Total Synthesis of Bacterial 5-(3-Indolyl)oxazole Alkaloids: Pimprinols A–C

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This paper is dedicated to the memory of Professor József Reiter.

Abstract

Pimprinols A, B, and C are bacterial 5-(3-indolyl)oxazole alkaloids that have been isolated from Streptomyces sp. Lv3–13. In this paper, we report a new synthesis of pimprinol A and the first total synthesis of pimprinol B and pimprinol C. In addition, antipodes of the naturally occurring pimprinols A and C, as well as the racemates of these two alkaloids were also prepared. In the pivotal step, the 1,3-oxazole ring was constructed by a Nicolaou's modified Robinson–Gabriel cyclization.

Key words oxazole, natural products, bacterial alkaloids, pimprinols A–C, total synthesis

Oxazole ring-containing compounds are significant representatives of natural products and synthetic pharmaceuticals.1–5 The bacterial alkaloids pimprinols A–C [(R)-1, 2, (R)-3; Figure 1], which belong to the 5-(3-indolyl)oxazole family, were isolated from the rare actinomycetes, Streptomyces sp. Lv3–13 by Müller and co-workers in 2012.6 All three extracted alkaloids [(R)-1, 2, (R)-3] were described as yellow oils and their structures were elucidated by UV, 1D NMR spectroscopy, and by HRMS (ESI, +) analysis. The absolute configurations of pimprinol A [(R)-1] and C [(R)-3] were determined by Mosher ester analysis.

The only known synthesis of pimprinol A [(R)-1] was described in 2014 by Wu et al. (Scheme 1).7 In this one-pot method, compound (R)-1 was prepared by condensation of 1-[(1H-indol-3-yl)ethanone (4) with l-threonine (5; 2 equiv) in the presence of I2 in DMSO at 110 °C. The product was obtained in 70% yield and 96% enantiomeric excess as a pale-brown solid. The alkaloids pimprinol B (2) and C [(R)-3] have not yet been synthesized.

Herein, we would like to report a new total synthesis of pimprinol A [(R)-1] and the first total synthesis of pimprinol B (2) and C [(R)-3]. In addition, antipodes and racemates of pimprinol A and C were also prepared.

Initially, the synthesis of racemic pimprinol A [(rac)-1] was investigated starting from the easily available dL-alanine [(rac)-6; Scheme 2]. 2-Chloro-1-methyl-2-oxoethyl acetate [(rac)-7] was prepared as previously reported.8–10 Reaction of (rac)-6 with NaNO2 in glacial acetic acid, followed by treatment with an excess of SOCl2, afforded compound (rac)-7. Intermediate (rac)-9 was obtained by acylation of tryptamine (8) with (rac)-7 in the presence of Et3N in 88% yield. Oxidation of (rac)-9 with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in a THF–water solvent mixture at 0 °C led to the corresponding acylamino-ketone (rac)-10 in

![Figure 1](image-url)
excellent yield. The Robinson–Gabriel cyclization of acyl- 
amino-ketone (rac)-10 with propylphosphonic anhydride (T3P®) under microwave conditions11 was unsuccessful, with the starting material being decomposed. Subsequent-
ly, the ring-closure reaction was attempted using Nicolaou's protocol with POCl₃ in pyridine at room temperature. In this reaction, the desired 1,3-oxazole derivative (rac)-11 was obtained in 80% yield. Removal of the acetyl group by alkaline hydrolysis furnished the target molecule, racemic pimprinol A [(rac)-1], in almost quantitative yield.

By following the above synthetic route, natural (+)-pimprinol A [(R)-1] and its enantiomer (−)-pimprinol A [(S)-1] were prepared starting from (R)-alanine [(R)-6] and (S)-alani-
ne [(S)-6], respectively. It is important to note that the substitution of the amino group in alanine occurs by double inversion.10,11 Natural (+)-pimprinol A [(R)-1] was obtained in four steps from known (1R)-2-chloro-1-methyl-2-
 oxyethyl acetate [(R)-7] in 60% overall yield and in 98% ee. (−)-Pimprinol A [(S)-1] was synthesized from the corre-
 sponding acid chloride (S)-7 in a similar overall yield (61%). The enantiomeric purity was 98% also in the final product, which was determined by chiral chromatographic separation on a polysaccharide stationary phase (column: 150 × 4.6 mm Lux 5
μm amylose-1, temperature: 20 °C, mobile phase: acetonitrile with 0.1% ethanolamine).

Racemic pimprinol C [(rac)-3] was prepared from the known 1-(chlorocarbonyl)propyl acetate [(rac)-13]8,14 by using an analogous procedure in four steps in 88% overall yield (Scheme 2). The natural alkaloid pimprinol C [(R)-3] and its enantiomer [(S)-3] were synthesized in a similar manner starting from (1R)-[(R)-15] and (1S)-1-(chloro-
carbonyl)propyl acetate [(S)-13],16 respectively. The latter compounds were obtained in more than 80% yield and in 98% ee.

Next, the synthesis of pimprinol B (2) was studied from two readily available oxazole derivatives; methyl [5-(1H-
 indol-3-yl)-1,3-oxazol-2-yl] acetate (21) and the natural product labradorin 5 (22; Scheme 3). First, tryptamine (8) was converted into compounds 21 and 22 through a three-
step procedure involving acylation with the appropriate acyl chlorides, DDQ mediated oxidation, and T3P®-promot-
ed Robinson–Gabriel cyclodehydration under microwave conditions in a vent-and-resale vessel. The reaction of ester 21 with MeMgI or MeLi was unsuccessful. In both cases the starting material was recovered. It is hypothesized that the reaction of oxazole 21 with Grignard or organolithium re-
agent produced an inactive dianion by deprotonation of both the indole NH and the active methylene group. Water addition to, or epoxidation of, the isopropylidene double bond in labradorin 5 (22) was unsuccessful with various re-
agents, such as H₂SO₄/H₂O at room temperature,17 poly-
phosphoric acid (PPA) at 90 °C,18 Hg(OAc)₂/THF–H₂O then NaOH/NaBH₄,19 HCl/THF–H₂O at reflux,20 and meta-chlоро-
p eroxybenzoic acid (mCPBA) at 0 °C.21 Finally, upon treat-
ment of labradorin 5 (22) with 50% aqueous H₂SO₄ in boiling 1,4-dioxane22 for 4 days, pimprinol B (2) was produced with 15% conversion and in 11% isolated yield. The main component of the residue was the starting material, with some decomposition detected. It is assumed that the poor reactivity of the isopropylidene double bond in compound 22 is caused by extensive conjugation.

Finally, a more efficient total synthesis of pimprinol B (2) was elaborated starting from commercially available 3-
hydroxy-3-methylbutanoic acid (23; Scheme 4). Protection of the tertiary hydroxyl group of 23 with acetyl chloride af-
forded carboxylic acid 24.23 The latter intermediate and tryptamine (8) were coupled according to Methods A and B. First carbonyldiimidazole (CDI) as coupling agent was used
in the amide formation but this resulted in the required product in only moderate yield. However, applying 1-[bis(dimethylamino)-methylene]-1H-1,2,3-triazolo[4,5-b]pyridinium 3-oxide hexafluorophosphate (HATU) and Hünig’s base, furnished the corresponding amide \(^\text{25}\) in good yield. Although Method B resulted in a higher yield, the final product was contaminated with HATU, which was difficult to eliminate. Subsequent oxidation of intermediate \(^\text{25}\) with DDQ in a THF–water solvent mixture provided \(\text{\textbeta}-\text{keto amide } \text{26}\). Reaction of compound \(^\text{26}\) with POCl\(_3\) in pyridine, followed by alkaline hydrolysis of the ester group generated pimprinol B in 17% (Method A) and 30% (Method B) overall yields.

Pimprinols A–C were obtained as colorless crystals with sharp melting points, unlike the isolated samples.\(^6\) The analytical data of these synthesized alkaloids are in agreement with those reported for the natural products. The only significant difference was found in the specific rotation values.\(^6\)

In conclusion, a convergent synthesis of racemic and optically active pimprinols A and C has been developed from readily available amino acids in six steps using practical and convenient synthetic methodology. Furthermore, the first total synthesis of optically inactive pimprinol B was accomplished in five steps starting from commercially available 3-hydroxy-3-methylbutanoic acid. In addition, 25 new
Reactions under microwave conditions were carried out with a MicroSYNTH T640 in ‘vent-and-reseal’ vessels with an ATC-FO automatic temperature control and limitation of maximum power to 200–300 W. All melting points were determined with a Büchi B-540 capillary melting point apparatus and are uncorrected. IR spectra were obtained with a Bruker Alpha FT-IR spectrophotometer in KBr pellets or film. 1H and 13C NMR spectra were recorded in DMSO-d6, CDCl3, or CD3OD in 5 mm tubes at r.t., with a Bruker Avance III HD 600 (600 and 150 MHz for 1H and 13C NMR spectra, respectively), or a Bruker Avance III 400 (400 and 100 MHz for 1H and 13C NMR spectra, respectively) spectrometer with the deuterium signal of the solvent as the internal standard. Chemical shifts (δ) and coupling constants (J) are given in ppm and in Hz, respectively. The following abbreviations were used to designate multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, sp = septet, m = multiplet, br = broad. Mass spectra were recorded with a Bruker TOF MAXIS Impact mass spectrometer coupled to a Dionex Ultimate 3000 RS HPLC system with a diode array detector. Reactions were monitored by thin-layer chromatography (TLC) carried out on silica gel plates (60 F254) using UV light as visualizing agent. Purifications by flash column chromatography were carried out using Merck 107736 silica gel 60 H film. 1H and 13C NMR spectra were recorded in DMSO-d6, CDCl3 or CD3OD (6, CDCl 3 or DMSO-d6) using UV light as visualizing agent. Purifications by flash column chromatography were carried out using Merck 107736 silica gel 60 H film. 1H and 13C NMR spectra were recorded in DMSO-d6, CDCl3 or CD3OD (6, CDCl 3 or DMSO-d6) using UV light as visualizing agent. 13C NMR (150 MHz, CDCl3): δ = 170.3, 169.4, 163.3, 127.3, 122.23, 122.16, 119.6, 118.6, 112.7, 111.3, 70.6, 39.5, 25.0, 20.9, 17.9 ppm.

(1R)-2-[(1H-Indol-3-yl)ethyl]amino]-1-methyl-2-oxoethyl acetate [(rac)-9]12

Yield: 3.151 g (91%); brown oil; [α]20 + 13.7 (c 1.0, MeOH).

IR (film): 3406, 3299, 1739, 1660, 1537, 1233, 745, 426 cm–1.


J2 8.2 Hz, 1 H), 6.18 (br s, 1 H), 5.15 (q, J = 6.9 Hz, 1 H), 3.69–3.54 (m, 1 H), 3.00 (t, J = 6.7 Hz, 2 H), 1.93 (s, 3 H), 1.43 (d, J = 6.8 Hz, 3 H).

13C NMR (150 MHz, CDCl3): δ = 170.3, 169.4, 163.2, 127.3, 122.20, 122.15, 119.5, 118.6, 112.6, 111.3, 70.5, 39.6, 25.0, 20.8, 17.9.


(1S)-2-[(1H-Indol-3-yl)ethyl]amino]-1-methyl-2-oxoethyl acetate [(S)-9]12

Yield: 3.428 g (99%); brown oil; [α]20 –17.5 (c 1.0, MeOH).

IR (film): 3405, 3308, 1735, 1664, 1540, 1233, 1096, 744 cm–1.


(1S,2R)-9

Yield: 3.594 g (94%); brown oil.

IR (film): 3406, 3299, 1739, 1660, 1537, 1223, 745, 426 cm–1.


J2 8.2 Hz, 1 H), 6.18 (br s, 1 H), 5.15 (q, J = 6.9 Hz, 1 H), 3.69–3.54 (m, 1 H), 3.00 (t, J = 6.7 Hz, 2 H), 1.93 (s, 3 H), 1.43 (d, J = 6.8 Hz, 3 H).

13C NMR (150 MHz, CDCl3): δ = 170.3, 169.4, 163.3, 127.3, 122.23, 122.16, 119.6, 118.6, 112.7, 111.3, 70.6, 39.5, 25.0, 20.9, 17.9.

(1R)-1-[(2-[(1-Indol-3-yl)ethyl]carbamoyl]propyl acetate [(R)-14]

Yield: 3.994 g (99%); brown oil; [α]28 +17.1 (c 1.0, MeOH).

IR (KBr): 3405, 3306, 1738, 1666, 1536, 1232, 745, 426 cm⁻¹.

1H NMR (600 MHz, CDCl₃): δ = 8.17 (br s, 1 H), 7.61 (d, J = 7.9 Hz, 1 H), 7.38 (d, J = 8.2 Hz, 1 H), 7.26 (br s, 1 H), 7.23 (t, J = 7.9 Hz, 1 H), 7.18 (t, J = 7.9 Hz, 1 H), 7.04 (d, J = 2.3 Hz, 1 H), 6.13 (br s, 1 H), 5.10 (q, J = 4.7 Hz, 1 H), 3.69–3.62 (m, 3 H), 3.61–3.53 (m, 3 H), 3.00 (t, J = 6.7 Hz, 2 H), 1.93 (s, 3 H), 1.91–1.85 (m, 1 H), 1.84–1.77 (m, 1 H), 0.88 (t, J = 7.4 Hz, 3 H).

13C NMR (150 MHz, CDCl₃): δ = 169.5, 169.56, 136.3, 127.3, 122.23, 122.19, 119.6, 118.6, 112.7, 111.3, 74.9, 39.4, 25.1, 25.0, 20.8, 9.0.


Yield: 2.259 g (62%) brown oil.

IR (film): 3393, 3307, 1738, 1655, 1437, 830, 746, 559 cm⁻¹.

1H NMR (600 MHz, CDCl₃): δ = 8.50 (br s, 1 H), 7.59–7.56 (m, 1 H), 7.34–7.31 (m, 1 H), 7.19–7.14 (m, 1 H), 7.11–7.07 (m, 1 H), 7.02 (br s, 1 H), 6.98 (d, J = 2.3 Hz, 1 H), 3.65 (s, 3 H), 3.59 (q, J = 6.9 Hz, 2 H), 3.21 (s, 2 H), 2.89–2.84 (m, 2 H).

13C NMR (150 MHz, CDCl₃): δ = 169.5, 165.0, 136.3, 127.1, 122.2, 121.9, 119.2, 118.5, 112.4, 51.2, 41.2, 39.9, 24.9.

Preparation of Ketoamines 10, 15, 19, 20, 26; General Procedure

The appropriate amide was dissolved in THF–H₂O (9:1, 60 mL). To this solution was added 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ; 2 mmol, 2 equiv) in several portions at 0 °C. After addition was complete, the mixture was stirred at the same temperature for 2 h (until the consumption of the starting material as indicated by TLC). The mixture was then poured into EtOAc (150 mL) and extracted with 10% aq. NaHCO₃ (4 × 85 mL) dried over MgSO₄, filtered, and evaporated to give the desired ketoamide. Analytical samples were obtained by recrystallization from EtOH.

2-[(2-[(1-Indol-3-yl)ethyl]amino]-1-methyl-2-oxoethyl acetate [(R)-10]

Yield: 1.096 g (95%); colorless crystals; mp 128–130 °C (EtOH).

IR (KBr): 3278, 3116, 1737, 1666, 1633, 1243, 1048, 756 cm⁻¹.

1H NMR (600 MHz, CDCl₃): δ = 12.03 (br s, 1 H), 8.43 (d, J = 3.1 Hz, 1 H), 8.30 (t, J = 5.6 Hz, 1 H), 8.16 (d, J = 7.4 Hz, 1 H), 7.49 (d, J = 7.9 Hz, 1 H), 7.36–7.27 (m, 2 H), 5.07 (q, J = 6.9 Hz, 1 H), 4.48 (d, J = 6.9 Hz, 2 H), 2.10 (s, 3 H), 1.39 (d, J = 7.2 Hz, 3 H).

13C NMR (150 MHz, CDCl₃): δ = 190.0, 170.5, 169.9, 136.3, 133.9, 125.6, 123.1, 121.3, 114.1, 112.4, 69.8, 45.6, 21.0, 18.1.

1H NMR (600 MHz, DMSO-d6): δ = 12.0 (br s, 1 H), 8.43 (s, 1 H), 8.42 (br s, 1 H), 8.33 (s, 1 H), 8.15 (s, 1 H), 8.12 (s, 1 H), 7.98 (s, 1 H), 7.16–7.12 (m, 2 H), 5.67 (s, 1 H), 4.48 (d, J = 6.8 Hz, 2 H), 2.09 (s, 3 H), 1.39 (d, J = 6.8 Hz, 3 H).

1C NMR (150 MHz, DMSO-d6): δ = 190.8, 166.4, 149.0, 136.6, 133.7, 125.6, 123.0, 122.0, 113.9, 112.4, 74.4, 45.6, 25.1, 21.0, 9.5.


Methyl 3-[[2-(1H-Indol-3-yl)-2-oxoethyl]amino]-3-oxopropionate (19)
Yield: 1.086 g (99%); pale-brown crystals; mp 173–176 °C (EtOH).
IR (KBr): 3302, 3219, 1741, 1667, 1625, 1437, 1208, 743 cm–1.
1H NMR (600 MHz, CDCl3): δ = 7.86 (br s, 1 H), 8.35 (t, J = 3.7 Hz, 1 H), 7.96 (d, J = 3.1 Hz, 2 H), 7.49–7.43 (m, 1 H), 7.37–7.30 (m, 2 H), 4.70 (d, J = 4.3 Hz, 2 H), 3.80 (s, 3 H), 3.45 (s, 2 H), 3.59 (q, J = 6.9 Hz, 2 H), 3.21 (s, 2 H), 2.89–2.94 (m, 2 H).
1C NMR (150 MHz, CDCl3): δ = 188.4, 169.2, 165.1, 136.1, 131.1, 125.2, 124.1, 123.1, 122.2, 115.4, 111.6, 52.6, 46.6, 41.3.
HRMS: m/z [M + H]+ calcd for C16H16N2O4: 279.0594; found: 275.1024.

N-[[2-(1H-Indol-3-yl)-2-oxoethyl] morpholin-4-yl]acetamide (20)
Yield: 1.015 g (99%); colorless crystals; mp 243–245 °C (EtOH, decomp.)(lit.7 mp 233–235 °C).
IR (KBr): 3335, 3243, 1737, 1630, 1435, 926, 742 cm–1.
1H NMR (600 MHz, DMSO-d6): δ = 11.99 (br s, 1 H), 8.43 (s, 1 H), 8.22–8.12 (m, 1 H), 8.05 (t, J = 5.6 Hz, 1 H), 7.53–7.45 (m, 1 H), 7.28–7.16 (m, 2 H), 5.81 (s, 1 H), 4.48 (d, J = 5.8 Hz, 1 H), 2.10 (s, 3 H), 1.81 (s, 3 H).
1C NMR (100 MHz, DMSO-d6): δ = 190.8, 166.4, 149.0, 136.6, 133.7, 125.6, 123.0, 122.0, 119.1, 114.3, 113.2, 45.6, 27.0, 19.5.

3-[[2-(1H-Indol-3-yl)ethyl]amino]-1,1-dimethyl-3-oxopropyl acetate (26)
Yield: 696 mg (55%); colorless crystals; mp 169–171 °C (EtOH, decomp.).
IR (KBr): 3328, 3243, 1737, 1630, 1431, 1251, 1144, 746 cm–1.
1H NMR (600 MHz, DMSO-d6): δ = 12.01 (br s, 1 H), 8.43 (s, 1 H), 8.20–8.12 (m, 2 H), 7.52–7.47 (m, 1 H), 7.25–7.17 (m, 2 H), 4.47 (d, J = 3.2 Hz, 1 H), 2.74 (s, 2 H), 1.93 (s, 3 H), 1.51 (s, 6 H).
1C NMR (150 MHz, DMSO-d6): δ = 190.4, 170.1, 169.1, 136.6, 133.8, 125.6, 123.1, 122.0, 114.2, 112.4, 74.4, 45.6, 25.1, 21.0, 9.5.

Formation of Oxazoles 11, 16, 27 in the Presence of POCl3 and Pyridine; General Procedure
Ketoamide (10, 15, 26; 0.6 mmol) was dissolved in pyridine (2 mL), POCl3 (3.24 mmol, 5.4 equiv) was added at r.t. and the reaction mixture was stirred for 3 hours. After the reaction was complete (TLC monitoring), EtOAc (40 mL) and 10% aq. NaHCO3 (60 mL) were added to the mixture, the phases were separated, and the aqueous phase was further extracted with EtOAc (3 × 40 mL). The combined organic extracts were washed with water (60 mL) and brine (60 mL), then dried (MgSO4), filtered and evaporated to afford the appropriate products. Analytical samples were obtained by recrystallization from aqueous EtOH.

1-[5-(1H-Indol-3-yl)-1,3-oxazol-2-yl]ethyl acetate (rac-11)
Yield: 130 mg (80%); pale-brown crystals; mp 139–141 °C (EtOH-H2O).
IR (KBr): 3473, 3171, 1750, 1634, 1495, 1221, 1044, 741 cm–1.
1H NMR (600 MHz, CD3OD): δ = 7.80 (dd, J = 0.4 Hz, 15 J = 7.9 Hz, 1 H), 7.65 (s, 1 H), 7.44 (d, J = 8.1 Hz, 1 H), 7.25 (s, 1 H), 7.20 (t, J = 7.1 Hz, 1 H), 7.16 (t, J = 7.8 Hz, 1 H), 6.01 (q, J = 6.8 Hz, 1 H), 2.12 (s, 3 H), 1.69 (d, J = 6.7 Hz, 3 H).
H NMR (600 MHz, CD$_3$OD): $\delta$ = 7.81 (d, $J$ = 7.9 Hz, 1 H), 7.65 (s, 1 H), 7.46 (d, $J$ = 8.1 Hz, 1 H), 7.26 (s, 1 H), 7.24–7.19 (m, 1 H), 7.18–7.14 (m, 1 H), 6.02 (q, $J$ = 6.8 Hz, 1 H), 2.13 (s, 3 H), 1.69 (d, $J$ = 6.7 Hz, 3 H).

13C NMR (150 MHz, CD$_3$OD): $\delta$ = 171.6, 161.3, 151.0, 138.2, 125.3, 124.3, 123.5, 121.5, 120.4, 119.5, 112.9, 112.0, 105.0, 66.2, 20.8, 11.6.

HRMS: $m/z [M + H]^+$ calcd for C$_{24}$H$_{24}$N$_2$O$_4$: 375.1748; found: 375.1744.

1H NMR (600 MHz, CD$_3$OD): $\delta$ = 7.80 (d, $J$ = 7.9 Hz, 1 H), 7.65 (s, 1 H), 7.46 (d, $J$ = 8.1 Hz, 1 H), 7.26 (s, 1 H), 7.24–7.19 (m, 1 H), 7.18–7.14 (m, 1 H), 6.02 (q, $J$ = 6.8 Hz, 1 H), 2.13 (s, 3 H), 1.69 (d, $J$ = 6.7 Hz, 3 H).

13C NMR (150 MHz, CD$_3$OD): $\delta$ = 171.6, 161.3, 151.0, 138.2, 125.3, 124.3, 123.5, 121.5, 120.4, 119.5, 112.9, 112.0, 105.0, 66.2, 20.8, 11.6.

HRMS: $m/z [M + H]^+$ calcd for C$_{24}$H$_{24}$N$_2$O$_4$: 375.1748; found: 375.1744.

1H NMR (600 MHz, CD$_3$OD): $\delta$ = 7.80 (d, $J$ = 7.9 Hz, 1 H), 7.65 (s, 1 H), 7.46 (d, $J$ = 8.1 Hz, 1 H), 7.26 (s, 1 H), 7.24–7.19 (m, 1 H), 7.18–7.14 (m, 1 H), 6.02 (q, $J$ = 6.8 Hz, 1 H), 2.13 (s, 3 H), 1.69 (d, $J$ = 6.7 Hz, 3 H).

13C NMR (150 MHz, CD$_3$OD): $\delta$ = 171.6, 161.3, 151.0, 138.2, 125.3, 124.3, 123.5, 121.5, 120.4, 119.5, 112.9, 112.0, 105.0, 66.2, 20.8, 11.6.

HRMS: $m/z [M + H]^+$ calcd for C$_{24}$H$_{24}$N$_2$O$_4$: 375.1748; found: 375.1744.
Preparation of Pimprinol Alkaloids 1–3; General Procedure

Acetoxy-protected oxazole (11, 16 or 27; 0.7 mmol) was dissolved in MeOH (28 mL) and aq. NaOH (3.08 mmol in 0.5 mL water, 4.4 equiv) was added. The reaction mixture was stirred at r.t. until the reaction was complete, then the solvent was evaporated. The residue was taken up in a mixture of EtOAc (50 mL) and water (50 mL), and the phases were separated. The aqueous mixture was extracted with further EtOAc (3 × 30 mL) and the combined organic phases were dried over MgSO₄, filtered and evaporated. The products were purified by recrystallization from MeCN.

1-[(1-Indol-3-yl)-1,3-oxazol-2-yl]propan-1-ol [(rac]-1

Yield: 155 mg (97%); pale-yellow crystals; mp 157–160 °C (MeCN) (lit.6 mp 151–152 °C).

IR (KBr): 3266, 1681, 1440, 1376, 1128, 1098, 972, 732 cm⁻¹.

Yield: 149 mg (83%); colorless crystals; mp 159–160 °C (MeCN).

IR (KBr): 3221, 1638, 1445, 1338, 1241, 1084, 974, 751 cm⁻¹.


\[(\text{1R})-1-[(1\text{-Indol-3-yl})-1,3\text{-oxazol-2-yl}]\text{propan-1-ol} \times \text{(rac)-1}\]

\[(\text{1R})-1-[(1\text{-Indol-3-yl})-1,3\text{-oxazol-2-yl}]\text{propan-1-ol} \times \text{(rac)-1}\]

\[\text{mp} \times 151–152°C; [\alpha]_D^{27} +12.8 (c 1.0, MeOH).\]

IR (KBr): 3285, 1587, 1438, 1258, 1125, 966, 732 cm⁻¹.

\[(\text{1R})-1-[(1\text{-Indol-3-yl})-1,3\text{-oxazol-2-yl}]\text{propan-1-ol} \times \text{(rac)-1}\]

\[\text{Yield: 158 mg (93%); 98% ee; colorless crystals; mp 143–145 °C (MeCN); [\alpha]_D^{27} +12.8 (c 1.0, MeOH).}\]

\[\text{IR (KBr): 3221, 1638, 1445, 1338, 1241, 1084, 974, 751 cm⁻¹.}\]

\[\text{IR (KBr): 3285, 1587, 1438, 1258, 1125, 966, 732 cm⁻¹.}\]

\[\text{HRMS: m/z [M + H]+ calcd for C₁₄H₁₅N₂O₂: 243.1128; found: 243.1128.}\]

Supporting Information

Supporting information for this article is available online at https://doi.org/10.1055/s-0039-1690336.

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