Synthesis of (5*R*)-4-Methyl-5-phenyl-1,3,4-oxadiazinan-2-one and Some *N*-Acyl Derivatives from (*R*)-Phenylglycine

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Abstract: (*5R*)-4-Methyl-5-phenyl-1,3,4-oxadiazinan-2-one was synthesized from (*R*)-phenylglycine in five steps and in 65% overall yield. In addition, a convenient and practical method for N-acylation of 1,3,4-oxadiazinan-2-one directly with acids in the presence of DCC and catalytic quantities of DMAP is described. The acylated products were obtained in excellent yields.

Key words: (*R*)-phenylglycine, 1,3,4-oxadiazinan-2-ones, heterocycles, acylation, carboxylic acids

In 1968, Trepanier and co-workers[1] reported the first synthesis of the 3,4,5,6-tetrahydro-2*H*-1,3,4-oxadiazin-2-ones **2** as candidates for central nervous system stimulant activity. The synthesis of substituted 1,3,4-oxadiazinan-2-ones has attracted attention because of their promising general application as chiral auxiliaries in asymmetric aldol addition reactions.[2]

Heterocycles **2** (Figure 1) were synthesized by Hitchcock and co-workers[3] from (1*R*,2*S*)-ephedrine and (1*S*,2*S*)-pseudoephedrine, which have limited utility in creating diverse 1,3,4-oxadiazinan-2-ones, because the N^4-position is substituted with a methyl group and both the C-5 and C-6 substituents are fixed (methyl and phenyl groups, respectively).

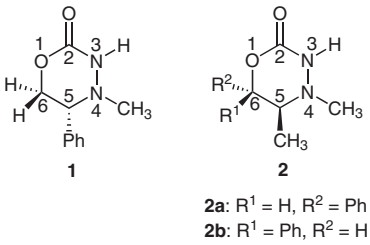
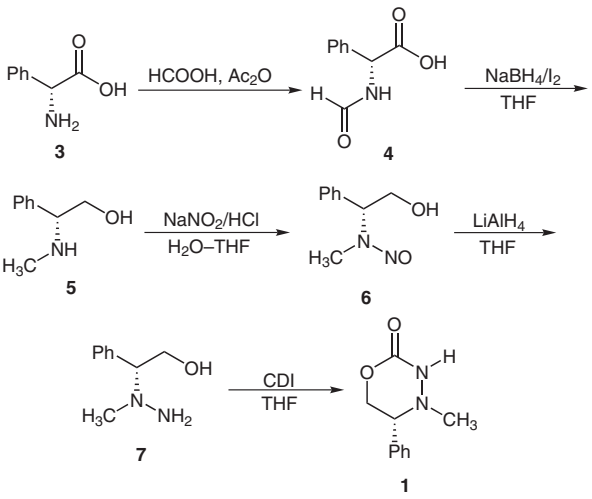


Figure 1 1,3,4-Oxadiazinan-2-ones (**1** and **2**)

We have developed another 1,3,4-oxadiazinan-2-one framework – the (*5R*)-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one (**1**) – starting from (*R*)-phenylglycine (**3**), which can be replaced by other amino acids; these are excellent templates for the creation of new 1,3,4-oxadiazinan-2-ones due to the wide range and diversity of these chiral starting materials. Therefore, we present in this paper the synthesis of the heterocycle **1** (Scheme 1) and a simple method to prepare the N^3-acylated-1,3,4-oxadiazinan-2-ones (Scheme 2). The synthesis of heterocycle **1** was readily performed in five steps from (*R*)-phenylglycine (**3**) on a multigram scale without chromatographic purification in 65% overall yield.

The starting point was the synthesis of *N*-formyl-(*R*)-phenylglycine (**4**), which was obtained in quantitative yield by the treatment of (*R*)-phenylglycine (**3**)[4] with formic acid and acetic anhydride (Scheme 1).



Scheme 1

Compound **4** was cleanly reduced[5] to *N*-methyl-(*R*)-phenylglycinol (**5**) with $NaBH_4/I_2$ in THF in 94% yield. Compound **5** was treated[6] with $NaNO_2$ in the presence of aqueous HCl and THF to conveniently give the desired *N*-methyl-*N*-nitrosamine (**6**) in 96% yield. *N*-Nitrosamine **6** was reduced[7] with $LiAlH_4$ in THF leading to hydrazine **7**.[8] Subsequent treatment[9] with carbonyldiimidazole (CDI) furnished the cyclic diazacarbamate **1** in 75% yield.

DCC and DMAP are known as synthetically useful and mild reagents for the preparation of esters and amides.[10,11] This chemistry was used to prepare (in one step) the N^3-acylated 1,3,4-oxadiazinan-2-ones **8a–j** using carboxylic acids, DCC, and DMAP (cat., 5 mol%) in CH_2Cl_2, at room temperature (Scheme 2). The N^3-acylated products **8a–j** were obtained in excellent yields (Table 1).

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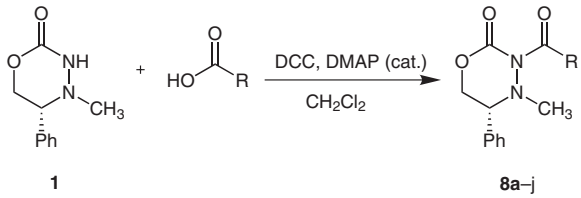
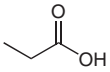
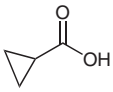
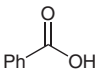
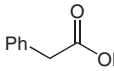
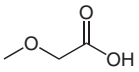
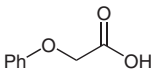
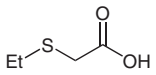
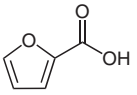
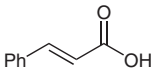


Scheme 2

Table 1 Synthesis of N^3-Acyl-(*5R*)-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-ones **8a–j** from Carboxylic Acids and 1,3,4-Oxadiazinan-2-one **1** Using DCC and DMAP

Entry	Product	RCOOH	Time (h)	Yield (%)[a]
1	**8a**		2.5	90
2	**8b**		3	92
3	**8c**		5	90
4	**8d**		12	87
5	**8e**		16	85
6	**8f**		2	85
7	**8g**		20	90
8	**8h**		5	83
9	**8i**		24	90
10	**8j**		8	80

[a] Isolated yields after chromatography.

The reaction does not require rigorously dried solvents or reagents, and eliminates the need for strong bases, such as BuLi or LiH. In addition, arylacetic acids and conjugated enoic acids can be employed to provide the desired N^3-acyl-oxadiazinan-2-ones free of by-products.

In conclusion, we have prepared (*5R*)-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one in a five-step reaction and 65% overall yield. In addition, the method described provides a mild and efficient process for N^3-acylation mediated by DCC/DMAP, resulting in a large variety of N^3-acylated-oxadiazinan-2-ones and this method should be easily extend to acylations with more complex substrates. The initial reaction can also be extended to other amino acids besides (*R*)-phenylglycine described in this paper.

NMR spectra were recorded on a Varian Unity Inova 1 and on a Bruker DRX 500 spectrometer operating at 299.948 MHz or 500.132 MHz (^{1}H NMR), and 75.429 MHz or 125.773 MHz (^{13}C NMR). ^{1}H and ^{13}C chemical shifts (δ) are reported in ppm relative to TMS as internal standard. Coupling constants (*J*) are given in Hz. IR spectra were measured on a MB-100 Michelson-Bomem FTIR instrument. Elemental analyses were carried out on a Perkin Elmer 2400 CHN-standard analyzer. Low resolution mass spectra were recorded on a SHIMADZU QP5050A GC-MS spectrometer (DB5 column, EI). Mps were measured on a Büchi melting point apparatus. Optical rotations were determined at 25 °C with a JASCO DIP-370 polarimeter (1 dm cell). Column chromatography was performed on Merck silica gel 60 (230–400 mesh). All reactions were conducted with magnetic stirring in oven-dried glassware under anhyd N_2. Solvents were purified and dried according to standard procedures. Other reagents were commercially available.

(2*R*)-2-(*N*-Formyl)amino-2-phenylacetic Acid (4)

Ac_2O (185 mL) was added dropwise to a mixture of (*R*)-phenylglycine (**3**; 40.00 g, 264 mmol) in formic acid (550 mL, 99%) at such a rate that the temperature of the reaction mixture was maintained between 5–15 °C. After the addition was complete the mixture was stirred at r.t. for 1 h; iced-water (400 mL) was introduced and the mixture was concentrated at reduced pressure to give **4** as white crystals in 100% yield (47.41 g); mp 178.1–178.8 °C (dec.) (Lit.[12] 178 °C); $[\alpha]_D^{25}$ –247.0 (*c* 1.00, MeOH); {Lit.[12] $[\alpha]_D^{20}$ –252.0 (*c* 1.00, MeOH)}.

^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.92 (d, 1 H, ^3J = 7.7 Hz), 8.08 (s, 1 H), 7.39–7.28 (m, 5 H), 5.39 (d, 1 H, ^3J = 7.7 Hz).

(2*R*)-2-(*N*-Methyl)amino-2-phenylethanol (5)

To a stirred solution of amino acid **4** (38.00 g, 180 mmol), $NaBH_4$ (19.38 g, 510 mmol), and anhyd THF (500 mL) cooled to 0 °C in an ice bath, was slowly added dropwise a solution of I_2 (53.85 g, 212 mmol) in THF (200 mL). Upon addition of I_2 gas evolution occurred, once this had ceased the flask was heated at reflux for 18 h and then cooled to r.t.; MeOH was added cautiously until the mixture became clear. After stirring for 30 min, the solvent was removed by rotary evaporator leaving a white paste, which was dissolved by the addition of KOH (20% aq, 200 mL). The resulting solution was stirred for 1 h and extracted with CH_2Cl_2 (3 × 150 mL). The organic extracts were dried over Na_2SO_4 and concentrated under vacuum, affording **5** as a colorless liquid in 94% yield (30.15 g, 200 mmol); $[\alpha]_D^{25}$ –85.5 (*c* 1.08, $CHCl_3$).

IR (film): 3303, 3063, 2855, 2798, 1455, 1060, 1024, 761, 702 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.36–7.22 (m, 5 H), 3.72–3.54 (m, 3 H), 3.07 (br s, 2 H), 2.29 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 140.31, 128.57, 127.56, 127.39, 66.68, 66.55, 34.13.

(2*R*)-2-(*N*-Methylnitroso)amino-2-phenylethanol (6)

To a solution of **5** (26.50 g, 175 mmol) in THF (75 mL) was added an aq solution of HCl (3 M, 75 mL, 225 mmol) followed by the addition of $NaNO_2$ (13.95 g, 202 mmol); the resulting mixture was stirred for 12 h. The mixture was then diluted with a sat. aq solution of $NaHCO_3$ until its pH was >7. The reaction mixture was extracted with EtOAc (4 × 100 mL), washed with a sat. solution of brine (80 mL), dried (Na_2SO_4), and the solvent was removed by rotary evaporation to give **6** as an orange oil (30.50 g, 96%); $[\alpha]_D^{25}$ –4.0 (*c* 1.17, $CHCl_3$)

IR (film): 3390, 3063, 3034, 2941, 2885, 1439, 1342, 1195, 1069, 1045, 704 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.39–7.23 (m, 5 H), 5.43 (dd, ^3J = 9.0 Hz, ^3J = 4.6 Hz, 1 H), 4.44 (dd, ^2J = 12.2 Hz, ^3J = 9.0 Hz, 1

H), 4.17 (dd, ^2J = 12.2 Hz, ^3J = 4.6 Hz, 1 H), 3.58 (s, 1 H), 2.94 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 135.47, 129.10, 128.78, 127.28, 69.87, 62.95, 31.57.

(5*R*)-4-Methyl-5-phenyl-1,3,4-oxadiazinan-2-one (1)

To a stirred suspension of $LiAlH_4$ (20.10 g, 529 mmol) in THF (500 mL) was added dropwise a solution of **6** (30.50 g, 170 mmol) in THF (250 mL) at r.t. The mixture was then heated at reflux for 6 h. The cooled and stirred mixture was quenched with H_2O (20 mL), 15% aq NaOH (20 mL), H_2O (60 mL), filtered, dried (Na_2SO_4), and the solvent was removed by rotary evaporation. This process afforded **7** as a viscous yellow oil (27.65 g, 98%), which was >95% pure, as determined by ^{1}H NMR spectroscopy. The hydrazine **7** was directly converted into the corresponding oxadiazinone derivative **1** due to its facile decomposition. CDI (35.02 g, 216 mmol) was added to a solution of **7** (27.65 g, 166 mmol) in THF (180 mL). The mixture was stirred for 24 h at r.t., concentrated, dissolved in H_2O (70 mL), and extracted with CH_2Cl_2 (3 × 15 mL). The organic extracts were washed with brine (50 mL), dried (Na_2SO_4), and evaporated. This process yielded a yellow solid, which was purified by recrystallization (EtOAc–hexane) to give heterocycle **1** as white crystals (23.93 g, 75%); $[\alpha]_D^{25}$ –100.6 (*c* 1.08, $CHCl_3$); mp 103–104 °C.

IR (KBr): 3353, 3208, 3090, 2957, 2790, 1725, 1477, 1363, 1306, 1152, 1082, 901, 882, 749, 725, 698 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.37 (s, 1 H), 7.39–7.33 (m, 5 H), 4.55–4.42 (m, 2 H), 3.84 (dd, *J* = 8.1 Hz, *J* = 3.6 Hz, 1 H), 2.52 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 152.93, 135.06, 128.98, 128.72, 127.78, 68.52, 62.70, 44.00.

MS (EI): *m*/*z* (%) = 192 (36), 118 (34), 105 (18), 104 (83), 103 (19), 91 (21), 78 (27), 77 (36), 40 (100).

Anal. Calcd for $C_{10}H_{12}N_2O_2$ (192.21): C, 62.49; H, 6.29; N, 14.57. Found: C, 62.53; H, 6.43; N, 14.77.

N^3-Acylation; General Procedure

To a mixture of 1,3,4-oxadiazinan-2-one (**1**; 500 mg, 2.60 mmol), DMAP (16 mg, 0.13 mmol) and the corresponding carboxylic acid (2.86 mmol) in CH_2Cl_2 (4 mL) at 0 °C, under a nitrogen atmosphere, DCC was added in one portion (590 mg, 2.86 mmol). The temperature of the resulting suspension was allowed to reach r.t. Stirring was continued until no starting material was left, as confirmed by TLC. The dicyclohexylurea formed was filtered and the precipitate washed with CH_2Cl_2 (20 mL). The filtrate was washed with a sat. aq solution of $NaHCO_3$ (15 mL) and dried over Na_2SO_4. Filtration and evaporation yielded the crude compounds **8a–j**, which were purified by flash chromatography on silica gel (hexane–EtOAc, 6:4).

(5*R*)-3-Acetyl-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one (8a)

Yield: 90%; white crystals; mp 102–103 °C; $[\alpha]_D^{25}$ +44.5 (*c* 1.00, $CHCl_3$).

IR (CCl_4): 3068, 2963, 2922, 1770, 1727, 1454, 1372, 1254, 1217, 1070 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.40–7.34 (m, 5 H), 4.84 (dd, ^2J = 11.7 Hz, ^3J = 5.7 Hz, 1 H), 4.66 (dd, ^2J = 11.7 Hz, ^3J = 7.8 Hz, 1 H), 4.35 (dd, ^3J = 7.8 Hz, ^3J = 5.7 Hz, 1 H), 2.80 (s, 3 H), 2.38 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.86, 150.27, 135.51, 129.01, 128.65, 127.04, 67.84, 62.07, 42.72, 24.80.

MS (EI): *m*/*z* (%) = 234 (1), 192 (90), 118 (20), 105 (15), 104 (100), 103 (11), 101 (18), 91 (13), 78 (15), 77 (18).

Anal. Calcd for $C_{12}H_{14}N_2O_3$ (234.25): C, 61.53; H, 6.02; N, 11.96. Found: C, 61.52; H, 5.83; 12.11.

(5*R*)-4-Methyl-5-phenyl-3-propionyl-1,3,4-oxadiazinan-2-one (8b)

Yield: 92%; white crystals; mp 103–104 °C; $[\alpha]_D^{25}$ +36.3 (*c* 1.02, $CHCl_3$).

IR (CCl_4): 3067, 2984, 2943, 2801, 1769, 1730, 1458, 1257, 1218, 1189 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.30 (m, 5 H), 4.82 (dd, ^2J = 11.5 Hz, ^3J = 5.6 Hz, 1 H), 4.66 (dd, ^2J = 11.5 Hz, ^3J = 7.8 Hz, 1 H), 4.35 (dd, ^3J = 7.8 Hz, ^3J = 5.6 Hz, 1 H), 2.85–2.59 (m, 2 H), 2.78 (s, 3 H), 1.08 (t, ^3J = 7.3 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 173.70, 150.13, 135.59, 128.97, 128.58, 127.05, 67.71, 61.98, 42.61, 29.88, 8.84.

MS (EI): *m*/*z* (%) = 192 (94), 118 (22), 105 (17), 104 (100), 103 (12), 101 (20), 91 (15), 78 (15), 77 (21).

Anal. Calcd for $C_{13}H_{16}N_2O_3$ (248.28): C, 62.89; H, 6.50; N, 11.28. Found: C, 63.17; H, 6.53; 11.53.

(5*R*)-3-(Cyclopropylcarbonyl)-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one (8c)

Yield: 90%; white crystals; mp 89–91 °C; $[\alpha]_D^{25}$ +37.6 (*c* 0.96, $CHCl_3$).

IR (CCl_4): 3067, 3016, 2962, 2801, 1766, 1739, 1713, 1451, 1389, 1259, 1188 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.39–7.33 (m, 5 H), 4.77 (dd, ^2J = 11.5 Hz, ^3J = 5.8 Hz, 1 H), 4.57 (dd, ^2J = 11.5 Hz, ^3J = 8.6 Hz, 1 H), 4.35 (dd, ^3J = 8.6 Hz, ^3J = 5.8 Hz, 1 H), 2.82 (s, 3 H), 2.59–2.53 (m, 1 H), 1.10–1.07 (m, 2 H), 0.94–0.88 (m, 2 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 174.06, 150.48, 135.79, 128.98, 128.62, 127.07, 68.17, 63.07, 43.52, 13.21, 10.41 (2 C).

MS (EI): *m*/*z* (%) = 192 (9), 118 (11), 104 (29), 103 (17), 78 (18), 77 (18), 69 (48), 42 (22), 41 (100), 39 (76).

Anal. Calcd for $C_{14}H_{16}N_2O_3$ (260.29): C, 64.60; H, 6.20; N, 10.76. Found: C, 64.60; H, 6.25; N, 10.95.

(5*R*)-3-Benzoyl-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one (8d)

Yield: 87%; white crystals; mp 91–92 °C; $[\alpha]_D^{25}$ +20.0 (*c* 1.03, $CHCl_3$).

IR (CCl_4): 3067, 3032, 3004, 2800, 1777, 1753, 1709, 1602, 1453, 1278, 1251 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.48–7.29 (m, 10 H), 4.95 (dd, ^2J = 11.7 Hz, ^3J = 5.7 Hz, 1 H), 4.75 (dd, ^2J = 11.7 Hz, ^3J = 7.0 Hz, 1 H), 4.43 (m, 1 H), 3.00 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.94, 151.08, 135.98, 134.32, 131.97, 129.11, 128.63, 128.16, 127.96, 126.89, 67.76, 62.65, 43.96.

MS (EI): *m*/*z* (%) = 296 (3), 161 (13), 105 (100), 77 (48), 51 (17).

Anal. Calcd for $C_{17}H_{16}N_2O_3$ (296.32): C, 68.91; H, 5.44; N, 9.45. Found: C, 68.65; H, 5.59; N, 9.63.

(5*R*)-4-Methyl-5-phenyl-3-(phenylacetyl)-1,3,4-oxadiazinan-2-one (8e)

Yield: 85%; colorless viscous oil; $[\alpha]_D^{25}$ +88.3 (*c* 1.09, $CHCl_3$).

IR (CCl_4): 3066, 3034, 3006, 2802, 1770, 1722, 1602, 1497, 1454, 1264 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.37–7.16 (m, 10 H), 4.70 (dd, ^2J = 11.4 Hz, ^3J = 5.6 Hz, 1 H), 4.36 (m, 1 H), 4.26 (dd, ^3J = 8.0 Hz,

^3J = 5.6 Hz, 1 H), 4.05 (AB system, Δν = 54.6 Hz, ^2J = 15.4 Hz, 2 H), 2.75 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 170.83, 150.66, 135.54, 133.92, 129.38, 129.01, 128.65, 128.55, 127.09, 127.04, 67.98, 62.86, 43.24, 42.91.

MS (EI): *m*/*z* (%) = 311 (1), 193 (13), 192 (100), 104 (34), 91 (52), 65 (17), 43 (21).

Anal. Calcd for $C_{18}H_{18}N_2O_3$ (310.35): C, 69.66; H, 5.85; N, 9.03. Found: C, 69.98; H, 5.94; N, 8.92.

(5*R*)-3-(Methoxyacetyl)-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one (8f)

Yield: 85%; white crystals; mp 116–117 °C; $[\alpha]_D^{25}$ +24.9 (*c* 1.00, $CHCl_3$).

IR (CCl_4): 3068, 3034, 2925, 2826, 1775, 1740, 1455, 1257, 1215, 1190 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.42–7.30 (m, 5 H), 4.90 (dd, ^2J = 11.6 Hz, ^3J = 5.2 Hz, 1 H), 4.78 (dd, ^2J = 11.6 Hz, ^3J = 6.5 Hz, 1 H), 4.35 (AB system, Δν = 60.4 Hz, ^2J = 17.2 Hz, 2 H), 4.36 (dd, ^3J = 6.5 Hz, ^3J = 5.2 Hz, 1 H), 3.36 (s, 3 H), 2.82 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 169.75, 149.49, 134.99, 129.06, 128.73, 127.05, 73.09, 67.15, 60.93, 59.22, 42.25.

MS (EI): *m*/*z* (%) = 177 (4), 118 (31), 104 (26), 103 (19), 91 (25), 89 (12), 78 (25), 77 (41), 65 (18), 63 (16), 56 (23), 55 (10), 51 (47), 50 (22), 45 (100), 43 (28), 42 (60), 39 (29).

Anal. Calcd for $C_{13}H_{16}N_2O_4$ (264.28): C, 59.08; H, 6.10; N, 10.60. Found: C, 58.71; H, 5.90; N, 10.63.

(5*R*)-4-Methyl-3-(phenoxyacetyl)-5-phenyl-1,3,4-oxadiazinan-2-one (8g)

Yield: 90%; white crystals; mp 112–114 °C; $[\alpha]_D^{25}$+17.7 (*c* 1.00, $CHCl_3$).

IR (CCl_4): 3068, 3033, 2966, 2799, 1777, 1742, 1600, 1495, 1257, 1191 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.42–7.35 (m, 5 H), 7.25–7.17 (m, 2 H), 6.97–6.91 (m, 1 H), 6.71–6.66 (m, 2 H), 4.93 (AB system, Δν = 63.0 Hz, ^2J = 17.4 Hz, 2 H), 4.92 (dd, ^2J = 11.7 Hz, ^3J = 5.1 Hz, 1 H), 4.76 (dd, ^2J = 11.7 Hz, ^3J = 5.7 Hz, 1 H), 4.35 (dd, ^3J = 5.7 Hz, ^3J = 5.1 Hz, 1 H), 2.85 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 168.30, 157.79, 149.48, 135.10, 129.47, 129.10, 128.72, 127.11, 121.55, 114.71, 68.53, 67.09, 60.83, 42.48.

MS (EI): *m*/*z* (%) = 326 (7), 205 (35), 192 (16), 161 (30), 132 (72), 118 (30), 117 (23), 107 (21), 104 (21), 103 (14), 91 (26), 79 (16), 78 (21), 77 (100), 65 (19), 51 (33), 43 (48), 42 (36), 39 (23).

Anal. Calcd for $C_{18}H_{18}N_2O_4$ (326.35): C, 66.25; H, 5.56; N, 8.58. Found: C, 66.29; H, 5.54; N, 9.02.

(5*R*)-3-[(Ethylthio)acetyl]-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one (8h)

Yield: 83%; light-yellow oil; $[\alpha]_D^{25}$ +42.0 (*c* 1.09, $CHCl_3$).

IR (CCl_4): 3068, 3030, 2969, 2804, 1770, 1713, 1455, 1276, 1173, 1125 cm^{-1}.

^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.41–7.33 (m, 5 H), 4.79 (dd, ^2J = 11.5 Hz, ^3J = 5.6 Hz, 1 H), 4.63 (m, 1 H), 4.36 (dd, ^3J = 8.1 Hz, ^3J = 5.6 Hz, 1 H), 3.69 (AB system, Δν = 178.9 Hz, ^2J = 14.1 Hz, 2 H), 2.80 (s, 3 H), 2.58–2.47 (m, 2 H), 1.21 (t, ^3J = 7.4 Hz, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 169.48 150.59, 135.61, 129.25, 128.91, 127.35, 68.30, 62.79, 43.10, 35.77, 26.47, 14.51.

MS (EI): *m*/*z* (%) = 192 (12), 133 (13), 118 (57), 104 (100), 103 (53), 91 (41), 89 (26), 78 (72), 77 (85), 65 (37), 63 (35), 56 (35), 52 (24), 51 (94), 50 (50), 43 (45), 42 (92), 39 (63).

Anal. Calcd for $C_{14}H_{18}N_2O_3S$ (294.37): C, 57.12; H, 6.16; N, 9.52. Found: C, 56.70; H, 6.02; N, 9.59.

(5*R*)-3-(2-Furoyl)-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one (8i)

Yield: 90%; colorless viscous oil; $[\alpha]_D^{25}$ +41.6 (*c* 1.00, $CHCl_3$).

IR (CCl_4): 3067, 3035, 3005, 2804, 1778, 1700, 1576, 1475, 1296, 1258 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.52 (dd, ^3J = 1.7 Hz, ^4J = 0.8 Hz, 1 H), 7.42–7.30 (m, 5 H), 7.20 (dd, ^3J = 3.6 Hz, ^4J = 0.8 Hz, 1 H), 6.50 (dd, ^3J = 3.6 Hz, ^3J = 1.7 Hz, 1 H), 4.76 (dd, ^2J = 11.4 Hz, ^3J = 6.0 Hz, 1 H), 4.51 (dd, ^2J = 11.4 Hz, ^3J = 9.7 Hz, 1 H), 4.37 (dd, ^3J = 9.7 Hz, ^3J = 6.0 Hz, 1 H), 2.95 (s, 3 H).

^{13}C NMR (75 MHz, $CDCl_3$): δ = 158.34, 151.43, 146.18, 145.94, 135.91, 129.01, 128.61, 126.62, 119.19, 112.15, 68.95, 64.80, 44.96.

MS (EI): *m*/*z* (%) = 286 (6), 229 (9), 174 (9), 161 (45), 118 (10), 104 (11), 95 (100), 77 (10), 43 (20), 39 (31).

Anal. Calcd for $C_{15}H_{14}N_2O_4$ (286.28): C, 62.93; H, 4.93; N, 9.79. Found: C, 62.92; H, 4.80; N, 10.01.

(5*R*)-3-[(2*E*)-Cinnamoyl]-4-methyl-5-phenyl-1,3,4-oxadiazinan-2-one (8j)

Yield: 80%; colorless viscous oil; $[\alpha]_D^{25}$ +4.40 (*c* 1.05, $CHCl_3$).

IR (CCl_4): 3087, 3065, 3032, 2802, 1763, 1737, 1700, 1621, 1449, 1333, 1255, 1188 cm^{-1}.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.81 (d, ^3J = 15.6 Hz, 1 H), 7.56–7.34 (m, 10 H), 7.30 (d, ^3J = 15.6 Hz, 1 H), 4.81 (dd, ^2J = 11.5 Hz, ^3J = 5.7 Hz, 1 H), 4.61 (dd, ^2J = 11.5 Hz, ^3J = 8.5 Hz, 1 H), 4.38 (dd, ^3J = 8.5 Hz, ^3J = 5.7 Hz, 1 H), 2.87 (s, 3 H).

^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.62, 150.56, 145.73, 135.63, 134.66, 130.44, 129.03, 128.85, 128.66, 128.37, 127.03, 117.98, 68.13, 62.85, 43.54.

MS (EI): *m*/*z* (%) = 322 (4), 132 (10), 131 (100), 104 (10), 103 (30), 76 (26), 51 (11).

Anal. Calcd for $C_{19}H_{18}N_2O_3$ (322.36): C, 70.79; H, 5.63. Found: C, 70.49; H, 5.70; N, 8.46.

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