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Article

The Crystal and Molecular Structure of (*2Z*)-2-[3-(4-Methoxybenzoyl)-4,4-dimethyl-1,2-oxazolidin-2-ylidene]-1-(4-methoxyphenyl)ethanone

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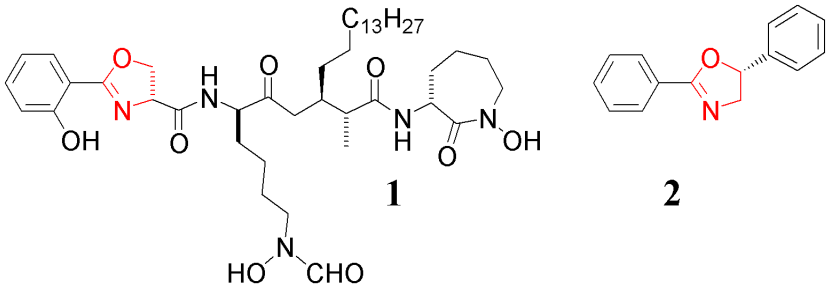
Abstract: The crystal and molecular structure of the title compound, *viz.*, (*2Z*)-2-[3-(4-methoxybenzoyl)-4,4-dimethyl-1,2,-oxazolidin-2-ylidene]-1-(4-methoxyphenyl)ethanone (**4**), is reported. Compound **4** crystallises from toluene/hexanes mixtures in the $P2_1/c$ space group with eight molecules in the unit cell. The unit cell parameters are: a = 20.9410(11) Å, b = 8.7523(5) Å, c = 21.2291(9) Å; β = 93.529(3)° and V = 3883.5(3) Å^3. There are two structurally distinct molecules of **4** found in the solid-state which differ primarily in terms of the observed torsion angles and the overall intramolecular spacing between the aromatic groups. Bond lengths and angles of this tertiary amide are otherwise typical. This is the first crystallographically characterised example of this class of oxazoline precursors, which have previously found application in the syntheses of other heterocycles. Density functional theory (B3LYP 6-311++G** level of sophistication) has likewise been applied to estimate the gas-phase structure of the title compound.

Keywords: oxazoline; X-ray crystal structure; tertiary amide; ketone; azole; oxazole; DFT

1. Introduction

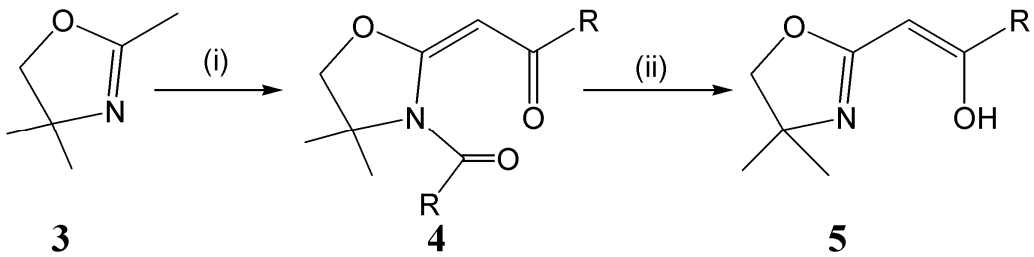
The 2-oxazolines, a sub-class of the azoles, consist of a 5-membered ring system consisting of one *O*- and one *N*-atom separated by a single carbon; these latter two atoms being formally sp^2 hybridised [1,2]. The group itself represents an important heterocyclic functionality as these molecules are routinely used as ligands in coordination chemistry [3-6] and catalysis [7-10], as directing groups in chemical modification strategies [11-14] and as a protecting group for carboxylic acids [15-18]. The ring is also found in a number of natural products, many of which have been the subject of total synthesis. Examples of these include complex molecules such as *Basilibactin A* down to very simple small molecules such as *Oxytriphine* (**1** and **2**, respectively: Figure 1) [19-21].

Figure 1. The molecular structures of the natural products *Brasilibactin A* (**1**) and *Oxytriphine* (**2**).



Sometime ago, Tohda and co-workers presented [22] a facile two-step strategy for the synthesis of enol-containing oxazolines initiating from 2,4,4-trimethyl-2-oxazoline (**3**). This protocol (Scheme 1) involves the (*i*) treatment of **3** with base (NEt_3) in the presence of two equiv. of a benzoyl- or alkoyl-chloride to yield an intermediate ethanone. This latter compound is then hydrolysed with excess alcoholic base (*ii*) to yield the desired enol-oxazoline product (**5**: Scheme 1). Materials such as **4** have found application in the production of other heterocycles [23] and as general synthetic intermediates [24-27]. A compound of general formula **4** (Scheme 1) has not previously been the subject of study *via* single crystal X-ray diffraction. In this report, we detail the solid-state properties of an example of crystalline **4** in which the R group (Scheme 1) is $–C_6H_4OCH_3$-*p* (*i.e.*, **4**: derived from 4-anisic acid).

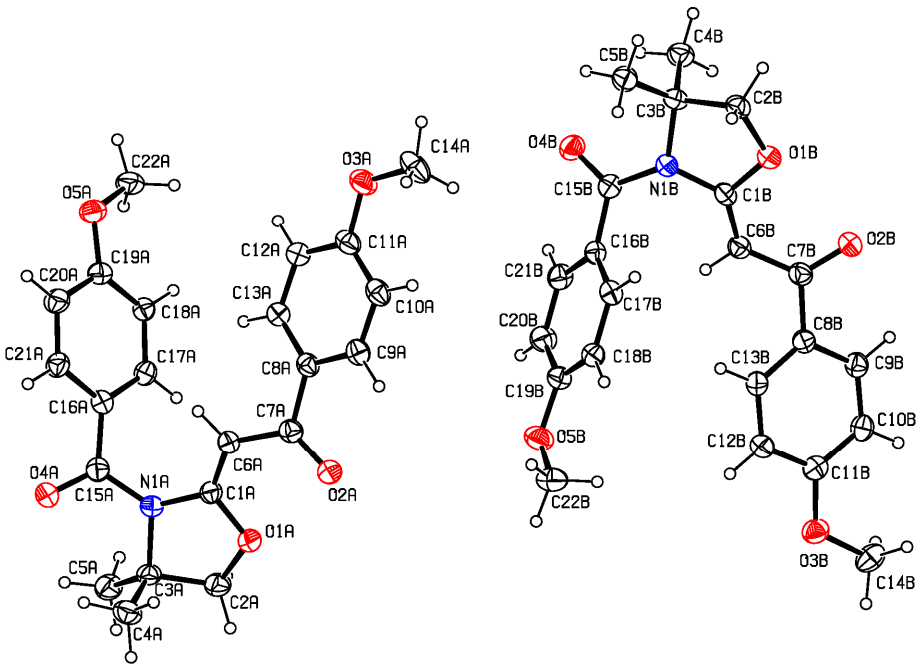
Scheme 1. The synthesis of enol-oxazolines (**5**) according to the method of Tohda [22]; specific conditions to yield **4**: (*i*) 2 × *p*-MeO-C_6H_4-C(=O)Cl / NEt_3 / MeCN / Δ.



2. Results and Discussion

As noted above, the title compound is the first crystallographically characterised example of this class of tertiary amides; solvent free crystals of **4** were obtained from equal volume mixtures of C_7H_8 and hexanes. A list of selected bond lengths and angles appears in Table 1. A noteworthy feature of the crystal form is the presence of two structurally distinct molecules of **4** (Molecule A and B) which are found in the unit cell (Figure 2).

Figure 2. ORTEP representations (50% probability) of the two distinct molecules of **4** found in the unit cell: Molecule A (left) and Molecule B (right).



These differ primarily in the torsion angles observed and the relative spacing of the two intramolecular aromatic rings (Table 1). Specifically for Molecule A, the O2A-C7A-C8A-C9A, C6A-C7A-C8A-C13A and N1A-C15A-C16A-C17A torsions are all narrower (20.6(5)°, 22.0(6)° and 33.9(5)°, respectively) than their respective angles observed for Molecule B (24.2(6)°, 28.8(5)° and 38.2(5)°, respectively). In the case of Molecule A, the relative spacing and twisting of the two aromatic rings results in a longer C22A•••O3A distance (6.66 Å) than that observed for the same spacing in B (6.27 Å). The heterocyclic rings in both molecules display deviations from planarity of 9.7° (Molecule A) and 8.0° (Molecule B) [21] as measured by their respective N1-C1-O1-C3 torsion angles. The bond lengths observed (Table 1) for the various functional groups are well within the expected ranges for such bonds and hence are otherwise unsurprising [28]. A crystal packing diagram is found in Figure 3. This molecule was also subjected to examination of its gas-phase structure using Density Functional Theory (DFT) at the B3LYP 6-311++G** level of sophistication. The calculated bond lengths and angles also appear in Table 1. The DFT measurements do a reasonable job at mimicking the solid-state structure (Table 1); interestingly rotation of the C6-C7 bond to a situation in which the C7-O2 ketone functionality is rotated approximately 180° relative to that of Molecules A or B is found to be a more

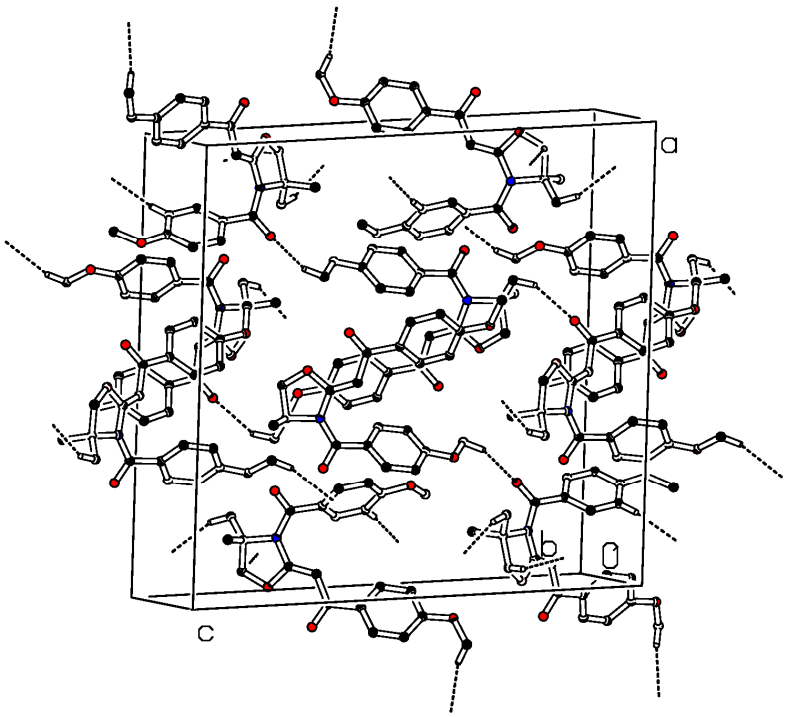
stable gas-phase configuration by approximately 3.0 kJ/mol. The gas-phase form is also predicted, perhaps not surprisingly, to have a longer C22•••O3 distance (d_{calc} = 9.00 Å). Of the three torsion angles mentioned above, the gas-phase form is closer to that of Molecule A with the respective values of 15.8°, 20.1° and 22.0°. The calculated deviation from planarity of the heterocycle (estimated similarly *via* the N1-C1-O1-C3 torsion, *vide supra*) is 12.5°.

Table 1. Selected bond lengths (Å) and angles (°) for observed unit cell Molecules A and B (standard deviations in parentheses) and their respective calculated parameters (DFT B3LYP 6-311++G**).

Molecule A		Calculated	Molecule B	
Designation	**Parameter**	**Parameter**	**Parameter**	**Designation**
O1A-C1A	1.351(4)	1.361	1.351(4)	O1B-C1B
O1A-C2A	1.456(5)	1.440	1.459(5)	O1B-C2B
O2A-C7A	1.231(4)	1.234	1.248(4)	O2B-C7B
O4A-C15A	1.222(4)	1.214	1.222(4)	O4B-C15B
N1A-C15A	1.401(5)	1.427	1.405(5)	N1B-C15B
N1A-C1A	1.405(5)	1.377	1.407(5)	N1B-C1B
N1A-C3A	1.496(5)	1.500	1.496(5)	N1B-C3B
C1A-C6A	1.344(5)	1.363	1.350(5)	C1B-C6B
C6A-C7A	1.456(5)	1.451	1.438(5)	C6B-C7B
C7A-C8A	1.489(5)	1.501	1.491(5)	C7B-C8B
C1A-C6A-C7A	125.5(4)	–125.74*	126.0(4)	C1B-C6B-C7B
O2A-C7A-C8A	119.9(3)	119.41	119.0(4)	O2B-C7B-C8B
O4A-C15A-N1A	119.4(3)	118.85	118.9(3)	O4B-C15B-N1B

* see text.

Figure 3. A crystal packing diagram for compound **4**.



3. Experimental Section

3.1. General

Compound **4** was prepared using the protocols described by Tohda and co-workers [22]. Crystals suitable for X-ray diffraction were obtained by recrystallisation of the said material from a sample dissolved in an equal volume mixture of warm toluene and hexanes which was allowed to cool and slowly evaporate at room temperature.

3.2. Data Collection and Refinement

The diffraction data of **4** were acquired and the data refined as described previously [29].

Crystal data (**4**). $C_{22}H_{23}NO_4$, 381.41 g mol^{-1}. Crystal size: 0.36 × 0.22 × 0.22 mm^3. Monoclinic, $P2_1/c$ (no. 14), a = 20.9410(11) Å, b = 8.7523(5) Å, c = 21.2291(9) Å, β = 93.529(3)°, V = 3883.5(3) Å^3, Z = 8. Mo-$K\alpha$: λ = 0.71073 Å; T = 150(1) K; θ range: 2.65° to 25.14°; Index ranges: $-24 \leq h \leq 24$, $-10 \leq k \leq 10$, $-25 \leq l \leq 25$; D_{calc} = 1.305 mg/m^3; 17679 reflections measured of which 6659 were symmetrically independent; R_{int} = 0.087; $F(000)$ = 1616; Abs. coeff.: 0.093 mm^{-1}; Abs. corr.: semi-empirical from equivalents; Parameters/Restraints: 514/0. Max./min.: 0.990/0.701; completeness to θ at 25.00° = 96.4%. R values: $R1$/w$R2$ for 6659 reflections with [$I > 2\sigma(I)$]: 0.0727/0.1872; for all data: 0.1167/0.2117; GOF on F^2: 1.083, largest difference peak and hole: 0.235/−0.286 eÅ^{-3}. CCDC number: 841810. Copies of the data can be obtained free of charge from the authors or on application to the Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge CB2 1EZ U.K. (fax: +44 1223 336033; E-mail: deposit@ccdc.cam.ac.uk; website: http://www.ccdc.cam.uk/conts/retrieving .html).

*3.3. Density Functional Treatment of **4***

The calculated parameters (Table 1) for a hypothetical gas phase molecule of **4** were derived using DFT at the B3LYP 6-311++G** level of theory using software (*Spartan 10.0*®) and parameters as previously described [29]. Zero point energy calculations were also carried out and no imaginary frequencies or vibrations were noted. Data files (.mol) are available from the authors on request.

4. Conclusions

The crystal and molecular structure of the title compound, *viz*., (*2Z*)-2-[3-(4-methoxybenzoyl)-4,4-dimethyl-1,2,-oxazolidin-2-ylidene]-1-(4-methoxyphenyl)ethanone (**4**), has been reported. These data represent the first crystallographically characterised example of this class of tertiary amides. The gas phase structure of **4** has also been estimated by DFT and the calculated parameters are in good agreement with those observed in the solid-state form.

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