auxiliaries) (*R*)- or (*S*)-**2** (SuperQuats) (*R*)- or (*S*)-**3** (DIOZ) (*R*)- or (*S*)-**4** (TRIOZ)

2. Preparation of the Starting Materials. – We have now prepared a number of oxazolidinone derivatives **5**–**15** and the phenylmenthol derivative **16** of α,β-unsaturated carboxylic acids, to test and compare the reactivities and diastereoselectivities in *Michael* additions to their enoylic (*i.e.*, **5**, **7**–**10**, and **12**–**15**) or nitroolefinic (*i.e.*, **6** and **11**) C=C bonds.

The substrates **5**–**16** for conjugate additions were prepared according to known procedures: the *classical Evans*-type acryloyl-oxazolidinone **5** [2b][7] was nitrated

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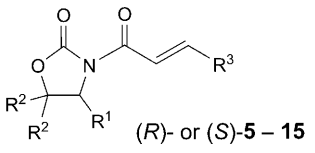
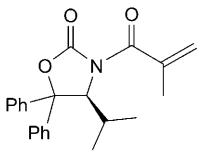
[6]) Besides our group [4], the groups of *Gibson et al.* [5b], and *Davies* and wo-workers [3b] have also tested auxiliary **3**. In two papers and in a patent, the preparation of **3** has been described previously [3g][5]. The term DIOZ (=3-(1-methylethyl)-5,5-diphenyloxazolidin-2-one) for compound **3** was first used in an advertisement of the *Shiratori Pharmaceutical Company*, which offered both enantiomers for sale.

[7]) A *SciFinder* search for *N*-enoyl-4-phenyloxazolidinone **1** (R = Ph) produced 200 references, 28 alone by *Hruby* and co-workers, who had first reported the superiority of this auxiliary for *Michael* additions [6].

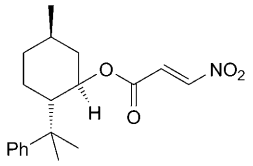


(*R*)- or (*S*)-**5** – **15**

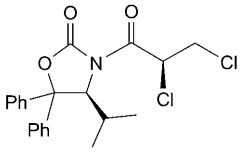


8b

	5	**6**	**7**	**8a**	**9**	**10**	**11**	**12**	**13**	**14**	**15**
R^1	Bn	Bn	^{i}Pr	^{i}Pr	^{i}Pr	^{i}Pr	^{i}Pr	Ph	Ph	Ph	Ph
R^2	H	H	Ph	Ph	Ph	Ph	Ph	Ph	Ph	Ph	Ph
R^3	H	NO_2	H	Me	Ph	4-MeO-C_6H_4	NO_2	H	Me	CF_3	Ph



16



17

(→**6**) by addition of NO_2Cl to the C=C bond, followed by HCl elimination with AcONa as base [8]. With a similar procedure[8]) acryloyl-DIOZ **7** gave nitro compound **11** (for crystal structure, see *Table 1*). The enoyl-oxazolidinones **7**–**10** and **12**–**15** were prepared[9]) from the corresponding parent heterocycles **3** (DIOZ) or **4** (TRIOZ), and enoyl-chlorides or anhydrides, as described in the literature [4a] and in the *Exper. Part*. The phenylmenthol-derived[10]) nitro-acrylate **16** was obtained according to a published procedure [9]. X-Ray crystal structures of the acryloyl-oxazolidinones **5**, **11**, and **12**, are shown in *Table 1*. As in numerous published structures of other 3-acyl-oxazolidinones and as in the product structures, also listed in *Table 1*, the exocyclic N–CO bond has s-*trans* configuration, with OC(2)–N–C(1′)=O torsion angles close to 180°.

3. Conjugate Additions to the Cinnamoyl- and Crotonoyl-Oxazolidinones 8–10, 13–15. – All reactions were carried out with excess organocuprates as nucleophiles, generated from *Grignard* reagents MeMgBr, PhMgBr, or 4-MeOPhMgBr and CuBr·SMe_2 (ratio 2:1)[11]). In *Table 2*, the yields and diastereoselectivities are listed, together with values reported in the literature for analogous additions to enoyl-oxazolidinones (*Entries 1–7*) other than DIOZ and TRIOZ derivatives (*Entries 8–17*). With the

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[8]) We did not succeed in preparing the corresponding nitro-acryloyl-TRIOZ from acryloyl-TRIOZ **12**.

[9]) Compound **7** was first prepared (59% yield) by *Meinrad Brenner* (ETH-Zürich Dissertation No. 14409, 2001), using the anhydride method. Most acrylations were carried out by first treating DIOZ or TRIOZ, with BuLi or MeMgBr, and then with the corresponding acid chloride.

[10]) Phenylmenthol was introduced as a chiral auxiliary by *Corey* and *Ensley* [9a].

[11]) The copper trick for directing *Grignard* reagents from the 1,2- to the 1,4-mode of addition to α,β-unsaturated carbonyl compounds was introduced by *Kharash* and *Tawney* [10a]. For leading references to the use of CuBr·SMe_2, see [10b].

Table 1. *X-Ray Crystal Structures of Starting Materials* **5**, **11**, *and* **12** *of the Dichloro Derivative* **17**, *and of the Products* **19**, **24a**, **24c**, *and* **25c**. For crystal data, see *Table 3* in the *Exper. Part*.

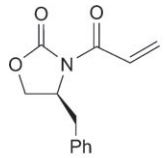
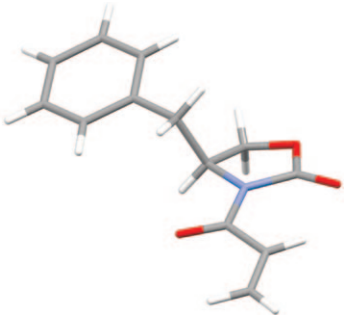
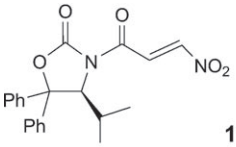
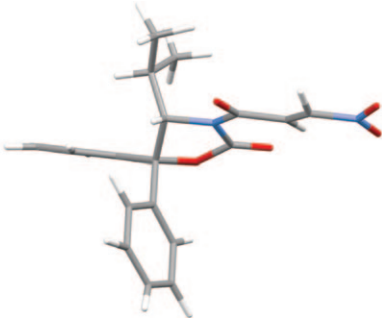
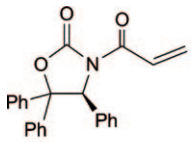
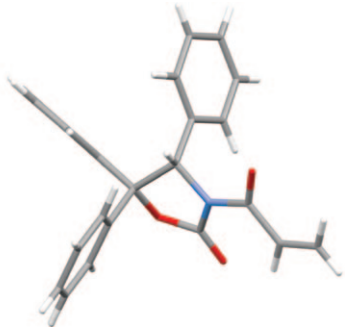
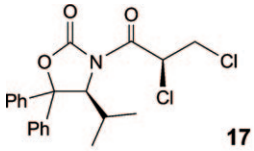
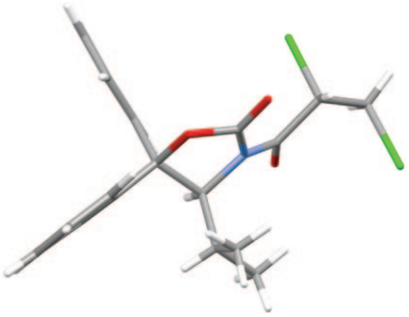
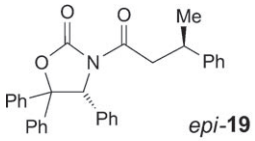
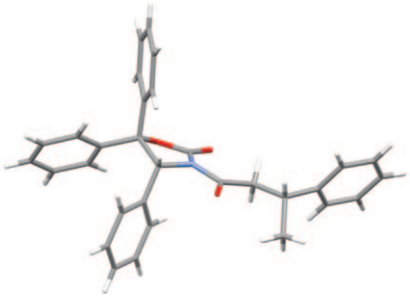
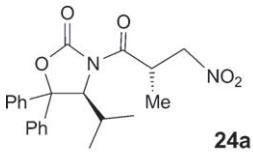
 **5**	
 **11**	
 **12**	
 **17**	

Table 1 (cont.)

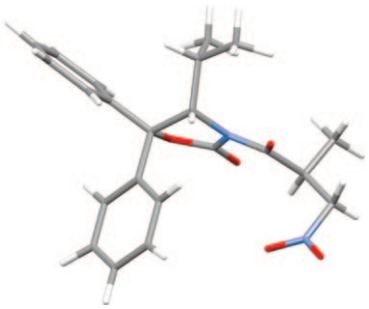


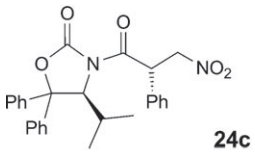
epi-**19**



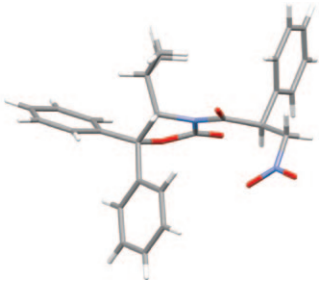


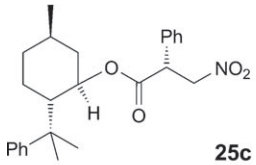
24a





24c





25c

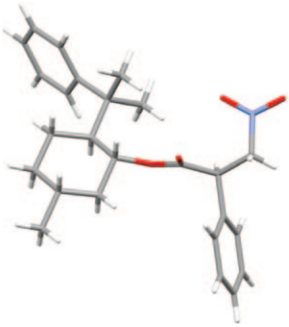
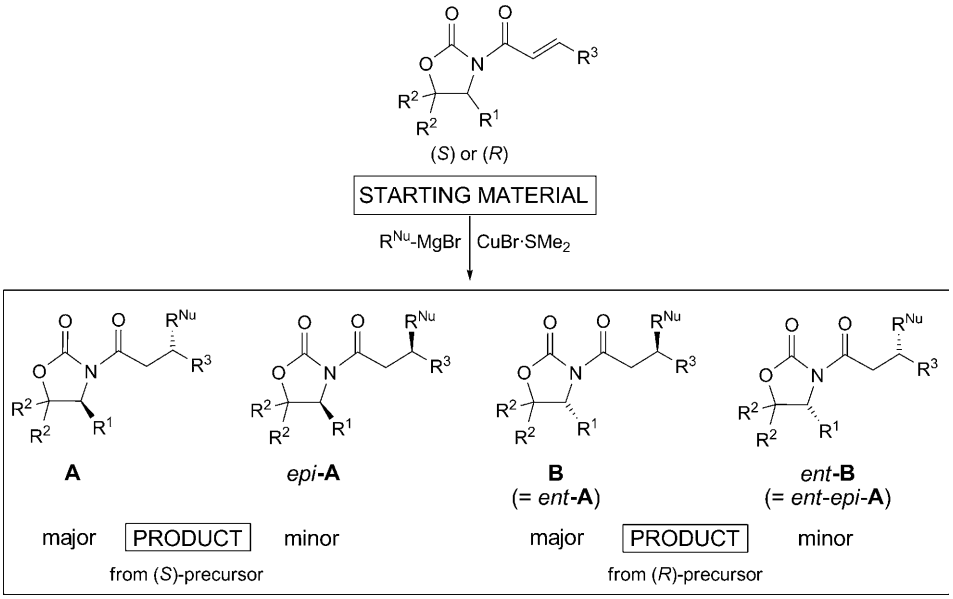


Table 2. *Examples of Diastereoselective Conjugate Additions of* Grignard *Reagents/CuBr·SMe$_2$ to 3-Enoyl-4-benzyl-, -4-isopropyl-, and -4-phenyl-Substituted Oxazolidinones from the Literature* (*Entries 3–9*) *and from the Present Investigation* (*Entries 1*, *2*, and *10–17*). Some of the data (*Entries 1*, *2*, and *11*) are taken from [11], with no experimental details given herein. In all cases, the solution of the *Michael* acceptor was added to the organometallic reagent at low temperatures (– 30° in THF). For the X-ray crystal structure of *epi*-**19**, see *Table 1*. All diastereoisomer ratios **A**/*epi*-**A** and **B**/*epi*-**B** were determined by NMR peak integrations with the crude products. The yields are total yields of major and minor products of type **A** or **B**. In most cases, recrystallization led to diastereoisomerically pure samples of the major isomer (see *Exper. Part*).



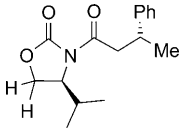
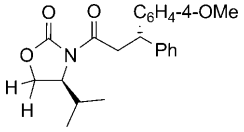
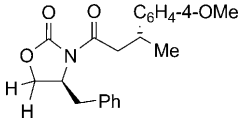
Entry	Starting material	Product				
		Major	No.	Yield [%]	Ratio **A**/*epi*-**A** **B**/*epi*-**B**	Ref.
1					65 : 35	[11]
2					66 : 34	[11]
3				85	55 : 45	[6]

Table 2 (cont.)

Entry	Starting material	Product				
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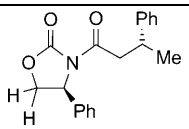
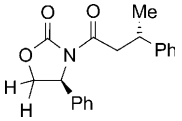
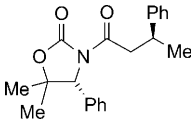
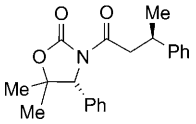
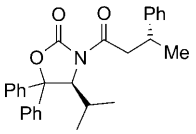
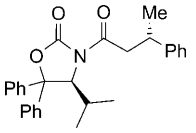
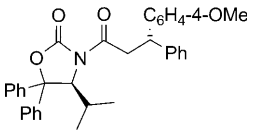
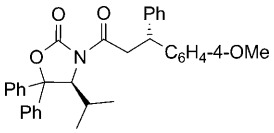
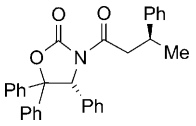
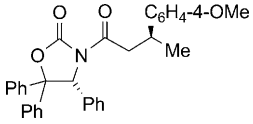
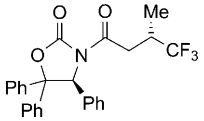
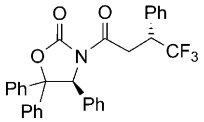
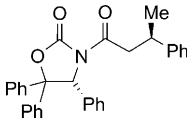
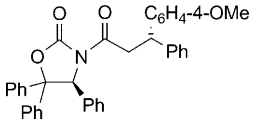
4				90	99 : 1	[6]
5				90	74 : 26	[6]
6				67	97 : 3	[3a]
7				87	96 : 4	[3a]
8	(*S*)-**8**			86 92	67 : 33 70 : 30	[4a] [11]
9	(*S*)-**9**			90	67 : 33	[4a]
10	(*S*)-**9**		**18**	88	85 : 15	this work
11	(*S*)-**10**		*epi*-**18**	78	82 : 18	this work
12	(*R*)-**13**		**19**	53 71	98 : 2 96 : 4	[11] this work

Table 2 (cont.)

Entry	Starting material	Product				
		Major	No.	Yield [%]	Ratio **A**/*epi*-**A** **B**/*epi*-**B**	Ref.
13	(*R*)-**13**		**20**	74	91 : 9	this work
14	(*S*)-**14**		**21**	55	61 : 39	this work
15	(*S*)-**14**		**22**	60	69 : 31	this work
16	(*R*)-**15**		*epi*-**19**	71 68	93 : 7 96 : 4	[11] this work
17	(*S*)-**15**		**23**	64	97 : 3	this work

exception of the CF_3-substituted acceptors (*Entries 14* and *15*), the diastereoselectivities of addition to 3-enoyl-4-phenyl-oxazolidinones are above 90%; with ^{i}Pr groups in the 4-position, the selectivities tend to be near 2 : 1 (*Entries 8* and *9*) or 4 : 1 (*Entries 10* and *11*); the yields are moderate to excellent; the configurations of the major products as shown in **A** and **B** (*Table 2*) are assigned by analogy with literature assignments, and in one case (*epi*-**19**, *Entry 16* of *Table 2*) by X-ray-structure analysis (see *Table 1*)[12]).

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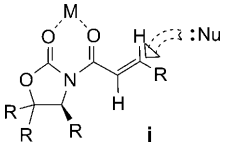
[12]) This is compatible with the assumption that a metal complex of the enoyl-oxazolidinone of s-*cis*-configuration around the exocyclic N–CO bond [2] is approached by the nucleophile from the face of the trigonal β-carbonyl C-atom that is remote from the R group at C(4) of the heterocycle, as shown here for an (*S*)-oxazolidinone derivative (see **i**).

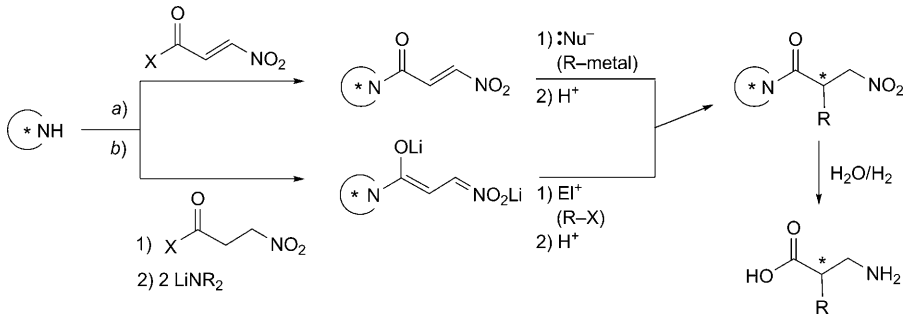


i

In view of the fact that the TRIOZ derivatives (*Entries 12–17* of *Table 2*) do not seem to perform better than simpler 3-enoyl-4-phenyl-oxazolidinones (*Entries 4–7*), the advantage of using TRIOZ as an auxiliary for overall enantioselective conjugate additions (*Scheme 1*) remains to be the high crystallization tendency of its derivatives and the facile removal of this auxiliary group (similar to that of DIOZ [4a,e]).

4. Experiments with the NO_2 Derivatives 11, 16, and 26. – In our pursuit of new routes to β^2-amino acids [4h], we have now employed *N*-(nitropropenyl)- and *N*-(nitropropanoyl)-oxazolidinones in two processes, which are related by *umpolung* [12] (*Scheme 2*): with respect to the C=O group, conjugate addition of a nucleophile to a 3-nitroacrylate system, where $C{=}C{-}NO_2$ is a much stronger *Michael* acceptor than C=C−COR, constitutes an *umpolung* (nucleophilic attack occurs in the *α-carbonyl*, rather than in the *β-carbonyl position*; see *Route a* in *Scheme 2*). On the other hand, a doubly deprotonated nitropropanoate system is attacked by *electrophiles* in *β*-position to the N-atom (an enolate is more reactive than a nitronate; see *Route b* in *Scheme 2*) [13].

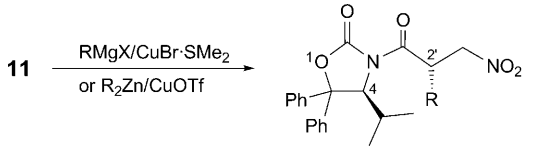
Scheme 2. *Two Possible Routes with Chiral Auxiliaries to β^2-Amino Acids. a*) *Michael* addition in *α*-carbonyl position of a nitroacryloyl derivative. *b*) Alkylation of a doubly deprotonated 3-nitropropanoyl derivative. Both processes lead to *α*-substituted *β*-nitropropanoic acid derivatives, hydrogenation of which will produce β^2-amino acids.



Removal of the auxiliary from the 'common' product and hydrogenation of the NO_2 group will lead to β^2-amino acid derivatives of the same general type, but with the R group stemming from a nucleophilic reagent (R-metal) in the first case (*Route a*) and from an electrophlic reagent (R−X) in the second case (*Route b*). Thus, the two transformations *a* and *b* are an *umpolung* of each other.

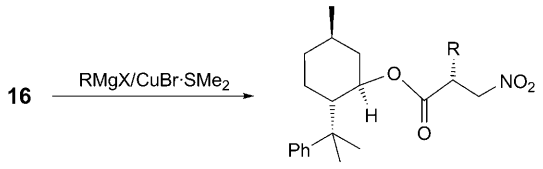
The results of addition of organomagnesium and organozinc reagents (in the presence of Cu^I salts) to nitroacryloyl derivatives **11** and **16** are shown in *Scheme 3*. The yields are generally modest, and so are the diastereoselectivities. In most cases, pure samples were prepared by flash chromatography and/or recrystallization. The configurations of two adducts, *i.e.*, **24a** and **24c**, to the nitroacryloyl-oxazolidinone **11** and of one of the adducts, **25c**, to the nitroacrylate ester **16** were determined by X-ray crystal-

Scheme 3. *Conjugate Addition of Mg/Cu and Zn/Cu Reagents to* N-*3-(Nitroacryloyl)-DIOZ* **11** *and to the 3-Nitroacrylate Ester* **16** *of Phenylmenthol.* All reactions were carried out in THF at dry-ice temperature, by adding a soln. of the nitro compound to the organometallic reagent. The yields of **24a**–**24c** and **25c** refer to materials obtained after recrystallization. The yields of **25a** and **25b** are those obtained after flash chromatography. The dr values were determined by NMR spectroscopy of the crude products. For X-ray-crystal structures of **24c** and **25c**, see *Table 1*.



24a–24c + 2'-*epi*-**24a–24c**

	R	Yield [%]	**24**/*epi*-**24**
24a	Me (RMgBr)	40	65:35
24b	^{i}Pr (RMgCl)	40	80:20
24b	^{i}Pr (R_2Zn)	40	25:75
24c	Ph (RMgBr)	55	95:5



25a–25c + *epi*-**25a–25c**

	R	Yield [%]	**25**/*epi*-**25**
25a	Me	36	78:22
25b	^{i}Pr	73	51:49
25c	Ph	42	80:20

structure analysis (*Table 1*); the configurations of the three major products **24b**, and **25a** and **25b** are assigned by analogy[13])[14]).

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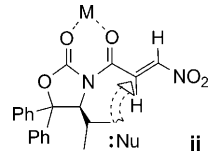
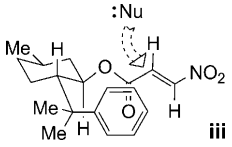
[13]) As in the case of 'normal' conjugate additions to 3-enoyl-oxazolidinones (*Table 2* and *Footnote 12*), the stereochemical course of reaction is compatible with the assumption that the R group of the organometallic reagent is preferentially transferred from the face opposite to the ^{i}Pr group at C(4) of a metal complex with s-*cis*-configuration around the exocyclic N–CO bond (see **ii**). The reversal observed with the Zn reagent (→ mainly *epi*-**24b**) may be taken as an indication that there is no metal chelation in this case, *i.e.*, the acylated oxazolidinone reacts in its preferred 'dipol-minimized' s-*trans* configuration [2] with an *anti*-arrangement of the 2 C=O groups (*cf.* the crystal structures in *Table 1* and the discussion in *Sect. 2*, above).



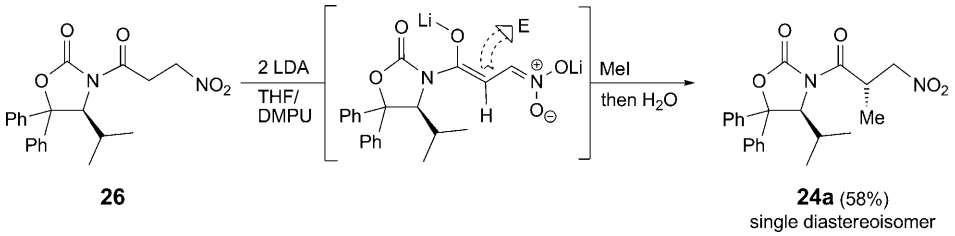
ii

[14]) The stereochemical course of reactions of phenylmenthol derivatives is commonly explained by assuming steric hindrance of a π-face by the neighboring Ph group ('π-stacking'; see textbooks of stereochemistry, *e.g.*, [14]). This is in agreement with the assigned configuration of our major diastereoisomers **25a**–**c** (see **iii**).



iii

Scheme 4. *Methylation of the Li_2-Enolate/Nitronate of* N-*(3-Nitropropanoyl)-DIOZ* **26** *with MeI*



26 **24a** (58%)
single diastereoisomer

Finally, we have prepared the *N*-(nitropropanoyl)-DIOZ **26**, which was methylated through a dilithio derivative to give product **24a** (*Scheme 4*), identical with the sample obtained by methylcuprate addition to the nitroacryloyl-DIOZ **11** (*cf. Scheme 3*)[15]). Other, less reactive alkylating reagents, such as BnBr, gave only traces of desired product. This may not be surprising, in view of the previously observed [3b][4a] rather poor yields of Li-enolate alkylations using 5,5-diphenyl-substituted oxazolidinone derivatives[16]). Further experiments with other auxiliaries are in progress, in the hope that this attractive general approach to β^2-amino acid[17]) precursors may eventually become general and practical.

5. Conclusions. – The triphenyl-oxazolidinone auxiliary TRIOZ has turned out to give higher diastereoselectivities in conjugate additions, and the nitroacryloyl-DIOZ may be used for diastereoselective preparations of β^2-amino acid precursors. The yields and selectivities observed with the DIOZ and TRIOZ derivatives are not better than those reported for analogous auxiliaries, including phenylmenthol, so that the main

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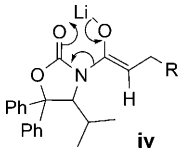
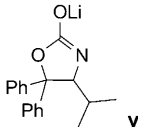
[15]) As indicated by the drawing of the intermediate dilithio-derivative in *Scheme 4*, the configuration of the product **24a** (safely assigned by X-ray analysis; see *Table 1*) is, again (*cf. Footnotes 12–14*), compatible with a metal-chelated structure; the stereochemical course of the reaction follows the general rules for reactions of *Evans* Li-enolates with electrophiles [2].

[16]) This is caused by the instability of the Li-enolates of this type with respect to Li-oxazolidinone elimination **iv** → **v** (recovery and *N*-alkylation of DIOZ!), a process, which does not occur with the corresponding Ti-enolates [4] (and which is less pronounced, with the analogous 5,5-dimethyl-substituted oxazolidinone derivatives [3b]).

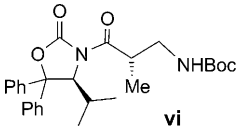


iv



v

[17]) In a preliminary experiment, reduction of **24a** with *Raney*-Ni in the presence of Boc_2O gave the DIOZ-derivative **vi** of β^2hAla in 75% yield. The analytical data were in agreement with those reported in [4a].



vi

advantage is the high crystallinity of all products, combined with the milder removal of the auxiliary groups, which has previously been demonstrated in other DIOZ applications [4]. In the preliminary experiment with a DIOZ Li_2-enolate-nitronate, another new route to β^2-amino acid precursors has been outlined, for which, however, a better auxiliary will have to be identified. With a single exception (Zn/Cu reagent → *epi*-**24b**), the stereochemical courses of all reactions are compatible with metal-chelated oxazolidinone derivatives as reactive intermediates.

The contribution to this work by *P. Kälin* and *M. Schneider* (Elementary Analyses unit of Laboratorium für Organische Chemie), *R. Häfliger*, *L. Bertschi*, and *O. Greter* (MS Service), and Dr. *W. B. Schweizer* and *M. Solar* (X-Ray Service unit of Laboratorium für Organische Chemie) are gratefully acknowledged.

Experimental Part

1. *General*. All reactions were performed under Ar in dried glassware using anh. solvents except when using aq. reagents. All chemicals were of reagent grade and used as supplied, unless stated otherwise. Solvents for extractions and chromatography were of technical grade and were distilled prior to use. Sat. hydrocarbon solvents were kept over Na wire. Extracts were dried over $MgSO_4$. Anal. TLC: pre-coated *Merck* silica gel *60 F254* plates (0.25 mm). Flash column chromatography (FC): *Fluka* silica gel *60* (230–400 mesh). Melting points (M.p.): *Büchi 510* melting point apparatus; uncorrected. Optical rotations ($[\alpha]_D^{20}$): *Jasco P-2000 Polarimeter*. IR Spectra: neat solid/oil on a *Perkin-Elmer precisely Universal ATR Sampling Accessory*; in cm^{-1}. ^{1}H-, ^{13}C-, and ^{19}F-NMR spectra: *Bruker AVANCE* (^{1}H: 300 MHz, ^{13}C: 75 MHz), *DRX* (^{1}H: 400 MHz, ^{13}C: 101 MHz), and *AV* (^{1}H: 400 MHz, ^{13}C: 101 MHz) spectrometer, or *Varian Gemini-300* XL (^{1}H: 300 MHz, ^{19}F: 282 MHz, ^{13}C: 75 MHz) spectrometer; chemical shifts (δ) in ppm relative to Me_4Si (0.00 ppm). MS: *VG Tribrid* (EI), *IonSpecUltima 4.7-T-FT Ion Cyclotron Resonance* (ICR; HR-MALDI; in 2,5-dihydroxybenzoic acid matrix) mass spectrometer. Elemental analyses were performed by the Microanalytical Laboratorium at the Laboratory for Organic Chemistry, ETH Zürich.

2. *Preparation of the Starting Materials. (*S*)-3-[(*E*)-3-Nitroprop-2-enoyl]-4-(phenylmethyl)oxazolidin-2-one* ((*S*)-**6**). Compound (*S*)-**5** [2b] (1.15 g, 5.0 mmol) was suspended in Et_2O (25 ml) and cooled to 0°. In a separate flask, to ice-cooled 100% HNO_3 (1.26 ml, 30 mmol) was added during 10 min $ClSO_3H$ (1.0 ml, 15 mmol, 3 equiv.), immediately NO_2Cl was formed, which was transferred by a slow stream of N_2 into the reaction mixture. After 1 h, additional $ClSO_3H$ (1.0 ml, 15 mmol, 3 equiv.) was added to the HNO_3, and the NO_2Cl was transferred into the reaction mixture. The resulting yellow soln. was stirred for an additional 1 h at r.t., and then the reaction was quenched by the addition of H_2O (20 ml). The mixture was extracted with Et_2O. The org. layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The crude product (1.54 g) was dissolved in Et_2O (35 ml) and treated with AcONa (410 mg, 5 mmol) and a trace hydrochinone. The mixture was heated for 5 h under reflux. After cooling to r.t., the mixture was filtered and then concentrated under reduced pressure. The residual oil was dissolved in AcOEt (5 ml) and treated with hexane (13 ml), and the precipitated (*S*)-**6** was filtered off (130 mg). The mother liquid was concentrated under reduced pressure, and by FC (toluene) additional product was isolated to give overall (*S*)-**6** (260 mg, 20%). Yellow crystals. M.p. 144–150°. $[\alpha]_D^{20} = +77.2$ ($c = 0.88$, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 3011*w*, 1788*s*, 1692*s*, 1542*s*, 1385*s*, 1351*s*, 1113*m*, 1050*m*, 1001*m*, 950*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 2.85 (*dd*, $J = 13.5$, 9.5, 1 H, $PhCH_2$); 3.35 (*dd*, $J =$ 13.5, 3.4, 1 H, $PhCH_2$); 4.26–4.35 (*m*, CH_2O); 4.74–4.80 (*m*, CHN); 7.2–7.38 (*m*, 10 arom. H); 7.77 (*d*, $J = 13.3$, =CH); 8.47 (*d*, $J = 13.2$, =CH). ^{13}C-NMR (100 MHz, $CDCl_3$): 37.5 (CH_2); 55.4 (CH); 66.8 (CH_2); 126.9, 127.7, 129.2, 129.4 (CH); 134.4 (C); 149.1 (CH); 152.8, 161.2 (C). MS (EI): 276 (1, M^+), 230 (13), 158 (5), 100 (9), 91 (100). Anal. calc. for $C_{13}H_{12}N_2O_5$ (276.25): C 56.52, H 4.38, N 10.14; found: C 56.43, H 4.53, N 9.97.

*(*S*)-4-(1-Methylethyl)-5,5-diphenyl-3-[(*E*)-prop-2-enoyl]oxazolidin-2-one* ((*S*)-**7**). To an ice-cold suspension of (*S*)-**3** (2.81 g; 10.0 mmol) in THF (40 ml) was added a soln. of MeMgBr (3.5 ml, 10.5 mmol,

3M in Et_2O) during 10 min. At the end of the addition, the deprotonated DIOZ precipitated. The resulting white suspension was stirred for an additional 30 min at 0° and then cooled to −70°. Within 5 min, acroyl chloride (1 ml, 10.5 mmol) was added, and the mixture was allowed to warm to r.t. overnight. The reaction was quenched with sat. aq. NH_4Cl soln. (10 ml), and the mixture was extracted with Et_2O. The org. layer was washed with sat. aq. NH_4Cl soln., dried ($MgSO_4$), and concentrated under reduced pressure. The residue was triturated with hexane (30 ml) to yield (*S*)-**7** (3.24 g, 90%). Colorless solid. R_f (hexane/AcOEt 2:1) 0.7. M.p. 146°. $[\alpha]_D^{20} = -232$ ($c = 1.00$, CH_2Cl_2). IR ($CHCl_3$): 3011*w*, 2969*w*, 1779*s*, 1689*m*, 1619*w*, 1494*w*, 1450*w*, 1408*m*, 1364*m*, 1322*m*, 1151*w*, 1120*w*, 1050*w*, 1002*m*, 984*w*, 958*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.78 (*d*, $J = 6.8$, Me); 0.90 (*d*, $J = 7.0$, Me); 1.96–2.04 (*m*, MeC*H*); 5.46 (*d*, $J = 3.4$, CHN); 5.85 (*dd*, $J = 10.5, 1.8$, 1 H, CH_2); 6.50 (*dd*, $J = 17.0, 1.8$, 1 H, CH_2); 7.25–7.49 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.4, 21.8 (Me); 30.1, 65.5 (CH); 89.5 (C); 125.7, 126.0, 127.1, 128.0, 128.4, 128.6, 128.9 (CH); 131.9 (CH_2); 138.2, 142.2, 152.9, 164.8 (C). MS (EI): 335 (2, M^+), 292 (13), 291 (9), 237 (11), 220 (10), 195 (36), 194 (26), 184 (12), 183 (8), 167 (19), 166 (12), 165 (26), 109 (19), 105 (22), 77 (13), 55 (100), 41 (9). Anal. calc. for $C_{21}H_{21}NO_3$ (335.40): C 75.20, H 6.31, N 4.18; found: C 75.28, H 6.41, N 4.20.

*(*S*)-4-(1-Methylethyl)-3-[(*E*)-1-oxobut-2-enyl]-5,5-diphenyloxazolidin-2-one* ((*S*)-**8a**). Starting from (*S*)-**3**, (*S*)-**8a** was prepared as described in [4a]. Yield and anal. data were in agreement with those reported in [4a].

*(*S*)-4-(1-Methylethyl)-3-(2-methylprop-2-enoyl)-5,5-diphenyloxazolidin-2-one* ((*S*)-**8b**). To an ice-cold suspension of (*S*)-**3** (0.4 g, 1.42 mmol) in THF (5 ml) was added a soln. of MeMgBr (0.5 ml, 1.5 mmol, 3M in Et_2O) during 10 min. At the end of the addition, the deprotonated DIOZ precipitated. The resulting white suspension was stirred for an additional 30 min at 0° and then cooled to −70°. Within 5 min, methacroyl chloride (0.34 ml, 3.55 mmol) was added, and the reaction mixture was allowed to warm to r.t. overnight. The reaction was quenched with sat. aq. NH_4Cl soln. (10 ml), and the mixture was extracted with Et_2O. The org. layer was washed with sat. aq. NH_4Cl soln., dried ($MgSO_4$), and concentrated under reduced pressure. FC (pentane/Et_2O 9:1) yielded (*S*)-**8b** (0.42 g, 85%). Colorless solid. R_f (pentane/Et_2O 2:1) 0.8. M.p. 111–113°. $[\alpha]_D^{20} = -181.1$ ($c = 0.5$, $CHCl_3$). IR ($CHCl_3$): 2968*w*, 1789*s*, 1686*m*, 1494*w*, 1450*m*, 1365*w*, 1324*m*, 1176*m*, 1001*w*, 918*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.80 (*d*, $J = 6.5$, Me); 0.92 (*d*, $J = 6.85$, Me); 1.92 (*s*, Me); 2.00–2.04 (*m*, Me_2CH); 5.07 (*s*, 1 H, CH_2); 5.28 (*d*, $J = 1.2$, 1 H, CH_2); 5.38 (*d*, $J = 3.4$, CHN); 7.24–7.37 (*m*, 6 arom. H); 7.40–7.44 (*m*, 2 arom. H); 7.50–7.53 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 16.4; 19.4; 21.8; 30.1; 64.9; 89.5; 119.7; 125.6; 125.8; 127.9; 128.3; 128.5; 128.8; 138.0; 139.3; 142.3; 152.1; 170.6. MS (EI): 721 ([2 M + Na]$^+$), 388 ([M + K]$^+$), 372 ([M + Na]$^+$), 350 ([M + 1]$^+$). Anal. calc. for $C_{22}H_{23}NO_3$ (349.43): C 75.62, H 6.63, N 4.01; found: C 75.66, H 6.75, N 4.02.

*(*S*)-4-(1-Methylethyl)-3-[(*E*)-3-phenylprop-2-enoyl]-5,5-diphenyloxazolidin-2-one* ((*S*)-**9**). Starting from (*S*)-**3**, (*S*)-**9** was prepared as described in [4a]. Yield and anal. data were in agreement with those reported in [4a].

*(*S*)-3-[(*E*)-3-(3-Methoxyphenyl)prop-2-enoyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* ((*S*)-**10**). To an ice-cold suspension of (*S*)-**3** (602 mg, 2.14 mmol) in THF (10 ml) was added a soln. of BuLi (1.45 ml, 2.35 mmol, 1.6M in hexane) during 5 min. After stirring for 5 min, (*E*)-3-(4-methoxyphenyl)prop-2-enoyl chloride (505 mg, 2.57 mmol) in THF (2 ml) was added, and the mixture was allowed to warm to r.t. overnight. The reaction was quenched with sat. aq. NH_4Cl soln. (10 ml), and the mixture was extracted with Et_2O. The org. layer was washed with 1M HCl, 1M NaOH, and brine, dried ($MgSO_4$), and concentrated under reduced pressure. FC (pentane/AcOEt 15:1) yielded (*S*)-**10** (674 mg, 71%). Colorless solid. M.p. 159–161°. $[\alpha]_D^{20} = -89.2$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2968*w*, 1775*s*, 1676*m*, 1599*s*, 1574*w*, 1512*s*, 1450*w*, 1348*m*, 1257*m*, 1172*s*, 1030*m*, 987*w*, 829*m*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.81 (*d*, $J = 6.9$, Me); 0.93 (*d*, $J = 6.9$, Me); 1.97–2.09 (*m*, Me_2CH); 3.82 (*s*, MeO); 5.54 (*d*, $J = 3.4$, CHN); 6.86–6.92 (*m*, 2 arom. H); 7.23–7.45 (*m*, 8 arom. H); 7.50–7.56 (*m*, 4 arom. H); 7.72 (*d*, $J = 15.7$, ArylCH=C*H*); 7.80 (*d*, $J = 15.7$, ArylC*H*=CH). ^{13}C-NMR (75 MHz, $CDCl_3$): 17.0, 21.0 (Me); 28.8 (CH); 55.4 (Me); 64.4 (CH); 89.3 (C); 114.2, 114.3, 125.7, 126.0, 127.4, 127.9, 128.4, 128.9, 130.4 (CH); 138.4, 142.4 (C); 146.4 (CH); 153.1, 161.7, 165.3 (C). MS (MALDI): 480 (10, [M + K]$^+$), 464 (100, [M + Na]$^+$), 442 (6, [M + H]$^+$). Anal. calc. for $C_{28}H_{27}NO_4$ (441.53): C 76.17, H 6.16, N 3.17; found: C 76.14, H 6.23, N 3.14.

*(*S*)-4-(1-Methylethyl)-3-[(*E*)-3-nitroprop-2-enoyl]-5,5-diphenyloxazolidin-2-one* ((*S*)-**11**) *and (*S*)-3-(2,3-Dichloropropanoyl)-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**17**). Compound (*S*)-**7** (5.03 g, 13.95 mmol) was suspended in Et_2O (110 ml) and cooled to 0°. In a separate flask, to ice-cooled 100% HNO_3 (3.47 ml, 83.7 mmol) was added during 10 min $ClSO_3H$ (2.8 ml, 41.9 mmol), immediately NO_2Cl was formed, which was transferred by a slow stream of N_2 into the reaction mixture. After 1 h, additional $ClSO_3H$ (2.8 ml, 41.9 mmol) was added to the HNO_3, and the NO_2Cl was transferred into the reaction mixture. The resulting yellow soln. was stirred for an additional 1 h at r.t., and then the reaction was quenched by the addition of H_2O (90 ml). The mixture was extracted with Et_2O. The org. layer was washed with H_2O and brine, dried ($MgSO_4$), and concentrated under reduced pressure. FC (pentane/AcOEt 9:1) yielded (*S*)-**11** (1.42 g, 22%) as yellow solid and **17** (1.31 g, 23%) as colorless solid.

*Data of (*S*)-***11***.* R_f (hexane/AcOEt 4:1) 0.53. M.p. 112°. $[\alpha]_D^{20} = -185$ ($c = 1.05$, CH_2Cl_2). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6.8, Me); 0.92 (*d*, *J* = 7, Me); 2.02–2.09 (*m*, Me_2CH); 5.46 (*d*, *J* = 3.4, CHN); 7.26–7.49 (*m*, 10 arom. H); 7.68 (*d*, *J* = 13.2, =CH); 8.38 (*d*, *J* = 13.2, =CH). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.3; 21.8; 30.1; 65.2; 90.4; 125.4; 125.8; 126.8; 128.3; 128.6; 129.0; 129.2; 137.5; 141.6; 149.2; 152.3; 161.1. Anal. calc. for $C_{21}H_{20}N_2O_5$ (380.39): C 66.31, H 5.30, N 7.36; found: C 66.23, H 5.46, N 7.02.

Data of **17***.* R_f (hexane/AcOEt 4:1) 0.63. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.80 (*d*, *J* = 6.7, Me); 0.93 (*d*, *J* = 7, Me); 1.97–2.05 (*m*, Me_2CH); 3.80 (*dd*, *J* = 10.7, 4.5, 1 H, CH_2); 4.12 (*dd*, *J* = 10.7, 9.7, 1 H, CH_2); 5.41 (*d*, *J* = 3.3, CHN); 5.78 (*dd*, *J* = 9.7, 4.5, CH); 7.26–7.45 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.2; 21.7; 29.8; 42.8; 51.3; 90.2; 125.6; 125.9; 128.2; 128.5; 128.8; 128.9; 137.6; 152.3; 166.3. Anal. calc. for $C_{21}H_{21}N_1O_3Cl_2$ (406.30): C 62.07, H 5.21, N 3.45, Cl 17.45; found: C 62.44, H 5.29, N 3.50, Cl 16.89.

*(*S*)-4,5,5-Triphenyl-3-[(*E*)-prop-2-enoyl]oxazolidin-2-one* ((*S*)-**12**). To an ice-cold suspension of (*S*)-**4** (3.15 g, 10.0 mmol) in THF (40 ml) was added a soln. of MeMgBr (3.5 ml, 10.5 mmol, 3M in Et_2O) during 10 min. At the end of the addition, the deprotonated TRIOZ precipitated. The resulting white suspension was stirred for an additional 30 min at 0° and then cooled to −70°. Within 5 min, acryloyl chloride (1.0 ml, 10.5 mmol) was added, and the mixture was allowed to warm to r.t. overnight. The reaction was quenched with sat. aq. NH_4Cl soln. (10 ml), and the mixture was extracted with Et_2O. The org. layer was washed with sat. aq. NH_4Cl soln., dried ($MgSO_4$), and concentrated under reduced pressure. FC (hexane/AcOEt 8:1) yielded (*S*)-**12** (1.58 g, 40%). Colorless solid. R_f (hexane/AcOEt 1:1) 0.8. M.p. 136–137°. $[\alpha]_D^{20} = -236$ ($c = 1.00$, CH_2Cl_2). ^{1}H-NMR (400 MHz, $CDCl_3$): 5.81 (*dd*, *J* = 10.3, 1.6, 1 H, $=CH_2$); 6.20 (*s*, CHN); 6.42 (*dd*, *J* = 17.1, 1.6, 1 H, $=CH_2$); 6.92–7.61 (*m*, 16 arom. H, $CH=CH_2$). ^{13}C-NMR (100 MHz, $CDCl_3$): 66.1; 89.2; 126.0; 126.2; 127.2; 127.5; 127.6; 127.7; 128.2; 128.3; 128.9; 129.0; 132.3; 137.9; 141.7; 152.6; 164.0. Anal. calc. for $C_{24}H_{19}NO_3$ (369.41): C 78.03, H 5.18, N 3.79; found: C 77.85, H 5.37, N 3.77.

*(*S*)- or (*R*)-3-[(*E*)-But-2-enoyl]-4,5,5-triphenyloxazolidin-2-one* ((*S*)- or (*R*)-**13**). To an ice-cold suspension of (*S*)- or (*R*)-**4** (3.70 g, 11.7 mmol) in THF (50 ml) was added BuLi (8.6 ml, 13.8 mmol, 1.6M in hexane) over a period of 25 min. During addition, the TRIOZ dissolved, and, after an additional 35 min at 0°, a clear yellow soln. was obtained. Within 15 min, crotonoyl chloride (1.73 ml, 16.2 mmol) was added, and the mixture was allowed to warm to r.t. overnight. The reaction was quenched with sat. aq. NH_4Cl soln. (25 ml), and the mixture was extracted with Et_2O. The org. layer was washed with 1M HCl, 1M NaOH, and brine, dried ($MgSO_4$), and concentrated under reduced pressure. FC (hexane/AcOEt 8:1) yielded (*S*)- or (*R*)-**13** (*ca.* 3.6 g, *ca.* 80%). M.p. 150–152°. (*S*)-**13**: $[\alpha]_D^{20} = -232.3$ ($c = 1$, $CHCl_3$). (*R*)-**13**: $[\alpha]_D^{20} = +240.8$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3007*w*, 1778*s*, 1687*m*, 1638*m*, 1495*w*, 1449*m*, 1341*s*, 1179*m*, 1059*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 1.91 (*d*, *J* = 8.5, Me); 6.27 (*s*, CHN); 7.02–7.44 (*m*, 13 arom. H, CH=CH); 7.63–7.65 (*m*, 2 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 18.5 (Me); 66.1 (CH); 89.0 (C); 121.7, 126.3, 128.9 (CH); 135.9, 138.1, 141.8 (C); 147.5 (CH); 152.8, 164.1 (C). Anal. calc. for $C_{25}H_{21}NO_3$ (383.44): C 78.31, H 5.52, N 3.65; found: C 78.23, H 5.48, N 3.68.

*(*S*)-3-[(*E*)-4,4,4-Trifluorobut-2-enoyl]-4,4,5,5-triphenyloxazolidin-2-one* ((*S*)-**14**). To an ice-cold suspension of (*S*)-**4** (2.31 g, 7.3 mmol) in THF (50 ml) was added BuLi (4.85 ml, 7.8 mmol, 1.6M in hexane) over a period of 10 min. During addition, the TRIOZ dissolved, and, after an additional 35 min at 0°, a clear yellow soln. was obtained. Within 15 min, a soln. of 4,4,4-trifluorocrotonoyl chloride[18]) (1.28 g, 8.1 mmol) in THF (10 ml) was added, and the mixture was allowed to warm to r.t. overnight. The

[18]) Prepared according to a literature procedure [15].

reaction was quenched with sat. aq. NH_4Cl soln. (10 ml), and the mixture was extracted with AcOEt. The org. layer was washed with 1M HCl, 1M NaOH, and brine, dried ($MgSO_4$), and concentrated under reduced pressure to yield (*S*)-**14** (2.77 g, 63%). M.p. 153–154°. $[\alpha]_D^{20} = -188.1$ (c = 1, $CHCl_3$). IR ($CHCl_3$): 3032*w*, 1774*s*, 1698*m*, 1496*w*, 1450*w*, 1349*s*, 1305*s*, 1276*m*, 1150*s*, 1033*w*, 1016*w*, 1000*w*, 973*w*, 639*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 6.27 (*s*, CH); 7.78 (*dq*, *J* = 15.3, 6.3, CH=C*H*CF_3); 7.02–7.14 (*m*, 10 arom. H); 7.39–7.48 (*m*, 3 arom. H); 7.62–7.66 (*m*, 2 arom. H); 7.91 (*dq*, *J* = 15.3, 1.8, C*H*=$CHCF_3$). ^{13}C-NMR (75 MHz, $CDCl_3$): 66.2 (CH); 89.7 (C); 122.0 (*q*, *J* = 269.0, CF_3); 125.8, 126.1, 127.3, 127.4, 127.6, 127.8, 128.4, 128.5, 129.1 (CH); 132.2 (*q*, *J* = 35.8, CH); 134.9, 137.5, 141.3 (C); 152.3, 161.6 (C). ^{19}F-NMR (282 MHz, $CDCl_3$): −65.20 (*dd*, *J* = 6.5, 1.7, CF_3). Anal. calc. for $C_{25}H_{18}F_3NO_3$ (437.42): C 68.65, H 4.15, N 3.20; found: C 68.42, H 4.41, N 3.15.

*(*S*)- or (*R*)-4,5,5-Triphenyl-3-[(*E*)-3-phenylprop-2-enoyl]oxazolidin-2-one* ((*S*)- or (*R*)-**15**). To an ice-cold suspension of (*S*)- or (*R*)-**4** (3.60 g, 11.4 mmol) in THF (50 ml) was added BuLi (8.55 ml, 13.6 mmol, 1.6M in hexane) over a period of 10 min. During addition, the TRIOZ dissolved, and, after an additional 35 min at 0°, a clear yellow soln. was obtained. Within 15 min, a soln. of cinnamoyl chloride (2.47 g, 14.8 mmol) in THF (8 ml) was added, and the reaction mixture was allowed to warm to r.t. overnight. The reaction was quenched with sat. aq. NH_4Cl soln. (25 ml), and the mixture was extracted with AcOEt. The org. layer was washed with 1M HCl, 1M NaOH, and brine, dried ($MgSO_4$), and concentrated under reduced pressure. The residue was triturated twice with hot hexane (30 ml) to yield (*S*)- or (*R*)-**15** (*ca.* 5.0 g, *ca.* 90%). Colorless solid. M.p. >240°. (*S*)-**15**: $[\alpha]_D^{20} = -234.6$ (*c* = 1, $CHCl_3$). (*R*)-**15**: $[\alpha]_D^{20} = +242.8$ (*c* = 1, $CHCl_3$). IR ($CDCl_3$): 3008*w*, 1777*s*, 1681*m*, 1617*m*, 1496*w*, 1450*m*, 1344*s*, 1170*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 6.34 (*s*, CHN); 7.06–7.25 (*m*, 10 arom. H); 7.37–7.39 (*m*, 4 arom. H); 7.41–7.46 (*m*, 2 arom. H); 7.55–7.58 (*m*, 2 arom. H); 7.66–7.68 (*m*, 2 arom. H); 7.76 (*d*, *J* = 15.7, PhCH=C*H*); 7.92 (*d*, *J* = 15.7, PhC*H*=CH). ^{13}C-NMR (100 MHz, $CDCl_3$): 66.2 (CH); 89.1 (C); 116.8, 126.9, 128.9 (CH); 134.4, 138.0, 141.8 (C); 146.9 (CH); 152.8, 164.4 (C). Anal. calc. for $C_{30}H_{28}NO_3$ (445.51): C 80.88, H 5.20, N 3.14; found: C 80.72, H 5.50, N 3.16.

3. *Conjugate Additions to the Cinnamoyl- and Crotonoyl-oxazolidinones. General Procedure 1* (*GP 1*). To a Cu^IBr-DMS (1.5 equiv.) suspension in THF (2.5 ml/mmol) was added at −40° the appropriate *Grignard* reagent (3 equiv., as 1M soln. in THF). After 10 min, the temp. was adjusted to −40 or −70°, and the acyl-TRIOZ derivative (1 equiv.) as a soln. in THF (5 ml/mmol) was added dropwise. After stirring for 30 min at −35 or −70°, the mixture was allowed to warm to r.t. (1–2 h), and the reaction was quenched with sat. aq. NH_4Cl soln., and the mixture was extracted with AcOEt. The org. layer was washed with 1M HCl, 1M NaOH, and brine, dried ($MgSO_4$), and concentrated under reduced pressure to yield the crude products which were analyzed by NMR for determination of the dr. FC and crystallization yielded the 1,4-addition products.

*(*S*)-3-[(*S*)- or (*R*)-3-(4-Methoxyphenyl)-3-phenylpropanoyl]-4-(1-methylethyl)-5,5-diphenyloxazolidin-2-one* (**18** or *epi*-**18**). Compound (*S*)-**9** (113 mg, 0.275 mmol) was treated with a soln. of (4-MeOPh)MgBr (0.825 ml, 0.825 mmol, 1M in THF), or (*S*)-**10** (121 mg, 0.275 mmol) with a soln. of PhMgBr (0.825 ml, 0.825 mmol, 1M in THF) at −30°, according to *GP 1*. Purification of the crude product by FC (pentane/AcOEt 15:1) yielded **18** (110 mg, 88%, dr 85:15) or *epi*-**18** (78%, dr 82:18). Colorless solid. For anal. purposes, a sample was re-crystallized from hexane to afford diastereomerically pure **18** (dr ≥ 99:1). M.p. 138–140°. $[\alpha]_D^{20} = +156.9$ (*c* = 1, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2966*w*, 2837*w*, 1779*s*, 1703*m*, 1610*w*, 1511*s*, 1450*m*, 1372*m*, 1319*w*, 1176*s*, 1034*w*, 831*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.61 (*d*, *J* = 6.7, Me); 0.65 (*d*, *J* = 7.0, Me); 1.82–1.92 (*m*, Me_2CH); 3.44 (*dd*, *J* = 16.5, 7.9, 1 H, CH_2); 3.74 (*s*, MeO); 3.74 (*dd*, *J* = 16.5, 7.9, 1 H, CH_2); 4.56 (*dd*, *J* = 7.9, 7.9, PhC*H*); 5.28 (*d*, *J* = 3.2, CHN); 6.75–6.79 (*m*, 2 arom. H); 7.08–7.20 (*m*, 7 arom. H); 7.24–7.41 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.1, 21.4 (Me); 29.8 (CH); 40.8 (CH_2); 45.8 (CH); 55.2 (Me); 64.4 (CH); 89.4 (C); 113.9, 125.6, 125.9, 126.3, 127.5, 127.9, 128.3, 128.5, 128.5, 128.9, 128.9 (CH); 135.6, 138.1, 142.2, 143.5, 153.1, 158.1, 171.1 (C). MS (MALDI): 558 (11, $[M+K]^+$), 542 (100, $[M+Na]^+$), 498 (32). Anal. calc. for $C_{34}H_{33}NO_4$ (519.64): C 78.59, H 6.40, N 2.70; found: C 78.52, H 6.46, N 2.64.

*(*R*)-4,5,5-Triphenyl-[(*S*)-3-phenylbutyanoyl]oxazolidion-2-one* (**19**). Compound (*R*)-**13** (667 mg, 1.74 mmol) was treated at −40° with a soln. of PhMgBr (5.22 ml, 5.22 mmol, 1M in THF) according to *GP 1* to yield the crude product (dr 96:4). FC (pentane/AcOEt 9:1) and crystallization from hexane/AcOEt yielded **19** (568 mg, 71%; pure diastereoisomer). Colorless solid. R_f (hexane/AcOEt 4:1) 0.48.

M.p. 112–114°. $[\alpha]_D^{20} = +232.7$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3032*w*, 1781*s*, 1705*m*, 1495*w*, 1450*m*, 1365*m*, 1333*m*, 1172*m*, 1081*w*, 1033*w*, 998*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.18 (*d*, $J = 6.6$, Me); 3.08–3.33 (*m*, CH_2, CH); 6.16 (*s*, CH); 6.91–7.22 (*m*, 15 arom. H); 7.43–7.46 (*m*, 3 arom. H); 7.63–7.67 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 21.5 (Me); 36.1 (CH_2); 43.3 (CH); 65.9 (CH); 88.9 (C); 125.9, 126.1, 126.2, 126.8, 127.2, 127.4, 127.6, 127.9, 128.1, 128.3, 128.8, 128.9 (CH); 135.4, 137.8, 141.7, 145.2, 171.0 (C). Anal. calc. for $C_{31}H_{27}NO_3$ (461.55): C 80.67, H 5.90, N 3.03; found: C 80.51, H 5.98, N 3.01.

*(*R*)-4,5,5-Triphenyl-[(*R*)-3-phenylbutanoyl]oxazolidion-2-one* (*epi*-**19**). Compound (*R*)-**15** (537 mg, 2.61 mmol) was treated at −40° with a soln. of MeMgBr (3.75 ml, 5.25 mmol, 1.4M in THF/toluene) according to *GP 1* to yield the crude product (dr 96:4). FC (hexane/AcOEt 4:1) and crystallization from hexane/AcOEt yielded *epi*-**19** (547 mg, 68%; pure diastereoisomer). Colorless solid. M.p. 153–155°. $[\alpha]_D^{20} = +156.3$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 2990*w*, 1780*s*, 1706*m*, 1464*w*, 1450*m*, 1367*m*, 1332*m*, 1170*m*, 1064*w*, 1034*w*, 999*w*, 629*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.20 (*d*, $J = 6.9$, Me); 3.11–3.371 (*m*, CH_2, CH); 6.12 (*s*, CH); 7.01–7.19 (*m*, 15 arom. H); 7.35–7.38 (*m*, 3 arom. H); 7.50–7.53 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 22.2 (Me); 35.9 (CH_2); 43.2 (CH); 66.0 (CH); 125.9, 126.2, 126.7, 127.4, 127.6, 128.1, 128.2, 128.3, 128.8, 128.9 (CH); 135.7, 137.9, 141.5, 145.6, 170.9 (C). Anal. calc. for $C_{31}H_{27}NO_3$ (461.55): C 80.67, H 5.90, N 3.03; found: C 80.52, H 6.08, N 2.99.

*(*R*)-3-[(*S*)-3-(4-Methoxyphenyl)butanoyl]-4,5,5-triphenyloxazolidin-2-one* (**20**). Compound (*R*)-**13** (667 mg, 1.74 mmol) was treated at −40° with a soln. of 4-MeOPhMgBr (5.22 ml, 5.22 mmol, 1.4M in THF) according to *GP 1* to yield the crude product (dr 91:9). FC (pentane/AcOEt 15:1) yielded **20** (631 mg, 74%; mixture of diastereoisomers). Colorless solid. M.p. 120.5–122°. $[\alpha]_D^{20} = +206.8$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3032*w*, 2663*w*, 1780*s*, 1705*m*, 1611*w*, 1514*m*, 1450*w*, 1365*m*, 1332*m*, 1248*m* (br.), 1035*w*, 999*w*, 831*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.18 (*d*, $J = 6.3$, Me); 3.06–3.35 (*m*, CH, CH_2); 3.78 (*s*, MeO); 6.17 (*s*, CH); 6.75–6.79 (*m*, 2 arom. H); 6.90–7.10 (*m*, 12 arom. H); 7.41–7.50 (*m*, 3 arom. H); 7.65–7.68 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 22.0 (Me); 35.7 (CH_2); 43.7 (CH); 55.3 (Me); 66.1 (CH); 88.9 (C); 113.7, 126.0, 127.2, 127.4, 127.6, 127.7, 128.0, 128.1, 128.8, 128.9 (CH); 135.5, 137.3, 137.8, 141.7, 152.6, 157.9, 171.0 (C). Anal. calc. for $C_{32}H_{29}NO_4$ (491.57): C 78.19, H 5.95, N 2.85; found: C 78.24, H 6.08, N 2.83.

*(*S*)-4,5,5-Triphenyl-3-[(*S*)-4,4,4-trifluoro-3-methylbutanoyl]oxazolidin-2-one* (**21**). Compound (*S*)-**14** (437 mg, 1.0 mmol) was treated at −40° with a soln. of MeMgBr (2.2 ml, 3.0 mmol, 1.4M in THF/toluene) according to *GP 1* to yield the crude product (dr 61:39). FC (pentane/AcOEt 9:1) yielded **21** (248 mg, 55%; mixture of diastereoisomers). Colorless solid. M.p. 52–53°. $[\alpha]_D^{20} = -184.2$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3032*w*, 1783*s*, 1709*m*, 1496*w*, 1450*w*, 1332*m*, 1271*m*, 1174*m*, 1132*m*, 1087*w*, 1034*w*, 998*w*, 909*w*, 636*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 1.05 (*t*, $J = 6.6$, Me); 2.77–2.88 (*m*, CH); 2.93–3.35 (*m*, CH_2); 6.25 (*s*, CH, minor diastereoisomer); 6.26 (*s*, CH, major diastereoisomer); 7.02–7.15 (*m*, 10 arom. H); 7.40–7.48 (*m*, 3 arom. H); 7.63–7.68 (*m*, 2 arom. H). ^{19}F-NMR (282 MHz; $CDCl_3$): −73.27 (*d*, $J = 8.7$, CF_3, major diastereoisomer); −73.28 (*d*, $J = 8.7$, CF_3, minor diastereoisomer). Anal. calc. for $C_{26}H_{22}F_3NO_3$ (453.45): C 68.87, H 4.89, N 3.09; found: C 66.20, H 4.85, N 2.91.

*(*S*)-4,5,5-Triphenyl-3-[(*R*)-4,4,4-trifluoro-3-phenylbutanoyl]oxazolidin-2-one* (**22**). Compound (*S*)-**14** (437 mg, 1.00 mmol) was treated at −40° with a soln. of PhMgBr (3.0 ml, 3.0 mmol, 1M in THF) according to *GP 1* to yield the crude product (dr 69:31). FC (pentane/AcOEt 9:1) yielded **22** (311 mg, 60%; mixture of diastereoisomers). Colorless solid. M.p. 103–106°. $[\alpha]_D^{20} = -157.3$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3032*w*, 1782*s*, 1710*m*, 1496*w*, 1450*w*, 1390*w*, 1363*w*, 1332*m*, 1250*m*, 1166*m*, 1034*w*, 1115*m*, 1033*w*, 999*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.39–3.54 (*m*, CH); 3.75–4.03 (*m*, CH_2); 6.04 (*s*, CH, minor diastereoisomer); 6.12 (*s*, CH_2, major diastereoisomer); 6.71–7.10 (*m*, 10 arom. H); 7.23–7.62 (*m*, 10 arom. H). ^{19}F-NMR (282 MHz, $CDCl_3$): −69.95 (*d*, $J = 8.7$, CF_3, major diastereoisomer); −69.83 (*d*, $J = 8.7$, CF_3, minor diastereoisomer). Anal. calc. for $C_{31}H_{24}F_3NO_3$ (515.52): C 72.22, H 4.69, N 2.72; found: C 72.01, H 4.97, N 2.55.

*(*S*)-3-[(*S*)-3-(4-Methoxyphenyl)-3-phenylpropanoyl]-4,5,5-triphenyloxazolidin-2-one* (**23**). Compound (*S*)-**15** (775 mg, 1.74 mmol) was treated at −40° with a soln. of 4-MeOPhMgBr (5.22 ml, 5.22 mmol, 1.4M in THF) according to *GP 1* to yield the crude product (dr 97:3). FC (pentane/AcOEt 9:1) yielded **23** (614 mg, 64%; pure diastereoisomer). Colorless solid. M.p. 165–168°. $[\alpha]_D^{20} = -170.6$ ($c = 1$, $CHCl_3$). IR ($CHCl_3$): 3008*w*, 1779*s*, 1707*m*, 1610*w*, 1512*m*, 1496*w*, 1450*w*, 1373*m*, 1332*m*, 1248*m*, 1034*w*, 1000*w*, 831*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 3.68, 3.72 (*d*, $J = 7.8$, CH_2); 3.75 (*s*, MeO); 4.50 (*d*,

$J = 7.8$, CH); 6.09 (*s*, CH); 6.72–6.75 (*m*, 2 arom. H); 6.87–7.19 (*m*, 17 arom. H); 7.39–7.41 (*m*, 3 arom. H); 7.52–7.55 (*m*, 2 arom. H). ^{13}C-NMR (75 MHz, $CDCl_3$): 41.0 (CH_2); 45.7 (CH); 55.1 (CH_3); 65.8 (CH); 89.0 (C); 113.8, 126.0, 126.2, 127.2, 127.4, 127.6, 127.9, 128.1, 128.4, 128.7, 128.8, 128.9 (CH); 135.2, 135.3, 137.7, 141.5, 143.5, 152.7, 158.0, 170.5 (C). Anal. calc. for $C_{37}H_{31}NO_4$ (553.65): C 80.27, H 5.64, N 2.53; found: C 80.29, H 5.68, N 2.51.

*(*S*)-4-(1-Methylethyl)-3-(2-methyl-3-nitropropanoyl)-5,5-diphenyloxazolidin-2-one* (**24a**). *a*) Compound (*S*)-**11** (380 mg, 0.83 mmol) was treated at $-70°$ with a soln. of MeMgBr (1.0 ml, 3.0 mmol, 3M in Et_2O) according to *GP 1* to yield the crude product (dr 65:35). Crystallization from hexane yielded **24a** (150 mg, 40%). The same compound was obtained by methylation of the nitropropanoyl derivative **26** as described in the following procedure.

b) A soln. of ^{i}Pr$_2$NH (0.79 ml, 4.54 mmol) in DMPU/THF (1:5; 20 ml) was cooled to $-35°$. To this cold soln., BuLi (2.84 ml, 4.54 mmol, 1.6M in hexane) was added, and the mixture was stirred for 10 min at *ca.* $-35°$ and then for 20 min at $-76°$. A soln. of **26** (0.764 g, 2.0 mmol) in DMPU/THF (1:5, 5 ml) was then added at once, and stirring was continued for 60 min. To the soln. of this double deprotonated nitro-DIOZ derivative MeI (0.158 ml, 2.54 mmol) was added at $-76°$, and the mixture was allowed to warm to $-25°$ over 4 h. AcOH (0.114 ml, 2.0 mmol) was added, followed after 5 min by H_2O (10 ml), and the hydrolyzed mixture was allowed to warm to r.t., H_2O and Et_2O were added, the org. layer was separated, and the aq. layer was extracted twice with Et_2O. The combined org. layers were washed successively with H_2O, sat. aq. $NaHCO_3$ soln., and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Purification by FC (hexane/AcOEt 4:1) and crystallization from hexane/AcOEt yielded diastereomerically pure **24a** (456 mg, 58%). Colorless powder. R_f (hexane/AcOEt 4:1) 0.44. M.p. 171–173°. $[\alpha]_D^{20} = -183.4$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 2970*w*, 1781*s*, 1700*m*, 1555*s*, 1495*w*, 1451*m*, 1395*s*, 1378*s*, 1317*w*, 1259*w*, 1212*m*, 1178*m*, 1053*m,* 993*w*, 761*m*, 703*m*, 666*w*, 638*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.70 (*d*, $J =$ 6.8, Me); 0.79 (*d*, $J = 6.8$, Me); 1.28 (*d*, $J = 7.2$, Me); 1.88–1.94 (*m*, Me_2CH); 4.18 (*dd*, $J = 14.8$, 4.4, 1 H, CH_2); 4.21–4.28 (*m*, MeC*H*); 4.76 (*dd*, $J = 14.8$, 10.0, 1 H, CH_2); 5.34 (*d*, $J = 3.2$, CHN); 7.21–7.35 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 14.9, 16.3, 21.8 (Me); 29.9, 36.2, 64.3 (CH); 75.1 (CH_2); 90.1 (C); 125.8, 126.0, 128.1, 128.4, 128.9, 129.0 (CH); 138.0, 141.5, 152.5, 173.2 (C). EI-MS: 396.17 (2, M^+), 353.11, 238.08, 220.12, 195.08, 183.08, 165.07. Anal. calc. for: $C_{22}H_{24}N_2O_5$ (396.44): C 66.65, H 6.10, N 7.07; found: C 66.67, H 5.93, N 7.03.

*(*S*)-4-(1-Methylethyl)-3-[(*S*)-2-(1-methylethyl)-3-nitropropanoyl]-5,5-diphenyloxazolidin-2-one* (**24b**). Compound (*S*)-**11** (380 mg, 0.83 mmol) was treated at $-70°$ with a soln. of ^{i}PrMgBr (1.5 ml, 3.0 mmol, 2M in Et_2O) according to *GP 1* to yield the crude product (dr 80:20) (**24b**/*epi*-**24b**). Crystallization from hexane/Et_2O yielded **24b** (150 mg, 40%; mixture of diastereoisomers). Colorless solid. ^{1}H-NMR (300 MHz, $CDCl_3$; main diastereoisomer): 0.77 (*d*, $J = 6.9$, Me); 0.91 (*d*, $J = 7.6$, Me); 0.93 (*d*, $J = 6.9$, Me); 1.13 (*d*, $J = 6.9$, Me); 1.9–2.1 (*m*, Me_2CH); 2.25–2.4 (*m*, Me_2CH); 4.15–4.23 (*m*, CH); 4.26 (*dd*, $J = 2.9$, 14.5, 1 H, CH_2); 4.86 (*dd*, $J = 11.2$, 14.7, 1 H, CH_2); 5.45 (*d*, $J = 3$, CHN); 7.29–7.42 (*m*, 10 arom. H).

*(*S*)-4-(1-Methylethyl)-3-[(*R*)-2-(1-methylethyl)-3-nitropropanoyl]-5,5-diphenyloxazolidin-2-one* (*epi*-**24b**). A soln. of (*S*)-**11** (380 mg (0.83 mmol) in Et_2O (10 ml) was treated at r.t. with Cu^{II}-triflate (15 mg, 0.04 mmol). The yellow soln. was cooled to $-45°$, and a soln. of (^{i}Pr$_2$)Zn (1.1 ml, 1.1 mmol, 1M in Et_2O) was added during 20 min. The resulting red soln. was stirred for an additional 40 min at $-40°$ and then warmed to 0° during 45 min, and then the reaction was quenched with sat. aq. NH_4Cl soln., and the mixture was extracted with Et_2O. The org. layer was washed with sat. aq. NH_4Cl soln., dried ($MgSO_4$), and concentrated under reduced pressure to yield the crude product with a dr 75:25 (*epi*-**24b**/**24b**). Crystallization from hexane yielded *epi*-**24b** (150 mg, 40%; mixture of diastereoisomers). Colorless solid. ^{1}H-NMR (400 MHz, $CDCl_3$): 0.56 (*d*, $J = 6.9$, Me); 0.63 (*d*, $J = 6.9$, Me); 0.84 (*d*, $J = 6.8$, Me); 0.91 (*d*, $J =$ 7, Me); 1.48–1.55 (*m*, Me_2CH); 1.97–2.05 (*m*, Me_2CH); 4.43 (*dd*, $J = 14.8$, 3.0, 1 H, CH_2); 4.51–4.56 (*m*, CH); 4.94 (*dd*, $J = 14.8$, 11.2, 1 H, CH_2); 5.39 (*d*, $J = 3.1$, CHN); 7.24–7.54 (m, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.0; 18.0; 19.8; 21.5; 28.7; 29.9; 45.7; 65.7; 73.2; 125.4; 125.6; 128.0; 128.5; 128.6; 128.8; 128.9; 137.6; 152.8; 172.3. MALDI-MS: 446.04 ($[M + Na]^+$). Anal. calc. for $C_{24}H_{28}N_2O_5$ (424.49): C 67.91, H 6.65, N 6.60; found: C 67.96, H 6.71, N 6.50.

*(*S*)-4-(1-Methylethyl)-3-[(*S*)-3-nitro-2-phenylpropanoyl]-5,5-diphenyloxazolidin-2-one* (**24c**). Compound (*S*)-**11** (380 mg, 0.83 mmol) was treated at $-70°$ with a soln. of PhMgBr (3.0 ml, 3.0 mmol, 1M in

THF) according to *GP 1* to yield the crude product (dr 95:5). Crystallization from hexane yielded diastereomerically pure **24c** (200 mg, 55%). Colorless solid. R_f (hexane/AcOEt 4:1) 0.9. M.p. 168°. $[\alpha]_D^{20} = -226$ ($c = 1$, CH_2Cl_2). ^{1}H-NMR (400 MHz, $CDCl_3$): 0.39 (*d*, *J* = 6.7, Me); 0.72 (*d*, *J* = 7, Me); 1.80–1.88 (*m*, Me_2CH); 4.46 (*dd*, *J* = 15.1, 4.16, 1 H, CH_2); 5.24 (*dd*, *J* = 15.1, 11.0, 1 H, CH_2); 5.45 (*d*, *J* = 3.1, CHN); 5.66 (*dd*, *J* = 11.0, 4.2, PhC*H*); 7.25–7.46 (*m*, 15 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 15.6; 21.6; 30.1; 46.2; 64.3; 75.1; 89.8; 125.9; 125.9; 128.0; 128.3; 128.7; 128.8; 128.9; 129.0; 129.1; 132.4; 137.9; 141.5; 152.2; 170.5. Anal. calc. for $C_{27}H_{26}N_2O_5$ (458.51): C 70.73, H 5.72, N 6.11; found: C 70.45, H 5.64, N 6.12.

*(1*R,*2*S,*5*R*)-5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 2-Methyl-3-nitropropanoate* (**25a**). Compound **16** (1.0 g, 3.0 mmol) was treated at −70° with a soln. of MeMgBr (3.7 ml, 10.9 mmol, 3M in THF) according to *GP 1* to yield the crude product (dr 78:22). FC (hexane/AcOEt 10:1) yielded **25a** (380 mg, 36%; mixture of diasterioisomers). Oily residue. IR ($CHCl_3$): 2955*w*, 2922*w*, 2870*w*, 1725*s*, 1601*w*, 1556*s*, 1549*s*, 1495*w*, 1473*w*, 1455*w*, 1413*w*, 1375*m*, 1345*w*, 1240*m*, 1241*s*, 1228*m*, 1199*m*, 1174*s*, 1095*m*, 1094*m*, 977*m*, 961*m*, 908*w*, 845*w*, 774*w*, 764*m*, 742*m*, 699*s*, 627*m*. ^{1}H-NMR (600 MHz, $CDCl_3$): 0.87, 8.8 (2*d*, *J* = 6.6, Me); 0.94, 1.05 (2*d*, *Me*CH); 0.85–0.97 (*m*, CH_2); 1.18, 1.19, 1.29, 1.31 (4*s*, *Me*CPh); 1.10–1.20 (*m*, 1 H, CH_2); 1.43–1.52 (*m*, MeC*H*); 1.66–1.71 (*m*, 1 H, CH_2); 2.08–2.12 (*m*, CH); 2.34–2.40, 2.56–2.62 (2*m*, MeC*H*); 3.91 (*dd*, *J* = 14, 6.2, 1 H, CH_2NO_2, minor diastereoisomer); 3.96 (*dd*, *J* = 14, 5.5, 1 H, CH_2NO_2, minor diastereoisomer); 4.00 (*dd*, *J* = 14, 6.2, 1 H, CH_2NO_2, major diastereoisomer); 4.21 (*dd*, *J* = 14, 7.7, 1 H, CH_2NO_2, major diastereoisomer); 4.81 (*dt*, *J* = 10.7, 4.4, CH–O, major diastereoisomer); 4.84 (*dt*, *J* = 10.7, 4.4, CH–O, minor diastereoisomer); 7.11–7.33 (*m*, 5 arom. H). ^{13}C-NMR (150 MHz, $CDCl_3$): 13.4; 14.1; 21.7; 23.3; 23.6; 26.3; 26.4; 29.1; 29.4; 31.2; 34.5; 37.3; 37.4; 39.4; 39.5; 49.2; 49.9; 50.0; 75.6; 75.65; 75.7; 76.4; 125.1; 125.2; 125.25; 125.3; 128.0; 128.1; 151.9; 151.2; 170.9; 171.5. Anal. calc. for $C_{20}H_{29}NO_4$ (347.45): C 69.14, H 8.41, N 4.03; found: C 69.16, H 8.41, N 4.00.

*(1*R,*2*S,*5*R*)-5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 3-Methyl-2-(nitromethyl)butanoate* (**25b**). Compound **16** (1.0 g, 3.0 mmol) was treated at −70° with a soln. of ^{i}PrMgBr (5.5 ml, 10.9 mmol, 2M in THF) according to *GP 1* to yield the crude product (dr 51:49). FC (hexane/AcOEt 10:1) yielded **25b** (830 mg, 73%; mixture of diastereoisomers). Oily residue. IR ($CHCl_3$): 2956*w*, 2922*w*, 2871*w*, 1726*s*, 1601*w*, 1556*s*, 1549*s*, 1495*w*, 1473*w*, 1456*w*, 1413*w*, 1375*m*, 1346*w*, 1242*m*, 1228*m*, 1199*m*, 1175*s*, 1095*m*, 978*m*, 961*m*, 909*w*, 845*w*, 845*w*, 774*w*, 764*m*, 742*m*, 699*s*, 627*m*. ^{1}H-NMR (600 MHz, $CDCl_3$; *ca.* 1:1 mixture of epimers): 0.74, 0.82 (2*d*, Me); 0.86–1.00 (*m*, CH_2, 2 Me); 1.06–1.16 (*m*, CH); 1.17, 1.20, 1.30, 1.31 (4*s*, 2 Me); 1.43–1.52 (*m*, CH); 1.63–1.78, 1.83–1.88, 1.90–1.95 (3*m*, 2 CH_2); 2.07–2.16 (*m*, CH); 2.42–2.45, 2.55–2.58 (2*m*, C*H*COO); 3.91, 4.53 (2*dd*, 1 H, CH_2NO_2); 4.08, 4.17 (2*dd*, 1 H, CH_2NO_2); 4.72, 4.85 (2*dt*, CH–O); 7.11–7.33 (*m*, 5 arom. H). ^{13}C-NMR (150 MHz, $CDCl_3$; *ca.* 1:1 mixture of epimers): 18.8; 19.4; 19.5; 20.1; 21.7; 21.8; 23.9; 24.7; 26.5; 26.7; 27.8; 28.3; 28.5; 28.6; 31.2; 31.3; 34.5; 34.6; 39.5; 39.6; 41.3; 41.4; 48.0; 48.8; 49.6; 50.3; 72.7; 72.8; 76.0; 76.1; 125.0; 125.1; 125.3; 125.4; 127.9; 128.1; 151.7; 151.9; 170.5; 170.9. Anal. calc. for $C_{22}H_{33}NO_4$ (375.50): C 70.37, H 8.86, N 3.73; found: C 70.51, H 8.73, N 3.72.

*(1*R,*2*S,*5*R*)-5-Methyl-2-(1-methyl-1-phenylethyl)cyclohexyl 3-Nitro-2-phenylpropanoate* (**25c**). Compound **16** (1.0 g, 3.0 mmol) was treated at −70° with a soln. of PhMgBr (10.9 ml, 10.9 mmol, 1M in THF) according to *GP 1* to yield the crude product (85%, dr 80:20). Crystallization from AcOEt/hexane yielded diastereomerically pure **25c** (520 mg, 42%). Colorless solid. M.p. 115°. $[\alpha]_D^{20} = -87.9$ (c = 0.5, $CHCl_3$). IR ($CHCl_3$): 2955*w*, 2922*w*, 2870*w*, 1725*s*, 1601*w*, 1556*s*, 1473*w*, 1455*w*, 1413*w*, 1375*m*, 1345*w*, 1240*m*, 1228*m*, 1199*m*, 1173*s*, 1094*m*, 1032*w*, 977*m*, 960*m*, 908*w*, 845*w*, 773*w*, 764*m*, 741*m*, 699*s*, 627*m*. ^{1}H-NMR (600 MHz, $CDCl_3$): 0.57 (*dd*, *J* = 23, 11, Me); 0.77 (*d*, *J* = 6.5, *Me*CH); 0.80 (*ddd*, *J* = 25.0, 13.0, 3.6, 1 H, CH_2CHMe); 1.08 (*dq*, *J* = 13.2, 3.4, 1 H, CH_2CHCPh); 1.20 (*s*, *Me*CPh): 1.34 (*s*, *Me*CPh); 1.38–1.44 (*m*, MeC*H*); 1.61–1.66 (*m*, 1 H each, CH_2CHMe, CH_2CHO); 1.75–1.80 (*m*, 1 H, CH_2CHCPh); 1.99–2.03 (*m*, CHCPh); 3.49 (*dd*, *J* = 8.9, 6.1, CHCOO); 4.35 (*dd*, *J* = 14.3, 6.1, 1 H, CH_2NO_2); 4.73 (*dt*, *J* = 10.7, 4.2, CH–O); 4.81 (*dd*, *J* = 14.3, 8.9, 1 H, CH_2NO_2); 6.92–7.37 (*m*, 10 arom. H). ^{13}C-NMR (150 MHz, $CDCl_3$): 21.6, 23.4 (Me); 26.3 (CH_2); 29.1 (Me); 31.1 (CH); 34.5 (CH_2); 39.5 (C); 40.3 (CH_2); 48.2, 50.02 (CH); 75.5 (CH_2); 76.0 (CH); 125.2, 125.5, 127.7, 128.0, 128.2, 129.0 (CH); 133.8, 152.0, 169.73 (C). Anal. calc. for $C_{25}H_{31}NO_4$ (409.52): C 73.32, H 7.63, N 3.42; found: C 73.11, H 7.48, N 3.41.

(S)-4-(1-Methylethyl)-3-(3-nitropropanoyl)-5,5-diphenyloxazolidin-2-one (**26**). *a*) BuLi (33.1 ml, 52.9 mmol, 1.6M in hexane) was added slowly to a suspension of (*S*)-**3** (14.2 g, 50.4 mmol) in THF

Table 3. *Experimental Details for the X-Ray Structures of* **5**, **11**, **12**, **17**, epi-**19**, **24a**, **24c**, *and* **25c**

	5 [2b]	**11**	**12**	**17**	*epi*-**19**	**24a**	**24c**	**25c**
CCDC No.[a])	753205	753206	753207	753208	753209	753210	753211	753212
Chemical formula	$C_{13}H_{13}NO_3$	$C_{21}H_{20}N_2O_5$	$C_{24}H_{19}NO_3$	$C_{21}H_{21}Cl_2NO_3$	$C_{31}H_{27}NO_3$	$C_{22}H_{24}N_2O_5$	$C_{27}H_{26}N_2O_5$	$C_{25}H_{31}NO_4$
M_r	231.25	380.40	369.42	406.31	461.56	396.44	458.51	409.52
Crystal size [mm]	0.5 × 0.36 × 0.1	0.2 × 0.2 × 0.08	0.28 × 0.08 × 0.06	0.5 × 0.14 × 0.04	0.4 × 0.02 × 0.006	0.21 × 0.18 × 0.15	0.28 × 0.2 × 0.2	0.42 × 0.21 × 0.12
Space group	$P2_1/c$, monoclinic	$P2_12_12_1$, orthorhombic	$P2_1$, monoclinic	$P2_1$, monoclinic	$P2_12_12_1$, orthorhombic	$P2_12_12_1$, orthorhombic	$P2_1$, monoclinic	$P2_12_12_1$, orthorhombic
a [Å]	13.2541 (4)	8.1342(10)	6.2781(4)	11.74(9)	6.1271(4)	9.1660(2)	11.3865(4)	6.3941(10)
b [Å]	5.9599 (2)	13.6164(10)	15.5661(7)	8.99(3)	18.5938(14)	10.9238(2)	9.0646(4)	11.6222(2)
c [Å]	15.2605 (6)	17.670(3)	20.6012(11)	9.61(2)	21.519(2)	21.3608(2)	12.3294(4)	30.7392(5)
α [°]	90.00	90.00	90.00	90.00	90.00	90.00	90.00	90.00
β [°]	105.5885(14)	90.00	93.074(2)	91.0(4)	90.00	90.00	107.449(2)	90.00
γ [°]	90.00	90.00	90.00	90.00	90.00	90.00	90.00	90.00
V [Å^3]	1161.13(7)	1957.1(4)	2010.4(2)	1014.0(9)	2451.6(3)	2138.80(8)	1214.01(8)	2284.34(6)
Z	4	4	4	2	4	4	2	4
ρ_{calc} [g · cm^{-3}]	1.323	1.291	1.221	1.331	1.251	1.231	1.254	1.191
μ [mm^{-1}]	0.095	0.077	0.081	3.051	0.080	0.088	0.087	0.080
Temp. [K]	223	298	298	298	203	223	203	223
θ_{max} [°]	27.49	53.87	24.93	49.90	22.47	27.48	27.52	27.46
$I > 2\sigma(I)$								
Reflexions:								
measured	4940	1402	6148	2077	9648	4854	5097	4599
independent	2655	1387	6143	1130	3196	4838	5091	4580
observed	1882	1303	4988	820	2545	4342	4393	4185
Variables	206	333	505	219	311	358	307	271
H-Atom treatment	refined	refined	constr.	constr.	not refined	refined	constr.	constr.
R(all)	0.0707	0.0595	0.1063	0.1665	0.0838	0.0588	0.0639	0.0719
R(gt)	0.0462	0.0567	0.0884	0.1226	0.0646	0.0515	0.0527	0.0648
Δ/σ_{max}	0.004	0.002	0.041	0.040	0.000	0.006	0.024	0.000
$\Delta\rho_{max}$ [e Å^3]	0.176	0.372	0.315	0.485	0.206	0.221	0.301	0.408

[a]) Copies of the data can be obtained, free of charge, on application to the *Cambridge Crystallographic Data Centre* (*CCDC*), 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336033; e-mail: deposit@ccdc.cam.ac.uk).

(200 ml) at $-40°$. The mixture was allowed to warm up to $-10°$ over 15 min. and then cooled down to $-70°$, followed by dropwise addition of a soln. of 3-nitropropanoyl chloride[19]) (6.93 g, 50.4 mmol) in THF (10 ml) so that the temp. did not exceed $-50°$. After addition, the mixture was stirred for 1 h at $-65°$, followed by slow warm-up to r.t. The reaction was then quenched with half-sat. NH_4Cl (50 ml), and the mixture was extracted with AcOEt. The org. layers were washed with sat. aq. $NaHCO_3$, H_2O, and brine, dried ($MgSO_4$), and concentrated under reduced pressure. Purification by FC (hexane/AcOEt 4:1) afforded besides **7** (product of HNO_2 elimination; 2.98 g, 17%) and (*S*)-**3** (1.87 g, 13%), **26** (4.94 g, 26%) as a colorless powder. For anal. purposes, a sample was recrystallized from hexane/AcOEt.

b) To a mixture of (*S*)-**7** (1.0 g, 3 mmol) and $NaNO_2$ (1.5 g, 22.5 mmol) in THF (10 ml) at 50° was added AcOH (1.25 ml, 22.5 mmol) during 2 h. The reaction was quenched with sat. aq. $NaHCO_3$ soln., and the mixture was extracted with Et_2O. The org. layer was washed with sat. aq. NH_4Cl soln. and brine, dried ($MgSO_4$), and concentrated under reduced pressure. FC (pentane/Et_2O 9:1) yielded beside unreacted (*S*)-**7** (0.32 g, 32%), **26** (0.43 g, 55%). Colorless solid. R_f (pentane/Et_2O 2:1) 0.5. M.p. 93–96°. $[\alpha]_D^{20} = -212.2$ ($c = 1.0$, $CHCl_3$). IR ($CHCl_3$): 2970*w*, 1779*s*, 1705*m*, 1556*s*, 1495*w*, 1450*m*, 1386*s*, 1372*s*, 1319*m*, 1265*m*, 1245*w*, 1211*m*, 1178*m*, 1052*m*, 1002*m*, 988*m*, 948*w*, 909*w*, 869*w*, 843*w*, 761*m*, 733*m*, 704*m*, 666*w*, 638*w*. ^{1}H-NMR (300 MHz, $CDCl_3$): 0.78 (*d*, $J = 6.9$, Me); 0.87 (*d*, $J = 6.9$, Me); 1.98 (*m*, CH); 3.29 (*ddd*, $J = 19.2$, 6.9, 4.2, 1 H, CH_2); 3.69 (*ddd*, $J = 18.9$, 8.1, 4.2, 1 H, CH_2); 4.58–4.75 (*m*, CH_2NO_2); 5.38 (*d*, $J = 3.3$, CH); 7.28–7.46 (*m*, 10 arom. H). ^{13}C-NMR (100 MHz, $CDCl_3$): 16.29, 21.73 (Me); 29.9 (CH); 32.3 (CH_2); 64.8 (CH); 68.9 (CH_2); 90.1 (C); 125.6, 125.9, 128.1, 128.5, 128.8, 129.0 (CH); 137.8, 141.9, 153.0, 168.9 (C). EI-MS: 382.15 (2, M^+), 339.09, 220.12, 195.08, 183.08, 165.07. Anal. calc. for: $C_{21}H_{22}N_2O_5$ (382.41): C 65.96, H 5.80, N 7.33; found: C 66.05, H 5.94, N 7.31.

4. Determination of the X-Ray Structures (*Table 3*). All structures were determined by the X-ray service unit of the Laboratorium für Organische Chemie, ETH-Zürich. Suitable single crystals were measured on a *Bruker–Nonius Kappa CCD* diffractometer with MoK_α radiation ($\lambda = 0.71073$ Å, graphite monochromator). Structures were solved by direct methods (SIR97) [17] and refined by full-matrix least-squares on F^2 (SHELXL97) [18]. If possible, H-atoms were located from a difference electron-density map or constrained at ideal positions and included in the refinement. The absolute configurations are derived from the known senses of chirality of the chiral auxiliaries.

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