

Full Paper

## Synthesis, NMR and Crystallographic Studies of 2-Substituted Dihydroquinazolinones Derived from (*S*)-Phenylethylamine

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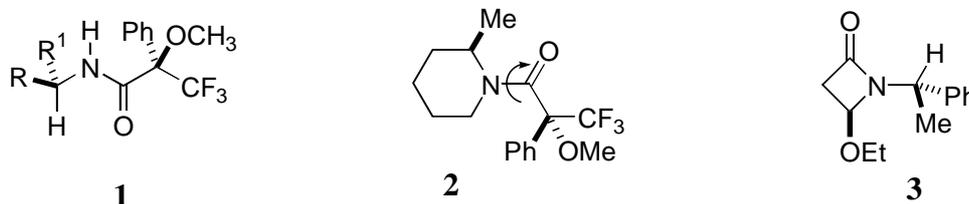
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**Abstract:** 2,3-Dihydro-3-[(*S*)-1-phenethyl]quinazolinone and some new 2-substituted derivatives bearing isopropyl, *o*-nitrophenyl and *p*-nitrophenyl groups were prepared in 40-90% yield by amidation of isatoic anhydride with (*S*)-phenylethylamine, followed by condensation with triethyl orthoformate, isopropylaldehyde, *o*-nitro- and *p*-nitrobenzaldehyde, respectively. The two 2-substituted dihydroquinazolinones obtained either by using isopropylaldehyde, *o*-nitro- or *p*-nitrobenzaldehyde, were separated and purified before their NMR spectra in CDCl<sub>3</sub> solutions were recorded. The detection of the low energy conformation of O=C-N-phenethyl segment in solution allowed the correlation of the NMR data with the configuration of newly stereogenic carbon C-2; thus, one diastereomer was labeled *SS* while the other was *RS*. Configurations determined by the NMR method were corroborated by X-ray diffraction analysis. X-ray structures of each diastereomeric series showed characteristic conformational types: a propeller-like for the *SS* and a hairpin for the *RS* series. Interatomic distances of the hairpin conformation suggest the existence of intramolecular face-to-face interactions between two aromatic rings.

**Keywords:** Chiral dihydroquinazolinones,  $\pi$ -stacking interactions, NMR method, configurational analysis.

## Introduction

Amidation of chiral primary amines with single enantiomers of methoxytrifluoromethylphenylacetyl chloride and related derivatizing agents is commonly used to determine the configuration of new stereogenic centers by  $^1\text{H-NMR}$  spectroscopy [1]. The detection of the low energy conformation **1** of the resulting amides is fundamental to establish the correlation between the chemical shifts ( $\delta$ ) of the hydrogen nuclei of the amine moiety and the configuration of the chiral derivatizing agent [2]. Although this strategy can be used to study the configuration of cyclic secondary amines, inherent ring conformations and slow rotation about amide bonds (see **2**) make it difficult to interpret the NMR spectra [3]. In this context, incorporation of a 1-arylethyl group as the amidic nitrogen substituent, might be the recommended strategy to avoid free rotation about amide bond. Studies carried out with chiral four- and five-membered cyclic amides prepared from a single enantiomer of either arylethylisocyanates [4] or phenylethylamine [5], showed that interaction between the methine hydrogen of the 1-phenethyl group and the carbonyl-oxygen favors the low-energy conformer **3**. Thus, the configuration of new stereogenic centers located in the neighborhood of the 1-phenethyl group, were readily determined from the chemical shifts and the orientation of phenyl ring [4,5].



Since the 1-phenethyl group can be removed from the heterocycle by hydrogenolysis [6], this strategy is comparable to classical chiral derivatizing methods. In a previous report [5b], we studied the effect of bulky substituents on the orientation of 1-phenethyl group of five-membered ring amides; this time we wish to report the applicability of 1-phenethyl group to six-membered ring amides. Herein we report the synthesis and configurational analysis of some new 2,3-dihydro-3-[(*S*)-1-phenethyl]-quinazolinones **8-11**.

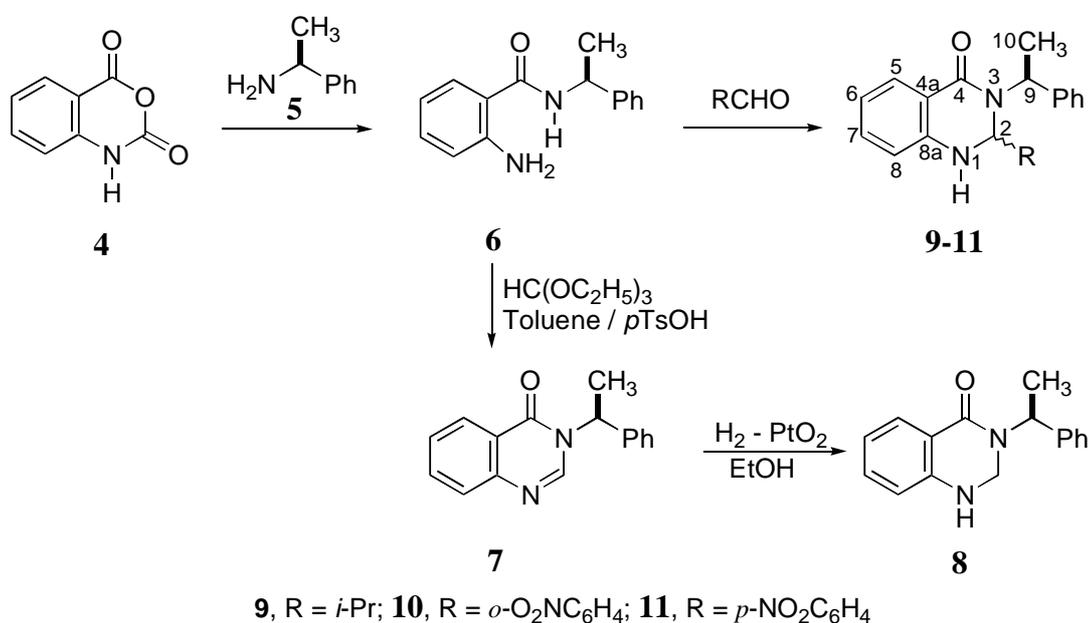
## Results and Discussion

### *Synthesis of dihydroquinazolinones*

The studied products were prepared by the sequence shown in Scheme 1 [7,8]. The reaction of isatoic anhydride (**4**) with (*S*)-1-phenylethylamine (**5**) gave benzamide **6**, which was treated with triethyl orthoformate and *p*-toluenesulfonic acid to give **7**. Catalytic hydrogenation of **7** gave 2,3-dihydro-3-[(*S*)-1-phenethyl]-4-quinazolinone (**8**). It should be noted that under these conditions

reductive cleavage of the 1-phenethyl group did not occur, due to the fact that the likelihood of removing this group from an amide is minimal. On the other hand, reactions of **6** with isobutyraldehyde, *o*-nitro- or *p*-nitrobenzaldehyde, gave the corresponding 2-substituted 2,3-dihydro-3-[(*S*)-1-phenethyl]quinazolinones **9-11** in nearly 3:2 diastereomeric ratio and 40-90% yields (see Experimental section). Based on the assumption that the configuration of (*S*)-1-phenylethylamine does not change in the two-reaction process [9], we assigned the *S* configuration to the C9 carbon of **8** (see the numbering system in Scheme 1). Consequently, the configurations of new compounds **9-11** could only be *SS* and *SR*. Pure diastereomers **9-11** were successfully separated by flash chromatography [10] and analyzed independently by NMR to produce two data sets for each diastereomeric pair. The first eluted diastereomer was labeled as the "less polar" and the next one, as the "more polar". Hereafter, we use the notation **A** and **B** for the "less polar" and "more polar" diastereomer, respectively.

Scheme 1



### Structure and chemical shift correlations

The studied 2,3-dihydro-3-[(*S*)-1-phenethyl]quinazolinones have rigid structures with limited degrees of freedom for single bond rotation. Their low energy molecular models, constructed with the MM2 subroutine of CS Chem 3D Pro® program [11], show little pyramidalization of the N1 and N3 nitrogens, which are both almost coplanar with the fused carbocyclic ring. The half chair conformation of the six-membered heterocyclic ring shows C2 out of the plane, with one pseudo-axial and one pseudo-equatorial bond. The substituent attached to C2 is invariably pseudo-axial.

To highlight the usefulness of the NMR method, only  $\delta$  values of specific hydrogen atoms attached to sp<sup>3</sup> carbons are commented briefly (however, complete data is given in the Experimental section). In the <sup>1</sup>H-NMR spectrum of **8**, the diastereotopic hydrogens attached to C2 (H2) constitute the AB part of an ABC system. In the spectra of **9A** and **9B**, H2 constitutes the A part of an ABC system, while in the spectra of **10** and **11**, H2 constitutes the A part of an AB spin-spin system. For any diastereomeric pair,  $\delta$  values of H2 (Table 1) showed large differences ( $\Delta\delta = \delta_{\text{H2 of A}} - \delta_{\text{H2 of B}}$ ) and therefore, H2 can be

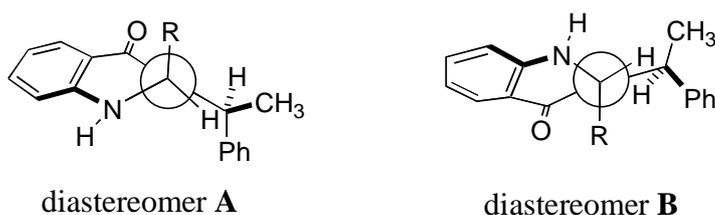
used as the pivotal nucleus to determine the configuration of C2. To fulfill the configurational analysis, one needs to know the dominant conformation of 1-phenethyl group.

**Table 1.**  $\delta_{H2}$  Values of dihydroquinazolinones **8-11**, obtained from 400 MHz spectra of 0.5 M solutions in  $CDCl_3$  containing TMS at 25 °C.

Compound	$\delta$ diastereomer <b>A</b>	$\delta$ diastereomer <b>B</b>	$\Delta\delta$ (ppb)
<b>8</b>	4.174, 4.463	–	–
<b>9</b>	4.19	4.535	-340
<b>10</b>	6.035	6.138	-103
<b>11</b>	5.481	5.674	-193

Experience and MM2 calculations of the  $O=C-CHCH_3Ph$  segment [5a] have shown that in the absence of a large substituent in the proximity of such segment, the most stable conformation of the 1-phenethyl group is that in which the methine hydrogen eclipses the carbonyl carbon [4,5]. Assuming that the steric interaction of the substituent at C2 does not alter this low energy conformer, the position of H2 and the phenyl ring could be inferred from  $\delta_{H2}$ . Accordingly, diastereomers **A** must have H2 in front of the phenyl ring, so that the configuration of C2 in these diastereomers must be *S*, and *R* that of diastereomers **B** (Figure 1). The same conclusion can be drawn by applying this interpretation to the observed  $\delta_{CH}$  of isopropyl group of **9A** and **9B**, as well as to the observed  $\delta_{Me}$  (C10) of **10A** and **10B** or **11A** and **11B**. In **9B**, for instance, the methine hydrogen of the isopropyl lies in the diamagnetic zone of the phenyl ring ( $\Delta\delta_{CH} = -750$  ppb) and in similar way, methyl C10 of **10A** and **11A** lies in the diamagnetic zone of nitrophenyl ring ( $\Delta\delta_{Me} = -509$  and  $-464$  ppb, respectively).

**Figure 1.** The conformation of 1-phenethyl group, is the key point to assign the absolute configuration of new stereogenic carbon C2 of diastereomers **A** and **B** by routine  $^1H$ -NMR experiments.

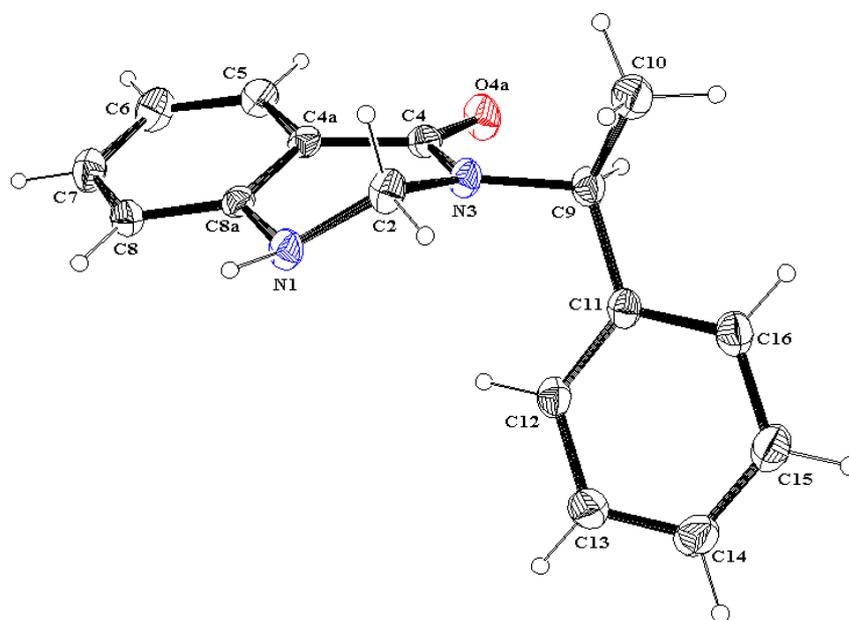


### X ray diffraction

To support the configurational analysis based on NMR spectra, the single crystals of **8**, **9A**, **10B**, **11A** and **11B** were analyzed by X-ray diffraction [12]. The structures were solved with the SHELXS97® program [13], under the assumption that the stereogenic carbon of the 1-phenethyl moiety retained the configuration of (*S*)-1-phenylethylamine. The ORTEP drawing of **8** (Figure 2) contains the following features: a *peri*-type interaction of the carbonyl with H5 twists the half-chair conformation of the heterocyclic ring, deviating N3 and C4 from the plane of the fused carbocyclic ring. The pyramidal N1 is aligned with the latter ring and the tetrahedral methylene C2 is out of the

plane, with one hydrogen pseudo-axial and other pseudo-equatorial. Methine hydrogen H9 is practically coplanar with the carbonyl group ( $\varphi$  H9-C9-N3-C4 =  $-5.0^\circ$ ) and close to the carbonyl-oxygen; the distance between H9 and O4 is 2.33 Å. These features prove that the low energy conformation of the 1-phenethyl group is not only a consequence of pure steric interactions of the substituents attached to C2 and N3, but also of the C-H $\cdots$ O hydrogen bond. According to the conformation of crystalline **8**, H2<sub>pseudo-equatorial</sub> is within the shielding zone of the phenyl ring and its NMR signal should be expected at high field. The observed chemical shifts of H2<sub>pseudo-equatorial</sub> and H2<sub>pseudo-axial</sub> are consistent with this expectation, see Table 1.

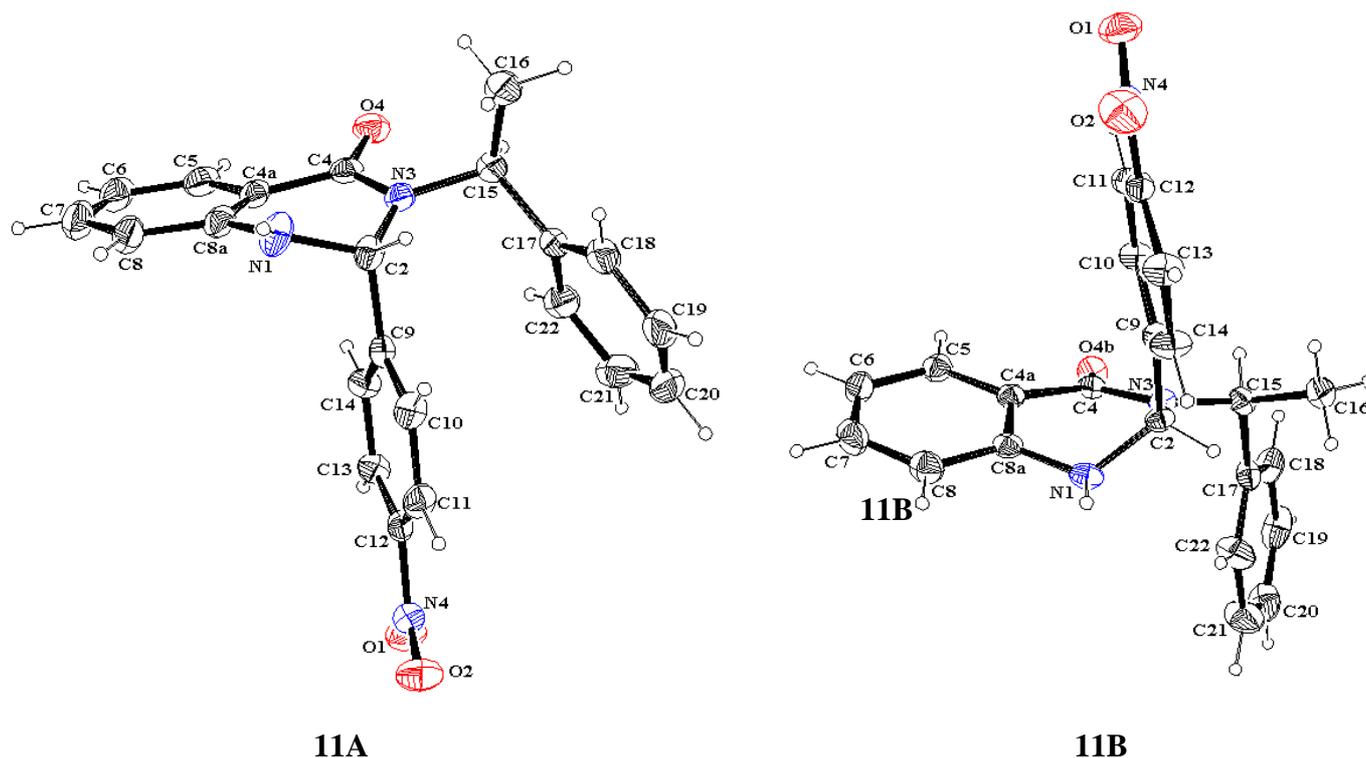
**Figure 2.** ORTEP drawing of compound **8** showing the *syn*-like conformation of carbonyl C4 and hydrogen attached to C9.



The X-ray structures of **9A**, **10B**, **11A** and **11B** show that isopropyl, *o*-nitro and *p*-nitro groups do not alter the typical conformation of the 1-phenethyl group. We chose **11A** and **11B** to summarize the molecular features of these 2-substituted 2,3-dihydro-3-[(*S*)-1-phenethyl]quinazolinones. Thus, X-ray structures **11A** and **11B** (Figure 3), show essentially the same half-chair conformation of the heterocyclic ring described above for **8**. Due to the allylic 1,3-effect [14], the *p*-nitrophenyl group is oriented pseudo-axial. In **11A**, the aromatic ring of *p*-nitrophenyl group is oriented towards the N3-C2 bond while in **11B**, it is oriented towards the heterocyclic ring ( $\varphi$  N3-C2-C<sub>ipso</sub>-C<sub>ortho</sub> =  $15.5^\circ$  and  $-42.2^\circ$ , respectively). In **11A**, the methine hydrogen of the 1-phenethyl group is much more deviated from the carbonyl plane than in **11B** ( $\varphi$  H15-C15-N3-C4 =  $44.3^\circ$  and  $-18.1^\circ$ , respectively) but the distance between H15 and O4 is still within the accepted values for hydrogen bonding [15]. The relative orientation of *p*-nitrophenyl and phenyl rings is the marked difference between structures of **11A** and **11B**. In the crystalline structure, **11A** assumes a propeller-like conformation. In contrast, **11B** assumes a hairpin conformation in which the phenyl and *p*-nitrophenyl rings are *syn*-like and slightly displaced from each other, so their planes are not parallel. Interatomic distances between *ipso* carbons C9-C17 (3.12 Å) and *para* carbons C12-C20 (4.57 Å), however, are small enough to suggest the existence of a stabilizing intramolecular  $\pi$ -stacking interaction between the two aromatic rings [16].

Thus, in addition to the above mentioned C-H $\cdots$ O hydrogen bond, the crystal lattice **11B** might be stabilized by intramolecular face-to-face and intermolecular face-to-edge interactions. The analysis of X ray structures of **10B**, 2,3-dihydro-2-(*S*)-phenyl-3-[(*R*)-1-phenethyl]- and 2,3-dihydro-2-(*S*)-*o*-methoxy-phenyl-3-[(*R*)-1-phenethyl] quinazolinone [7], are consistent with the features mentioned above for **11B**.

**Figure 3.** ORTEP drawings showing the propeller-like and hairpin conformations of compounds **11A** and **11B**, respectively. It should be noticed that substituents are labeled with a particular numbering system.



## Conclusions

We have prepared the new compounds **8**, **9A**, **9B**, **10A**, **10B**, **11A** and **11B**, and have characterized them by NMR, elemental analysis and X-ray diffraction. Experimental data of studied compounds revealed that a *syn*-like conformation of the methine hydrogen of the phenethyl group and the carbonyl oxygen is the dominant conformation in CDCl<sub>3</sub> solution and in the solid state. Based on this conformation and on the shielding effect caused by phenyl ring on neighboring protons, we assigned the *SS* configuration to **9A**, **10A** and **11A**, and the *RS* one to **9B**, **10B** and **11B**. The crystalline structure of the *SS* diastereomeric series derived from monosubstituted benzaldehydes has a propeller-like conformation while the *RS* series assumes a hairpin conformation. Interatomic distances of the latter arrangement suggest the existence of stabilizing intramolecular  $\pi$ -stacking interaction between two aromatic rings.

## Experimental

### General

All melting points were determined with a Büchi apparatus and are uncorrected. Specific rotations were measured in a PerkinElmer 341 polarimeter at 24 °C and  $\lambda = 589$  nm. Elemental analysis (CHN) was performed on an Elementar Vario EL III elemental analyzer. Proton and  $^{13}\text{C}$ -NMR spectra were obtained from 0.5 M solutions in  $\text{CDCl}_3$ , containing a small amount of TMS, and recorded on an Inova 400 spectrometer equipped with a 5 mm  $^1\text{H}$  probe at 25 °C. All chemical shifts are from TMS signal and  $^1\text{H}$ -NMR data are given in the standard format:  $\delta$  units, integration, signal multiplicity and coupling constants in Hertz. X-ray diffraction analysis was carried out with an APEX-Bruker diffractometer. The structures were solved by SHELXS97 method and refined by full-matrix least squares. For each crystal, heavy atoms were refined anisotropically while hydrogen atoms were located in the calculated positions.

### Synthesis of dihydroquinazolinones

2,3-Dihydro-3-[(*S*)-1-phenethyl]-4(1*H*)-quinazolinone (**8**) and its 2-substituted derivatives **9-11**, were prepared by minor variations of published procedures [17,7]. The physical and spectroscopic data reported herein were obtained with pure diastereomers recrystallized from dichloromethane-hexane.

#### 2,3-Dihydro-3-[(*S*)-1-phenethyl]-4(1*H*)-quinazolinone (**8**)

Quinazolinone **7** was prepared according to a known procedure [17] and then it was hydrogenated in the following way: a solution of **7** (0.5 g) in EtOH (10 mL) was mixed with commercial  $\text{PtO}_2$  catalyst (0.05 g) and exposed to 30 psi of hydrogen during 2 h at 25 °C with shaking in a Parr hydrogenator. The catalyst was filtered through Celite<sup>®</sup> and the resulting solution was concentrated in a rotavapor. The crude residue was purified via flash chromatography to give compound **8** (0.48 g, 95% yield): White solid, mp 119-121 °C;  $[\alpha]_{\text{D}}^{24} = -91.7 \text{ deg cm}^2 \text{ g}^{-1}$ ,  $c = 1.0$  in  $\text{CH}_3\text{OH}$ ;  $^1\text{H-NMR}$   $\delta$  1.57 (3H, d,  $J = 7.2$  Hz), 4.17 (1H, dd,  $J = 2.4, 9.2$  Hz), 4.22 (1H, s), 4.46 (1H, dd,  $J = 2.0, 9.2$  Hz), 6.10 (1H, q,  $J = 7.1$  Hz), 6.63 (1H, d,  $J = 8.0$  Hz), 6.88 (1H, ddd,  $J = 7.9, 7.9, 0.8$  Hz), 7.24 – 7.41 (6H, m), 7.99 (1H, dd,  $J = 7.8, 1.6$  Hz);  $^{13}\text{C-NMR}$   $\delta$  16.3, 49.8, 55.0, 115.0, 118.1, 119.9, 127.3, 127.6, 128.7, 129.2, 133.2, 140.2, 147.6, 163.4. Anal. calcd. for  $\text{C}_{16}\text{H}_{16}\text{N}_2\text{O}$ : C, 76.10; H, 6.40; N, 11.02. Found: C, 76.16; H, 6.39; N, 11.10. X-Ray crystallographic data of **8** is available as supporting information [12].

#### 2,3-Dihydro-(2*S*)- and 2,3-dihydro-(2*R*)-isopropyl-3-[(*S*)-1-phenethyl]-4(1*H*)-quinazolinone (**9A** and **9B**, respectively)

The crude mixture of **9A** and **9B**, obtained from **6** (1 g, 4.0 mmol) and isobutyraldehyde (0.5 mL, 5.0 mmol) was purified by flash chromatography (silica gel, hexane-dichloromethane-ethyl acetate 70:30:10) to afford 0.44 g of **9A** and 0.30 g of **9B**. Compound **9A** was thus isolated as white solid, mp 137-139 °C;  $[\alpha]_{\text{D}}^{24} = -118 \text{ deg cm}^2 \text{ g}^{-1}$ ,  $c = 0.7$  in  $\text{CHCl}_3$ ;  $^1\text{H-NMR}$   $\delta$  0.78 (3H, d,  $J = 6.8$  Hz), 0.87

(3H, d,  $J = 6.8$  Hz), 1.68 (3H, d,  $J = 7.4$  Hz), 2.00 (1H, m), 4.19 (1H, dd,  $J = 3.6, 7.6$  Hz), 4.28 (1H, s), 6.08 (1H, q,  $J = 7.4$  Hz), 6.52 (1H, d,  $J = 8.0$  Hz), 6.76 (1H, ddd,  $J = 7.8, 7.8, 0.7$  Hz), 7.18 – 7.41 (6H, m), 7.88 (1H, dd,  $J = 7.7, 1.1$  Hz);  $^{13}\text{C-NMR}$   $\delta$  17.2, 18.7, 19.0, 36.6, 52.8, 70.1, 113.8, 118.6, 118.6, 127.8, 128.7, 128.7, 128.8, 133.4, 141.0, 146.5, 163.6; Anal. calcd. for  $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}$ : C, 77.52; H, 7.53; N, 9.52. Found: C, 77.30; H, 7.32; N, 9.00. X-Ray crystallographic data of **9A** is available as supporting information [12]. Diastereomer **9B** was isolated as a white solid, mp 141–142 °C;  $[\alpha]_{\text{D}}^{24} = -24$  deg  $\text{cm}^2 \text{g}^{-1}$ ,  $c = 1.1$  in  $\text{CHCl}_3$ ;  $^1\text{H-NMR}$   $\delta$  0.60 (3H, d,  $J = 7.0$  Hz), 0.65 (3H, d,  $J = 7.0$  Hz), 1.25 (1H, m), 1.75 (3H, d,  $J = 7.0$  Hz), 4.47 (1H, s), 4.53 (1H, dd,  $J = 7.4, 3.0$  Hz), 5.81 (1H, q,  $J = 7.0$  Hz), 6.56 (1H, d,  $J = 8.0$  Hz), 6.78 (1H, ddd,  $J = 7.5, 7.5, 1.2$  Hz), 7.19 – 7.51 (6H, m), 7.87 (1H, dd,  $J = 7.6, 1.5$  Hz);  $^{13}\text{C-NMR}$   $\delta$  17.1, 17.7, 18.7, 34.9, 54.2, 71.5, 113.7, 118.8, 118.8, 127.8, 128.0, 128.7, 128.9, 133.4, 133.2, 145.9, 163.3; Anal. Calcd. for  $\text{C}_{19}\text{H}_{22}\text{N}_2\text{O}$ : C, 77.52; H, 7.53; N, 9.52. Found: C, 77.00; H, 7.20; N, 9.10.

*2,3-Dihydro-(2S)- and 2,3-dihydro-(2R)-o-nitrophenyl-3-[(S)-1-phenethyl]-4(1H)-quinazolinone (10A and 10B, respectively)*

The crude mixture of **10A** and **10B**, obtained from **6** (1 g, 4.0 mmol) and *o*-nitrobenzaldehyde (0.75 g, 5 mmol) was purified by flash chromatography to afford 0.75 g of **10A** and 0.70 g of **10B**. Compound **10A** was thus isolated as yellowish solid, mp 104 °C;  $[\alpha]_{\text{D}}^{24} = 31$  deg  $\text{cm}^2 \text{g}^{-1}$ ,  $c = 1$  in  $\text{CHCl}_3$ ;  $^1\text{H-NMR}$   $\delta$  1.18 (3H, d,  $J = 7.2$  Hz), 5.19 (1H, br d,  $J \approx 2.4$  Hz), 6.03 (1H, d,  $J = 3.2$  Hz), 6.26 (1H, q,  $J = 7.2$  Hz), 6.45 (1H, dd,  $J = 8.0, 0.4$  Hz), 6.86 (1H, ddd,  $J = 7.4, 7.4, 0.8$  Hz), 7.20 – 7.24 (1H, m); 7.25 – 7.56 (9H, m), 7.63 (1H, dd,  $J = 8.0, 1.2$  Hz);  $^{13}\text{C-NMR}$   $\delta$  17.5, 51.5, 63.0, 115.2, 116.3, 119.6, 125.8, 127.8, 128.1, 128.8, 128.9, 129.0, 129.7, 134.0, 134.0, 136.7, 140.3, 143.9, 146.9, 163.8. Anal. calcd. for  $\text{C}_{22}\text{H}_{19}\text{N}_3\text{O}_3$ : C, 70.76; H, 5.13; N, 11.25. Found: C, 70.67; H, 5.45; N, 10.5. Diastereomer **10B** was isolated as a yellowish solid, mp 173–175 °C;  $[\alpha]_{\text{D}}^{25} = -359$  deg  $\text{cm}^2 \text{g}^{-1}$ ,  $c = 1$  in methanol;  $^1\text{H-NMR}$   $\delta$  1.69 (3H, d,  $J = 6.8$  Hz), 5.24 (1H, br d,  $J \approx 2.0$  Hz), 6.14 (1H, d,  $J = 2.8$  Hz), 6.17 (1H, q,  $J = 7.5$  Hz), 6.45 (1H, ddd,  $J = 8.1, 0.9, 0.5$  Hz), 6.85 (1H, ddd,  $J = 7.5, 7.5, 1.2$  Hz), 7.16 (1H, ddd,  $J = 7.5, 7.5, 1.2$  Hz), 7.19 – 7.63 (9H, m), 8.02 (1H, dd,  $J = 7.8, 0.8$  Hz);  $^{13}\text{C-NMR}$   $\delta$  17.2, 52.0, 62.8, 114.9, 116.7, 119.6, 124.7, 128.0, 128.2, 128.4, 128.6, 128.7, 133.3, 133.9, 136.0, 137.4, 144.0, 146.5, 163.7; Anal. calcd. for  $\text{C}_{22}\text{H}_{19}\text{N}_3\text{O}_3$ : C, 70.76; H, 5.13; N, 11.25. Found: C, 70.80; H, 5.10; N, 11.24. X-Ray crystallographic data of **10B** is available as supporting information [12].

*2,3-Dihydro-(2S)- and 2,3-dihydro-(2R)-p-nitrophenyl-3-[(S)-1-phenethyl]-4(1H)-quinazolinone (11A and 11B, respectively)*

The crude mixture of **11A** and **11B**, obtained from **6** (1 g, 4 mmol) and *p*-nitrobenzaldehyde (0.75 g, 5 mmol) was purified by flash chromatography to afford 0.39 g of **11A** and 0.21 g of **11B**. Compound **11A** was thus isolated as a yellowish solid, mp 180–182 °C;  $[\alpha]_{\text{D}}^{25} = 454.5$  deg  $\text{cm}^2 \text{g}^{-1}$ ,  $c = 1$  in  $\text{CHCl}_3$ ;  $^1\text{H-NMR}$   $\delta$  1.27 (3H, d,  $J = 6.8$  Hz), 4.60 (1H, br d,  $J \approx 2.4$  Hz), 5.48 (1H, d,  $J = 3.2$  Hz), 6.37 (1H, q,  $J = 7.2$  Hz), 6.46 (1H, dd,  $J = 8.8, 0.6$  Hz), 6.90 (1H, ddd,  $J = 7.3, 7.3, 0.8$  Hz), 7.23 (1H, ddd,  $J = 6.9, 6.9, 1.2$  Hz), 7.21 – 8.14 (9H, m), 8.04 (1H, dd,  $J = 7.6, 1.6$  Hz);  $^{13}\text{C-NMR}$   $\delta$  17.7, 51.4, 66.8, 115.5, 117.3, 120.4, 124.3, 126.7, 127.41, 128.1, 128.9, 134.0, 140.2, 143.5, 148.1, 149.0, 162.8;

Anal. calcd. for C<sub>22</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>: C, 70.76; H, 5.13; N, 11.25. Found: C, 70.78; H, 5.18; N, 11.17. Diastereomer **11B** was isolated as a yellowish solid, mp 194-196 °C;  $[\alpha]_D^{25} = -423 \text{ deg cm}^2 \text{ g}^{-1}$ ,  $c = 1$  in methanol; <sup>1</sup>H-NMR δ 1.73 (3H, d,  $J = 7.2$  Hz), 4.63 (1H, d,  $J = 2.0$  Hz), 5.67 (1H, d,  $J = 2.4$  Hz), 6.21 (1H, q,  $J = 7.1$  Hz), 6.47 (1H, dd,  $J = 8.4, 0.4$  Hz), 6.91 (1H, ddd,  $J = 7.5, 7.5, 0.9$  Hz), 6.96 – 7.02 (1H, m), 7.17 – 7.81 (9H, m), 8.02 (1H, dd,  $J = 7.8, 1.2$  Hz); <sup>13</sup>C-NMR δ 17.1, 51.8, 67.1, 115.3, 117.3, 120.4, 123.5, 126.3, 128.0, 128.2, 128.3, 128.8, 134.0, 138.4, 143.8, 147.4, 148.0, 162.6; Anal. calcd. for C<sub>22</sub>H<sub>19</sub>N<sub>3</sub>O<sub>3</sub>: C, 70.76; H, 5.13; N, 11.25. Found: C, 70.57; H, 5.17; N, 11.05. X-Ray crystallographic data of **11A** and **11B** is available as supporting information [12].

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*Sample Availability:* Small samples (a few milligrams) of **8**, **9**, **10** and **11** are available from the authors.