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Chemistry

DIETHYL 2,2′-(1*H*-1,2,4-TRIAZOLE-3,5-DIYL)DIACETATE: SYNTHESIS STRATEGIES, CHEMICAL BEHAVIOR, CRYSTAL STRUCTURE AND HIRSHFELD SURFACE ANALYSIS

Oleksandr Vashchenko[1], Dmytro Khomenko[1], Roman Doroshchuk[1], Oleksandr Vynohradov[1], Ilona Raspertova[1,✉], Volodymyr Trachevskii[2], Sergiu Shova[3], Rostyslav Lampeka[1]

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Abstract. 1,2,4-Triazolyl-3,5-diacetic acid ethyl ester was synthesized by condensation of hydrazine hydrate and N-acyl ethyl 3-ethoxy-3-iminopropanoate. Other methods for the synthesis are considered and their comparative analysis is carried out. The molecular structure of the title compound was established by X-ray analysis. Hirshfeld surface analysis was performed to investigate intermolecular interactions.

Keywords: 1,2,4-triazole, iminoesters, NMR spectroscopy, X-ray analysis, Hirshfeld surface analysis.

1. Introduction

1,2,4-Triazoles are prominent representatives of nitrogen-containing heterocycles, comprising five-membered rings with two carbon atoms and three nitrogen atoms positioned at the 1st, 2nd and 4th positions. With all atoms sp^2-hybridized, these structures exhibit aromatic character, akin to pyrazole and imidazole, suggesting their potential utility in studying various biochemical processes[1–3]. In drug design, triazoles are increasingly utilized as bioisosteres and linkers to enhance the potency of lead molecules, with the introduction of additional functional groups enhancing specific properties[4–8]. Notably, carboxyl and ether groups are well-known pharmacophores in the design of compounds with anti-inflammatory activity[9].

In our previous work, we investigated the synthesis and modification of derivatives of 1,2,4-triazolyl carboxylic[10] and acetic acids[11, 12], highlighting their potential for constructing target substances due to the presence of numerous diversification points. Furthermore, 1,2,4-triazoles show promise as ligands for complexing metal ions, prompting our interest in exploring their catalytic[13, 14], fluorescent[14, 15], and cytotoxic activities[16], particularly with chelators like 3-(2-pyridile)-1,2,4-triazole.

Recently, our focus has extended to copper(II) coordination compounds with different 1,2,4-triazole-containing chelators, demonstrating the crucial role of chelating arms in forming specific coordination compounds. Additionally, we have reported the complexation of "hybrid" ligands containing both 2-pyridyl and carboxyethyl substituents connected through carbon atoms to the 1,2,4-triazole core, yielding both typical and unusual coordination compounds with copper(II)[13, 17] and palladium (II)[18].

As a logical extension of our previous studies and to expand the chemical space of 1,2,4-triazoles, we propose investigating 1,2,4-triazolyl diacetic acid derivatives. However, a literature analysis revealed that 1,2,4-triazolyl-3,5-diacetic acid has not been synthesized previously, with only one study focusing on the synthesis of the corresponding diethyl ester. Kiseleva *et al.* achieved the synthesis of 1,2,4-triazolyl-3,5-diacetic acid diethyl esters from ethyl 3-ethoxy-3-iminopropanoate hydrochloride and hydrazine with low yield[19]. Therefore, prior to investigating the coordination chemistry of 1,2,4-triazolyl-3,5-diacetic acid, we sought to improve the methodology for its synthesis. In this paper, we present the molecular structure and two novel synthesis routes for 1,2,4-triazolyl-3,5-diacetic acid diethyl ester, starting from chloroethylmalonate.

2. Experimental

2.1. Materials

All the starting materials and solvents were obtained from Enamine Ltd. and UORSY, and were used as received.

[1] Department of Chemistry, Taras Shevchenko National University of Kyiv, 64/13, Volodymyrska str., Kyiv, 01601, Ukraine
[2] G.V. Kurdyumov Institute for Metal Physics, N.A.S. of Ukraine, 36, Academician Vernadsky Blvd., Kyiv, 03680, Ukraine
[3] "PetruPoni" Institute of Macromolecular Chemistry, 41 A, Aleea Gr. GhicaVoda, Iasi, 700487, Romania
✉ *ilonabatyuk@gmail.com*

2.2. Methods

^{1}H NMR spectra were recorded on Varian Mercury 400 (400 MHz) spectrometer. ^{13}C NMR spectra were recorded on AVANCE-400 Bruker (100.613 MHz) spectrometer. All spectra are referenced to DMSO-d_6 residual DMSO peak (^{1}H NMR δ = 2.50 ppm; ^{13}C NMR δ = 39.5 ppm). Coupling constants are quoted to the nearest 0.1 Hz. Splitting patterns are abbreviated as follows: singlet (*s*), doublet (*d*), triplet (*t*), quartet (*q*), multiplet (*m*), broad singlet (*brs*) and combinations thereof. Elemental analyses were carried out with Perkin-Elmer 2400 CHN Analyzer. Melting points (°C, uncorrected) were measured with OptiMelt Automated Melting Point System (MPA 100). The IR spectra (KBr, pellet) were recorded with Spektrum BX Perkin Elmer spectrometer.

2.3. Experimental Procedures

TR^1 (Eq. (1)): Hydrazine hydrate (10.4 mL, 0.2 mol) was added to a stirred solution of ethyl 3-ethoxy-3-iminopropanoate (80 g, 0.5 mol) in 500 mL dry ethanol. The internal temperature was maintained between –5 °C and 0 °C. After complete addition of hydrazine hydrate, the reaction mixture was slowly heated to room temperature and stirred for an additional 2 hours. The precipitated 3-amino-1H-pyrazol-5-ol was filtered off, and the resulting solution was refluxed for 24 hours. The reaction mixture was then concentrated *in vacuo* and the residue was recrystallized from 500 mL of toluene to yield **TR^1** as white crystals. (yield 29 %).

TR^1 (Eq. (2a)): Sodium ethylate (0.02 mol, 0.46 g of sodium in 25 mL of ethanol) was added to a solution of Ethyl malonyl hydrazide hydrochloride (4.0 g, 0.022 mol) in 25 mL of dry ethanol. The precipitated sodium chloride was filtered off, and then ethyl 3-ethoxy-3-iminopropanoate (3.8 g, 0.024 mol) was added to the solution. The reaction mixture was refluxed for 6 hours and then concentrated *in vacuo.* The resulting residue was recrystallized from 20 mL toluene to yield **TR^1** as white crystals (yield 20 %).

TR^1 (Eq. 2b): Chlorethylmalonate (1.92 mL, 0.015 mol) was added dropwise to a solution of ethyl 3-ethoxy-3-iminopropanoate (1.59 g, 0.01 mol) and N,N-diisopropylethylamine (1.9 mL, 0.0115 mol) in 25 mL of dichloromethane. The internal temperature was maintained between 0 °C and +5 °C. After complete addition of chlorethylmalonate, the reaction mixture was slowly heated to room temperature and stirred for 6 hours. The solution was then washed with water (3×10 mL), dried over sodium sulfate, and concentrated in vacuo. The resulting brown oil was dissolved in 25 mL of dry ethanol, and hydrazine hydrate was added. The reaction mixture was stirred for 16 hours and then concentrated *in vacuo.* The resulting residue was recrystallized from 10 mL toluene to give **TR^1** as white crystals. (yield 42 %). M.p. 104–106 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 1.18 (6H, *t*, *J* = 6.0 Hz, $\underline{CH_3}CH_2$), 3.70 (2H, *s*, CH_2), 3.82 (2H, *s*, CH_2), 4.09 (4H, *d*, *J* = 6.0 Hz, $CH_3\underline{CH_2}$), 13.67 (1H, *brs*, NH). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.9, 32.2, 34.2, 60.3, 60.4, 150.0, 157.0, 168.2, 169.3. IR (KBr, cm^{-1}): 3422, 2993, 1733, 1624, 1457, 1384, 1333, 1201, 1034. Anal. calc. for $C_{10}H_{15}N_3O_4$: C, 49.79; H, 6.27; N, 14.72. Found: C, 49.51; H, 6.492; N, 17.62.

3-Amino-1H-pyrazol-5-ol (1). 3-Amino-1H-pyrazol-5-ol was one of the byproducts in Eq. (1). Brown crystals (yield 38 %). M.p. >220 °C. ^{1}H NMR (400 MHz, DMSO-d_6): *δ* = 3.07 (1.66 H); 4.19 (0.21 H); 5.65 (0.49 H); 5.86 (1.56 H); 8.69 (0.33 H); 9.83 (0.70 H). IR (KBr, cm^{-1}): 3333, 3166, 1687, 1604, 768, 551. Anal. calc. for $C_3H_5N_3O$: C, 36.36; H, 5.09; N, 42.40. Found: C, 36.42; H, 4.98; N, 42.41.

Na$_2$TR^2. Sodium hydroxide (0.8 g, 0.02 mol) was added to a solution of **TR^1** (2.41 g, 0.01 mol) in 15 mL of water, and the mixture was refluxed for 6 hours. The solution was then concentrated in vacuo, and the resulting oil was stirred in 10 mL of DMF for 2 hours. The resulting white precipitate was filtered off, washed with DMF (3×5 mL) and then washed with diethyl ether (3×5 mL) to yield **Na$_2$TR^2** as white crystals. (yield 95 %). M.p. >220 °C. ^{1}H NMR (400 MHz, D_2O): δ = 3.63 (4H, CH_2). ^{13}C NMR (100 MHz, D_2O): δ = 34.2, 154.7, 175.4. IR (KBr, cm^{-1}): 3382, 1595, 1386, 1263, 1067, 682. Anal. calc. for $C_6H_5N_3Na_2O_4$: C, 31.46; H, 2.99; N, 18.34. Found: C, 31.48; H, 3.02; N, 18.28.

TR^2. Hydrochloric acid (2.81 N, 1.78 mL) was added dropwise to the aqueous solution of **Na$_2$TR^2** (0.558 g, 0.0025 mol) in 0.5 mL of water. The solution was stirred at 0 °C for 5 minutes and the resulting white precipitate was filtered off, washed with cold water (3×1 mL) and dried in air to yield **TR^2** as white powder (yield 11 %). M.p. 97–98 °C. ^{1}H NMR (400 MHz, DMSO-d_6): δ = 3.63 (4H, CH_2). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 33.5, 154.1, 170.4. IR (KBr, cm^{-1}): 3324, 1971, 1696, 1545, 1403, 1269, 1019, 793. Anal. calc. for $C_6H_7N_3O_4$: C, 38.93; H, 3.81; N, 22.70. Found: C, 38.92; H, 3.79; N, 22.75.

TR^3. Methyl iodide (1.63 g, 0.0115 mol) was added to a solution of **TR^1** (2.4 g, 0.01 mol) and potassium carbonate (2.07 g, 0.015 mol) in 50 mL DMF. The reaction mixture was stirred at room temperature for 6 hours. Subsequently, the reaction mixture was concentrated *in vacuo*, and the resulting residue was diluted with water and extracted with methyl *tert*-butyl ether (3×10 mL). The combined organic layers were washed with water (1×10 mL), dried over Na_2SO_4, and concentrated *in vacuo* to yield pure **TR^3** as a yellow oil (yield 20 %). ^{1}H NMR (400 MHz, DMSO-d_6): *δ* = 1.18 (3H, *t*, *J* = 7.2 Hz, $\underline{CH_3}CH_2$), 1.20 (3H, *t*, *J* = 7.2 Hz,

$\underline{CH_3}CH_2$), 3.64 (2H, *s*, CH_2), 3.75 (3H, *s*, CH_3), 4.00 (2H, *s*, CH_2), 4.07 (2H, *d*, *J* = 6.0 Hz, $CH_3\underline{CH_2}$), 4.12 (2H, *d*, *J* = 6.0 Hz, $CH_3\underline{CH_2}$). ^{13}C NMR (100 MHz, DMSO-d_6): δ = 13.9, 14.0, 31.7, 34.1, 35.1, 60.5, 61.1, 149.8, 155.9, 168.0, 169.2. IR (KBr, cm^{-1}): 3559, 2985, 1733, 1508, 1377, 1333, 1260, 1188, 1034. Anal. calc. for $C_{10}H_{15}N_3O_4$: C, 51.76; H, 6.71; N, 16.46. Found: C, 51.78; H, 6.67; N, 16.41.

Ethyl malonyl hydrazide (3). Chlorethylmalonate (3.76 g, 0.025 mol) was added dropwise to a solution of *tert*-butoxycarbonyl hydrazide (3.3 g, 0.025 mol) and N,N-diisopropylethylamine (4.76 mL, 0.0288 mol) in 50 mL of dichloromethane. The internal temperature was maintained between 0 °C and +5 °C. After the addition of all chlorethylmalonate the reaction mixture was slowly heated to room temperature and stirred for 6 hours. The solution was then washed with water (3×10 mL), dried over sodium sulfate, and concentrated in vacuo. The resulting brown oil was dissolved in 50 mL of 0.5 M HCl in dry ethanol. The reaction mixture was stirred for 18 hours and the precipitate was filtered off, washed with ethanol (3×2 mL) and dried to yield ethyl malonyl hydrazide hydrochloride as white crystals (yield 38 %). M.p. 118–120 °C. ^{1}H NMR (400 MHz, DMSO-d_6): 1.19 (3H, *t*, *J* = 6.8 Hz, $\underline{CH_3}CH_2$), 3.44 (2H, *s*, CH_2), 4.10 (2H, *d*, *J* = 6.0 Hz, $CH_3\underline{CH_2}$), 5.49 (2H, *brs,* NH), 11.36 (1H, *s*, NH). IR (KBr, cm^{-1}): 3197, 2673, 2920, 1745, 1596, 1495, 1403, 1277, 1144. Anal. calc. for $C_5H_{11}N_2O_3Cl$: C, 32.89; H, 6.07; N, 15.34. Found: C, 32.68; H, 6.21; N, 15.63.

2.4. Crystal Data Collection and Refinement

Crystallographic measurements for compound **TR^1** were carried out with an Oxford-Diffraction XCALIBUR E CCD diffractometer equipped with graphite-monochromated Mo-K_α radiation. The crystals were placed 40 mm from the CCD detector. Single crystals were positioned at 40 mm from the detector and 555 and 244 frames were measured each for 25, 5, s over 1° scan width for **TR^1** respectively. The unit cell determination and data integration were carried out using the CrysAlis package of Oxford Diffraction[20]. The structures were solved by direct methods using Olex2[21] software with the SHELXS structure solution program and refined by full-matrix least-squares on F^2 with SHELXL-97[22]. Atomic displacements for non-hydrogen, non-disordered atoms were refined using an anisotropic model. The hydrogen atoms have been placed by Fourier Difference accounting for the hybridisation of the supporting atoms and the possible presence of hydrogen bonds in the case of donor atoms.

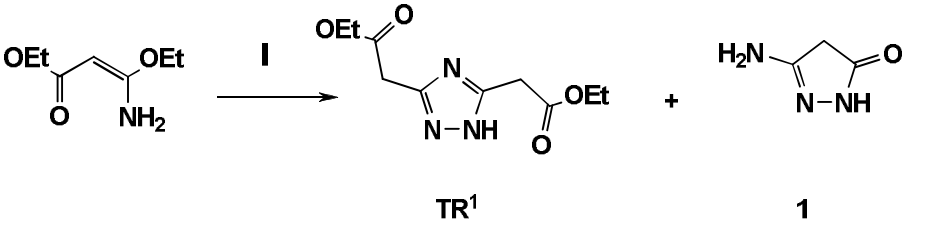
TR^1. Empirical formula: $C_{10}H_{15}N_3O_4$, *Mr* = 241.25 g mol^{-1}, size 0.45x0.10×0.10 mm^3, monoclinic, space group $P2_1/n$, *a* = 5.0374(5) Å, *b* = 19.404(2) Å, *c* = 12.2055(12) Å, β = 96.114(10), *V* = 1186.3(2) $Å^3$, *Z* = 4, ρ_{calcd} = 1.351 g cm^{-3}, μ(Mo*K*α) = 0.106 mm^{-1}, *F*(000) = 512, 4761 reflections in *h*(–5/5), *k*(–23/22), *l*(–14/14), measured in the range 3.95 ≤ Θ ≤ 50.05, completeness Θ_{max}=100 %, 2078 independent reflections, R_{int} = 0.0571, 156 parameters, 0 restraints, R_{1obs}=0.0607, wR_{2obs} = 0.1127, R_{1all} = 0.0793, $wR2_{all}$ = 0.1213, GoF = 1.106, largest difference peak and hole: 0.32/–0.22 e A^{-3}.

3. Results and Discussion

3.1. Synthetic Procedures

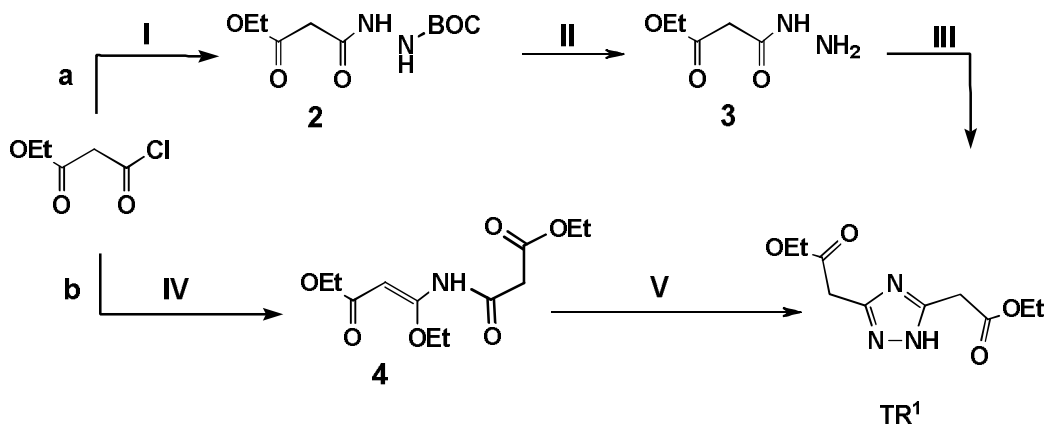
As described above, the reaction of ethyl 3-ethoxy-3-iminopropanoate hydrochloride with hydrazine leads to the formation of 1,2,4-triazolyl-3,5-diacetic acid ethyl ester only in 33 % yield[19]. Slight changes in reaction conditions and the use of ethyl 3-ethoxy-3-iminopropanoate in the form of a base didn`t increase the reaction yield. Unsurprisingly, aminopyrazolone **1** was one of the byproducts in this reaction (Eq. (1))[23]. Therefore, we decided to explore alternative routes for the synthesis of **TR^1** (Eq. 2). The synthesis of 1,2,4-triazolyl-3,5-diacetic acid diethyl ester **TR^1** was performed in three steps (Eq. (2a)) or two steps (Eq. (2b)) starting from commercially available chloroethylmalonate.

For the preparation of **TR^1** according to Eq. (2a), we used a fairly common method for the synthesis of the 1,2,4-triazole heterocycle from ethyl 3-ethoxy-3-iminopropanoate and ethyl malonyl hydrazide. BOC-hydrazide **2** was prepared according to a standard procedure[24] from BOC-hydrazine and chloroethylmalonate. Removal of the BOC-protection yielded hydrochloride **3** in high yields. Heating ethyl malonyl hydrazide with ethyl 3-ethoxy-3-iminopropanoate at reflux resulted in the formation of **TR^1** with an overall yield 20 %.



(1)

TR^1 **1**



(2)

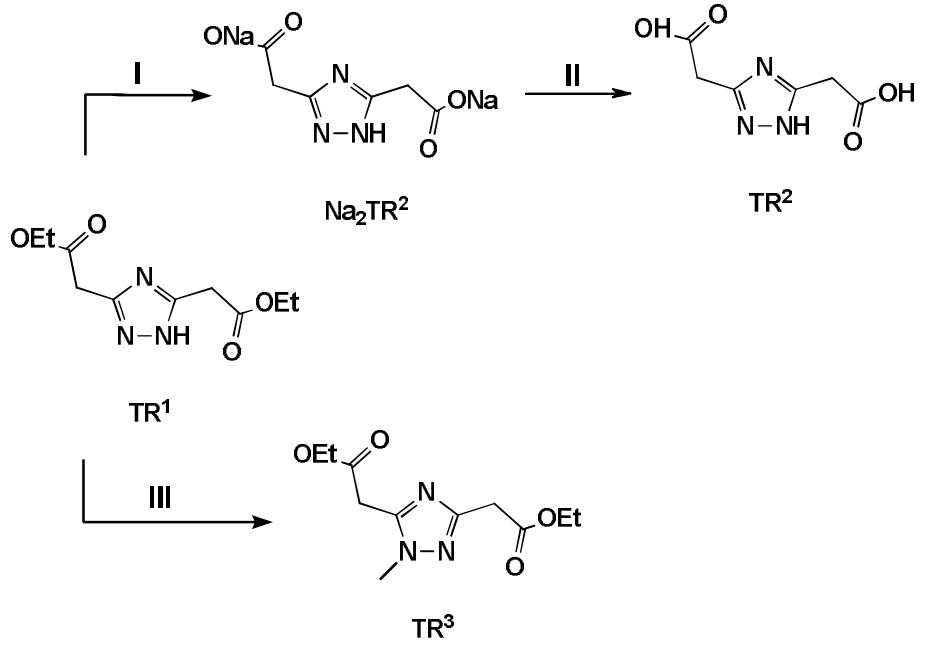
Conditions and reagents: (I) hydrazine hydrate, ethanol, 0–5 °C, stirring for 2 hours; reflux 18 hours.

Conditions and reagents: (I) BOC-hydrazine, N,N-diisopropylethylamine, dichloromethane, 0–5 °C, 1 hour; (II) HCl, ethanol, rt, 6 hours; (III) ethyl 3-ethoxy-3-iminopropanoate, ethanol, reflux, 6 hours; (IV) ethyl 3-ethoxy-3-iminopropanoate, N,N-diisopropylethylamine, dichloromethane, 0–5 °C, 6 hours; (V) hydrazine hydrate, ethanol, rt, 4 hours.

The reaction of 3-ethoxy-3-iminopropanoate with chloroethylmalonate produced intermediates **4**. Subsequent reaction of imidate **4** with hydrazine yielded the title compound. The overall yield of this reaction was 42 %, which was higher than that obtained with Eq. (2a) or the previously described method[19]. It should be noted that potentially this reaction could also be used for the synthesis of N^1 or N^2 substituted 1,2,4-triazolyl-3,5-diacetic acid diethyl esters[25]. The identity of **TR^1** obtained by different methods was confirmed using ^{1}H NMR, ^{13}C NMR, IR-spectroscopy, and elemental analysis.

Starting from **TR^1**, we obtained the corresponding disodium salt **Na_2TR^2**, diacid **TR^2** and N^1-methylated diester **TR^3** (Eq. (3)).

Conditions and reagents: (I) NaOH, water, reflux, 4 hours; (II) 2.5N HCl, water, 5 °C; (III) methyl iodide, N,N-dimethylformamide, K_2CO_3, stirring, rt, 6 hours.



(3)

3.2. Spectroscopy

In the IR spectra of **TR^1**, there are strong peaks at 1738 cm^{-1} assigned to stretching vibrations ν(C=O) and at 1202 cm^{-1} assigned to bending vibrations ν(C-O-C) of ester groups.

A characteristic feature in the ^{13}C NMR spectra for **TR^1** in DMSO-d_6 solution is the separate position of all carbon signals, except the methyl group, which was not observed in the ^{13}C NMR spectra acquired in $CDCl_3$ solution (Fig. 1). The same observation was made for the signals of methylene groups in the ^{1}H NMR spectrum.

This may be due to the slow interconversion of tautomers, resulting in non-equivalence of atoms situated close to the triazole. This phenomenon can be caused not only by the formation of intramolecular hydrogen bonds but also by association with dimethyl sulfoxide molecules, which stabilize tautomers[15]. However, the presence of an acidic proton in **TR^1** is the reason for the broadening of carbon signals in the ^{13}C NMR spectra, especially manifested in the ^{13}C NMR spectra of **TR^1** in $CDCl_3$ solution. Here, the low intensity of quaternary carbons, together with the possibility of **TR^1** existing in several tautomeric forms, results in the absence of precise signals from triazolic carbons.

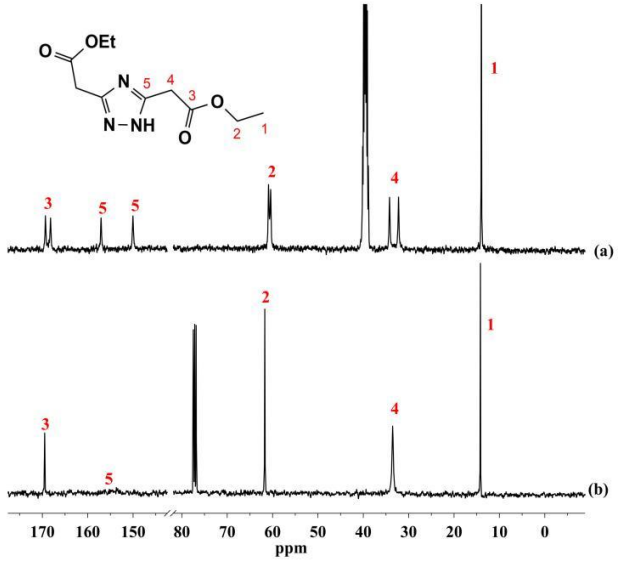


Fig. 1. ^{13}C NMR spectra of TR^1 in DMSO-d_6 (a) and $CDCl_3$ (b)

3.3. X-Ray Analysis of TR^1

The single crystal X-ray study confirmed that compound **TR^1** has a molecular crystal structure consisting of neutral molecules, as shown in Fig. 2. No co-crystallized solvent was found in the crystal. The main crystal structure motif of **TR^1** can be described as a parallel packing of weakly interacting infinite chains formed by the intermolecular hydrogen bonding of N2-H groups as donors towards N1 atoms as acceptors. The structure of the one-dimensional supramolecular chain is depicted in Fig. 3.

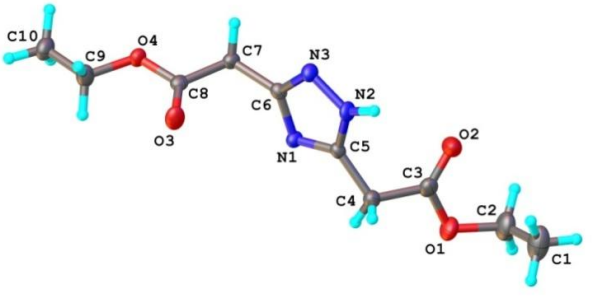


Fig. 2. X-ray molecular structure of **TR^1** with atom labeling scheme and thermal ellipsoids at 50 % probability level

3.4. Hirshfeld Surface Analysis

The Hirshfeld surface analysis and the associated two-dimensional fingerprint plots were performed using Crystal Explorer 17.5 software[26], with a standard resolution of the three-dimensional d_{norm} surfaces plotted over a fixed color scale of –0.5024 (red) to 1.2024 (blue) a.u. The dark-red spots arise as a result of short interatomic contacts and represent negative d_{norm} values on the surface, while the other weaker intermolecular interactions appear as light-red spots. View of the three-dimensional Hirshfeld surface of the title compound plotted over d_{norm} are shown in Fig. 4. The Hirshfeld surface representations with the function fragment patch plotted onto the surface are in the range of 0.0000 to 14.0000 with the mean value of 7.3638 (Fig. 5).

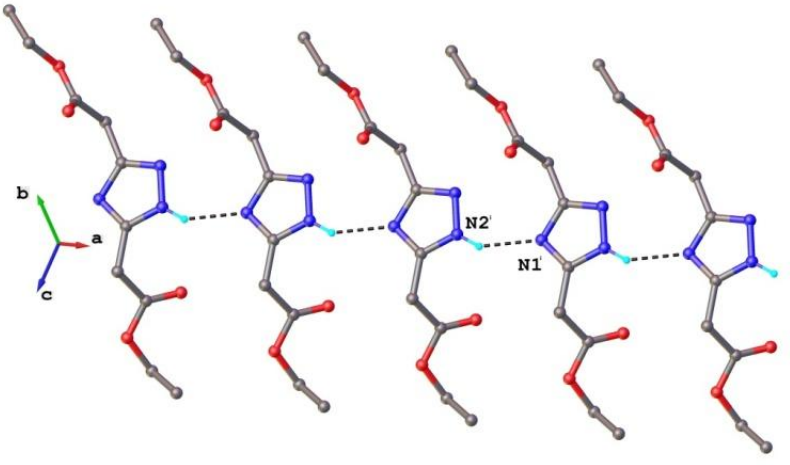


Fig. 3. View of the 1D supramolecular architecture in the crystal structure of **TR^1**.
H-bond parameters: N2-H···N1 [N2-H 0.88 Å, H···N1 2.09 Å, N2···N1(1 + *x*, *y*, *z*) 2.866(3) Å, N2-H···N1 146.6°].
Only H-atoms involved in hydrogen bonding are shown for clarity

The coordination environment of the title molecule is determined by observing the color patches on the Hirshfeld surface, which indicate proximity to neighboring molecules. Also the Hirshfeld surfaces mapped over d_{norm} and fragment patches are shown for the H···H (Fig. 6, *a*), H·O/O···H (Fig. 6, *b*), H···N/N···H (Fig. 6, *c*) and H···C/C···H (Fig. 6, *d*) contacts, the overall two-dimensional fingerprint plot and the decomposed two-dimensional fingerprint plots are given in Fig. 7. The red spots appearing near N1 and H2 atoms indicate their roles as the respective donors or acceptors in the N–H···N hydrogen bonds. The most significant contributions to the overall crystal packing are from H···H (45.4 %), H···O/O···H (29.5 %), H···N/N···H (17 %) and H···C/C···H (5.4 %) contacts. There is a small contribution from N···C/C···N (1.2 %) weak intermolecular contacts. The smallest contribution of the other weak intermolecular contacts (N···O/O···N – 0.9 %, C···O/O···C – 0.3 %, C···C – 0.1 % and O···O – 0.1 %) has a negligible effect on the packing. The relative percentage contributions to the overall Hirshfeld surface by elements: H···all atoms – 69 %, O···all atoms –16.8 %, N···all atoms – 10.4 % and C···all atoms – 3.8 %. The Hirshfeld surface representations with the function fragment patch plotted onto the surface also illustrate the significance of hydrogen atom contacts in the formation of crystal packing. Also, quantitative physical properties of the Hirshfeld surface for this compound were obtained, such as molecular volume (289.95 Å^3), surface area (296.67 Å^2), globularity (0.714), as well as asphericity (0.513).

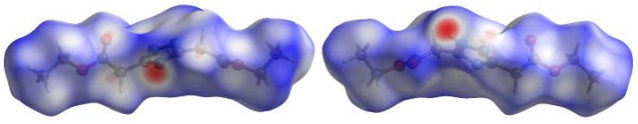


Fig. 4. View of the three-dimensional Hirshfeld surface of the title compound plotted over d_{norm}

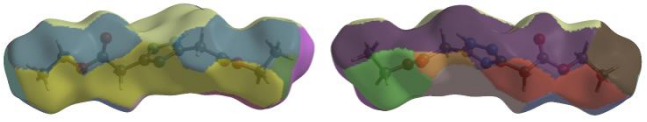


Fig. 5. The Hirshfeld surface representation with the function fragment patch plotted onto the surface

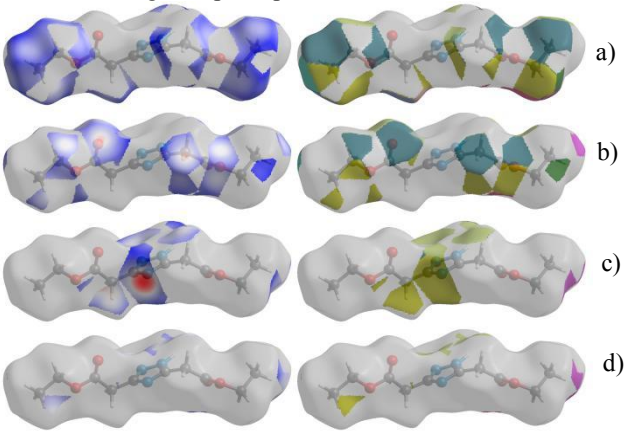


Fig. 6. Hirshfeld surfaces mapped over d_{norm} and fragment patches for (a) H···H, (b) H···O/O···H, (c) H···N/N···H and (d) H···C/C···H interactions

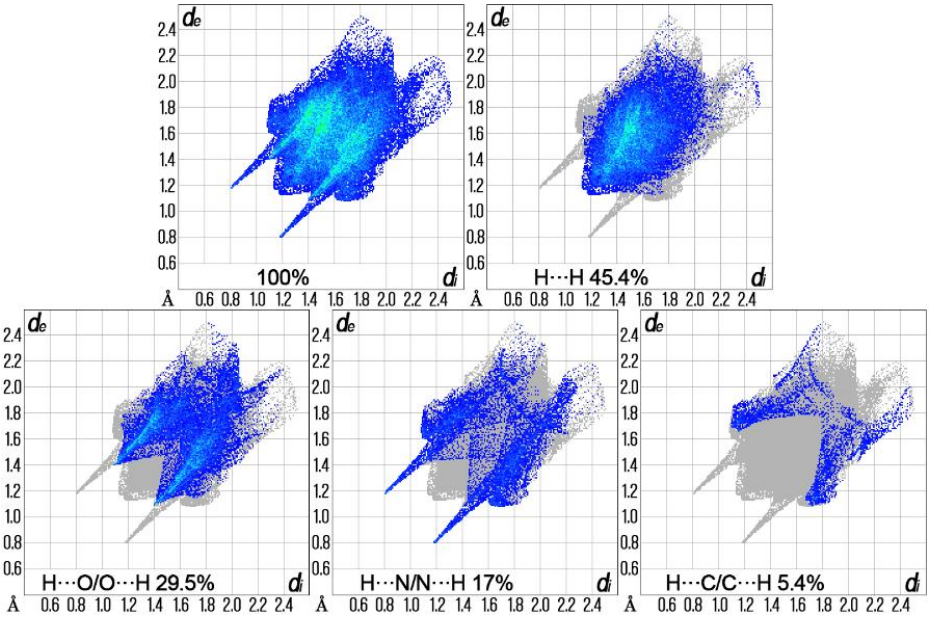


Fig. 7. The overall two-dimensional fingerprint plot and those delineated into specified interactions

4. Conclusions

Two novel synthetic routes for the preparation of 1,2,4-triazolyl-3,5-diacetic acid diethyl ester were explored. While the traditional method gives low product yield, modifications involving 3-ethoxy-3-iminopropanoate and chloroethylmalonate showed promising results, enhancing the overall yield to 20 % and 42 %, respectively. These alternative routes offer efficient pathways for the synthesis of target substances and potentially its derivatives. The crystal structure of the title compound was established using X-ray analysis. The crystal structure revealed the formation of one-dimensional supramolecular chains driven by intermolecular hydrogen bonding interactions, offering valuable information for understanding its solid-state behavior and potential applications. This compound served as the precursor for obtaining three new compounds, namely N-methyl-1,2,4-triazolyl-3,5-diacetic acid ethyl ester, 1,2,4-triazolyl-3,5-diacetic acid and 1,2,4-triazolyl-3,5-diacetic acid disodium salt. According to the Hirshfeld surface analysis, the most significant contributions to the overall crystal packing are from H···H (45.4 %), H···O/O···H (29.5 %), H···N/N···H (17 %) and H···C/C···H (5.4 %) contacts. H-atom contacts play a crucial role in determining the crystal packing. The abundance of interactions involving hydrogen atoms indicates that Van der Waals forces and hydrogen bonding are the primary contributors to the crystal structure. The globularity value (0.714) for **TR**[1] is less than one, suggesting a modest deviation from a spherical surface and indicating that this molecular surface is more structured compared to a sphere. The asphericity, which is a measure of the anisotropy of the crystal and is 0.513, shows a noticeable deviation from isotropy.

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ДІЕТИЛ 2,2'-(1*H*-1,2,4-ТРІАЗОЛ-3,5-ДІІЛ)ДІАЦЕТАТ: СТРАТЕГІЇ СИНТЕЗУ, ХІМІЧНА ПОВЕДІНКА, КРИСТАЛІЧНА СТРУКТУРА Й АНАЛІЗ ПОВЕРХНІ ГІРШФЕЛЬДА

Анотація. *Етиловий естер 1,2,4-триазоліл-3,5-діоцтової кислоти синтезовано конденсацією гідразин-гідрату та N-ацил-етил-3-етокси-3-імінопропаноату. Розглянуто інші методи синтезу та виконано їхній порівняльний аналіз. Молекулярну будову досліджуваної сполуки встановлено за допомогою рентгеноструктурного аналізу. Для детального аналізу міжмолекулярних взаємодій здійснено аналіз поверхні Гіршфельда.*

Ключові слова: *1,2,4-триазол, іміноестери, ЯМР спектроскопія, рентгеноструктурний аналіз, аналіз поверхні Гіршфельда.*