Pergamon

Tetrahedron 55 (1999) 7331–7344

TETRAHEDRON

Nickel(II)-catalyzed Michael Additions. Formation of Quaternary Centers and Diastereoselective Addition of Enantiopure *N*-Acetoacetyl-4-benzyloxazolidin-2-one

Jaume Clariana,[a] Nicanor Gálvez,[a] Caroline Marchi,[a] Marcial Moreno-Mañas,*[a] Adelina Vallribera,[a] and Elies Molins[b]

[a]*Department of Chemistry, Universitat Autònoma de Barcelona, Cerdanyola, 08193-Barcelona, Spain, e-mail: iqorb@cc.uab.es*
[b]*Institut de Ciència de Materials de Barcelona (CSIC), Campus de la UAB, E-08193-Cerdanyola, Spain*

Received 1 February 1999; revised 30 March 1999; accepted 15 April 1999

Abstract

$Ni(acac)_2$ and Ni(salicylaldehydate)$_2$ are effective catalysts for conjugate additions of 2-methyl-1,3-dicarbonyl compounds to Michael acceptors. Significant diastereomeric excesses are obtained in the Michael additions of enantiopure *N*-acetoacetyl-4-benzyloxazolidinones. Reaction of the latter compound with aryl isocyanates affords unsymmetrical diamides of malonic acid.

Keywords: Nickel Catalysis; Conjugate Addition; Quaternary Centers; Chiral Induction; Amides of Malonic Acid

1. Introduction

Conjugate addition of active methylene compounds to activated π-systems (Michael addition) is one of the oldest and most useful constructive methods dating back to more than one hundred years.[1] However, the use of basic catalysts generates some limitations as the formation of by-products through unwanted side reactions can occur.

Some salts and complexes of transition metals and of lanthanides catalyze the conjugate addition of active methylene (and methyne) compounds.[2,3] The limitations caused by basic catalysts as well as the advantages offered by the alternative use of transition metal and lanthanide salts and complexes under essentially neutral conditions have been recently discussed in a review.[3] Saegusa reported in 1972 that the combination of Cu_2O or $Cu(acac)_2$ with cyclohexyl isocyanide catalyzes the conjugate addition of many activated methylene and methyne groups with a limited number of electrophiles (acrylate, propiolate, crotonate and acrylonitrile).[4] Since then many papers proposing several different metal species have appeared.[3,5] Of particular significance is the work of Echavarren and coworkers on the generalized use of $RuH_2(PPh_3)_4$,[6] a catalyst previously proposed by Murahashi only for nucleophiles featuring cyano groups.[7]

0040-4020/99/$ - see front matter
PII: S0040-4020(99)00358-0

Asymmetric versions of this metal-catalyzed conjugate addition have been reported.[3,8] In all cases induction is generated by incorporating enantiomerically pure ligands into the metal coordination sphere as in the conversion of **1** into **2** (Figure 1). Related work by Shibasaki relies on lanthanum-BINOL[9] or on heterobimetallic (Al - Li, Na, K, or Ba; La - Na) combinations of BINOL.[10] To the best of our knowledge the strategy which has the chiral inductor in the nucleophile, exemplified in the Michael addition of **3** to afford **4** (Figure 1), has never been reported.

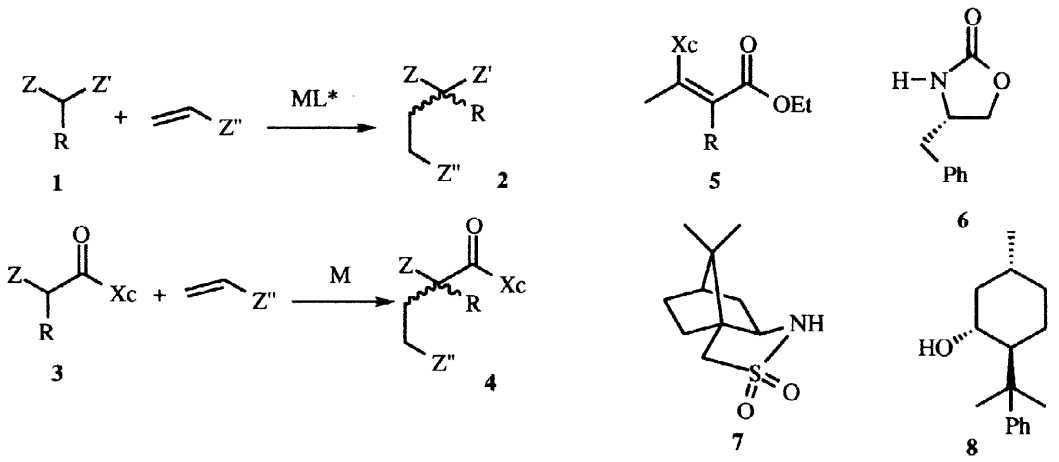


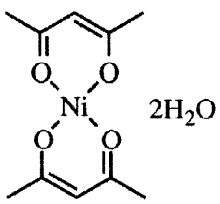
Figure 1. Different approaches to diastereoselective alkylation and Michael addition of active methylene compounds.

Diastereoselective alkylation of activated methylene or methyne groups in open-chain compounds is more broadly precedented than Michael additions. Alkylation of menthyl acetoacetate (**3**, Z = $COCH_3$, R = H, X_C = O-menthyl) led to modest diastereoisomeric excesses (de).[11] Our group has explored the alkylations of *N*-acetoacetyl derivatives of enantiomerically pure 4-benzyloxazolidin-2-ones, Oppolzer sultam, and 8-phenylmenthol (**3**, Z = $COCH_3$, R = H, CH_3, H-X_C = **6**, **7**, **8**),[12] inductor **8** permitting an efficient preparation of enantiomerically pure 4,4-disubstituted-2-pyrazolin-5-ones.[12b] In monoalkylations (**3**, R = H) diastereoisomeric integrity of the final product is compromised by the remaining active proton, and in dialkylations (**3**, R = different from H) steric hindrance imposes some limitations. However, for **3** (Z = CN) remarkable diastereoselective dialkylations have been achieved,[13,14] mainly as the key step in the synthesis of enantiomerically pure non natural amino acids, by Cativiela and coworkers.[14] Transition-metal induced diastereoselective alkylations have been also reported. Thus, our group has described the cobalt(II)-mediated alkylation of **3** (Z = $COCH_3$, R = H, H-X_C = **6**) in connection with the synthesis of enantiomerically pure (1-adamantyl)glycine,[15] and Snider reported the copper(II)-manganese(III) mediated free-radical cyclization of **3** (R = allyl, Z = $-COCH_2CH_2C(CH_3)=CH_2$).[16] Conjugate addition of **3** (Z = $COCH_3$, R = H, H-X_C = **7**) has been successfully used in a preparation of 2-amino-4-aryl-4*H*-pyrans.[17]

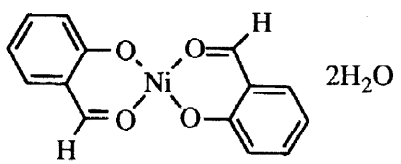
The alternative approach consists of incorporation of the chiral inductor in the form of an enamine as in **5** (Figure 1). Thus, Koga has reported alkylation and conjugate additions on substrates **5**[18] and this method has been adopted by Georg in a preparation of enantiomerically pure α,α-disubstituted glycines[19] and by Stille in an aza-annulation leading to the formation of asymmetric quaternary centers.[20]

2. Results and Discussion

From the several metal salts and complexes proposed in the literature we selected the catalyst Ni(acac)$_2$, **9**, (Figure 2) studied by Nelson[21] since it offers good reactivity for a broad selection of nucleophiles and electrophiles. Soon we noticed that the efficient Ni(acac)$_2$ produces small amounts of by-products arising from the acetylacetone ligand acting as nucleophile.[2] Consequently we moved to the equally efficient but cleaner Ni(salicylaldehydate)$_2$, **10**, (Figure 2) which *a priori* presents the added advantage of allowing the activity of the catalyst to be tuned by introducing different substituents at the aromatic ring.



9: Ni(acac)$_2$·2H$_2$O

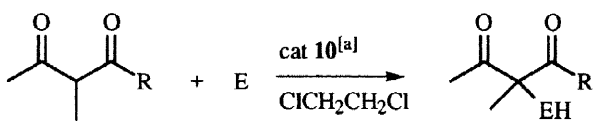


10: Ni(salicylaldehydate)$_2$·2H$_2$O

Figure 2. Ni(II) catalysts.

Table 1.

Michael additions of 3-methyl-2,4-pentanedione and of ethyl 2-methyl-3-oxobutanoate to several Michael acceptors.



11

11a: R = CH_3

11b: R = OEt

12a-h

12a,b : EH = $CH_2CH_2COCH_3$

12c,d : EH = $CH_2CH_2COCH_2CH_3$

12e,f : EH = N(COOEt)NHCOOEt

12g : EH = CH_2CH_2-(N=)

12h : EH = $C(CO_2Me)=CHCO_2Me$

Entry	E	11	T(°C)	Time	Product	Yield (%)
1	$CH_2=CHCOCH_3$	**11a**	100	15h	**12a**	83
2	$CH_2=CHCOCH_3$	**11b**	100	39h	**12b**	87
3	$CH_2=CHCOCH_2CH_3$	**11a**	100	17h	**12c**	55
4	$CH_2=CHCOCH_2CH_3$	**11b**	100	50h	**12d**	77
5	EtOCON=NCOOEt	**11a**	50	20h	**12e**	96
6	EtOCON=NCOOEt	**11b**	50	23h	**12f**	73
7	2-vinylpyridine	**11a**	130	48h	**12g**	18
8	$MeO_2CC\equiv CCO_2Me$	**11a**	50	42h	**12h**[b]	27

[a] 0.1 Equivalents of catalyst **10**; [b] *cis-trans* mixture.

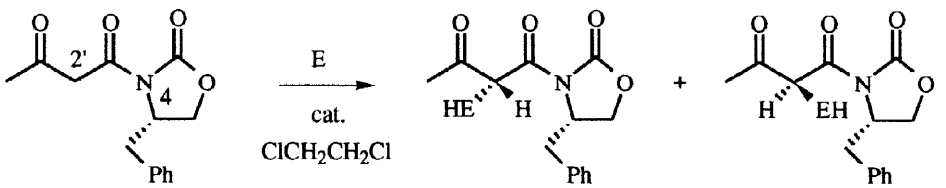
Formation of quaternary centers by metal-catalyzed Michael addition is a topic of current interest.[3-8] We report here that Ni(salicylaldehydate)$_2$, **10**, is an efficient catalyst for reactions of a series of Michael acceptors with 3-methyl-2,4-pentanedione, **11a**, and ethyl 2-methyl-3-oxobutanoate, **11b**. Products **12** were obtained in good yields after some optimization work, as shown in Table 1. Unfortunately, (4*S*)-2'-methylacetoacetyl-4-benzyloxazolidin-2-one (**11**, HR = HX_C = **6**) is inert under the same conditions.

(4*S*) And (4*R*)-*N*-acetoacetyl-4-benzyloxazolidin-2-one, **13** and **ent-13** respectively, were prepared as previously described.[22] Conjugate additions of **13** to methyl and ethyl vinyl ketone gave excellent chemical yields (82-97%) and moderate diastereomeric excesses (Table 2, entries 1-4). Azodicarboxylates were the best Michael acceptors under our conditions, at 0 °C we observed des up to 78% for dibenzyl azodicarboxylate (Table 2, entry 7) and 64% de for diethyl azodicarboxylate (Table 3, entry 3). Owing to hindered rotation at the amide bonds, the ^{1}H (^{13}C) NMR spectra of all these products are complex unless acquired at high temperature. Catalyst **10** gave similar yields and des as **9** (compare entries 1 and 3, and 5 and 6 of Table 2) but reactions were cleaner.

No variation in des is observed along time for the reaction of dibenzyl azodicarboxylate (Table 2, entry 9) indicating kinetic control of the Michael addition. However, slow epimerization is noticed after 5 days in the presence of catalyst. When pure **15a** is submitted to reaction conditions (Table 2, entry 3) no epimerization is observed after 39h.

Table 2.

Ni(II) mediated reactions of (4*S*)-acetoacetyl-4-benzyloxazolidin-2-one, **13**, with Michael acceptors.



13 (4*S*) **14a-e** (4*S*, 2'*R*) **15a-e** (4*S*,2'*S*)

For **14a** and **15a** : EH = $CH_2CH_2COCH_3$, **14b** and **15b** : EH = $CH_2CH_2COCH_2CH_3$,
14c and **15c** : EH = N(COOEt)NHCOOEt, **14d** and **15d** : EH = N(COOBzl)NHCOOBzl,
14e and **15e** : EH = CH_2CH_2-(N)

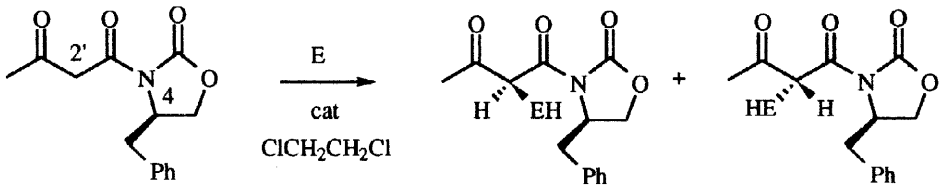
Entry	E	cat[a]	T(°C)	Time	Products	dr[c] (2'*R*:2'*S*)	Yield[d] (%)
1	CH_2=CHCOCH$_3$	**9**	r.t.	17h	**14a+15a**	65:35	97
2	CH_2=CHCOCH$_3$	**9**	0	10d	**14a+15a**	70:30	83
3	CH_2=CHCOCH$_3$	**10**	r.t	39h	**14a+15a**	69:31	88
4	CH_2=CHCOCH$_2$CH$_3$	**10**[b]	r.t.	4d	**14b+15b**	70:30	82
5	EtOCON=NCOOEt	**9**	r.t	18h	**14c+15c**	73:27	94
6	EtOCON=NCOOEt	**10**	r.t.	12h	**14c+15c**	74:26	97
7	BzlOCON=NCOOBzl	**9**	0	4d	**14d+15d**	89:11	100
8	BzlOCON=NCOOBzl	**10**	r.t.	17h	**14d+15d**	70:30	100
9	BzlOCON=NCOOBzl	**10**	0	72h	**14d+15d**	69:31	100
10	BzlOCON=NCOOBzl	**10**	50	17h	**14d+15d**	63:27	100
11	2-vinylpyridine	**10**	reflux	1d	**14e+15e**	60:40	65

[a] 0.1 Equivalents of catalyst unless otherwise stated; [b] 0.05 Equivalents of catalyst; [c] Calculated from ^{1}H NMR integration; [d] Overall yield before separation.

Results obtained from **ent-13** are summarized in Table 3. Di-*tert*-butyl azodicarboxylate has been recommended for base catalyzed asymmetric Michael reactions.[23]

However, under our conditions no reaction occurs at room temp. and although quantitative addition takes place at 50 °C no de is observed (Table 3, entry 4).

Table 3.
Ni(II) mediated reactions of (4*R*)-acetoacetyl-4-benzyloxazolidin-2-one, **ent-13**, with Michael acceptors.[a]

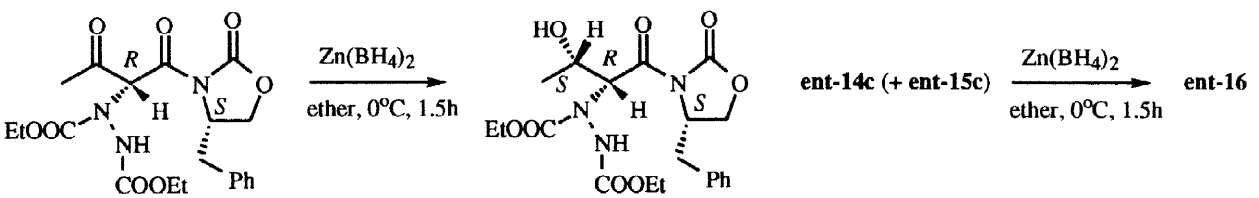


ent-13 (4*R*) **ent-14c,f** (4*R*,2'*S*) **ent-15c,f** (4*R*, 2'*R*)

Entry	E	cat[a]	T (°C)	Time	Products	dr[b] (2'*S*:2'*R*)	Yield[c] (%)
1	EtOCON=NCOOEt	9	r.t.	17h	**ent-14c+ent-15c**	73:27	95
2	EtOCON=NCOOEt	10	r.t.	12h	**ent-14c+ent-15c**	74:26	97
3	EtOCON=NCOOEt	9	0	3d	**ent-14c+ent-15c**	82:18	93
4	tBuOCON=NCOOtBu	9	50	48h	**ent-14f+ent-15f**	50:50	90

[a] 0.1 Equivalents of catalyst; [b] Calculated from ^{1}H NMR integration; [c] Overall yield before separation.

The major diastereoisomers were easily separated by column chromatography when alkyl vinyl ketones were used as electrophiles (E). In other cases no isolation was possible without epimerization and for dialkyl azodicarboxylates a decrease in de was noticed after column chromatography.



14c (+15c) **16**

Scheme 1

Therefore, we envisaged conversion of **14-15** into non-easily epimerizable materials. We were inspired by the reported zinc borohydride reduction of products **3** (Z = CH3CO) which afforded **3** (Z = CH3CHOH) in a diastereoselective manner (only *syn* or *threo* diastereoisomer).[24] Indeed, stereoselective reduction of a mixture of **14c** + **15c** (73:27) with zinc borohydride allowed us to isolate **16** in pure form (49% yield, Scheme 1) which features stereochemistry 2'*R*, 3'*S* (*syn* or *threo*) at the new stereogenic centers as shown by X-ray diffractions analysis (Figure 3, for details see experimental section). Thus, the major diastereoisomer **14c** from the Michael addition has *R* configuration at the initially created stereogenic center. Similarly, reduction of a mixture of **ent-14c** + **ent-15c** (81:19), gave **ent-16** in 57% yield, exhibiting identical melting point and spectroscopic behaviour as **16** but with opposite specific rotation.

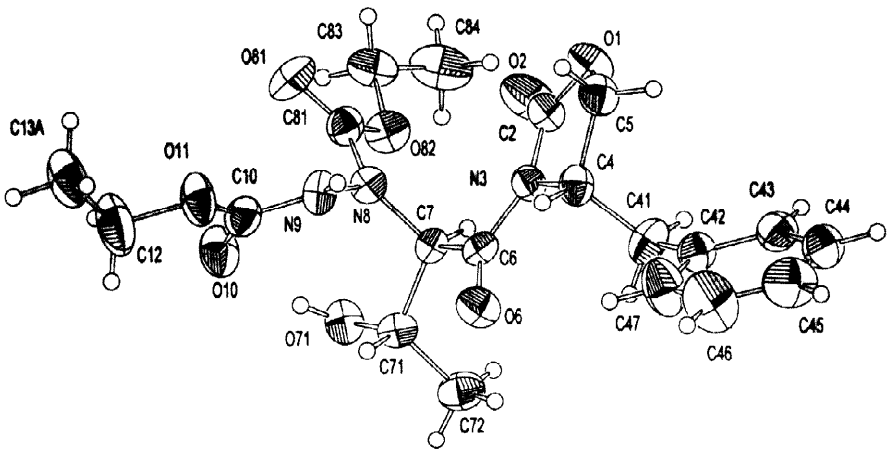


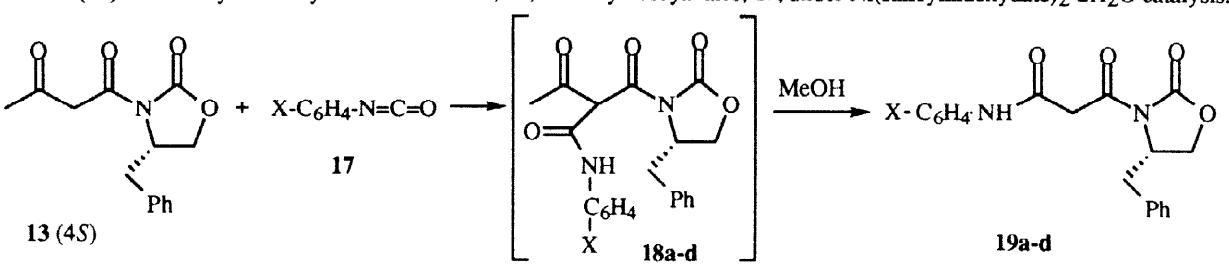
Figure 3. Molecular Structure of **16** by X-ray analysis. The configuration at C7 is *R*.

We assume the same chirality for the major diastereoisomers **14a-e** as for **14c**. Starting from **ent-13**, the major diastereoisomers are **ent-14c,f**. Note that from (4*S*)-oxazolidinone major Michael adducts of *R* configuration are obtained. The observed induction under nickel catalysis is the same as that observed for cobalt-mediated alkylation of (4*S*)-3-acetoacetyl-4-benzyloxazolidin-2-ones.[15]

Other Michael acceptors were tested. Dimethyl acetylenedicarboxylate, 2-butenal and 2-methylpropenal gave high chemical yields at 50 °C. However, four products were produced in each case and isolation of pure isomers was not achieved. Acrylonitrile, ethyl acrylate and 1-nitrostyrene were inert even at 150 °C.

Table 4.

Reaction of (4*S*)-acetoacetyl-4-benzyloxazolidin-2-one, **13**, with aryl isocyanates, **17**, under Ni(salicylaldehydate)$_2$·2H$_2$O catalysis.[a]

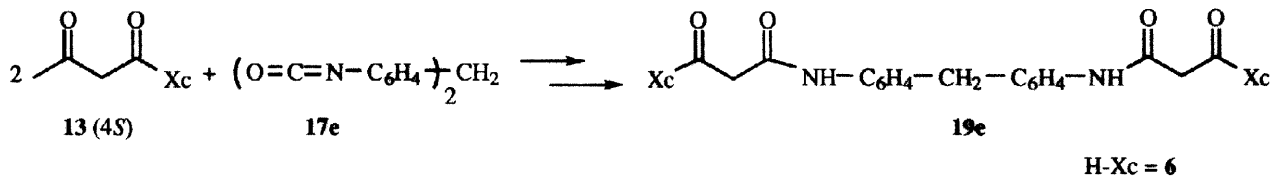


Entry	X (17)	T(°C)	Time	Product	Yield (%)
1	H (**17a**)	r.t.	5h	**19a**	65
2	4-OCH$_3$ (**17b**)	r.t.	17h	**19b**	65
3	4-Cl (**17c**)	r.t.	70h	**19c**	86
4	4-CF$_3$ (**17d**)	r.t.	40h	**19d**	75

[a] 0.1 equivalents of **10**.

Reactions of β-dicarbonyl compounds with isocyanates under catalysis by Ni(acac)$_2$ had been described by Nelson and coworkers.[2,21a] Phenyl isocyanate, **17a**, reacts with **13** at room temp. to afford diastereomeric adducts **18a** (Table 4) which solvolyze in methanol to β-diamide **19a**. In Table 4 we summarize the results obtained for several aryl isocyanates, all

of them giving **19** in good yields.[25] For 4,4'-methylenebis(phenylisocyanate), **17e**, reaction of two equivalents of **13** affords **19e** in 37% yield (Scheme 2).



Scheme 2

3. Conclusion

Nickel (salicylaldehydate)$_2$, **10**, is an excellent catalyst for Michael addition under neutral conditions. Nickel complex **10** catalyzes the formation of quaternary centers by Michael addition. The reactions are very clean and free of side products since **10** itself is inert at its α position. Useful diastereoselectivities have been achieved in the Michael addition of enantiomerically pure 3-acetoacetyl-4-benzyloxazolidin-2-ones to several Michael electrophiles. The resulting products are stereochemically labile and easily epimerized. However, reduction of the ketone group to secondary alcohol occurs with high diastereoselectivity and the reduction products are sterically stable. We are at present studying the conversion of the highly functionalized alcohols of type **16** into target molecules.

4. Experimental section

X-ray Crystallographic Study:[26]

A summary of the crystal data and data collection parameters for compound **16** is given in Table 5. A crystal of approximate dimensions of 0.10x0.12x0.20 mm was mounted on an Enraf-Nonius CAD4 diffractometer equipped with a graphite monochromator. Using MoKα radiation and the ω-2θ scan mode, 3202 independent reflections were collected. The structure was solved by direct methods (SHELXS-86) and refined by full-matrix least-squares (SHELXL-93). C13 atom presents two equally populated disordered positions (only one is shown in the ORTEP drawing). Hydrogen atoms were introduced in calculated positions and refined using two isotropic temperature factors (methyl and non-methyl groups). Thermal vibration for non H-atoms was assumed to be anisotropic.

Table 5. Crystal data and structure refinement for **16.**

empirical formula	$C_{20}H_{27}N_3O_8$	F (000)	928
formula weight	437.45	standard intensity decay	0.8%
temperature	293 (2) K	PSI scan absorption correction	Max: 0.9997, min: 0.9773
wavelength	0.71069 A	theta range for data collection	2.10 to 29.96 deg.
crystal system	orthorhombic	index ranges	0<=h<=13, 0<=k<=14, 0<=l<=18
space group	P 2_1 2_1 2_1	reflections collected	3202
unit cell dimensions	a = 11.484 (2) A	independent reflections	3202
	b = 12.189 (3) A	refinement method	full-matrix least-squares on F^2
	c = 15.926 (3) A	data / parameters	3202 / 294
volume	2229.3 (8) A^3	goodness-of-fit on F^2	1.055
Z	4	final R indices [I<2σ(I)]	R1 = 0.0654, wR2 = 0.1212
density (calculated)	1.303 Mg/m^3	R indices (all data)	R1 = 0.1861, wR2 = 0.1513
absorption coefficient	0.101 mm^{-1}	Largest diff. peak and hole	0.209 and -0.222 e.A^{-3}

General Method for Preparation of Compounds **12a-h**:

3-Acetyl-3-methyl-2,6-heptanedione **12a**[27]: methyl vinyl ketone (3.0 mL, 34.0 mmol) was added to a stirred mixture of 3-methyl-2,4-pentanedione, **11a**, (3.01 g, 26.0 mmol) and Ni(salicylaldehydate)$_2$·2H$_2$O (0.778 g, 2.6 mmol) in 1,2-dichloroethane (80 mL). The resulting solution was stirred at 100 °C during 15 hours. Then 100 mL of methylene chloride were added and the organic solution was washed with 1M hydrochloric acid, with a saturated solution of potassium carbonate and with water. The organic layer was dried with anhydrous sodium sulfate and the solvent evaporated to afford **12a** (3.976 g, 83% yield) as a colourless oil, bp 100 °C (1 mmHg), lit. bp 99-102 °C (1 mmHg): IR (film): ν = 2974, 2930, 1700, 1425 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.35 (s, 3H), 2.08 (m, 2H), 2.13 (s, 6H), 2.14 (s, 3H), 2.35 (apparent dd, J = 14.8 and 6.8 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 18.4, 26.3, 27.4, 29.7, 38.2, 65.1, 207.2 (3C); MS (70eV) (*m/z*): 142 (31), 85 (54), 43 (100).

Ethyl 2-acetyl-2-methyl-5-oxohexanoate **12b**[28] was prepared from **11b** following the same procedure as for **12a** in 87% yield as a colourless oil, bp 104 °C (1 mmHg), lit. bp 92 °C (0.5 mmHg): IR (film): ν = 2985, 2938, 1714 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.27 (t, J = 7.13 Hz, 3H), 1.33 (s, 3H), 2.05-2.20 (m, 2H), 2.14 (s, 3H), 2.16 (s, 3H), 2.43 (m, 2H), 4.19 (q, J = 7.13 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 14.0, 19.2, 26.1, 28.3, 29.9, 38.5, 58.6, 61.4, 172.6, 205.4, 207.3; MS (70eV) (*m/z*): 172 (33), 126 (21), 115 (32), 98 (65), 87 (32), 43 (100), 42 (41).

3-Acetyl-3-methyl-2,6-octanedione **12c** was prepared as a colourless oil from **11a** following the same procedure as for **12a** in 55% yield after distillation: bp 125 °C (0.1 mmHg); IR (film): ν = 2978, 2938, 1713, 1700, 1420 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.04 (t, J = 7.3 Hz, 3H), 1.33 (s, 3H), 2.07-2.34 (m, 4H), 2.13 (s, 6H), 2.41 (q, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 7.7, 18.6, 26.5, 27.7, 35.9, 37.0, 65.4, 207.2 (2C), 210.1; MS (70eV) (*m/z*): 156 (31), 85 (85), 72 (50), 57 (48), 43 (100). Anal. Calcd for $C_{11}H_{18}O_3$: C 66.64, H 9.15. Found: C 66.40, H 9.15.

Ethyl 2-acetyl-2-methyl-5-oxoheptanoate **12d** was prepared as a colourless oil in 77% yield from **11b** following the same procedure as for **12a**: IR (film): ν = 2982, 2940, 1714, 1459 cm^{-1}; ^{1}H NMR ($CDCl_3$): δ = 1.04 (t, J = 7.3 Hz, 3H), 1.27 (t, J = 7.3 Hz, 3H), 1.33 (s, 3H), 2.04-2.13 (m, 2H), 2.16 (s, 3H), 2.35-2.47 (m, 4H), 4.20 (q, J = 7.3 Hz, 2H); ^{13}C NMR ($CDCl_3$): δ = 7.3, 13.9, 19.1, 26.0, 28.3, 35.8, 37.1, 58.6, 61.3, 172.3, 205.3, 209.9; MS (70eV) (*m/z*) : 186 (29), 115 (37), 112 (71), 43 (100). Anal. Calcd for $C_{12}H_{20}O_4$: C 63.14, H 8.83. Found: C 63.15, H 8.69.

3-Methyl-3-(N,N'-bis(ethoxycarbonyl)hydrazino)-2,4-pentanedione **12e** was prepared as an orange oil from **11a** following the same procedure as for **12a** in 96% yield after chromatography through a silica gel column eluting with a mixture of hexanes and diethyl ether (2:1). IR (film): ν = 3303, 2987, 1723, 1246 cm^{-1}; ^{1}H NMR (at 336 K, [D$_8$] toluene): δ = 1.30 (t, J = 7.3 Hz, 6H), 1.61 (s, 3H), 2.37 (s, 6H), 4.21-4.36 (m, 4H), 6.75 (s, 1H); ^{13}C NMR (at 336 K, [D8] toluene) (complex spectrum due to hindered rotation of amide bonds): δ = 14.0, 14.3, 19.5-20.7, 25.8, 61.5-63.2, 80.6, 156.7, 157.0, 202.8; MS (70eV) (*m/z*): 173 (32), 127 (25), 43 (100), 42 (41); HRMS: Calcd for $C_{12}H_{20}N_2O_6$: [M$^+$+1] 289.1426. Found: 289.1412.

Ethyl 2-methyl-2-(N,N'-bis(ethoxycarbonyl)hydrazino)-3-oxobutanoate **12f** was prepared as an orange oil from **11b** following the same procedure as for **12a** in 73% yield after chromatography through a silica gel column eluting with a mixture of hexanes and diethyl ether (2:1): IR (film): ν = 3306, 2986, 1728, 1246 cm^{-1}; ^1H NMR (at 336 K, [D_8] toluene): δ = 0.99-1.09 (m, 9H), 1.63 (s, 3H), 2.27 (s, 3H), 3.95-4.09 (m, 6H); ^{13}C NMR (at 336 K, [D_8] toluene) (complex spectrum due to hindered rotation of amide bonds): δ = 13.9, 14.4, 19.5, 25.1, 61.9-63.2, 77.0, 156.7, 169.3, 199.2; MS (70eV) (*m/z*): 319 (4) [M^++1], 203 (74), 188 (86), 157 (80), 129 (50), 43 (68), 42 (78); Anal. Calcd for $C_{13}H_{22}N_2O_7$: C 49.05, H 6.97, N 8.80. Found: C 49.15, H 6.94, N 8.56.

3-Methyl-3-(2-(2-pyridyl)ethyl)-2,4-pentanedione **12g** was prepared as an oil from **11a** following the same procedure as for **12a** in 18% yield after chromatography through a silica gel column eluting with a mixture of hexanes and diethyl ether (2:1): IR (film): ν = 1716, 1698, 1593, 1474 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.44 (s, 3H), 2.16 (s, 6H), 2.24-2.31 (m, 2H), 2.59-2.66 (m, 2H), 7.10-7.18 (m, 2H), 7.60 (t, J = 8 Hz, 1H), 8.52 (d, J= 5.1 Hz, 1H); ^{13}C NMR ($CDCl_3$): δ = 18.0, 26.4, 32.9, 34.1, 66.2, 121.2, 122.8, 136.4, 149.2, 160.8, 207.2; MS (70eV) (*m/z*): 220 (1) [M^++1], 176 (41), 106 (38), 43 (26); Anal. Calcd for $C_{13}H_{17}NO_2$: C 71.21, H 7.81, N 6.39. Found: C 70.75, H 7.99, N 6.31.

Dimethyl 2-(1-acetyl-1-methyl-2-oxopropyl)-2-butenedionate **12h** was prepared as an orange oil from **11a** following the same procedure as for **12a** in 27% yield after chromatography through a silica gel column eluting with a mixture of hexanes and diethyl ether (4:1): IR (film): ν = 2956, 1727 cm^{-1} (broad); ^1H NMR ($CDCl_3$): δ = 1.58 (s, 3H), 2.24 (s, 6H), 3.76 (s, 3H), 3.79 (s, 3H), 6.07 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 18.7, 27.0, 52.1, 69.0, 124.2, 164.6, 145.8, 166.8, 203.6; MS (70eV) (*m/z*): 182 (65), 154 (31), 151 (30), 123 (42), 43 (100); Anal. Calcd for $C_{12}H_{16}O_6$: C 56.25, H 6.29. Found: C 56.11, H 6.31.

General Procedure for Preparation of Compounds **14a-e** *and* **15a-e**.

(4S)-4-Benzyl-N-(2-acetyl-1,5-dioxohexyl)oxazolidin-2-ones **14a** *and* **15a** (Run 2 of Table 2): methyl vinyl ketone (0.96 g, 0.014 mole) was added to a mixture of **13**, (3.00 g, 0.011 mol) and $Ni(acac)_2{\cdot}2H_2O$ (0.29 g, 0.001 mol) in 1,2-dichloroethane (50 mL) at 0 °C and under magnetic stirring. The resulting solution was stirred at 0 °C during 10 days, washed with 1M hydrochloric acid and with water. The organic layer was dried and evaporated. The resulting oil was a mixture of **14a** and **15a** in a ratio ca. 70:30 (40% de) determined by integration of the ^1H NMR signals of one of the $C\underline{H}_2$-Ph protons at δ 3.30 and 3.38. The residue was purified by chromatography through silica-gel using methylene chloride/diethyl ether 75/25 as eluent to give 0.99 g (26%) of **15a** and 2.02 g (57%) of **14a**. Starting material **13** (16% yield) was recovered.

(4S)-4-Benzyl-N-((2R)-2-acetyl-1,5-dioxohexyl)oxazolidin-2-one **14a**: oil; IR (film): ν = 1776, 1714 cm^{-1}(broad); ^1H NMR ($CDCl_3$): δ = 2.12 (s, 3H), 2.15 (m, 2H), 2.33 (s, 3H), 2.59 (apparent t, J = 7.3 Hz, 2H), 2.73 (dd, J = 13.5 and 9.9 Hz, 1H), 3.38 (dd, J = 13.5 and 3.3 Hz, 1H), 4.16 (m, 2H), 4.52 (dd, J= 7.3 and 5.1 Hz, 1H), 4.63 (m, 1H), 7.20-7.50 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 20.8, 28.8, 29.8, 37.4, 40.8, 55.3, 57.3, 66.3, 127.2, 128.9 (2C), 129.4, (2C), 135.2, 153.6, 169.0, 204.0, 207.4; $[\alpha]_D$ = -14 (c = 0.56, $CHCl_3$); Anal. Calcd for $C_{18}H_{21}NO_5$: C 65.24, H 6.38, N 4.23. Found: C 65.49, H 6.23, N 4.14.

(4S)-4-Benzyl-N-((2S)-2-acetyl-1,5-dioxohexyl)oxazolidin-2-one **15a**: oil; IR (film): ν = 1776, 1715 cm^{-1}(broad); ^1H NMR ($CDCl_3$): δ = 2.14 (s, 3H), 2.16 (m, 2H), 2.30 (s, 3H), 2.58 (apparent t, J = 6.9 Hz, 2H), 2.75 (dd, J = 13.5 and 9.5 Hz, 1H), 3.30 (dd, J = 13.5 and 3.6 Hz, 1H), 4.14 (dd, J= 9.1 and 2.3 Hz, 1H), 4.22 (apparent t, J = 9.1 Hz, 1H), 4.57 (dd, J = 6.9 and 5.5 Hz, 1H), 4.72 (m, 1H), 7.20-7.50 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 21.0, 28.8, 29.8, 37.9, 40.9, 55.1, 57.8, 66.6, 127.3, 128.9 (2C), 129.3 (2C), 135.0, 153.7, 169.0, 204.3, 207.3; $[\alpha]_D$ = +125 (c = 1.21, $CHCl_3$).

(4S)-4-Benzyl-N-((2R)-2-acetyl-1,5-dioxoheptyl)oxazolidin-2-one **14b**: oil; IR (film): ν = 1777, 1713 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.05 (t, J = 7.3 Hz, 3H), 2.17 (m, 2H), 2.36 (s, 3H), 2.43 (q, J = 7.3 Hz, 2H), 2.58 (t, J = 7.3 Hz, 2H), 2.76 (dd, J = 13.2 and 9.5 Hz, 1H), 3.41 (dd, J = 13.2 and 3.7 Hz, 1H), 4.20 (m, 2H), 4.55 (dd, J= 7.3 and 5.1 Hz, 1H), 4.66 (ddd, J = 9.5, 6.6, and 3.7 Hz, 1H), 7.23-7.37 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 7.7, 21.0, 28.8, 35.8, 37.4, 39.5, 55.3, 57.5, 66.4, 127.2, 128.9, 129.4, 135.3, 153.6, 169.0, 204.1, 210.3; $[\alpha]_D$ = +98 (c = 1.00, $CHCl_3$); Anal. Calcd for $C_{19}H_{23}NO_5$: C 66.07, H 6.71, N 4.06. Found: C 65.89, H 6.77, N 4.07.

(4S)-4-Benzyl-N-((2S)-2-acetyl-1,5-dioxoheptyl)oxazolidin-2-one **15b**: oil; IR (film): ν = 1778, 1714cm^{-1}; ^1H NMR ($CDCl_3$): δ = 1.07 (t, J = 7.3 Hz, 3H), 2.19 (m, 2H), 2.33 (s, 3H), 2.44 (q, J = 7.3 Hz, 2H), 2.58 (t, J = 7.3 Hz, 2H), 2.79 (dd, J = 13.2 and 9.5 Hz, 1H), 3.30 (dd, J = 13.2 and 3.7 Hz, 1H), 4.21 (m, 2H), 4.59 (dd, J= 7.3 and 5.1 Hz, 1H), 4.74 (ddd, J = 9.5, 6.6, and 3.7 Hz, 1H), 7.18-7.36 (m, 5H); ^{13}C NMR ($CDCl_3$): δ = 7.7, 21.2, 28.8, 35.9, 38.0, 39.6, 55.2, 58.0, 66.5, 127.4, 128.9, 129.3, 129.4, 135.0, 153.7, 169.1, 204.4, 210.1; Anal. Calcd for $C_{19}H_{23}NO_5$: C 66.07, H 6.71, N 4.06. Found: C 65.55, H 6.77, N 4.07.

(4R)-4-Benzyl-3-(2-(N,N'-bis(etoxycarbonyl)hydrazino)-1,3-dioxobutyl)oxazolidin-2-ones **ent-14c** and **ent-15c**: white foam; IR (KBr): ν = 1783, 1734, 1708 cm^{-1}; ^1H NMR (at 331K, $CDCl_3$): δ = 1.25 (m, 12H), 2.39 (s, 3H), 2.42 (s, 3H), 2.79 (m, 2H), 3.22 (dd, J = 13.9 and 3.6 Hz, 1H), 3.41 (dd, J = 13.9 and 3.7 Hz, 1H), 4.16 (m, 12H), 4.62 (m, 2H), 6.40 (s, 2H), 6.85 (broad s, 2H), 7.10-7.40 (m, 10H); ^{13}C NMR (at 335K, [D_6] DMSO): δ = 13.5 and 13.7 (4C), 27.1, 27.3, 36.3, 36.4, 54.3 (2C), 60.7, 62.2 (4C), 66.7, 66.8, 70.0, 71.3, 126.3, 126.4, 128.0 (4C), 129.0 (4C), 134.8, 135.1, 153.0 and 153.1 and 155.0 and 155.4 (6C), 165,6 (2C), 197.2 (2C); Anal. Calcd for $C_{20}H_{25}N_3O_8$: C 55.17, H 5.79, N 9.65. Found: C 55.01, H 5.91, N, 9.56.

(4S)-4-Benzyl-3-(2-(N,N'-bis(benzyloxycarbonyl)hydrazino)-1,3-dioxobutyl)oxazolidin-2-ones **14d** and **15d:** white foam; IR (film): ν = 1781, 1730, 1704 cm^{-1}; ^1H NMR (at 320 K, [D_8] toluene): δ = 2.60 (broad s, 3H), 2.65 (broad s, 3H), 2.77 (apparent dd, 2H), 3.11 (dd, J = 13.5 and 3.3 Hz, 1H), 3.38 (dd, J = 13.9 and 3.7 Hz, 1H), 3.82 (m, 4H), 4.55 (m, 2H), 5.22 (m, 8H), 6.85 (broad s, 2H), 7.10-7.50 (m, 30H), 7.82 (s, 2H); ^{13}C NMR (at 320 K, [D_8] toluene): δ = 29.5 (2C), 38.8, 38.9, 56.3 (2C), 68.3, 68.5, 69.0 and 70.3 (4C), 71.7, 72.6, 128.6, 128.7, 129.2, 129.3, 129.5, 129.8, 129.9, 130.0, 130.1, 130.2, 130.4, 130.8, 130.9, 136.5 (2C), 137.0 (2C), 137.3, 137.6, 138.7, 155.0 and 155.1 and 157.2 and 157.7 (6C), 169.3, 169.4, 199.2, 199.5; Anal. Calcd for $C_{30}H_{29}N_3O_8$: C 64.39, H 5.22, N 7.51. Found C 64.67, H 5.37, N 7.35.

(4S)-4-Benzyl-N-((2R)-2-(2-pyridylethyl)-1,3-dioxobutyl)oxazolidin-2-ones **14e** and **15e**: oil; IR (film): ν = 1777, 1716 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 2.29 (s, 3H), 2.31 (s, 3H), 2.35-2.50 (m, 4H), 2.72-3.00 (m, 6H), 3.31 (dd, J = 13.2 and 3.7 Hz, 1H), 3.43 (dd, J = 13.2 and 3.7 Hz, 1H), 4.13-4.26 (m, 4H), 4.58-4.78 (m, 4H), 7.11-7.13 (m, 14H), 7.60 (dt, J = 7.7 and 1.5 Hz, 1H), 7.63 (dt, J = 7.7 and 1.5 Hz, 1H), 8.54 (apparent t, 2H); ^{13}C NMR ($CDCl_3$): δ= 26.9 (2C), 28.5 (2C), 35.7 (2C), 37.2, 37.6, 54.8, 55.1, 57.6, 58.1, 66.1, 66.2, 121.2 (2C), 122.7 (2C), 126.9 and 127.1 and 128.8 and 134.8 and 135.1 (12C), 136.3 (2C), 149.0, 149.1, 153.4 (2C), 160.2, 160.3, 168.6, 168.7, 203.9, 204.2; Anal. Calcd for $C_{21}H_{22}N_2O_4$: C 68.84, H 6.05, N 7.65. Found: C 68.50, H 6.15, N 7.42.

(4R)-4-Benzyl-3-(2-N,N'-bis(tert-butoxycarbonyl)hydrazino)-1,3-dioxobutyl)oxazolidin-2-ones **ent-14f** and **ent-15f**: white foam; IR (KBr): ν = 1784, 1734, 1707 cm^{-1}; ^1H NMR (at 331 K, $CDCl_3$): δ = 1.42 (s, 18H), 1.45 (s, 9H), 1.47 (s, 9H), 2.38 (s, 3H), 2.41 (s, 3H), 2.80 (m, 2H), 3.21 (dd, J = 13.5 and 3.3 Hz, 1H), 3.40 (dd, J = 13.9 and 3.6 Hz, 1H), 4.15 (m, 4H), 4.63 (m, 2H), 6.26 (broad s, 2H), 6.70 (broad s, 2H), 7.00-7.45 (m, 10H); ^{13}C NMR (at 335 K, [D_6] DMSO): δ = 27.0 (2C), 27.3 and 27.5 (12C), 36.2, 36.5, 54.1, 54.3, 66.6, 66.7, 79.8 (2C), 81.6, 81.7, 126.3, 126.4, 128.0 (4C), 128.95 (4C), 134.9, 135.2, 153.1 and 154.4 (6C), 165.9 (2C), 197.6 (2C); Anal. Calcd for $C_{24}H_{33}N_3O_8$: C 58.64, H 6.77, N 8.55. Found: C 58.76, H 6.61, N 8.45.

(4S)-4-Benzyl-3-((2R,3S)-2-(N,N'-bis(ethoxycarbonyl)hydrazino)-3-hydroxy-1-oxobutyl)oxazolidin-2-one **16**: a 0.27M solution of zinc borohydride in diethyl ether (50 mL, 0.013 mol) was added to a solution of a mixture of **14c** and **15c** (73:27) (5.1 g, 0.01 mole) in anhydrous diethyl ether (10 mL) under nitrogen at 0 °C. After stirring for 1.5 h at 0 °C, 1M hydrochloric acid was added (20 mL). The organic layer was washed, dried over sodium sulfate and evaporated. Chromatographic separation of the residue under pressure through silica-gel using diethyl ether as eluent gave 2.3 g (49% yield) of pure **16** as a white solid, mp 152-153 °C; IR (KBr) : ν = 3409, 3232, 1790, 1722, 1702 cm^{-1}; ^1H NMR (at 335 K, [D_6] DMSO) : δ = 1.20 (m, 9H), 2.94 (dd, J = 13.5 and 8.0 Hz, 1H), 3.10 (dd, J = 13.5 and 3.6 Hz, 1H), 4.10 (m, 6H), 4.32 (apparent t, J = 8.8 Hz, 1H), 4.59 (m, 1H), 5.70 (d, J = 8.4 Hz, 1H), 7.10-7.40 (m, 5H), 8.70 (broad s, 1H); ^{13}C NMR (335 K, [D_6] DMSO) : δ = 13.5, 13.7, 18.8, 36.9, 54.7, 60.7, 61.5, 63.1, 63.7, 66.1, 126.3, 128.0 (2C), 128.8 (2C), 135.3, 152.1, 155.2, 156.3, 168.1; $[\alpha]_D$ = +32 (c = 1.08, $CHCl_3$); Anal. Calcd for $C_{20}H_{27}N_3O_8$: C 54.91, H 6.22, N 9.60. Found: C 55.04, H 6.12, N 9.61.

A similar reaction from **ent-14c** plus **ent-15c** (81:19) afforded **ent-16** (57 %), mp 149-151 °C; $[\alpha]_D$ = -32 (c = 1.00, $CHCl_3$).

General Method for Preparation of Compounds **19a-e:**

N-Phenyl-3-((4S)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl)-3-oxopropanamide **19a**: The same general procedure as for **14** + **15** was used with **13** (0.27 g, 1.05 mmole), Ni(salicylaldehydate)$_2$·$2H_2O$, **10**, (0.023 g, 5 % mol) and phenyl isocyanate (0.358 g, 3.23 mmole) in 8 mL of 1,2-dichloroethane. The residue was identified as a mixture of diastereomers **18**. After solvolysis in MeOH (10 min), 0.238 g (65%) of pure compound **19a** was isolated: oil; IR (film): ν = 3314, 1782, 1707, 1669 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 2.75 (dd, J = 13.5 and 9.5 Hz, 1H), 3.24 (dd, J = 13.5 and 2.9 Hz, 1H), 4.10 (m, 4H), 4.63 (m, 1H), 7.05-7.27 (m, 8H), 7.52 (d, J = 7.7 Hz, 2H), 8.88 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 37.5,

44.6, 55.1, 66.5, 120.1, 120.3, 124.5, 127.3, 128.9, 129.4, 135.0, 137.7, 153.9, 164.2, 166.8; MS (70eV) (*m/z*): 338 (3) [M^+], 135 (20), 93 (100), 43 (20); Anal. calcd for $C_{19}H_{18}N_2O_4$: C 67.45, H 5.36, N 8.28. Found: C 66.83, H 5.55, N 8.27.

N-(4-Methoxyphenyl)-3-((4S)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl)-3-oxopropanamide **19b**: oil; IR (film): ν = 3314, 1783, 1706, 1663, 1512, 1362, 1241 cm^{-1}; ^1H NMR ($CDCl_3$) : δ = 2.76 (dd, J = 13.5 and 9.1 Hz, 1H), 3.26 (dd, J = 13.5 and 2.9 Hz, 1H), 3.72 (s, 3H), 4.04 (s, 2H), 4.07-4.19 (m, 2H), 4.16-4.71 (m, 1H), 6.78 (d, J = 9.1Hz, 2H), 7.13-7.29 (m, 5H), 7.41 (d, J = 7.9 Hz, 2H), 8.69 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 37.3, 44.2, 55.0, 66.3, 113.9, 121.8, 127.1, 128.8, 129.2, 130.7, 134.9, 153.6, 156.3, 163.8, 166.8; MS (70 eV) (*m/z*): 369 (46) [M^++1], 195 (100), 192 (21), 178 (89), 124 (85); Anal. Calcd for $C_{20}H_{20}N_2O_5$: C 65.21, H 5.47, N 7.60. Found: C 65.13, H 5.47, N 7.46.

N-(4-Chlorophenyl)-3-((4S)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl)-3-oxopropanamide **19c**: white solid, mp 53-55 °C; IR (KBr): ν = 3325, 1782, 1707, 1687 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 2.80 (dd, J = 13.5 and 9.5 Hz, 1H), 3.28 (dd, J = 13.5 and 3.3 Hz, 1H), 4.07-4.25 (m, 4H), 4.70 (m, 1H), 7.14-7.48 (m, 9H), 8.82 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 37.6, 44.2, 55.2, 66.6, 121.8, 127.5, 129.0, 129.4, 153.8, 163.3, 166.6; MS (70 eV) (*m/z*): 374 (2) [M^++2], 372 (6) [M^+], 129 (34), 127 (100), 117 (52), 91 (55); HRMS: Calcd for $C_{19}H_{17}ClN_2O_4$: 372.0876. Found: 372.0882.

N-(4-Trifluoromethylphenyl)-3-((4S)-4-benzyl-2-oxo-1,3-oxazolidin-3-yl)-3-oxopropanamide **19d**: oil; IR (film): ν = 3350, 1782, 1713, 1609 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 2.80 (dd, J = 13.9 and 9.5 Hz, 1H), 3.28 (dd, J = 13.9 and 3.3 Hz, 1H), 4.12-4.21 (m, 4H), 4.71 (m, 1H), 7.13-7.27 (m, 5H), 7.48 (d, J = 8.8 Hz, 2H), 9.07 (s, 1H); ^{13}C NMR ($CDCl_3$): δ = 37.4, 44.5, 55.1, 66.6, 119.5, 126.0, 126.1, 127.4, 128.9, 129.2, 134.6, 140.6, 153.9, 164.3, 166.4; MS (70eV) (*m/z*): 406 (4) [M^+], 161 (100), 92 (60), 91 (53), 86 (68), 43 (41); HRMS: Calcd for $C_{20}H_{17}F_3N_2O_4$: 406.1140. Found: 406.1140.

Compound **19e**: Prepared as **19a** using two equivalents of **13**. Compound **19e** was obtained with 37% yield as an oil. IR (film): ν = 3317, 2924, 1781, 1707, 1667, 1362 cm^{-1}; ^1H NMR ($CDCl_3$): δ = 2.84 (dd, J = 13.5 and 9.2 Hz, 2H), 3.31 (dd, J = 13.5 and 3.3 Hz, 2H), 3.91 (s, 2H), 4.02 (d, J = 15.3 Hz, 2H), 4.14 (d, J = 15.3 Hz, 2H), 4.18-4.30 (m, 4H), 4.75 (m, 2H), 7.12 (d, J = 8.8 Hz, 4H), 7.16-7.28 (m, 10H), 7.44 (d, J = 8.8 Hz, 4H), 8.36 (s, 2H); ^{13}C NMR ($CDCl_3$): δ = 37.6, 40.7, 44.2, 55.3, 66.5, 120.2, 127.5, 129.0, 129.4, 134.7, 135.6, 137.5, 153.9, 162.8, 166.7; MS (70eV); m/z (%): 246 (55), 178 (95), 117 (58), 92 (55), 91 (100), 86 (46), 65 (29), 42 (30); HRMS: Calcd for $C_{39}H_{36}N_4O_8$: [M^++1] 689.2611. Found: 689.2609.

Acknowledgements

Financial support from DGICYT (Ministry of Education and Science of Spain; project PB93-0896), CIRIT (Generalitat de Catalunya; project SGR96-0030 and predoctoral grant to N.G), and UAB (predoctoral grant to J.C.) is gratefully acknowledged. We are indebted to URQUIMA S.A. (Dr Joan Bladé) for the generous gift of oxazolidinones.

References

(1) (1a) Jung, M.E. Stabilized Nucleophiles with Electron Deficient Alkenes and Alkynes, Vol. 4, Chapter 1.1. In *Comprehensive Organic Synthesis*; Ed. by Trost B.M. and Fleming I.; Pergamon Press, **1991**. (1b) Perlmutter, P. *Conjugate Addition Reactions in Organic Synthesis*; Pergamon Press, **1992**.

(2) For a general review on the stoichiometric and catalytic use of transition metal complexes of β-dicarbonyl compounds see: Moreno-Mañas, M.; Marquet, J.; Vallribera, A. *Tetrahedron* **1996**, *52*, 3377-3401.

(3) For a specific review on the transition metal and lanthanide catalysis of the Michael addition of β-dicarbonyl compounds see: Christoffers, J. *Eur. J. Org. Chem.* **1998**, 1259-1266.

(4) Saegusa, T.; Ito, Y.; Tomita, S.; Kinoshita, H. *Bull. Chem. Soc. Jpn.* **1972**, *45*, 496-499.

(5) For other examples recently reported on ytterbium catalysis see: (5a) Kotsuki, H.; Arimura, K. *Tetrahedron Lett.* **1997**, *38*, 7583-7586. (5b) Keller, E.; Feringa, B.L. *Synlett* **1997**, 842-844.

(6) Gómez-Bengoa, E.; Cuerva, J.M.; Mateo, C.; Echavarren, A.M. *J. Am. Chem. Soc.* **1996**, *118*, 8553-8565.

(7) (7a) Murahashi, S.-I.; Naota, T.; Taki, H.; Mizuno M.; Takaya, H.; Komiya, S.; Mizuho, Y.; Oyasato, N.; Hiraoka, M.; Hirano, M.; Fukuoka, A. *J. Am. Chem. Soc.* **1995**, *117*, 12436-12451. (7b) For a recently reported different Ru catalysts see Alvarez, S.G.; Hasegawa, S.; Hirano, M.; Komiya, S. *Tetrahedron Lett.* **1998**, *39*, 5209-5212.

(8) For other recently reported asymmetric Rh catalysis: (8a) Sawamura, M.; Hamashima, H.; Shinoto, H.; Ito, Y. *Tetrahedron Lett.* **1995**, *36*, 6479-6482. (8b) Inagaki, K.; Nozaki, K.; Takaya, H. *Synlett* **1997**, 119-120.

(9) (9a) Sasai, H.; Arai, T.; Satow, Y.; Houk, K.N.; Shibasaki, M. *J. Am. Chem. Soc.* **1995**, *117*, 6194-6198. (9b) Arai, T.; Sasai, H.; Aoe, K.; Okamura, K.; Date, T.; Shibasaki, M. *Angew. Chem. Int. Ed. Engl.* **1996**, *35*, 104-106. (9c) Sasai, H.; Emori, E.; Arai, T.; Shibasaki, M. *Tetrahedron Lett.* **1996**, *37*, 5561-5564.

(10) Sasai, H.; Ari, T.; Shibasaki, M. *J. Am. Chem. Soc.* **1994**, *116*, 1571-1572.

(11) Bram, G.; Cabaret, D.; Welvart, Z.; Geraghty, N.W.A.; Garvey, J. *Tetrahedron Lett.* **1988**, *29*, 4615-4618.

(12) (12a) Moreno-Mañas, M.; Sebastián, R.M.; Vallribera, A.; Molins, E. *Tetrahedron* **1995**, *51*, 10795-10800. (12b) Moreno-Mañas, M.; Sebastián, R.M.; Vallribera, A.; Molins, E.; Espinosa, E. *Tetrahedron:Asymmetry* **1997**, *8*, 1525-1527.

(13) Hamamoto, T.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1986**, *27*, 2463-2464.

(14) (14a) Cativiela, C.; Diaz-de-Villegas, M.D.; Gálvez, J.A. *Tetrahedron* **1994**, *50*, 9837-9846. (14b) Cativiela, C.; Diaz-de-Villegas, M.D.; Gálvez, J.A. *Tetrahedron* **1996**, *52*, 687-694. (14c) Badorrey, R.; Cativiela, C.; Diaz-de-Villegas, M.D.; Gálvez, J.A.; Lapena, Y. *Tetrahedron: Asymmetry* **1997**, *8*, 311-317.

(15) Gálvez, N.; Moreno-Mañas, M.; Vallribera, A.; Molins, E.; Cabrero, A. *Tetrahedron Lett.* **1996**, *37*, 6197-6200.

(16) Zhang Q.; Mohan R.M.; Cook L.; Kazanis S.; Peisach D.; Foxman B.M.; Snider B.B. *J. Org. Chem.*, **1993**, *58*, 7640-7651.

(17) (17a) Martín, N.; Martínez-Grau, A.; Seoane, C.; Marco, J.L. *Tetrahedron Lett.* **1993**, *34*, 5627-5630. (17b) Marco, J.L.; Martín, N.; Martínez-Grau, A.; Seoane, C.; Albert, A.; Cano, F.H. *Tetrahedron* **1994**, *50*, 3509-3528.

(18) (18a) Tomioka, K.; Ando, K.; Takemasa, Y.; Koga, K. *J. Am. Chem. Soc.* **1988**, *106*, 2718-2719. (18b) Ando, K.; Takemasa, Y.; Tomioka, K.; Koga, K. *Tetrahedron* **1993**, *49*, 1579-1588. (18c) Ando, K.; Yasuda, K.; Tomioka, K.; Koga, K. *J. Chem. Soc., Perkin Trans. I* **1994**, 277-282. (18d) Ando K.; Seo W.; Tomioka K.; Koga K. *Tetrahedron*, **1994**, *50*, 13081-13088.
(19) Georg, G.I.; Guan, X.; Kant, J. *Tetrahedron Lett.* **1988**, *29*, 403-406.
(20) Barta, N.S.; Brode, A.; Stille, J.R. *J. Am. Chem. Soc.* **1994**, *116*, 6201-6206.
(21) (21a) Nelson J.H.; Howells P.N.; DeLullo G.C.; Landen, G.L.; Henry R.A. *J. Org. Chem.* **1980**, *45*, 1246-1249. (21b) Nelson J.H.; Howells P.N.; Landen, G.L.; DeLullo G.C.; Henry R.A. *Fundam. Res. Homogeneous Catal.* **1979**, *3*, 921-939.
(22) Gálvez, N.; Moreno-Mañas, M.; Padrós, I.; Sebastián, R.M.; Serra, N.; Vallribera, A. *Polyhedron* **1995**, *14*, 1397-1399.
(23) Willliams, R.S. in *Synthesis of Optically Active α-Amino Acids* ; Chapter 3; Pergamon Press: Oxford, **1989**.
(24) (24a) Ito, Y.; Katsuki, T.; Yamaguchi, M. *Tetrahedron Lett.* **1984**, *25*, 6015-6016. (24b) Nakata, T.; Nagao, S.; Oishi, T. *Tetrahedron Lett.* **1985**, *26*, 6465-6468.
(25) For a recent preparation of unsymmetrical diamides of malonic acid see Lee, H.K.; Lee, J.P.; Lee, G.H.; Pak, C.S.; *Synlett* **1996**, 1209-1210.
(26) Crystallographic data for structure **16** reported in this paper have been deposited at the Cambridge Crystallographic Data Center (deposition number 103.216).
(27) Terashima, S.; Sato, S.; Koga, K. *Tetrahedron Lett.* **1979**, *36*, 3469-3472.
(28) Kreiser, W.; Below, P. *Tetrahedron Lett.* **1981**, *22*, 429-432.