Diastereoselective Alkylation of Acetoacetates of Chiral Inductors. Synthetic Applications

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Dedicated to Prof. Raymond N. Castle, *in memoriam*

Diastereoselective alkylations of acetoacetates of chiral inductors are reviewed. The formed products are starting materials for the preparation of enantiomerically pure amino acids, 4,4-disubstituted 2-pyrazolin-5-ones, and of oxazoles and pyrazoles incorporating the chiral inductors.

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Introduction.

Some precedents of the diastereoselective alkylation of β-dicarbonyl compounds have been reported. Introduction of a chiral inductor in the alcohol or amine group of ketoesters or ketoamides is a current strategy [1]. β-Cyano as activating group [2] has been used in successful preparations of enantiopure amino acids by Cativiela and coworkers [3]. An alternative strategy is based on the incorporation of the chiral inductor in the form of an enamine of the β-ketoester [4-6].

We have investigated the diastereoselective alkylation of acetoacetates of chiral inductors aimed at the preparation of enantiomerically pure amino acids (Figure 1). Several chiral inductors have been tested, mainly Oppolzer's sultam [7], Evans oxazolidinones [8], menthol, 8-phenylmenthol, and D-ribonolactone acetonide [9]. We present in this paper a review on our own achievements as well as results yet unpublished.

An examination of Figure 1 reveals that: i. stereochemistry of monoalkylated derivatives could be compromised

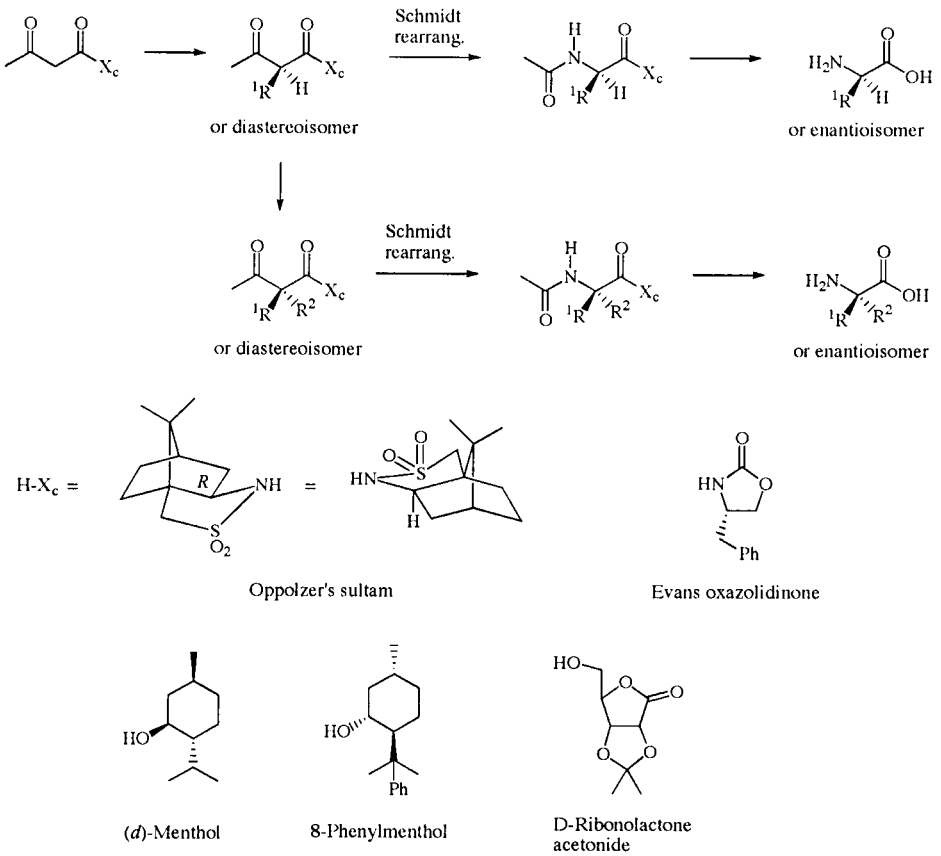


Figure 1

by the presence of an acidic proton in the intercarbonyl position, thus rendering epimerization possible; ii. the acetyl group of the ketoesters or ketoamides ought to be converted into acetylamino group by Schmidt rearrangement; iii. final deprotection would provide the required amino acids.

Three different types of alkylation were envisaged: i. alkylation under conventional basic conditions; ii. alkylation mediated by Co(II) for alkyl halides precursor of stabilized free radicals [10]; and iii. alkylation under acidic conditions with substrates precursors of stabilized carbenium ions.

Alkylation Under Basic Conditions (Method A).

The summary of results is in Figure 2. Reasonable diastereomeric ratios were achieved in the monoalkylation of *N*-acetoacetyl-(*R*)-bornane-10,2-sultam, **1**. However, second alkylation failed [11].

Low diastereomeric ratios were obtained in the first alkylation of *N*-acetoacetyl-(*S*)-4-benzyloxazolidin-2-one, **3**. Again, second alkylation presented many problems [11]. As anticipated, epimerization was observed even under very mild alkylation conditions and during purification procedures.

(*d*)-Menthyl 2-methylacetoacetate, **5**, was efficiently alkylated, but diastereoselectivity was low in the second alkylation.

8-Phenylmenthyl 2-methylacetoacetate, **7**, was well alkylated in the second alkylation with several alkyl halides. The diastereomeric ratios were interesting. However, both Schmidt rearrangement and transesterification failed on the dialkylated compounds **8** [12].

2-Methyl and 2-butyl acetoacetates of D-ribonolactone acetonide (**9** and **10**) gave the best results. The chiral inductor has the first stereodifferentiating center one atom more separated from the intercarbonyl position than

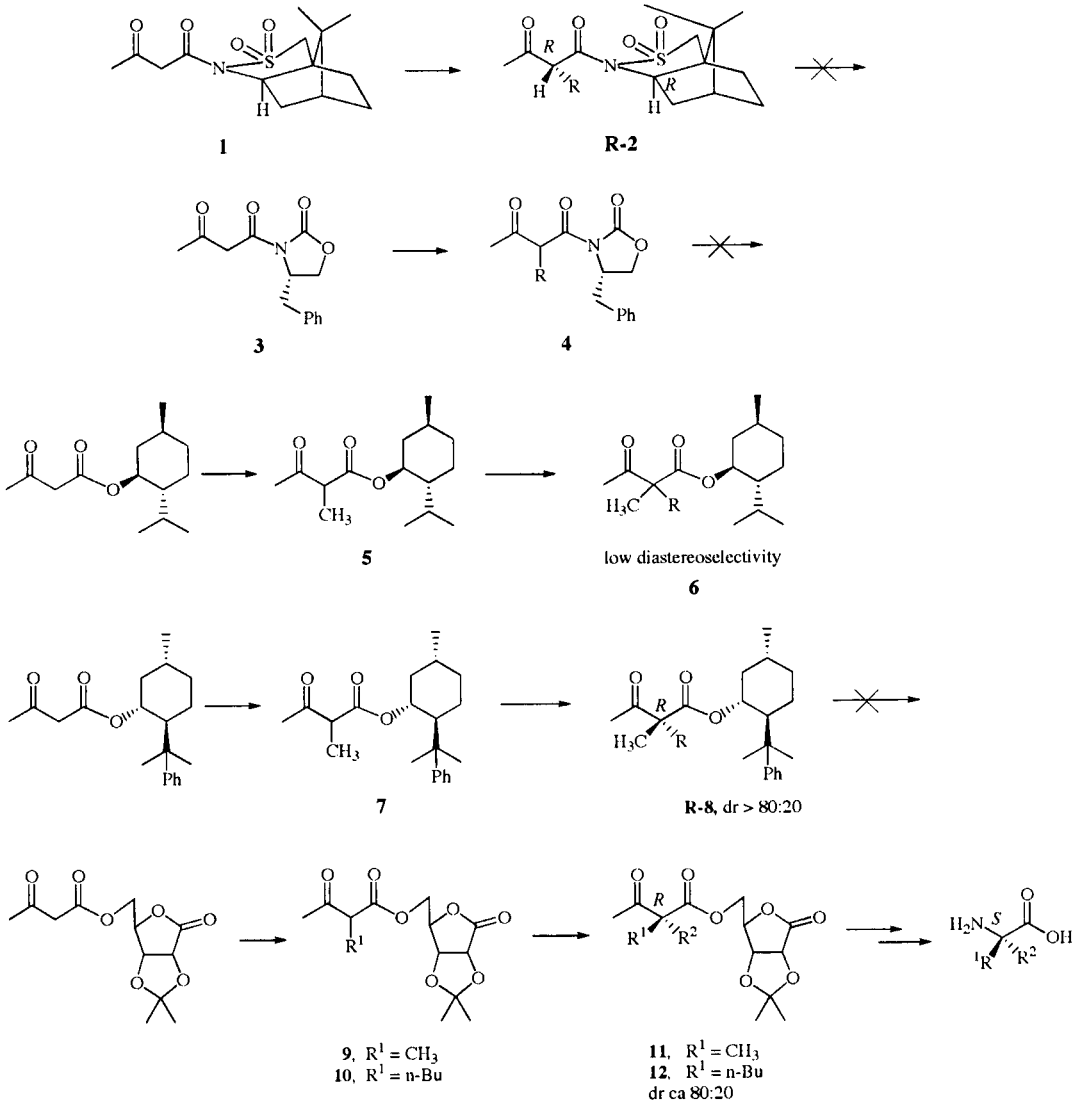
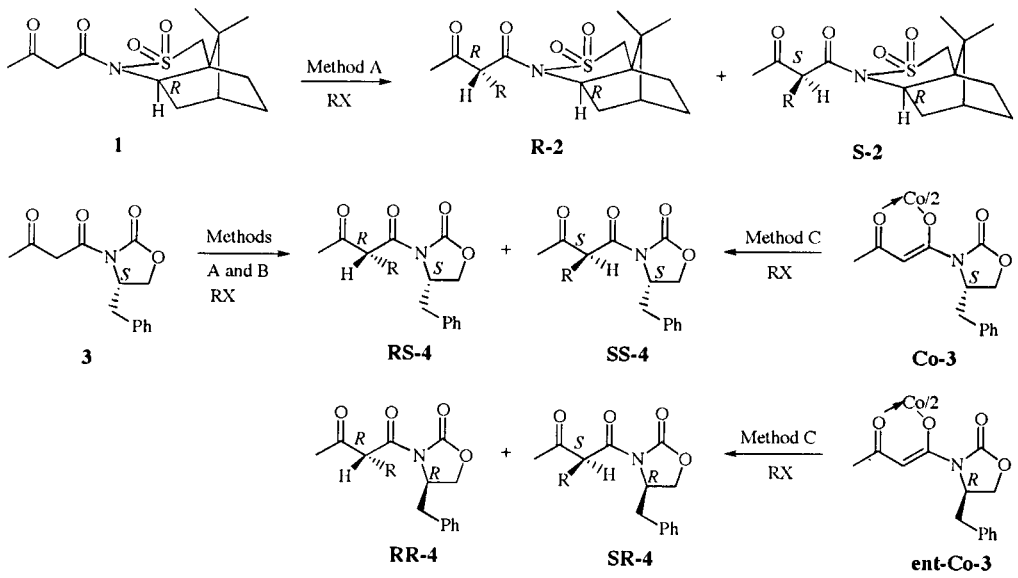


Figure 2



Method A: K_2CO_3/acetone; R: -CH_3, -CH_2Ph, -CH_2CH=CHPh, -$CH_2COPhBr$-4, -CH_2PhCl-4, -CH_2CH=CH_2, -CH_2COOEt, -CH_2CH_2Ph, -CH_2PhBr-4

Method B: K_2CO_3/$[PhCH_2NMe_3]_2$ $[CoCl_4]$/$CHCl_3$; R: -CH_2Ph, -CH_2PhCl-4, -CH_2CH=CH_2, -CH_2CH=CHPh, -$CH_2COPhBr$-4, -CH_2COOEt, -CH_2PhBr-4, -$CHPh_2$, 9-fluorenyl

Method C: $CHCl_3$, heat; R: -$CHPh_2$, 1-adamantyl, -CH_2Ph, 9-fluorenyl

Figure 3

Table 1

Alkylations of Figure 3

Entry	1 or 3	X-R	Method	t (°C)	Product	Yield (%) [a]	dr (R:S)	Remarks	Ref.
1	**1**	I-CH_3	A	40	**2a**	92	60:40	[b]	[11]
2	**1**	Br-CH_2Ph	A	Room temp	**2b**	100	>95:5	X-Ray [c]	[11]
3	**1**	Br-CH_2CH=CHPh	A	Room temp	**2e**	73	73:27	[b]	[11]
4	**1**	Br-$CH_2COPhBr$-4	A	Room temp	**2f**	89	62:38	[b]	[11]
5	**3**	I-CH_3	A	40	**4a**	92		[d]	[11]
6	**3**	Br-CH_2Ph	A	40	**4b**	ca 100	50:50		[11]
7	**3**	Br-CH_2Ph	A	-15	**4b**	ca 100	65:35	[e]	[11]
8	**3**	Br-CH_2Ph	A	-40	**4b**	50	68:32	[e]	[11]
9	**3**	Cl-CH_2PhCl-4	A	40	**4c**	79	72:28	[e]	[11]
10	**3**	Cl-CH_2PhCl-4	A	Reflux	**4c**	94	60:40	[e]	[11]
11	**3**	Br-CH_2CH=CH_2	A	40	**4d**	ca 100		[d]	[11]
12	**3**	Br-CH_2CH=CHPh	A	40	**4e**	ca 100		[d]	[11]
13	**3**	Br-$CH_2COPhBr$-4	A	40	**4f**	ca 100		[d]	[11]
14	**3**	I-CH_2COOEt	A	40	**4g**	ca 100	40:60	X-Ray [f]	[11]
15	**3**	Br-CH_2PhBr-4	A	40	**4i**	ca 100	62:38	X-Ray [g]	This work
16	**3**	Br-CH_2Ph	B	50	**4b**	[h]	81:19	[i], [j]	This work
17	**3**	Cl-CH_2Ph	B	50	**4b**	[h]	50:50		This work
18	**3**	Cl-CH_2PhCl-4	B	50	**4c**	ca 100		[d]	This work
19	**3**	Br-CH_2CH=CH_2	B	50	**4d**	[h]		[d]	This work
20	**3**	Br-CH_2CH=CHPh	B	50	**4e**	[h]		[d]	This work
21	**3**	Br-$CH_2COPhBr$-4	B	50	**4f**	[h]		[d]	This work
22	**3**	I-CH_2COOEt	B	50	**4g**	[h]	57:43	X-Ray [k]	This work
23	**3**	Br-CH_2PhBr-4	B	50	**4i**	61 + 16	77:23	X-Ray [l]	This work
24	**3**	Br-$CHPh_2$	B	50	**4k**	50	82:18	X-Ray [m]	[14]
25	**3**	9-bromofluorene	B	50	**4l**	84	79:21	[n], [o]	[14]
26	**Co-3**	Br-$CHPh_2$	C	Reflux	**4k**	58	73:27	[p]	This work
27	**Co-3**	1-bromoadamantane	C	140	**4m**	56	32:24	[q]	[14]
28	**ent-Co-3**	Br-CH_2Ph	C	100	**4b**	62	50:50		This work
29	**ent-Co-3**	Br-$CHPh_2$	C	50	**4k**	70	22:78	[r]	[14]

Table 1 (continued)

Entry	1 or 3	X-R	Method	t (°C)	Product	Yield (%) [a]	dr (R:S)	Remarks	Ref.
30	**ent-Co-3**	9-bromofluorene	C	100	**4l**	42	41:59	[o]	This work
31	**ent-Co-3**	1-bromoadamantane	C	175	**4m**	35	50:50		This work

[a] Overall yield of both diastereoisomers unless otherwise stated (Entry 23). [b] Configurations assigned by analogy to entry 2. [c] Cambridge Structural Database (CSD) reference code ZIBYAK. [d] Low dr and lack of X-ray information prevents us from assigning configuration to both isomers. [e] Configurations assigned by analogy to entry 15. [f] X-Ray of the major isomer. CSD reference code ZIBYEO. [g] See Entry 23. [h] Compounds not isolated, dr were determined by integration of nmr signals and comparison of data in Ref. [11]. [i] Configurations assigned by analogy to entry 23. [j] ^1H nmr of the major diastereoisomer is coincident with that of the major diastereoisomer of entries 7 and 8. [k] See entry 14. [l] X-Ray of the minor isomer. CSD deposition number CCDC 139148. [m] X-Ray of the major isomer. CSD reference code TOTDIP. [n] Configurations assigned by analogy to entry 24. [o] Epimerizable diastereoisomers. [p] For configuration assignment see entry 24. [q] Ratio refers to yields of isolated products; cobalt(II) chloride bistriphenylphosphine and lanthanum(III) bromide hexahydrate were added as catalysts; isomer **S-4m** was converted into (*S*)-(1-adamantyl)glycine. [r] Major isomer was converted into known amino acid.

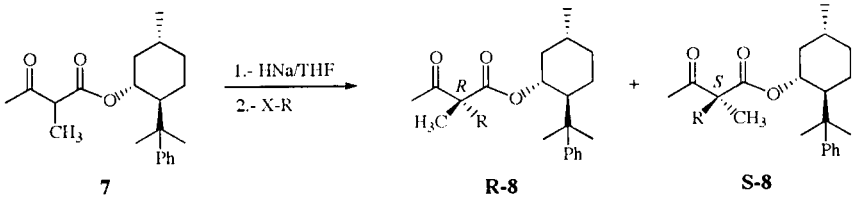
8-phenylmenthol. However, the diastereomeric ratios were practically the same, and the dialkylated compounds **11** and **12**, being esters of a primary alcohol, were more easily transesterified. Further Schmidt rearrangement and elimination of the acetyl group and chiral inductor afforded enantiomerically pure α,α-disubstituted glycines [13].

Alkylation Under Basic Conditions, Oppolzer's Sultam (Figure 3).

The results are in Figure 3 and Table 1. Alkylation of **1** with benzyl bromide (entry 2) afforded the best result since only diastereoisomer **R-2b** was observed. X-Ray diffraction revealed *R* configuration at the new stereogenic center. On the basis of this finding the same *R* stereochemistry was assigned to all other major diastereoisomers (Entries 1, 3, and 4). Since dialkylations failed this inductor was not studied further.

Alkylation Under Basic Conditions, Evans Oxazolidinone (Figure 3).

X-Ray diffraction on the major isomer (**S-4g**) of entry 14 showed *S* stereochemistry at the intercarbonyl position. Although the diastereomeric excess was low, this was at that time the only basis to propose, even with caution, the same *S* stereochemistry to all other major diastereoisomers [11]. Today we have reasons to believe that configurations should be reversed for compounds featuring a 4-X-benzyl group at the intercarbonyl position (Entries 7-10 and 15). Thus, the cobalt mediated alkylation of **3** with 4-bromobenzyl bromide (Entry 23) gave two diastereoisomers in a ratio 77:23. The minor one (**S-4i**) showed *S* configuration at the new stereogenic center by X-ray diffraction. Therefore, the major isomer of Entry 23 is *R*. This major isomer is also the major isomer in the alkylation under basic conditions (Entry 15). On the other



7 **R-8** **S-8**

Figure 4

Table 2

Alkylations of Figure 4

Entry	X-R	t (°C)	Products (%) [a]	dr R-8:S-8	Remarks	Ref.
1	Br-CH_2Ph	-78 to rt	**8b** (62)	83:17	X-Ray [b]	[12]
2	Cl-CH_2Ph-Cl-4	-78 to rt	**8c** (29) [c]	72:28	X-Ray [b]	[12]
3	Br-CH_2CH=CHPh	-78 to rt	**8e** (57)	82:18	[d]	[12]
4	I-CH_2CH_2Ph	-78 to rt	**8h** (41)	85:15	[d]	[12]

[a] Overall yields of both diastereoisomers. [b] Major isomer. CSD reference codes NAZSOW (for **8b**) and NAZSUC (for **8c**). [c] Yield corresponds to isolated **R-8c**. [d] Configurations assigned by analogy to entries 1 and 2.

hand, coming back to the cobalt-mediated alkylations, we observed that the ratios of isomers from alkylations with benzyl bromide (Entry 16) and with the 4-Br analogue (Entry 23) are similar, and it is reasonable to accept a similar behavior for both benzylic alkylating agents. Moreover, the major isomer of benzyl bromide reaction of Entry 16 (cobalt mediated reaction) is also the major isomer of the alkylation performed under basic conditions (Entries 7 and 8). Therefore, we believe that configurational assignments at the intercarbonyl position should be revised, at least for 4-X-benzyl groups (X = H, Cl, Br) as indicated in Table 1. Being conservative, we prefer to consider unsafe any configurational assignment for other substituents when neither X-ray evidences nor strong analogies are available (Entries 11-13).

Alkylation Under Basic Conditions, 8-Phenylmenthol (Figure 4).

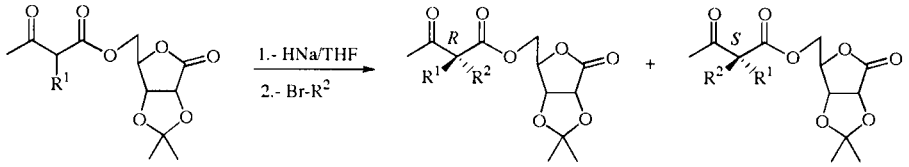
Alkylation of 8-phenylmenthyl 2-methylacetoacetate, **7**, proved quite satisfactory (Table 2). Diastereomeric excesses were interesting and diastereoisomers **8** were easily separated by column chromatography. Moreover, two of them were studied by X-ray diffraction, thus ofering a safe basis for configurational assignment. Major isomers were *R*. However, both Schmidt rearrangement and transesterification under different experimental conditions failed. Transesterification to the ethyl esters was attempted since ethyl ester for R = benzyl was known including stereochemistry [5].

Alkylation Under Basic Conditions, D-Ribonolactone Acetonide (Figure 5).

Alkylation of 2-methyl and 2-butylacetoacetate of D-ribonolactone acetonide (**9** and **10**) was efficient from several viewpoints: yield, diastereoisomeric excesses, facility of separation of the major diastereoisomer, and its conversion into amino acids (Table 3). We performed experiments on ketoester **10**, featuring a butyl group to check the generality of our method. Yields for second alkylations were of the same order as for **9**. However, following reactions leading to amino acids gave lower yields, but the method being still quite useful. Configurational assignments were made by converting **R-11** and **R-12** into 4,4-disubstituted 3-methyl-2-pyrazolin-5-ones **15** (See Figure 8), and comparison of the Cotton effect of the heterocycles with that of the 3-methyl-2-pyrazolin-5-ones obtained from the corresponding 8-phenylmenthyl esters **R-8**. In the 8-phenylmenthyl series X-ray data were available for **R-8b** and **R-8c** (Table 2).

Cobalt-mediated Alkylation, Evans Oxazolidinone (Figure 3).

We have reported that cobalt(II) complexes of β-dicarbonyl compounds are alkylated with alkyl halides precursors of stabilized free radicals [10]. The mechanism is quite complex, consisting of two propagation connected cycles, one for each ligand, and featuring an initiation step in which the halogen atom of the alkyl halide is transferred to a Co(II) species already present in the reaction medium. Thus, the reactions are autocat-



9, $R^1 = CH_3$
10, R^1 = n-Bu

R-11, $R^1 = CH_3$
R-12, R^1 = n-Bu

S-11, $R^1 = CH_3$
S-12, R^1 = n-Bu

Figure 5

Table 3
Alkylations of Figure 5

Entry	R^1	R^2	t (°C)	Products (%) [a]	dr R-11:S-11 or R-12:S-12	Remarks	Ref.
1	CH_3	$-CH_2Ph$	-78 to rt	**11b** (69)	75:25	[b]	[13]
2	CH_3	$-CH_2CH{=}CHPh$	-78 to rt	**11e** (71)	78:22	[b]	[13]
3	CH_3	$-CH_2Ph$-Br-4	-78 to rt	**11i** (64)	80:20	[b]	[13]
4	CH_3	$-CH_2$-2-naphthyl	-78 to rt	**11j** (74)	80:20	[b]	[13]
5	n-Bu	$-CH_2Ph$-Br-4	-78 to rt	**12i** (75)	80:20	[b]	[13]
6	n-Bu	$-CH_2$-2-naphthyl	-78 to rt	**12j** (69)	80:20	[b]	[13]

[a] Overall yields of both diastereoisomers. [b]Configuration assignment based on Cotton effect of pyrazolin-5-ones **15** (Figure 8).

alytic since cobalt(II) halide is the other reaction product. However, initial addition of cobalt(II) in soluble form catalyzes the reaction, which is performed in chloroform in neutral media, thus tolerating alkyl halides incompatible with basic conditions [10d,e]. There is a variation using a base suspended in chloroform in the presence of soluble Co(II) species [10c]. Since benzhydryl, 9-fluorenyl, and 1-adamantyl are typical radicals incorporated into intercarbonyl positions by cobalt-mediated alkylations, we performed experiments on the *N*-acetoacetyl derivative **3** of Evans oxazolidinone. The summary is in Figure 6. Some of the products **R-4** so prepared were converted into monosubstituted (*S*)-alkylglycines featuring benzhydryl, 9-fluorenyl, and 1-adamantyl substituents [14].

Cobalt-mediated Alkylation, Evans Oxazolidinone. Basic Conditions and Cobalt Catalysis (Method B) (Figure 3 and Table 1).

Several alkylating agents were tested (Entries 16-25 of Table 1). X-Ray diffraction of two compounds was decisive for configurational assignment (Entries 23 and 24). Reaction of **3** with 4-bromobenzyl bromide (Entry 23) was fundamental for configurational reassignment of several products as already commented. An important conclusion is that bromide is a much better leaving group than chloride in this type of reactions.

Cobalt-mediated Alkylation on Cobalt Complexes, Evans Oxazolidinone. Neutral Conditions (Method C).

Two sets of experiments were performed with the cobalt complexes of (*S*) and (*R*)-4-benzyloxazolidinones, **Co-3** and **ent-Co-3** (Entries 26-31 of Table 1). Note that the 1-adamantyl group was introduced, although the high temperature required prevented high diastereoisomeric excesses (Entries 27 and 31). In the first case the oxazolidinone acts as a resolution agent rather than as a chiral inductor. The 1-adamantyl derivative of R configuration was converted into (*S*)-1-adamantylglycine [14]. The diastereoisomeric excesses were good for benzhydryl bromide (Entries 26 and 29). The 9-fluorenyl derivatives were easily epimerizable. Final amino acids were all known, which was an added data for configurational assignment of the new stereogenic centers, since Schmidt rearrangements take place with retention of configuration of the migrating center [15].

Alkylation Under Acidic Conditions, Evans Oxazolidinone (Figure 7).

These results are in Table 4. Xanthydrol, thiaxanthydrol, and dibenzosuberenol (5*H*-dibenzo[*a*,*d*]cycloheptene-5-ol) are precursors of relatively stable carbenium ions. The two first alcohols are substrates for the alkylation of β-diketones in acidic media [16]. The three alcohols are alkylated under mild acid catalysis to afford diastereoisomeric mixtures with

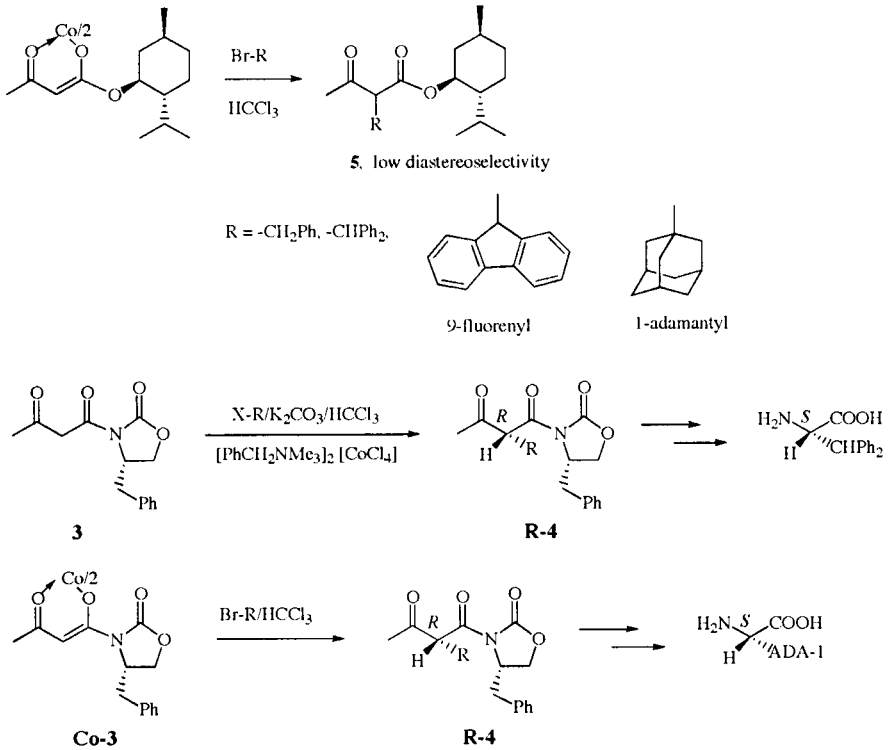


Figure 6

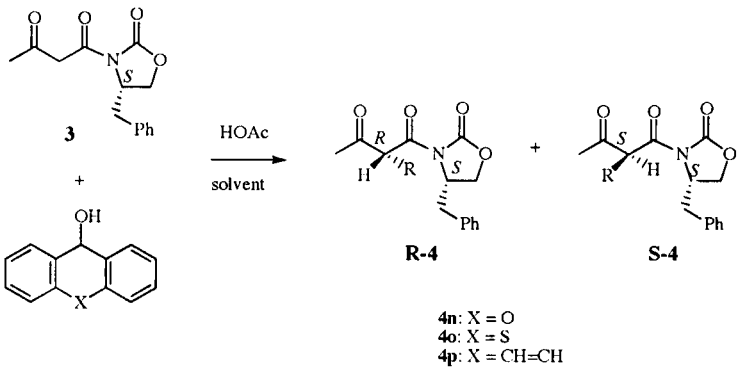


Figure 7

Table 4

Alkylations of Figure 7

Entry	X	Solvent/ t (°C)	Products (%) [a]	dr R-4:S-4	Remarks	Ref.
1	O	EtOH/rt	**4n** (97)	71:29	[b]	this work
2	S	EtOH/rt	**4o** (98)	79:21	X-Ray [c]	this work
3	CH=CH	t-BuOH/rt	**4p** (ca 100)	79:21	[b]	this work

[a] Overall yield of both diastereoisomers. [b] Configuration assignment by analogy to Entry 2. [c] Major isomer. CSD deposition number CCDC 139147.

reasonable diastereoisomeric excesses. X-Ray diffraction permitted to assign *R* configuration to the major isomer (**R-4o**) of the reaction with thiaxanthydrol (Entry 2). On this basis, the same stereochemistry is assigned to the major isomers of Entries 1 and 3. Attempts to perform Schmidt rearrangement on major isomers failed.

Preparation of Nitrogen-containing 5-Membered Heterocyclic Compounds (Figure 8).

Schmidt rearrangement is a crucial step in the transformation into amino acids. We have found that the combination

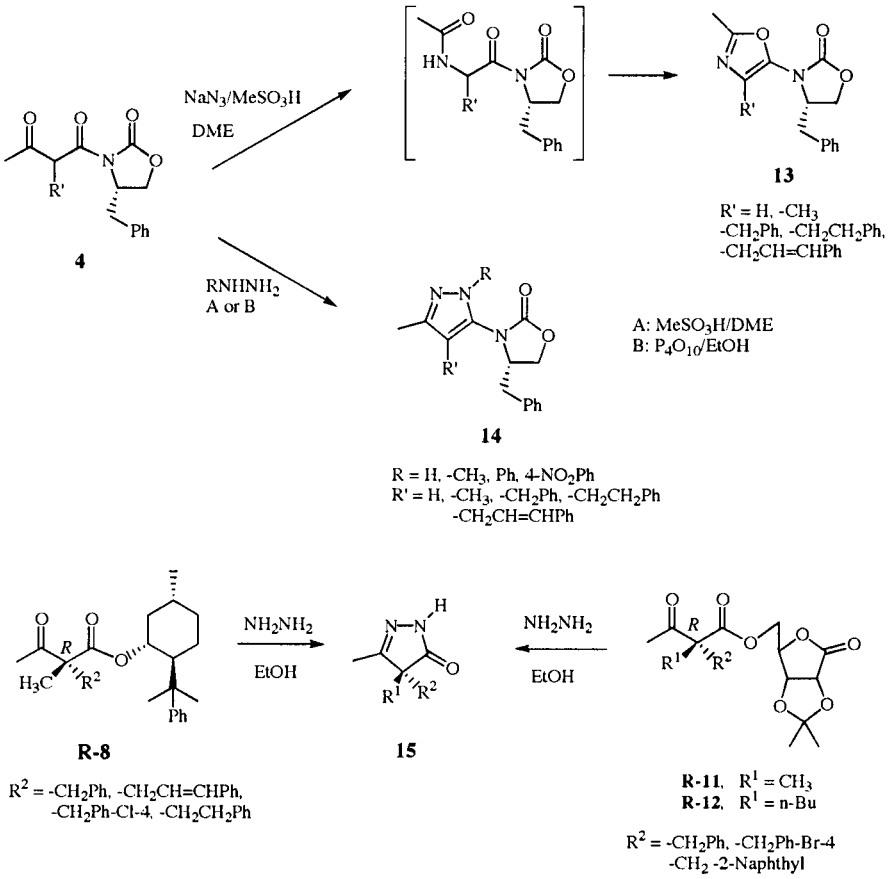


Figure 8

of sodium azide and methanesulfonic acid in dimethoxyethane is efficient and safer [17] than other reported alternatives based on the use of chloroform [15]. When these experimental conditions were applied to compounds **4**, Schmidt rearrangement was followed by cyclization to oxazoles **13** featuring the enantiopure oxazolidinone at C-5 [17]. Recently similar results have been reported by Lautens *et al.* [18]. The obvious alternative for this type of cyclization is the formation of 5-hydroxyoxazole and recovery of the chiral inductor. This peculiar cyclization depends on the very acidic conditions. We anticipated that strongly acidic conditions could in general vary the usual selection of leaving group in cyclizations leading to five-membered heterocycles. Thus we applied this idea to the formation of pyrazoles **14** featuring the Evans oxazolidinone [19]. In sharp contrast, treating **4** with hydrazine in ethanol in the absence of acid affords the corresponding pyrazolone, the Evans oxazolidinone being recovered [19].

On the other hand, treatment of major diastereoisomers **R-8** with hydrazine hydrate at 140°C afforded 4,4-disubstituted 3-methyl-2-pyrazolin-5-ones **15**, in enantiomerically pure form, with practically quantitative recovery of 8-phenylmenthol [12]. This is a very useful reaction since absolute configuration of **15** is known by correlation with configuration of **R-8b,c** for which X-ray is available [12]. Pyrazolinones **15** obtained both from **R-8** and from **R-11** and **R-12** exhibit a very strong positive Cotton effect, which is a safe basis to confirm that both families of ketoesters belong to the same stereochemical family [13].

Summary.

As anticipated monoalkylation of chiral derivatives of acetoacetic acid leads to stereochemically delicate products due to the presence of an intercarbonylic proton. Probably Oppolzer's sultam is the best inductor if only monoalkylation is looked for [11].

Dialkylation is efficient with 8-phenylmenthol in terms of only diastereoselectivity [12]. However, difficulties are experienced in further transformation of products. D-ribonolactone acetonide produces diastereoselectivities only slightly lower than 8-phenylmenthol. However, further transformations are clearly more facile. In other words, D-ribonolactone acetonide is the best inductor in order to prepare amino acids as well as 2-pyrazolin-5-ones, **15** [13].

The cobalt method is very good for alkyl halides precursors of stabilized free radicals such as benzhydryl bromide and 9-bromofluorene [14]. 1-Adamantyl group can only be introduced by the cobalt method [14]. In this case we can not compare the performances of several inductors since only Evans oxazolidinone was tested.

EXPERIMENTAL

Experimental details for reactions made in basic media have been throughly described in references [11-13]. The cobalt methods [10,14] as well as the compounds prepared through them have been also fully described [10,11,14]. Here we describe in detail the experiment of Entry 23, Table 1 as a typical procedure leading to a new compound.

N-(2'-(4-Bromobenzyl)acetoacetyl)-4-benzyloxazolidin-2-ones (**4i**); (Entry 23, Table 1).

A mixture of **3** (1.37 g, 5.24 mmole), potassium carbonate (0.95 g, 6.89 mmoles), bis(benzyltrimethylammonium) tetrachlorocobaltate [20] (0.287 g, 0.57 mmole), and chloroform (6 ml) was stirred at 50°C for 45 minutes. Then, 4-bromobenzyl bromide (1.370 g, 5.50 mmoles) was added and the stirring and temperature were maintained for 23 hours. The mixture was partitioned between chloroform and 1*M* hydrochloric acid. The organic layer was dried with sodium sulfate and evaporated. The oily residue (2.34 g) was chromatographed through silica gel with hexanes - diethyl ether (1:1) to afford both diastereoisomers and unreacted **3** (0.30 g, 22%).

(2'*R*,4*S*)-*N*-(2'-(4"-Bromobenzyl)acetoacetyl)-4-benzyloxazolidin-2-one (**R-4i**) (1.37 g, 61%) was an oil, ir (film): 1776, 1719, 1702, 1389, 1359, 1267, 1233, 1215, 1072, 732, 705 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.25 (s, 3H), 2,70 (dd, J = 9.9 and 13.5 Hz, 1H), 3.00 (dd, J = 5.1 and 13.9 Hz, 1H), 3.22 (dd, J = 9.5 and 13.9 Hz, 1H), 3.33 (dd, J = 3.3 and 13.5 Hz, 1H), 4.02 (apparent t, J = 9.1 Hz, 1H), 4.08 (dd, J = 2.9 and 9.1 Hz, 1H), 4.52 (m, 1H), 4.87 (dd, J = 5.1 and 9.5 Hz, 1H), 7.05-7.33 (m, 7H), 7.38 (d, J = 8.4 Hz, 2H); ^{13}C nmr (deuteriochloroform): δ 29.4, 32.8, 37.2, 55.2, 60.0, 66.3, 120.6, 127.2, 128.8, 129.4, 130.8, 131.6, 135.0, 137.2, 153.9, 168.5, 202.8; $[\alpha]_D$ = +8.9 (chloroform, c = 1.58).

(2'*S*,4*S*)-*N*-(2'-(4"-Bromobenzyl)acetoacetyl)-4-benzyloxazolidin-2-one (**S-4i**) (0.36 g, 16%) was a solid, mp 109-110°C (pentane - dichloromethane - diethyl ether), ir (KBr): 1769, 1707 (sh), 1697, 1396, 1373, 1357, 1263, 1233, 1116, 748, 704 cm^{-1}; ^1H nmr (deuteriochloroform): δ 2.20 (s, 3H), 2.62 (dd, J = 8.8 and 13.5 Hz, 1H), 2.90 (dd, J = 3.3 and 13.5 Hz, 1H), 3.04 (dd, J = 5.1 and 13.9 Hz, 1H), 3,26 (dd, J = 9.5 and 13.9, 1H), 4.08 (dd, J = 3.3 and 9.1 Hz, 1H), 4.18 (apparent t, J = 9.1 Hz, 1H), 4.69 (m, 1H), 4.96 (dd, J = 5.1 and 9.5 Hz, 1H), 6.92 (m, 2H), 7.18 (m, 5H), 7.42 (d, J = 8.4 Hz, 2H); ^{13}C nmr (deuteriochloroform): δ 29.3, 33.2, 37.4, 54.9, 60.4, 66.2, 120.7, 127.4, 128.8, 129.3, 130.9, 131.7, 134.5, 137.2, 154.1, 168.3, 203.2; $[\alpha]_D$ = +116.7 (chloroform, c = 1.05).

Anal. Calcd for $C_{21}H_{20}BrNO_4$: C, 58.62: H, 4.68: N, 3.25. Found: C, 58.82: H, 4.66: N, 3.26.

N-(2'-(1-Adamantyl)acetoacetyl)-(4*S*)-4-benzyloxazolidin-2-ones (**4m**); (Entry 27, Table 1).

A mixture of cobalt complex **Co-3** (5.00 g, 8.0 mmoles), 1-bromoadamantane (3.55 g, 16.0 mmoles), cobalt(II) chloride bis(triphenylphosphine) (0.54 g, 0.8 mmole) in ethanol-free chloroform (7.5 ml) was heated under magnetic stirring in a closed reactor to 80°C for 20 hours and at 100°C for 14 hours. No reaction was observed. Then, lanthanum(III) bromide hexahydrate (0.40 g, 0.82 mmole) was added and the mixture was gradually heated in the closed reactor. At 140°C the color changed to blue and the reactor was maintained at 140°C for 48 hours. After cooling, the mixture was partitioned between dichloromethane and diluted hydrochloric acid. The organic phase was washed with water, dried and evaporated. The residue was chromatographed through silica gel to afford both diastereoisomers **4m** and *N*-(1-adamantyl)-(4*S*)-4-benzyloxazolidin-2-one.

N-((2'*R*)-2'-(1-Adamantyl)acetoacetyl)-(4*S*)-4-benzyloxazolidin-2-one (**RS-4m**) (2.12 g, 32%) was a solid, mp 89-90°C (hexanes –dichloromethane – diethyl ether); ir (KBr): 2911, 2848, 1783, 1721, 1689 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.60-2.04 (m, 15H), 2.35 (s, 3H), 2.71 (dd, J = 9.9 and 13.2 Hz, 1H), 3.30 (dd, J = 2.9 and 13.2 Hz, 1H), 4.16 (m, 2H), 4.68 (m, 1H), 4.86 (s, 1H), 7.15-7.35 (m, 5H); ^{13}C nmr (deuteriochloroform): δ 28.4, 33.3, 36.4, 37.2, 38.0, 40.0, 55.3, 65.7, 66.3, 127.1, 128.7, 129.2, 134.9, 153.3, 167.2, 202.6; $[\alpha]_D$ = +21 (chloroform, c = 1.00).

N-((2'*S*)-2'-(1-Adamantyl)acetoacetyl)-(4*S*)-4-benzyloxazolidin-2-one (**SS-4m**) (1.56 g, 24%) was a solid, mp 161-162°C (hexanes – ethyl acetate); ir (KBr): 2902, 2851, 1779, 1721, 1690 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.65-2.05 (m, 15H), 2.32 (s, 3H), 2.64 (dd, J = 10.2 and 13.1 Hz, 1H), 3.39 (dd, J = 3.7 and 13.1 Hz, 1H), 4.11 (m, 2H), 4.70 (m, 1H), 4.93 (s, 1H), 7.18-7.40 (m, 5H); ^{13}C nmr (deuteriochloroform): δ 28.5, 34.4, 36.5, 38.1, 38.6, 40.1, 55.4, 65.8, 66.4, 127.2, 128.8, 129.2, 135.0, 153.5, 167.6, 202.9; $[\alpha]_D$ = +56 (chloroform, c = 1.00).

Anal. Calcd for $C_{24}H_{29}NO_4$: C, 72,88; H, 7.39; N, 3.54. Found: C, 72.78; H, 7.40; N, 3.55.

N-(1-Adamantyl)-(4*S*)-4-benzyloxazolidin-2-one (0.73g) was a solid, mp 115-117°C (hexanes – dichloromethane – diethyl ether); ir (KBr): 2968, 2912, 2853, 1743 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.65-1.90 (m, 6H), 2.05-2.38 (m, 9H), 2.68 (dd, J = 11.0 and 13.5 Hz, 1H), 3.18 (dd, J = 2.9 and 13.5 Hz, 1H), 3.82-4.06 (m, 3H), 7.05-7.40 (m, 5H); ^{13}C nmr (deuteriochloroform): δ 29.5, 36.0, 40.3, 54.4, 56.2, 65.5, 126.9, 128.7, 129.0, 136.3, 155.9; $[\alpha]_D$ = +33 (chloroform, c = 1.00).

Anal. Calcd for $C_{20}H_{25}NO_2$: C, 77.13; H, 8.09; N, 4.49. Found: C, 77.11; H, 8.16; N, 4.43.

N-(2'-(9''-Xanthenyl)acetoacetyl)-4-benzyloxazolidin-2-ones (**4n**) (Entry 1, Table 4).

A mixture of xanthydrol (0.300 g, 1.585 mmoles), (4*S*)-4-benzyloxazolidin-2-one (**3**) (0.376 g, 1.441 mmoles), acetic acid (1 ml) and ethanol (1 ml) was stirred at room temperature for 16 hours. The formed solid (isomer *S*, 0.157 g) was filtered off. The filtrate was evaporated to dryness to afford an oil (0.514 g) which was chromatographed through silica gel with hexanes - diethyl ether (3:2) to afford xanthene (0.016 g) [21], (2'*R*,4*S*)-*N*-(2'-(9''-xanthenyl)acetoacetyl)-4-benzyloxazolidin-2-one (**R-4n**) (0.465 g), and (2'*S*,4*S*)-*N*-(2'-(9''-xanthenyl)acetoacetyl)-4-benzyloxazolidin-2-one (**S-4n**) (0.030 g). Overall yield was 97%.

(2'*R*,4*S*)-*N*-(2'-(9''-Xanthenyl)acetoacetyl)-4-benzyloxazolidin-2-one (**R-4n**), was an oil, ir (film on KBr): 1780, 1721, 1697, 1478, 1358, 1254, 762 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.74 (s, 3H), 2.73 (dd, J = 13.2 and 9.5 Hz, 1H), 3.27 (dd, J = 13.2 and 2.9 Hz, 1H), 3.87 (t, J = 8.4, 1H), 4.03 (dd, J = ca. 9 and 2.0 Hz, 1H), 4.45 (m, 1H), 5.04 (d, J = 8.8 Hz, 1H), 5.13 (d, J = 8.8 Hz, 1H), 7.04 (m, 2H), 7.1-7.4, 11H); ^{13}C nmr (deuteriochloroform): δ 31.5, 37.4, 39.2, 55.5, 64.6, 66.2, 116.9, 122.4, 123.2, 123.7, 123.9, 127.3, 128.3, 128.5, 128.9, 129.1, 129.4, 129.5, 135.0, 153.0, 153.4, 167.1, 202.5; ms: m/z 441 (M,1), 221 (9), 182 (17), 181 (100), 152 (11), 92 (9); $[\alpha]_D$ = +98 (chloroform, c = 1.036).

Anal. Calcd. for $C_{27}H_{23}NO_5$: C, 73.45; H, 5.26; N, 3.17. Found: C, 73.37; H, 5.28; N, 3.10.

(2'*S*,4*S*)-*N*-(2'-(9''-Xanthenyl)acetoacetyl)-4-benzyloxazolidin-2-one (**S-4n**) presented mp 200-202°C; ir (KBr): 1763, 1710, 1485, 1263, 761 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.70 (s, 3H), 2.60 (dd, J = 13.9 and 8.8 Hz, 1H), 3.05 (dd, J = 13.2 and 2.9 Hz, 1H), 4.05 (dd, J = 8.8 and 2.9 Hz, 1H), 4.13 (dd, J = *ca.* 9 and 8.8 Hz, 1H), 4.73 (m, 1H), 5.0-5.1 (nearly collapsed AB system, 2H), 6.85 (bs, 2H), 7.06 (m, 2H), 7.2-7.3 (m, 8H), 7.42 (d, J = 7.3 Hz, 1H); ^{13}C nmr (deuteriochloroform): δ 32.0, 39.3, 39.7, 54.7, 65.1, 66.0, 116.9, 122.1, 123.5, 123.7, 124.2, 127.3, 128.4, 128.6, 128.9, 129.3, 129.4, 134.5, 153.2, 153.4, 153.8, 167.0, 203.3; ms: m/z 441 (M,1), 221 (12), 182 (17), 181 (100), 152 (9); $[\alpha]_D$ = +96 (chloroform, c = 1.155).

Anal. Calcd. for $C_{27}H_{23}NO_5$: C, 73.45; H, 5.26; N, 3.17. Found: C, 73.30; H, 5.42; N, 3.15.

N-(2'-(9''-Thiaxanthenyl)acetoacetyl)-4-benzyloxazolidin-2-ones (**4o**).

A mixture of thiaxanthydrol (1.000 g, 4.872 mmoles), (4*S*)-4-benzyloxazolidin-2-one (**3**) (0.849 g, 3.248 mmoles), acetic acid (3.4 ml) and ethanol (3.4 ml) was stirred at room temperature for 21 hours. The formed solid (isomer *R* and thiaxanthone [21], 1.055 g) was filtered off. The filtrate was evaporated and the residue contained **3** (nmr monitoring). Therefore, this mixture was further treated in the darkness with thiaxanthydrol (0.246 g, 1.199 mmoles) in ethanol (1 ml) and acetic acid (1 ml) under stirring for 17 hours. The formed solid (isomer **R-4o**, thiaxanthene [21], and thiaxanthone [21], 0.348 g) was filtered off and the filtrate was evaporated to afford an oily residue (0.527 g). The combined solids containing **R-4o** were chromatographed through a silica gel column with hexanes - diethyl ether (8:2), to afford thiaxanthene [21] (0.070 g), thiaxanthone [21] (0.387 g), and **R-4o** (0.848 g). The oily residue was chromatographed with hexanes - diethyl ether (9:1) to afford thiaxanthene [21] (0.041 g), thiaxanthone [21] (0.061 g), **R-4o** (0.270 g), and **S-4o** (0.301 g). The overall yield of **4o** was 98%.

(2'*R*,4*S*)-*N*-(2'-(9''-Thiaxanthenyl)acetoacetyl)-4-benzyloxazolidin-2-one (**R-4o**) was a solid, mp 176-177°C; ir (KBr): 1775, 1710, 1696, 1390, 1354, 1262, 761, 739 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.61 (s, 3H), 2.72 (dd, J = 13.2 and 9.5 Hz, 1H), 3.27 (dd, J = 13.2 and 2.9 Hz, 1H), 3.92 (apparent t, J = 8.4 Hz, 1H), 4.05 (dd, J = 9.5 and 2.2 Hz, 1H), 4.41 (m, 1H), 5.13 (d, J = 11.0 Hz, 1H), 5.62 (d, J = 11.0 Hz, 1H), 7.22 (m, 10H), 7.47 (m, 2H), 7.58 (m, 1H); ^{13}C nmr (deuteriochloroform): δ 31.2, 37.1, 48.4, 55.3, 56.2, 66.1, 126.5, 126.9, 127.0, 127.2, 127.3, 127.4, 128.8, 129.4, 130.2, 130.8, 134.1, 135.2, 153.0, 166.8, 203.3; ms: m/z 198 (16), 197 (100), 165 (13); $[\alpha]_D$ = +53 (chloroform, c = 1.070).

Anal. Calcd for $C_{27}H_{23}NO_4S$: C, 70.88; H, 5.08; N, 3.06. Found: C, 70.70; H, 5.25; N, 3.04.

(2'*S*,4*S*)-*N*-(2'-(9''-Thiaxanthenyl)acetoacetyl)-4-benzyloxazolidin-2-one (**S-4o**) was an oil, ir (film on KBr): 1777, 1720, 1694, 1393, 1358, 1253, 1225, 1199, 758 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.50 (s, 3H), 2.46 (dd, J = 13.5 and 7.7 Hz, 1H), 2.76 (dd, J = 13.5 and 3.3, 1H), 3.98 (dd, J = 9.5 and 3.6, 1H), 4.10 (apparent t, J = 8.7 Hz, 1H), 4.66 (m, 1H), 5.13 (d, J = 11.0 Hz, 1H), 5.73 (d, J = 11.0 Hz, 1H), 6.70 (bd, 2H), 7.22 (m, 8H), 7.51 (m, 2H), 7.65 (bd, 1H); ^{13}C nmr (deuteriochloroform): δ 31.5, 37.0, 48.9, 54.4, 56.4, 65.8, 126.6, 127.0, 127.3, 127.4, 127.5, 128.8, 129.2, 130.0, 131.1, 133.5, 134.2, 134.3; ms: m/z 198 (17), 197 (100), 165 (11); $[\alpha]_D$ = +81 (chloroform, c = 1.020).

Anal. Calcd for $C_{27}H_{23}NO_4S$: C, 70.88; H, 5.08; N, 3.06. Found: C, 71.06; H, 5.58; N, 2.81.

N-(2'-(5''*H*-Dibenzo[*a,d*]cyclohepten-5''-yl)acetoacetyl)-4-benzyloxazolidin-2-ones (**4p**).

These isomers were obtained as for **4n**, from **3** (0.191 g, 0.731 mmole) and dibenzosuberenol (5*H*-dibenzo[*a,d*]cyclohepten-5-ol)

(0.171 g, 0.821 mmole), in acetic acid (2.0 ml) and *tert*-butanol (0.8 ml). Overall yield was nearly quantitative.

(2'*R*,4*S*)-*N*-(2'-(5"*H*-Dibenzo[*a*,*d*]cyclohepten-5"-yl)acetoacetyl)-4-benzyloxazolidin-2-one (**R-4p**) presented mp 186-187°C; ir (KBr): 1773, 1708, 1694 (sh), 1351, 1263 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.62 (s, 3H), 2.61 (dd, J = 13.2 and 9.5 Hz, 1H), 3.15 (dd, J = 13.9 and 2.9 Hz, 1H), 3.83 (apparent t, J = 8.0 Hz, 1H), 3,98 (dd, J = 9.5 and 2.2 Hz, 1H), 4.21 (m, 1H), 4.95 (d, J = 11.7 Hz, 1H), 5.76 (d, J = 11.7 Hz, 1H), 7.00-7.15 (m, 4H), 7.16-7.45 (m, 10H), 7.53 (d, J = 7.3 Hz, 1H); ^{13}C nmr (deuteriochloroform): δ 31.3, 37.1, 53.7, 55.2, 55.4, 66.0, 127.8, 128.2, 128.8, 129.2, 129.4, 129.7, 130.6, 130.9, 131.4, 133.9, 134.8, 134.9, 136.2, 136.9, 153.1, 166.9, 203.5; ms: m/z 451 (M,2), 203 (31), 202 (32), 192 (17), 191 (100), 190 (45), 189 (75), 165 (43), 91 (34); $[\alpha]_D$ = +42 (chloroform, c = 1.150).

Anal. Calcd for $C_{29}H_{25}NO_4$: C, 77.13; H, 5.59; N, 3.10. Found: C, 77.08; H, 5.75; N, 2.99.

(2'*S*,4*S*)-*N*-(2'-(5"*H*-Dibenzo[a,d]cyclohepten-5"-yl)acetoacetyl)-4-benzyloxazolidin-2-one (**S-4p**) presented mp 132-133°C; ir (KBr): 1776, 1721, 1693, 1393, 1358, 1263, 1201 cm^{-1}; ^1H nmr (deuteriochloroform): δ 1.60 (s, 3H), 2.19 (dd, J = 13.9 and 8.0 Hz, 1H), 2.50 (dd, J = 13.9 and 3.7 Hz, 1H), 3.96 (dd, J = 8.8 and 3.7 Hz, 1H), 4.06 (t, J = 8.8 Hz, 1H), 4.53 (m, 1H), 5.02 (d, J = 11.7 Hz, 1H), 5.94 (d, J = 11.7 Hz, 1H), 6,73 (m, 2H), 7.12 (s, 2H), 7.15-7.40 (m, 10H), 7.55 (d, J = 8.0 Hz, 1H); ^{13}C nmr (deuteriochloroform): δ 31.6, 36.8, 54.3, 54.4, 55.6, 65.7, 127.0, 127.2, 127.4, 128.8, 129.2, 129.3, 129.9, 130.6, 131.1, 131.5, 131.8, 134.1, 134.6, 134.9, 136.3, 136.8, 153.2, 166.9, 203.5; ms: m/z 451 (M,1), 192 (18), 191 (100), 190 (6), 189 (8), 165 (6), 91 (8); $[\alpha]_D$ = +71 (chloroform, c = 0.045).

Anal. Calcd for $C_{29}H_{25}NO_4$: C, 77.13; H, 5.59; N, 3.10. Found: C, 76.90; H, 5.64; N, 2.85.

Single Crystal X-Ray-diffraction of **S-4i**.

A colourless prismatic single crystal of dimensions 0.39 x 0.35 x 0.25 mm^3 was selected for the X-Ray experiment which was performed on an Enraf-Nonius CAD4 diffractometer using MoKα radiation. Resulting crystal data were: a = 10.714(2), b = 6.235(5), c = 15.109(3) Å, α = 90.00(3), β = 95.210(10), γ = 90.00(3)°, V = 1005.1(9) $Å^3$, Z = 2, D_X = 1.422 Mg/m^3, μ = 2.070 mm^{-1}, monoclinic P 2_1. Up to 2Θ = 52.5°, 2310 reflections were collected, -13<=h<=13, -7<=k<=0, 0<=l<=18, which were reduced and corrected from the Lorenz, polarisation and absorption (PSI scan, max. and min. transmission 0.6256 and 0.4990) effects. The structure was solved by direct methods (*SHELXS-97*) [22] and refined by full-matrix least-squares on F^2 (*SHELXL-97*) [22]. Final R indices for [I>2sigma(I)] were R1 = 0.0927, wR2 = 0.2515 and those for all data were R1 = 0.2473, wR2 = 0.2946. The absolute structure parameter was -0.02(4), which allows us to establish the absolute configuration. The largest peak and hole in the last Fourier map were 0.625 and -1.255 e.$Å^{-3}$.

Single crystal X-Ray-diffraction of **R-4o**.

A colourless prismatic single crystal of dimensions 0.39 x 0.25 x 0.15 mm^3 was selected for the X-Ray experiment which was performed on an Enraf-Nonius CAD4 diffractometer using MoKα radiation. Resulting crystal data were: a = 7.397(3), b = 15.410(3), c = 19.390(2) Å, V = 2210.2 $Å^3$, Z = 4, D_X = 1.375 Mg/m^3, μ = 0.182 mm^{-1}, orthorhombic P $2_12_12_1$. Up to 2Θ = 60°, 3633 reflections were collected, 0<=h<=10, 0<=k<=21, 0≤=l≤=27, which were reduced and corrected from the Lorenz, polarisation and absorption (PSI scan, max. and min. transmission 0.9983 and 0.9714) effects. The structure was solved by direct methods (*SHELXS-97*) [22] and refined by full-matrix least-squares on F^2 (*SHELXL-97*) [22]. Final R indices for [I>2sigma(I)] were R1 = 0.055, wR2 = 0.104 and those for all data were R1 = 0.151, wR2 = 0.121. The absolute structure parameter was -0.22(13), which allows us to establish the absolute configuration. The largest peak and hole in the last Fourier map were 0.21 and -0.26 e.$Å^{-3}$.

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REFERENCES AND NOTES

[1a] G. Bram, D. Cabaret, Z. Welvart, N. W. A. Geraghty, and J. Garvey, *Tetrahedron Lett.*, **29**, 4615 (1988); [b] Q. Zhang, R. M. Mohan, L. Cook, S. Kazanis, D. Peisach, B. M. Foxman, and B. B. Snider, *J. Org. Chem.*, **58**, 7640 (1993); [c] J. L. Marco, N. Martín, A. Martínez-Grau, C. Seoane, A. Albert, and F. H. Cano, *Tetrahedron*, **50**, 3509 (1994).

[2] T. Hamamoto, T. Katsuki, and M. Yamaguchi, *Tetrahedron Lett.*, **27**, 2463 (1986).

[3a] C. Cativiela, M. D. Diaz-de-Villegas, and J. A. Gálvez, *Tetrahedron: Asymmetry*, **5**, 261 (1994); [b] C. Cativiela, M. D. Diaz-de-Villegas, and J. A. Gálvez, *Tetrahedron*, **50**, 9837 (1994); [c] C. Cativiela and M. D. Diaz-de-Villegas, *Tetrahedron*, **51**, 5921 (1995); [d] C. Cativiela, M. D. Diaz-de-Villegas, and J. A. Gálvez, *Tetrahedron*, **52**, 687 (1996); [e] R. Badorrey, C. Cativiela, M. D. Diaz-de-Villegas, J. A. Gálvez, and Y. Lapena, *Tetrahedron: Asymmetry*, **8**, 311 (1997).

[4a] K. Tomioka, K. Ando, Y. Takemasa, and K. Koga, J. *Am. Chem. Soc.*, **106**, 2718 (1988); [b] K. Ando, Y. Takemasa, K. Tomioka, and K. Koga, *Tetrahedron*, **49**, 1579 (1993); [c] K. Ando, K. Yasuda, K. Tomioka, and K. Koga, J. *Chem. Soc., Perkin Trans. I*, 277 (1994). [d] K. Ando, W. Seo, K. Tomioka, and K. Koga, *Tetrahedron*, **50**, 13081 (1994).

[5] G. I. Georg, X. Guan, and J. Kant, *Tetrahedron Lett.*, **29**, 403 (1988).

[6] N. S. Barta, A. Brode, and J. R. Stille, *J. Am. Chem. Soc.*, **116**, 6201 (1994).

[7] For a review on the use of Oppolzer's sultam see: W. Oppolzer, *Tetrahedron*, **43**, 1969 (1987).

[8] For a review on the use of Evans oxazolidinones and related amino alcohols see: D. J. Ager, I. Prakash, and D. R. Schaad, *Chem. Rev.*, **96**, 835 (1996).

[9] For reviews on the use of carbohydrates and derivatives as chiral inductors see: [a] H. Kunz and K. Rück, *Angew. Chem., Int. Ed. Engl.* **32**, 336 (1993); [b] P.G. Hultin, M.A. Earle, and M. Sudharshan, *Tetrahedron*, **53**, 14823 (1997).

[10a] J. Marquet and M. Moreno-Mañas, *Synthesis*, 348 (1979); [b] A. González, J. Marquet, and M. Moreno-Mañas, *Tetrahedron*, **42**, 4253 (1986); [c] A. González, J. Marquet, and M. Moreno-Mañas, *Tetrahedron Lett.*, **29**, 1469 (1988); [d] A. Vallribera, J. Marquet, M. Moreno-Mañas, and E. Cayón, *Tetrahedron*, **49**, 6437 (1993); [e] A. Vallribera, N. Serra, J. Marquet, and M. Moreno-Mañas, *Tetrahedron*, **49**, 6451 (1993); [f] M. Moreno-Mañas, J. Marquet, and A. Vallribera, *Tetrahedron*, **52**, 3377 (1996).

[11] M. Moreno-Mañas, R. M. Sebastián, A. Vallribera, and E. Molins, *Tetrahedron*, **51**, 10795 (1995).

[12] M. Moreno-Mañas, R. M. Sebastián, A. Vallribera, E. Molins, and E. Espinosa, *Tetrahedron: Asymmetry*, **8**, 1525 (1997).

[13] M. Moreno-Mañas, R. M. Sebastián, E. Trepat, and A. Vallribera, *Tetrahedron: Asymmetry*, **10**, 4211 (1999).

[14] N. Gálvez, M. Moreno-Mañas, A. Vallribera, E. Molins, and A. Cabrero, *Tetrahedron Lett.*, **37**, 6197 (1996).

[15a] A. Campbell and J. Kenyon, *J. Chem. Soc.*, 25 (1946); [b] H. Wolff, *Org. React.*, **3**, 307 (1946); [c] G. I. Koldobskii, G. F. Tereshchenko, E. S. Gerasimova, and L. I. Bagal, *Russ. Chem. Rev.* **40**, 835 (1971); [d] J. March, Advanced Organic Chemistry, Reactions, Mechanisms and Structure, 4th ed., Wiley Interscience, New York, 1992. (15b).

[16a] E. Sawicki and V. T. Oliverio, *J. Org. Chem.*, **21**, 183 (1956); [b] E. Y. Gren and G. Vanags, *Dokl. Akad. Nauk S.S.S.R.*, **133**, 588 (1960).

[17] N. Gálvez, M. Moreno-Mañas, R.M. Sebastián, and A. Vallribera, *Tetrahedron*, **52**, 1609 (1996).

[18] M. Lautens and A. Roy, *Org. Lett.*, **2**, 555 (2000).

[19] M. Moreno-Mañas, R.M. Sebastián, A. Vallribera, and F. Carini, *Synthesis*, 157(1999).

[20] For preparation of bis-tetraalkylammonium tetrahalogenometallates and metal complexes of acetoacetates of chiral inductors see: N. Gálvez, M. Moreno-Mañas, I. Padrós, R. M. Sebastián, N. Serra, and A. Vallribera, *Polyhedron*, **14**, 1397 (1995).

[21] Secondary alcohols xanthydrol and its thia analogue have propensity to desproportionate to the methylene and ketone groups in acidic media: [a] C. Finzi, *Gazz. Chim. Ital.* **62**, 211 (1932); [b] O. I. Magidson, *Ber.*, **58B**, 433 (1925).

[22] G. M. Sheldrick, *SHELXS-97*. Program for the solution of crystal structures, University of Göttingen, Germany, 1997.