



Communication / Preliminary communication

Synthesis and crystal structure of (*R*, 4*R*)-3-[(*N*-benzyl-*N*-hydroxy-amino)-(1*H*-indol-3-yl)-methyl]-oxazolidin-2-one

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Abstract

The preparation and the crystal structure of the title compound are described. The unit-cell dimensions are: $a = 8.711(4)$, $b = 12.549(3)$, $c = 20.643(4)$ Å, $\beta = 92.21(4)^\circ$. Space group is the monoclinic $P2_1/c$ with $Z = 4$. The crystal structure determination was run by using 4560 independent reflections with a final R -value of 0.052 ($R_w = 0.083$). **To cite this article:** *M. David et al., C. R. Chimie 7 (2004)*.

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Résumé

La préparation du présent composé et sa structure cristalline sont décrites. L'étude cristallographique montre qu'il est monoclinique, avec une maille de dimensions : $a = 8,711(4)$, $b = 12,549(3)$, $c = 20,643(4)$ Å, $\beta = 92,21(4)^\circ$. Le groupe spatial est $P2_1/c$, avec $Z = 4$. La détermination de l'arrangement atomique, effectuée à l'aide de 4560 réflexions indépendantes, conduit à une valeur finale de $R = 0,052$ ($R_w = 0,083$). **Pour citer cet article :** *M. David et al., C. R. Chimie 7 (2004)*.

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Mots clés : Structure cristalline ; *N*-Hydroxylamines ; Nitrones ; Nucléophiles ; Noyaux indoliques ; *N*-Hydroxylamines indoliques

1. Introduction

N-Hydroxylamines are a very interesting class of compounds in organic chemistry, because of their interest as intermediates in the preparation of highly

functionalized amino derivatives. They may be prepared by reaction of nitrones with nucleophiles [1–15]. So, we have previously shown that *N*-hydroxylamines, obtained by reaction of nitrones with alkyl 3-lithiopropiolates, could be transformed into the corresponding γ -amino α,β -saturated esters [12], γ -(*N*-benzyl)amino α,β -ethylenic esters and/or α,β -ethylenic γ -lactames [3], γ -(*N*-*t*-butoxycarbonyl) amino α,β -ethylenic esters [6] and γ -(*N*-*t*-

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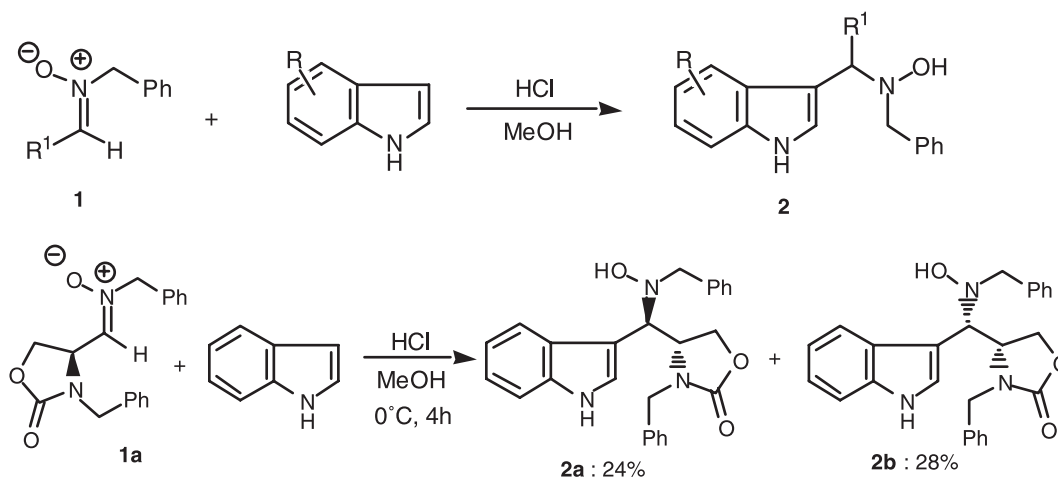


Fig. 1. Preparation scheme of the title compound.

butoxycarbonyl)amino α,β -dihydroxy esters [15]. The study of the reactivity of nitrones with indolic rings was also carried out [16,17], leading to the development of a synthetic approach of indolic *N*-hydroxylamines (Fig. 1). In this paper, we describe the preparation, by this method, of (*R*, *4R*)-3-[(*N*-

benzyl-*N*-hydroxy-amino)-(1*H*-indol-3-yl)-methyl]-oxazolidin-2-one **2a** and its (*S*, *4R*) diastereomer **2b** from α -chiral nitronium salt **1a** and indole [18] (Fig. 1). We also disclose the crystal structure analysis of compound **2a** (Fig. 2).

2. Preparation

The experimental procedure is as follows.

To a stirred methanolic solution of anhydrous hydrochloric acid (obtained by addition of 0.461 ml (0.506 g, 6.45 mmol) of acetyl chloride in 28 ml of distilled methanol), at 0 °C and under argon, was added a solution of 1.0 g (3.22 mmol) of nitronium salt **1a** and 0.377 g (3.22 mmol) of indole in 7 ml of distilled methanol. The resulting mixture was stirred at 0 °C for 4 h and then diluted by addition of dichloromethane. A saturated aqueous solution of sodium hydrogencarbonate was then added. After decantation, the aqueous layer was extracted three times with acetyl acetate. The combined organic layers were washed with brine and dried over anhydrous magnesium sulfate. After filtration and evaporation of solvents under vacuum, the crude product was purified by silica gel chromatography using a mixture of ether: pentane (1:7) as eluent to afford 0.331 g (0.78 mmol) of pure *N*-hydroxylamine **2a** and 0.379 g (0.89 mmol) of its diastereomer **2b** as white solids. The yields are respectively 24% and 28%.

Fig. 1 schematizes the experimental process for the preparation of indolic *N*-hydroxylamines **2a** and **2b**.

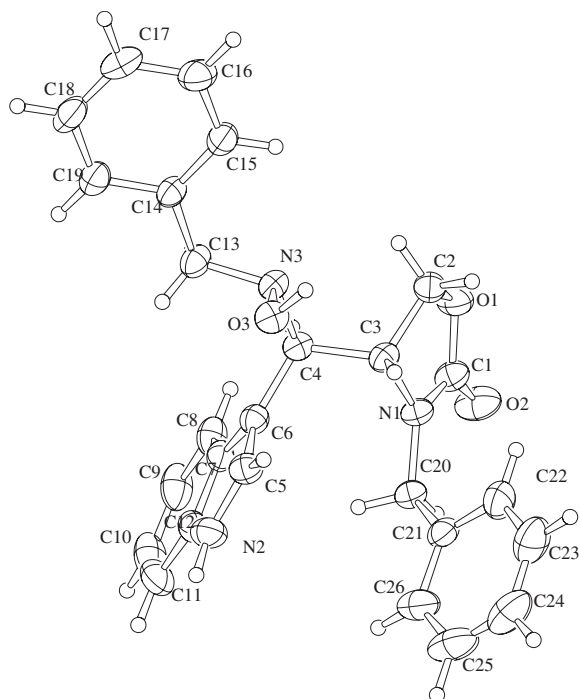


Fig. 2. Perspective view of the title compound performed using ORTEP II.

Experimental data for **2a**. mp : 88 °C. $[\alpha]_D^{20} = -5.1$ ($c = 1.1$; CHCl₃). ¹H NMR (300 MHz, CDCl₃) δ 3.72 (ABq, $J_{AB} = 13.0$ Hz, $\delta_A - \delta_B = 87.1$ Hz, 2H); 3.80–3.98 (broad s, 1H); 4.15–4.30 (m, 3H); 4.51 (broad s, 1H); 4.67 (s, 1H); 4.87 (d, $J = 14.9$ Hz, 1H); 6.86–7.00 (m, 2H); 7.04–7.14 (m, 1H); 7.16–7.37 (m, 11H); 7.40 (d, $J = 8.1$ Hz, 1H); 8.54 (broad s, 1H). ¹³C NMR (75.5 MHz, CDCl₃) δ 47.1 (CH₂); 55.8 (CHN); 62.3 (CH₂); 63.2 (CHN); 65.4 (CH₂); 108.6 (C); 111.5 (CH); 118.4 (CH); 120.1 (CH); 122.5 (CH); 124.3 (CH); 127.5 (CH); 127.6 (C); 127.7 (2 CH); 128.4 (CH); 128.7 (CH); 129.4 (CH); 135.7 (C); 136.1 (C); 137.4 (C); 159.5 (CO). IR (film): 3410 and 3300 (ν_{NH} and ν_{OH}), 1730 cm⁻¹ (ν_{CO} oxazolidinone). Mass spectrum (DCI, NH₃ + isobutane) m/z 428 (MH⁺), 305. Anal. calcd for C₂₆H₂₅N₃O₃: C, 73.05; H, 5.89; N, 9.83; found: C, 72.91; H, 6.17; N, 9.64. Experimental data for **2b**. mp: 88 °C. $[\alpha]_D^{20} = -23.7$ ($c = 0.75$; CHCl₃). ¹H NMR (300 MHz, CDCl₃) δ 3.64 (ABq, $J_{AB} = 13.0$ Hz, $\delta_A - \delta_B = 16.1$ Hz, 2H); 3.85–4.03 (m, 2H); 4.11 (broad s, 1H); 4.37–4.50 (m, 2H); 4.90 (ABq, $J_{AB} = 15.0$ Hz, $\delta_A - \delta_B = 93.8$ Hz, 2H); 6.85–7.40 (m, 14H); 7.54 (d, $J = 7.8$ Hz, 1H); 8.60 (broad s, 1H). ¹³C NMR (75.5 MHz, CDCl₃) δ 47.1 (CH₂); 54.7 (CHN); 62.3 (CH₂); 65.4 (CH₂); 66.3 (CHN); 107.3 (C); 111.5 (CH); 119.0 (CH); 120.3 (CH); 122.5 (CH); 124.5 (CH); 127.5 (CH); 127.8 (2 CH); 128.0 (C); 128.4 (CH); 129.0 (CH); 129.4 (CH); 135.7 (C); 136.8 (C); 137.3 (C); 159.3 (CO). IR (film): 3420 and 3340 (ν_{NH} and ν_{OH}), 1730 cm⁻¹ (ν_{CO} oxazolidinone). Mass spectrum (DCI, NH₃ + isobutane) m/z 428 (MH⁺), 305.

3. Structural determination

A crystal fragment with a size of 0.18 × 0.12 × 0.10 mm³ was used for the collection of diffraction data run with an Enraf-Nonius CAD4 diffractometer, operating with the copper radiation (1.5418 Å), monochromatized by a graphite plate. Measurements were performed within a range of 3 to 72° (θ). In this explored area ($\pm h, k, l$) h varies from -10 to 10, k from 0 to 15 and l from 0 to 25. A total of 4560 independent reflections ($R_{int} = 0.048$) were extracted among the 4599 scanned reflections. All reflections were measured with an $\omega/2\theta$ scan within an angular range of 1.20° for a maximum time of 80 s. Two intensity reference reflections measured every two hours

showed a decay of 6.74% during measurements run at room temperature. Unit-cell dimensions were determined and refined from a set of 25 reflections selected between 21.6 and 27.10°(θ). Some additional data are: $D_x = 1.259$, $F(000) = 904$, $V = 2256(1)$ Å³, $\mu = 0.672$ cm⁻¹.

The observed extinction rules: $0k0$ ($k = 2n+1$) and $h0l$ ($l = 2n+1$) lead unambiguously to the $P2_1/c$ space group. No absorption correction was applied. The crystal structure was solved using a direct method [19]. All non-hydrogen atoms were refined anisotropically, while hydrogen atoms located by geometry were not. The weighting scheme used corresponds to $w = [\sigma^2(F_o) + p^2/4|F_o|^2]^{-1}$ with $p = 0.06$. For 3584 reflections corresponding to $I/\sigma(I) > 2$, the final R value is 0.052 ($R_w = 0.083$). The residual electronic densities in the final Fourier difference map spread between

Table 1
Atomic coordinates and thermal parameters. Estimated standard deviations are given in parentheses

Atoms	$x(\sigma)$	$y(\sigma)$	$z(\sigma)$	B_{eq}
O(1)	1.1940(1)	0.13858(9)	0.77428(6)	0.0636(3)
O(2)	1.1957(2)	0.2977(1)	0.72608(7)	0.0820(4)
O(3)	0.6986(1)	-0.01914(8)	0.83677(5)	0.0537(3)
N(1)	0.9727(2)	0.2017(1)	0.73478(6)	0.0495(3)
N(2)	0.4992(2)	0.2832(1)	0.79437(8)	0.0674(4)
N(3)	0.8307(1)	0.03136(9)	0.86924(6)	0.0459(3)
C(1)	1.1241(2)	0.2200(1)	0.74288(8)	0.0575(4)
C(2)	1.0840(2)	0.0531(1)	0.77946(8)	0.0560(4)
C(3)	0.9281(2)	0.1063(1)	0.77047(7)	0.0458(3)
C(4)	0.8559(2)	0.1333(1)	0.83546(7)	0.0441(3)
C(5)	0.5835(2)	0.1911(1)	0.79550(8)	0.0559(4)
C(6)	0.7213(2)	0.2072(1)	0.82797(7)	0.0470(4)
C(7)	0.7216(2)	0.3167(1)	0.84789(7)	0.0496(4)
C(8)	0.8296(2)	0.3824(1)	0.88121(8)	0.0616(5)
C(9)	0.7920(3)	0.4869(2)	0.8910(1)	0.0827(6)
C(10)	0.6532(3)	0.5293(2)	0.8686(1)	0.1000(7)
C(11)	0.5456(3)	0.4681(2)	0.8363(1)	0.0860(6)
C(12)	0.5819(2)	0.3615(1)	0.82592(8)	0.0616(4)
C(13)	0.7872(2)	0.0493(1)	0.93606(7)	0.0559(4)
C(14)	0.7817(2)	-0.0515(1)	0.97540(7)	0.0504(4)
C(15)	0.8638(2)	-0.1418(1)	0.96092(8)	0.0632(5)
C(16)	0.8577(3)	-0.2313(1)	0.99942(9)	0.0740(6)
C(17)	0.7702(3)	-0.2323(2)	1.05295(9)	0.0737(6)
C(18)	0.6882(2)	-0.1434(2)	1.06819(8)	0.0743(6)
C(19)	0.6933(2)	-0.0536(1)	1.02971(8)	0.0630(5)
C(20)	0.8732(2)	0.2754(1)	0.69864(7)	0.0546(4)
C(21)	0.7832(2)	0.2280(1)	0.64241(7)	0.0562(4)
C(22)	0.8292(2)	0.1377(2)	0.61079(9)	0.0776(6)
C(23)	0.7483(3)	0.1016(2)	0.5557(1)	0.0988(8)

–0.18 and 0.19 e Å⁻³. The final atomic coordinates and the equivalent thermal factors are gathered in Table 1. All calculations as well as the ORTEP view [20] were made using the TeXsan crystallographic system [21].

4. Supplementary material available

Hydrogen coordinates, anisotropic thermal parameters, tables of interatomic distances and bond angles involving hydrogen atoms are available. Supplementary material data have been deposited at the Cambridge Crystallographic Data Center, 12 Union Road, Cambridge CB2 1EZ, UK, as supplementary publication No. 216151 and are available on request from the CCDC.

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