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Synthesis and single crystal structure of N-Dansyl-o-n-pentoxy aniline

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Here we present a three step synthesis of 5-(dimethylamino)-N-(2-(pentyloxy)phenyl)naphthalene-1-sulfonamide. The first step, is producing of o-n-pentoxynitrobenzene using a classical alkylation of o-nitrophenols. The second step provides o-n-pentoxyaniline using a catalytic transfer hydrogenation. In the last step the title compound is obtained by reacting dansyl(5-(dimethylamino)naphthalene-1-sulfonyl) chloride and o-n-pentoxyaniline in a two phase system. Single crystals of N-dansyl-o-n-pentoxy aniline were obtained from isopropyl/water solution (1:1 *v/v*). The crystal structure was solved in the monoclinic $P2_1/c$ space group with unit cell parameters a = 11.926(2), b = 17.328(5), c = 10.9760(14), β = 99.4457(18)°, and Z = 4. The molecular structure is stabilized by an intramolecular C–H…O interaction, while the crystal structure is stabilized by N–H…O hydrogen bonds.

Keywords: Dansyl chloride, (pentyloxy)aniline, single crystal, DTA-TGA

INTRODUCTION

Dansyl chloride, chemically known as 5-(dimethylamino)naphthalene-1-sulfonyl chloride, is a versatile and widely used fluorescent probe in chemistry and biochemistry[1–3]. Its popularity stems from its high fluorescence intensity and the ability to react with primary and secondary amines, forming stable dansyl derivatives[4, 5]. These derivatives are fluorescent and can be easily detected and quantified by fluorescence spectroscopy, making dansyl chloride an essential tool in qualitative and quantitative analysis of amines in complex mixtures[6, 7]. The high fluorescence efficiency of dansyl derivatives allows for the detection of very low concentrations of target molecules[8, 9]. A high sensitivity and specificity can be obtained if dansyl chloride derivatives are obtained and specifically labeled for a range of biomolecules [8]. The compound (pentyloxy)aniline, is a notable organic molecule that integrates both an aniline (phenylamine) and a pentyloxy group[10, 11]. This combination of aromatic and aliphatic moieties provides to (pentyloxy)aniline quite distinct chemical properties and potential applications, particularly in the fields of organic chemistry and materials science[12]. The specific electronic properties of aniline combined with the flexibility and solubility conveyed by the pentyloxy group could be advantageous in designing materials for pharmaceutical applications. Combining the insights from Dansyl chloride and (pentyloxy)aniline into a comprehensive compound e.g. 5-(dimethylamino)-N-(2-(pentyloxy) phenyl)naphthalene-1-sulfonamide establishes an intriguing synergy of properties and discloses a large field for potential applications stemming from properties of both parent compounds. Having in mind the bioactive nature of aniline derivatives in pharmaceutical contexts, the title compound could serve as a novel probe or therapeutic scaffold. The (pentyloxy)aniline portion might increase the solubility and thus biological distribution, membrane permeability, etc. The Dansyl group hints at applications as a fluorescent marker in biological systems or in the field of organic electronics e.g. as organic semiconductors, photodetectors, or light-emitting diodes (LEDs).

Herein we report the synthesis of 5-(dimethylamino)-N-(2-(pentyloxy)phenyl)naphthalene-1-sulfonamide using well established protocols (Scheme 1) and its crystal structure.

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MATERIALS AND METHODS

Synthesis of N-dansyl-o-n-pentoxy aniline

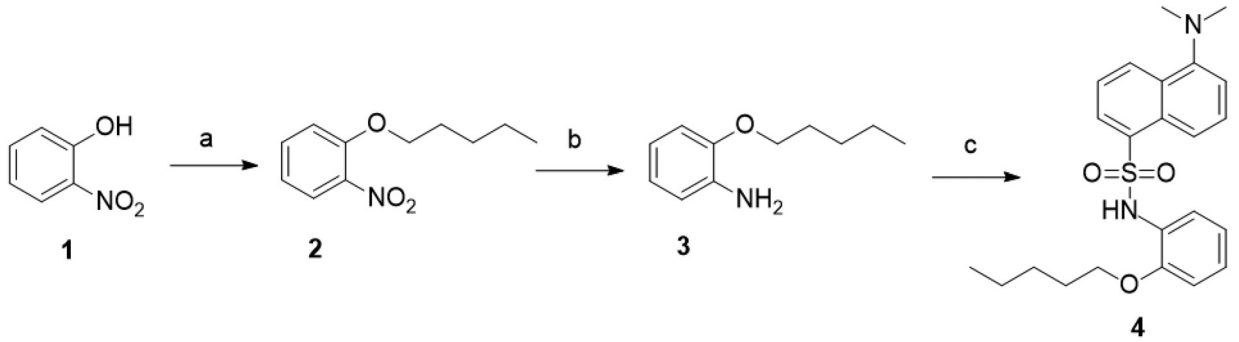
All reagents were purchased from Alfa Aesar or Sigma Aldrich and were used without further purification. The title compound N-dansyl-o-n-pentoxy aniline was prepared by a three step synthetic protocol (Scheme 1). First, o-n-pentoxynitrobenzene (**2**, Scheme 1) was obtained according to a standard procedure [13] by refluxing o-nitrophenol (0.1 mol), n-bromopentane (0.11 mol) and anhydrous K_2CO_3 (0.1 mol) as a base in dry acetone for 48 h. The isolation and purification procedures involved distillation of the acetone, extraction of the residue with water/benzene mixture, washing with 10% NaOH, distillation of the benzene at ambient pressure and finally vacuum distillation of the residual oil. The o-n-pentoxynitrobenzene (b.p. 160-165 at 5 mm Hg) was obtained in 85% yield. In the second step, o-n-pentoxynitrobenzene was then reduced by catalytic transfer hydrogenation [14] with hydrazine hydrate ($NH_2NH_2 \times H_2O$) and nickel boride (Ni_2B) as a catalyst to obtain o-n-pentoxyaniline (**3**, b.p. 148–156 °C at 5 mm Hg, yield 95%). Finally, o-n-pentoxyaniline (**3**) was reacted with dansyl (5-(dimethylamino)naphthalene-1-sulfonyl) chloride in a two phase system, dichloromethane and 10% sodium hydroxide water solution. After washing the reaction mixture with 3% hydrochloric acid and water, the product, N-dansyl-o-n-pentoxy aniline, was crystallized from isopropyl alcohol/water to obtain green crystals, m.p. 68–70, yield 90%.

Single crystal X-ray diffraction

Suitable single crystals of the title compound were mounted on glass capillaries. The intensity and diffraction data were collected on Agilent SupernovaDual diffractometer equipped with an Atlas CCD detector using micro-focus Cu*K*α radiation (λ = 1.54184 Å, respectively). The structures were solved by direct methods and refined by the full-matrix least-squares method on F^2 with ShelxS and ShelxL programs[15,16]. All non-hydrogen atoms, were located successfully from Fourier map and were refined anisotropically. Hydrogen atoms were placed at calculated positions using a riding scheme (*Ueq* = 1.2 for $C\text{-}H_{aromatic}$ = 0.93 Å and $C\text{-}H_{methylene}$ = 0.97 Å) while the N hydrogen was located from Fourier map. The ORTEP [17] views of the molecule present in the asymmetric unit and the most important crystallographic parameters from the data collection and refinement are shown in Fig. 1 and Table 1 respectively. Selected bonds lengths, angles and torsion angles are given in Table 2. The figures concerning crystal structure description and comparison were prepared using Mercury software (version 4.0) [18]. Complete crystallographic data for the reported structure were deposited in the CIF format with the Cambridge Crystallographic Data Centre as 2344357. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html, or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; Fax: +441223336033; E-mail: depos-it@ccdc.cam.ac.uk.

RESULTS AND DISCUSSION

The original intention for creating a novel organic compound by leveraging the structural and functional traits of Dansyl chloride and (pentyloxy) aniline was successfully achieved by integrating a three-step synthetic protocol, described above. Emulating the methodology for integrating organic molecules with specific functionalities the goal was



Scheme 1. General synthetic procedure for the preparation of N-dansyl-o-n-pentoxy aniline – (a) bromopentane, anxydrous K_2CO_3, dry acetone, reflux, 48h, (b) NH_2NH_2 x H_2O, cat. Ni_2B and (c) dansyl chloride, 10% aq. NaOH/DCM.

Table 1. Most important crystallographic parameters for structures **4**

Compound	4
Empirical formula	$C_{23}H_{28}N_2O_3S$
Formula weight	412.53
Temperature/K	290
Crystal system	Monoclinic
Space group	$P2_1/c$
a/Å	11.926(2)
b/Å	17.328(5)
c/Å	10.9760(14)
α/°	90.0
β/°	99.457(18)
γ/°	90.0
Volume/Å^3	2237.4(7)
Z	4
ρ_{calc} (g/cm^3)	1.225
μ/mm^{-1}	1.486
F(000)	880.0
Crystal size/mm^3	0.32 × 0.25 × 0.2
Radiation, λ [Å]	Cu Kα (λ = 1.54184)
2Θ range for data collection/°	7.516 to 154.966
Index ranges	$-14 \le h \le 14$, $-21 \le k \le 17$, $-8 \le l \le 13$
Reflections collected/ independent	8322/4322
R_{int}/ R_{sigma}	R_{int} = 0.0359, R_{sigma} = 0.0334
Data/restraints/parameters	4322/1/270
Goodness-of-fit on F^2	1.136
Final R indexes [I>=2σ (I)]	$R1$ = 0.0884, $wR2$ = 0.2694
Final R indexes [all data]	$R1$ = 0.1141, $wR2$ = 0.3088
Largest diff. peak/hole / e Å^{-3}	0.82/-0.34
CCDC number	2344357

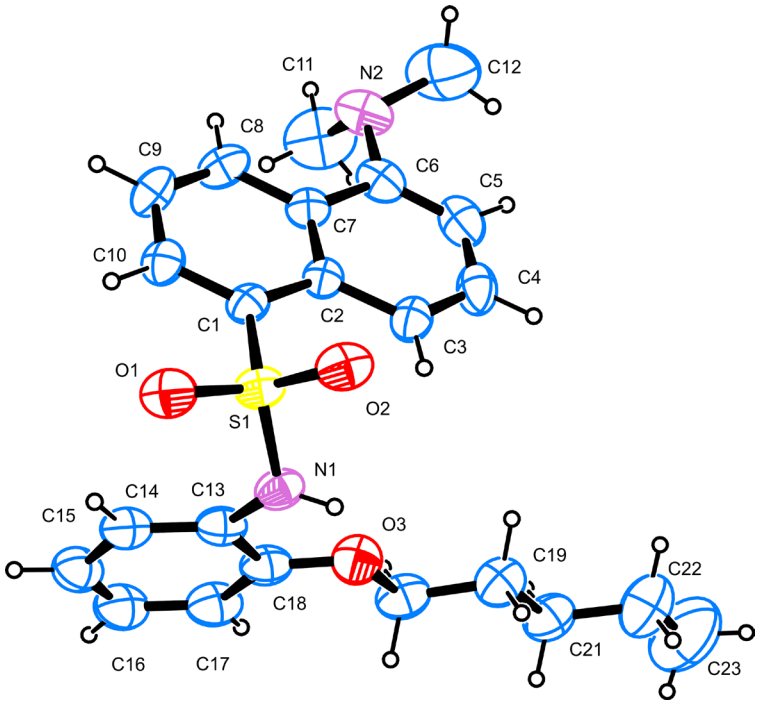


Fig. 1. *ORTEP* view of molecule present in the asymmetric unit of **4** along with employed numbering scheme; displacement ellipsoids are at 50% probability and hydrogen atoms are shown as spheres with arbitrary radii.

Table 2. Selected bond lengths s and angles for **4**

Bond lengths						Bond angles							
Atom	Atom	distance	Atom	Atom	distance	Atom	Atom	Atom	Angle	Atom	Atom	Atom	Angle
S1	O2	1.422(3)	C9	C10	1.413(6)	O2	S1	O1	118.8(2)	C6	N2	C12	113.8(6)
S1	O1	1.426(3)	C9	C8	1.337(6)	O2	S1	N1	105.87(19)	C11	N2	C6	116.1(5)
S1	N1	1.628(3)	N2	C6	1.418(6)	O2	S1	C1	109.35(19)	C11	N2	C12	103.0(7)
S1	C1	1.774(4)	N2	C11	1.405(9)	O1	S1	N1	108.0(2)	C6	C5	C4	121.1(4)
O3	C18	1.347(6)	N2	C12	1.474(9)	O1	S1	C1	107.08(19)	N2	C6	C7	118.2(4)
O3	C19	1.441(5)	C5	C6	1.368(8)	N1	S1	C1	107.26(17)	C5	C6	C7	118.5(4)
N1	C13	1.421(5)	C5	C4	1.376(7)	C18	O3	C19	118.6(4)	C5	C6	N2	123.3(4)
C3	C2	1.423(6)	C17	C16	1.400(8)	C13	N1	S1	123.8(3)	C3	C4	C5	122.5(4)
C3	C4	1.356(6)	C14	C13	1.372(7)	C4	C3	C2	120.0(5)	C1	C10	C9	119.3(4)
C18	C17	1.394(7)	C14	C15	1.391(7)	O3	C18	C17	125.6(5)	C18	C17	C16	119.2(5)
C18	C13	1.406(6)	C20	C19	1.489(8)	O3	C18	C13	115.9(4)	C13	C14	C15	119.8(5)
C2	C7	1.417(5)	C20	C21	1.549(7)	C17	C18	C13	118.6(5)	C19	C20	C21	110.2(4)
C2	C1	1.429(5)	C21	C22	1.503(10)	C3	C2	C1	123.6(4)	C18	C13	N1	116.3(4)
C7	C6	1.459(5)	C16	C15	1.334(8)	C7	C2	C3	118.5(3)	C14	C13	N1	123.0(4)
C7	C8	1.402(6)	C22	C23	1.542(14)	C7	C2	C1	117.9(3)	C14	C13	C18	120.5(4)
C1	C10	1.364(6)				C2	C7	C6	119.4(4)	O3	C19	C20	107.8(4)

Table 3. Hydrogen Bonding and weak interaction for **4**

D	H	A	d(D-H)/Å	d(H-A)/Å	d(D-A)/Å	D-H-A/°
C14	H14	O1	0.93	2.45	3.072(6)	124.5
N1	H1	O2[1]	0.824(18)	2.42(2)	3.190(5)	157(3)
N1	H1	O3	0.824(18)	2.22(3)	2.625(5)	110(3)

symmetry operation: [1] *2-x,1-y,1-z*

to create an organic molecule with distinct photophysical properties and potential applications in areas such as bioimaging, material science, pharmaceuticals and possibly optoelectronics.

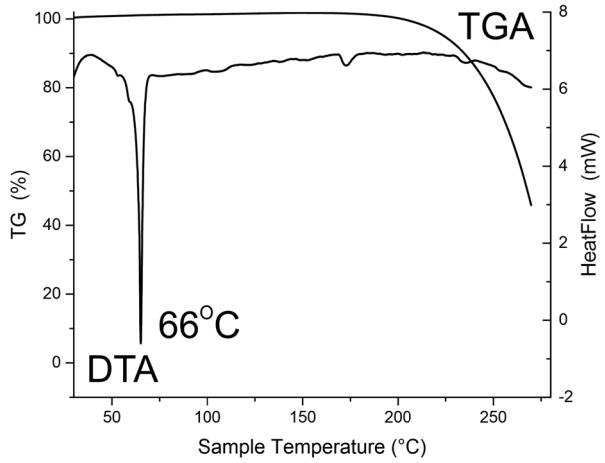


Fig. 2. DTA-TGA thermogram of compound **4**.

The thermal stability of the reported compound was studied with differential thermal analysis (DTA) and thermo-gravimetric analysis (TGA). The DTA thermogram (Fig. 2) reveals a sharp *endothermic* effect spanning from ~48 °C to 72 °C. This effect is attributed to the melting of the compound e.g. the destruction off the crystal structure. Having in mind the presence of a pentoxy moiety in the molecule, the relatively low melting temperature for such a compound is expected. There are two very shallow effect at ~160 and 230 °C probably related the decomposition of the compound. The TGA curve shows that compound **4** conserved its molecular structure up to ~160 °C. With the increase of the temperature above 160 °C significant weight losses are registered thus e.g. thermal decomposition of compound **4** is observed.

The crystal structure of compound **4** discloses that the bond lengths and angles are comparable to similar compounds bearing a chain on the aniline moiety [19–22] or possessing a Dansyl moiety [23–26] (Table 2). The molecular geometry is stabi-

lized by a weak C–H…O intramolecular interaction (Table 3). It is quite probable that one of the shallows endothermic effects visible on the DTA thermogram is related to the disruption of the intramolecular interaction, followed by the decomposition of compound **4**. Adjacent molecules of **4** interact through two N–H…O hydrogen bonding interactions that produce a dimmer with an $R^2_2(8)$ graph set motif [27] (Fig. 3).

The crystal packing of the molecules of **4** does not reveal additional hydrogen bonding or weak interactions. The flexible pentyl chains are locked in between two Dansyl moieties (Fig. 4) thus the steric hindrance is minimized.

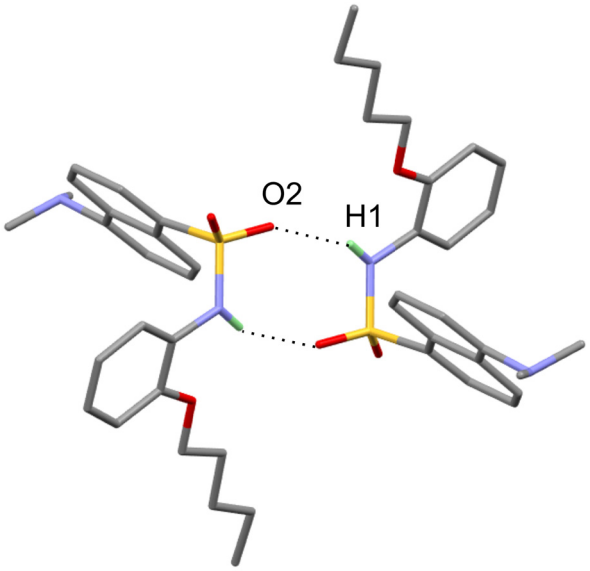


Fig. 3. Hydrogen bonding interactions (for details see Table 3) stabilizing the three-dimensional arrangement in compound **4**.

CONCLUSIONS

The title compound N-Dansyl-o-n-pentoxy aniline was obtained in good yield by a classical three-step reactions starting using o-nitrophenol, n-bromopentane and dansyl (5-(dimethylamino)naphthalene-1-sulfonyl) chloride as starting reagents. The product was purified and characterized using powder and single-crystal XRD, DTA-TGA analyses. The single-crystal XRD analysis revealed that the compound crystallizes in the monoclinic $P2_1/c$ space group, the molecular structure being stabilized by an intramolecular interactions, while the crystal packing is governed by N-H…O hydrogen bonding and the flexibility of the pentoxy chains.

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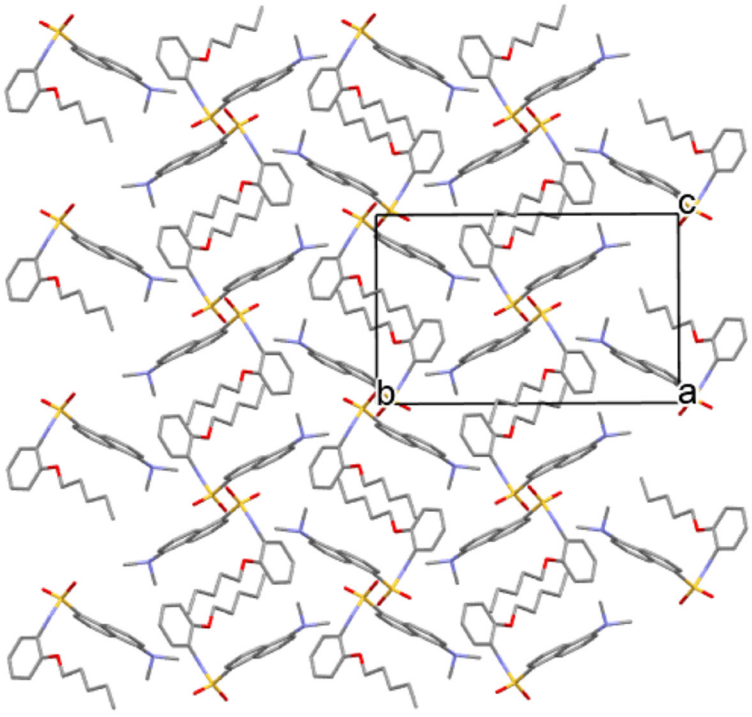

Fig. 4. Crystal packing arrangement in **4** disclosing the pseudo parallel positing of the pentoxy chains.

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