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Synthesis and Structural Characterisation of (*E*)-N-(3,4,5-Trimethoxybenzylidene)aniline

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Abstract

The parent Schiff base of the N-(3,4,5-trimethoxybenzylidene)aniline series, (*E*)-N-(3,4,5-trimethoxybenzylidene)aniline (C₁₆H₁₇NO₃), was synthesised by microwave condensation of 3,4,5-trimethoxybenzaldehyde with aniline and structurally characterised by spectroscopic and single-crystal X-ray diffraction methods. The known 4-F, 4-Cl and 4-Br analogues of this series crystallise isotypically with each other in the non-centrosymmetric space group P21 (*Z* = 2); the parent (*X* = H) compound reported here adopts the related but distinct centrosymmetric space group P21/*n* (*Z* = 4) despite closely comparable unit-cell metrics. The compound crystallises with one molecule in the asymmetric unit and adopts an *E* configuration about the imine C7=N1 bond [1.2734(14) Å] while the trimethoxyphenyl and phenyl rings are twisted relative to one another by 63.11(4°), while the imine bridge remains close to coplanar with the trimethoxyphenyl ring. This completes this structural series providing a halogen-free reference for this family of tubulin-polymerisation-inhibitor-related Schiff bases.

Keywords Schiff base · Imine · Trimethoxy · Microwave · Crystal structure

Introduction

Imines (Schiff bases) formed by condensation of aromatic aldehydes with primary amines remain one of the most extensively studied classes of organic crystal structures, owing to their straightforward synthesis and their use as intermediates and ligands and relative ease of crystallisation. In the solid state, their structural conformation, in particular, the dihedral angle between the two aromatic rings flanking the C=N bond, varies significantly with the type and position of ring substituents, making this class highly valuable for understanding structure–property relationships in medically relevant motifs.

Beyond their crystallographic interest, Schiff bases are of substantial pharmaceutical significance. The azomethine (–CH=N–) group is a versatile pharmacophore in its own right, and simple aryl-imine compounds and their metal complexes have been reported to display antibacterial, antifungal, antiviral, anti-inflammatory and antioxidant activities, among others, with recent reviews cataloguing this broad pharmacological profile in detail [1]. This combination of biological versatility with the ease and low cost of Schiff-base synthesis continues to drive structural studies of new aryl-imine compounds as a foundation

for structure–activity work, and has in parallel motivated the development of faster, greener synthetic routes; including microwave-assisted condensations, which give the same aryl-imine products as conventional reflux in a fraction of the time and with reduced solvent and energy use [2].

Among these, Schiff bases bearing a 3,4,5-trimethoxyphenyl (TMP) ring are of particular pharmaceutical interest because the TMP group is a well-established pharmacophore in anticancer medicinal chemistry. It occurs in natural tubulin-binding agents such as colchicine and podophyllotoxin, and in synthetic tubulin polymerisation inhibitors related to combretastatin A-4, where the three symmetrically arranged methoxy substituents make essential hydrophobic and electronic contacts within the colchicine-binding site of β -tubulin; removal or repositioning of the methoxy pattern typically causes a marked loss of activity [3]. Aryl–imine (Schiff base) linkages built from 3,4,5-trimethoxybenzaldehyde have themselves been incorporated into several series of tubulin-polymerisation-inhibitor-related and cytotoxic hybrid molecules [4, 5], reflecting continuing interest in the solid-state conformation of this pharmacophore-bearing imine core as a template for further pharmaceutical elaboration (for example as a synthetic precursor to the corresponding trimethoxybenzamide or thiazole/pyrrolizine hybrids reported as cytotoxic tubulin-polymerisation inhibitors).

A series of para-substituted N-(3,4,5-trimethoxybenzylidene)anilines, $X-C_6H_4-N=CH-C_6H_2(OMe)_3$, has previously been structurally characterised for $X = 4-Cl$ [6], $4-Br$ [7] and $4-F$ [8]; these three halogen-substituted members are isotypic with each other, crystallising in the non-centrosymmetric space group P21 ($Z = 2$) with similar unit-cell metrics but differing dihedral angles between the aromatic rings (38.3 – 47.6°). Despite this, the parent, unsubstituted-aniline member of the series ($X = H$), the simplest and most direct precursor for comparison, and the member most directly relevant to the pharmacologically privileged TMP-imine core described above, does not appear to have been reported. To complete this structural series and to provide a halogen-free structural reference against which the electronic and steric effects of the para substituents can be assessed, we synthesised and structurally characterised (E)-N-(3,4,5-trimethoxybenzylidene)aniline by single-crystal X-ray diffraction, using a rapid microwave-assisted condensation route in place of the conventional prolonged reflux typically used for this compound class.

Experimental Section

Materials and Methods

All reactions were performed in air unless otherwise noted; all reagents and solvents were obtained from commercial sources and were used without further purification unless otherwise noted. High resolution electron spray mass spectrometry (HRMS) of the compound was conducted by Gary Hessman of the School of Chemistry, Trinity College Dublin on a Waters TOF mass spectrometer. Solid state infrared (IR) spectra were collected with a Shimadzu IRSPIRIT-TX spectrometer outfitted with an Attenuated Total Reflectance (ATR) accessory in the range 400 – 4000 cm^{-1} . Abbreviations used to describe signal shape and intensity: w = weak; m = medium; s = strong. Proton nuclear magnetic resonance (^1H NMR) spectra were recorded on a Varian 400 MHz instrument; spectra were recorded in $CDCl_3$ unless otherwise stated and chemical shifts (ppm) are referenced to $Si(CH_3)_4$ for ^1H NMR. Abbreviations used to describe signal multiplicity: s = singlet; d = doublet; t = triplet; m = multiplet.

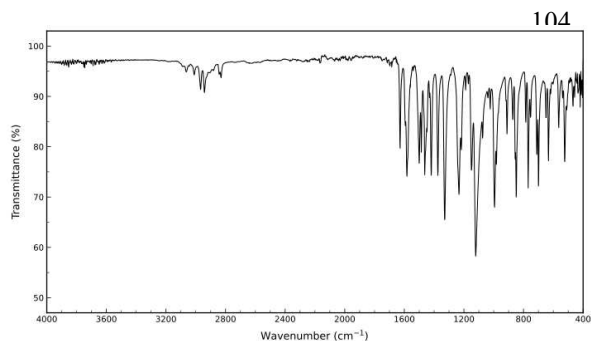
Synthesis of (E)-N-(3,4,5-Trimethoxybenzylidene)aniline (1)

The title compound was prepared by a microwave-assisted condensation, adapting the general method of Border et al. [2]. 3,4,5-Trimethoxybenzaldehyde (1.05 equiv., 1.13 g) and aniline (1 equiv., 0.5 g) were dissolved in 5 mL of toluene in a 10 mL microwave vial. The vial was then placed in a CEM Discover 2.0 microwave reaction system and was heated at 150 °C, 150 W for 30 min. After irradiation, the reaction mixture was transferred to a flask and the solvent removed under vacuum. The crude product was then recrystallised at room temperature using the minimum amount of 2-propanol to give the desired compound. Recrystallisation from methanol by slow evaporation over several days afforded colourless, plate-like single crystals of the title compound suitable for single crystal X-ray diffraction. White solid (1.08 g, 74%).

¹H NMR (400 MHz, CDCl₃) δ 8.34 (s, 1H), 7.40 – 7.36 (m, 2H), 7.24 – 7.18 (m, 3H), 7.15 (s, 2H), 3.94 (s, 6H), 3.91 (s, 3H).



IR (cm⁻¹): 3063.89 (w), 3010.71 (w), 2967.60 (w), 2941.73 (w), 2829.64 (w), 1628.23 (w), 1593.74 (w), 1582.24 (w), 1500.33 (w), 1485.96 (w), 1462.96 (w), 1447.15 (w), 1419.85 (w), 1375.30 (w), 1329.31 (m), 1233.03 (w), 1217.22 (w), 1149.68 (w), 1120.93 (m), 1074.95 (w), 994.47 (w), 981.54 (w), 911.12 (w), 855.07 (w), 849.32 (w), 784.65 (w), 768.85 (w), 709.93 (w), 699.87 (w), 632.32 (w), 563.34 (w), 523.10 (w).



HRMS (ESI) m/z [M+H]⁺: found 272.1284 [C₁₆H₁₈NO₃]⁺, calc. 271.1281, found [M+Na]⁺ 294.1092 [C₁₆H₁₇NNaO₃]⁺, calc. 294.1101

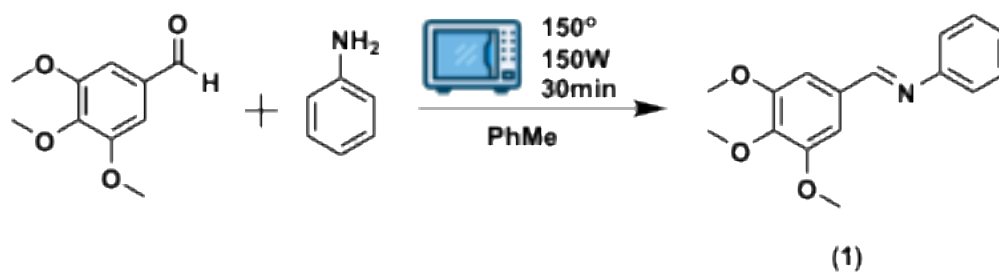
X-ray Structure Determination

Single-crystal X-ray diffraction data for (1) were collected at 110.1(3) K using graphite-monochromated Cu K α radiation ($\lambda = 1.54184$ Å) on a SuperNova, Dual, Cu at home/near, Atlas four-circle diffractometer. Data collection and cell refinement were performed with CrysAlisPro [10]; an empirical multi-scan absorption correction using spherical harmonics (SCALE3 ABSPACK) was applied. The structure was solved by dual-space methods with SHELXT [11] and refined against F^2 with SHELXL-2018/3 [12] within the Olex2 [13] program suite. All non-hydrogen atoms were refined anisotropically, aromatic and imine C–H hydrogen atoms were placed in calculated positions and refined riding on their parent atoms with Uiso(H) = 1.2Ueq(C); methyl hydrogens were refined as idealised rotating groups with Uiso(H) = 1.5Ueq(C). A summary of the crystallographic data and structure-refinement parameters is given in Table 1.

Results and Discussion

Synthesis

The title compound was obtained via a microwave-assisted Schiff-base condensation of 3,4,5-trimethoxybenzaldehyde with aniline in toluene (Scheme 1.), adapting the general method of Border et al. [2]. Heating at 150 °C for 30 min under microwave irradiation gave the desired compound in good yield (74%) within a fraction of the time typically required for the conventional prolonged-reflux protocols used to prepare the related 4-halo analogues in this series (which can lead to unwanted by-product formation), consistent with the broader advantages of microwave-assisted condensation reported for aryl-imine synthesis more generally. Attempts were made to follow the solvent free methodology as described in [2], this gave high yields of the desired product, however there were significant difficulties in isolation. The product would solidify in the microwave reaction vial upon cooling forming a very difficult to solubilise waxy solid; which was difficult to remove from microwave vial and any remaining impurities or molecular sieves (that had been used as a drying solid). Consequently a slight modification of the procedure was utilised with toluene as a solvent without molecular sieves. After reaction the presence of the solvent allowed the easy decanting of the pale yellow solution and compound (1) could the crude product could be isolated in good yield. Sequential recrystallisation, first from 2-propanol and then by slow evaporation from methanol, afforded colourless, plate-like crystals suitable for single-crystal X-ray diffraction. The spectroscopic and mass-spectrometric data obtained (^1H NMR, IR, HRMS) were fully consistent with those previously reported for this compound [9], confirming both the identity and purity of the material prior to structural analysis.



Scheme 1. Microwave synthesis of (*E*)-N-(3,4,5-Trimethoxybenzylidene)aniline (1).

Crystal Structure

The title compound (1) crystallises in the monoclinic space group $P2_1/n$, of which the asymmetric unit consists of a single molecule of (*E*)-*N*-(3,4,5-trimethoxybenzylidene)aniline, $C_{16}H_{17}NO_3$ (Fig. 1., thermal ellipsoid plot drawn at 50% of probability). The imine bond $C7=N1$ [1.2734(14) Å] is consistent with reported C=N distances in related trimethoxybenzylidene-aniline Schiff bases and confirms the expected *E* (trans) configuration about the imine linkage, as indicated by the $C8-C7=N1-C4$ torsion angle of 176.87(9)°. The $C7-C8$ bond to the trimethoxyphenyl ring [1.4685(14) Å] and the $N1-C4$ bond to the aniline ring [1.4171(13) Å] both fall within the normal range for such conjugated single bonds (Table 2); these values are compared directly with the isotypic 4-F, 4-Cl and 4-Br analogues in Table 3.

Least-squares planes calculated through the two six-membered rings ($C8-C13$ for the trimethoxyphenyl ring A and $C1-C6$ for the aniline ring B) show that both rings are individually planar, with r.m.s. deviations of 0.016 Å (ring A) and 0.007 Å (ring B). The dihedral angle between the two ring planes is 63.11(4)° (Table 2), indicating a considerably more twisted conformation than in the corresponding 4-halo analogues (4-fluoro 47.58(11)° [8]), 4-chloro (40.5(11)°, [6]) and 4-bromo (38.3(1)° calculated in this work from [6-8], Table 4). The imine carbon (C7) and, to a lesser extent, the imine nitrogen (N1) and the ipso aniline carbon (C4) lie close to the trimethoxyphenyl ring plane (0.0751(16), 0.304(18) and 0.270(2) Å, respectively), so that the twist between the two aromatic rings is accommodated essentially entirely at the $C7=N1-C4$ hinge rather than by rotation of the imine unit out of the trimethoxyphenyl plane. Because para substitution on the aniline ring (F, Cl, Br) tends to be associated with smaller inter-ring dihedral angles in this series, the larger twist found here for the unsubstituted ($X = H$) parent suggests that para-halogen substitution favours a somewhat flatter overall conformation, most plausibly through subtle differences in crystal packing rather than through any electronic effect transmitted across the imine bridge, since the imine bond length itself changes only marginally across the series. The three methoxy substituents at C10, C11 and C12 of the trimethoxyphenyl ring are arranged in the usual 3,4,5-pattern; the central methoxy oxygen (O2) is twisted markedly out of the attached-ring plane ($C15-O2-C11-C10 = 109.39(11)^\circ$, $C15-O2-C11-C12 = -72.67(13)^\circ$), whereas the two flanking methoxy groups (O1/C14 and O3/C16) lie much closer to the ring plane ($O1-C10-C11-O2 = 1.44(14)^\circ$ and $O3-C12-C11-O2 = 0.57(15)^\circ$), a pattern that mirrors the steric relief seen for the central methoxy group in other 3,4,5-trimethoxyphenyl Schiff bases and is a recognised structural signature of this substituent pattern (Table 2).

The three halogenated 4-Cl, 4-Br and 4-F analogues are isotypic with each other, crystallising in the non-centrosymmetric space group $P2_1$ ($Z = 2$) with comparable *a*, *b* and *c* axes and β close to 105° (Table 4.). The title compound instead crystallises in the centrosymmetric space group $P2_1/n$ ($Z = 4$) (Fig. 3); although a different space group, the unit-cell volume per molecule (V/Z) is remarkably consistent across three of the four compounds, 371.3 Å³ (H, this work), 371.8 Å³ (F) and 369.3 Å³ (Cl), with only the bromo analogue notably more open (387.6 Å³), indicating a closely similar packing efficiency despite the change in space-group symmetry on going from the halogenated to the unsubstituted derivative. The principal structural variable across the series remains the inter-ring dihedral angle, which the parent ($X = H$) compound extends to its largest value so far reported for this family.

Figure 3. shows the packing within the unit cell of (1) projecting the down the c axis. The four molecules generated within the outlined ab cell arise from the single general-position molecule of the asymmetric unit through the combined action of the 21 screw axes, the n-glide plane and the inversion centres characteristic of P21/n. Despite this difference in space-group symmetry, the resulting packing motif is broadly similar across the four structures: molecules associate as offset, roughly parallel chains propagating along the b axis, rather than through any face-to-face or otherwise strongly directional arrangement. Neighbouring chains are linked only by the weak C–H···O and C–H···N contacts identified in the Hirshfeld surface analysis below; due to imine nitrogen and the three methoxy oxygens acting exclusively as acceptors.

Structural comparison with Related N-(3,4,5-Trimethoxybenzylidene)arylamines

Beyond the para-halogenated anilines discussed above, the Cambridge Structural Database [14] contains several further selected examples in which the amine component condensed with 3,4,5-trimethoxybenzaldehyde is varied more substantially: naphthalen-1-amine ([15], 2,3-dimethylaniline [16], 2-aminophenol [17] and 3,4-dichloroaniline [18]. In order to compare these literature examples with (1) synthesised in this study, the inter-ring dihedral angle for each was recalculated from the deposited atomic coordinates using the same least-squares-plane procedure applied to the title compound and the results (together with those determined for 4-F, 4-Cl and 4-Br structural analogues) directly compared in Table 5.

The determined dihedral angles span a wide range, from 8.3° for the 3,4-dichloroaniline analogue to 63.11(4)° for that of compound (1). The naphthalen-1-amine analogue (55.7(1)°) is the closest in magnitude to the title compound; the peri-hydrogen at C8 of the naphthalene ring system produces a steric environment around the imine nitrogen broadly similar to that created by ortho C–H interactions in the unsubstituted phenyl ring, so that both compounds twist to a comparable extent. The 2,3-dimethylaniline analogue (36.2(1)°) is markedly less twisted than the parent despite carrying an ortho-methyl substituent, suggesting that the crystal-packing forces stabilising this particular structure outweigh the additional steric bulk at C8 of the amine ring. The 3,4-dichloroaniline analogue is essentially coplanar (8.3(2)°); this compound was reported as part of a study of elastically flexible molecular crystals in which planar, well-stacked packing motifs were deliberately sought [18], and the very small dihedral angle found here is consistent with that design intent.

The 2-aminophenol analogue is a special case: two crystallographically independent molecules are present in the asymmetric unit (dihedral angles 21.4(2)° and 18.5(2)°), and each carries an intramolecular O1–H1···N1 hydrogen bond [2.687(6) Å] that locks the phenolic ring into a near-planar, chelate-like arrangement with the imine nitrogen, similar to the classic enol-imine tautomer seen in salicylaldehyde-derived Schiff bases. This intramolecular hydrogen bond, which is structurally impossible for (1) and subsequent structural analogues discussed in Table 5 (none of which carries an ortho-donor group on the amine ring), is the most plausible reason why both independent molecules of the 2-aminophenol analogue adopt comparatively small dihedral angles despite the absence of any para- or ortho-alkyl/halogen substituent of the kind otherwise associated with flatter conformations in this series. Overall, Table 5. shows that the inter-ring dihedral angle in this compound family is governed by a combination of amine-ring sterics, the possibility of an intramolecular hydrogen bond, and crystal-packing preferences, rather than by

any single dominant electronic effect of the amine substituent; compound (1) has an unusually large dihedral angle reflective of absence of any of the flattening influences (ortho-donor hydrogen bonding, engineered planar packing, or a bulky peri-substituent counterbalanced by favourable stacking) present in the other family members.

Hirshfeld Surface Analysis

The Hirshfeld surface of (1) was computed in CrystalExplorer from the refined structure and mapped with d_{norm} over the range -0.65 to 1.7 (Fig. 2a, b). Across both faces of the surface the d_{norm} mapping is dominated by white and blue regions, indicating that the great majority of the molecular periphery is in contact with neighbouring molecules at or beyond the sum of van der Waals radii. Only small, pale red/pink patches are visible, situated in the vicinity of the methoxy oxygen atoms and, more faintly, near the imine nitrogen. This is consistent with the absence of any strong hydrogen-bond donor in the molecule, the imine nitrogen and the three methoxy oxygens are acceptors only, with no N–H or O–H donor present, consequently packing is due exclusively by weak C–H $\cdots$ O and C–H $\cdots$ N contacts together with more diffuse H $\cdots$ H van der Waals contacts, rather than by any classical hydrogen bond.

The full two-dimensional fingerprint plot (Fig. 2c) shows a broad, relatively featureless distribution spanning $d_i + d_e \approx 2.2$ – 4.0 Å with two short, narrow spikes projecting toward the lower-left corner ($d_i, d_e \approx 1.0$ – 1.4 Å), the classic signature of a small number of short, directional donor/acceptor contacts superimposed on a much larger population of longer, non-directional contacts. Decomposition of the surface by contact type shows that H $\cdots$ H contacts (Fig. 2d) account for the visually dominant fraction of the surface (52.3%). The H $\cdots$ O and O $\cdots$ H contacts (Fig. 2e, f) are comparatively minor (6.7 and 7.7% respectively) in area but map onto the two short spikes identified in the full plot, confirming that the methoxy oxygens are the principal acceptors of weak C–H $\cdots$ O interactions in the structure; the H $\cdots$ O plot (own H atoms donating toward a neighbouring O) shows a sharper, shorter spike than the reciprocal O $\cdots$ H plot (own O atoms accepting from a neighbouring H within the unit cell), indicating that the two directions of this contact are not perfectly symmetric across the surface. A further, smaller H $\cdots$ N contribution (2.4%, Fig. 2g) occupies a less extreme, longer-contact region of the plot than H $\cdots$ O, consistent with the imine nitrogen acting as a weaker and less directional acceptor than the methoxy oxygens in this structure. Shape-index, curvedness and C $\cdots$ C-resolved fingerprint data were subsequently generated to probe directly for π – π stacking (Fig. 2h–j). The shape-index surface (Fig. 2h) shows numerous small, roughly circular concave (red) patches scattered across the trimethoxyphenyl and aniline ring faces. However, these red patches are not paired with an adjacent, similarly sized convex (blue) patch of complementary outline on the same face. The absence of this diagnostic signature of offset or face-to-face π – π stacking between neighbouring aromatic rings is consistent with individual short C–H $\cdots$ π or C–H $\cdots$ O contacts rather than an extended stacking interaction. The curvedness surface (Fig. 2i) supports this interpretation: the ring faces are subdivided by sharp, dark-blue boundary lines into a mosaic of small, moderately curved (cyan/green) patches rather than one large, flat, low-curvedness region, which is what a genuine π -stacked contact would produce. Finally, the C $\cdots$ C resolved fingerprint plot (Fig. 2j) shows a broad, diffuse distribution of points spanning roughly $d_e = d_i = 1.0$ – 2.9 Å, with no sharp spike at $d_e \approx d_i \approx 1.8$ Å (0% contribution), the characteristic signature of ordered offset π – π stacking. This evidence is indicative that π – π stacking does

not make a significant contribution to the crystal packing of (1), consistent with the twisted, non-coplanar (63.1°) relationship between the two aromatic rings established above.

Conclusions

The parent, unsubstituted-aniline member of the Schiff-base series, N-(3,4,5-trimethoxybenzylidene)aniline, was synthesised by microwave methods and its crystal structure determined at 110 K. The compound adopts the expected E configuration about the imine bond and crystallises in the centrosymmetric space group P21/n ($Z = 4$), a related but distinct space group from the non-centrosymmetric P21 ($Z = 2$) shared by its isotypic 4-Cl, 4-Br and 4-F congeners, despite closely comparable unit-cell metrics and volume per molecule; it also shows a notably larger dihedral angle (63.11(4)°) between its two aromatic rings than any of the halogen-substituted analogues. Extending the comparison to four further N-(3,4,5-trimethoxybenzylidene)arylamines whose crystal structures are available in the CSD (naphthalen-1-amine, 2,3-dimethylaniline, 2-aminophenol and 3,4-dichloroaniline analogues) shows that the inter-ring dihedral angle across this compound family spans more than 50°, governed by amine-ring sterics, and crystal-packing preferences rather than by a single electronic effect. This completes the parent-plus-halogen family of structures for this pharmacophore-related Schiff base, situates it within the broader family of trimethoxybenzylidene-arylamines structures, and provides a halogen-free reference point for future structure–property and structure–activity comparisons within this series.

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Author Contributions

[Camil Dali-Youcef: Review & editing, Methodology, Data curation. Shrinivas Jahagirdar: Review & editing, Methodology, Data curation. Roderick C. Jones: Writing, Supervision, Conceptualisation]

Data Availability

Crystallographic data for the structure reported in this article has been deposited with the Cambridge Crystallographic Data Centre [2578710]. These data are available free of charge from the Cambridge Crystallographic Data Centre via <https://www.ccdc.cam.ac.uk/structures/>. Data will be made available on request.

Declarations

298 **Competing interests** The authors declare no competing interests.

299

300 **Table 1**

301 *Crystallographic data, details of data collection and structure-refinement parameters for (E)-N-(3,4,5-*
 302 *trimethoxybenzylidene)aniline (1)*

Formula	C ₁₆ H ₁₇ NO ₃
M [g mol ⁻¹]	271.30
T [K]	110.1(3)
Crystal system	monoclinic
Space group	P21/n
a [Å]	11.43780(10)
b [Å]	10.39410(10)
c [Å]	12.99630(10)
β [°]	105.9940(10)
V [Å ³]	1485.26(2)
Z	4
F(000)	576
ρ _{calcd} [g cm ⁻³]	1.213
Radiation, λ [Å]	Cu Kα, 1.54184
μ [mm ⁻¹]	0.683
Absorption correction	multi-scan (spherical harmonics, SCALE3 ABSPACK)
Crystal size, mm	0.261 × 0.193 × 0.109
Crystal colour and shape	colourless, plate
T _{max} , T _{min}	1.00000, 0.70977
R _{int}	0.0338
Reflections all	36324
Independent	3105
[I > 2σ(I)]	2766
Goodness-of-fit on F ²	1.041
Final R1 [I > 2σ(I)]	0.0357
Final R1 (all data)	0.0403
wR2 [I > 2σ(I)]	0.0917
wR2 (all data)	0.0965
Largest diff. peak and hole (e Å ⁻³)	0.180, -0.183

303

Table 2*Selected bond lengths, torsion angles and bond angles for (I)*

Parameter	Value
Bond lengths (Å)	
C7=N1 (imine)	1.2734(14)
C7–C8 (imine–trimethoxyphenyl ring)	1.4685(14)
N1–C4 (imine–aniline ring)	1.4171(13)
Torsion / dihedral angles (°)	
C8–C7=N1–C4 (imine torsion)	176.87(10)
Inter-ring dihedral angle A/B	63.11(4)
Bond angles (°)	
N1=C7–C8	122.54(9)
C7=N1–C4	117.57(9)
C10–O1–C14	116.74(8)
C11–O2–C15	113.86(8)
C12–O3–C16	116.85(9)

Table 3*Selected bond lengths (Å) and torsion angle (°) for the title compound, compared with the isotypic 4-F, 4-Cl and 4-Br analogues*

Parameter	H (this work)	F [8]	Cl [6]	Br [7]
C7=N1 (imine)	1.2734(14)Å	1.258(2)°	1.282(4)Å	1.268(3)Å
C(imine)–C(ipso, TMP ring)	1.4685(14)Å	1.455(3)Å	1.466(4)Å	1.464(3)Å
N(imine)–C(ipso, aniline ring)	1.4171(13)Å	1.411(3)Å	1.417(4)Å	1.421(2)Å
C(ar)–C=N–C(ar) torsion	176.87(9)°	-177.3(2) ^a	-178.9(3) ^a	179.19(18)
Inter-ring dihedral angle (A/B)	63.11(4)	47.58(11) ^a	40.5(11) ^a	38.3(1) ^a

^aCalculated from literature cif files from [6-8].**Table 4***Comparison of unit-cell parameters and inter-ring dihedral angles across the para-X series of N-(3,4,5-trimethoxybenzylidene)anilines*

X (para)	Space group	a (Å)	b (Å)	c (Å)	β (°)	Dihedral angle A/B (°)	Reference
H (this work)	P21/n	11.4378(1)	10.3941(1)	12.9963(1)	105.994(1)	63.11(4)	this work

F	P21	7.1147(9)	8.3841(9)	12.9217(13)	105.266(5)	47.58(11) ^a	[8]
Cl	P21	7.2012(2)	8.1870(1)	12.9734(3)	105.050(2)	40.5(11) ^a	[6]
Br	P21	7.1951(4)	8.3722(5)	13.2882(8)	104.413(3)	38.3(1) ^a	[7]

Table 5

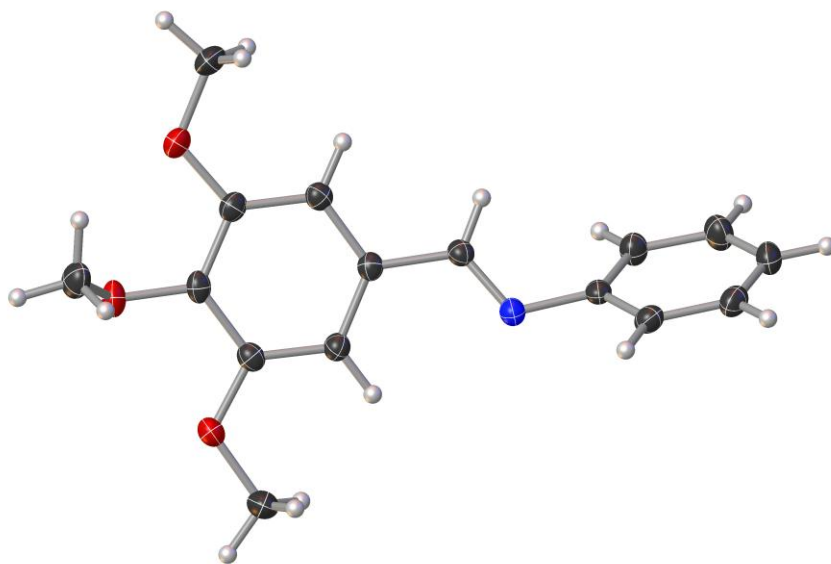
Inter-ring dihedral angle across a wider series of N-(3,4,5-trimethoxybenzylidene)arylamines, ranked from largest to smallest angle

Amine component	Formula	Space group	Dihedral angle (°)	CCDC no.	Reference
Aniline (H) — this work	C ₁₆ H ₁₇ NO ₃	P21/n	63.11(4)	2578710	this work
Naphthalen-1-amine	C ₂₀ H ₁₉ NO ₃	P21/n	55.7(1) ^a	979036	[15]
4-Fluoroaniline	C ₁₆ H ₁₆ FNO ₃	P21	47.58(11) ^a	—	[8]
4-Bromoaniline	C ₁₆ H ₁₆ BrNO ₃	P21	38.3(1) ^a	—	[7]
2,3-Dimethylaniline	C ₁₈ H ₂₁ NO ₃	P21/n	36.2(1) ^a	1864422	[16]
4-Chloroaniline	C ₁₆ H ₁₆ ClNO ₃	P21	40.5(11) ^a	—	[6]
2-Aminophenol, mol. 1	C ₁₆ H ₁₇ NO ₄	I2 (Z' = 2)	21.4(2) ^a	1919490	[17]
2-Aminophenol, mol. 2	C ₁₆ H ₁₇ NO ₄	I2 (Z' = 2)	18.5(2) ^a	1919490	[17]
3,4-Dichloroaniline	C ₁₆ H ₁₅ Cl ₂ NO ₃	Pna21	8.3(2) ^a	1840966	[18]

^aCalculated directly from supplied cif files.

319

320 **Figure 1**



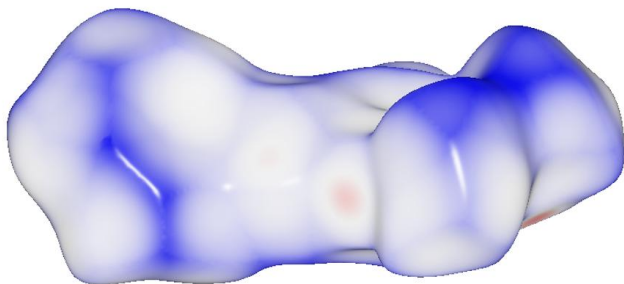
321

322 *Molecular structure of the title compound showing the asymmetric unit, with non-hydrogen atoms drawn as*
323 *anisotropic displacement ellipsoids [50% probability level] and hydrogen atoms as small spheres of arbitrary radius,*
324 *generated from the refined atomic coordinates. Carbon atoms are grey, nitrogen blue and oxygen red; the E*
325 *configuration about the C7=N1 imine bond and the twist between the trimethoxyphenyl and aniline rings described*
326 *in the text are both apparent from this view.*

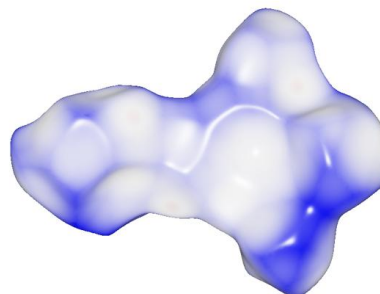
327

328 **Figure 2**

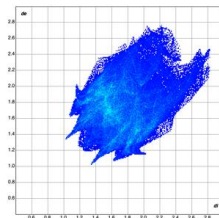
(a) dnorm surface — view 1



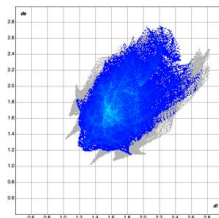
(b) dnorm surface — view 2 (rotated)



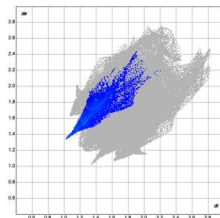
(c) Full



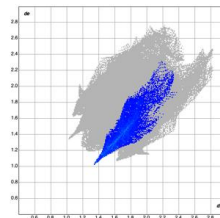
(d) H...H



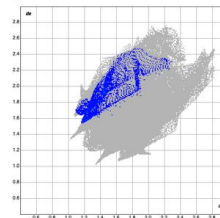
(e) H...O



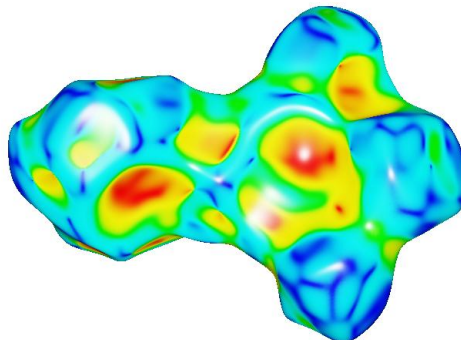
(f) O...H



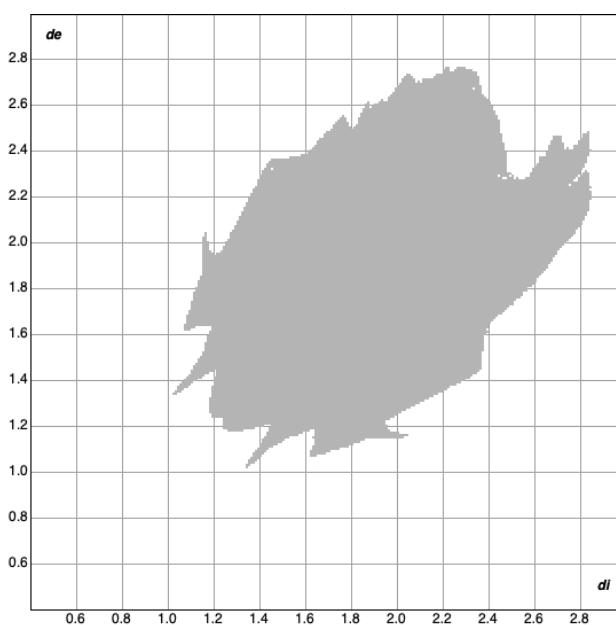
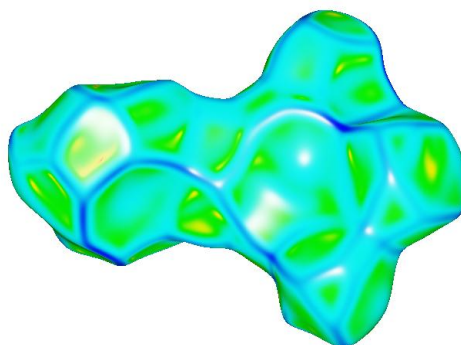
(g) H...N



329

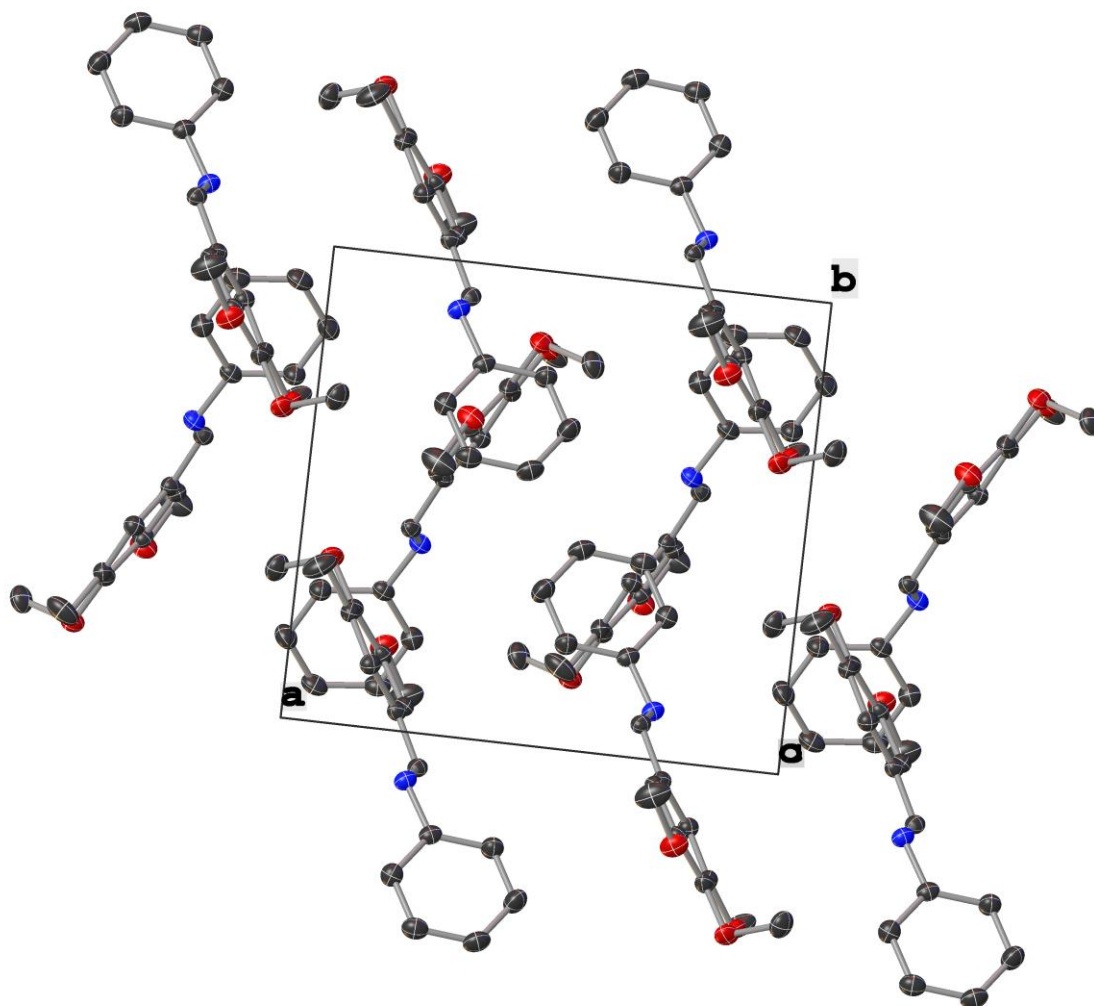


330



Hirshfeld surface analysis of the title compound. (a, b) dnorm-mapped Hirshfeld surface shown in two orientations (colour scale -0.65 to 1.7); faint pink/red patches mark the shortest intermolecular contacts. (c) Full two-dimensional fingerprint plot. (d–g) Fingerprint plots resolved by contact type: $H\cdots H$, $H\cdots O$, $O\cdots H$ and $H\cdots N$, respectively (blue = selected contact type; grey = full surface, shown for reference). (h) Shape-index-mapped Hirshfeld surface (standard red–green–blue scale). (i) Curvedness-mapped Hirshfeld surface (standard blue-to-green scale, flat regions dark blue). (j) $C\cdots C$ -resolved two-dimensional fingerprint plot (d_e , d_i in Å).

Figure 3



Crystal packing of the title compound viewed down the *c* axis, with non-hydrogen atoms drawn as anisotropic displacement ellipsoids at 50% probability level, hydrogen atoms are omitted for clarity.

Table 6

Hirshfeld surface contact-type breakdown for the title compound

Contact type	Approx. surface region (d_i , d_e / Å)	Relative contribution (visual)	% of surface area
H...H	≈ 1.6 – 2.6 (broad, central)	dominant	[52.3 %]
H...O	≈ 1.0 – 1.6 (sharp spike)	minor but resolved	[6.7 %]
O...H	≈ 1.3 – 2.0 (broader spike)	minor but resolved	[7.7 %]
H...N	≈ 1.6 – 2.4 (diffuse patch)	small	[2.4 %]
C...C	d_i , $d_e \approx 1.0$ – 2.9 (broad, no spike at 1.8)	diffuse; no π – π stacking signature	[to be inserted]

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