

## Enantioselective Synthesis of 2-(2-Arylcyclopropyl)glycines: Conformationally Restricted Homophenylalanine Analogs

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Dedicated to Professor Wolfgang Steglich on the occasion of his 70th birthday

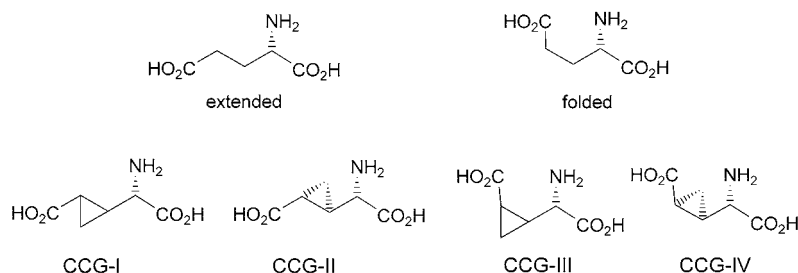
Starting from simple aromatic aldehydes and acetylfuran, (*E*)-1-(furan-2-yl)-3-arylprop-2-en-1-ones (**2**) were synthesized in high yields. Cyclopropanation of the C=C bond with trimethylsulfoxonium iodide (Me<sub>3</sub>SO<sup>+</sup>I<sup>−</sup>) furnished (furan-2-yl)(2-arylcyclopropyl)methanones **3** in 90–97% yields. Selective conversion of cyclopropyl ketones to their (*E*)- and (*Z*)-oxime ethers **5** and oxazaborolidine-catalyzed stereoselective reduction of the C=N bond followed by separation of the formed diastereoisomers, furnished (2-arylcyclopropyl)(furan-2-yl)methanamines **6** in optically pure form and high yield. Oxidation of the furan ring of (*S,S,S*)-, (*S,R,R*)-, (*R,S,S*)-, and (*R,R,R*)-**6a** afforded the four stereoisomers of  $\alpha$ -(2-phenylcyclopropyl) glycine (**1a**).

**Introduction.** – Conformationally restricted  $\alpha$ -amino acids [1] are important tools for studying the spatial requirements for receptor affinity and the biological activity of natural amino acids and peptides [2]. Replacement of natural amino acids in bioactive peptides by conformationally restricted amino acids has led to a better understanding of their bioactive conformations [3][4]. Since L-Glu is a major neurotransmitter in the mammalian central nervous system, its mimetics are of possible interest in studies on (and eventually for the treatment of) pathological processes such as *Alzheimer's* or *Huntington's* disease, as well as *Parkinsonism* or neuronal damage resulting from cerebral ischemia and epilepsy [5].

The importance of L-Glu triggered the synthesis of analogs, ones that are even more specifically agonistic than L-Glu, that activate both metabotropic and ionotropic glutamate receptors [6]. Among these,  $\alpha$ -carboxycyclopropylglycines (CCGs) are the most prominent; the extended conformer of L-Glu, which is equivalent to CCG-I and -II, activates the metabotropic Glu receptor, and the NMDA receptor is activated by a folded conformer of L-Glu, which is equivalent to CCG-III and -IV [7].

Several methods have been described in the literature for the enantioselective synthesis of CCG derivatives [7–10], but there are few examples of enantioselective syntheses of (arylcyclopropyl)-substituted glycines. Actually,  $\alpha$ -(2-phenylcyclopropyl)-glycine (**1a**) seems to be the only example. *Silverman* and *Zelechonok* [11] described

<sup>1)</sup> Authors responsible for X-ray crystal-structure analyses.



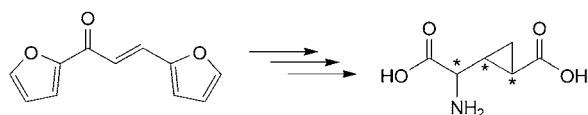
the synthesis of racemic *trans*-**1a** from *trans*-2-phenylcyclopropane-1-carbaldehyde in 34% yield by means of the *Strecker* synthesis. This compound was designed to probe the mechanism of the silver(I)-peroxydisulfate and silver(II)-picolinate oxidation of amino acids and whether an  $\alpha$ -amino radical is an important intermediate in either reaction. The multistep *enantioselective* synthesis of this compound from (*S*)-serine was described by *Bernabe* and co-workers [12], the key step being the dibromocyclopropanation of *tert*-butyl 2,2-dimethyl-4-(2-phenylethenyl)-1,3-oxazolidine-3-carboxylate. An analogous sequence was also followed, starting from (*R*)-serine. The absolute configuration of the cyclopropane ring was determined by NMR techniques.

Optically active furan-2-amine derivatives have received much attention due to their importance as building blocks for the synthesis of a considerable number of N-containing natural products such as  $\alpha$ -amino acids [13],  $\beta$ -lactams [14], indolizidines [15], quinolizidines [16], and piperidine alkaloids [17].

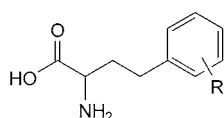
The development of an *enantioselective* synthesis capable of producing both enantiomers of furan-2-amines would allow access to many interesting compounds. In connection with some other projects, we, thus, developed a new method for the *enantioselective* synthesis of furan-2-amines and amino acids. Some preliminary results in this context have already been reported [18].

In a previous paper [9a], we described the *stereoselective* synthesis of CCG-I and -II starting from 1,3-di(2-furyl)prop-2-en-1-one (*Scheme 1*). The method covers the selective formation of the corresponding (*E*)- and (*Z*)-oximes, *enantioselective* reduction of their ethers with chiral oxazaborolidine complexes, and oxidation of the furan rings [18].

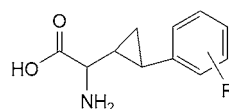
Scheme 1



As an extension of our studies, we report herein a new representative method for the *stereoselective* synthesis of all stereoisomers of *trans*- $\alpha$ -(2-phenylcyclopropyl)glycine (**1a**) and precursor derivatives thereof, *i.e.*, conformationally restricted analogs of homophenylalanine.

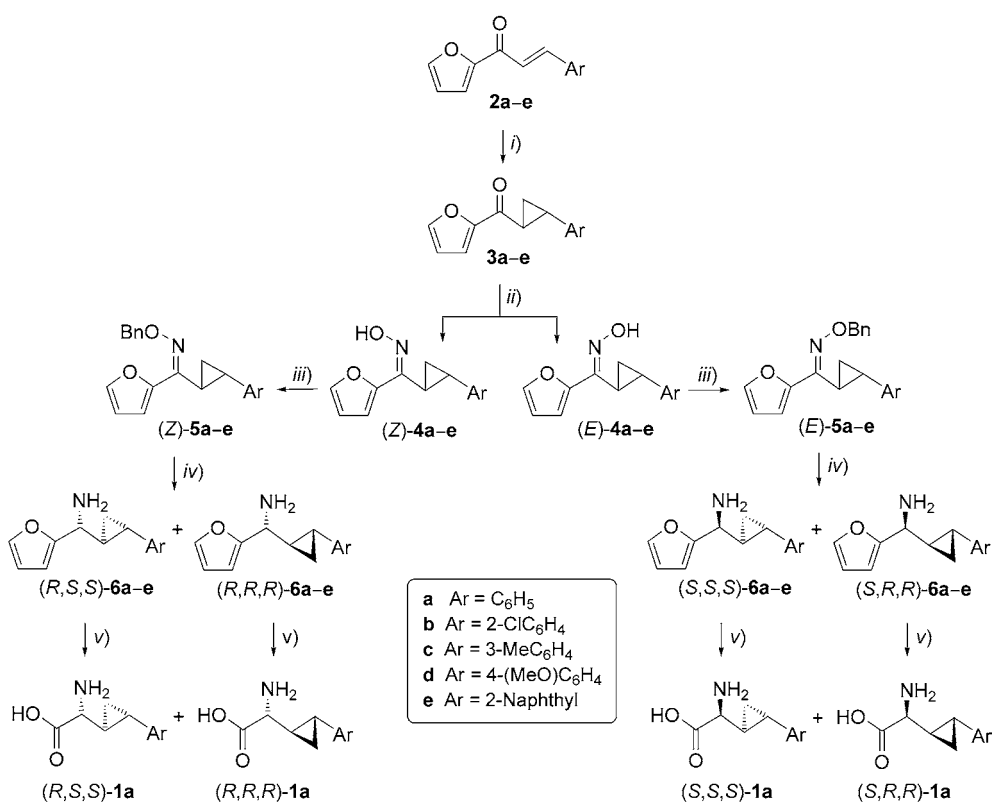


Homophenylalanine (HPhe)



conformationally restricted HPhe

**Results and Discussion.** – As shown in *Scheme 2*, the 1-(furan-2-yl)-3-arylprop-2-en-1-ones **2a–e** were chosen as starting materials for the synthesis of the target molecules, where the C=C bond serves as a cyclopropane-ring precursor and the furyl ring as a masked carboxylate. Compounds **2a–e** were readily synthesized from 2-acetylfuran and different aryl aldehydes in basic medium in 70–95% yield. *Simmons–Smith* cyclopropanation in the next step gave the products in very low yields [19], since  $\alpha,\beta$ -unsaturated carbonyl and carboxyl compounds are generally unreactive under these conditions. Fortunately, trimethylsulfoxonium iodide turned out to be the choice

*Scheme 2*

*i*) Me<sub>3</sub>SO<sup>+</sup>I<sup>−</sup>, DMSO, NaH. *ii*) For (*E*)-oxime ethers: NH<sub>2</sub>OH · HCl, NaOH, EtOH, H<sub>2</sub>O; for (*Z*)-oxime ethers: NH<sub>2</sub>OH · HCl, NaOAc, EtOH. *iii*) BnBr, NaH, DMF. *iv*) Chiral amino alcohol, such as (−)-**9** (see *Table 2*), BH<sub>3</sub> · SME<sub>2</sub>, THF. *v*) O<sub>3</sub>, CH<sub>2</sub>Cl<sub>2</sub>, −78°C; or RuO<sub>2</sub>, NaIO<sub>4</sub>, r.t.

Table 1. Absolute Configurations and Reaction Yields (in %) of Compounds **2–6**

Substituent	<b>2</b>	<b>3</b>	<b>4</b>	<b>5</b>	<b>6<sup>a)</sup></b>
<b>a:</b> Ar = C <sub>6</sub> H <sub>5</sub>	90	95	84 ( <i>E</i> ) 77 ( <i>Z</i> )	92 ( <i>E</i> ) 96 ( <i>Z</i> )	45 ( <i>S,S,S</i> ) 41 ( <i>S,R,R</i> ) 46 ( <i>R,S,S</i> ) 43 ( <i>R,R,R</i> )
<b>b:</b> Ar = 2-ClC <sub>6</sub> H <sub>4</sub>	95	97	83 ( <i>E</i> ) 78 ( <i>Z</i> )	95 ( <i>E</i> ) 95 ( <i>Z</i> )	40 ( <i>S,S,S</i> ) 43 ( <i>S,R,R</i> ) 39 ( <i>R,S,S</i> ) 44 ( <i>R,R,R</i> )
<b>c:</b> Ar = 3-MeC <sub>6</sub> H <sub>4</sub>	89	96	86 ( <i>E</i> ) 77 ( <i>Z</i> )	89 ( <i>E</i> ) 90 ( <i>Z</i> )	44 ( <i>S,S,S</i> ) 44 ( <i>S,S,S</i> ) 41 ( <i>R,S,S</i> ) 43 ( <i>R,R,R</i> )
<b>d:</b> Ar = 4-(MeO)C <sub>6</sub> H <sub>4</sub>	75	95	74 ( <i>E</i> ) 82 ( <i>Z</i> )	87 ( <i>E</i> ) 96 ( <i>Z</i> )	46 ( <i>S,S,S</i> ) 41 ( <i>S,S,S</i> ) <sup>b)</sup> 44 ( <i>R,S,S</i> ) <sup>b)</sup> 45 ( <i>R,R,R</i> )
<b>e:</b> Ar = 2-Naphthyl	70	90	78 ( <i>E</i> ) 80 ( <i>Z</i> )	76 ( <i>E</i> ) 83 ( <i>Z</i> )	42 ( <i>S,S,S</i> ) 39 ( <i>S,R,R</i> ) <sup>b)</sup> 40 ( <i>R,S,S</i> ) <sup>b)</sup> 44 ( <i>R,R,R</i> )

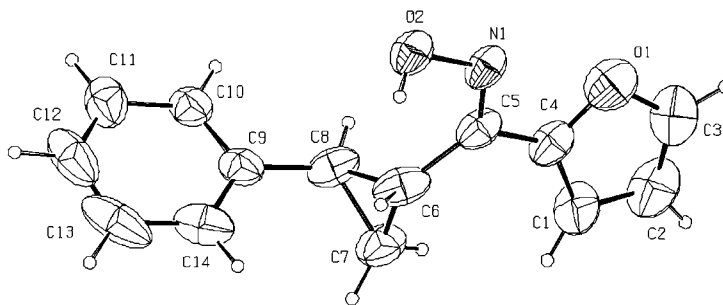
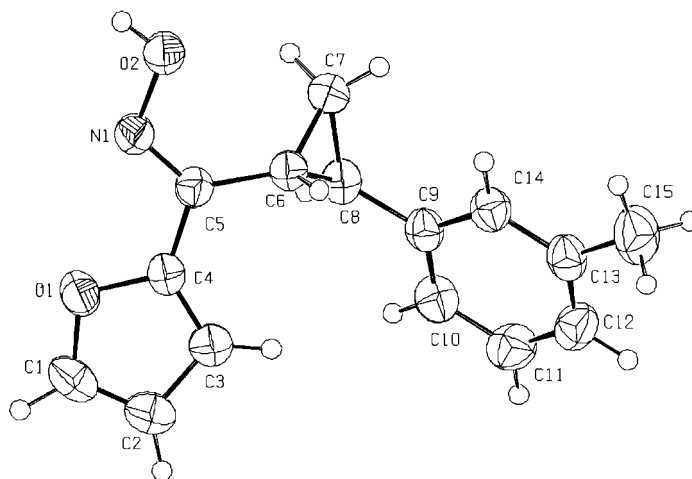
<sup>a)</sup> For the formation of chiral oxazaborolidines, (–)-(1*R*,2*S*)-norephedrine (**9**) was used. <sup>b)</sup> Stereoisomers could not be separated.

for the cyclopropanation of the enone C=C bond, giving rise to **3a–3e** in 90–97% yield after only 20 min reaction time in DMSO.

In the next step, ketones **3a–e** were selectively converted to the oximes (*E*)- and (*Z*)-**4a–e** in good yields. Reaction of **3a–e** with H<sub>2</sub>NOH·HCl/NaOH gave the (*E*)-oximes (74–86%), whereas reaction with H<sub>2</sub>NOH·HCl/AcONa in EtOH led to (*Z*)-oximes (77–82%), with only small amounts of the corresponding opposite isomers being formed. Assignment of the (*E*)/(*Z*)-configuration, which is crucial for the stereocontrol of the final products [18], was made by <sup>1</sup>H-NMR analyses and was supported by X-ray crystal-structure analyses of (*E*)-**4a**, (*E*)-**4c**, and (*Z*)-**4c** (see Figs. 1, 2, and 3, resp.).

The crystal structure of compound (*E*)-**4a** is shown in Fig. 1. Intramolecular bond distances and angles, calculated from the final coordinates, are close to the average of values found in organic molecules. The shortest intermolecular distances between non-H-atoms are 2.745(6) [O(2),N(1'); (1–*x*, –*y*, 1–*z*)] and 2.929 Å [N(1),N(1'); (1–*x*, –*y*, 1–*z*)]. The ring moieties are practically planar, with maximum deviations of 0.0158(1) and 0.0210(1) Å for C(1) and C(13), respectively. The dihedral angle between the least-squares planes of the two rings is 63.75°.

In compound (*E*)-**4c** (Fig. 2), there are H-bonds between the N- and O-atoms of neighboring molecules, which results in dimeric structures. The distance O(2)–H···N(1') (–*x*, –*y*, –*z*) is 2.763 Å, with an angle of 139.58°. The H-bridged centrosymmetric dimers are oriented along the *c*-axis of the orthorhombic unit cell. The shortest interdimeric contact distances, which are less than the sum of the *Van der Waals* radii, are 2.44 [H(1),H(7'') Å; (1–*x*, –*y*, –*z*)]; 2.63 [O(2),H(10); (–1+*x*, *y*, *z*)], and 2.75 Å [H(2), O(1); (–*x*, –*y*, –*z*)]. The furyl ring is planar, with double-bond lengths of 1.331(3) (C(1)=C(2)) and 1.345(2) Å (C(3)=C(4)). The phenyl ring is also planar with C–C distances between 1.379(3) and 1.394(2) Å. The dihedral angle between the least-squares planes of the furyl and phenyl rings is 40.51°.

Fig. 1. X-Ray crystal structure of (E)-**4a**Fig. 2. X-Ray crystal structure of (E)-**4c**

Crystals of (Z)-**4c** consist of H-bridged centrosymmetric dimers lined up along the *b*-axis of the monoclinic unit-cell in a zig-zag mode (Fig. 3). The intermolecular H-bond (O(2)–H(2')  $\cdots$  N(1) within the dimer is 2.81 Å long, with an angle of 146° (symmetry code:  $1 - x, 1 - y, -z$ ). In addition to the intermolecular H-bonds, several interdimeric contacts shorter than the sum of the *Van der Waals* radii are observed. The shortest of these contact distances have the following values: 2.23 [H(7A), H(2'); ( $1 - x, 1 - y, -z$ )]; 2.75 [H(7B), O(2); ( $1 + x, y, z$ )], and 2.81 Å [H(8), C(2); ( $x, 1/2 - y, -1/2 + z$ )]. The network of H-bonds and other intermolecular interactions hold the structure together. The furyl and the phenyl rings are planar, with a maximum deviation of 0.016(3) and 0.033(5) Å for C(2) and C(13), respectively. A least-squares-plane calculation shows that the dihedral angle between these two moieties is 88.61(11)°.

The configuration of the oximes **4** could also be determined by analysis of the <sup>1</sup>H-NMR resonances of the furyl rings: H–C(3) of (E)-**4a** appeared as a *d* at 6.81 ppm, whereas the same H-atom in (Z)-**4a** showed a downfield shift, appearing at 7.52 ppm.

The purity of (E)- and (Z)-**4a–4e** was demonstrated by GLC (gas/liquid chromatography) analysis of the corresponding *O*-benzyl oximes **5a–5e** obtained in high yields with BnBr and NaH in DMF. No isomerization was observed during this conversion. All these oxime ethers were viscous oils and were purified by flash

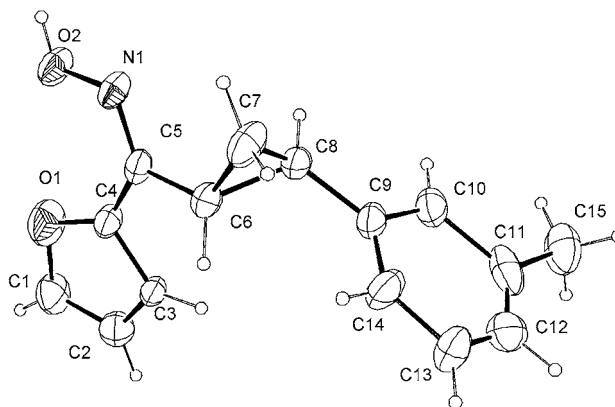


Fig. 3. X-Ray crystal structure of (Z)-4c

chromatography (FC). We also synthesized these *O*-benzyl oximes directly from the enones in the presence of *O*-benzylhydroxylamine hydrochloride. However, this procedure gave a mixture of isomers, which was separated by FC to afford the (*E*)- and (*Z*)-oxime ethers in only 28 and 36% yield, respectively.

Oxime ethers are compounds often used for the conversion of C=O to NH<sub>2</sub> groups [20]. Even more so, acetophenone oxime ethers can be stereoselectively converted to amines with BH<sub>3</sub>/oxazaborolidine complexes in high enantiomeric excess [21].

For the oxazaborolidine-catalyzed enantioselective reduction of the *O*-benzyloximes **5a–5e** with BH<sub>3</sub>·SMe<sub>2</sub> to **6a–6e**, **5a** was used as the reference starting material, and different reaction conditions were applied (Table 2). The highest selectivity was obtained when the borane/amino alcohol/oxime ether ratio was *ca.* 2.5:1.25:1.0. The amino alcohols **7–9** were used to form the oxazaborolidine complexes [22]. As shown in Table 2, they gave comparable results in terms of both selectivity and yield. For commercial reasons, compound **9** was used in most cases. After usual work-up, the diastereoisomeric mixtures of amines were separated by FC to give (*S,S,S*)- and (*S,R,R*)-**6a**. Under the same conditions, the reduction of (*Z*)-**5a** gave (*R,R,R*)- and

Table 2. Oxazaborolidine-Catalyzed Reduction of (*E*)- and (*Z*)-**4a** to Different Stereoisomers of **6** with BH<sub>3</sub>·SMe<sub>2</sub> in the Presence of Chiral Aminoalcohols (**7–9**). The absolute configurations of the products were assigned by comparing their optical rotations with literature data.

Product	<div style="display: flex; justify-content: space-around; align-items: center;"> <div style="text-align: center;">   <b>7</b> </div> <div style="text-align: center;">   <b>8</b> </div> <div style="text-align: center;">   <b>9</b> </div> </div>		
( <i>S,S,S</i> )- <b>6a</b> [%]	43	45	45
( <i>R,R,R</i> )- <b>6a</b> [%]	41	39	43
( <i>S,R,R</i> )- <b>6a</b> [%]	44	41	41
( <i>R,S,S</i> )- <b>6a</b> [%]	46	45	46

(*R,S,S*)-**6a**. Similar results were obtained with **5b–5e**, as substrates affording **6b–e** in pure form and good yields (*Table 1*). The absolute configurations of the products were determined by comparison of their specific rotations with published values. The results of the above enantioselective reduction, *i.e.*, formation of (*S*)-amine from (*E*)-oxime ether, and *vice versa*, were in accordance with our preliminary results (synthesis of CCG enantiomers) [9a]. The purity of the products was determined by NMR spectroscopy. Both the yields and purities of the isolated amines **6a** showed that the reductions occurred with high selectivity. The high diastereo- and enantioselectivities of the process and the finding that the diastereoisomers can be purified by FC make our method valuable.

The effect of the *O*-protecting group on the reduction of oxime ethers was also investigated. When the reduction was carried out with a (*Z*)-*O*-methyl oxime of type **5a** in the presence of oxazaborolidine complexes with **9**, very low selectivities were observed. As suggested previously [18], the benzyl group is superior to aliphatic groups, probably for steric and electronic reasons.

The oxidation of the furan ring of **6a** was first attempted by ozonolysis at low temperature, followed by the formation of the HCl salt. However, this method gave low yields of **1a** and many side products. Fortunately, RuO<sub>2</sub>/NaIO<sub>4</sub> oxidation [23], followed by HCl-salt formation, afforded the product in high yield.

As proposed for related catalytic systems [18a], the formation of low-energy *cis*-pentalane is favored because the  $\beta$ -binding of BH<sub>3</sub>·THF to oxazaborolidine forms very strained *trans*-pentalane, which is disfavored. As apparent from *Table 1*, the configuration of the oxime ether is the dominant factor with respect to the stereoselective formation of the amines **6**. It appears that the oxime N-atom rather than the C-atom is responsible for the high selectivity.

**Conclusions.** – We have described a very efficient route for the stereoselective synthesis of  $\alpha$ -(2-arylcypropyl)glycines from readily accessible 3-aryl-1-(2-furyl)-prop-2-en-1-ones **2**. Cyclopropanation with trimethylsulfoxonium iodide (Me<sub>3</sub>SO<sup>+</sup>I<sup>–</sup>), selective formation of (*E*)- and (*Z*)-oxime ethers **5**, oxazaborolidine-catalyzed reduction to **6**, and separation of the formed diastereoisomers furnished (2-arylcypropyl)-2-furylmethanamines,  $\alpha$ -(2-arylcypropyl)glycine precursors, in optically pure form and high yields. As a representative example, the oxidation of the furan rings of (*S,S,S*)-, (*S,R,R*)-, (*R,S,S*)-, and (*R,R,R*)-**6a** furnished the corresponding isomers of  $\alpha$ -(2-phenylcypropyl)glycine (**1a**). Our approach benefits from the fact that all compounds required can be readily prepared, that diastereoisomer formation proceeds in high yields, and that the absolute configurations of the final products (**1**) can be controlled by choosing the appropriate stereoisomerically pure *O*-benzyloxime.

#### Experimental Part

*General.* Flash chromatography (FC): silica gel 60 (40–63  $\mu$ m). Optical rotations: Autopol IV automatic polarimeter. <sup>1</sup>H- and <sup>13</sup>C-NMR Spectra: Bruker DPX-400 (400 and 100 MHz, resp.); chemical shifts  $\delta$  in ppm rel. to SiMe<sub>4</sub>, coupling constants *J* in Hz.

*General Procedure for the Synthesis of Enones 2a–2e.* To a stirred soln. of the arene-aldehyde (1 equiv.) in H<sub>2</sub>O (*ca.* 2 ml per mmol) at r.t. was added a 0.1% aq. KOH soln. (100 mg in 10 ml of H<sub>2</sub>O). After stirring the mixture for 15 min at r.t., acetylfuran (1.33 equiv.) was added at once, and the mixture was stirred for 12 h

(monitored by TLC). Then, the mixture was acidified with  $\text{H}_2\text{SO}_4$ , extracted with  $\text{Et}_2\text{O}$  ( $3 \times 30$  ml), dried ( $\text{MgSO}_4$ ), and concentrated under reduced pressure. The products were purified by FC (Hex/AcOEt 6:1  $\rightarrow$  3:1).

(*E*)-1-(Furan-2-yl)-3-phenylprop-2-en-1-one (**2a**). Yield: 90%. Colorless solid. M.p. 81–83° (hexane/ $\text{Et}_2\text{O}$ ).  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 6.61 (*dd*,  $J = 1.7, 3.6, 1$  H); 7.34 (*dd*,  $J = 0.5, 3.6, 1$  H); 7.41–7.53 (*m*, 3 H); 7.54 (*d*,  $J_{AB} = 15.8, 1$  H); 7.63–7.72 (*m*, 3 H); 7.91 (*d*,  $J_{AB} = 15.8, 1$  H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 112.9; 117.9; 121.6; 129.1; 129.5; 130.7; 134.8; 144.3; 146.9; 154.1; 178.4.

(*E*)-3-(2-Chlorophenyl)-1-(furan-2-yl)prop-2-en-1-one (**2b**). Yield: 95%. Viscous oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 6.60 (*dd*,  $J = 1.6, 3.5, 1$  H); 7.35–7.55 (*m*, 5 H); 7.44 (*d*,  $J_{AB} = 15.8, 1$  H); 7.60 (*d*,  $J = 0.5, 1$  H); 8.21 (*d*,  $J_{AB} = 15.8, 1$  H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 112.5; 117.5; 124.2; 127.0; 127.9; 130.3; 131.1; 133.3; 135.6; 139.7; 139.7; 146.5; 153.7; 177.7.

(*E*)-1-(Furan-2-yl)-3-(3-methylphenyl)prop-2-en-1-one (**2c**). Yield: 89%. Viscous oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 2.21 (*s*, 3 H); 6.41 (*dd*,  $J = 1.4, 3.4, 1$  H); 7.01–7.12 (*m*, 2 H); 7.17 (*d*,  $J = 3.5, 1$  H); 7.25–7.27 (*m*, 2 H); 7.31 (*d*,  $J_{AB} = 15.8, 1$  H); 7.47 (*br. s*, 1 H); 7.65 (*d*,  $J_{AB} = 15.8, 1$  H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 21.6; 112.8; 117.5; 121.3; 126.1; 129.1; 129.5; 131.7; 135.0; 138.7; 144.3; 146.5; 154.2; 177.9.

(*E*)-1-(Furan-2-yl)-3-(4-methoxyphenyl)prop-2-en-1-one (**2d**). Yield: 75%. Viscous oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 3.71 (*s*, 3 H); 6.54 (*dd*,  $J = 1.6, 3.5, 1$  H); 6.81 (*d*,  $J_{AB} = 8.7, 2$  H); 7.15 (*d*,  $J = 3.6, 1$  H); 7.27 (*d*,  $J_{AB} = 15.8, 1$  H); 7.57 (*d*,  $J_{AB} = 8.7, 2$  H); 7.59 (*d*,  $J = 0.6, 1$  H); 7.71 (*d*,  $J_{AB} = 15.9, 1$  H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 55.6; 112.8; 114.7; 117.0; 119.2; 127.9; 130.6; 144.1; 146.1; 154.4; 162.1; 178.1.

(*E*)-1-(Furan-2-yl)-3-(2-naphthyl)prop-2-en-1-one (**2e**). Yield: 70%. Viscous oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 6.51 (*dd*,  $J = 1.6, 3.4, 1$  H); 7.27 (*d*,  $J = 3.5, 1$  H); 7.39–7.75 (*m*, 10 H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 112.6; 117.7; 121.7; 127.1; 127.7; 128.2; 129.1; 131.2; 132.6; 133.8; 134.8; 144.4; 146.6; 146.7; 153.4; 154.3; 178.3.

*General Procedure for the Cyclopropanation of Compounds of Type 2.* To a stirred soln. of NaH (1 equiv.) in DMSO (*ca.* 2 ml per mmol) under Ar gas at r.t. was added  $\text{Me}_3\text{SO}^+\text{I}^-$  (1.3 equiv.). After stirring for 15 min, the enone (**2a–e**; 1 equiv.), in DMSO (*ca.* 1 ml per mmol) was added at once with a syringe. The resulting dark mixture was stirred for 20 min at r.t., and poured onto ice-water, which was extracted with  $\text{Et}_2\text{O}$  ( $3 \times 75$  ml). The combined org. layers were dried ( $\text{MgSO}_4$ ) and concentrated under reduced pressure. The crude products were purified by FC (hexane/AcOEt 6:1  $\rightarrow$  3:1).

(Furan-2-yl)(2-phenylcyclopropyl)methanone (**3a**). Yield: 95%. Colorless solid. M.p. 91–93° (hexane/ $\text{Et}_2\text{O}$ ).  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 1.52 (*ddd*,  $J = 4.0, 6.8, 8.1, 1$  H); 1.91 (*ddd*,  $J = 4.1, 5.1, 9.1, 1$  H); 2.74 (*ddd*,  $J = 4.0, 6.5, 9.0, 1$  H); 2.83 (*ddd*,  $J = 4.1, 5.2, 8.1, 1$  H); 6.62 (*dd*,  $J = 1.7, 3.5, 1$  H); 7.11–7.31 (*m*, 6 H); 7.67 (*d*,  $J = 1.5, 1$  H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 18.9; 28.9; 29.4; 112.3; 116.7; 126.2; 126.5; 127.6; 140.3; 146.4; 153.2; 187.2. Anal. calc. for  $\text{C}_{14}\text{H}_{12}\text{O}_2$  (212.24): C 79.22, H 5.70; found: C 79.38, H 5.62.

[2-(2-Chlorophenyl)cyclopropyl](furan-2-yl)methanone (**3b**). Yield: 97%. Viscous oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 1.57 (*ddd*,  $J = 4.2, 6.9, 8.1, 1$  H); 1.84 (*ddd*,  $J = 4.3, 6.7, 8.3, 1$  H); 2.71 (*ddd*,  $J = 5.1, 6.8, 8.0, 1$  H); 2.85 (*ddd*,  $J = 4.3, 7.1, 8.1, 1$  H); 6.54 (*dd*,  $J = 1.6, 3.4, 1$  H); 7.13–7.32 (*m*, 5 H); 7.62 (*d*,  $J = 1.0, 1$  H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 17.1; 26.9; 27.1; 112.1; 116.7; 126.5; 127.1; 127.7; 129.1; 135.4; 137.4; 146.3; 152.8; 186.7. Anal. calc. for  $\text{C}_{14}\text{H}_{11}\text{ClO}_2$  (264.69): C 68.16, H 4.49; found: C 68.36, H 4.61.

(Furan-2-yl)[2-(3-methylphenyl)cyclopropyl]methanone (**3c**). Yield: 96%. Viscous oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 1.27–1.31 (*m*, 1 H); 1.72–1.76 (*m*, 1 H); 2.23 (*s*, 3 H); 2.50–2.53 (*m*, 1 H); 2.69–2.73 (*m*, 1 H); 6.31 (*dd*,  $J = 1.3, 3.5, 1$  H); 6.31–7.18 (*m*, 5 H); 7.49 (*s*, 1 H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 19.2; 21.3; 29.3; 29.7; 112.7; 116.8; 123.6; 127.4; 127.7; 128.8; 138.3; 140.6; 146.4; 153.7; 187.3. Anal. calc. for  $\text{C}_{15}\text{H}_{14}\text{O}_2$  (226.27): C 79.62, H 6.24; found: C 79.48, H 6.33.

(Furan-2-yl)[2-(4-methoxyphenyl)cyclopropyl]methanone (**3d**). Yield: 95%. Viscous oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 1.34 (*ddd*,  $J = 4.1, 6.7, 8.1, 1$  H); 1.75 (*ddd*,  $J = 4.2, 5.1, 9.1, 1$  H); 2.63 (*ddd*,  $J = 4.1, 6.7, 9.2, 1$  H); 2.78 (*ddd*,  $J = 4.1, 5.2, 8.3, 1$  H); 3.84 (*s*, 3 H); 6.51 (*dd*,  $J = 1.7, 3.5, 1$  H); 6.74 (*d*,  $J_{AB} = 8.6, 2$  H); 7.01 (*d*,  $J_{AB} = 8.6, 2$  H); 7.10 (*d*,  $J = 3.4, 1$  H); 7.50 (*s*, 1 H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 19.1; 29.2; 29.4; 55.5; 112.6; 114.3; 116.5; 127.8; 132.7; 146.3; 153.8; 158.8; 187.4. Anal. calc. for  $\text{C}_{15}\text{H}_{14}\text{O}_3$  (242.27): C 74.36, H 5.82; found: C 74.58, H 5.61.

(Furan-2-yl)[2-(2-naphthyl)cyclopropyl]methanone (**3e**). Yield: 90%. Viscous oil.  $^1\text{H-NMR}$  (400 MHz,  $\text{CDCl}_3$ ): 1.55–1.61 (*m*, 1 H); 1.86–1.90 (*m*, 1 H); 2.77–2.87 (*m*, 2 H); 6.47 (*dd*,  $J = 1.6, 3.5, 1$  H); 7.15–7.73 (*m*, 9 H).  $^{13}\text{C-NMR}$  (100 MHz,  $\text{CDCl}_3$ ): 19.3; 29.5; 30.1; 112.7; 117.0; 124.9; 125.2; 125.9; 126.7; 127.8; 128.1; 128.6; 132.8; 133.8; 138.2; 146.7; 153.7; 187.4. Anal. calc. for  $\text{C}_{18}\text{H}_{14}\text{O}_2$  (262.30): C 82.42, H 5.38; found: C 82.57, H 5.21.

*General Procedure for the Synthesis of Oximes of Type 4. Method A ((E)-oximes):* The ketone (**3a–e**; 5 mmol),  $\text{NH}_2\text{OH} \cdot \text{HCl}$  (6 mmol), and NaOH (6 mmol) were mixed in anhyd. EtOH (15 ml) and stirred under



reflux for 12 h. The reaction was monitored by TLC. The hot soln. was filtered and evaporated. The remaining solid was dissolved in H<sub>2</sub>O and extracted with Et<sub>2</sub>O. The org. layer was washed with H<sub>2</sub>O and brine, and dried (MgSO<sub>4</sub>). Evaporation of the solvent afforded the crude (*E*)-oxime, which was purified either by FC (hexane/AcOEt 5 : 1 → 3 : 1) or recrystallization (hexane/Et<sub>2</sub>O).

**Method B** ((*Z*)-oximes): The ketone (**3a–e**; 5 mmol), NH<sub>2</sub>OH · HCl (6 mmol), and NaOAc (6 mmol) were mixed in anh. EtOH (15 ml) and stirred under reflux for 12 h. The reaction was monitored by TLC. The hot soln. was filtered and evaporated. The remaining solid was dissolved in H<sub>2</sub>O and extracted with Et<sub>2</sub>O. The org. layer was washed with H<sub>2</sub>O and brine, and dried (MgSO<sub>4</sub>). Evaporation of the solvent afforded the crude (*Z*)-oxime, which was purified either by FC (hexane/AcOEt 5 : 1 → 3 : 1) or recrystallization (hexane/Et<sub>2</sub>O).

(*E*)-(Furan-2-yl)(2-phenylcyclopropyl)methanone Oxime ((*E*)-**4a**). Yield: 84%. Colorless solid. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.55 (ddd, *J* = 5.5, 5.9, 9.2, 1 H); 1.82 (ddd, *J* = 5.1, 6.1, 8.8, 1 H); 2.41 (ddd, *J* = 5.6, 6.1, 9.1, 1 H); 2.67 (ddd, *J* = 5.5, 5.8, 8.8, 1 H); 6.42 (dd, *J* = 1.8, 3.4, 1 H); 6.81 (d, *J* = 3.6, 1 H); 7.21–7.45 (m, 5 H); 7.42 (d, *J* = 1.8, 1 H); 9.87 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 17.5; 21.8; 28.7; 112.8; 113.1; 128.2; 130.5; 143.5; 145.4; 151.2; 152.0. Anal. calc. for C<sub>14</sub>H<sub>13</sub>NO<sub>2</sub> (227.26): C 73.99, H 5.77, N 6.16; found: C 73.71, H 5.63, N 5.92.

(*Z*)-(Furan-2-yl)(2-phenylcyclopropyl)methanone Oxime ((*Z*)-**4a**). Yield: 77%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.34 (ddd, *J* = 5.6, 6.9, 8.1, 1 H); 1.62 (ddd, *J* = 5.1, 7.3, 8.0, 1 H); 2.31 (ddd, *J* = 5.3, 7.0, 8.3, 1 H); 2.45 (ddd, *J* = 5.3, 6.8, 7.9, 1 H); 6.51 (dd, *J* = 1.6, 3.2, 1 H); 7.11–7.24 (m, 5 H); 7.40 (d, *J* = 1.0, 1 H); 7.52 (d, *J* = 3.3, 1 H); 10.12 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 14.9; 22.6; 25.1; 111.1; 117.9; 125.9; 126.2; 128.3; 141.7; 143.4; 145.8; 146.9.

(*E*)-[2-(2-Chlorophenyl)cyclopropyl](furan-2-yl)methanone Oxime ((*E*)-**4b**). Yield: 83%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.21 (ddd, *J* = 5.6, 6.7, 8.9, 1 H); 1.72 (ddd, *J* = 5.5, 6.5, 9.1, 1 H); 2.34 (ddd, *J* = 6.0, 6.9, 9.2, 1 H); 2.84 (ddd, *J* = 6.1, 7.1, 8.9, 1 H); 6.31 (dd, *J* = 1.9, 3.4, 1 H); 6.52 (dd, *J* = 0.4, 3.6, 1 H); 7.01–7.27 (m, 4 H); 7.32 (dd, *J* = 0.4, 1.7, 1 H); 9.91 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.5; 18.9; 21.9; 111.0; 111.5; 127.2; 127.3; 127.8; 129.7; 135.7; 139.2; 143.8; 149.4; 150.5. Anal. calc. for C<sub>14</sub>H<sub>12</sub>ClNO<sub>2</sub> (261.70): C 64.25, H 4.62, N 5.35; found: C 64.52, H 4.73, N 5.52.

(*Z*)-[2-(2-Chlorophenyl)cyclopropyl](furan-2-yl)methanone Oxime ((*Z*)-**4b**). Yield: 78%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.24 (ddd, *J* = 5.1, 6.3, 9.1, 1 H); 1.52 (ddd, *J* = 6.1, 6.4, 8.9, 1 H); 2.31 (ddd, *J* = 5.5, 6.1, 8.7, 1 H); 2.55 (ddd, *J* = 5.7, 6.1, 9.0, 1 H); 6.42 (dd, *J* = 1.6, 3.5, 1 H); 7.01–7.24 (m, 4 H); 7.30 (d, *J* = 1.1, 1 H); 7.42 (d, *J* = 3.4, 1 H); 9.81 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.9; 22.8; 23.9; 113.4; 119.4; 127.9; 128.1; 128.5; 130.6; 136.9; 140.4; 143.8; 147.2; 147.7.

(*E*)-(Furan-2-yl)[2-(3-methylphenyl)cyclopropyl]methanone Oxime ((*E*)-**4c**). Yield: 86%. Colorless solid. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.31–1.36 (m, 1 H); 1.63–1.67 (m, 1 H); 2.23–2.25 (m, 1 H); 2.25 (s, 3 H); 2.45–2.50 (m, 1 H); 6.32 (t, *J* = 1.5, 1 H); 6.57 (d, *J* = 3.2, 1 H); 6.78–7.15 (m, 4 H); 7.36 (s, 1 H); 8.51 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 16.0; 20.2; 21.8; 24.1; 111.2; 111.5; 123.6; 127.3; 127.4; 128.8; 138.4; 141.7; 143.7; 149.6; 150.3. Anal. calc. for C<sub>15</sub>H<sub>15</sub>NO<sub>2</sub> (241.29): C 74.67, H 6.27, N 5.81; found: C 74.83, H 6.43, N 5.62.

(*Z*)-(Furan-2-yl)[2-(3-methylphenyl)cyclopropyl]methanone Oxime ((*Z*)-**4c**). Yield: 77%. Colorless solid. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.19–1.24 (m, 1 H); 1.49–1.54 (m, 1 H); 2.22–2.27 (m, 2 H); 2.27 (s, 3 H); 6.46 (dd, *J* = 1.7, 3.3, 1 H); 6.86–7.15 (m, 4 H); 7.38 (br. s, 2 H); 8.74 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.5; 21.8; 23.0; 25.6; 112.7; 118.4; 123.7; 127.4; 128.7; 138.3; 140.6; 142.1; 143.2; 146.7; 147.5.

(*E*)-(Furan-2-yl)[2-(4-methoxyphenyl)cyclopropyl]methanone Oxime ((*E*)-**4d**). Yield: 74%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.25–1.28 (m, 1 H); 1.53–1.57 (m, 1 H); 2.18–2.21 (m, 1 H); 2.47–2.51 (m, 1 H); 3.65 (s, 3 H); 6.41 (dd, *J* = 1.7, 2.8, 1 H); 6.56 (d, *J* = 2.7, 1 H); 6.75 (d, *J*<sub>AB</sub> = 8.5, 2 H); 7.12 (d, *J*<sub>AB</sub> = 8.6, 2 H); 7.49 (s, 1 H); 8.71 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.6; 19.8; 22.6; 55.6; 111.1; 111.5; 112.4; 114.2; 114.3; 127.9; 133.7; 143.7; 149.6; 150.2; 158.3. Anal. calc. for C<sub>15</sub>H<sub>15</sub>NO<sub>3</sub> (257.28): C 70.02, H 5.88, N 5.05; found: C 68.74, H 5.66, N 4.91.

(*Z*)-(Furan-2-yl)[2-(4-methoxyphenyl)cyclopropyl]methanone Oxime ((*Z*)-**4d**). Yield: 82%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.18–1.21 (m, 1 H); 1.48–1.51 (m, 1 H); 2.17–2.27 (m, 2 H); 3.61 (s, 3 H); 6.47 (dd, *J* = 1.6, 3.4, 1 H); 6.47 (d, *J*<sub>AB</sub> = 8.5, 2 H); 7.01 (d, *J*<sub>AB</sub> = 8.4, 2 H); 7.35 (br. s, 2 H); 9.02 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.0; 22.7; 25.1; 55.6; 112.5; 114.3; 118.4; 127.8; 134.2; 143.1; 146.4; 146.6; 147.5; 158.5.

(*E*)-(Furan-2-yl)[2-(2-naphthyl)cyclopropyl]methanone Oxime ((*E*)-**4e**). Yield: 78%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.43–1.48 (m, 1 H); 1.73–1.78 (m, 1 H); 2.32–2.37 (m, 1 H); 2.64–2.69 (m, 1 H); 6.30 (d, *J* = 1.6, 1 H); 6.58 (d, *J* = 3.3, 1 H); 7.14–7.69 (m, 8 H); 8.83 (br. s, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 16.0; 20.4; 24.5; 111.2; 111.6; 125.0; 125.2; 125.6; 126.5; 126.8; 127.8; 128.6; 132.7; 133.9; 139.3; 143.7; 149.8; 150.1. Anal. calc. for C<sub>18</sub>H<sub>15</sub>NO<sub>2</sub> (277.32): C 77.96, H 5.45, N 5.05; found: C 77.79, H 5.52, N 4.91.

(*Z*)-(Furan-2-yl)[2-(2-naphthyl)cyclopropyl]methanone Oxime ((*Z*)-**4e**). Yield: 80%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.30–1.35 (*m*, 1 H); 1.47–1.53 (*m*, 1 H); 1.83–1.87 (*m*, 1 H); 2.74–2.79 (*m*, 1 H); 6.38 (*dd*, *J* = 1.5, 3.5, 1 H); 7.10–7.66 (*m*, 9 H); 8.98 (*br. s*, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.5; 23.3; 29.6; 112.5; 117.0; 118.5; 124.9; 125.4; 125.9; 126.4; 126.7; 127.9; 128.1; 128.2; 128.4; 128.7; 143.1; 146.6.

*General Procedure for the Synthesis of Oxime Ethers of Type 5.* To a stirred soln. of NaH (1.3 equiv.) in DMF (*ca.* 10 ml per mmol) under Ar gas at 0° was added the oxime (**4a–e**; 1 equiv.), in DMF (*ca.* 5 ml per mmol). The mixture was stirred for 2 h at r.t. Benzyl bromide (1.04 equiv.) was added, and stirring was continued overnight. Careful addition of H<sub>2</sub>O (until no more gas was observed) was followed by extraction with AcOEt (3 × 50 ml). The combined org. layers were dried (MgSO<sub>4</sub>) and concentrated under reduced pressure to give the crude product, which was purified by FC (Hexane/AcOEt 6:1 → 4:1).

(*E*)-(Furan-2-yl)(2-phenylcyclopropyl)methanone O-Benzylloxime ((*E*)-**5a**). Yield: 92%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.31 (*ddd*, *J* = 4.1, 6.5, 9.0, 1 H); 1.61 (*ddd*, *J* = 4.1, 5.0, 8.8, 1 H); 2.20 (*ddd*, *J* = 5.3, 6.0, 9.1, 1 H); 2.54 (*ddd*, *J* = 5.3, 6.1, 8.7, 1 H); 5.21 (*s*, 2 H); 6.31 (*dd*, *J* = 1.9, 3.4, 1 H); 6.63 (*d*, *J* = 3.1, 1 H); 7.01–7.32 (*m*, 11 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.4; 20.4; 23.7; 76.6; 110.5; 110.9; 126.1; 127.3; 127.6; 128.0; 128.1; 128.2; 137.4; 141.2; 143.0; 149.3; 149.7. Anal. calc. for C<sub>21</sub>H<sub>19</sub>NO<sub>2</sub> (317.38): C 79.47, H 6.03, N 4.41; found: C 79.66, H 5.84, N 4.66.

(*Z*)-(Furan-2-yl)(2-phenylcyclopropyl)methanone O-Benzylloxime ((*Z*)-**5a**). Yield: 96%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.11–1.21 (*m*, 1 H); 1.61–1.74 (*m*, 1 H); 2.20–2.42 (*m*, 2 H); 5.12 (*s*, 2 H); 6.21 (*dd*, *J* = 1.5, 3.3, 1 H); 7.12–7.53 (*m*, 12 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.6; 22.5; 25.7; 76.8; 111.9; 117.5; 125.8; 126.2; 128.2; 128.3; 128.6; 128.9; 137.6; 142.0; 142.3; 145.9; 146.2.

(*E*)-[2-(2-Chlorophenyl)cyclopropyl](furan-2-yl)methanone O-Benzylloxime ((*E*)-**5b**). Yield: 95%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.06–1.14 (*m*, 1 H); 1.56–1.64 (*m*, 1 H); 2.22–2.27 (*m*, 1 H); 2.66–2.71 (*m*, 1 H); 5.07 (*s*, 2 H); 6.23 (*dd*, *J* = 1.7, 3.2, 1 H); 6.43 (*d*, *J* = 3.4, 1 H); 6.90–7.26 (*m*, 10 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.6; 19.6; 22.2; 77.2; 110.1; 111.7; 127.1; 127.5; 127.8; 128.2; 128.3; 128.5; 128.7; 129.6; 138.0; 143.7; 147.6; 150.4; 150.7. Anal. calc. for C<sub>21</sub>H<sub>18</sub>ClNO<sub>2</sub> (351.83): C 71.69, H 5.16, N 3.98; found: C 71.78, H 5.23, N 3.62.

(*Z*)-[2-(2-Chlorophenyl)cyclopropyl](furan-2-yl)methanone O-Benzylloxime ((*Z*)-**5b**). Yield: 95%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.10 (*ddd*, *J* = 3.9, 6.1, 8.1, 1 H); 1.62 (*ddd*, *J* = 4.2, 5.6, 8.1, 1 H); 2.45 (*ddd*, *J* = 4.9, 5.6, 8.6, 1 H); 2.63 (*ddd*, *J* = 4.1, 5.1, 8.9, 1 H); 5.24 (*s*, 2 H); 6.42 (*dd*, *J* = 1.7, 3.4, 1 H); 7.11–7.34 (*m*, 11 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.2; 21.7; 23.8; 77.3; 112.4; 117.9; 127.1; 127.2; 127.5; 128.1; 128.2; 128.6; 128.7; 136.8; 138.9; 139.5; 143.4; 146.9; 147.5.

(*E*)-(Furan-2-yl)[2-(3-methylphenyl)cyclopropyl]methanone O-Benzylloxime ((*E*)-**5c**). Yield: 89%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.17–1.21 (*m*, 1 H); 1.44–1.48 (*m*, 1 H); 2.04–2.09 (*m*, 1 H); 2.13 (*s*, 3 H); 2.27–2.32 (*m*, 1 H); 5.07 (*s*, 2 H); 6.24 (*dd*, *J* = 1.8, 3.3, 1 H); 6.49 (*d*, *J* = 3.3, 1 H); 6.74–7.21 (*m*, 9 H); 7.27 (*d*, *J* = 1.0, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.9; 21.8; 23.2; 24.3; 77.6; 111.4; 111.6; 123.7; 127.4; 127.6; 128.2; 128.6; 128.8; 138.0; 138.3; 141.8; 143.7; 149.8; 150.5. Anal. calc. for C<sub>22</sub>H<sub>21</sub>NO<sub>2</sub> (331.41): C 79.73, H 6.39, N 4.23; found: C 79.61, H 8.47, N 4.42.

(*Z*)-(Furan-2-yl)[2-(3-methylphenyl)cyclopropyl]methanone O-Benzylloxime ((*Z*)-**5c**). Yield: 90%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.26–1.33 (*m*, 1 H); 1.68–1.72 (*m*, 1 H); 2.31–2.36 (*m*, 1 H); 2.38 (*s*, 3 H); 2.44–2.48 (*m*, 1 H); 5.26 (*s*, 2 H); 6.51 (*dd*, *J* = 1.7, 3.4, 1 H); 7.01–7.46 (*m*, 11 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 16.1; 21.9; 23.0; 26.2; 77.4; 112.5; 118.0; 123.8; 127.2; 127.5; 128.3; 128.6; 128.8; 128.9; 138.3; 142.6; 142.9; 146.7; 146.8.

(*E*)-(Furan-2-yl)[2-(4-methoxyphenyl)cyclopropyl]methanone O-Benzylloxime ((*E*)-**5d**). Yield: 87%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.16–1.21 (*m*, 1 H); 1.47–1.52 (*m*, 1 H); 2.05–2.10 (*m*, 1 H); 2.31–2.36 (*m*, 1 H); 3.64 (*s*, 3 H); 5.11 (*s*, 2 H); 6.31 (*br. s*, 1 H); 6.53 (*d*, *J* = 3.1, 1 H); 6.64 (*d*, *J*<sub>AB</sub> = 8.5, 2 H); 6.92 (*d*, *J*<sub>AB</sub> = 8.5, 2 H); 7.15–7.31 (*m*, 6 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.6; 20.5; 23.7; 55.5; 77.4; 111.1; 111.5; 114.2; 127.9; 128.2; 128.6; 128.7; 133.7; 138.0; 143.5; 149.8; 150.5; 158.5. Anal. calc. for C<sub>22</sub>H<sub>21</sub>NO<sub>3</sub> (347.41): C 76.06, H 6.09, N 4.03; found: C 76.22, H 5.91, N 4.82.

(*Z*)-(Furan-2-yl)[2-(4-methoxyphenyl)cyclopropyl]methanone O-Benzylloxime ((*Z*)-**5d**). Yield: 96%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.05–1.10 (*m*, 1 H); 1.51–1.56 (*m*, 1 H); 2.16–2.26 (*m*, 2 H); 3.65 (*s*, 3 H); 5.10 (*s*, 2 H); 6.34 (*dd*, *J* = 1.7, 3.4, 1 H); 6.73 (*d*, *J*<sub>AB</sub> = 8.6, 2 H); 7.14 (*d*, *J*<sub>AB</sub> = 8.5, 2 H); 7.17–7.31 (*m*, 7 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 15.4; 22.7; 25.6; 55.7; 77.4; 112.5; 114.3; 117.9; 127.9; 128.1; 128.2; 128.3; 128.7; 128.9; 134.6; 138.3; 143.0; 146.8; 158.5.

(*E*)-(Furan-2-yl)[2-(2-naphthyl)cyclopropyl]methanone O-Benzylloxime ((*E*)-**5e**). Yield: 76%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.35–1.49 (*m*, 1 H); 1.52–1.78 (*m*, 1 H); 2.21–2.35 (*m*, 1 H); 2.52–2.61 (*m*, 1 H); 5.12 (*s*, 2 H); 6.32 (*dd*, *J* = 1.6, 3.3, 1 H); 6.59 (*d*, *J* = 3.2, 1 H); 7.12–7.77 (*m*, 13 H). <sup>13</sup>C-NMR (100 MHz,

CDCl<sub>3</sub>): 15.8; 20.9; 24.6; 77.2; 111.5; 117.9; 125.6; 126.4; 127.8; 128.0; 128.1; 128.2; 128.4; 128.6; 128.7; 132.6; 133.9; 138.7; 139.3; 143.6; 149.7; 150.3. Anal. calc. for C<sub>25</sub>H<sub>21</sub>NO<sub>2</sub> (367.44): C 81.72, H 5.76, N 3.81; found: C 81.93, H 5.57, N 3.97.

(*Z*)-(Furan-2-yl)[2-(2-naphthyl)cyclopropyl]methanone O-Benzoyloxime ((*Z*)-**5e**). Yield: 83%. Viscous oil. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.12–1.24 (*m*, 2 H); 1.61–1.70 (*m*, 1 H); 2.31–2.42 (*m*, 1 H); 5.09 (*s*, 2 H); 6.27 (*dd*, *J* = 1.7, 3.5, 1 H); 7.12–7.59 (*m*, 14 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 16.1; 23.4; 26.6; 77.5; 112.6; 118.2; 125.0; 125.5; 126.5; 128.0; 128.1; 128.2; 128.4; 128.5; 134.1; 138.3; 138.9; 140.2; 142.9; 142.9; 146.5; 146.9.

**General Procedure for the Synthesis of Amines 6 from Oxime-Ethers 5.** To a stirred mixture of one of the chiral amino alcohols (**7–9**; 1.5 equiv.) in anh. THF (*ca.* 5 ml per mmol) under Ar gas at r.t. was added BH<sub>3</sub>·SMe<sub>2</sub>. The mixture was stirred for 8 h at r.t., then, the oxime ether (**5a–e**; 1 equiv.) in anh. THF (*ca.* 3 ml per mmol) was added dropwise. After 48 h, 1*N* HCl was added, until a white precipitate was formed. Finally, aq. NaOH soln. was added, and the layers were separated. The aq. layer was extracted with Et<sub>2</sub>O (2 × 25 ml), and the combined org. layers were dried (MgSO<sub>4</sub>) and evaporated. The crude products were purified by FC (hexane/AcOEt/MeOH 1:1:1).

(*S*)-(Furan-2-yl)[(1*S*,2*S*)-2-phenylcyclopropyl]methanamine ((*S,S,S*)-**6a**) and (*R*)-(Furan-2-yl)[(1*R*,2*R*)-2-phenylcyclopropyl]methanamine ((*R,R,R*)-**6a**). Yields: 45 and 43%, resp. Viscous oils. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +37.5 (*c* = 0.5, CHCl<sub>3</sub>) for (*S,S,S*)-**6a**, and [ $\alpha$ ]<sub>D</sub><sup>20</sup> = –34.5 (*c* = 0.5, CHCl<sub>3</sub>) for (*R,R,R*)-**6a**. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 1.27–1.31 (*m*, 2 H); 1.64–1.67 (*m*, 1 H); 2.17–2.19 (*m*, 1 H); 2.67 (*br. s*, 2 H); 3.74 (*d*, *J* = 8.4, 1 H); 6.17 (*d*, *J* = 3.4, 1 H); 6.26 (*dd*, *J* = 1.6, 3.5, 1 H); 7.18–7.65 (*m*, 6 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 14.4; 21.7; 28.9; 55.6; 105.3; 110.5; 126.2; 126.5; 126.8; 128.1; 128.6; 128.7; 142.4; 158.1.

(*S*)-(Furan-2-yl)[(1*R*,2*R*)-2-phenylcyclopropyl]methanamine ((*S,R,R*)-**6a**) and (*R*)-(Furan-2-yl)[(1*S*,2*S*)-2-phenylcyclopropyl]methanamine ((*R,S,S*)-**6a**). Yields: 41 and 46%, resp. Viscous oils. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = –61.4 (*c* = 0.6, CHCl<sub>3</sub>) for (*S,R,R*)-**6a**, and [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +55.7 (*c* = 0.6, CHCl<sub>3</sub>) for (*R,S,S*)-**6a**. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 0.91–1.12 (*m*, 2 H); 1.57–1.59 (*m*, 1 H); 1.89–1.92 (*m*, 1 H); 2.58 (*br. s*, 2 H); 3.62 (*d*, *J* = 8.2, 1 H); 6.11 (*d*, *J* = 3.2, 1 H); 6.24 (*dd*, *J* = 1.7, 3.4, 1 H); 6.96–7.42 (*m*, 6 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 14.2; 21.8; 28.9; 54.2; 105.2; 110.5; 126.0; 126.4; 126.8; 127.8; 128.6; 128.7; 141.9; 158.2. Anal. calc. for C<sub>14</sub>H<sub>15</sub>NO (212.28): C 78.84, H 7.09; found: C 78.93, H 7.33.

(*S*)-[1*S*,2*S*]-2-(2-Chlorophenyl)cyclopropyl[(furan-2-yl)methanamine] ((*S,S,S*)-**6b**) and (*R*)-[1*R*,2*R*]-2-(2-Chlorophenyl)cyclopropyl[(furan-2-yl)methanamine] ((*R,R,R*)-**6b**). Yields: 40 and 44%, resp. Viscous oils. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +2.6 (*c* = 0.5, CHCl<sub>3</sub>) for (*S,S,S*)-**6b**, and [ $\alpha$ ]<sub>D</sub><sup>20</sup> = –56.2 (*c* = 0.5, CHCl<sub>3</sub>) for (*R,R,R*)-**6b**. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 0.95–0.98 (*m*, 2 H); 1.34–1.39 (*m*, 1 H); 2.11–2.14 (*m*, 1 H); 2.33 (*br. s*, 2 H); 3.52 (*d*, *J* = 8.3, 1 H); 6.12 (*d*, *J* = 3.2, 1 H); 6.21 (*dd*, *J* = 1.8, 3.4, 1 H); 6.08–7.31 (*m*, 5 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 12.4; 20.2; 28.9; 54.3; 105.3; 104.7; 126.7; 127.3; 128.7; 129.5; 135.4; 139.6; 141.8; 157.6. Anal. calc. for C<sub>14</sub>H<sub>14</sub>ClNO (247.72): C 67.88, H 5.70; found: C 67.63, H 5.66.

(*S*)-[1*R*,2*R*]-2-(2-Chlorophenyl)cyclopropyl[(furan-2-yl)methanamine] ((*S,R,R*)-**6b**) and (*R*)-[1*S*,2*S*]-2-(2-chlorophenyl)cyclopropyl[(furan-2-yl)methanamine] ((*R,S,S*)-**6b**). Yields: 43 and 39%, resp. Viscous oils. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = –74.7 (*c* = 0.3, CHCl<sub>3</sub>) for (*S,R,R*)-**6b**, and [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +77.1 (*c* = 0.3, CHCl<sub>3</sub>) for (*R,S,S*)-**6b**. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 0.71–0.95 (*m*, 2 H); 1.44–1.47 (*m*, 1 H); 1.89 (*br. s*, 2 H); 2.18–2.21 (*m*, 1 H); 3.62 (*d*, *J* = 8.3); 6.14 (*d*, *J* = 3.3, 1 H); 6.18 (*dd*, *J* = 1.7, 3.5, 1 H); 6.84–7.28 (*m*, 5 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 12.8; 19.0; 27.9; 53.1; 105.2; 110.2; 110.4; 127.2; 129.6; 135.4; 139.9; 141.8; 158.1.

(*S*)-(Furan-2-yl)[(1*S*,2*S*)-2-(3-methylphenyl)cyclopropyl]methanamine ((*S,S,S*)-**6c**) and (*R*)-(Furan-2-yl)[(1*R*,2*R*)-2-(3-methylphenyl)cyclopropyl]methanamine ((*R,R,R*)-**6c**). Yields: 44 and 43%, resp. Viscous oils. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +78.4 (*c* = 0.5, CHCl<sub>3</sub>) for (*S,S,S*)-**6c**, and [ $\alpha$ ]<sub>D</sub><sup>20</sup> = –76.3 (*c* = 0.6, CHCl<sub>3</sub>) for (*R,R,R*)-**6c**. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 0.90–0.96 (*m*, 1 H); 1.34–1.41 (*m*, 1 H); 1.78–1.83 (*m*, 1 H); 2.23 (*s*, 3 H); 2.38 (*br. s*, 2 H); 3.47 (*d*, *J* = 8.2, 1 H); 6.06 (*d*, *J* = 3.1, 1 H); 6.21 (*dd*, *J* = 1.9, 3.0, 1 H); 6.76–7.06 (*m*, 4 H); 7.26 (*s*, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 14.2; 21.7; 21.8; 28.6; 54.1; 105.3; 110.4; 123.4; 126.8; 127.1; 128.6; 138.2; 141.9; 142.6; 158.0. Anal. calc. for C<sub>15</sub>H<sub>17</sub>NO (227.30): C 79.26, H 7.54; found: C 79.52, H 7.68.

(*S*)-(Furan-2-yl)[(1*R*,2*R*)-2-(3-methylphenyl)cyclopropyl]methanamine ((*S,R,R*)-**6c**) and (*R*)-(Furan-2-yl)[(1*S*,2*S*)-2-(3-methylphenyl)cyclopropyl]methanamine ((*R,S,S*)-**6c**). Yields: 44 and 41%, resp. Viscous oils. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = –15.9 (*c* = 0.4, CHCl<sub>3</sub>) for (*S,R,R*)-**6c**, and [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +18.9 (*c* = 0.5, CHCl<sub>3</sub>) for (*R,S,S*)-**6c**. <sup>1</sup>H-NMR (400 MHz, CDCl<sub>3</sub>): 0.80–0.88 (*m*, 2 H); 1.30–1.36 (*m*, 1 H); 1.69–1.74 (*m*, 1 H); 2.20 (*s*, 5 H); 3.37 (*d*, *J* = 8.0, 1 H); 6.05 (*d*, *J* = 2.9, 1 H); 6.17 (*t*, *J* = 1.9, 1 H); 6.69–7.17 (*m*, 4 H); 7.21 (*s*, 1 H). <sup>13</sup>C-NMR (100 MHz, CDCl<sub>3</sub>): 14.3; 21.8; 22.0; 29.0; 54.1; 105.2; 110.5; 123.4; 126.4; 126.8; 128.7; 138.1; 141.8; 142.7; 158.1.

(*S*)-(Furan-2-yl)[(1*S*,2*S*)-2-(4-methoxyphenyl)cyclopropyl]methanamine ((*S,S,S*)-**6d**) and (*R*)-(Furan-2-yl)[(1*R*,2*R*)-2-(4-methoxyphenyl)cyclopropyl]methanamine ((*R,R,R*)-**6d**). Yields: 46 and 45%, resp. Viscous oils. [ $\alpha$ ]<sub>D</sub><sup>20</sup> = +12.4 (*c* = 1.1, CHCl<sub>3</sub>) for (*S,S,S*)-**6d**, and [ $\alpha$ ]<sub>D</sub><sup>20</sup> = –9.2 (*c* = 0.9, CHCl<sub>3</sub>) for (*R,R,R*)-**6d**. <sup>1</sup>H-NMR

(400 MHz,  $\text{CDCl}_3$ ): 0.81–0.92 (*m*, 2 H); 1.25–1.28 (*m*, 1 H); 1.75 (br. *s*, 2 H); 1.26–1.29 (*m*, 1 H); 3.40 (*d*,  $J = 8.3$ , 1 H); 3.68 (*s*, 3 H); 6.05 (*d*,  $J = 3.1$ , 1 H); 6.19 (*dd*,  $J = 1.6$ , 3.0, 1 H); 6.71 (*dd*,  $J_{AB} = 8.6$ , 2 H); 6.89 (*dd*,  $J_{AB} = 8.6$ , 2 H); 7.25 (*s*, 1 H).  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ): 13.7; 21.0; 28.5; 54.3; 55.6; 105.1; 110.4; 114.2; 127.5; 134.6; 141.8; 158.2; 158.5. Anal. calc. for  $\text{C}_{15}\text{H}_{17}\text{NO}_2$  (243.30): C 74.05, H 7.04; found: C 74.33, H 7.33.

(*S*)-(Furan-2-yl)[(1*S*,2*S*)-2-(2-naphthyl)cyclopropyl]methanamine ((*S,S,S*)-**6e**) and (*R*)-2-(Furan-2-yl)[(1*R*,2*R*)-2-(2-naphthyl)cyclopropyl]methanamine ((*R,R,R*)-**6e**). Yields: 42 and 44%, resp. Viscous oils.  $[\alpha]_{\text{D}}^{20} = +98.3$  ( $c = 0.5$ ,  $\text{CHCl}_3$ ) for (*S,S,S*)-**6e**, and  $[\alpha]_{\text{D}}^{20} = -101.6$  ( $c = 0.6$ ,  $\text{CHCl}_3$ ) for (*R,R,R*)-**6e**.  $^1\text{H}$ -NMR (400 MHz,  $\text{CDCl}_3$ ): 1.01–1.14 (*m*, 2 H); 1.55–1.57 (*m*, 1 H); 1.98–2.02 (*m*, 1 H); 2.57 (br. *s*, 2 H); 3.52 (*d*,  $J = 8.3$ , 1 H); 6.07 (*d*,  $J = 3.4$ , 1 H); 6.18 (br. *s*, 1 H); 7.12–7.74 (*m*, 8 H).  $^{13}\text{C}$ -NMR (100 MHz,  $\text{CDCl}_3$ ): 14.5; 22.1; 28.6; 54.1; 105.5; 110.5; 124.4; 125.2; 125.4; 126.4; 127.7; 127.9; 128.3; 132.4; 133.4; 139.9; 142.0. Anal. calc. for  $\text{C}_{18}\text{H}_{17}\text{NO}$  (263.33): C 82.10, H 6.51; found: C 82.24, H 6.68.

*General Procedure for the Oxidation of the Furan Ring of Compounds of Type 6. By Ozonolysis.* Through a soln. of (*S,S,S*)-**6a** and (*S,R,R*)-**6a** (3 mmol) in MeOH (25 ml), cooled to  $-78^\circ$ , was passed  $\text{O}_3$  for 15 min (blue color). Then, Ar gas was bubbled at this temp. through the soln. to remove excess  $\text{O}_3$ . The soln. was allowed to warm to r.t., and HCl gas was passed through the soln. (salt formation). The crude product was purified by recrystallization.

*By Oxidation with  $\text{RuO}_2/\text{NaIO}_4$ .*  $\text{RuO}_2 \cdot \text{H}_2\text{O}$  (0.066 mmol) was added to a mixture of  $\text{NaIO}_4$  (29.8 mmol) in  $\text{H}_2\text{O}$  (13 ml), MeCN (19 ml), and  $\text{CCl}_4$  (13 ml), and the mixture was stirred for 30 min. Compounds (*S,S,S*)- and (*S,R,R*)-**6a** (1.8 mmol) were added, and the mixture was stirred for 2 h at r.t. The org. layer was separated, the aq. phase was washed with  $\text{CH}_2\text{Cl}_2$  ( $4 \times 20$  ml) and brine, dried ( $\text{Na}_2\text{SO}_4$ ), and concentrated. The residue was

Table 3. Crystallographic Data<sup>a</sup> of (*E*)-**4a**, (*E*)-**4c**, and (*Z*)-**4c**

	( <i>E</i> )- <b>4a</b>	( <i>E</i> )- <b>4c</b>	( <i>Z</i> )- <b>4c</b>
Crystallized from	Hexane/Et <sub>2</sub> O	Hexane/Et <sub>2</sub> O	Hexane/Et <sub>2</sub> O
Empirical formula	$\text{C}_{14}\text{H}_{13}\text{NO}_2$	$\text{C}_{15}\text{H}_{15}\text{NO}_2$	$\text{C}_{15}\text{H}_{15}\text{NO}_2$
Formula weight [g mol <sup>-1</sup> ]	227.26	241.29	241.29
Unit-cell dimensions <i>a</i> [Å]	13.9937(12)	6.9182(11)	7.3515(12)
<i>b</i> [Å]	6.1683(11)	14.3302(12)	14.2047(11)
<i>c</i> [Å]	14.3233(14)	25.5885(14)	12.6422(14)
$\beta$ [°]	103.068(4)	90	91.106(2)
Cell volume [Å <sup>3</sup> ]	1204.3(3)	2536.8(5)	1319.9(3)
Crystal system	monoclinic	orthorhombic	monoclinic
Space group	$P2_1/n$	$Pbca$	$P2_1/c$
<i>Z</i>	4	8	4
$D_x$ [g cm <sup>-3</sup> ]	1.253	1.263	1.214
$\mu$ (MoK $\alpha$ ) [mm <sup>-1</sup> ]	0.084	0.084	0.081
Scan type	$\omega/2\theta$	$\omega/2\theta$	$\omega/2\theta$
$\theta_{\text{max}}$ [°]	22.74	26.29	26.28
Absorption correction	none	none	none
Total reflections measured	3406	4282	4334
Symmetry-independent reflections	1625	2572	2071
Reflections used [ $I \geq 2\sigma(I)$ ]	974	2013	1278
Parameters refined	155	163	163
Final <i>R</i>	0.079	0.046	0.077
<i>wR</i>	0.245	0.120	0.240
$\Delta\rho$ (max; min) [e Å <sup>-3</sup> ]	0.295; -0.173	0.194; -0.325	0.346; -0.206

<sup>a</sup>) Crystallographic data (excluding structure factors) for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as deposition No. CCDC-212026 for (*E*)-**4a**, CCDC-212027 for (*E*)-**4c**, and CCDC-212028 for (*Z*)-**4c**. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ UK (fax: +44(1223)336033; e-mail: deposit@ccdc.com.ac.uk).

dissolved in MeOH (20 ml) and filtered through a small pad of *Celite*. Then, HCl gas was passed through the soln. (salt formation), and the crude product was purified by recrystallization.

(S,S,S)- $\alpha$ -(2-Phenylcyclopropyl)glycine ((S,S,S)-**1a**). M.p. 210°.  $[\alpha]_D^{20} = +71.0$  ( $c = 0.4$ , H<sub>2</sub>O).

(R,R,R)- $\alpha$ -(2-Phenylcyclopropyl)glycine ((R,R,R)-**1a**). M.p. 215°.  $[\alpha]_D^{20} = -76.0$  ( $c = 0.2$ , H<sub>2</sub>O).

*X-Ray Crystal-Structure Analyses.* X-ray diffraction intensities were collected with a CAD-4 diffractometer. Graphite monochromated MoK $\alpha$  radiation ( $\lambda = 0.71073$  Å) was used. Data reduction involved Lorentz and polarization corrections. The structures of (E)-**4a** (Fig. 1), (E)-**4c** (Fig. 2), and (Z)-**4c** (Fig. 3) were solved by direct methods and refined by full-matrix least-squares techniques. All non-H-atoms were refined with anisotropic displacement parameters. The H-atoms were placed geometrically by 0.84–1.00 Å from their parent atoms, then a riding model with  $U_{iso}(H) = 1.3U_{eq}(C,O)$  was applied. Scattering factors were taken from *International Tables for X-ray Crystallography*. The following computer programs were used: CAD4-EXPRESS [24] for data collection and cell parameters, the SHELXL package [25] for structure solution and refinement, and PLATON 2000 [26] for molecular graphics. For more details, see Table 3.

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