

Two Crystal Forms of 4-{(2*E*)-2-[1-(4-Methoxyphenyl)ethylidene]hydrazinyl}-8-(trifluoromethyl)quinoline

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Abstract The Schiff base, 4-{(2*E*)-2-[1-(4-methoxyphenyl)ethylidene]hydrazinyl}-8-(trifluoromethyl)quinoline, crystallizes in two polymorphic forms depending on the solvent. One of these forms is monoclinic (**1M**), space group $P2_1/c$ with $a = 10.2906(10)$ Å, $b = 8.9211(7)$ Å, $c = 18.4838(15)$, $\beta = 97.271(8)^\circ$, and the other is orthorhombic (**1O**), space group $Pbca$, unit-cell parameters: $a = 13.6485(12)$ Å, $b = 9.0588(9)$ Å, $c = 27.400(2)$ Å. The molecules in either crystalline form have similar bond lengths and angles, but one is nearly planar while the other has a significant twist. In monoclinic form the dihedral angle between terminal ring planes is $17.26(8)^\circ$ while in the orthorhombic one it is $26.11(5)^\circ$, and in this latter case the central chain is almost coplanar with the quinoline ring system while in the former these two planes are significantly twisted. The crystal structures of both forms are determined

by the interplay of van der Waals forces and weak directional interactions C–H \cdots F, $\pi\cdots\pi$ stacking, and—in the case of **1M**—short intermolecular C–F \cdots N contact. The crystals of **1M** decomposes slowly into the powder while the other form is stable. The powder diffraction pattern of the product of decomposition of **1M** is similar to that calculated for **1O**. This suggests that the decomposition is a consequence of the phase transition of the less stable monoclinic into more stable orthorhombic form.

Keywords Schiff bases · Polymorphism · Powder diffraction · Conformation · Crystal packing

Introduction

The syntheses and structures of Schiff bases have attracted much attention in biology and chemistry due to their model character and practical applications [1, 2]. It was found that the properties of these compounds are directly related to the presence of the intramolecular hydrogen bond and the conjugative interactions in the molecules [3, 4]. Some Schiff bases were reported to possess various biological activities, for instance antimicrobial, anti-inflammatory, antifungal or antitumor [5–12].

Fluorinated organic compounds have attracted attention due to the ability of fluorine to act as polar hydrogen or hydroxyl mimic. Therefore, substitution of hydrogen by fluorine has been a strategy in designing molecules for biological activity studies [13].

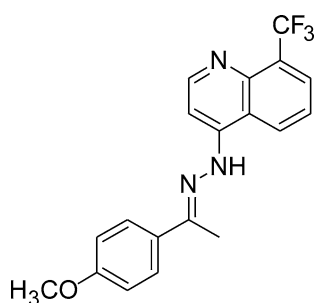
Recently we have published, crystal structures and theoretical studies of four Schiff bases derived from 4-hydrazinyl-8-(trifluoromethyl)quinoline have been reported [14] and the crystal structure of (E)-1-(4-methylphenyl)ethanone [8-(trifluoromethyl)quinolin-4-yl]hydrazone [15]. In the course of

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Scheme 1 4-((2E)-2-[1-(4-methoxyphenyl)ethylidene]hydrazinyl)-8-(trifluoromethyl)quinoline

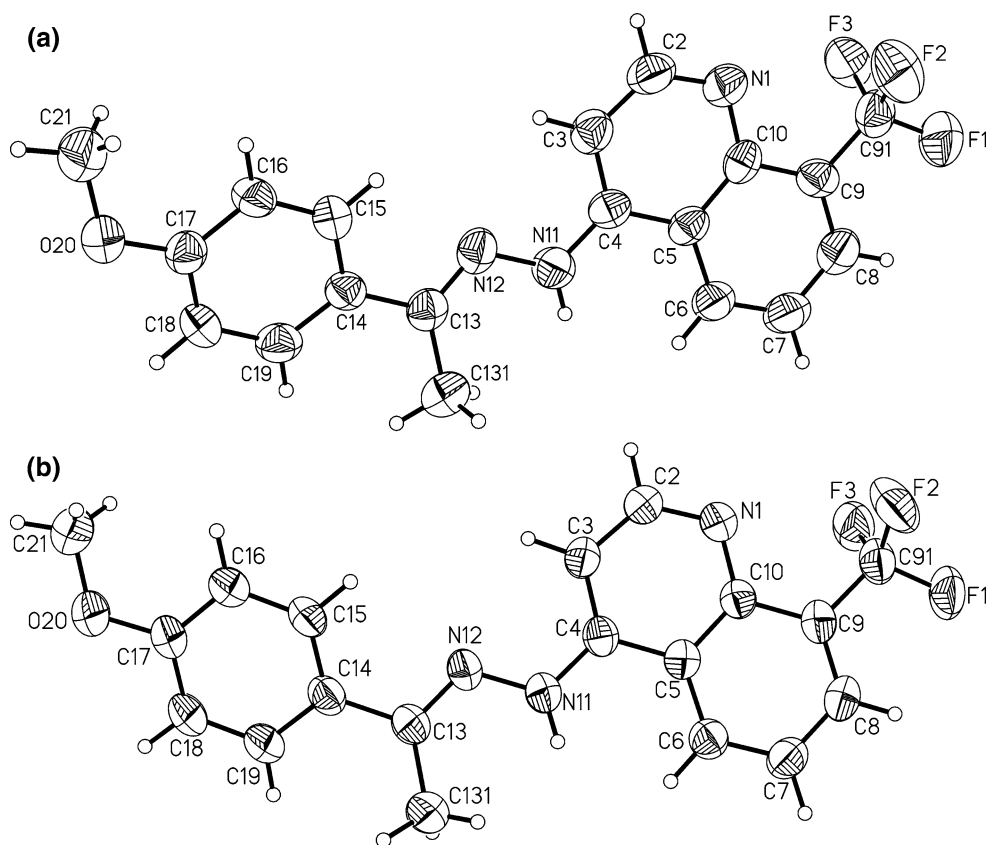
our studies on these derivatives we have prepared the new compound, 4-((2E)-2-[1-(4-methoxyphenyl)ethylidene]hydrazinyl)-8-(trifluoromethyl)quinoline (**1**, Scheme 1). It turned out that crystallization from different solvents gave two different crystal forms. The X-ray diffraction analysis showed that these forms are in fact two polymorphic forms of **1**: less stable monoclinic (**1M**), crystallized from THF, and more stable orthorhombic (**1O**) which was obtained from a methanol solution. It can be only hypothesized that the different properties of the solvents, for instance their ability or inability to donate/accept hydrogen bonds, might be important for the formation of polymorphic forms.

Molecular Structure

The molecules of **1** in both forms do not differ significantly (Fig. 1a, b), however the overall conformation which can be estimated by the dihedral angles between the planar fragments: the phenyl ring (A), central C–C=N–N–C chain (B) and the quinoline ring system (C) has some systematic differences. Figure 2 shows a comparison of two molecules fitted onto the plane of central extended chain. It can be seen that in the case of **1M** the two ring system planes are similarly twisted with respect to the central plane and these twists add to $17.26(8)^\circ$. In the molecule of **1O** the quinoline ring system is almost coplanar with the central chain plane, while the phenyl ring is significantly—by almost 25° —twisted (cf. Table 1).

The normal probability plots [16, 17]—which in principle show the deviation from the statistical distribution of differences between two sets of data—calculated for the bond lengths and bond angles show that the differences between the two molecules are mainly statistical but the deviations are significant. The R^2 correlation factor between the experimental and ideal values is almost perfect for bond angles, of 0.989, while for bond lengths it is much lower, equals to 0.862. It might be noted that the large part of this deviation comes from the methoxy group (which might be influenced by the

Fig. 1 Anisotropic ellipsoid representation of the molecules of **1** from monoclinic (a) and orthorhombic (b) forms, together with atom labeling scheme [23]. The ellipsoids are drawn at 50% probability level, hydrogen atoms are depicted as spheres with arbitrary radii



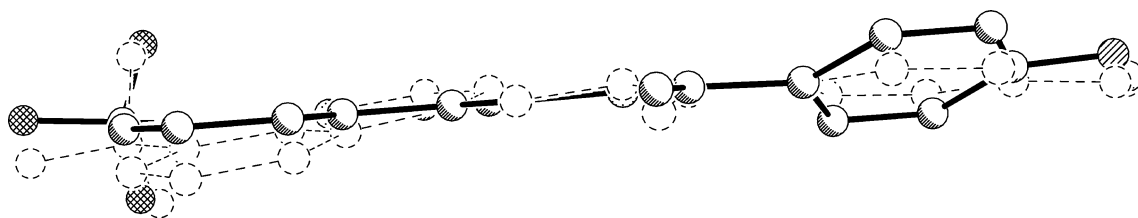


Fig. 2 Comparison of molecules **1** [23] fitted onto the central C=N–N–C–C plane (dashed lines—**1M**, solid lines—**10**)

thermal motion); when this group is excluded from the calculations, R^2 increases to 0.93.

Crystal Packing

There are also some important differences in the crystal packing. The molecule **1** is devoid of the good hydrogen bond acceptors and in both forms the good hydrogen bond donor—N–H group—is not involved in any hydrogen bonding interactions, nor in any short intermolecular contacts. The crystal packing is mostly caused by the interplay of van der Waals, stacking and weak hydrogen bonding interactions.

Table 1 Selected geometrical parameters (Å, °) with *su*'s in parentheses (the last section describes the deviations from mean planes and the dihedral angles between these planes)

	1M	10
N1–C2	1.325(2)	1.3157(19)
N1–C10	1.364(3)	1.3636(18)
C4–N11	1.374(3)	1.3697(17)
N11–N12	1.386(2)	1.3751(16)
N12–C13	1.282(2)	1.2882(17)
C2–N1–C10	114.6(2)	115.97(12)
C4–N11–N12	118.3(2)	119.04(12)
N11–N12–C13	117.3(2)	117.91(12)
C3–C4–N12–C13	–5.6(4)	0.1(2)
C4–N11–N12–C13	–171.6(2)	–179.78(13)
N11–N12–C13–C14	173.91(18)	177.23(12)
C13–C14–C15–C16	–176.7(2)	177.28(15)
N12–C13–C14–C15	–15.2(3)	–24.5(2)
C16–C17–O20–C21	9.8(3)	10.1(3)
A/B	9.3(2)	24.89(4)
B/C	8.5(2)	1.45(13)
A/C	17.28 (9)	26.11(5)
A	0.0019(16)	0.0127(12)
B	0.1027(17)	0.0226(10)
C	0.041(2)	0.0151(12)

A denotes the phenyl ring, B the central C=C=N–N–C chain, and C the quinolone ring system)

In **1M** there is stacking between the quinoline ring systems (interplanar distance of ca. 3.68 Å) which organizes the molecules into centrosymmetric dimers. There is also relatively short C–F⋯N12 ($-x, -y, 1-z$) contact: F⋯N 2.898(2) Å, C–F⋯N angle of 126.8(3)°. Such contacts are relatively rare: in the CSD ([18], ver. of Nov. 2010 last update May 2011; only organic) we have found only 28 examples of C–F⋯N(aromatic) contacts closer than sum of F and N van der Waals radii (3.02 Å), the shortest has been reported in the structure of 4,4'-(pyridine-2,6-diylbis(carbonylimino)) bis(1-methylpyridinium)bis(trifluoromethanesulfonate) one of 2.817 Å [19]. There are also some very weak C–H⋯F contacts; they are listed in Table 2.

In the crystal structure of **10** the molecules are also stacked, and also the quinoline rings are stacked with the mean interplanar distance between the molecules related by the inversion center at (1/2, 1/2, 0) of 3.47 Å. In this structure however there is no exotic C–F⋯N interactions but more common weak—but definitely one of the shortest known—C–H⋯F contacts (cf. Table 3).

Figures 3 and 4 show the crystal packing of both forms, showing similar packing motifs: zig-zag chains of molecules. In the crystal structure of **1M** (Fig. 3) the dihedral angle between the consecutive molecules in the chain are roughly 90° and the weak interaction join the neighbouring chains into pairs but there are no directional interactions

Table 2 Short contact data (Å, °) 110 K

D	H	A	D–H	H⋯A	D⋯A	D–H⋯A
1M						
C2	H2	F3 ⁱ	0.93	2.76	3.582(3)	148
C8	H8	F3 ⁱⁱ	0.93	2.77	3.574(3)	145
C15	H15	F3 ⁱⁱⁱ	0.93	2.67	3.242(3)	120
C16	H16	F3 ⁱⁱⁱ	0.93	2.60	3.204(3)	123
10						
C21	H21B	F2 ^{iv}	0.96	2.39	3.030(2)	124
C131	H13C	O20 ^v	0.96	2.55	3.4994(19)	170

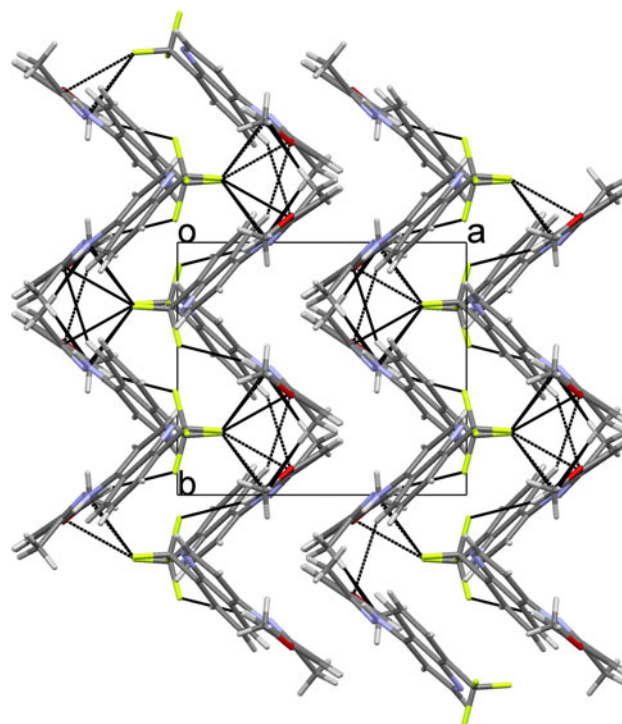
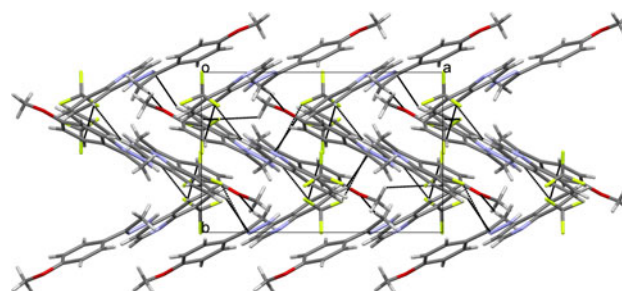
Symmetry codes: ⁱ $-x, 1-y, 1-z$; ⁱⁱ $-x, -1/2+y, 3/2-z$; ⁱⁱⁱ $x, 1/2-y, -1/2+z$; ^{iv} $-x, 1-y, -z$; ^v $-x, 1/2+y, 1/2-z$

Table 3 Crystal and experimental data

Compound	1M	2O
Formula	C ₁₉ H ₁₆ FN ₃ O	
Formula weight	359.35	
Crystal system	Monoclinic	Orthorhombic
Space group	<i>P</i> 2 ₁ / <i>c</i>	<i>Pbca</i>
<i>a</i> (Å)	10.2906(10)	13.6485(12)
<i>b</i> (Å)	8.9211(7)	9.0588(9)
<i>c</i> (Å)	18.4838(15)	27.400(2)
β (°)	97.271(8)	90
<i>V</i> (Å ³)	1683.2(3)	3387.7(5)
<i>Z</i>	4	8
<i>D_x</i> (g cm ⁻³)	1.42	1.41
<i>F</i> (000)	744	1,488
μ (mm ⁻¹)	0.11	0.95
Crystal size (mm)	0.3 × 0.1 × 0.1	0.4 × 0.2 × 0.2
Θ Range (°)	2.54–25.00	4.57–75.57
<i>hkl</i> range	−12 ≤ <i>h</i> ≤ 9 −10 ≤ <i>k</i> ≤ 10 −21 ≤ <i>l</i> ≤ 19	−14 ≤ <i>h</i> ≤ 17 −11 ≤ <i>k</i> ≤ 10 −33 ≤ <i>l</i> ≤ 32
Reflections		
Collected	9,451	8,385
Unique (<i>R</i> _{int})	2,966 (0.054)	3,438 (0.015)
With <i>I</i> > 2σ(<i>I</i>)	1,079	2,872
Number of parameters	238	277
Weighting scheme		
A	0.01	0.0678
B	0	0.4024
<i>R</i> (<i>F</i>) [<i>I</i> > 2σ(<i>I</i>)]	0.037	0.041
<i>wR</i> (<i>F</i> ²) [<i>I</i> > 2σ(<i>I</i>)]	0.047	0.116
<i>R</i> (<i>F</i>) [all data]	0.139	0.048
<i>wR</i> (<i>F</i> ²) [all data]	0.051	0.120
Goodness of fit	0.90	1.084
Max/min Δρ (e Å ⁻³)	0.14/−0.14	0.25/−0.19

between the pairs. In **1O** the similar dihedral angles are smaller, of ca. 61°, and the interactions seem to connect all the molecules into one three-dimensional structure. This might be connected with the smaller stability of the form **1M**.

We have observed that both forms are stable in the temperature range 90–295 K; however the structure **1M** slowly (during a month) changes into the powder. The diffraction pattern of this powder is almost identical with the simulated pattern of **1O** (Fig. 5a, b). On the other hand, **1O** does not change for a long time—till now it is more than 2 years—therefore this form can be regarded as more stable form of the title compound.

**Fig. 3** Crystal packing of **1M** as seen along *z*-direction; C–H...F and F...N contacts (see text) are shown as dashed lines [24]**Fig. 4** Crystal packing of **1O** as seen along *z*-direction; C–H...F and C–H...O contacts (see text) are shown as dashed lines [24]

Experimental

A solution of 4-hydrazino-8-(trifluoromethyl)quinoline (2.2 g, 10 mol) and 4-methoxy acetophenone (1.5 g, 10.2 mol) in 10 mL of ethanol was refluxed for 24 h under nitrogen atmosphere and in absence of light. The reaction mass was then cooled and the solid separated was collected by filtration (Scheme 2). **1M**: recrystallized from THF, M.P.: 447–449 K. **1O**: recrystallized from methanol, M.P.: 444–445 K.

X-ray diffraction data were collected at room temperature by the ω -scan technique, for **1M** on a KUMA KM4CCD four-circle diffractometer equipped with Sapphire CCD-detector [20] using graphite-monochromatized MoK α radiation

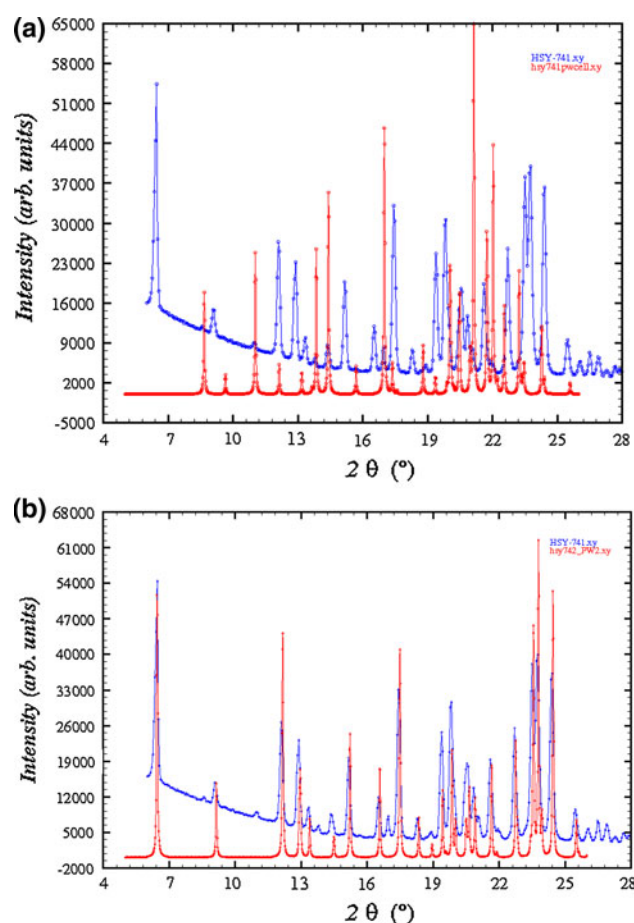
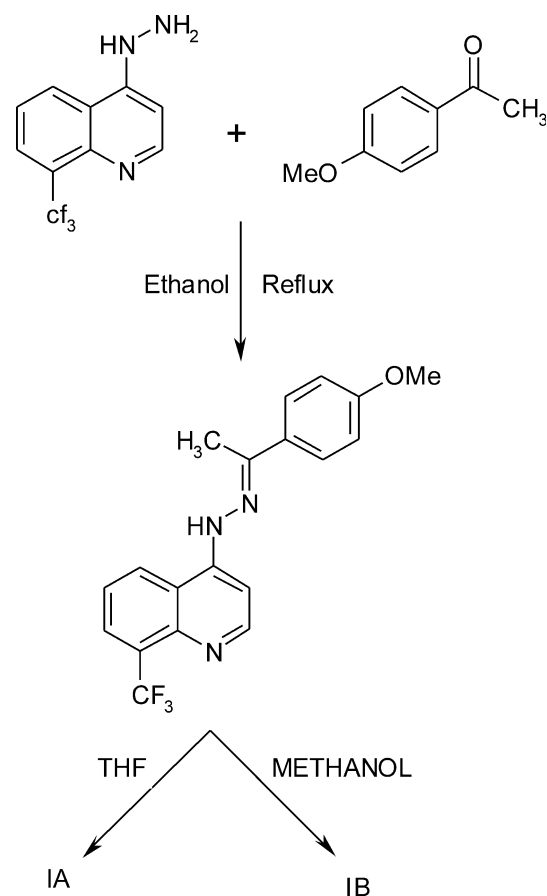


Fig. 5 The comparison of the experimental powder diffraction pattern of the powder resulting from the decomposition of single crystals of **1M** with the patterns calculated from the single crystal structures of **a 1M** and **b 1O**

($\lambda=0.71073\text{\AA}$), and for **1O** on a SuperNova four-circle diffractometer equipped with Atlas CCD-detector [20] using mirror-monochromatized $\text{CuK}\alpha$ radiation from high-flux micro-focus source ($\lambda = 1.54178\text{\AA}$). The data were corrected for Lorentz-polarization effects as well as for absorption [20]. Accurate unit-cell parameters were determined by a least-squares fit of 1727 (**1M**) and 4961 (**1O**) reflections of highest intensity, chosen from the whole experiment. The structures were solved with SIR92 [21] and refined with the full-matrix least-squares procedure on F^2 by SHELXL97 [22]. Scattering factors incorporated in SHELXL97 were used. The function $\sum w(|F_o|^2 - |F_c|^2)^2$ was minimized, with $w^{-1} = [\sigma^2(F_o)^2 + (A \cdot P)^2 + B \cdot P]$, where $P = [\text{Max}(F_o^2, 0) + 2F_c^2]/3$. The final values of A and B are listed in Table 1. All non-hydrogen atoms were refined anisotropically, all hydrogen atoms in **1M** and methyl hydrogens in **1O** were placed in calculated positions and were refined as ‘riding’ on their parent atoms; the U_{iso} ’s of hydrogen atoms were set as 1.2 (1.5 for methyl groups) times the U_{eq} value of the appropriate carrier atom; all other hydrogen



Scheme 2 Reaction pathway

atoms in **1O** were found in difference Fourier maps and isotropically refined. Relevant crystal data are listed in Table 3, together with refinement details.

Powder diffraction pattern for **1M** was measured with Bruker AXS D8 Advance diffractometer ($\text{CuK}\alpha$ radiation, $\lambda = 1.54178\text{\AA}$) equipped with Johansson monochromator and silicon strip detector LynxEye.

Crystallographic data (excluding structure factors) for the structural analysis has been deposited with the Cambridge Crystallographic Data Centre, Nos. CCDC 765241 (**1M**) and 765242 (**1O**). Copies of this information may be obtained free of charge from: The Director, CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK. Fax: +44(1223)336-033, e-mail: deposit@ccdc.cam.ac.uk, or www.ccdc.cam.ac.uk.

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