Acta Crystallographica Section C
Crystal Structure Communications
ISSN 0108-2701

2,2,2-Trifluoro-*N*-(1a,2,7,7a-tetrahydronaphtho[2,3-*b*]oxiren-3-yl)-acetamide by X-ray powder diffraction

Mwaffak Rukiah* and Thaer Assaad

Department of Chemistry, Atomic Energy Commission of Syria (AECS), PO Box 6091, Damascus, Syrian Arab Republic
Correspondence e-mail: cscientific@aec.org.sy

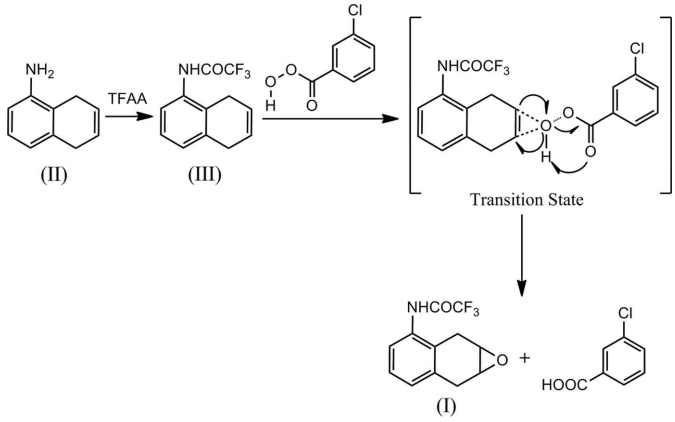
Received 21 June 2010
Accepted 3 August 2010
Online 18 August 2010

The title compound, $C_{12}H_{10}F_3NO_2$, an important precursor in the preparation of benzovesamicol analogues for the diagnosis of Alzheimer's disease, was prepared by the epoxidation of 5,8-dihydronaphthalen-1-amine using 3-chloroperoxybenzoic acid. The structure was determined by X-ray powder diffraction, multinuclear NMR spectroscopy and FT–IR spectroscopy. A pair of molecules form intermolecular N—H···O hydrogen bonds, involving the amino and oxirene groups, to produce a dimer.

Comment

2,2,2-Trifluoro-*N*-(1a,2,7,7a-tetrahydronaphtho[2,3-*b*]oxiren-3-yl)acetamide, (I), is an important precursor for the preparation of benzovesamicol analogues (Zea-Ponce *et al.*, 2005; Jung *et al.*, 1990; Mulholland & Jung, 1992; Mulholland *et al.*, 1993; Nicolas *et al.*, 2007), which are used in cholinergic nerve imaging for the diagnosis of Alzheimer's disease and in other research areas (Mazère *et al.*, 2008). This compound is a useful synthetic intermediate and has the advantage of high reactivity at the epoxide ring for introducing additional functionality as part of a more extensive molecular transformation.

The title compound, (I), was prepared as presented in the reaction scheme. The synthesis started with the protection of the amine function of 5,8-dihydronaphthalen-1-amine, (II), by trifluoroacetic anhydride (TFAA) to obtain the corresponding amide, (III), in 99% yield. The next step involved the epoxidation of the alkene, (III), by reaction with *m*-CPBA (3-chloroperbenzoic acid) to produce the corresponding epoxide, (I), in 78% yield. The major by-product of the alkene epoxidation reaction, however, is the carboxylic acid precursor of the epoxide. The reaction proceeds *via* a concerted mechanism, as proposed by Bartlett (1950), in which the alkene and the electrophilic peroxy O atom coordinate with a concomitant expulsion of the carboxylic acid and release of the epoxide (Smith, 2002). The transition state of this reaction has been characterized and is usually represented as shown in the scheme.



We employed laboratory powder X-ray diffraction data to solve and refine the crystal structure of (I). This compound crystallizes as a fine white powder and it was not possible to isolate a sample of sufficient size and quality for a single-crystal analysis. This is an 18-atom (non-H) problem, which requires careful measurement and interpretation of the in-house data in order to optimize the quality of the results. Over the past 10 years, the crystal structures of a number of compounds of pharmaceutical interest have been determined by X-ray powder data, essentially as a last resort in the absence of single crystals of sufficient quality (Chan *et al.*, 1999; Shankland *et al.*, 2004; Chernyshev *et al.*, 2003; Kiang *et al.*, 2003; Rukiah *et al.*, 2004; van der Lee *et al.*, 2005).

The details of the solution and refinement of (I) merit a brief comment. We shall refer to the three stages of crystal structure determination from diffraction data: (i) unit-cell determination and space-group assignment, (ii) structure solution and (iii) structure refinement. Structure solution, which aims to obtain an initial approximation to the structure, using the unit cell and space group determined in the first stage, tends to be more arduous with powder data. The final step, refinement, is commonly carried out using the Rietveld method. Structure solution for (I) was initially attempted using the traditional approach (direct methods) with the

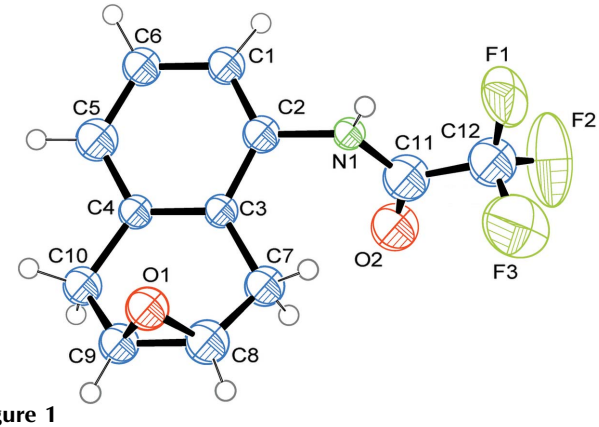


Figure 1
The molecular structure of (I), showing the atomic numbering scheme. Displacement ellipsoids are drawn at the 50% probability level; only the F atoms were refined anisotropically.

 doi:10.1107/S0108270110031124

program *EXPO2004* (Altomare *et al.*, 2004); all of our attempts failed. We then used Monte Carlo simulated annealing (parallel tempering algorithm) to solve the structure in direct space using the program *FOX* (Favre-Nicolin & Černý, 2002). *FOX* solves structures by altering the positions, orientations and conformations of the molecule(s) in the unit cell, maintaining the space-group symmetry, until a good match is obtained between the calculated and observed intensities. One molecule of (I) was introduced randomly with the possibility to translate, to rotate around its centre of mass and to modify its three torsion angles. The degree of freedom for the molecular replacement is nine. H atoms were ignored during the structure solution. The model found by this program was introduced into the program *GSAS* (Larson & Von Dreele, 2004), interfaced by *EXPGUI* (Toby, 2001) for Rietveld refinements. All non-H bond distances were restrained to their expected values. Before the final refinement, H atoms of CH and CH_2 groups were introduced geometrically and the H atom of the amide was located in a Fourier difference synthesis. The H atoms were refined as riding atoms. The final refinement cycles were performed using isotropic displacement parameters for C, N and O atoms and anisotropic displacement parameters for F. No restraints were used for these displacement parameters. It was necessary to use anisotropic displacement parameters for F to obtain good agreement between the calculated and observed profile at the final stage of the refinement. Of course, the data were of sufficient quality to permit free refinement of these parameters. Intensities were corrected for absorption effects with a function for a flat plate sample in transmission geometry (function number 5 in *GSAS*) with a μd value of 0.2517, determined experimentally. The preferred orientation was modelled using a spherical harmonic description as per Von Dreele (1997) with 20 coefficients. The use of the preferred orientation correction leads to better molecular geometry with better agreement factors.

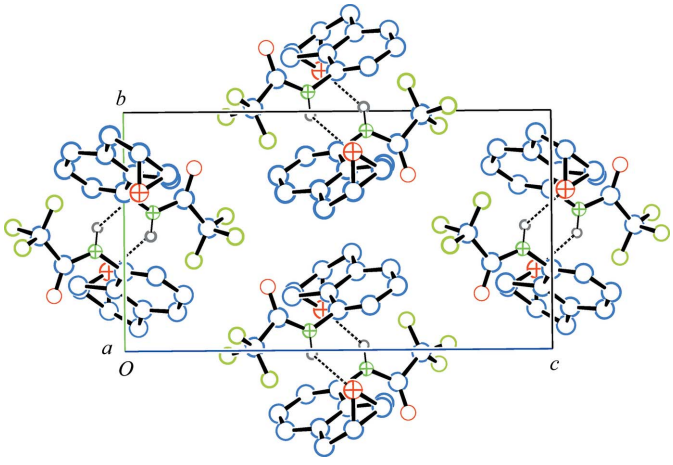


Figure 2
A view of (I) along the *a* axis, showing N—H···O hydrogen bonding (dashed lines), which results in the formation of dimers between inversion-related molecules. H atoms not involved in the motifs have been omitted for clarity.

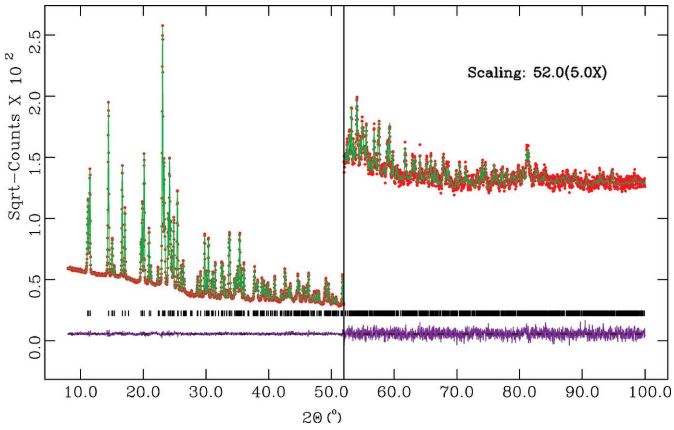


Figure 3
Final observed (points), calculated (line) and difference profiles for the Rietveld refinement of (I).

Compound (I) crystallizes with one molecule in the asymmetric unit in the space group $P2_1/c$ (Fig. 1). All bond lengths and angles in (I) are in their normal ranges (Allen *et al.*, 1987). The epoxide group, which is the most interesting function in (I), has normal geometry (Table 1). The benzene ring plus C7 and C10 are coplanar [maximum deviation is 0.035 (11) Å for C5, when the latter is not used in the calculation of the plane]. The non-F atoms of the acetamide function lie in a plane tilted 62.6 (6)° from the benzene plane. Intermolecular N—H···O hydrogen bonds (Table 2) link two independent molecules in a self-recognition pattern to form a dimer (Fig. 2).

The results of the structure analysis by powder diffraction can be correlated with the spectroscopic data obtained for this compound. The IR spectrum of (I) gave the expected band at 3440 cm^{-1} which corresponds with the NH group. The characteristic absorption bands of the $COCF_3$ group appeared at 1715 and 1170 cm^{-1} for the CO and CF_3 groups, respectively. The epoxide bands appeared at 3000 (stretch) and 800 cm^{-1} (bending), which fall within their normal ranges. The ^{1}H NMR spectrum of (I) gave multiplets at 2.95 and 3.40 p.p.m., which are attributed to the two CH_2 and two CH groups. The three aromatic H atoms (attached to C1, C6 and C5; Fig. 1) appeared as a multiplet at 7.17 p.p.m. A singlet at 8.18 p.p.m. corresponds to the amide group. The ^{13}C NMR of (I) showed 12 singlets corresponding to 12 different C-atom environments in the molecule at their expected chemical shifts.

Experimental

All chemical reagents and solvents were of commercial quality and were used as received. IR spectra were recorded on a Jasco FT–IR 300E spectrometer. NMR spectra were recorded on a Bruker Biospin 400 spectrometer (400 MHz for ^{1}H and 100 MHz for ^{13}C). Chemical shifts (d) were expressed in p.p.m. relative to TMS (tetramethylsilane) as an internal standard. The melting point was determined in a Stuart SMP3 melting point apparatus. Microanalysis was performed using a EURO EA analyzer.

5,8-Dihydronaphthalen-1-amine, (II) (25 g, 177 mmol), was dissolved in benzene (84 ml) and the solution cooled to 273 K. Trifluoroacetic anhydride (TFAA; 24.7 ml) was added slowly due to the exothermicity of the reaction. The ammonium salt began to

precipitate immediately, but the reaction solution was homogenous upon complete addition of the anhydride. The solution was kept at 273 K for 1 h, after which benzene and trifluoroacetic acid were removed under reduced pressure. More benzene was added, then evaporated in order to aid the removal of trifluoroacetic acid. A beige powder of (III) was obtained without purification in 99% yield (41.5 g). The amide, (III), was dissolved in Et_2O (150 ml), then 3-chloroperoxybenzoic acid (70.66 g, 0.204 mmol, 50–55% pure) was added. The solution was maintained at 283 K throughout the addition and then left stirring at room temperature for 5 h. The epoxide, (I), was collected by filtration and washed with Et_2O (yield: 34.7 g, 78%; m.p. 453 K). Analysis found for $C_{12}H_{10}F_3NO_2$: C 56.36, H 4.14, N 4.88%; calculated: C 56.04, H 3.92, N 5.45%.

Crystal data

$C_{12}H_{10}F_3NO_2$
M_r = 257.21
Monoclinic, $P2_1/c$
a = 8.0594 (5) Å
b = 8.8122 (5) Å
c = 15.9964 (9) Å
β = 99.4514 (7)°
V = 1120.66 (11) Å^3
Z = 4
Cu $K\alpha_1$ radiation, λ = 1.54060 Å
μ = 1.20 mm^{-1}
T = 298 K
flat sheet, 7 × 7 mm

Data collection

Stoe transmission Stadi-P diffractometer
Specimen mounting: powder extended between two Mylar foils
Data collection mode: transmission
Scan method: step
Absorption correction: for a cylinder mounted on the φ axis; as implemented and documented in *GSAS* (Larson & Von Dreele, 2004)
T_{min} = 0.522, T_{max} = 0.545
$2\theta_{min}$ = 7.96°, $2\theta_{max}$ = 99.94°, $2\theta_{step}$ = 0.02°

Refinement

R_p = 0.022
R_{wp} = 0.030
R_{exp} = 0.024
$R(F^2)$ = 0.04069
χ^2 = 1.613
4600 data points
246 parameters
54 restraints
H-atom parameters constrained

Table 1
Selected geometric parameters (Å, °).

O1—C8	1.455 (5)	C8—C9	1.463 (5)
O1—C9	1.451 (5)		
C8—O1—C9	60.4 (3)	O1—C9—C8	59.9 (3)
O1—C8—C9	59.7 (3)		
C3—C7—C8—O1	−43.7 (7)	O1—C9—C10—C4	48.5 (7)

The X-ray powder diffraction pattern was obtained with a Stoe Stadi-P diffractometer using monochromatic Cu $K\alpha_1$ radiation (λ = 1.5406 Å) selected with an incident beam curved-crystal germanium Ge(111) monochromator, using Stoe transmission geometry (horizontal set-up) with a linear position-sensitive detector (PSD). The powder was ground and loaded between two Mylar foils and fixed in the sample holder with a mask of suitable internal diameter (7.0 mm). Data were collected at room temperature and pressure over the angular range 8–100° (2θ) with a step length of the PSD of 0.5° (2θ) and a counting time of 240 s per step.

The first 20 lines of the powder pattern were indexed with the program *DICVOL04* (Boultif & Louër, 2004), using an absolute error of 0.02° (2θ) on the peak positions, on the basis of a monoclinic solution with the unit-cell dimensions a = 15.994 (3) Å, b = 8.8084 (17) Å, c = 8.0584 (14) Å, β = 99.45 (18)° and V = 1119.87 Å^3, with good figures of merit [M_{20} = 44.5, F_{20} = 115.5 (0.0047, 37)]. The space group was identified as $P2_1/a$ using the program *Check Group* interfaced by *WinPLOTR* (Roisnel & Rodriguez-Carvajal, 2001). Parameters a and c were interchanged to give the standard space-group setting, $P2_1/c$. The number of molecules per unit cell was estimated to be Z = 4, giving Z' = 1. The program *FOX* was employed for structure solution. In order to accelerate the process during the parallel tempering calculation, the powder pattern was truncated to 45° in 2θ (Cu $K\alpha_1$), corresponding to a real-space resolution of 2.0 Å. The model found by this program was introduced in the program *GSAS* (Larson & Von Dreele, 2004), interfaced by *EXPGUI* (Toby, 2001) for Rietveld refinements.

The background was refined using a shifted Chebyshev polynomial with 20 coefficients. The Thompson–Cox–Hastings (Thompson *et al.*, 1987) pseudo-Voigt profile function was used with an axial divergence asymmetry correction (Finger *et al.*, 1994). The two asymmetry parameters of this function S/L and D/L were both fixed at 0.0215 during the Rietveld refinement. Other details of the structure refinement appear in the *Comment* section. The observed and calculated powder patterns are shown in Fig. 3.

Data collection: *WinXPOW* (Stoe & Cie, 1999); cell refinement: *GSAS* (Larson & Von Dreele, 2004); data reduction: *WinXPOW*; program(s) used to solve structure: *FOX* (Favre-Nicolin & Černý, 2002); program(s) used to refine structure: *GSAS*; molecular graphics: *ORTEP-3* (Farrugia, 1997); software used to prepare material for publication: *publCIF* (Westrip, 2010).

Table 2
Hydrogen-bond geometry (Å, °).

D—H···A	D—H	H···A	D···A	D—H···A
N1—H1N1···O1^{i}	0.87	2.32	2.949 (9)	130

Symmetry code: (i) $-x+1, -y+2, -z+1$.

The authors thank Professor I. Othman, Director General, and Professor T. Yassine, Head of Chemistry, for their support and encouragement.

Supplementary data for this paper are available from the IUCr electronic archives (Reference: FA3231). Services for accessing these data are described at the back of the journal.

References

Allen, F. H., Kennard, O., Watson, D. G., Brammer, L., Orpen, A. G. & Taylor, R. (1987). *J. Chem. Soc. Perkin Trans. 2*, pp. S1–18.
Altomare, A., Caliandro, R., Camalli, M., Cuocci, C., Giacovazzo, C., Moliterni, A. G. G. & Rizzi, R. (2004). *J. Appl. Cryst.* **37**, 1025–1028.
Bartlett, P. D. (1950). *Rec. Chem. Prog.* **11**, 47.
Boultif, A. & Louër, D. (2004). *J. Appl. Cryst.* **37**, 724–731.
Chan, F. C., Anwar, J., Cernik, R., Barnes, P. & Wilson, R. M. (1999). *J. Appl. Cryst.* **32**, 436–441.
Chernyshev, V. V., Machon, D., Fitch, A. N., Zaitsev, S. A., Yatsenko, A. V., Shmakov, A. N. & Weber, H.-P. (2003). *Acta Cryst.* B**59**, 787–793.
Farrugia, L. J. (1997). *J. Appl. Cryst.* **30**, 565.
Favre-Nicolin, V. & Černý, R. (2002). *J. Appl. Cryst.* **35**, 734–743.
Finger, L. W., Cox, D. E. & Jephcoat, A. P. (1994). *J. Appl. Cryst.* **27**, 892–900.
Jung, Y. W., Van Dort, M. E., Gildersleeve, D. L. & Wieland, D. M. (1990). *J. Med. Chem.* **33**, 2065–2073.
Kiang, Y. H., Huq, A., Stephens, P. W. & Xu, W. (2003). *J. Pharm. Sci.* **92**, 1844–1853.

Larson, A. C. & Von Dreele, R. B. (2004). *GSAS*. Report LAUR 86-748. Los Alamos National Laboratory, New Mexico, USA.
Lee, A. van der, Richez, P. & Tapiero, C. (2005). *J. Mol. Struct.* **743**, 223–228.
Mazère, J., Prunier, C., Barret, O., Guyot, M., Hommet, C., Guilloteau, D., Dartigues, J. F., Auriacombe, S., Fabrigoule, C. & Allard, M. (2008). *NeuroImage*, **40**, 280–288.
Mulholland, G. K. & Jung, Y. W. (1992). *J. Labelled Comp. Radiopharm.* **31**, 253–259.
Mulholland, G. K., Jung, Y. W., Wieland, D. M., Kilbourn, M. R. & Kuhl, D. E. (1993). *J. Labelled Comp. Radiopharm.* **33**, 583–591.
Nicolas, G., Patrick, E., Roger, R. F., David, J. H., Sylvie, C., Lucette, G., Peter, R., Stefan, E., Sylvie, M., Sylvie, B., Michael, J. F., Denis, G. & Michael, K. (2007). *Synapse*, **61**, 962–970.
Roisnel, T. & Rodriguez-Carvajal, J. (2001). *Mater. Sci. Forum*, **378–381**, 118–123.
Rukiah, M., Lefebvre, J., Hernandez, O., van Beek, W. & Serpelloni, M. (2004). *J. Appl. Cryst.* **37**, 766–772.
Shankland, N., David, W. I. F., Shankland, K., Kennedy, A. R., Frampton, C. S. & Florence, A. J. (2004). *Chem. Commun.* **21**, 2204–2205.
Smith, M. A. (2002). *Organic Synthesis*, 2nd ed., pp. 234–246. New York: McGraw–Hill.
Stephens, P. W. (1999). *J. Appl. Cryst.* **32**, 281–289.
Stoe & Cie (1999). *WinXPow*. Stoe & Cie, Darmstadt, Germany.
Thompson, P., Cox, D. E. & Hastings, J. B. (1987). *J. Appl. Cryst.* **20**, 79–83.
Toby, B. H. (2001). *J. Appl. Cryst.* **34**, 210–213.
Von Dreele, R. B. (1997). *J. Appl. Cryst.* **30**, 517–525.
Westrip, S. P. (2010). *J. Appl. Cryst.* **43**, 920–925.
Zea-Ponce, Y., Mavel, S., Assaad, T., Kruse, S. E., Parsons, S. M., Emond, P., Chalon, S., Kruse, S., Giboureau, N., Kassiou, M. & Guilloteau, D. (2005). *Bioorg. Med. Chem.* **13**, 745–753.