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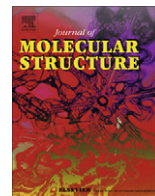


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Synthesis, characterization, and crystal structure of 2-iodo-3,4,5-trimethoxybenzoic acid

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H I G H L I G H T S

- ▶ The main advantage of the applied synthetic procedure is its operational simplicity.
- ▶ The experimental setup allows controlled addition of I₂ using less organic solvent.
- ▶ The structure of the reaction product has been identified.

A R T I C L E I N F O

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A B S T R A C T

This work describes the synthesis of 2-iodo-3,4,5-trimethoxybenzoic acid. The combination of iodine and silver trifluoroacetate (AgTFA) reagents was used successfully for the iodination of 3,4,5-trimethoxybenzoic acid. To improve the efficiency of the synthetic process a significant modification on the experimental design was also performed. The main structural features of the obtained aryl iodide were investigated by a single crystal X-ray diffraction analysis, FTIR, ¹H and ¹³C NMR spectroscopy.

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1. Introduction

Aryl halides and especially aryl iodides have attracted much attention due to their peculiar reactivity towards different organo-metallic reagents. They have served as important building blocks in the syntheses of various aromatic natural products, such as ellagitannins (Sanguin H-5) [1], terpenoids (Fronodosin B) [2], alkaloids (Psilocin [3], (–)-Quadrigenine C [4], Singulair [5–7], Michellamine B [8,9]), antibiotics (Arylomycin B) [10], and benzofuranes (Lepidezavirgatal) [11].

A wide variety of reagents has been reported as very efficient catalysts for iodination of aromatic compounds. The most used are: I₂–F₃CCOOAg, I₂–HgO, I₂–Ag₂SO₄, I₂–Cr₂O₃, I₂–Pb(OAc)₂, I₂–TiOAc, I₂–KI–Hg(OAc)₂, I₂–(Bu₄N)₂S₂O₈, I₂–Na₂S₂O₈, N-iodo-succinimide (NIS), NIS–CF₃SO₃H, ICl, NH₄I–oxone, NaOCl–NaI, etc. [12,13]. In all these cases the iodine or iodine-containing source is used in a combination with a strong activating agent in order to create an efficient iodonium donating system. Regarding

the mechanism, the active iodonium species are probably formed *in situ* and act as very reactive electrophiles (Scheme 1) [14,15].

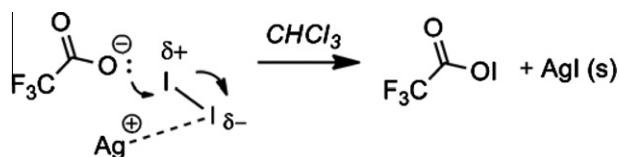
This work reports on carrying out the iodination of 3,4,5-trimethoxybenzoic acid by the implementation of a combination of iodine and silver trifluoroacetate (AgTFA) reagents (Scheme 2). The synthetic procedure developed by Janssen and Wilson has been successfully employed [16] for this purpose. With a slight modification in the construction of the experimental apparatus there has been no need of using a large amount of solvent. That has also ensured the slow and continuous insertion of iodine into the reaction medium. The structure of the obtained aryl iodide has been determined by single crystal X-ray diffraction, FTIR, ¹H NMR, and ¹³C NMR spectroscopy.

2. Materials and methods

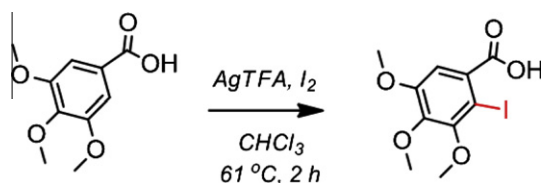
3,4,5-Trimethoxybenzoic acid (99+%, Alfa Aesar), Trifluoroacetic acid (Merck), Iodine (≥99.8%, Sigma–Aldrich), and Silver nitrate (>99.5%, Fluka) were used without further purification. The solvents chloroform, cyclohexane, toluene, and dichloromethane were received from Sigma–Aldrich and dried by standard methods.

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Scheme 1. Proposed mechanism of generation of trifluoroacetyl hypoiodite.



Scheme 2. Synthesis of 2-iodo-3,4,5-trimethoxybenzoic acid.

The Fourier transform infrared (FTIR) spectra were recorded on an IRAffinity-1 “Shimadzu” FTIR spectrophotometer with a MIRacle Attenuated Total Reflectance Attachment at a resolution of 4 cm^{-1} accumulating 50 scans and on a Bruker-Vector 22 spectrometer at a resolution of 4 cm^{-1} accumulating 50 scans (in this case the samples were prepared in KBr pellets).

The ^1H NMR and ^{13}C NMR spectra were recorded at 250 MHz on a Bruker Avance DRX 250 spectrometer using deuterated chloroform as a solvent and tetramethylsilane as an internal reference.

Melting points were determined in an open capillary tube on a Büchi Melting Point B-540 apparatus.

Diffraction data were collected at 150 K by ω -scan technique, on an Agilent Diffraction SuperNova Dual four-circle diffractometer equipped with an Atlas CCD detector using mirror-monochromatized $\text{MoK}\alpha$ radiation from a micro-focus source ($\lambda = 0.7107\text{ Å}$). A CrysAlis Pro program package was used for the determination of cell parameters, data integration, scaling and absorption correction [17]. The structures were solved by direct methods (SHELXS-97) [18] and refined by fullmatrix least-square procedures on F^2 (SHELXL-97) [18]. The non-hydrogen atoms were refined anisotropically and hydrogen atoms were placed at idealized positions and refined using the riding model. A summary of the fundamental crystal and refinement data is provided in Table 1. Crystallographic data (excluding structure factors) for the structural analysis was deposited with the Cambridge Crystallographic Data Centre, CCDC No. 872697. A copy 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.

3. Experimental

3.1. Synthesis of 2-iodo-3,4,5-trimethoxybenzoic acid

A 250 ml one-necked round bottom flask equipped with a magnetic stirring bar, a pressure-equalizing dropping funnel padded with a thin layer of glass wool, combined with a reflux condenser, and a two-way tap was charged with 1.5 g (7.07 mmol) of 3,4,5-trimethoxybenzoic acid and 1.56 g (7.07 mmol) of freshly prepared, dry silver trifluoroacetate. The reaction set-up was then evacuated repeatedly under vacuum, carefully flamed and refilled with argon, using a double-manifold system (argon/vacuum) connected to the two-way tap. After that, 1.83 g (7.20 mmol) of iodine¹ and 15 ml of

Table 1

Important crystallographic and refinement details for the title compound.

Compound	2-Iodo-3,4,5-trimethoxybenzoic acid
Chemical formula	$\text{C}_{10}\text{H}_{11}\text{O}_5\text{I}$
Mw	338.09
Crystal system	Monoclinic
SG	$P 2_1/c$
<i>a</i>	16.890(7) Å
<i>b</i>	4.2308(9) Å
<i>c</i>	18.049(7) Å
β	116.91(5)°
<i>V</i>	1150.1(7) Å ³
<i>Z</i>	4
<i>F</i> ₀₀₀	656
<i>D</i> _x	1.953 g cm ^{−3}
Radiation	$\text{MoK}\alpha$, $\lambda = 0.7107\text{ Å}$
Cell parameters	From 2182 reflections
μ	2.787 mm ^{−1}
<i>T</i>	150 (0.1) K
Crystal	Plate, colorless
Size	0.20 × 0.10 × 0.10 mm
Radiation source	SuperNova (Mo) X-ray source, monochromator: mirror
Detector	Atlas, resolution: 10.3974 pixels mm ^{−1}
Data collection	ω scans
Measured reflections	6414
Independent reflections	2758
Reflections with $I > 2\sigma(I)$	1634
<i>R</i> _{int}	0.0629
θ_{max}	29.31°
θ_{min}	3.37°
<i>h</i>	−1722
<i>k</i>	−55
<i>l</i>	−1822
Absorption correction	Multi-scan, CrysAlisPro, Oxford Diffraction Ltd., Version 1.171.35.15
<i>T</i> _{min} / <i>T</i> _{max}	0.4389, 1.000
Refinement	On F^2
Least-squares matrix:	Full
$R[F^2 > 2\sigma(F^2)]/\text{all}$	0.0857/0.1296
$wR(F^2)$	0.1784
<i>S</i> (GOF)	1.073
Parameters	149
Hydrogen site location:	Inferred from neighboring sites
$(\Delta/\sigma)_{\text{max}}$	<0.001
$\Delta\rho_{\text{max}}$	2.61 e Å ^{−3}
$\Delta\rho_{\text{min}}$	−1.53 e Å ^{−3}

The low precision of the structure and the relatively high $wR(F)^2$ are probably due to the combination of relatively smaller single crystals that were subject to a degradation under the X-ray beam (although data collection was carried out at 150 K).

chloroform were placed into the dropping funnel under an argon atmosphere. The flask was then heated to 65 °C² using an oil-bath. When the temperature was stabilized, the magnetic stirrer was switched on. After several minutes started the controlled (slow) addition of iodine into the flask;³ in our case, the complete dissolution and continuous supply of iodine (iodine crystals) into the reaction flask continued over 2.0 h by refluxing the solvent. Having completed the addition of iodine, the reaction mixture was refluxed for additional 2.5 h. Then, the reaction mixture was cooled to room temperature. The precipitate of silver iodide was removed by filtration⁴ and washed repeatedly with 5.0 ml chloroform. The obtained filtrate was concentrated to dryness under reduced pressure. After

² The reaction of F_3CCOOAg decomposition in the presence of I_2 does not occur appreciably below 100 °C [19].

³ The discoloration of the reaction mixture is a convenient measure of the reaction progress.

⁴ The use of filter paper with a smaller pore size is most suitable.

¹ The solubility of iodine, expressed in g/kg CHCl_3 at 25 °C is 49.7. Here, the amount of used CHCl_3 is insufficient to the complete dissolution of I_2 .

the solvent evaporation, the residue was dried additionally for 2.0 h at 70 °C to remove the excess of iodine and trifluoroacetic acid. The obtained light yellow residue was crystallized from a mixture of equal amounts (*v/v*) of dichloromethane and cyclohexane to afford 2-iodo-3,4,5-trimethoxybenzoic acid as colorless thin needles.⁵ Recrystallization was effectuated in a mixture of dichloromethane–cyclohexane–toluene (at a 1:2:1 volume ratio) at 4.0 °C for several days. The reaction product was analyzed by TLC; the presence of traces of 3,4,5-trimethoxybenzoic acid was not recorded (yield = 93.0%). Melting range: 151–152 °C (lit. 135–142 °C [20]; 142–145 °C [21]; 147–148 °C [22]). The recrystallization of 2-iodo-3,4,5-trimethoxybenzoic acid from dichloromethane and cyclohexane yielded needle-shaped crystals analytically pure and suitable for a single crystal X-ray diffraction analysis.

3.2. Preparation of Silver trifluoroacetate (AgTFA)

The synthesis of AgTFA was carried out according to the procedure described in Ref. [16].

Caution!!! All work with chloroform and trifluoroacetic acid must be done in a well-ventilated hood using protective clothing and gloves.

4. Results and discussion

2-Iodo-3,4,5-trimethoxybenzoic acid has been previously prepared by treatment of 2-iodo-3,4,5-trimethoxybenzyl alcohol with the Jones reagent (oxidation of the corresponding benzyl alcohol to benzoic acid) [20,22] and chosen by our simple and effective method of direct iodination of 3,4,5-trimethoxybenzoic acid with the catalytic system I_2 –AgTFA [21]. The I_2 –AgTFA couple is usually used in cases of using electron-poor arenes (such as haloarenes) and benzoic acid. Commonly, the reaction conditions are dependent on the chemical reactivity of the arene; e.g., the benzoic acid is been iodinated in nitrobenzene at 150 °C with 84% yield [15], the methyl ester of 3,4,5-trimethoxybenzoic acid in chloroform at room temperature with 45% yield [23], and 3,4,5-trimethoxybenzoic acid in chloroform with 99% yield [21]. Although, in most cases, the authors have not provided a detailed description of the preparative procedure, it is reasonable to expect that the iodination of aromatic hydrocarbons should be quantitative when using freshly prepared AgTFA, rigorously anhydrous conditions and inert atmosphere. The presence of unsuspected traces of moisture in the reaction mixture will lead to the hydrolysis of the *in situ* formed CF_3COOI intermediate to the corresponding low-active and unstable hypoiodous acid.

5. X-ray crystallography

Crystals of the title compound suitable for single crystal X-ray analysis were grown by slow evaporation from dichloromethane and cyclohexane. Attempts were made to optimize the crystal growth conditions, by varying the solvent and crystallization temperature however crystals grew only as thin needles. Initial attempts to perform data collection at ambient temperature resulted in a meltdown of the crystals. Thus a low temperature experiment had to be performed.

The title compound $C_{10}H_7IO_5$ crystallizes in the centrosymmetric $P2_1/c$ space group (No 14) with one molecule per asymmetric unit (Fig. 1). The structural features (bond distances and angles) of the 2-iodo-3,4,5-trimethoxybenzoic acid molecule are compara-

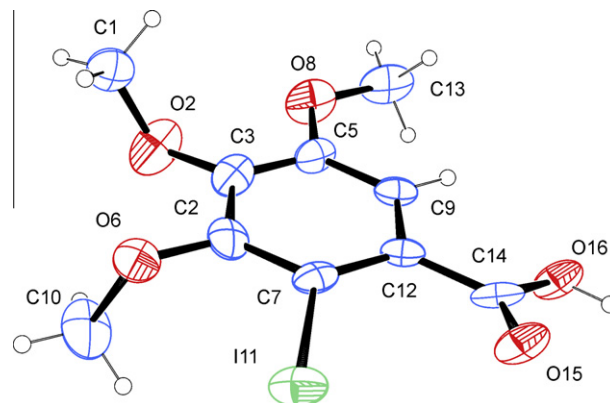


Fig. 1. Single-crystal X-ray structure of 2-iodo-3,4,5-trimethoxybenzoic acid. Displacement ellipsoids are drawn at the 50% probability level (the hydrogen atoms are represented by circles of arbitrary radii).

ble to those of similar compounds [24–26] (Table 2). The phenyl moiety is also nearly planar (rms of 0.008(4) Å) while the angle between COOH and aromatic ring mean planes is 71.07(4)°. A strong intramolecular interaction between the iodine and the carbonyl oxygen (O15...I11 3.056(5) Å) is present.

The COOH moieties of the molecules face each other in the crystal structure. The hydrogen bond between the OH and carbonyl oxygens (O16–H16...O15), typical for COOH groups, produces a bicyclic dimer ($R^2_2(8)$ motif) (Fig. 2a). Two of the three methoxy groups are involved in weak $CH_3...O$ interactions (C1H1B...O8, C1H1C...O2 and C13H13A,B and C...O16) (Fig. 2b, Table 3). Although the molecules are positioned on top of each other and thus produces a ladder motif, no stacking ($\pi... \pi$) of the phenyl rings has been observed (the distance between the mean planes of the rings is 4.969(6) Å).

6. FTIR analysis of the 2-iodo-3,4,5-trimethoxybenzoic acid

The vibrational frequency assignments were made by comparing the IR spectrum of the 2-iodo-3,4,5-trimethoxybenzoic acid with these of 3,4,5-trimethoxybenzoic acid and related derivatives [27–30]. Black squares in Figs. 4 and 5 mark the limits wherein frequencies characteristic of pentasubstituted phenyl ring may occur [31,32].

6.1. Methoxy group vibrations

In the FTIR spectrum of 2-iodo-3,4,5-trimethoxybenzoic acid (Fig. 3), the bands attributed to the asymmetric C–H stretching modes are observed at 2951 and 2936 cm^{-1} , and for the symmetric ones observed at 2828 cm^{-1} [32]. Bands involving the asymmetric and symmetric C–H deformation vibrations are detected at 1462, 1454, and 1444 cm^{-1} , respectively. In addition, three strong bands are also observed in the 1100–1130 cm^{-1} range, at 1000 cm^{-1} , and at 1267 cm^{-1} which can be attributed to the methoxy group vibrations, namely: O–CH₃ symmetric and asymmetric stretching vibrations as well as to C–OCH₃ absorption (Fig. 4). Bands at 774, 723, and 440 cm^{-1} , which can be attributed to the “C–OCH₃ stretching modes” and to C–OCH₃ bending vibrations have been also observed in the FTIR spectrum presented in Fig. 5. On the other hand, the bands detected at 1182 and 1195 cm^{-1} correlate well with the CH₃ rocking modes.

6.2. Phenyl ring vibrations

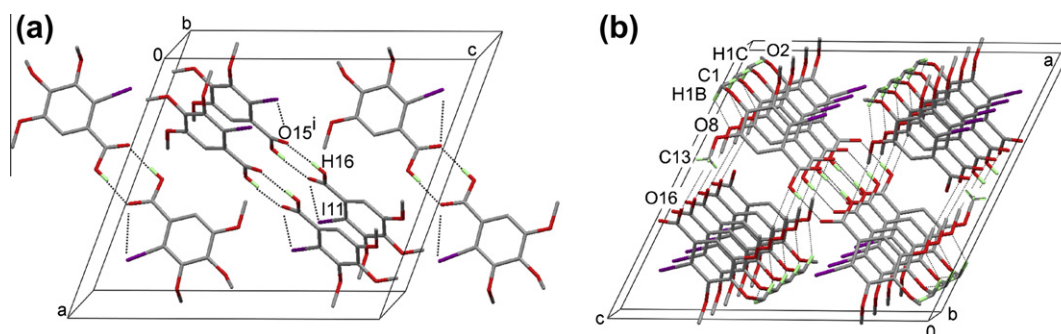
Typically there are two pairs of bands in the 1650–1320 cm^{-1} region consistent with the aromatic C=C stretching (tangential)

⁵ The crystallization process was initiated after the evaporation of a substantial part of the dichloromethane.

Table 2

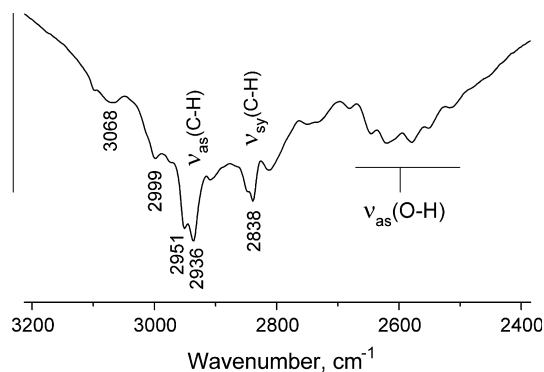
Selected bond distances, bond angles and torsion angles.

Bond distance	(Å)	Bond angle	(°)	Torsion angle	(°)
C7–I	2.106(10)	O15–C14–O16	122.0(3)	I11–C7–C2–C3	179.4(7)
C7–C2	1.399(15)	I11–C7–C2	114.0(9)	I11–C7–C12–C9	178.7(7)
C7–C12	1.408(15)	I11–C7–C12	125.3(3)	O15–C14–C12–C7	–16.5(3)
C12–C14	1.459(16)	C2–C7–C12	120.7(2)	O16–C14–C12–C7	164.5(9)
C12–C14	1.223(11)	C2–O6–C10	114.3(2)	C13–O8–C5–C9	2.5(7)
C5–O8	1.372(14)	C3–O2–C1	118.1(9)	C1–O2–C3–C5	–100.9(7)
C3–O2	1.361(14)	C5–O8–C13	118.2(2)	C10–O6–C2–C7	–102.6(6)
C2–O6	1.364(14)				
C13–O8	1.429(17)				
C1–O2	1.383(15)				
C10–O6	1.445(14)				

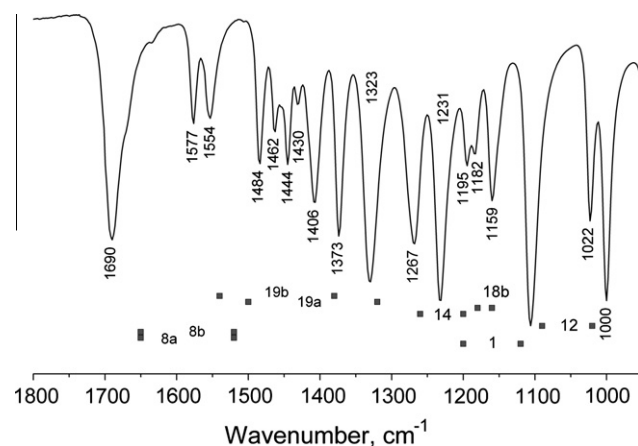
**Fig. 2.** A part of the crystal structure of 2-iodo-3,4,5-trimethoxybenzoic acid, showing hydrogen bonds and the interaction between the iodine and oxygen atoms (a) and a crystal packing diagram of 2-iodo-3,4,5-trimethoxybenzoic acid, viewed along the *b* axis (the hydrogen bonds are indicated by dashed lines) (b).**Table 3**

Hydrogen bonds and weak interactions in the title compound.

D–H...A	D–H (Å)	H...A (Å)	D–A (Å)	D–H...A (°)
Hydrogen bond				
O16–H16...O15 ⁱ	0.82	1.809	2.628(2)	175.8
Intramolecular interaction				
I11...O15			3.056(5)	
Weak interactions				
C1–H1B...O8 ⁱⁱ	0.96	2.66	3.368(16)	131.4
C1 H1C O2 ⁱⁱ	0.96	2.43	3.178(15)	134.4
C13–H13A...O16 ⁱⁱⁱ	0.96	2.88	3.216(18)	101.9

Symmetry codes: (i) $1 - x, -y, 1 - z$; (ii) $x, 1 + y, z$; (iii) $1 - x, -1/2 + y, 3/2 - z$.**Fig. 3.** FTIR spectrum of 2-iodo-3,4,5-trimethoxybenzoic acid in the high-frequency region.

vibrations. According to the well-known Wilson's notation these modes are designated as **8a**, **8b**, **19a**, and **19b** [33]. In general, the position and intensity of these modes are affected not only by the nature but also by the position and number of substituents

**Fig. 4.** FTIR spectrum of 2-iodo-3,4,5-trimethoxybenzoic acid in the wavenumber interval from 1800 to 950 cm^{-1} .

around the aromatic ring. In the spectrum of 2-iodo-3,4,5-trimethoxybenzoic acid three of these bands of medium intensity are observed at 1577, 1554, and 1484 cm^{-1} (Fig. 4). Interestingly the position of the fourth one cannot be located in the spectrum. It is most probably “hidden” in the series of bands attributed to the characteristic asymmetric and symmetric C–H deformation vibrations of the methyl groups or amongst the rest of bands localized in the range of 1320–1500 cm^{-1} .

According to Varsanyi [31] the frequency regions of **14** (Kekule mode), **1** (ring breathing), and of **12** (ring triangular angle bending) modes (radial vibrations) are at 1200–1260, 1120–1200, and 1020–1090 cm^{-1} , respectively. The frequency values of these modes presented in the spectrum in Fig. 4 are observed at 1231, 1182, and 1022 cm^{-1} .

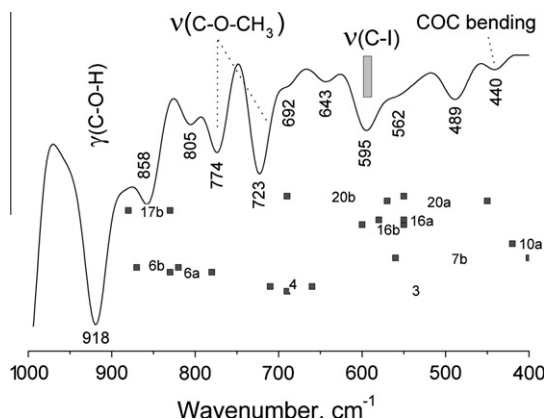


Fig. 5. FTIR spectrum of 2-iodo-3,4,5-trimethoxybenzoic acid (KBr) in the region of low frequencies ($1000\text{--}400\text{ cm}^{-1}$).

The bands of very weak to medium intensities observed at 858, 805, 692, 643, 562, 489 and 440 cm^{-1} are assigned to CCC deformations of the phenyl ring.

6.3. Carboxylic group vibrations

In the condensed state carboxylic acid dimers have a very broad and intense OH stretching band observed in the region of $3100\text{--}2500\text{ cm}^{-1}$. The intense CH stretching vibrations, combinations vibrations, as well as overtones of different functional groups are also located in the same wavenumber interval. In spite of all, the band at 2999 cm^{-1} can be assigned to the O–H stretching vibrations and the bands observed in the region of $2500\text{--}2680\text{ cm}^{-1}$ assigned to the asymmetric O–H...O stretching vibrations.

The considerable change in the profile of the spectral bands corresponding to the $\nu(\text{C=O})$ and $\nu(\text{C-O})$ vibrations has been used as an additional indication for the presence of iodine in the structure of the product. The observed shift in the position of the peak characteristic for carbonyl stretching towards to higher wavenumbers (1690 cm^{-1}), as compared with that of 3,4,5-trimethoxybenzoic acid (1680 cm^{-1}), is indicative for the presence of a strong intramolecular interaction (electrostatic effect transmitted through space) between the adjacent electronegative iodine and oxygen atoms. As a rule, the increase in C=O stretching frequency should be associated with the suppression of the contribution of dipolar carbonyl resonance form [34]. The strong intramolecular interaction between iodine and oxygen atoms is also confirmed by the single crystal X-ray diffraction analysis. The latter has revealed the presence of an intramolecular O...I interaction [O(15)–I(11)

distance $3.056(5)\text{ \AA}$], as well as, an expected electrostatic repulsion between O and I atoms reflected in the deviation from planar to “syn-periplanar” conformation between the carboxylic acid group and phenyl ring system (Fig. 6).

Noteworthy similar structural changes induced by a steric hindrance between adjacent bulky substituents (iodine atom and carboxylic group) have also been reported in the case of *ortho*-iodobenzoic acid (Fig. 6a) [35]. On contrary, in our case of 2-iodo-3,4,5-trimethoxybenzoic acid, the interplanar angle between the carboxyl group and the benzene ring has slightly decreased (Fig. 6b). Most probably, this phenomenon can be attributed to a negative hyperconjugative interaction between the nonbonding lone pair orbital on the iodine atom (n_I) and the antibonding $\pi_{\text{C=O}}^*$ orbital; an effect which should also be taken into consideration besides the primary field effect. Consequently, it is safe to say that this type of orbital interaction acts in a reverse manner to the field effect, i.e. it tends to favor the contribution of dipolar carbonyl resonance form and to restrict the dihedral C(7)–C(12)–C(14)–O(15) angle.

The single crystal X-ray diffraction analysis has also shown the presence of two equivalent O–H...O hydrogen bonds connecting two 2-iodo-3,4,5-trimethoxybenzoic acid molecules into an acid dimer. Since the hydrogen bonding acid dimers possess a center of symmetry, the two acid units will oscillate in-phase and out-of-phase with respect to each other. The out-of-phase (asymmetric) vibrations are IR-active and responsible for the appearance of the asymmetrical C=O stretching band in the range of $1700\text{--}1680\text{ cm}^{-1}$, C(O)–O stretching band at 1323 cm^{-1} , and in-plane and out-of-plane C–O–H bending vibrations at 1403 and 918 cm^{-1} , respectively. The band observed at 1373 cm^{-1} has also substantial O–H bending character. According to C. James et al. [36] the enhanced intensity of this band results from the intermolecular hydrogen bonding interaction.

6.4. C–I vibration

According to E. Mooney, the stretching modes of C–X groups (X = Cl, Br, and I) lie in the frequency range of $1129\text{--}480\text{ cm}^{-1}$ [37]. Usually, the iodine containing compounds absorb in a narrower frequency interval ($650\text{--}450\text{ cm}^{-1}$). In this study the band observed at 595 cm^{-1} is assigned to C–I stretching vibrations.

7. ^1H NMR and ^{13}C NMR analyses of 2-iodo-3,4,5-trimethoxybenzoic acid

The ^1H NMR spectrum of 2-iodo-3,4,5-trimethoxybenzoic acid (Fig. 7a) shows the expected three singlet signals for the three inequivalent MeO-groups at 3.88, 3.91, and 3.95 ppm. A singlet

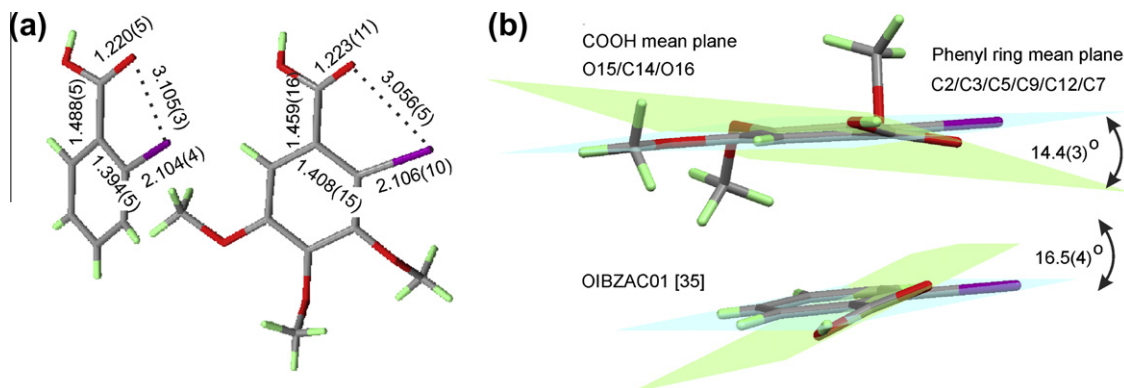


Fig. 6. Molecular structures of 2-iodo-3,4,5-trimethoxybenzoic acid and of *ortho*-iodobenzoic acid, and selected their bond lengths (Å) (a) and a graphical illustration of the interplanar angle between the mean planes of the COOH group and the phenyl ring (b).

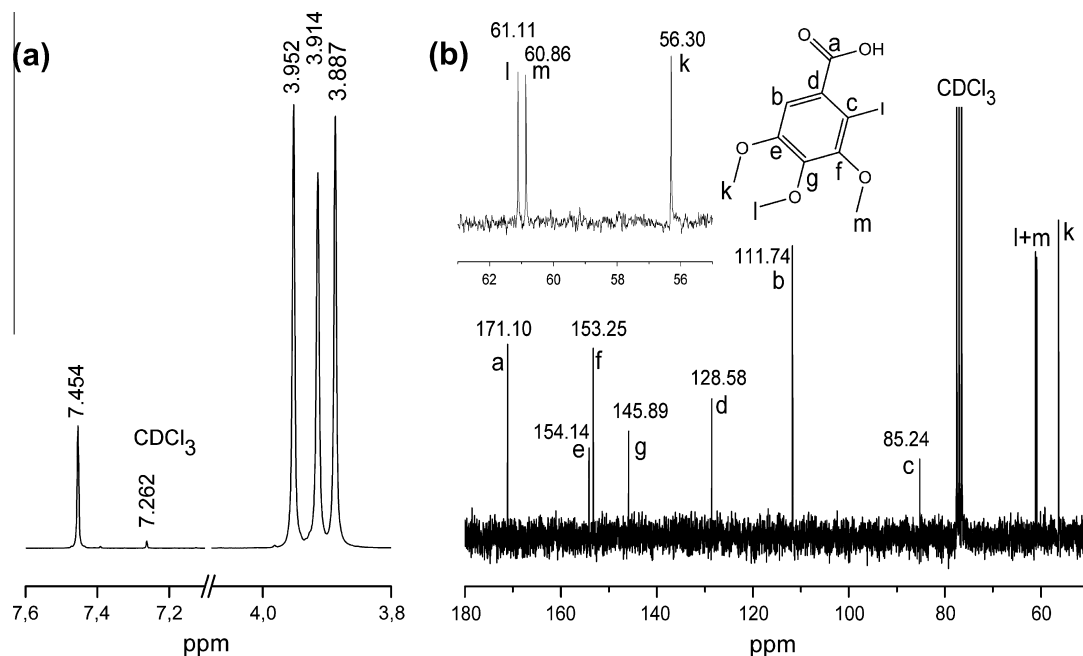


Fig. 7. ^1H NMR (a) and ^{13}C NMR (b) spectra of the 2-iodo-3,4,5-trimethoxybenzoic acid.

signal characteristic for a $=\text{C}-\text{H}$ proton at 7.45 ppm is also observed in the spectrum. The observed chemical shift in the $=\text{C}-\text{H}$ proton resonance from the expected position at 7.0 ± 0.02 ppm (estimated on the basis of the inductive effect of substituents) to downfield values might be attributed both to the presence of the aforementioned steric and electric (field) effects as well as to the presence of an anisotropy effect induced by the hydrogen bonded carboxylic groups.

The signals observed at 85.24, 111.74, 128.58, 145.89, 153.25, and 154.14 ppm in the ^{13}C NMR spectrum (Fig. 7b) have been assigned to the six aromatic carbon atoms. The signals observed at 56.30, 60.86, and 61.11 ppm have been assigned to the three methoxy carbons **k**, **m** and **l**, respectively, while the signal at 171.11 ppm has been assigned to the $-\text{COOH}$ carbon atom.

8. Conclusion

The presented synthetic procedure is a convenient route to the direct and high-yield synthesis of 2-iodo-3,4,5-trimethoxybenzoic acid. The product has been characterized by single crystal X-ray diffraction analysis, FTIR, ^1H NMR, and ^{13}C NMR spectroscopy to estimate the efficiency of the modified experimental design. This design allowing regular and continuous iodine loading into the reaction media, and a great reduction of the solvent used has a number of advantages to the preparative procedures reported so far.

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Appendix A. Supplementary material

Supplementary data associated with this article can be found, in the online version, at <http://dx.doi.org/10.1016/j.molstruc.2012.10.039>.

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