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Enantioselective synthesis of 4,5-disubstituted pyrrolidin-2-one derivatives with two stereocenters on the basis of Michael adducts

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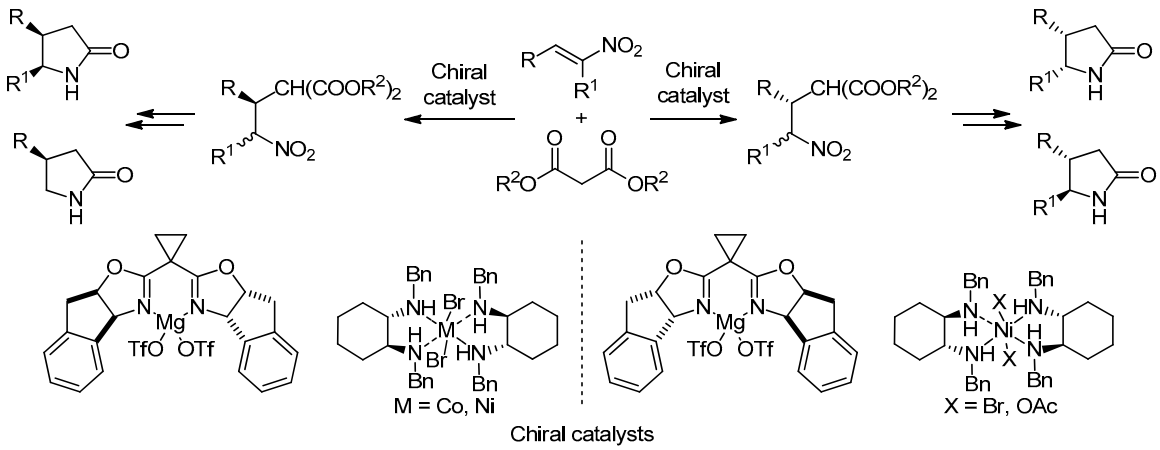


The addition of malonates to *trans*-β-alkyl-β-nitrostyrenes in the presence of chiral Mg^{2+} bisoxazoline complex and Ni^{2+} and Co^{2+} bis((*S*,*S*)- or (*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine) complexes resulted in the formation of Michael adducts with two stereocenters which were used as key precursors for the preparation of potentially biologically active enantiopure 4,5-disubstituted pyrrolidin-2-one derivatives.

Keywords: chiral Mg^{2+}, Ni^{2+}, and Co^{2+} complexes, 4,5-disubstituted pyrrolidin-2-ones, Michael adduct, asymmetric catalysis.

According to structure–activity relationships, the biological and pharmacological effectiveness of chiral γ-aminobutyric acid (GABA) and its cyclic pyrrolidin-2-one derivatives at the molecular level depends on the configuration of substituents providing optimal interaction with an appropriate receptor. Identification of stereoisomer with such properties usually involves the development of synthetic methodology suitable for the preparation of all possible isomers and their comparable biological testing. It explains the constant interest in the search for efficient chiral catalysts for the preparation of chiral Michael adducts and their subsequent conversion into biologically active compounds.

The above-mentioned conditions fully apply to investigations aimed at the synthesis of chiral drugs and biologically active compounds **1**–**8** on the basis of linear and cyclic GABA derivatives (Fig. 1). In the case of drugs **1**–**4** with one chiral center, their individual *R*- or *S*-enantiomers were obtained by the resolution of racemic molecules or by asymmetric synthesis in the presence of chiral catalysts.[1–5] The addition of a vicinal chiral center to the carbon skeleton of 2-pyrrolidinones **5**–**8** doubled the number of possible chiral enantiomers. The synthetic problems that arose during their preparation were also successfully solved by the usage of chiral catalysts, resulting in the formation of a pair of diastereoisomeric adducts usually as a mixture of *syn* and *anti* isomers suitable for their conversion into the target products.[6–8] A similar approach was developed for clausenamide **8** with three chiral centers in pyrrolidin-2-one heterocycle.[9]

In general, the majority of published data devoted to this problem have focused on the preparation of type **I**–**IV** adducts with one or two chiral centers that were successfully used as precursors in the preparation of mono- or disubstituted linear or cyclic GABA analogs with potential pharmaceutical application (Fig. 2).

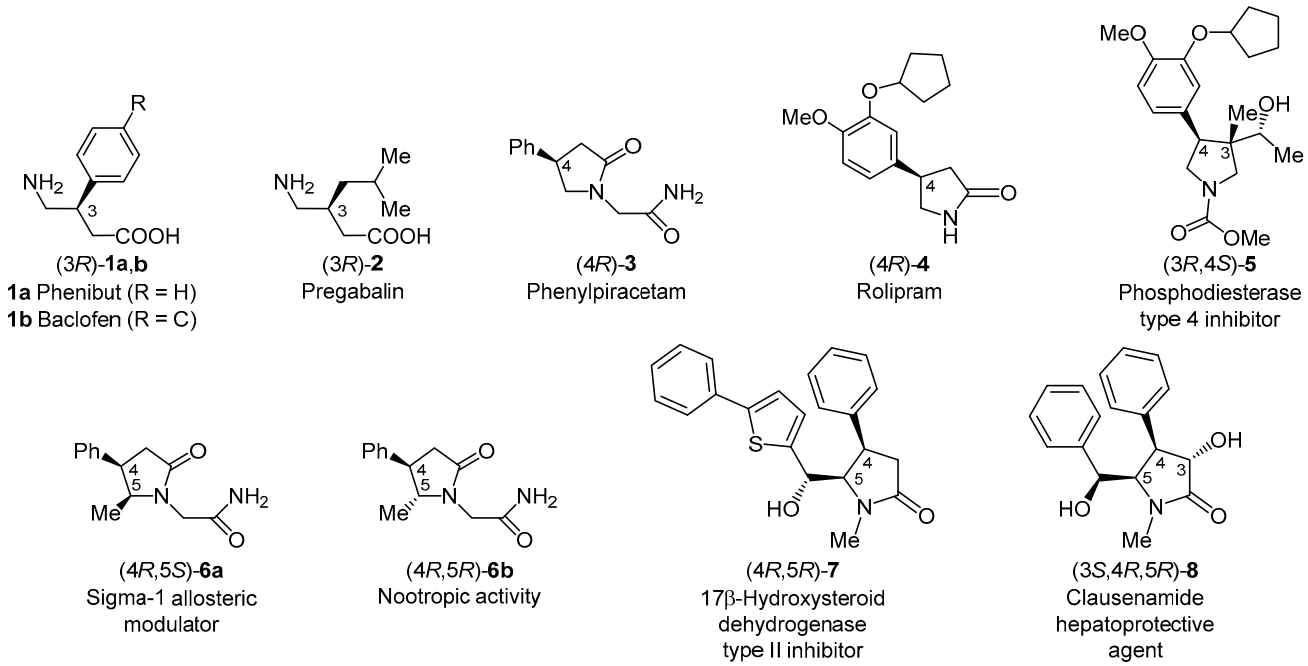


Figure 1. Chiral drugs and biologically active compounds on the basis of linear and cyclic GABA derivatives.

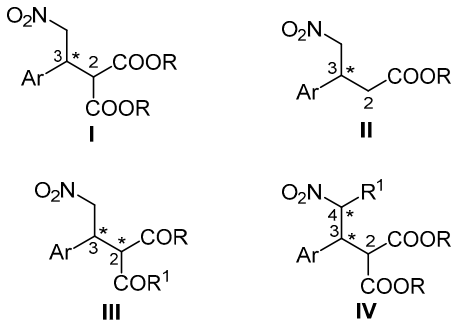


Figure 2. GABA precursors with one or two chiral centers.

According to the literature data, the catalysts used for the preparation of the above-mentioned substances can be divided into two categories: (1) complexes consisting of chiral ligands and metal ions[2,5a,6,10–14] and (2) chiral thiourea, guanidine derivatives, or nitrogen-containing heterocycles.[3,15–25] Despite the large number of studies carried out in the field of stereocontrolled Michael reactions leading to the preparation of the adducts of type **I**–**IV**, the possibilities of continued research in this direction are far from exhausted, especially regarding the synthesis of type **IV** compounds **13** and their further conversion into vicinally disubstituted enantiopure pyrrolidin-2-ones **14**, racetams **15**, or GABA **16** according to a common retrosynthetic design starting from nitroalkenes **9** or nitroalkanes **11** and malonic esters **10**, **12** (Scheme 1), which became the main purpose of the present research.

In accordance with the task described above, our efforts were focused on the preparation of Michael adducts **13** (Table 1) with vicinal chiral centers in positions 1 and 2 of the 2-nitroalkyl substituent with high *ee* values as a potentially easily separable mixture of enantiomers with *syn* or *anti* configuration suitable for conversion into four individual enantiopure 4,5-disubstituted pyrrolidin-2-ones **14**. In addition to the bis(oxazoline)Mg(OTf)$_2$ complexes **Aa** and **Ab** successfully employed for the preparation of type **I** adducts and adopted from Barnes research,[5a,7a] the following catalysts were also tested: (a) cinchona alkaloids cupreine (**Ba**) and cupreidine (**Bb**) which demonstrated excellent stereoselectivity in the case of unsubstituted nitrostyrene and malonate;[26] (b) Ni(II) bis((*S*,*S*)- or (*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine) complexes **C**–**E** characterized by high stereoselectivity in the case of nitrostyrene unsubstituted in the β-position and malonate;[10] (c) bis((*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine) complexes **F** with

Scheme 1. Retrosynthetic design leading to the stereocontrolled preparation of linear and cyclic disubstituted GABA derivatives

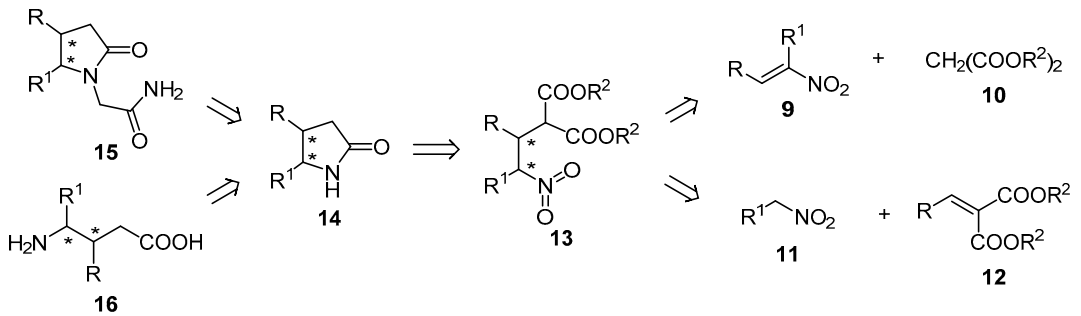
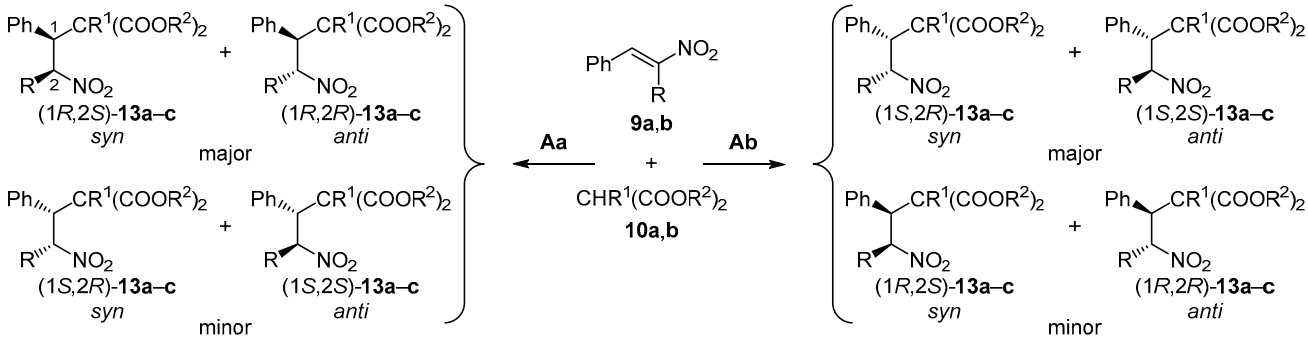


Table 1. Michael addition of malonates **10a**,**b** to *trans*-β-alkyl-β-nitrostyrenes **9a**,**b** in the presence of complexes **Aa** and **Ab**



Entry	Catalyst	Styrene	Malonate	R	R^1	R^2	Time, days	Product	Yield*, %	*ee***, %	*syn/anti****
1	**Aa**	**9a**	**10a**	Me	H	Et	7	**13a**	81	90 (90)	83/17 (80/20)
2	Base*[4]	**9a**	**10a**	Me	H	Et	7	**13a**	–	90 (90)	59/41 (60/40)
3	**Ab**	**9a**	**10a**	Me	H	Et	7	**13a**	79	80 (80)	63/37 (63/37)
4	**Aa**	**9b**	**10a**	Et	H	Et	7	**13b**	71	86 (78)	78/22 (68/32)
5	**Ab**	**9b**	**10a**	Et	H	Et	7	**13b**	72	84 (82)	73/27 (73/27)
6	**Aa**	**9a**	**10b**	Me	F	Me	4	**13c**	63	70 (76)	45/55 (48/52)
7	**Ab**	**9a**	**10b**	Me	F	Me	4	**13c**	51	94 (94)	53/47 (50/50)
8	TMG	**9a**	**10a**	Me	H	Et	1	**13a**	78	–	60/40
9	TMG	**9b**	**10a**	Et	H	Et	1	**13b**	69	–	65/35
10	TMG	**9a**	**10b**	Me	F	Me	1	**13c**	78	–	50/50

* Adducts were prepared in $CHCl_3$ (50 ml) containing malonate **9** (2.5 mmol), nitrostyrene **10** (2.5 mmol) in the presence of 30 mol % of catalyst, morpholine (12 ml, 0.14 mmol), and tetramethylguanidine (TMG) (12 ml, 0.09 mmol) at room temperature for 4–7 days. The evaluation of the content of individual diastereomers and enantiomers in adducts was performed on the basis of chiral HPLC retention time data after chromatographic purification of reaction product.

** *ee* Values for *syn* and *anti* (in brackets) diastereomers were calculated on the basis of HPLC data for the (1*R*,2*S*)/(1*S*,2*R*) and (1*R*,2*R*)/(1*S*,2*S*) pairs of enantiomers in accordance with the chirality of catalysts **Aa** and **Ab**.

*** *syn/anti* Diastereomeric ratios for the major and minor (in brackets) enantiomers were calculated on the basis of HPLC data for the integrated concentrations of the 1*R*,2*S*- and 1*R*,2*R*- or 1*S*,2*R*- and 1*S*,2*S*-stereoisomers in accordance with the chirality of catalysts **Aa** and **Ab**.

*[4] Chiral adduct **13a** (entry 1) after isolation was additionally treated by TMG at room temperature for 7 days.

Zn^{2+}, Mg^{2+}, Cu^{2+}, Fe^{3+}, Ba^{2+}, or Co^{2+} ions and (d) Co(II) bis((*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine) complex **G** (Fig. 3).

In addition to our previous research,[7a] it was found that complexes **Aa** and **Ab** provided high *ee* values for all four stereoisomers of adducts **13a**–**c** obtained by the conjugated addition of malonate **10a** not only to β-methyl-β-nitrostyrene **9a** (Table 1, entries 1–3), but also to its homolog **9b** (entries 4 and 5). According to literature data, a similar excess of *syn* stereoisomer (1*S*,3*R*)-**13b** was also obtained after the conjugated addition of nitropropane to benzylidenemalonate catalyzed by chiral *N*-spiro ammonium bromides.[25a]

The preferred formation of *syn* enantiomers **13a**,**b** with 1*R*,2*S*- or 1*S*,2*R*-configuration was also proved by the X-ray structural analysis of compound (1*R*,2*S*)-**13a** (Fig. 4). Similar tendency in the *syn*/*anti* ratio were observed even in the case of racemic compounds **13a**,**b** (entries 8, 9).

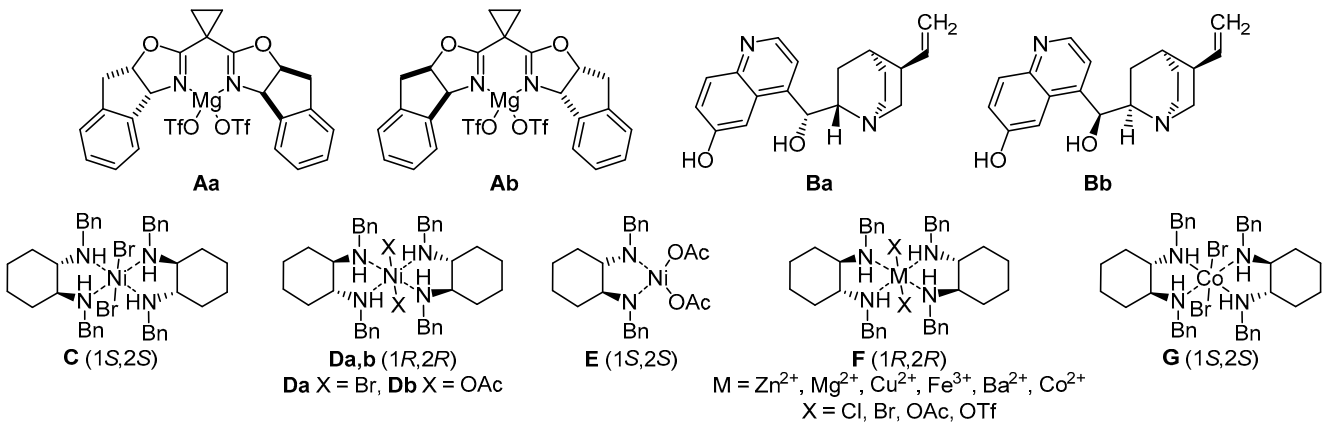


Figure 3. Chiral catalysts tested in the preparation of Michael adducts from nitroalkenes and malonates.

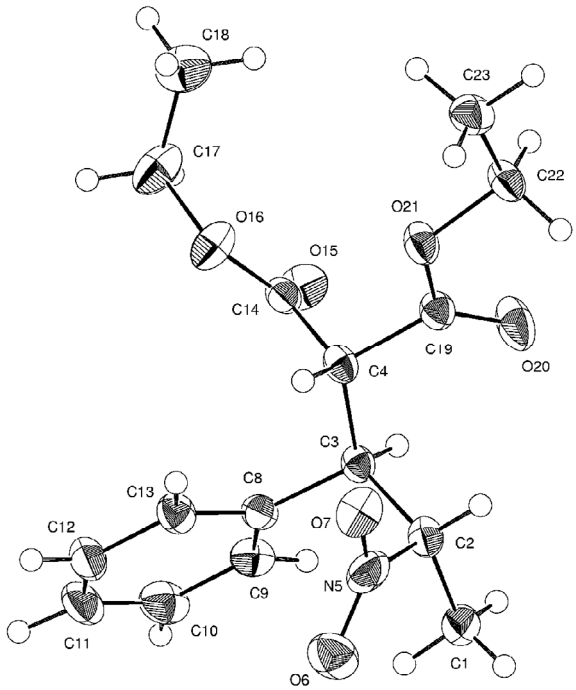


Figure 4. Molecular structure of compound (1*R*,2*S*)-**13a** with atoms representad as thermal vibration ellipsoids of 50% probability.

The higher stability of compound *syn*-(1*R*,2*S*)-**13b**, which has *gauche* conformation for the vicinal protons EtCH–CHPh, in comparison with its *anti*-(1*S*,2*R*)-**13b** isomer was proved using theoretical calculations of the potential energy surfaces (PES). In the case of compound *syn*-(1*R*,2*S*)-**13b** the two protons were characterized by a dihedral angle of $\phi_1 = 64.94°$. At the same time, the dihedral angle ϕ_2 between the vicinal protons PhCH–CH(COOEt)$_2$ was equal to 173.08° (Fig. 5). According to X-ray analysis data, molecule *syn*-(1*R*,2*S*)-**13a** is characterized with similar dihedral angles: $\phi_1 = 64.94°$ and $\phi_2 = 173.08°$.

In contrast, *anti* conformation of vicinal protons EtCH–CHPh and PhCH–CH(COOEt)$_2$ in compound (1*R*,2*R*)-**13b** isomer well agreed with the calculated dihedral angles of $\phi_1 = -169.62°$ and $\phi_2 = 164.99°$ in the appropriate conformer (Fig. 5). The calculated difference in free energies for the optimized conformers was positive and equal to 1.15 kcal/mol proving higher stability of compound *syn*-(1*R*,2*S*)-**13b**.

The *gauche* conformation for the vicinal protons at C-1 and C-2 stereocenters in compound **13a** could be partially changed in the favor of stereoisomers with an *anti* orientation. This effect was achieved by the treatment of the sample of compound **13a** obtained according to the procedure described in Table 1, entry 1, at room temperature in $CHCl_3$ for several days in the presence of a deprotonating agent such as a tetramethylguanidine (TMG) (Table 1, entry 2). It reduced the concentration of *syn* isomer (1*R*,2*S*)-**13a** by up to 23% in favor of *anti* isomer (1*R*,2*R*)-**13a** reaching the same *syn/anti* ratio as in the racemic mixture (entry 8) and with practically unchanged *ee* values in the beginning and the end of the experiment.

An increase in the concentration of the *anti* isomer observed in the experiments using styrene **9b** (Table 1, entries 4, 5, 9) and especially malonate **10b** (entries 6, 7, 10) indicated various possibilities to regulate the stereochemistry of C-2 atom in adducts **13a**–**c**.

However, the usage of this method is not very promising for the large-scale production of adducts due to the high concentration of catalysts **Aa** or **Ab** and a multiday duration of the reaction preferably at room temperature.

In continuation of the study, we applied cupreine (**Ba**) and cupreidine (**Bb**) catalysts which had been successfully used for the asymmetric preparation of type **I** Michael adducts.[26] Low *ee* values for stereoisomeric adducts **13a** presented in Scheme 2 demonstrated only moderate effectiveness of these catalysts.

Considerably better catalytic activity was demonstrated by chiral Ni(II) bis((*R*,*R*)- or (*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine) complexes **C**, **Da**,**b**, and **E** (Fig. 3) originally developed by Evans for the preparation of type **I** adducts.[10] According to the data presented in Table 2, the

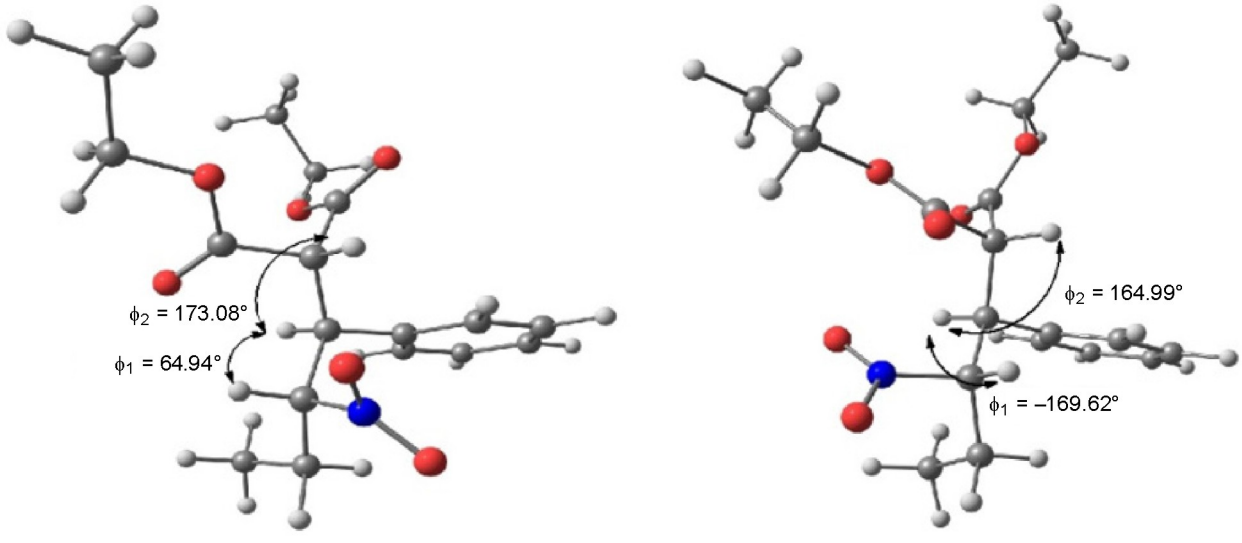


Figure 5. Calculated structure and dihedral angles for (1*R*,2*S*)-**13b** and (1*R*,2*R*)-**13b** conformers (Table 1, entry 4).

Scheme 2. Michael addition of malonate **10a** to *trans*-β-methyl-β-nitrostyrene (**9a**) in the presence of cupreine (**Ba**) and cupreidine (**Bb**)

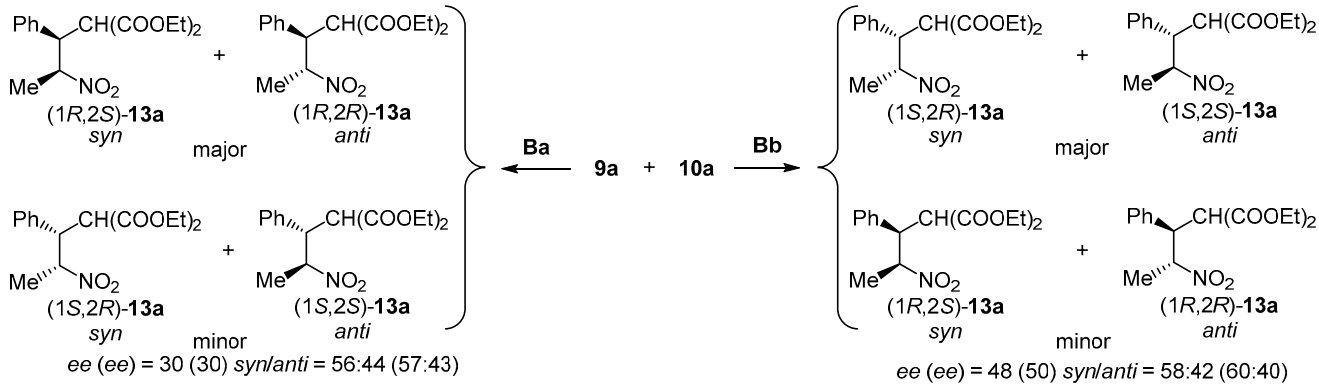
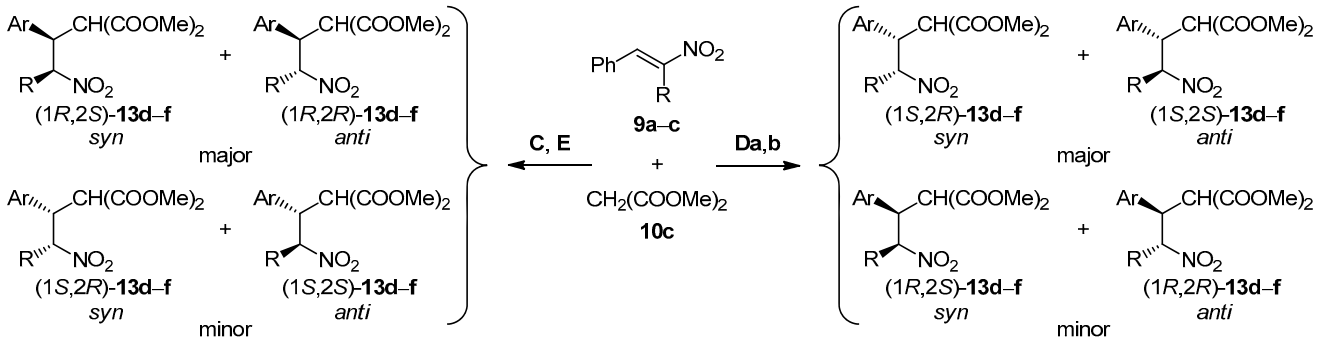


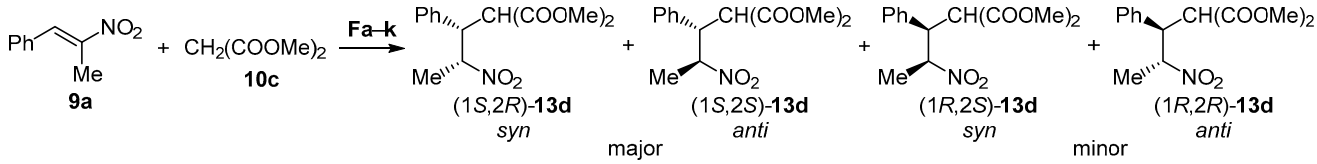
Table 2. Michael addition of malonate **10c** to *trans*-β-alkyl-β-nitrostyrenes **9a**–**c** in the presence of Ni^{2+} complexes **C**, **Da**,**b**, **E**



Entry	Catalyst*	Styrene	Ar	R	Temperature, °C	Time, h	Product	Yield, % *	*ee***, %	*syn/anti****
1	**C**	**9a**	Ph	Me	55	48	**13d**	54	90 (88)	72/28 (69/31)
2	**Da**	**9a**	Ph	Me	20	144	**13d**	46	88 (88)	70/30 (71/29)
3	**C**	**9a**	Ph	Me	55	72	**13d**	85	86 (90)	89/11 (84/16)
4	**Da**	**9a**	Ph	Me	55	72	**13d**	83	90 (94)	71/29 (79/21)
5	**E**	**9a**	Ph	Me	55	72	**13d**	62	84 (78)	53/47 (45/55)
6	**Da**	**9a**	Ph	Me	55	72	**13d**	84	90 (88)	56/44 (51/49)
7	**Db***[4]	**9a**	Ph	Me	55	72	**13d**	58	84 (77)	56/44 (48/52)
8	**C**	**9a**	Ph	Me	100	18	**13d**	87	76 (82)	60/40 (68/32)
9	**Da**	**9a**	Ph	Me	100	18	**13d**	86	82 (86)	62/38 (69/31)
10	**C***[5]	**9a**	Ph	Me	55	36	**13d**	95	84 (84)	58/42 (60/40)
11	**Da***[5]	**9a**	Ph	Me	55	36	**13d**	94	88 (88)	64/36 (75/25)
12	**C**	**9b**	Ph	Et	55	48	**13e**	45	80 (86)	58/42 (64/36)
13	**Da**	**9b**	Ph	Et	55	72	**13e**	75	82 (82)	62/38 (56/44)
14	**C**	**9c**	4-FC_6H_4	Me	55	72	**13f**	74	88 (84)	58/42 (48/52)
15	**Da**	**9c**	4-FC_6H_4	Me	55	72	**13f**	80	88 (90)	60/40 (65/35)
16	TMG	**9a**	Ph	Me	20	24	**13d**	78	–	51/49
17	TMG	**9b**	Ph	Et	20	24	**13e**	69	–	54/46
18	TMG	**9c**	4-FC_6H_4	Me	20	24	**13f**	78	–	60/40

* Reactions were performed in PhMe (10 ml) containing nitrostyrene **9a**–**c** (1.0 mmol), malonate **10c** (1.0 mmol), and Ni(II)-complex **C**, **Da**,**b**, **E** (6 mol %) in a screw cup vial at room or up to 100°C temperature controlling adduct formation by LC/MS analysis. The evaluation of the content of individual diastereomers and enantiomers in adducts was performed on the basis of chiral HPLC retention time data after chromatographic purification of reaction product.
** *ee* Values for *syn* and *anti* (in brackets) diastereomers were calculated as described for Table 1.
*** *syn/anti* Diastereomeric ratios for the major and minor (in brackets) enantiomers were calculated as described for Table 1.
*[4] Catalyst preparation was realized *in situ* directly in the reaction mixture.
*[5] Reaction was carried out in the absence of solvent.

Table 3. Michael addition of malonate **10c** to *trans*-β-alkyl-β-nitrostyrene (**9a**) in the presence of bis((*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine) complexes with metal ions **Fa**–**k***



Entry	Catalyst	Metal	X	Yield of compound **13d**, %	*ee***, %	*syn*/*anti****
1	**Fa**	Zn^{2+}	OAc	36	8 (24)	75/25 (67/33)
2	**Fb**	Zn^{2+}	OTf	38	64 (52)	60/40 (72/28)
3	**Fc**	Zn^{2+}	Cl	28	4 (0)	48/52 (63/37)
4	**Fd**	Zn^{2+}	Br	17	4 (0)	55/45 (57/43)
5	**Fe**	Mg^{2+}	OTf	82	54 (70)	80/20 (87/13)
6	**Ff**	Mg^{2+}	Cl	91	36 (40)	71/29 (73/27)
7	**Fg**	Cu^{2+}	OTf	33	58 (60)	67/33 (67/33)
8	**Fh**[a]	Fe^{3+}	OAc	30	4 (2)	60/40 (61/39)
9	**Fi**	Ba^{2+}	Cl	26	6 (6)	67/33 (67/33)
10	**Fj**	Co^{2+}	Cl	88	84 (84)	64/36 (66/64)
11	**Fk**	Co^{2+}	OAc	81	80 (78)	60/40 (55/45)

* Reactions were performed in PhMe (10 ml) containing nitrostyrene **9a** (1.0 mmol), malonate **10c** (1.0 mmol) using catalysts **Fa**–**k** (6 mol %) in a screw cup vial at 44°C controlling adduct formation by LC/MS analysis. Identification and quantitative evaluation of individual enantiomers in adducts **13d** was realized on the basis of chiral HPLC retention time data.
** *ee* Values for *syn* and *anti* (in brackets) diastereomers were calculated as described for Table 1.
*** *syn*/*anti* Diastereomeric ratios for the major and minor (in brackets) enantiomers were calculated as described for Table 1.

effectiveness of these complexes could be successfully extended to the preparation of adducts with two vicinal stereocenters with high *ee* values and increased diastereoselectivity toward the formation of *anti* isomers.

In addition, catalysts **C**, **Da**,**b**, and **E** preserved the important catalytic advantages developed in the Evans study such as relatively low catalyst loading (6 mol %), effectiveness in the absence of base and at elevated temperatures up to 100°C (Table 2, entries 8, 9). Moreover, the formation of type **IV** adducts with moderate results took place even in the absence of solvent (entries 10, 11). In the case of $Ni(OAc)_2$, its interaction with the ligand leading to the formation of catalytic complex **Db** was achieved *in situ* in a reaction mixture at 55°C (entry 7). The usage of β-nitrostyrenes **9b**,**c** modified in the β-position or aromatic ring resulted in the formation of adducts with similar characteristics.

The catalytic effectiveness of complexes **C**, **Da**,**b**, and **E** based on chiral *N*,*N*'-dibenzylcyclohexane-1,2-diamine ligands prompted us to explore the catalytic properties of the same ligand complexed with other metal ions. The data in Table 3 demonstrate the low catalytic efficiency or lack of it in the case of complexes **Fa**–**k** containing Zn^{2+}, Mg^{2+}, Fe^{3+}, Cu^{2+}, or Ba^{2+} ions. The only positive result was obtained in the presence of Co^{2+} complexes **Fj**,**k** (Table 3, entries 10 and 11). Similar catalytic properties for this ion were described for bis(imidazolidine)pyridine–$CoCl_2$ complex in 2019.[27]

In the continuation of this research, crystalline catalyst **G** on the basis $CoBr_2$ and two chiral (*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine ligands was prepared. Its X-ray analysis data (Fig. 6) demonstrated a *trans*-equatorial coordination of ligands with two H_2O molecules in apical positions, one of which was connected by hydrogen bonds with two bromine ions. The *ee* and *syn*/*anti* ratios values of stereoisomeric adducts **13d** prepared in the presence of compound **G** and presented in the Table 4 were similar to those demonstrated by catalyst **C** (Table 2, entries 1, 12, 14).

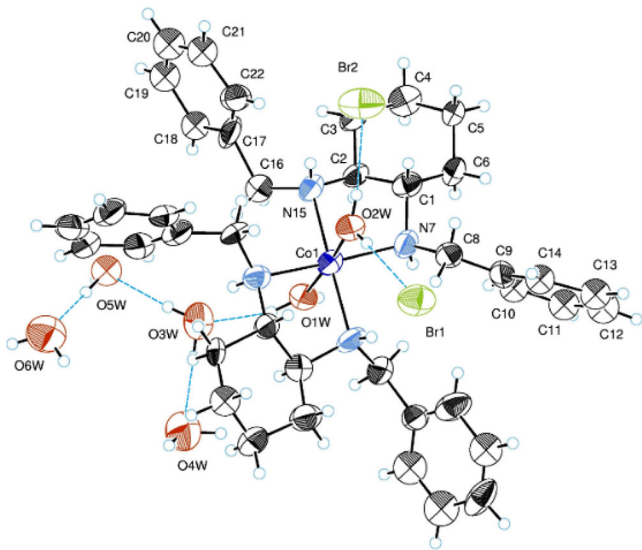
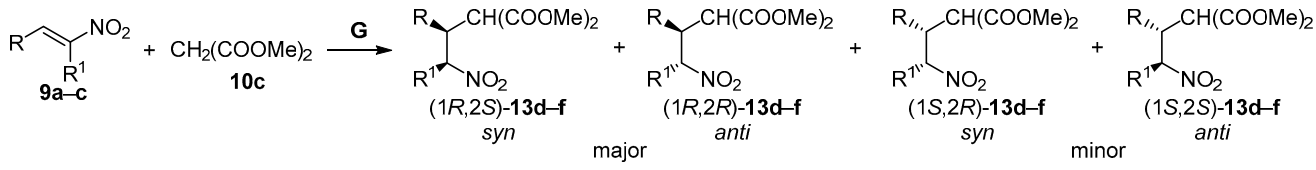


Figure 6. Molecular structure of cobalt(II) bis((*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine) complex **G** with atoms representad as thermal vibration ellipsoids of 50% probability.

Table 4. Michael addition of malonate **10c** to *trans*-β-alkyl-β-nitrostyrenes **9a**–**c** in the presence of a Co(II) bis((*S*,*S*)- *N*,*N*'-dibenzylcyclohexan-1,2-diamine) complex **G***



Entry	Styrene	R	R^1	Solvent	Product	Yield, %	*ee***, %	*syn*/*anti****
1	**9a**	Ph	Me	Me_2CO	**13d**	86	90 (62)	65/35 (29/71)
2	**9a**	Ph	Me	PhMe	**13d**	84	82 (90)	60/40 (76/24)
3	**9a**	Ph	Me	EtOAc	**13d**	81	84 (52)	66/34 (34/66)
4	**9b**	Ph	Et	PhMe	**13e**	78	82 (86)	60/40 (65/35)
5	**9c**	4-FC_6H_4	Me	PhMe	**13f**	85	78 (70)	58/42 (50/50)

* Reactions were performed in PhMe (10 ml) containing nitrostyrene **9a**–**c** (1.0 mmol), malonate **10c** (1.0 mmol) using catalyst **G** (6 mol %) in a screw cup vial for 24 h at 45°C controlling adduct formation by LC/MS analysis. The evaluation of the content of individual diastereomers and enantiomers in adducts was performed on the basis of chiral HPLC retention time data after chromatographic purification of reaction product.
** *ee* Values for *syn* and *anti* (in brackets) diastereomers were calculated as described for Table 1.
*** *syn*/*anti* Diastereomeric ratios for the major and minor (in brackets) enantiomers were calculated as described for Table 1.

The stereocontrolled preparation of new Michael adducts **13e**,**f** with two stereocenters in the C-1 and C-2 positions catalyzed by Ni(II) complexes **C** and **Da** allowed to transform them into four enantiopure 4,5-disubstituted pyrrolidin-2-ones **14a**,**b** using methodology developed in our previous study.[7a] It included: (a) hydrolysis and decarboxylation of enantiomerically enriched diastereomer mixtures (1*R*,2*S*)/(1*R*,2*R*) and (1*S*,2*R*)/(1*S*,2*S*) of the respective compounds **13e**,**f** into intermediate 4-nitrobutanoic acids followed by their conversion into appropriate methyl esters: (1*R*,2*S*)/(1*R*,2*R*)- and (1*S*,2*R*)/(1*S*,2*S*)-**17a**,**b**; (b) chromatographic separation of *syn* and *anti* diastereoisomers; (c) reduction and cyclization of individual methyl 4-nitrobutanoates (3*R*,4*S*)-, (3*R*,4*R*)-, (3*S*,4*R*)-, and (3*S*,4*S*)-**17a**,**b** into 4,5-disubstituted pyrrolidin-2-ones (4*R*,5*S*)-, (4*R*,5*R*)-, (4*S*,5*R*)-, and (4*S*,4*S*)-**14a**,**b** (Scheme 3). The corresponding racemic compounds **14a**,**b** have been described previously.[28]

Experimental realization of decarboxylation and reesterification processes (Scheme 3) in rather aggressive conditions created a risk of the racemization of intermediates **17e**,**f** and, accordingly, final products **14a**,**b**. However, the comparison of *ee* and *syn/anti* ratio data for the starting stereoisomeric mixtures (1*R*,2*S*)/(1*R*,2*R*)-**13e** and (1*S*,2*R*)/(1*S*,2*S*)-**13e** and four final products (4*R*,5*S*)-, (4*R*,5*R*)-, (4*S*,5*R*)-, and (4*S*,4*S*)-**14a** (Table 5) demonstrated retention of chiral stability during the whole process.

The presented study offers comparative analysis of the catalytic effectiveness of already known and new chiral catalysts in the preparation of Michael adducts with two vicinal stereocenters. The most promising were chiral Mg(II) bis(oxazoline)$_2$ complex, as well as Ni(II) or Co(II) bis((*S*,*S*)-

Scheme 3. Conversion of adducts **13e**,**f** into enantiopure 3,4-disubstituted pyrrolidin-2-ones **14a**,**b**

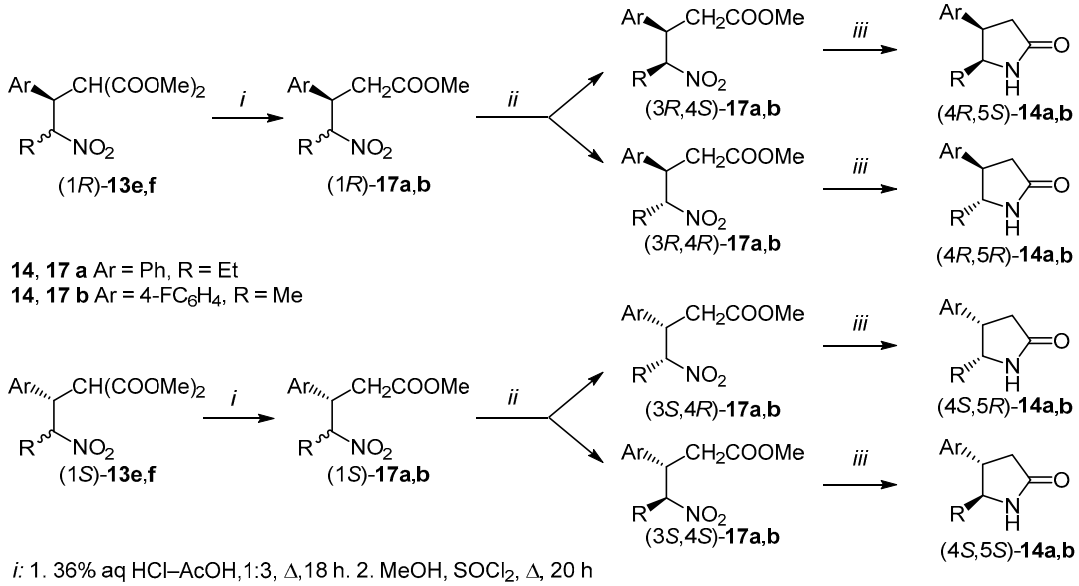


Table 5. Enantiomeric excess (*ee*) ratio of pyrrolidin-2-ones **14a** in comparison with the corresponding starting nitro adducts **13e**

Adducts **13e***	*ee***, %	*syn/anti****	Pyrrolidin-2-ones	*ee***, %	*cis/trans****
(1*R*,2*S*)/(1*R*,2*R*)-**13e**	80 (80)	58/42	*cis*-(4*R*,5*S*)-**14a**	83 (84)	90/10
			trans-(4*R*,5*R*)-**14a**	88 (86)	6/94
(1*S*,2*R*)/(1*S*,2*S*)-**13e**	82 (82)	62/38	*cis*-(4*S*,5*R*)-**14a**	82 (82)	91/9
			trans-(4*S*,4*S*)-**14a**	90 (82)	7/93

* Table 2, entries 12, 13.
** *ee* Values for major and minor (in brackets) diastereomers.
*** Data for the major enantiomer only.

or (*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine) complexes, which were successfully employed in the preparation of adducts with fixed configuration of C-1 and variable one of C-2 chiral center. In addition, the adducts thus obtained were successfully converted into enantiopure 4,5-disubstituted pyrrolidin-2-ones useful as key intermediates in the preparation and biological testing of appropriate racetams or GABA derivatives.

Experimental

The IR spectra were recorded on a Shimadzu IRPrestige-21 Fourier transform infrared spectrophotometer in thin films. The one-dimensional ^{1}H, ^{13}C, and ^{19}F NMR spectra (400, 100, and 376 MHz, respectively) and two-dimensional NOESY, ^{1}H–^{13}C HMBC, ^{1}H–^{13}C HSQC spectra were recorded on a Varian Mercury 400 instrument in $CDCl_3$ at 25°C. The chemical shifts of the hydrogen and carbon atoms are referred to the residual signals of $CDCl_3$ at 7.26 (^{1}H) and 77.0 (^{13}C) ppm, respectively. Complete ^{1}H and ^{13}C NMR signal assignments and the identification of stereochemistry of pairs of diastereomers were made by homonuclear and heteronuclear 2D NMR experiments with the special attention to homonuclear ^{1}H–^{1}H and heteronuclear ^{1}H–^{13}C coupling constants. The ^{19}F NMR signals were indirectly referenced to $CFCl_3$. LC/MS analysis data were obtained using a Waters Acquity UPLC system with a photodiode array detector, Acquity UPLC BEH C18 1.7 μm 2.1 × 50 mm column, and a Waters SQ2 mass spectrometer with single quadrupole detector and electrospray ionization. High-resolution mass spectra were recorded on a Micromass Quatro Micro™ instrument with electrospray ionization. The melting points were determined using a Boetius PNMK melting point apparatus and are reported uncorrected. Optical rotation measurement was performed on an automated Rudolf Research Analytical Polarimeter Autopol IV. Chiral HPLC measurements were performed on a Waters Alliance LC system equipped with 2695 separation module, quaternary pump, degasser, autosampler, column thermostat, and a Waters 2489 double-absorbed UV detector (employed at 210 nm wavelength) using a Chiralpak IA column (4.6 mm × 250 mm, 5 μm), and the output signal was monitored and processed using the Waters Empower 2 software; the enantiomeric elution order and the assignment of HPLC peaks were established by the usage of racemic adducts as external standards, X-ray crystallographic and ^{1}H NMR analysis data. The purity of the compounds was determined by TLC using Merck 60 F_{254} silica gel plates. Merck Kieselgel silica gel (0.063–0.230 mm) was used for column chromatography.

Cupreidine (**Bb**) was supplied by Toronto Research Chemicals. All other chemicals were supplied by Sigma-Aldrich.

Stereochemical assignements. The absolute configuration for diethyl (1*R*,2*S*)-, (1*R*,2*R*)-, (1*S*,2*R*)-, and (1*S*,2*S*)-2-(2-nitro-1-phenylpropyl)malonates **13a** was confirmed by their chemical conversion into enantiopure 2-(5-methyl-4-phenyl-2-oxopyrrolidin-1-yl)acetamides.[7a] The absolute configurations of their structural analogs **13b**–**f** were assigned by analogy on the basis of their HPLC data.

(3a*R*,8a*S*,3a'*R*,8a'*S*)-2,2'-Cyclopropane-1,1-diylbis-(8,8a-dihydro-3a*H*-indeno[1,2-*d*]oxazole)magnesium(II) triflate (Aa) and (3a*S*,8a*R*,3a'*S*,8a'*R*)-2,2'-cyclopropane-1,1-diylbis(8,8a-dihydro-3a*H*-indeno[1,2-*d*]oxazole)magnesium(II) triflate (Ab) were prepared according to literature method.[5a]

Bis((*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine)-nickel(II) bromide (C), bis((*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine)nickel(II) bromide (Da), bis((*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine)nickel(II) acetate (Db), and ((*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine)-nickel(II) acetate (E) were prepared according to literature method.[10]

Zn(II), Mg(II), Cu(II), Fe(II), Ba(II), and Co(II) complexes with (*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine Fa–k. A mixture of the appropriate metal salt (2 mmol) and (*R*,*R*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine (1177 mg, 4.0 mmol) in MeCN (50 ml) was heated at reflux for 5 h. Reaction mixture was cooled and evaporated under reduced pressure. The residue was dissolved in CH_2Cl_2 and filtered. The solvent from the filtrate was evaporated under reduced pressure to obtain the crude product used in experiments without additional purification.

Diaquabis((*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine)-cobalt(II) dibromide tetrahydrate (G). A mixture of $CoBr_2$ (437 mg, 2 mmol) and (*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine (1177 mg, 4.0 mmol) in MeCN (50 ml) was heated at reflux for 5 h. Reaction mixture was cooled and evaporated under reduced pressure, and the crude product was recrystallized from a mixture of EtOAc and 96% EtOH. Yield 1116 mg (80%), microcrystalline pale-green powder. $[\alpha]_{20}^{D}$ +63° (c 0.87, CH_2Cl_2). IR spectrum, ν, cm^{-1}: 3254, 3142, 3028, 2933, 2859, 1496, 1453, 1353, 1029, 948, 752, 700.

Addition of nitrostyrenes 9a,b to malonates 10a,b in the presence of chiral catalysts Aa or Ab (General method I).

$Mg(OTf)_2$ (160 mg, 0.5 mmol) and H_2O (13 μl) were added to a solution of (3a*R*,3'a*R*,8a*S*,8'a*S*)-2,2'-cyclopropylidenebis[3a,8a]dihydro-8*H*-indeno[1,2-*d*]oxazole or (3a*S*,3'a*S*,8a*R*,8'a*R*)-2,2'-cyclopropylidenebis[3a,8a]dihydro-8*H*-indeno[1,2-*d*]-oxazole (267 mg, 0.75 mmol) in $CHCl_3$ (amylene-stabilized) (5 ml) in a 250-ml reaction flask at room temperature. The mixture was stirred under argon for 1 h. Molecular sieves (1.0 g) were added to the mixture, and the mixture was stirred for additional 30 min. A solution of malonate **9a**,**b** (2.5 mmol), nitrostyrene **10a**,**b** (2.5 mmol), morpholine (12 μl, 0.14 mmol), and TMG (12 μl, 0.09 mmol) in $CHCl_3$ (45 ml) was added to the obtained suspension. The reaction mixture was stirred at room temperature 4–7 days while monitoring the progress of reaction by LC/MS. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure. The crude product was purified by column chromatography using as eluent petroleum ether – EtOAc, 5:1.

The addition of nitrostyrene 9a to malonate 10a in the presence of chiral catalysts Ba or Bb (General method II). A solution of malonate **9a** (0.67 mmol), nitrostyrene **10a** (0.67 mmol), and 4-[(*R*)-((2*S*,4*S*,5*R*)-5-ethenyl-1-azabicyclo-[2.2.2]octan-2-yl)(hydroxy)methyl]quinolin-6-ol (cupreine, **Ba**) or 4-[(*S*)-((2*R*,4*S*,5*R*)-5-ethenyl-1-azabicyclo[2.2.2]-oct-2-yl)(hydroxy)methyl]quinolin-6-ol (cupreidine, **Bb**) (21 mg, 0.067 mmol) in dry THF (8 ml) under N_2 atmosphere was stirred at room temperature for 2 days while monitoring the reaction by LC/MS. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the crude product was purified by column chromatography using as eluent petroleum ether – EtOAc, 5:1.

The addition of nitrostyrenes 9a–c to malonates 10c in the presence of chiral catalysts C–E (General method III). Nitrostyrene **9a**–**c** (1.0 mmol), malonate **10c** (1.0 mmol), and 6 mol % of Ni(II)-complexes **C**, **Da**,**b**, or **E** in PhMe (5 ml) or neat were placed in a screw cup vial and stirred at chosen temperature (Table 2) while controlling product formation by LC/MS. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the crude product was purified by column chromatography using as eluent petroleum ether – EtOAc, 5:1. In the case of catalyst **Db**, it was formed *in situ* by the addition $Ni(OAc)_2$ (4 mg, 0.0012 mmol) and (*S*,*S*)-*N*,*N*'-dibenzylcyclohexane-1,2-diamine (14 mg, 0.0024 mmol) into the reaction mixture of nitrostyrene **9a** (65 mg, 0.4 mmol) and malonate **10c** (52.8 mg, 0.4 mmol) in PhMe (5 ml).

The addition of nitrostyrene 9c to malonates 10c in the presence of chiral complexes Fa–k and G (General method IV) was performed at 44°C for 24 h using PhMe (10 ml) as solvent following general method III in all other details.

Preparation of racemic Michael adducts 13a–f (General method V). A solution of nitrostyrene **9a**–**c** (3.1 mmol), malonate **10a**–**c** (3.1 mmol), and TMG (0.31 mmol) in $CHCl_3$ (20 ml) was stirred at 20°C for 24 h estimating the degree of conversion by TLC. After the completion of the reaction, the reaction mixture was concentrated under reduced pressure and the crude product was purified by column chromatography (eluent petroleum ether – EtOAc, 5:1).

Preparation of enantiopure 3,4-disubstituted methyl 4-nitrobutanoates 17a,b (General method VI). The appropriate diastereoisomeric mixture of adduct **13e**,**f** (1.8 mmol) was hydrolized and decarboxylated in a refluxing mixture of 36% aqueous HCl and AcOH in the ratio of 1:3 (30 ml) for 18 h. After the completion of the reaction, the solution was cooled and concentrated under reduced pressure. The residue was purified by column chromatography using as eluent petroleum ether – EtOAc, 5:1. Isolated mixtures of *syn* and *anti* isomers of the respective intermediate 3,4-disubstituted 4-nitrobutanoic acids were dissolved in $SOCl_2$ (0.12 g, 1.0 mmol) and MeOH (20 ml) mixture and refluxed for 20 h. The reaction mixture was cooled and concentrated under reduced pressure. *Syn* and *anti* isomers were separated by column chromatography using as eluent petroleum ether – EtOAc, 5:1.

Preparation of enantiopure 4,5-disubstituted pyrroldin-2-ones 14a,b (General method VII). Enantiopure samples of methyl 4-nitrobutanoates **17a**,**b** (2.2 mmol) were hydrogenated in EtOH (40 ml) in the presence of 50% Raney Ni slurry in H_2O (1 ml) at 10 bar at 40°C for 20 h. After the completion of the reaction, the reaction mixture was cooled, and the catalyst was filtered off and washed with EtOH (30 ml). The filtrate was concentrated under reduced pressure. The residue was purified by silica gel column chromatography using as eluent CH_2Cl_2–EtOH, 20:1.

Diethyl 2-((1*R*,2*S*)- and (1*R*,2*R*)-2-nitro-1-phenylpropyl)malonate ((1*R*,2*S*)- and (1*S*,2*S*)-13a) and diethyl (1*S*,2*R*)- and (1*S*,2*S*)-2-(2-nitro-1-phenylpropyl)malonate ((1*S*,2*R*)- and (1*S*,2*S*)-13a)[7a] were prepared from nitrostyrene **9a** and malonate **10a** according to the general method I or II. Recrystallization of the isolated product from EtOAc–hexane mixture allowed to obtain colorless crystals of compound (1*R*,2*S*)-**13a**, mp 51–53°C, characterized by X-ray crystallography (Fig. 4).

Epimerization of compound (1*R*,2*S*)- and (1*S*,2*S*)-13a. The mixture of stereoisomers of compound (1*R*,2*S*)- and (1*S*,2*S*)-**13a** (50 mg, 0.15 mmol), prepared according to the general method I, and TMG (6 μl, 0.05 mmol) in $CHCl_3$ (5 ml) was stirred at room temperature for 7 days. The reaction mixture was concentrated under reduced pressure, and the residue was dissolved in CH_2Cl_2 (20 ml). The obtained solution was washed with 5% aqueous HCl (2×20 ml) and brine (2×50 ml), and the organic phase was dried over anhydrous Na_2SO_4. The drying reagent was removed by filtration, the solution was concentrated under reduced pressure, and the crude product underwent chiral HPLC analysis.

Diethyl (1*R*,2*S*)- and (1*R*,2*R*)-2-(2-nitro-1-phenylbutyl)-malonate ((1*R*,2*S*)- and (1*R*,2*R*)-13b) was prepared in the presence of catalyst **Aa** according to the general method I from nitrostyrene **9b** and malonate **10a**. Yield 0.60 g (71%), low melting solid. IR spectrum, ν, cm^{-1}: 2981, 2940, 1751, 1734, 1550, 1369. Found, *m*/*z*: 360.1418 $[M+Na]^+$. $C_{17}H_{23}NNaO_6$. Calculated, *m*/*z*: 360.1418.

Compound *syn*-(1*R*,2*S*/1*S*,2*R*)-13b. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.23–7.20 (3H, m, H Ph); 7.05–7.01 (2H,

m, H Ph); 4.93–4.87 (1H, m, CH); 4.26–4.18 (2H, m, CH_2); 4.14 (2H, q, J = 7.1, CH_2); 4.03 (1H, d, J = 10.9, CH); 3.85–3.75 (1H, m, CH); 1.83–1.74 (1H, m) and 1.69–1.59 (1H, m, CH_2); 1.24 (3H, t, J = 7.1, CH_3); 1.19 (3H, t, J = 7.1, CH_3); 0.85 (3H, t, J = 7.1, CH_3).^{13}C NMR spectrum, δ, ppm: 167.8; 167.1; 134.2; 129.3; 129.0; 128.4; 90.1; 62.1; 61.6; 54.1; 47.0; 24.5; 14.0; 13.6; 10.5.

Compound *anti*-(1*R*,2*R*/1*S*,2*S*)-13b. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.23–7.20 (3H, m, H Ph); 7.05–7.01 (2H, m, H Ph); 4.93–4.87 (1H, m, CH); 4.09–3.75 (6H, m, 2CH, $2CH_2$); 1.83–1.74 (1H, m) and 1.69–1.59 (1H, m, CH_2); 1.13 (3H, t, J = 7.1, CH_3); 0.97 (3H, t, J = 7.1, CH_3); 0.78 (3H, t, J = 7.2, CH_3). ^{13}C NMR spectrum, δ, ppm: 167.2; 166.8; 135.3; 129.3; 129.0; 128.2; 91.6; 62.0; 61.6; 54.6; 48.1; 24.6; 13.8; 13.7; 10.3.

Diethyl (1*S*,2*R*)- and (1*S*,2*S*)-2-(2-nitro-1-phenylbutyl)-malonate ((1*S*,2*R*)- and (1*S*,2*S*)-13b)[25a] was prepared in the presence of catalyst **Ab** according to the general method I from nitrostyrene **9b** and malonate **10a**. Yield 0.61 g (72%), low-melting solid. The IR, ^{1}H and ^{13}C NMR spectroscopic data were in agreement to those established for the mixture (1*R*,2*S*)- and (1*R*,2*R*)-**13b**.

Dimethyl (1*R*,2*S*)- and (1*R*,2*R*)-2-fluoro-2-(2-nitro-1-phenylpropyl)malonate ((1*R*,2*S*)- and (1*R*,2*R*)-13c) was prepared in the presence of catalyst **Aa** according to the general method I from nitrostyrene **9a** and malonate **10b**. Yield 0.49 g (63%), colorless crystals, mp 80–83°C. IR spectrum, ν, cm^{-1}: 2958, 1771, 1757, 1558, 1554, 1361. ^{13}C NMR spectrum: 165.9; 165.6; 165.0; 164.7; 164.6; 164.3; 164.0; 133.4; 132.7; 129.8; 129.7; 129.3; 128.9; 128.8; 128.7; 96.8; 94.7; 85.3; 85.2; 81.8; 54.0; 53.9; 53.3; 53.2; 52.6; 52.4; 18.3; 18.1. ^{19}F NMR spectrum, δ, ppm (*J*, Hz): –171.62 (d, J = 29.8); –170.51 (d, J = 29.5). Found, *m*/*z*: 336.0848. $[M+Na]^+$. $C_{14}H_{16}FNNaO_6$. Calculated, *m*/*z*: 336.0854.

Compound *syn*-(1*R*,2*S*/1*S*,2*R*)-13c. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.29–7.20 (5H, m, H Ph); 5.09–5.04 (1H, m, CH); 4.39 (1H, dd, J = 29.5, J = 10.1, CH); 3.89 (3H, s, CH_3); 3.39 (3H, s, CH_3); 1.57 (3H, d, J = 6.9, CH_3).

Compound *anti*-(1*R*,2*R*/1*S*,2*S*)-13c. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.29–7.20 (5H, m, H Ph); 5.09–5.04 (1H, m, CH); 4.43 (1H, dd, J = 29.8, J = 8.0, CH); 3.84 (3H, s, CH_3); 3.44 (3H, s, CH_3); 1.26 (3H, d, J = 6.9, CH_3).

Dimethyl (1*S*,2*R*)- and (1*S*,2*S*)-2-fluoro-2-(2-nitro-1-phenylpropyl)malonate ((1*S*,2*R*)- and (1*S*,2*S*)-13c) was prepared in the presence of catalyst **Ab** according to the general method I from nitrostyrene **9a** and malonate **10b**. Yield 0.40 g (51%), colorless crystals, mp 76–78°C. The IR, ^{1}H and ^{13}C NMR spectroscopic data were identical to those established for the mixture (1*R*,2*S*/1*S*,2*R*)- and (1*R*,2*R*/1*S*,2*S*)-**13c**.

Racemic diethyl 2-(2-nitro-1-phenylpropyl)malonate (13a) was prepared according to the general method V from nitrostyrene **9a** and malonate **10a**. Yield 0.78 g (78%), low-melting solid. The IR, ^{1}H and ^{13}C NMR spectroscopic data were in agreement with those of enantiomerically enriched (1*R*,2*S*/1*S*2*R*)-**13a** and (1*R*,2*R*, 1*S*,2*S*)-**13a**.

Racemic diethyl 2-(2-nitro-1-phenylbutyl)malonate (13b) was prepared according to the general method V from nitrostyrene **9b** and malonate **10a**. Yield 0.72 g (69%), low-melting solid. The IR, ^{1}H and ^{13}C NMR spectroscopic data were in agreement with those of enantiomerically enriched (1*R*,2*S*/1*S*,2*R*)-**13b** and (1*R*,2*R*/1*S*,2*S*)-**13b**.

Racemic dimethyl 2-fluoro-2-(2-nitro-1-phenylpropyl)-malonate (13c) was prepared according to the general method V from nitrostyrene **9a** and malonate **10b**. Yield 0.76 g (78%), colorless crystals, mp 70–77°C. The IR, ^{1}H and ^{13}C NMR spectroscopic data were in agreement with those of enantiomerically enriched (1*R*,2*S*/1*S,2R*)-**13c** and (1*R*,2*R*/1*S,2S*)-**13c**.

Dimethyl 2-((1*R*,2*S*)- and (1*R*,2*R*)-2-nitro-1-phenyl-propyl)malonate ((1*R*,2*S*)- and (1*R*,2*R*)-13d) and dimethyl (1*S*,2*R*)- and (1*S*,2*S*)-2-(2-nitro-1-phenylpropyl)-malonate ((1*S*,2*R*)- and (1*S*,2*S*)-13d) were prepared according to the general method III or IV from nitrostyrene **9a** and dimethyl malonate (**10c**). IR spectrum, ν, cm^{-1}: 2954, 2916, 2848, 1755, 1557, 1456, 1436. Found, *m*/*z*: 318.0946 $[M+Na]^+$. $C_{14}H_{17}NNaO_6$. Calculated, *m*/*z*: 318.0948.

Compound *syn*-(1*R*,2*S*/1*S*,2*R*)-13d. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.26–7.20 (5H, m, H Ph); 5.10 (1H, qd, J = 6.7, J = 4.5, CH); 4.20 (1H, d, J = 10.9, CH); 3.78 (1H, dd, J = 10.8, J = 4.5, CH); 3.69 (3H, s, CH_3); 3.37 (3H, s, CH_3); 1.37 (3H, d, J = 6.7, CH_3). ^{13}C NMR spectrum, δ, ppm: 168.4; 167.7; 134.0; 128.9; 128.7; 128.6; 83.0; 53.9; 53.1; 52.7; 49.0; 16.93.

Compound *anti*-(1*R*,2*R*/1*S*,2*S*)-13d. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.14–7.11 (2H, m, Ph); 7.07–6.97 (3H, m, H Ph); 5.02 (1H, dq, J = 8.0, J = 6.8, CH); 4.09 (1H, dd, J = 9.3, J = 7.9, CH); 3.84 (1H, d, J = 9.3, CH); 3.65 (3H, s, CH_3); 3.37 (3H, s, CH_3); 1.28 (3H, d, J = 6.7, CH_3). ^{13}C NMR spectrum, δ, ppm: 168.4; 167.2; 134.7; 129.1; 128.8; 128.6; 84.2; 54.3; 53.0; 52.6; 48.4; 16.4.

Dimethyl (1*R*,2*S*)- and (1*R*,2*R*)-2-(2-nitro-1-phenyl-butyl)malonate ((1*R*,2*S*)- and (1*R*,2*R*)-13e) and dimethyl (1*S*,2*R*)- and (1*S*,2*S*)-2-(2-nitro-1-phenylbutyl)malonate ((1*S*,2*R*)- and (1*S*,2*S*)-13e were prepared according to the general method III or IV from nitrostyrene **9b** and dimethyl malonate (**10c**). Low-melting solid. IR spectrum, ν, cm^{-1}: 2955, 1738, 1734, 1550, 1455, 1435, 1262. Found, *m*/*z*: 332.1114 $[M+Na]^+$. $C_{15}H_{19}NNaO_6$. Calculated, *m*/*z*: 332.1105.

Compound *syn*-(1*R*,2*S*/1*S*,2*R*)-13e. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.25–7.20 (3H, m, H Ph); 7.06–7.00 (2H, m, H Ph); 4.91–4.86 (1H, m, CH); 4.07 (1H, d, J = 10.6, CH); 3.83–3.78 (1H, m, CH); 3.75 (3H, s, CH_3); 3.36 (3H, s, CH_3); 1.82–1.74 (1H, m) and 1.70–1.61 (1H, m, CH_2); 0.90 (3H, t, J = 7.3, CH_3). ^{13}C NMR spectrum, δ, ppm: 168.3; 167.6; 134.2; 129.1; 128.8; 128.5; 90.1; 53.8; 53.1; 52.7; 47.8; 24.5; 10.5.

Compound *anti*-(1*R*,2*R*/1*S*,2*S*)-13e. ^{1}H NMR spectrum, δ, ppm (*J*, Hz): 7.25–7.20 (3H, m, H Ph); 7.06–7.00 (2H, m, H Ph); 4.96–4.91 (1H, m, CH); 3.96–3.92 (1H, m, CH); 3.79 (1H, d, J = 7.8, CH); 3.60 (3H, s, CH_3); 3.33 (3H, s, CH_3); 1.70–1.61 (1H, m) and 1.53–1.42 (1H, m, CH_2); 0.78 (3H, t, J = 7.3, CH_3). ^{13}C NMR spectrum, δ, ppm: 167.7; 167.3; 135.3; 128.8; 128.5; 128.4; 91.6; 54.4; 52.8; 52.6; 48.1; 25.0; 10.3.

Dimethyl (1*R*,2*S*)- and (1*R*,2*R*)-2-[1-(4-fluorophenyl)-2-nitropropyl]malonate ((1*R*,2*S*)- and (1*R*,2*R*)-13f) and

dimethyl (1*S*,2*R*)- and (1*S*,2*S*)-2-[1-(4-fluorophenyl)-2-nitropropyl]malonate ((1*S*,2*R*)- and (1*S*,2*S*)-13f) were prepared according to the general method III from nitrostyrene **9c** and dimethyl malonate (**10c**). Low-melting solid. IR spectrum, ν, cm^{-1}: 2956, 1737, 1734, 1550, 1512, 1436, 1229, 1165, 846. Found, *m*/*z*: 314.1040 $[M+H]^+$. $C_{14}H_{16}FNO_6$. Calculated, *m*/*z*: 314.1034.

Compound *syn*-(1*R*,2*S*/1*S*,2*R*)-13f. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.04–6.98 (2H, m, H Ph); 6.97–6.88 (2H, m, H Ph); 5.14–5.05 (1H, m, CH); 4.15 (1H, d, *J* = 10.8, CH); 3.73–3.67 (1H, m, CH); 3.75 (3H, s, CH_3); 3.39 (3H, s, CH_3); 1.37 (3H, d, *J* = 6.7, CH_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 168.2; 167.6; 162.7 (d, *J* = 248.0); 130.7; 130.6; 115.8; 115.6; 83.0; 53.8; 53.1; 52.8; 48.3; 17.0.

Compound *anti*-(1*R*,2*R*/1*S*,2*S*)-13f. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.16–7.11 (2H, m, H Ph); 6.97–6.88 (2H, m, H Ph); 5.04–4.97 (1H, m, CH); 4.12–4.05 (1H, m, CH); 3.79 (1H, d, *J* = 9.2, CH); 3.65 (3H, s, CH_3); 3.46 (3H, s, CH_3); 1.29 (3H, d, *J* = 6.8, CH_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 167.5; 167.1; 162.6 (d, *J* = 248.0); 130.9; 130.4; 115.9; 115.8; 84.0; 54.0; 53.0; 52.7; 47.7; 16.20.

Racemic dimethyl 2-(2-nitro-1-phenylpropyl)malonate (13d) was prepared according to the general method V from β-methyl-β-nitrostyrene (**9a**) and dimethyl malonate (**10c**), low-melting solid. The IR, ^1H and ^{13}C NMR spectroscopic data were in agreement with those established for the enantiomerically enriched samples of compound **13d**.

Racemic dimethyl 2-(2-nitro-1-phenylbutyl)malonate (13e) was prepared according to the general method V from β-ethyl-β-nitrostyrene (**9b**) and dimethyl malonate (**10c**), low-melting solid. The IR, ^1H and ^{13}C NMR spectroscopic data were in agreement with those established for the enantiomerically enriched samples of compound **13e**.

Racemic dimethyl 2-[1-(4-fluorophenyl)-2-nitropropyl]-malonate (13f) was prepared according to the general method V from nitrostyrene **9c** and dimethyl malonate (**10c**), colorless crystals, mp 70–77°C. The IR, ^1H and ^{13}C NMR spectroscopic data were in agreement with those established for the enantiomerically enriched samples of compound **13f**.

Methyl (3*R*,4*S*)-4-nitro-3-phenylhexanoate ((3*R*,4*S*)-17a) was prepared according to the general method VI from diastereomeric mixture (1*R*,2*S*/1*R*,2*R*)-**13e**. Yield 0.23 g (51%), low-melting solid. IR spectrum, ν, cm^{-1}: 2976, 1737, 1550, 1436, 701. ^1H NMR spectrum, δ, ppm (*J*, Hz); 7.26–7.17 (3H, m, H Ph); 7.12–7.07 (2H, m, H Ph); 4.67 (1H, ddd, *J* = 10.5, *J* = 7.9, *J* = 3.7, CH); 3.67–3.59 (1H, m, CH); 3.52 (3H, s, CH_3); 2.80 (1H, dd, *J* = 16.1, *J* = 6.0) and 2.66 (1H, dd, *J* = 16.1, *J* = 8.7, CH_2); 1.96–1.76 (2H, m, CH_2); 0.90 (3H, t, *J* = 7.3, CH_3). ^{13}C NMR spectrum, δ, ppm: 171.4; 137.9; 128.8; 128.0; 127.9; 93.5; 51.9; 45.0; 36.5; 24.5; 10.4. Found, *m*/*z*: 252.1225 $[M+H]^+$. $C_{13}H_{18}NO_4$. Calculated, *m*/*z*: 252.1230.

Methyl (3*R*,4*R*)-4-nitro-3-phenylhexanoate ((3*R*,4*R*)-17a) was prepared according to the general method VI from diastereomeric mixture (1*R*,2*S*/1*R*,2*R*)-**13e**. Yield 0.11 g (24%), low-melting solid. IR spectrum, ν, cm^{-1}: 2975, 2952, 1742, 1549, 1436, 1260, 702. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.28–7.19 (3H, m, Ph); 7.14–7.11 (2H, m, H Ph); 4.54 (1H, td, *J* = 10.6, *J* = 3.1, CH); 3.60–3.55 (1H, m, CH); 3.43 (3H, s, CH_3); 2.69 (1H, dd, *J* = 15.8, *J* = 10.5) and 2.56 (1H, dd, *J* = 15.7, *J* = 4.3, CH_2); 1.81–1.69 (1H, m) and 1.45–1.37 (1H, m, CH_2); 0.77 (3H, t, *J* = 7.4, CH_3). ^{13}C NMR spectrum, δ, ppm: 170.9; 137.9; 129.1; 128.1; 128.0; 94.1; 51.6; 45.6; 37.7; 25.6; 10.3. Found, *m*/*z*: 252.1236 $[M+H]^+$. $C_{13}H_{18}NO_4$.Calculated, *m*/*z*: 252.1230.

Methyl (3*S*,4*R*)-4-nitro-3-phenylhexanoate ((3*S*,4*R*)-17a) was prepared according to the general method VI from diastereomeric mixture (1*S*,2*S*/1*S*,2*R*)-**13e**. Yield 0.21 g (46%), low-melting solid. IR spectrum, ν, cm^{-1}: 2954, 1741, 1608, 1563, 1437, 1360, 1225, 1162, 836. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.26–7.17 (3H, m, H Ph); 7.12–7.07 (2H, m, H Ph); 4.69–4.64 (1H, ddd, *J* = 10.5, *J* = 7.9, *J* = 3.7, CH); 3.69–3.58 (1H, m, CH); 3.52 (3H, s, CH_3); 2.80 (1H, dd, *J* = 16.1, *J* = 6.0) and 2.66 (1H, dd, *J* = 16.1, *J* = 8.7, CH_2); 1.95–1.76 (2H, m, CH_2); 0.90 (3H, t, *J* = 7.3, CH_3). ^{13}C NMR spectrum, δ, ppm: 171.4; 137.9; 128.8; 128.0; 127.9; 93.5; 51.9; 45.0; 36.5; 24.5; 10.4. Found, *m*/*z*: 252.1237 $[M+H]^+$. $C_{13}H_{18}NO_4$. Calculated, *m*/*z*: 252.1230.

Methyl (3*S*,4*S*)-4-nitro-3-phenylhexanoate ((3*S*,4*S*)-17a) was prepared according to the general method VI from diastereomeric mixture (1*S*,2*S*/1*S*,2*R*)-**13e**. Yield 0.12 g (27%), low-melting solid. IR spectrum, ν, cm^{-1}: 2975, 1742, 1553, 1436, 1170, 702. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.28–7.19 (3H, m, H Ph); 7.14–7.11 (2H, m, H Ph), 4.54 (1H, td, *J* = 10.6, *J* = 3.1, CH); 3.61–3.52 (1H, m, CH); 3.43 (3H, s, CH_3); 2.69 (1H, dd, *J* = 15.7, *J* = 10.5) and 2.56 (1H, dd, *J* = 15.8, *J* = 4.3, CH_2); 1.81–1.69 (1H, m) and 1.45–1.37 (1H, m, CH_2); 0.77 (3H, t, *J* = 7.3, CH_3). ^{13}C NMR spectrum, δ, ppm: 170.9; 137.9; 129.1; 128.1; 127.7; 94.1; 51.8; 45.6; 37.7; 25.6; 10.3. Found, *m*/*z*: 252.1236 $[M+H]^+$. $C_{13}H_{18}NO_4$. Calculated, *m*/*z*: 252.1230.

Methyl (3*R*,4*S*)-3-(4-fluorophenyl)-4-nitropentanoate ((3*R*,4*S*)-17b) was prepared according to the general method VI from diastereomeric mixture (1*R*,2*S*/1*R*,2*R*)-**13f**. Yield 0.11 g (25%), low-melting solid. IR spectrum, ν, cm^{-1}: 2954, 1741, 1553, 1437, 1225, 836. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.14–7.04 (2H, m, H Ar); 6.96–6.89 (2H, m, H Ar); 4.80 (1H, quint, *J* = 6.9, CH); 3.67–3.59 (1H, m, CH); 3.52 (3H, s, CH_3); 2.78 (1H, dd, *J* = 16.1, *J* = 5.9) and 2.65 (1H, dd, *J* = 16.1, *J* = 9.0, CH_2); 1.48 (3H, d, *J* = 6.7, CH_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 171.2; 162.3 (d, *J* = 247.1); 133.4 (d, *J* = 3.4); 129.6 (d, *J* = 8.2); 115.8 (d, *J* = 21.5); 86.4; 52.0; 45.2; 36.2; 16.9. Found, *m*/*z*: 256.0847 $[M+H]^+$. $C_{12}H_{14}FNO_4$. Calculated, *m*/*z*: 256.0980.

Methyl (3*S*,4*R*)-3-(4-fluorophenyl)-4-nitropentanoate ((3*S*,4*R*)-17b) was prepared according to the general method VI from diastereomeric mixture (1*S*,2*S*/1*S*,2*R*)-**13f**. Yield 0.16 g (34%), low-melting solid. IR spectrum, ν, cm^{-1}: 2954, 2852, 1738, 1734, 1606, 1550, 1512, 1226, 837. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.12–7.03 (2H, m, H Ar); 6.96–6.90 (2H, m, H Ar); 4.80 (1H, dq, *J* = 7.6, *J* = 6.7, CH_2); 3.62 (1H, ddd, *J* = 9.0, *J* = 7.4, *J* = 5.7, CH_2); 3.52 (3H, s, CH_3); 2.78 (1H, dd, *J* = 16.1, *J* = 5.9) and 2.65 (1H, dd, *J* = 16.1, *J* = 9.0, CH); 1.48 (3H, d, *J* = 6.7, CH_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 171.2; 162.4 (d, *J* = 245.0); 133.4; 129.6 (d, *J* = 8.1); 115.8 (d,

J = 21.6); 86.4; 52.0; 45.2; 36.2; 16.9. Found, *m*/*z*: 256.0850 $[M+H]^+$. $C_{12}H_{14}FNO_4$. Calculated, *m*/*z*: 256.0980.

Methyl (3*S*,4*S*)-3-(4-fluorophenyl)-4-nitropentanoate ((3*S*,4*S*)-17b) was prepared according to the general method VI from diastereomeric mixture (1*S*,2*S*/1*S*,2*R*)-**13f**. Yield 0.09 g (20%), low-melting solid. IR spectrum, ν, cm^{-1}: 3005, 2954, 1741, 1606, 1555, 1511, 1437, 1226, 836. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.12–7.08 (2H, m, H Ar); 6.99–6.94 (2H, m, H Ar); 4.69 (1H, dq, *J* = 9.6, *J* = 6.7, CH); 3.62 (1H, td, *J* = 9.7, *J* = 4.9, CH); 3.47 (3H, s, CH_3); 2.69 (1H, dd, *J* = 15.8, *J* = 10.5) and 2.59 (1H, dd, *J* = 15.8, *J* = 4.3, CH_2); 1.27 (3H, d, *J* = 6.7, CH_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 172.4; 170.8; 162.3 (d, *J* = 246.0); 133.3; 129.8 (d, *J* = 7.8); 116.1 (d, *J* = 21.6); 86.8; 51.9; 45.5; 37.4; 17.6. Found, *m*/*z*: 256.0845 $[M+H]^+$. $C_{12}H_{14}FNO_4$. Calculated, *m*/*z*: 256.0980.

(4*R*,5*S*)-5-Ethyl-4-phenylpyrrolidin-2-one ((4*R*,5*S*)-14a) was prepared according to the general method VII from methyl (3*R*,4*S*)-4-nitro-3-phenylhexanoate ((3*R*,4*S*)-**17a**). Yield 0.32 g (77%), low-melting solid. IR spectrum, ν, cm^{-1}: 3221, 3087, 2965, 1702, 1454, 701. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.29–7.18 (3H, m, H Ph); 7.15–7.11 (2H, m, H Ph); 6.72–6.55 (1H, m, NH); 3.75–3.66 (2H, m, CH); 2.63–2.58 (2H, m, CH_2); 1.04–0.98 (2H, m, CH_2); 0.75 (3H, t, *J* = 7.4, CH_3). ^{13}C NMR spectrum, δ, ppm: 177.7; 139.1; 128.5; 128.1; 127.1; 60.1; 44.1; 35.9; 24.8; 10.8. Found, *m*/*z*: 190.1241 $[M+H]^+$. $C_{12}H_{16}NO$. Calculated, *m*/*z*: 190.1226.

(4*R*,5*R*)-5-Ethyl-4-phenylpyrrolidin-2-one ((4*R*,5*R*)-14a) was prepared according to the general method VII from methyl (3*R*,4*R*)-4-nitro-3-phenylhexanoate ((3*R*,4*R*)-**17a**). Yield 0.31 g (74%), low-melting solid. IR spectrum, ν, cm^{-1}: 3182, 3086, 2906, 2876, 1699, 1668, 1453, 1312, 757. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.51 (1H, br. s, NH); 7.29–7.23 (2H, m, H Ph); 7.21–7.15 (3H, m, H Ph); 3.49–3.55 (1H, m, CH); 3.12–3.07 (1H, m, CH); 2.71 (1H, dd, *J* = 17.2, *J* = 9.1) and 2.46 (1H, dd, *J* = 17.2, *J* = 8.8, CH_2); 1.65–1.53 (1H, m) and 1.53–1.40 (1H, m, CH_2); 0.88 (3H, t, *J* = 7.4, CH_3). ^{13}C NMR spectrum, δ, ppm: 177.3; 142.3; 128.9; 127.3; 127.1; 64.0; 46.9; 39.62; 28.4; 10.5. Found, *m*/*z*: 190.1234 $[M+H]^+$. $C_{12}H_{16}NO$. Calculated, *m*/*z*: 190.1226.

(4*S*,5*S*)-5-Ethyl-4-phenylpyrrolidin-2-one ((4*S*,5*S*)-14a) was prepared according to the general method VII from methyl (3*S*,4*S*)-4-nitro-3-phenylhexanoate ((3*S*,4*S*)-**17a**). Yield 0.29 g (70%), low melting solid. IR spectrum, ν, cm^{-1}: 3269, 3169, 3089, 2974, 2923, 1709, 1670, 1514, 818. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.30–7.24 (2H, m, H Ph); 7.22–7.17 (3H, m, H Ph); 7.09–6.54 (1H, m, NH); 3.53 (1H, td, *J* = 7.2, *J* = 4.7, CH); 3.15–3.04 (1H, m, CH); 2.72 (1H, dd, *J* = 17.2, *J* = 9.2, CH_2); 2.47 (1H, dd, *J* = 17.2, *J* = 8.8, CH_2); 1.64–1.57 (1H, m) and 1.49–1.42 (1H, m, CH_2); 0.87 (3H, td, *J* = 7.4, *J* = 1.0, CH_3). ^{13}C NMR spectrum, δ, ppm: 177.0; 142.2; 128.9; 128.5; 128.1; 127.3; 127.1; 63.8; 46.9; 39.5; 28.3; 10.5. Found, *m*/*z*: 190.1231 $[M+H]^+$. $C_{12}H_{16}NO$. Calculated, *m*/*z*: 190.1226.

(4*S*,5*R*)-5-Ethyl-4-phenylpyrrolidin-2-one ((4*S*,5*R*)-14a) was prepared according to the general method VII from methyl (3*R*,4*R*)-4-nitro-3-phenylhexanoate ((3*S*,4*R*)-**17a**). Yield 0.30 g (71%), low melting solid. IR spectrum, ν, cm^{-1}: 3221, 3089, 2965, 2934, 1705, 1454, 701. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.28–7.19 (3H, m, H Ph); 7.16–7.10 (2H, m, H Ph); 6.97–6.80 (1H, m, NH); 3.75–3.66 (2H, m, CH); 2.65–2.56 (2H, m, CH_2); 1.06–0.97 (2H, m, CH_2); 0.75 (3H, t, *J* = 7.4, CH_3). ^{13}C NMR spectrum, δ, ppm: 177.8; 139.2; 128.5; 128.1; 127.1; 60.2; 44.0; 36.0; 24.8; 10.9. Found, *m*/*z*: 190.1237 $[M+H]^+$. $C_{12}H_{16}NO$. Calculated, *m*/*z*: 190.1226.

(4*R*,5*S*)-4-(4-Fluorophenyl)-5-methylpyrrolidin-2-one ((4*R*,5*S*)-14b) was prepared according to the general method VII from methyl (3*R*,4*S*)-3-(4-fluorophenyl)-4-nitropentanoate ((3*R*,4*S*)-**17b**). Yield 0.26 g (60%), low-melting solid. IR spectrum, ν, cm^{-1}: 3246, 2974, 2930, 1699, 1513, 1224, 838. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.13–7.05 (2H, m, H Ar); 6.97–6.80 (3H, m, H Ar, NH); 4.02–3.94 (1H, m, CH); 3.66 (1H, q, *J* = 7.8, CH); 2.63–2.49 (2H, m, CH_2); 0.74 (3H, d, *J* = 6.6, CH_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 177.6; 161.9 (d, *J* = 245.6); 134.9; 129.4; 115.4 (d, *J* = 22.2); 53.7; 43.6; 36.8 (br. s); 17.5. Found, *m*/*z*: 194.0984 $[M+H]^+$. $C_{11}H_{13}FNO$. Calculated, *m*/*z*: 194.0976.

(4*R*,5*R*)-4-(4-Fluorophenyl)-5-methylpyrrolidin-2-one ((4*R*,5*R*)-14b) was prepared from diastereomeric mixture (1*R*,2*S*)- and (1*R*,2*R*)-**13f** according to the general methods VI and VII without isolation of intermediate (3*R*,4*S*)-**17b**. Yield 0.10 g (24%), low-melting solid. IR spectrum, ν, cm^{-1}: 3273, 3206, 2973, 2927, 1699, 1694, 1511, 1229. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.22–7.12 (2H, m, H Ar); 7.01–6.92 (2H, m, H Ar); 6.15 (1H, br. s, NH); 3.68–3.60 (1H, m, CH); 3.05–2.98 (1H, m, CH); 2.67 (1H, dd, *J* = 17.0, *J* = 8.8) and 2.47 (1H, dd, *J* = 17.0, *J* = 10.0, CH_2); 1.19 (3H, dd, *J* = 6.2, CH_3). ^{13}C NMR spectrum, δ, ppm: 176.1; 163.2; 160.8; 136.5; 128.9; 127.4; 115.8; 115.6; 57.7; 49.0; 39.3; 20.4. Found, *m*/*z*: 194.0990 $[M+H]^+$. $C_{11}H_{12}FNO$. Calculated, *m*/*z*: 194.0976.

(4*S*,5*S*)-4-(4-Fluorophenyl)-5-methylpyrrolidin-2-one ((4*S*,5*S*)-14b) was prepared according to the general method VII from methyl (3*S*,4*S*)-3-(4-fluorophenyl)-4-nitropentanoate ((3*S*,4*S*)-**17b**). Yield 0.28 g (65%), low-melting solid. IR spectrum, ν, cm^{-1}: 3278, 3198, 3089, 2975, 2923, 1709, 1512, 1229, 836. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.30–7.12 (3H, m, H Ar, NH); 6.99–6.92 (2H, m, H Ar); 3.64 (1H, dq, *J* = 7.5, *J* = 6.1, CH); 3.00 (1H, ddd, *J* = 10.0, *J* = 8.8, *J* = 7.7, CH); 2.67 (1H, dd, *J* = 17.0, *J* = 8.8) and 2.46 (1H, dd, *J* = 17.0, *J* = 10.0, CH_2); 1.18 (3H, d, *J* = 6.2, CH_3). ^{13}C NMR spectrum, δ, ppm (*J*, Hz): 176.7; 161.9 (d, *J* = 245.6); 136.6 (d, *J* = 3.0); 128.9 (d, *J* = 8.1); 115.7 (d, *J* = 21.2); 115.6; 57.9; 48.9; 39.6; 20.3. Found, *m*/*z*: 194.0986 $[M+H]^+$. $C_{11}H_{12}FNO$. Calculated, *m*/*z*: 194.0976.

(4*S*,5*R*)-4-(4-Fluorophenyl)-5-methylpyrrolidin-2-one ((4*S*,5*R*)-14b) was prepared according to the general method VII from methyl (3*S*,4*R*)-3-(4-fluorophenyl)-4-nitropentanoate ((3*S*,4*R*)-**17b**). Yield 0.31 g (71%), low-melting solid. IR spectrum, ν, cm^{-1}: 3242, 2974, 2931, 1699, 1511, 1224, 838. ^1H NMR spectrum, δ, ppm (*J*, Hz): 7.20–7.15 (2H, m, H Ar); 7.09–7.02 (2H, m, H Ar); 6.34 (1H, br. s, NH); 4.11–4.03 (1H, m, CH); 3.80–3.72 (1H, m,

CH); 2.75–2.61 (2H, m, CH_2); 0.83 (3H, d, J = 6.6, CH_3). ^{13}C NMR spectrum, δ, ppm (J, Hz): 177.1; 161.9 (d, J = 245.7); 134.8; 129.4 (d, J = 8.1); 115.4 (d, J = 21.2); 53.6; 43.5; 35.6; 17.6. Found, m/z: 194.0990 $[M+H]^+$. $C_{11}H_{12}FNO$. Calculated, m/z: 194.0976.

X-ray structural investigation of compounds 13a and G. Diffraction data of compound **13a** were collected at −130°C on a Bruker-Nonius KappaCCD diffractometer using monochromated MoKα radiation (λ 0.71073 Å). Crystal of compound **13a**: monoclinic; *a* 10.9551(5), *b* 6.8391(2), *c* 11.3130(5) Å; β 94.140(2)°; *V* 845.39(6) Å^3; *Z* 2; μ 0.101 mm^{-1}; d_{calc} 1.270 g·cm^{-3}; space group is $P2_1$. Diffraction data of catalyst **G** were collected at −73°C on a diffractometer Rigaku, XtaLAB Synergy, Dualflex, HyPix using monochromated CuKα radiation (λ 1.54184 Å). Crystal of catalyst **G**: monoclinic; *a* 14.106(2), *b* 15.400(3), *c* 21.097(3) Å; *V* 4582.8(11) Å^3; *Z* 4; μ 5.338 mm^{-1}; d_{calc} 1.327 g·cm^{-3}; space group is $P2_12_12_1$. The structure was solved with the help of the heavy-atom method and refined by full-matrix least-squares method using the SHELXL program.[29] For further details, see crystallographic data for compounds **13a** and **G** deposited at the Cambridge Crystallographic Data Center (deposits CCDC 1011584 and CCDC 1959822, respectively).

Quantum-chemical calculations were performed according to the DFT/B3LYP method in a 6-31G+* basis set, using the Jaguar 8.0 software.[30] The investigation of energy and molecular geometry as functions of the rotation around C(Ph)–C(NO_2) and C(Ph)–C(CO_2R^2)$_2$ bonds was performed by constraining these angles with a step of 20°, while the rest of coordinates were optimized.

Supplementary information file containing chiral HPLC data, ^1H and ^{13}C NMR and IR spectra, as well as high-resolution mass spectra of the synthesized products is available at the journal website at http://link.springer.com/journal/10593.

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