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	ISI (Dubai, UAE) = 1.582	РИНЦ (Russia) = 3.939	PIF (India) = 1.940
	GIF (Australia) = 0.564	ESJI (KZ) = 8.771	IBI (India) = 4.260
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Issue Article

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SYNTHESIS OF DICHLORODIAZADIENES AND HYDROZO DERIVATIVE OF α-KETOETHER AND ASSESSMENT OF THEIR ANTIBACTERIAL ACTIVITY: CRYSTAL STRUCTURE OF (E)-4-((1-(4-(TERT-BUTYL)PHENYL)-2,2-DICHLOROVINYL)DIAZENYL) BENZONITRILE (VII)

Abstract: *The new dichlorodiazadiene derivatives (I-VIII) and from solvolysis of II compound, which resulted in methyl (Z)-2-(4-(tert-butyl)phenyl)-2-(2-(p-tolyl)hydrazineylidene)acetate (**IX**) were synthesized, which exhibits a wide range of antimicrobial activity against grampositive and gramnegative bacteria. **IX** and (E)-1-(1-(4-(tert-butyl)phenyl)-2,2-dichlorovinyl)-2-(4-methoxyphenyl) diazene (**III**) showed high antimicrobial activity against Acinetobacter baumanii, Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Bacillus subtilis and Staphylococcus aureus, where the zone of inhibition was 1.3-2.6 and 1.3-2.1 times larger,respectively, compared with gentamicin. This substances have a wide range of inhibitory effect agent of gramnegative and grampositive bacteria and can be used as a disinfectant agent. In the crystal structure of **VII**, the molecules are connected by C—H···Cl, C---H…N, and C---Cl…π interactions, forming a 3D network.*

Key words: *dichlorodiazadiene derivatives, antibacterial activity, grampositive and gramnegative bacteria, Hirshfeld surface analysis.*

Language: *English*

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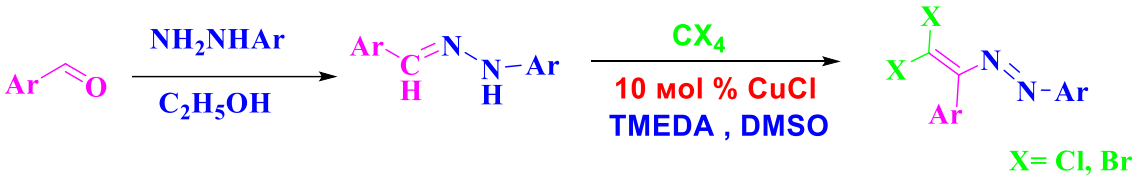
Introduction

The shortage of new antimicrobials and the rapid development of antimicrobial resistance pose a major challenge to health systems. In this regard, scientists are exploring new compounds of various origins as new antimicrobial substances. One –pot reactions are highly significant in industrial synthetic chemistry, and pharmaceutical chemistry applications for generation of structural diversity and libraries of drug-like molecules. These reactions as efficient methods have been widely used in the preparation of different bioactive compounds[1-5]

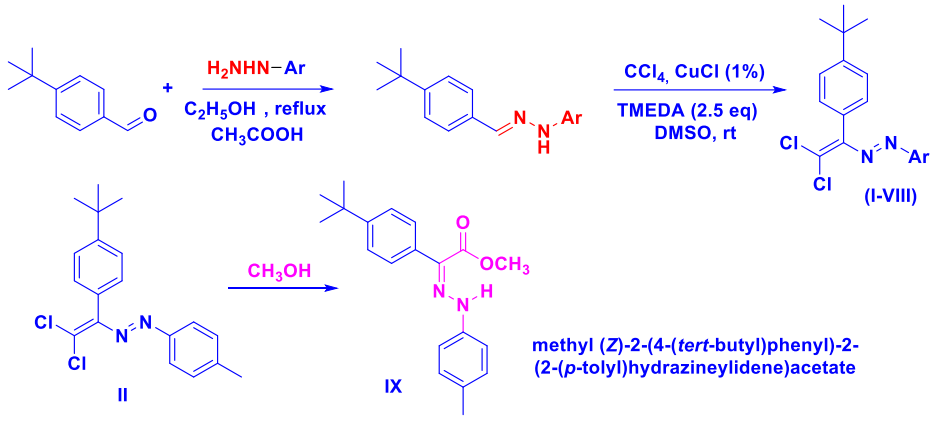
The synthesis of polyfunctional compounds, the study of their structure and properties is one of the directions of fine organic synthesis that have been studied in more detail in recent years. In this regard, the synthesis of dihalogendiazabutadienes from the reaction of N-substituted hydrazones of benzaldehyde derivatives with polyhalomethanes (CCl_4, CBr_4) in the presence of a CuCl catalyst[6-10], the investigation of their structural features by the RQA method[11-14] and the investigation of the factors affecting the direction of the reaction are distinguished by their relevance.



Scheme 1. Synthesis of dihalogendiazabutadienes

The presence of an attached diazadiene system in dihalogendiazabutadiene derivatives leads to their application as a new class of diazo dyes and the reaction of heminal halogen atoms with various nucleophiles to produce many important compounds (azidotriazoles, hydrozo derivatives of α-ketoethers, other nitrogen-containing heterocyclic compounds)[8,15] allows us to say how important this reaction is. Considering this, corresponding azo dyes (I-VIII) were synthesized based on 4-(tert-butyl)benzaldehyde and Hirshfeld surface analysis was studied[16]

At the same time, compound IX was synthesized from the solvolysis of compound II. In this study, the study of the antimicrobial properties of some of the newly synthesized dichlordiazadiene derivatives and the α-keto ether aryl-hydrazone like a solvolysis reaction product - and the results obtained from the structural studies of compound VII were discussed (Scheme 2).



Ar=4H (I), 4-CH_3 (II), 4-OCH_3 (III), 3-CH_3 (IV), 3,4-$(CH_3)_2$(V), 4-Cl (VI), 4-CN (VII), 4-I (VIII)

Scheme 2. Synthesis of dichlorodiazadienes and aryl hydrazone of α-keto ester

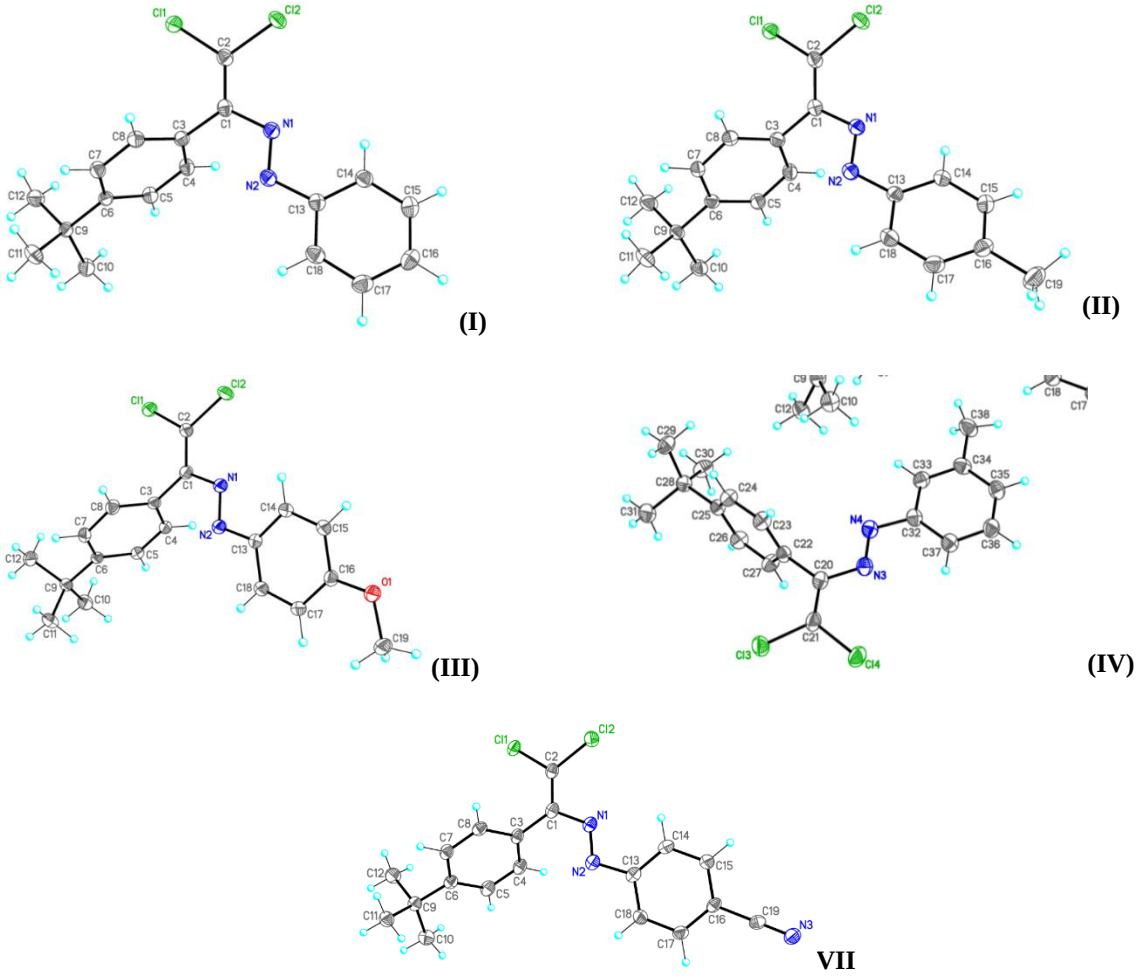


Figure 1. Molecular structures of compounds I-IV,VII

Result and Discussion

dichlorodiazadienes (**I-VIII**) were synthesized from the reaction of corresponding N-substituted hydrazones synthesized on the basis of t-Bu-benzaldehyde with CCl_4 in a catalytic amount of CuCl. Aryl hydrazones (**IX**) of α-keto esters were obtained from the solvolysis of dichlorodiazadiene in methyl alcohol at room temperature. Structures of obtained compounds were studied by NMR ^1H, ^{13}C spectroscopy and RSA analysis method. According to the NMR ^1H spectrum, signals of tertbutyl group were observed in the range of 1.39-1.44 ppm, and aromatic H atoms were observed in the range of 6.89-7.87 ppm. The signals of the groups (4-CH3, 4-OCH3, 3-CH3) in the hydrazine fragment were observed at 2.42, 3.88, 2.45 ppm. In the ^1H spectrum of substance (VIII), shift

to the weaker area (to the 12.45 ppm) due to the intramolecular H-bonding of the H atom in the NH group suggests us that it is in the Z-isomer form.

Antimicrobial activity of dichlorodiazadiene derivatives (I,III,IV) and methyl (Z)-2-(4-(tert-butyl)phenyl)-2-(2-(p-tolyl)hydrazineylidene) acetate IX.

The data obtained are presented in the table. All tested compounds exhibited antimicrobial activity to varying degrees against both gramnegative and grampositive bacteria.

Table 1. Antibacterial activity of dichlorodiazadiene derivatives

Test cultures		*Diameter of inhibition zone(mm), M ± m*				
		Compounds (0.3%)				Gentamicin (0.3%)
		I	**IX**	**III**	**IV**	
Gram negative bacteria	*Acinetobacter baumannii*	25.3±	30.0±	27.2±	28.8±	19.0±0.7
	Escherichia coli	26.2±	46.8±	38.2±	29.7±	18.0±0.6
	Klebsiella pneumoniae	23.5±	32.7±	33.3±	26.3±	20.0±0.1
	Pseudomonas aeruginosa	19.3±	33.2±	37.3±	17.5±	20.0±0.1
Gram positive bacteria	*Bacillus mesentericus*	23.2±	28.2±	27.3±	27.5±	26.0±1.3
	Bacillus subtilis	32.2±	31.0±	33.7±	34.3±	24.0±1.1
	Staphylococcus aureus	17.3±	35.3±	30.0±	19.8±	24.0±1.1

Note:
I (E)-1-(1-(4-(tert-butyl) phenyl)-2,2-dichlorovinyl)-2-phenyldiazene;
III(E)-1-(1-(4-(tert-butyl) phenyl)-2,2-dichlorovinyl)-2-(4-methoxy-phenyl) diazene;
IV (E)-1-(1-(4-(tert-butyl) phenyl)-2, 2-dichlorovinyl)-2-(m-tolyl) diazene
IX methyl (Z)-2-(4-(tert-butyl)phenyl)-2-(2-(p-tolyl)hydrazineylidene)acetate

Methyl (Z)-2-(4-(tert-butyl)phenyl)-2-(2-(p-tolyl)hydrazineylidene)acetate (**substance IX**) and (E) -1 - (1 - (4 – (tert-butyl) phenyl) – 2,2 – dichlorovinyl) – 2 – (4 – methoxyphenyl) diazene (**substance III**) showed high antimicrobial activity against *Acinetobacter baumanii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Staphylococcus aureus*, where the zone of inhibition **IX** and **III** was 1.3-2.6 and 1.3-2.1 times larger, respectively, compared with gentamicin (control). (E) - 1 - (1 - 4 - (tert-butyl) phenyl) - 2,2 - dichlorovinyl) - 2 - phenyldiazene (**substance I**) and (E) -1 - (1 - (4 - (tert-butyl) phenyl) - 2,2 - dichlorovinyl) - 2 - (m - tolyl) diazene (**substance IV**) showed high antimicrobial activity against *A. baumanii*, *E. coli*, *K. pneumoniae*, *B. subtilis*, where the zone of inhibition was, respectively, 1.2 - 1.5 and 1.3 - 1.7 times more than with gentamicin. *Acinetobacter baumanii*, *Bacillus mesentericus* and *B. subtilis* showed moderate sensitivity to all tested substances. However, *E. coli*, *K. pneumoniae*, *P. aeruginosa*, and *St. aureus* showed the greatest sensitivity to **substances IX** and **III**. Thus, sensitivity to **IX** and **III** was, respectively, in *E. coli* 1.6–1.8 and 1.3–1.5 times; in *K. pneumoniae*, 1.3–1.4 times; in *P aeruginosa* - by 1.7 - 1.9 and 1.9 - 2.1 times, in *St. aureus* - 1.7 - 2.0 and 1.5 - 1.8 times more compared to **substances I** and **IV**. The maximum antibacterial activity was shown by **substance XI** against *E. coli*, where the zone of inhibition was 1.8, 1.2, and 1.6 times larger compared to **substances I, III,** and **IV,** correspondingly. Hence, ntimicrobial activity varied depending on the spescies of bacteria and the inhibitory substances.

It should be noted that some synthetic organic substances have a more specific effect on microorganisms. specifically acted only on gramnegative bacteria and did not act grampositive and vice versa[4]; dimethyl 5-acetyl-1,3-disiano-4-hydroxy-4-methyl-2,6-diphenylcyclohexane-1,3-dicaoboxylate is more active (MIC-62.5 μg/ml) on *Pseudomonas aeruginosa*[5]; 2-hidroxy -3-allyi -5-isodesilbenzil) dietnylammonium chlorid had a specific bactericidal effect against *Staphylococcus aureus*[17]; 3-(4-chlorobenzyl)-5-(iodomethyl)

thiazolidine-2-thione did not affect bacteria, but inhibited the growth of fungi[18].

The results of the substance we studied **(I,III,IV and IX)** agree with the data, where 3-(4-chlorbenzyl) -5-(iodomethyl) thiazolidine - 2-thione inhibited the growth of gram-positive and gramnegative bacteria[18].

Structural studies of VII

Crystal data, data collection and structure refinement details are summarized in Table 2. The single crystal data of **VII** was collected on a Rigaku's XtaLAB Synergy Dual Source Single Crystal Diffractometer with graphite-monochromated Cu-K_α (1.54184 Å) at 100 K. With the CrysAlisPro software package, reduction and integration of the gathered data was done[20] . The crystal structure was solved by direct methods using SHELXT[21], and refined on F^2 by full-matrix least-squares procedures using SHELXL-2015[22]. Eventually, data were reduced and corrected for absorption using CrysAlisPro[20] . The C-bound H atoms were positioned geometrically and treated as riding atoms, C—H = 0.95 Å with U_{iso}(H) = 1.2U_{eq}(C) for aromatic H atoms and C—H = 0.98 Å with U_{iso}(H) = 1.5U_{eq}(C) for methyl H atoms. Owing to poor agreement between observed and calculated intensities, twenty-five were omitted in the final cycles of refinement. The molecular geometry calculations and drawings were performed with ORTEP-3 for Windows[23]. Software was used to prepare material: PLATON[24] and WinGX[23] .

The aromatic rings C3–C8 and C13–C18 of compound **VII (Fig. 1)** form a dihedral angle of 51.59(13)°. The title molecule adopts an *E* configuration with respect to the N1=N2 bond. The N1/N2/C1–C3/C13/Cl1/Cl2 unit is approximately planar [rms deviation of fitted atoms = 0.0667 Å], and makes dihedral angles of 58.22 (5) and 6.64 (12)°, respectively, with the C3–C8 and C13–C18 benzene rings. The values of the geometric parameters of **VII** are normal and compatible with those of the related compounds *viz.*: 4-{2,2-dichloro-1-[(*E*)-2-(4-methylphenyl)diazen-1-yl]ethenyl}-*N*, *N*-dimethylaniline[25], 1-(4-chlorophenyl)-2-[2,2-di-chloro-1-(4-fluorophenyl)ethenyl]diazene[26], 1-(4-chlorophenyl)-2-[2,2-dichloro-1-(4-nitrophen-yl)ethenyl]diazene[27] and 1-[2,2-dichloro-1-(4-nitro-phenyl)ethenyl]-2-(4-fluorophenyl)diazene[28].

In the crystal of **VII**, molecules are linked by C—H···Cl, C---H…N (Table 2) and C---Cl…π [C2---Cl1...Cg1^a: Cl1...Cg1^a=3.8158 (13) Å, C2---Cl1...Cg1^a (1-x, -y, 1-z) = 157.02(9)°; C2---Cl2...Cg2^b: Cl2...Cg2^b = 3.4704 (13) Å, C2---Cl2...Cg2^b = 93.78(9)°; Symmetry codes (*a*) 1 - x, - y, 1 - z, (*b*) x, - 1 + y, z; Cg1 and Cg2 are the centroids of the C3--C8 and C13--C18 benzene rings, respectively] interactions, forming a three-dimensional network to make the crystal structure stable (**Fig. 2**). π-π stacking interactions were not observed in the crystal structure of **VII**.

Table 3. Hydrogen-bond geometry (Å, °)

D—H···*A*	*D*—H	H···*A*	*D*···*A*	*D*—H···*A*
C4—H4···Cl1^{i}	0.95	2.79	3.741 (3)	176
C15—H15···N3^{ii}	0.95	2.61	3.545 (4)	169.00

Symmetry codes: (i) *x*, *y*+1, *z*; (ii) −*x*+2, *y*−1/2, −*z*+1/2.

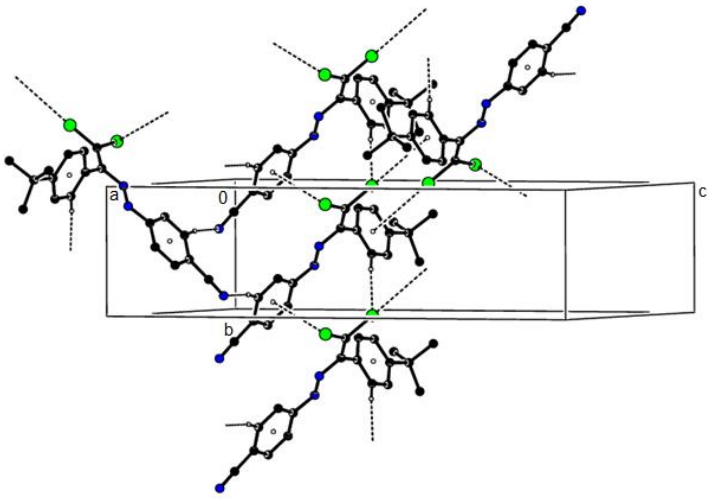


Fig. 2. A view of part of the molecular packing, showing C—H···Cl, C---H…N and C---Cl…π interactions.

Hirshfeld surface analysis of VII

The Hirshfeld surface analysis was carried out along the associated two-dimensional fingerprint plots generated using C*rystalExplorer17.5* [29]. The Hirshfeld surface is colour-mapped with the normalized contact distance, d_{norm}, from red (distances shorter than the sum of the van der Waals radii) through white to blue (distances longer than the sum of the van der Waals radii) with a fixed colour scale of -0.1260 (red) to +1.2999 (blue) a.u.

The Hirshfeld surfaces of **VII** mapped over d_{norm}, are given in **Fig. 3a**. The faint red spots indicate that short C---H…Cl and C---H…N contacts (Table 3) are significant in the crystal packing of the compound. **Fig. 3b, c** and d also exhibit the shape index (b), curvedness (c) and fragment paches surfaces of **VII**, respectively.

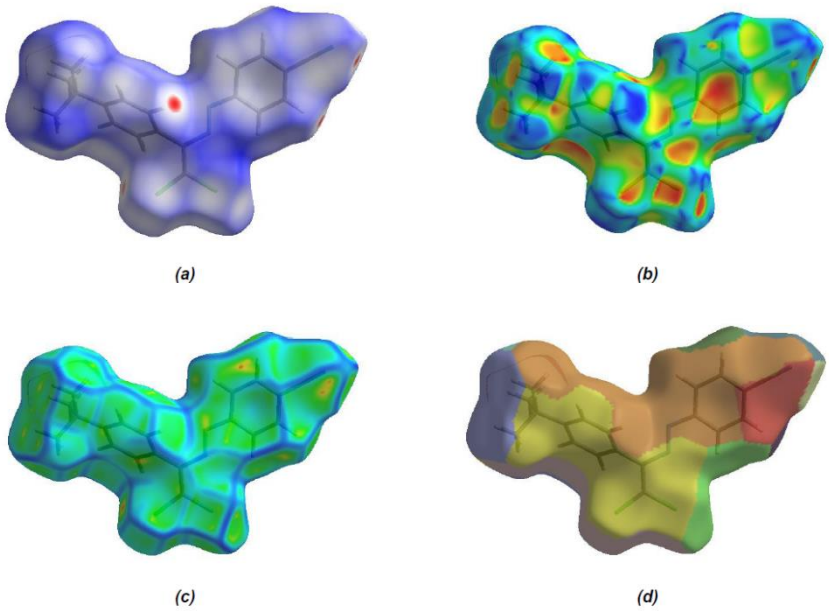


Fig. 3. (a) Hirshfeld surface mapped over d_{norm} with a fixed color scale in the range of -0.1260 au (red)–1.2999 au (blue), based on the length of the intermolecular contacts with respect to the sum of the van der Waals radii (red: shorter; blue: longer; white: same). (b) Hirshfeld surface mapped over the shape index (color scale: −1.0000 au – 1.0000 au). Blue areas represent bumps, and red regions indicate hollows. (c) Hirshfeld surface mapped over the curvedness (color scale: −4.0000 au – 0.4000 au). Flat regions are in green, while edges are in blue. (d) Unique (colored) region representations (fragment patches) based on atoms outside the Hirshfeld surface designed to indicate nearest neighbor molecule (color scale: 0.0000 au – 17.0000 au).

The full two-dimensional fingerprint plots for **VII** are given in **Fig 4**. The H…H contacts comprise 36.4 % of the total interactions. Besides this contact, N···H/H···N (17.1 %) and C···H/H···C (13.2 %) interactions make significant contributions to the total Hirshfeld surface. The percentage contributions of the Cl···C/C···Cl, C…C, N···C/C···N, Cl…Cl and Cl···N/N···Cl contacts are 5.6, 5.5, 1.2, 0.9 and 0.7 %, respectively.

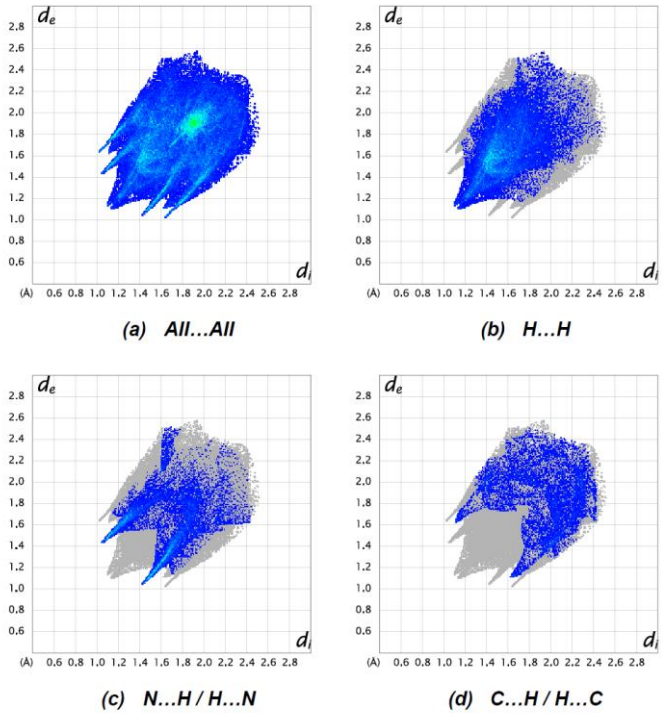


Fig. 4. Two-dimensional fingerprint plots of the Hirshfeld surface of VII, providing a visual summary of the frequency of each combination of d_e and d_i across the Hirshfeld surface. Points with a contribution to the surface are colored blue for a small contribution, and green for a great contribution. (a) All intermolecular contacts, (b) H···H contacts, (c) N···H/H···N contacts, (d) C···H/H···C contacts

Conclusion

The new dichlorodiazadiene derivatives were synthesized, which exhibits a wide range of antimicrobial activity against grampositive and gramnegative bacteria. **methyl (Z)-2-(4-(tert-butyl)phenyl)-2-(2-(p-tolyl)hydrazineylidene) acetate(substance IX)** and (E) -1 - (1 - (4 – (tert-butyl) phenyl) – 2,2 – dichlorovinyl) – 2 – (4 – methoxyphenyl) diazene (**substance III**) showed high antimicrobial activity against *Acinetobacter baumanii*, *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa*, *Bacillus subtilis* and *Staphylococcus aureus*, where the zone of inhibition was 1.3-2.6 and 1.3-2.1 times larger, respectively, compared with gentamicin. This substances have a wide range of inhibitory effect agent of gramnegative and grampositive bacteria and can be used as a disinfectant agent. In the crystal of VII, the molecules are linked by C—H···Cl, C---H…N, and C---Cl…π interactions, forming a 3D network to stabilize the crystal structure. π-π stacking interactions were not observed.

Experimental

General. The syntheses of compounds were carried out at the Organic Chemistry Department of Baku State University (Baku, Azerbaijan). The X-ray analyses of compounds I, II, III, IV and VII were carried out using the Bruker APEX II CCD (T 296 K, λMoK α - radiation, graphite monochromator, φ- and ω-scan) diffractometer. NMR 1H and 13C spectra were recorded using a Bruker Avance 300 (working frequency is 300 MHz) using CDCl3 solvent. SiMe4 (TMS) was used as an internal standard. Thin-layer chromatography (TLC) was performed on silhouette plate UB-254 and acidified KMnO4 solution; UV lamp rays were used to make spots visible. Column chromatography was performed on silica gel of Merk firm (63-200).

Synthetic procedure. Compounds (I)- (VI) were synthesized according to a literature protocol[6-7].

A 20-mL screw neck vial was charged with DMSO (10 mL), corresponding phenylhydrazones - ((E)-1-(4-(tert-butyl)benzylidene)-2-phenylhydrazine (252mg) for I, (E)-1-(4-(tert-butyl)benzylidene)-2-(p-tolyl) (266mg) for II, (E)-1-(4-(tert-

butyl)benzylidene)-2-(4-methoxyphenyl)hydrazine (276mg) for III, (E)-1-(4-(tert-butyl)benzylidene)-2-(m-tolyl)hydrazine for IV (266mg), (E)-1-(4-(tert-butyl)benzylidene)-2-(3,4-dimethylphenyl)hydrazine for V (280mg) and (E)-1-(4-(tert-butyl)benzylidene)-2-(4-chlorophenyl)hydrazine for VI (286mg), (E)-4-(2-(4-(tert-butyl)benzylidene)hydrazineyl) benzonitrile for VII (277mg), (E)-1-(4-(tert-butyl)benzylidene)-2-(4-iodophenyl)hydrazine for VIII (278mg) / (1mmol), respectively, tetramethylethylenediamine (TMEDA) (295 mg, 2.5mmol), CuCl (2 mg, 0.02 mmol) and CCl4 (20 mmol, 10 equiv). After 1-3 hours (until TLC analysis showed complete consumption of the corresponding Schiff base), the reaction mixture was poured into an ~0.01 M solution of HCl (100 mL, ~pH 2-3), and extracted with dichloromethane (3x20 mL). The combined organic phase was washed with water (3x50 mL), followed by brine (30 mL), dried over anhydrous Na_2SO_4 and concentrated in vacuo by rotary evaporator. The residue was purified by column chromatography on silica gel using appropriate mixtures of hexane and dichloromethane (3/1-1/1), and the corresponding diazenes were obtained. Compounds I-IV and VII were dissolved in dichloromethane (CH_2Cl_2) and then left at room temperature for slow evaporation; red and orange crystals of all compounds suitable for X-rays started to form after 2 day

I. (E)-1-(1-(4-(tert-butyl) phenyl)-2,2-dichlorovinyl)-2-phenyldiazene . Red solid (yiled 69%, 229.94mg); m.p. 87^{0}C. Anal. Calcd for C18H18Cl2N2 (*M* = 333.26): ^{1}H NMR (300MHz, $CDCl_3$) δ 7.87 (dd, *J* = 6.6, 2.9 Hz, 2H, arom), 7.54 – 7.47 (m, 5H, arom), 7.21 (d, *J* = 8.3 Hz, 2H, arom), 1.44 (s, 9H, -$C(CH_3)_3$). ^{13}C NMR (75MHz,$CDCl_3$) δ 31.8, 31.4, 123.3, 125.1, 129.0, 129.3, 129.7, 131.5, 135.1, 151.6, 152.2, 153.0: CCDC reference 2268431.

II. (E)-1-(1-(4-(tert-butyl)phenyl)-2,2-dichlorovinyl)-2-(p-tolyl)diazene. Red solid. (yield 71%, 246.56mg); mp 96^{0}C. Anal. Calcd for C19H20Cl2N2 (M = 347.28): 1 H NMR (300 MHz, CDCl3) δ 7.72 (d, *J* = 8.3 Hz, 2H, arom), 7.46 (d, *J* = 8.3 Hz, 2H, arom), 7.25 (d, *J* = 8.2 Hz, 2H, arom), 7.15 (d, *J* = 8.3 Hz, 2H, arom), 2.42 (s, 3H, -CH_3), 1.39 (s, 9H, -$C(CH_3)_3$). 13C NMR (75 MHz, CDCl3) 21.6, 31.3, 34.8, 123.3, 125.0, 129.4, 129.7, 129.7, 134.2, 142.2, 151.1, 151.5, 152.1. CCDC reference 2268430.

III. (E)-1-(1-(4-(tert-butyl) phenyl)-2,2-dichlorovinyl)-2-(4-methoxy-phenyl) diazene. Orange solid (yield 63%, 228.86mg); mp 127^{0}C. Analysis calculated for C19H20Cl2N2O (M = 363.28): 1 H NMR (300 MHz, CDCl3) δ 7.83 (d, *J* = 9.0 Hz, 2H, arom), 7.48 (d, *J* = 8.4 Hz, 2H, arom), 7.17 (d, *J* = 8.3 Hz, 2H, arom), 6.96 (d, *J* = 9.0 Hz, 2H, arom), 3.88 (s, 3H, -OCH_3), 1.41 (s, 9H, -$C(CH_3)_3$). 13C NMR (75 MHz, CDCl3) δ 31.3, 34.7, 55.5, 114.1, 125.0, 125.2, 129.6, 129.7, 132.9, 147.4, 151.4, 152.0, 162.5. CCDC reference 2268429.

IV. (E)-1-(1-(4-(tert-butyl) phenyl)-2, 2-dichlorovinyl)-2-(m-tolyl) diazene. An orange solid (yield 63%, 218.78mg); mp 66^{0}C. Anal. Calcd for C19H20Cl2N2 (M = 347.28): 1 H NMR (300 MHz, CDCl3) δ 7.66 (s, 2H, arom), 7.50 (d, *J* = 8.3 Hz, 2H, arom), 7.37 (dd, *J* = 9.7, 6.0 Hz, 1H, arom), 7.31 (s, 1H, arom), 7.19 (d, *J* = 8.3 Hz, 2H, arom), 2.45 (s, 3H, -CH_3), 1.43 (s, 9H, - $C(CH_3)_3$). 13C NMR (75 MHz, CDCl3) δ 21.3, 31.3, 34.8, 120.3, 124.0, 125.1, 128.8, 129.3, 129.7, 132.3, 134.7, 138.9, 151.5, 152.2, 153.0. CCDC reference 2268428.

V. (E)-1-(1-(4-(tert-butyl)phenyl)-2,2-dichlorovinyl)-2-(3,4-dimethylphenyl)diazene. An orange solid (yield 61%, 220.21mg); mp 97^{0}C. Anal. Calcd for C20H22Cl2N2 (M = 360.12). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.61 (dd, *J* = 11.2, 3.2 Hz, 2H, arom), 7.49 (d, *J* = 8.4 Hz, 2H, arom), 7.24 (d, *J* = 8.0 Hz, 1H, arom), 7.18 (d, *J* = 8.4 Hz, 2H, arom), 2.35 (s, 6H, - 3.4-$(CH_3)_2$), 1.43 (s, 9H, - $C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 19.8, 19.9, 31.3, 34.7, 120.7, 124.5, 125.0, 129.5, 129.7, 130.2, 133.7, 137.3, 140.9, 151.4, 151.5, 152.1.

VI. (E)-1-(1-(4-(tert-butyl)phenyl)-2,2-dichlorovinyl)-2-(4-chlorophenyl)diazene. Red solid (yield 75%, 275.63mg); mp 109^{0}C. Anal. Calcd for C18H17Cl3N2 (M = 367.70). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.76 (d, *J* = 8.7 Hz, 2H, arom), 7.44 (t, *J* = 9.4 Hz, 4H, arom), 7.13 (d, *J* = 8.3 Hz, 2H, arom), 1.38 (s, 9H, -$C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.3, 34.7, 124.4, 125.1, 129.0, 129.2, 129.6, 135.8, 137.4, 151.3, 151.7, 152.2.

VII. (E)-4-((1-(4-(tert-butyl)phenyl)-2,2-dichlorovinyl)diazenyl)benzonitrile. An orange solid (yield 65%, 232.7mg); mp 120^{0}C. Anal. Calcd for C19H17Cl2N3 (M = 358.27). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.80 (d, *J* = 8.5 Hz, 2H, arom), 7.53 (d, *J* = 8.5 Hz, 2H, arom), 7.46 (d, *J* = 8.2 Hz, 2H, arom), 7.13 (d, *J* = 8.2 Hz, 2H, arom), 1.38 (s, 9H, -$C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 31.31, 34.77, 98.44, 124.78, 125.12, 128.40, 128.97, 129.65, 136.07, 138.28, 151.71, 152.24, CCDC reference 2284693.

VIII. (E)-1-(1-(4-(tert-butyl)phenyl)-2,2-dichlorovinyl)-2-(4-iodophenyl)diazene. Red solid (yield 57%, 261.63mg); mp 97^{0}C. Anal. Calcd for C18H17Cl2IN2 (M = 459.15). ^{1}H NMR (300 MHz, Chloroform-d) δ 7.87 (d, *J* = 8.5 Hz, 2H, arom), 7.75 (d, *J* = 8.5 Hz, 2H, arom), 7.47 (d, *J* = 8.3 Hz, 2H, arom), 7.12 (d, *J* = 8.3 Hz, 2H, arom), 1.38 (s, 9H, -$C(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 29.71, 31.27, 34.80, 117.51, 120.32, 123.79, 124.60, 125.02, 125.25, 128.45, 129.54, 133.11, 162.32.

Compounds IX was synthesized according to a literature protocol[8]. (E)-1-(1-(4-(tert-butyl)phenyl)-2,2-dichlorovinyl)-2-(p-tolyl)diazene (II) (1 mmol, 347mg) and methanol (50 mL) were mixed at room

temperature. After completion of the reaction (until TLC analysis showed complete consumption of the corresponding dichlorodiazabutadiene, aproximetly 3-5h), the residue was purified by column chromatography on silica gel using appropriate mixtures of hexane and dichloromethane (v/v: 3/1).

IX. Synthesis of methyl (Z)-2-(4-(tert-butyl)phenyl)-2-(2-(p-tolyl)hydrazineylidene) acetate. Yellow solid (yield 56%, 181.67mg), m.p. 112^{0}C. Analysis calculated for C20H24N2O2 (*M* = 324.42), ^{1}H NMR (300 MHz, Chloroform-d) δ 12.45 (s, 1H,-NH), 7.64 (d, *J* = 8.4 Hz, 2H, arom), 7.46 (d, *J* = 8.4 Hz, 2H, arom), 7.24 (d, *J* = 8.5 Hz, 2H, arom), 7.17 (d, *J* = 8.5 Hz, 2H, arom), 3.91 (s, 3H, -OCH_3), 2.36 (s, 3H, -CH_3), 1.40 (s, 9H, -$(CH_3)_3$). ^{13}C NMR (75 MHz, $CDCl_3$) δ 20.7, 20.8, 31.2, 31.3, 51.6, 114.2, 124.9, 126.9, 128.2, 129.8, 131.9, 133.7, 140.9, 150.4, 164.3.

Test cultures and antibacterial assay

As test cultures, were used gram negative bacteria: *Acinetobacter baumannii* BDU-32, *Escherichia coli* BDU-12, *Klebsiella pneumoniae* BDU-44 and *Pseudomonas aeruginosa* BDU-49, and gram positive bacteria: *Bacillus mesentericus* BDU-51, *Bacillus subtilis* BDU-50, and *Staphylococcus aureus* BDU-23. All test cultures were taken from the collection of the Research Laboratory of Microbiology and Virology of Baku State University. Nutrient agar (Liofilchem) was used to cultivate bacterial species. Fresh 24 hours old cultures of bacteria were used in all experiments.

Methyl sulfoxide (DMSO) was used as solvant for the compounds. The test compounds solutions were prepared in concentration 0.3%.

The antibacterial activity of compounds were determined *in vitro* by standard agar well diffusion method[19]. A microbial suspension of test cultures (density 0.5 McFarland) in an amount of 0.1 µL was added in the surface of dense medium and smeared over the entire surface with a sterile glass spatula. Then, a hole with a diameter of 8 mm was opened with a sterile glass hole puncher. A solution of test substance in DMSO was added to the hole in an amount of 150 µL. Bacterial test cultures were incubated at 37°C for 24 hours. The zone of inhibition (the clear zone around the holes) was measured with a ruler in mm. DMSO and GENTAMICIN were used as a negative and positive control, correspondingly. All experiments were performed in 4 replicates and statistically processed.

Supplementary Material

1H and 13C spectra for compound I

1H spectra for compound II

1H and 13C spectra for compound III

1H and 13C spectra for compound IV

1H and 13C spectra for compound V

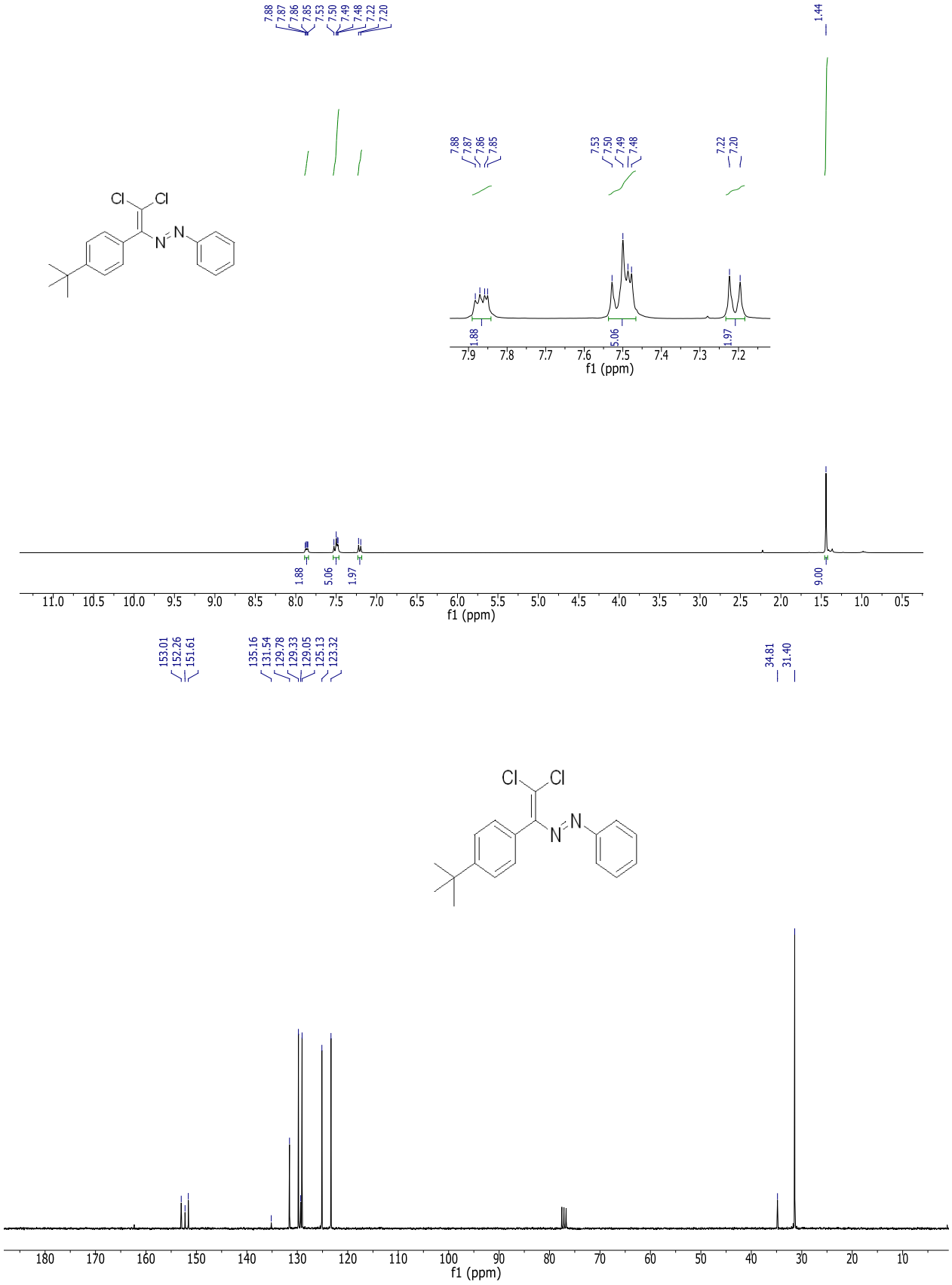
1H and 13C spectra for compound VI

1H spectra for compound VII

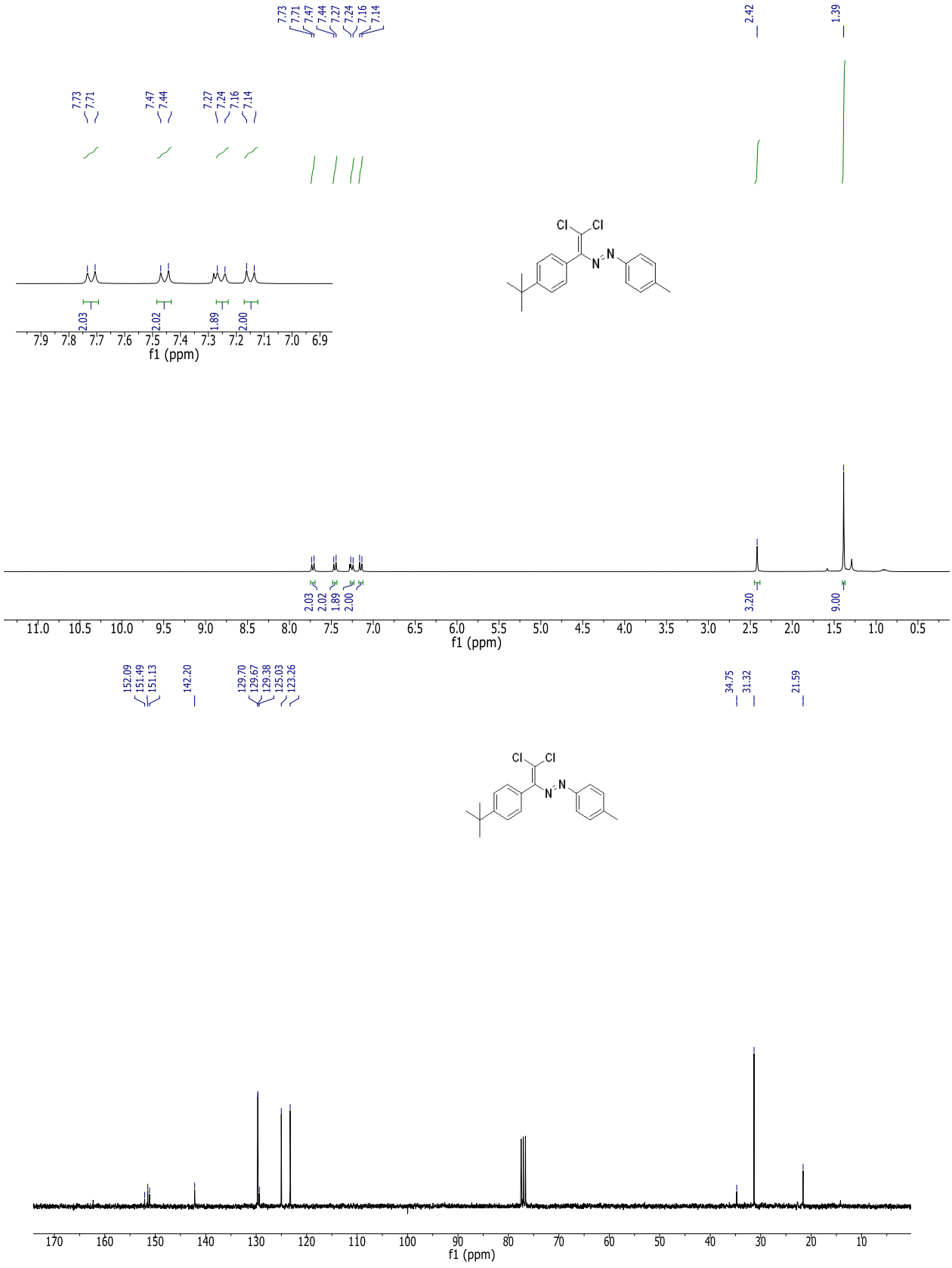
1H and 13C spectra for compound VIII

1H and 13C spectra for compound IX

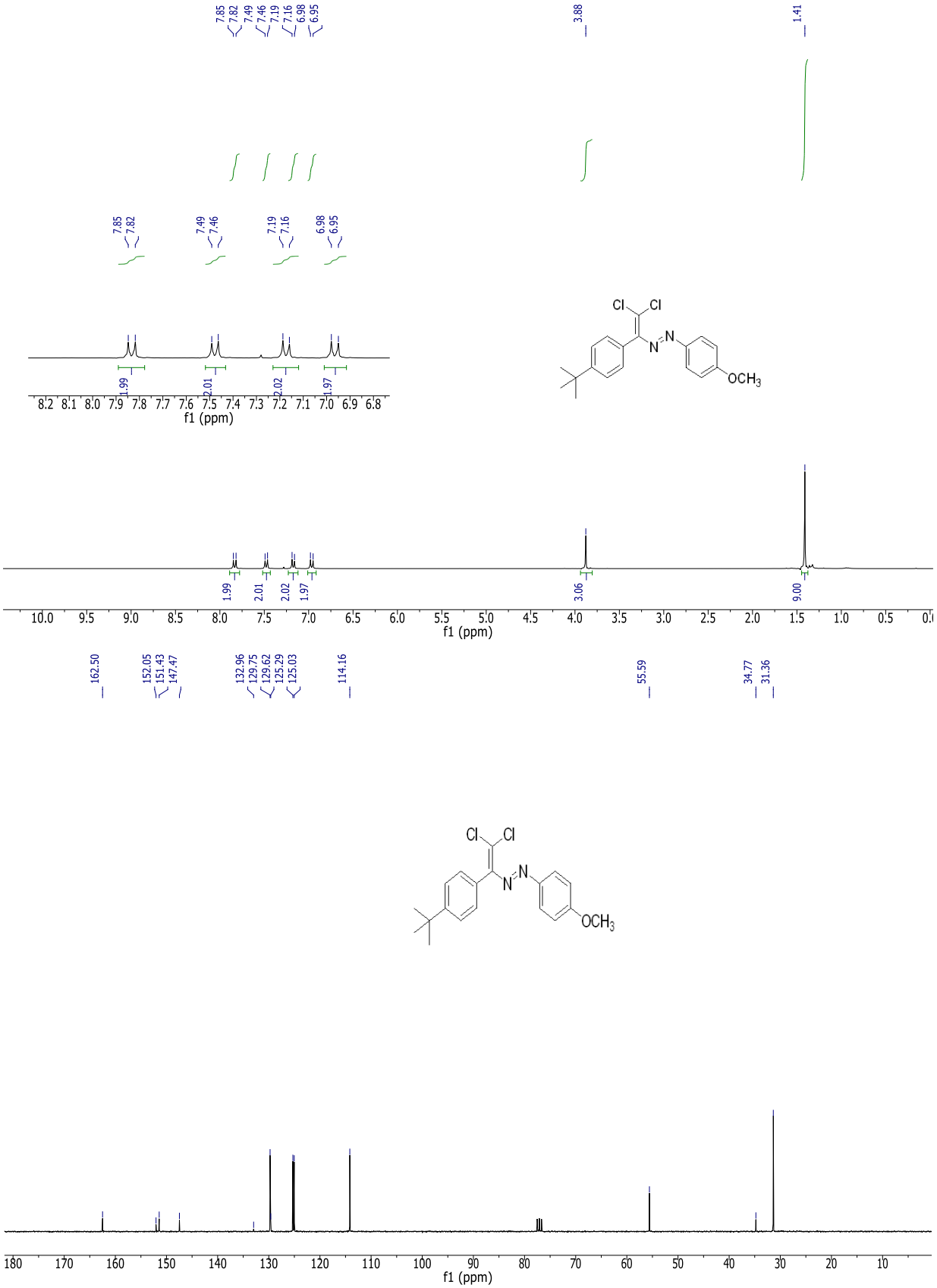
Crystal data, data collection and structure refinement details for compound VII



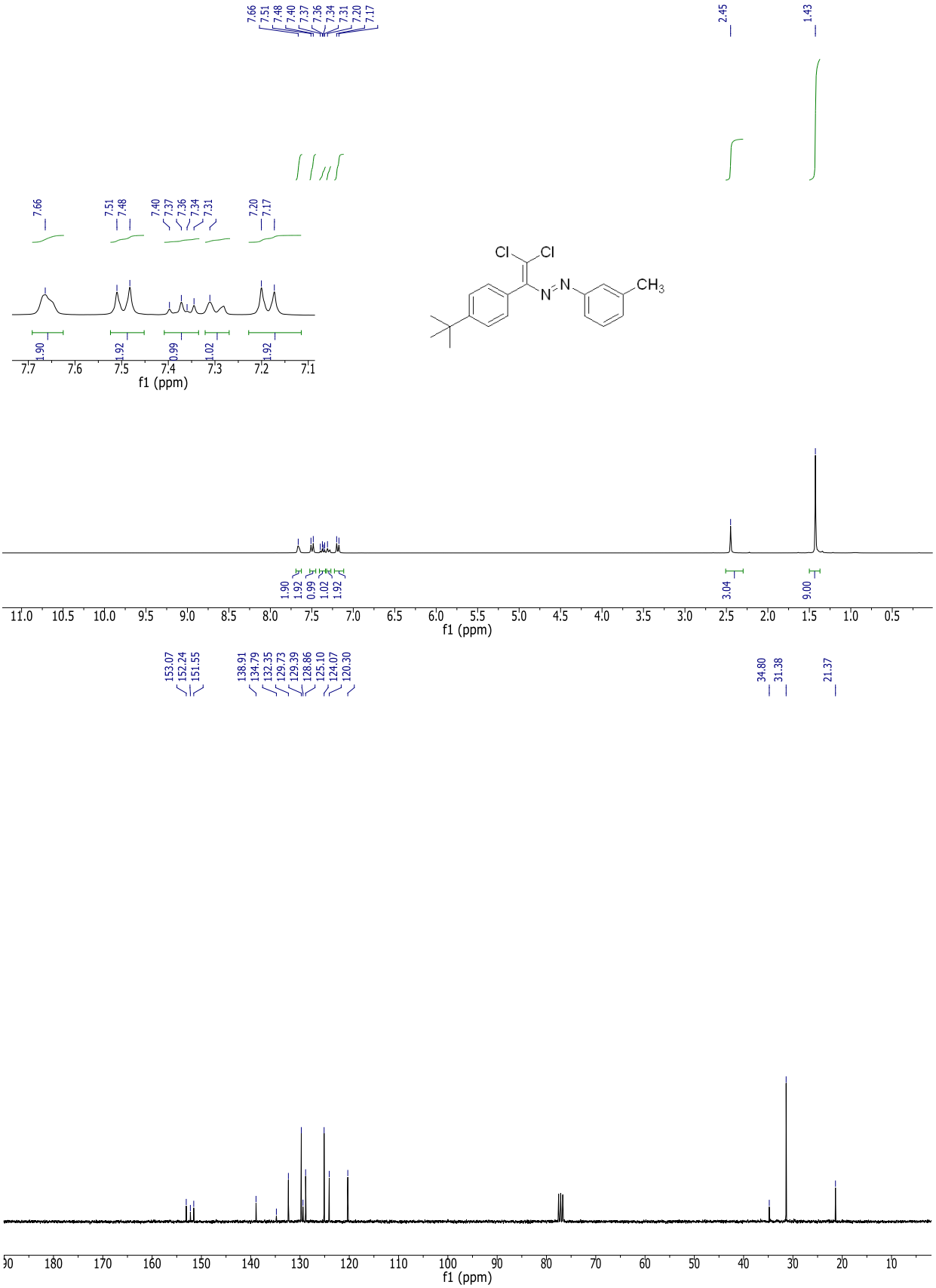
^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for I



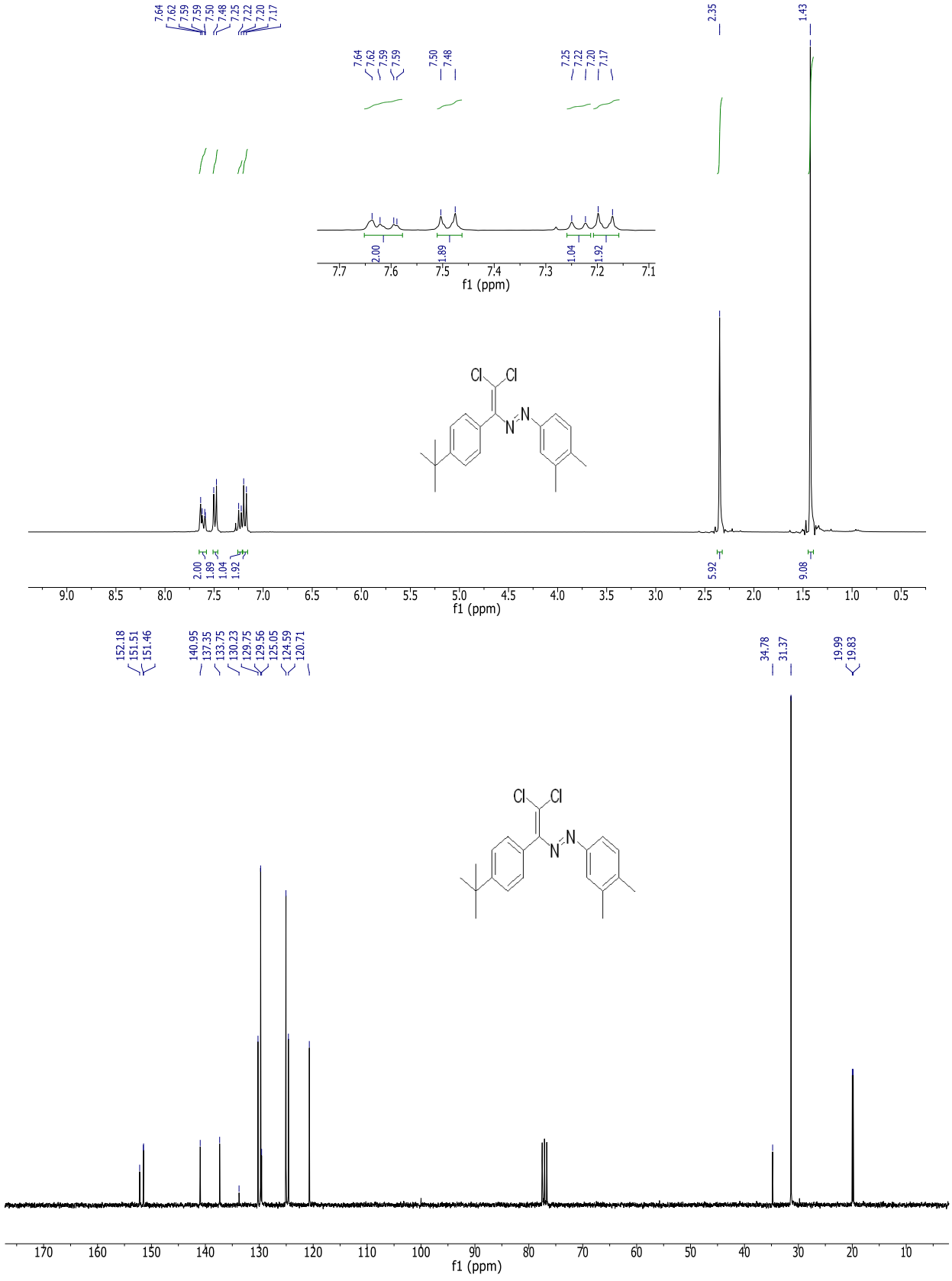
^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for II



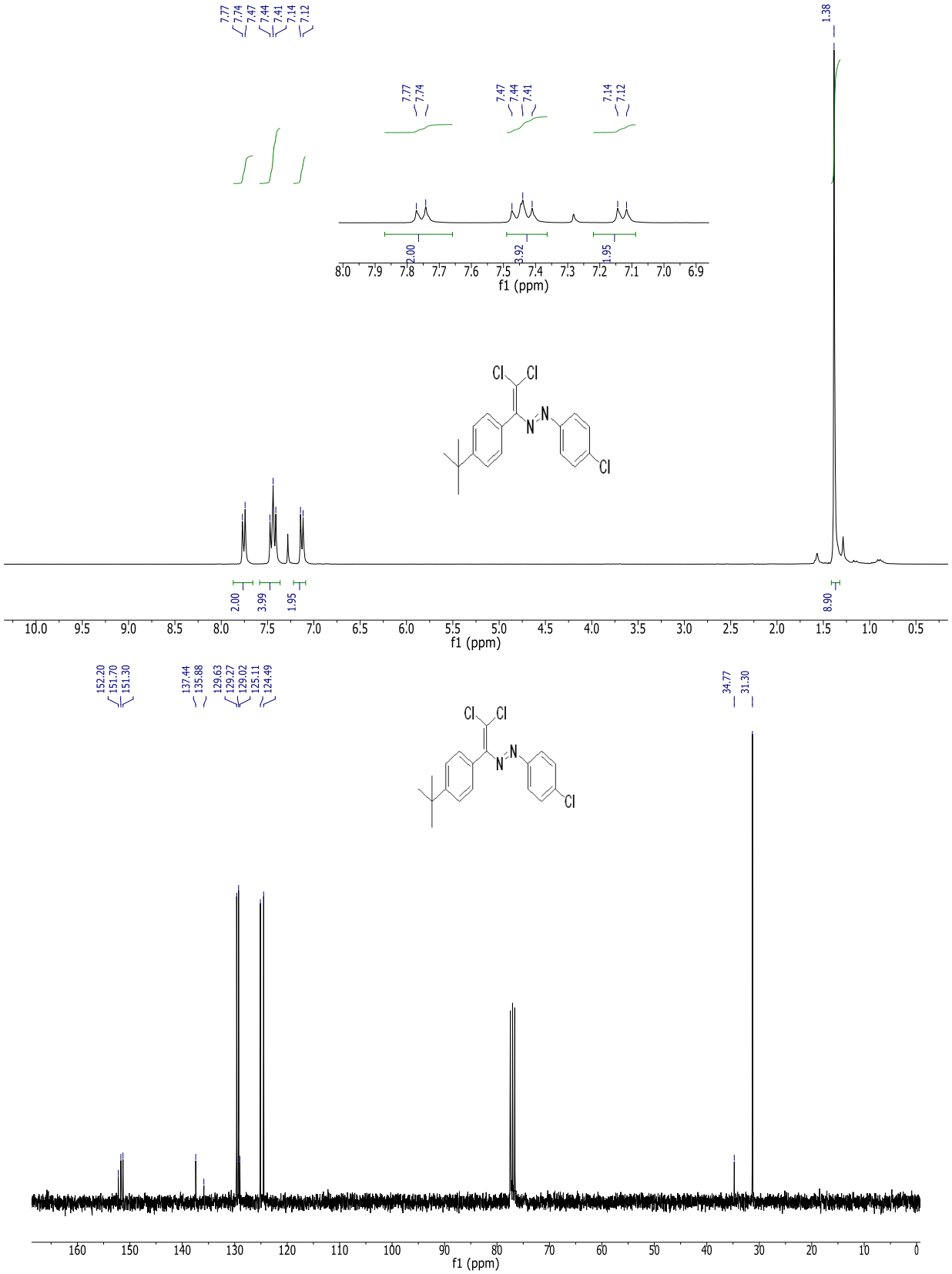
^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for III



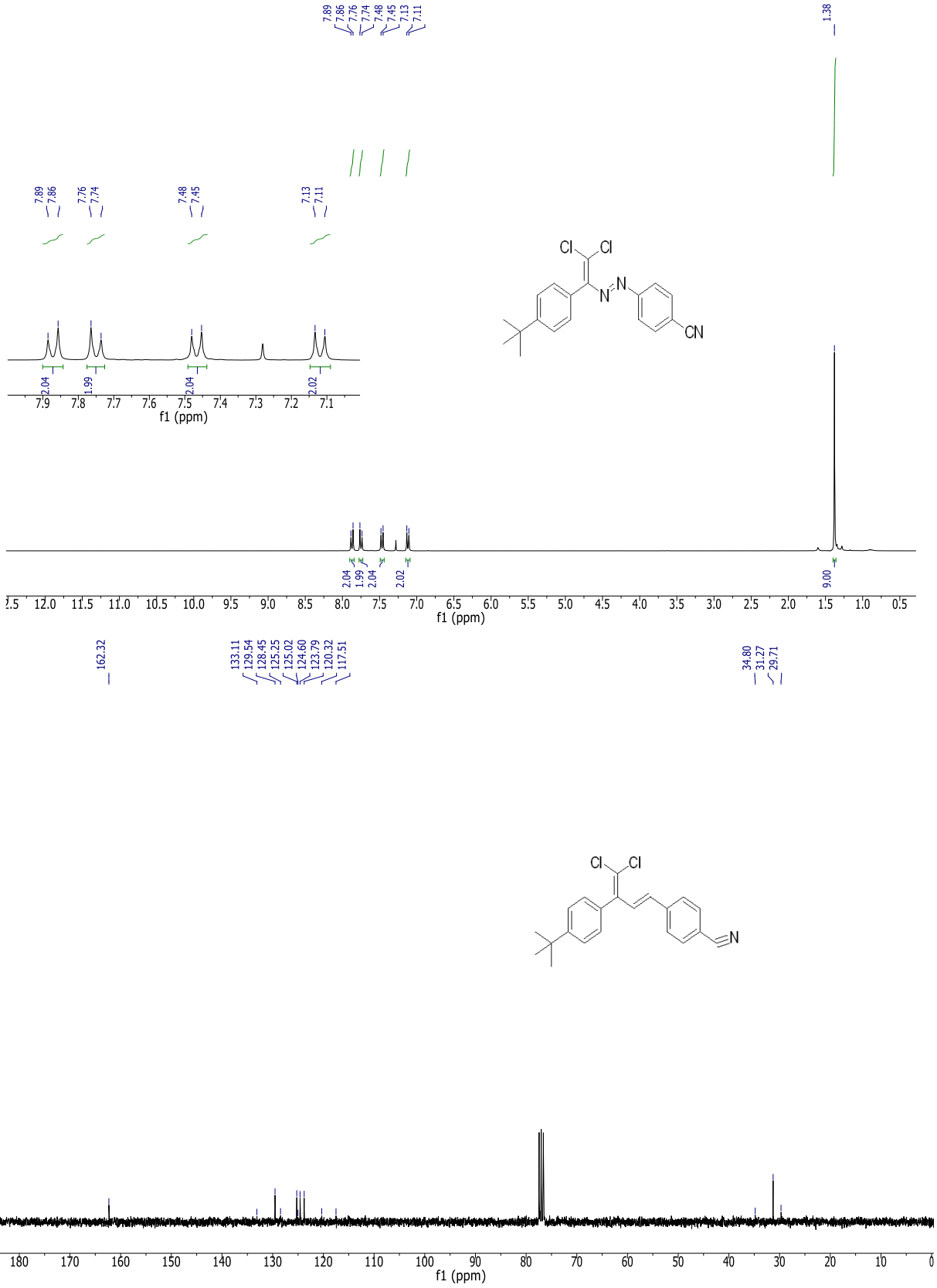
^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for IV



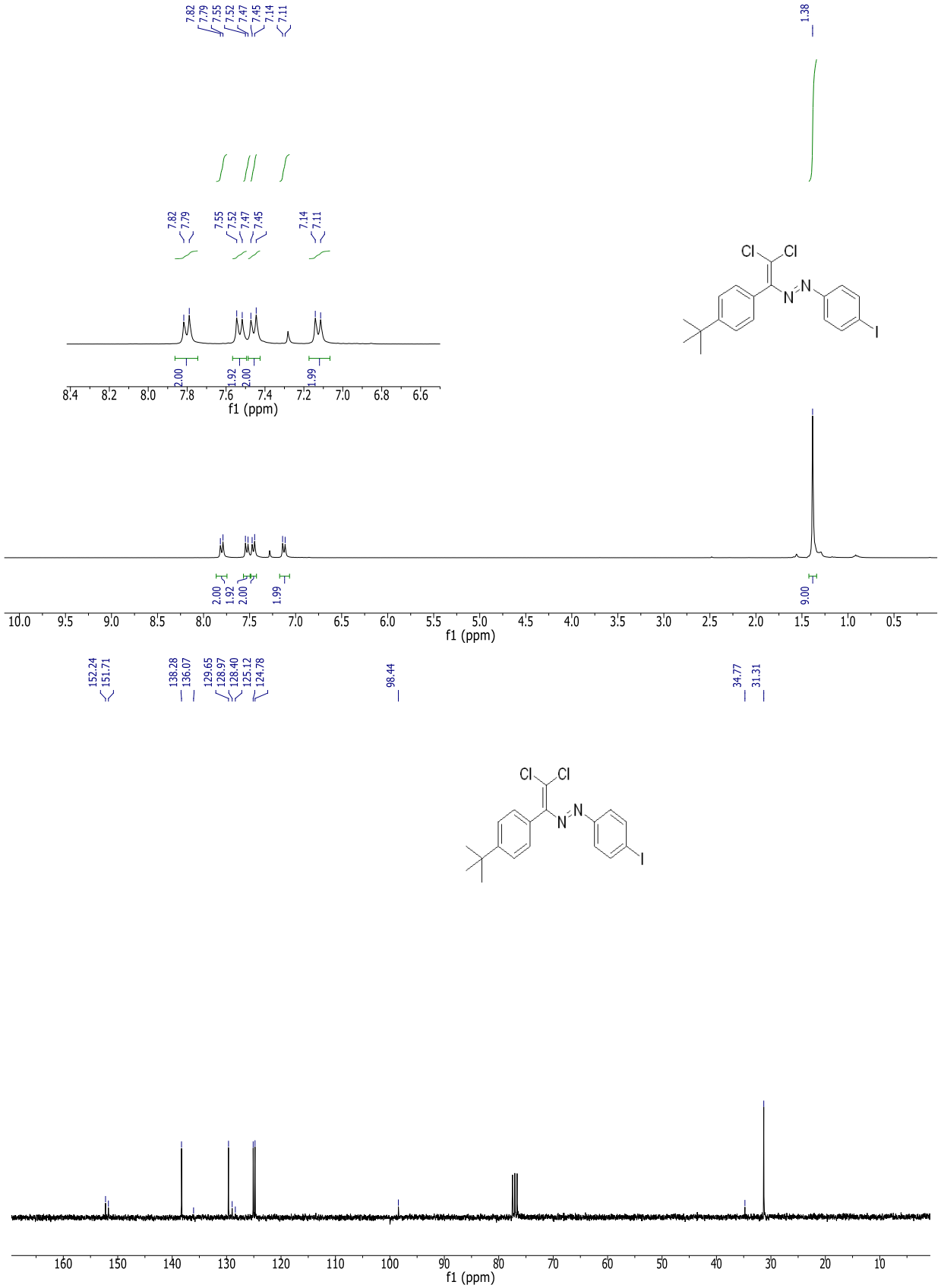
^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for V



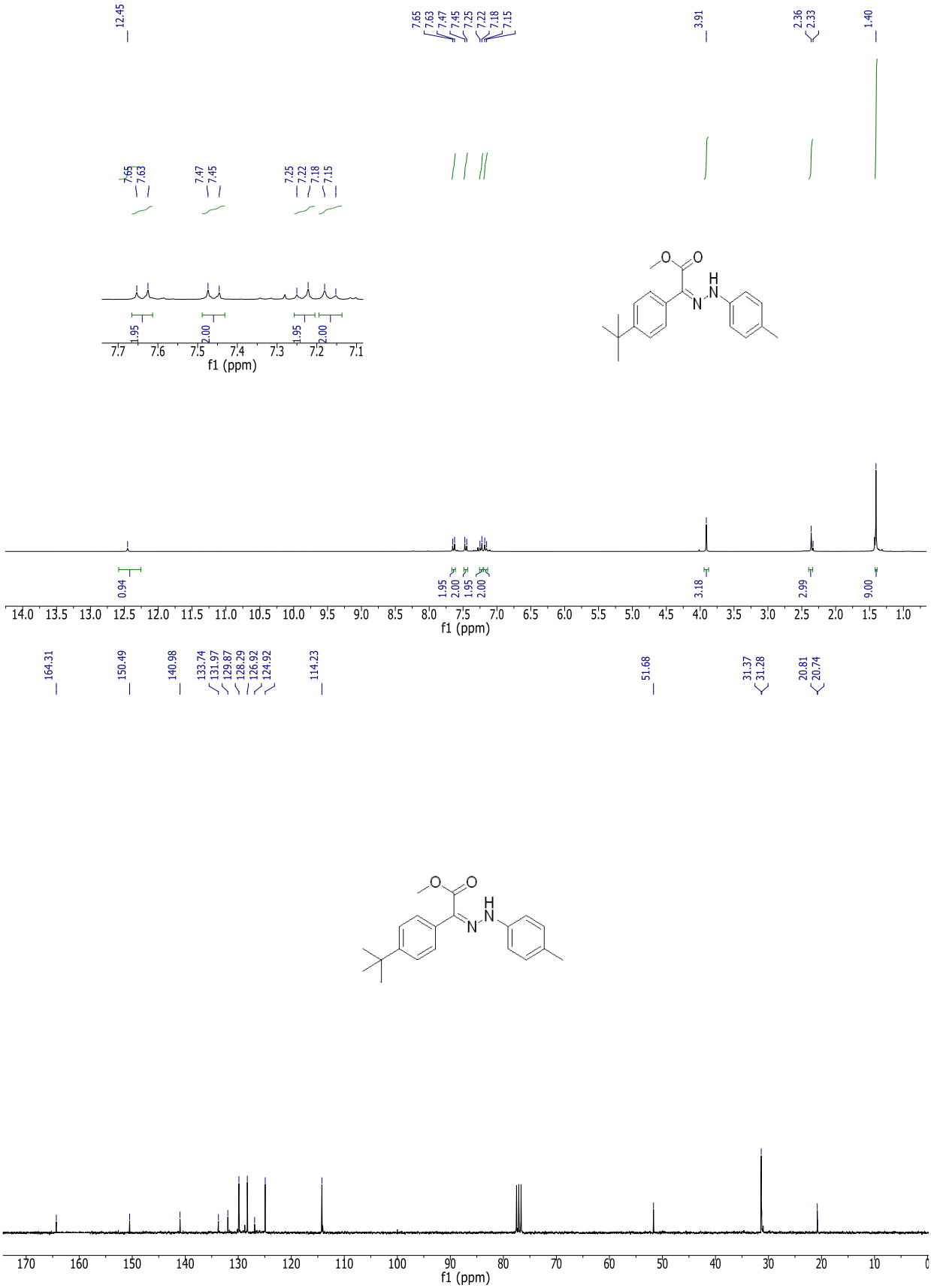
^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for VI



^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for VII



^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for VIII



^{1}H and ^{13}C NMR spectrum of synthesized compound in $CDCl_3$ solution for IX

Crystal data, data collection and structure refinement details for compound VII

Table 2. Experimental details

CCDC Deposition Number	2284693
Chemical formula	$C_{19}H_{17}Cl_2N_3$
M_r	358.26
Crystal system, space group	Monoclinic, $P2_1/c$
Temperature (K)	100
a, b, c (Å)	12.2479 (4), 6.30086 (18), 23.4804 (8)
β (°)	103.096 (3)
V (Å^3)	1764.91 (10)
Z	4
Radiation type	Cu $K\alpha$
μ (mm^{-1})	3.34
Crystal size (mm)	0.20 × 0.15 × 0.13
Diffractometer	XtaLAB Synergy, Dualflex, HyPix
Absorption correction	Multi-scan *CrysAlis PRO* 1.171.41.117a (Rigaku OD, 2021) Empirical absorption correction using spherical harmonics, implemented in SCALE3 ABSPACK scaling algorithm.
T_{min}, T_{max}	0.690, 1.000
No. of measured, independent and observed [$I > 2\sigma(I)$] reflections	20062, 3669, 3182
R_{int}	0.078
$(\sin \theta/\lambda)_{max}$ (Å^{-1})	0.634
$R[F^2 > 2\sigma(F^2)]$, $wR(F^2)$, S	0.066, 0.171, 1.02
No. of reflections	3669
No. of parameters	220
H-atom treatment	H-atom parameters constrained
$\Delta\rho_{max}$, $\Delta\rho_{min}$ (e Å^{-3})	1.21, −0.62

References:

1. Cioc, R. C., Ruijter, E., & Orru, R. V. (2014). Multicomponent reactions: advanced tools for sustainable organic synthesis. *Green Chemistry*, *16*(6), 2958-2975.
2. Di Pietro, O., Vicente-Garcia, E., Taylor, M. C., Berenguer, D., Viayna, E., Lanzoni, A., ... & Munoz-Torrero, D. (2015). Multicomponent reaction-based synthesis and biological evaluation of tricyclic heterofused quinolines with multi-trypanosomatid activity. *European Journal of Medicinal Chemistry*, *105*, 120-137.
3. Safa, K. D., Esmaili, M., & Allahvirdinesbat, M. (2016). Aqua-mediated one-pot synthesis of Biginelli dihydropyrimidinone/thiones (DHPMs), Hantzsch dihydropyridines (DHPs), and polysubstituted pyridines sonocatalyzed by metal-supported nanocatalysts. *Journal of the Iranian Chemical Society*, *13*, 267-277.
4. Ismiyev, A. I., Shoaib, M., Dotsenko, V. V., Ganbarov, K. G., Israilova, A. A., & Magerramov, A. M. (2020). Synthesis and Biological Activity of 8-(Dialkylamino)-3-aryl-6-oxo-2, 4-dicyanobicyclo [3.2. 1] octane-2, 4-dicarboxylic Acids Diethyl Esters. *Russian Journal of General Chemistry*, *90*, 1418-1425.
5. Israyilova, A., Shoaib, M., Ganbarov, K., Huseynzada, A., Hajiyeva, S., & Ismiyev, A. (2022). Antimicrobial activity and time kill curve study of newly synthesized dialkyl carboxylate cyclohexane derivative; A novel anti-Pseudomonas aeruginosa compound. *Acta Scientiarum. Technology*, *44*, e58868-e58868.
6. Maharramov, A. M., Shikhaliyev, N. Q., Suleymanova, G. T., Gurbanov, A. V., Babayeva, G. V., Mammadova, G. Z., ... & Pombeiro, A. J. (2018). Pnicogen, halogen and hydrogen bonds in (E)-1-(2, 2-dichloro-1-(2-nitrophenyl) vinyl)-2-(para-substituted phenyl)-diazenes. *Dyes and Pigments*, *159*, 135-141.
7. Shikhaliyev, N. Q., Ahmadova, N. E., Gurbanov, A. V., Maharramov, A. M., Mammadova, G. Z., Nenajdenko, V. G., ... & Pombeiro, A. J. (2018). Tetrel, halogen and hydrogen bonds in bis (4-((E)-(2, 2-dichloro-1-(4-substitutedphenyl) vinyl) diazenyl) phenyl) methane dyes. *Dyes and Pigments*, *150*, 377-381.
8. Spackman, P. R., Turner, M. J., McKinnon, J. J., Wolff, S. K., Grimwood, D. J., Jayatilaka, D., & Spackman, M. A. (2021). CrystalExplorer: A program for Hirshfeld surface analysis, visualization and quantitative analysis of molecular crystals. *Journal of Applied Crystallography*, *54*(3), 1006-1011.
9. Shikhaliyev, N. G., Maharramov, A. M., Suleymanova, G. T., Babazade, A. A., Nenajdenko, V. G., Khrustalev, V. N., ... & Tskhovrebov, A. G. (2021). Arylhydrazones of α-keto esters via methanolysis of dichlorodiazabutadienes: Synthesis and structural study. *Mendeleev Communications*, *31*(5), 677-679
10. Nenajdenko, V. G., Shikhaliyev, N. G., Maharramov, A. M., Atakishiyeva, G. T., Niyazova, A. A., Mammadova, N. A., ... & Tskhovrebov, A. G. (2022). Structural Organization of Dibromodiazadienes in the Crystal and Identification of Br··· O Halogen Bonding Involving the Nitro Group. *Molecules*, *27*(16), 5110.
11. Nenajdenko, V. G., Shikhaliyev, N. G., Maharramov, A. M., Bagirova, K. N., Suleymanova, G. T., Novikov, A. S., ... & Tskhovrebov, A. G. (2020). Halogenated diazabutadiene dyes: Synthesis, structures, supramolecular features, and theoretical studies. *Molecules*, *25*(21), 5013.
12. Shikhaliyev, N. G., Maharramov, A. M., Bagirova, K. N., Suleymanova, G. T., Tsyrenova, B. D., Nenajdenko, V. G., ... & Tskhovrebov, A. G. (2021). Supramolecular organic frameworks derived from bromoaryl-substituted dichlorodiazabutadienes via Cl··· Br halogen bonding. *Mendeleev Communications*, *31*(2), 191-193.
13. Shikhaliyev, N. G., Maharramov, A. M., Suleymanova, G. T., Babayeva, G. V., Mammadova, G. Z., Shikhaliyeva, I. M., ... & Nenajdenko, V. G. (2021). Halogen-bonding in 3-nitrobenzaldehyde-derived dichlorodiazadienes. *Organic Chemistry*, (part iii), 67-75.
14. Shikhaliyev, N. Q., Atioğlu, Z., Akkurt, M., Suleymanova, G. T., Babayeva, G. V., & Mlowe, S. (2021). Crystal structure and Hirshfeld surface analysis of (E)-4-({2, 2-dichloro-1-[4-(dimethylamino) phenyl] ethenyl} diazenyl) benzonitrile. *Acta Crystallographica Section E: Crystallographic Communications*, *77*(10), 994-998.
15. Atioğlu, Z., Akkurt, M., Shikhaliyev, N. Q., Mukhtarova, S. H., Suleymanova, G. T., & Toze, F. A. (2020). Crystal structure and Hirshfeld surface analysis of 4-{2, 2-dichloro-1-[(E)-(4-chlorophenyl) diazenyl] ethenyl}-N, N-dimethylaniline. *Acta Crystallographica Section E: Crystallographic Communications*, *76*(7), 1033-1037.

16. Tsyrenova, B. D., Khrustalev, V. N., & Nenajdenko, V. G. (2021). Synthesis of blue light emitting heterocycles via cyclization of 2-pyridine derived 4-azido-r1, 2, 3-triazoles. *Organic & Biomolecular Chemistry*, *19*(37), 8140-8152.
17. Maharramov, A., Shikhaliyev, N. Q., Qajar, A., Atakishiyeva, G. T., Niyazova, A., Khrustalev, V. N., ... & Bhattarai, A. (2023). Crystal structures and Hirshfeld surface analyses of (E)-1-[1-(4-tert-butylphenyl)-2, 2-dichloroethenyl]-2-phenyldiazene,(E)-1-[1-(4-tert-butylphenyl)-2, 2-dichloroethenyl]-2-(4-methylphenyl) diazene,(E)-1-[1-(4-tert-butylphenyl)-2, 2-dichloroethenyl]-2-(4-methoxyphenyl) diazene and (E)-1-[1-(4-tert-butylphenyl)-2, 2-dichloroethenyl]-2-(3-methylphenyl) diazene. *Acta Crystallographica Section E: Crystallographic Communications*, *79*(7).
18. Magerramov, A., Bayramov, M., Ganbarov, K., Mamedov, I., Javadova, Z., Israilova, A. (2021). *EurAsian patent, 2021, 037888*.
19. Mehrabani, M. G., Safa, K. D., Rahimi, M., Alyari, M., Ganbarov, K., & Kafil, H. S. (2020). Thiazolidine-2-thione and 2-imino-1, 3-dithiolane derivatives: synthesis and evaluation of antimicrobial activity. *Pharmaceutical Chemistry Journal*, *54*, 588-595.
20. Balouiri, M., Sadiki, M., & Ibnsouda, S. K. (2016). Methods for in vitro evaluating antimicrobial activity: A review. *Journal of pharmaceutical analysis*, *6*(2), 71-79.
21. Rigaku, O.D. (2021). *CrysAlis PRO*. Rigaku Oxford Diffraction, Yarnton, England.
22. Sheldrick, G. M. (2015). Crystal structure refinement with SHELXL. *Acta Crystallographica Section C: Structural Chemistry*, *71*(1), 3-8.
23. Sheldrick, G. M. (2015). SHELXT–Integrated space-group and crystal-structure determination. *Acta Crystallographica Section A: Foundations and Advances*, *71*(1), 3-8.
24. Farrugia, L. J. (2012). WinGX and ORTEP for Windows: an update. *Journal of Applied Crystallography*, *45*(4), 849-854.
25. Spek, A. L. J. (2003). Single-crystal structure validation with the program PLATON. *Journal of applied crystallography*, *36*(1), 7-13.
26. Özkaraca, K., Akkurt, M., Shikhaliyev, N. Q., Askerova, U. F., Suleymanova, G. T., Shikhaliyeva, I. M., & Bhattarai, A. (2020). Crystal structure and Hirshfeld surface analysis of 4-{2, 2-dichloro-1-[(E)-(4-fluorophenyl) diazenyl] ethenyl}-N, N-dimethylaniline. *Acta Crystallographica Section E: Crystallographic Communications*, *76*(6), 811-815.
27. Shikhaliyev, N. Q., Çelikesir, S. T., Akkurt, M., Bagirova, K. N., Suleymanova, G. T., & Toze, F. A. (2019). Crystal structure and Hirshfeld surface analysis of (E)-1-(4-chlorophenyl)-2-[2, 2-dichloro-1-(4-fluorophenyl) ethenyl] diazene. *Acta Crystallographica Section E: Crystallographic Communications*, *75*(4), 465-469.
28. Akkurt, M., Shikhaliyev, N. Q., Suleymanova, G. T., Babayeva, G. V., Mammadova, G. Z., Niyazova, A. A., ... & Toze, F. A. (2019). Crystal structures and Hirshfeld surface analyses of the two isotypic compounds (E)-1-(4-bromophenyl)-2-[2, 2-dichloro-1-(4-nitrophenyl) ethenyl] diazene and (E)-1-(4-chlorophenyl)-2-[2, 2-dichloro-1-(4-nitrophenyl) ethenyl] diazene. *Acta Crystallographica Section E: Crystallographic Communications*, *75*(8), 1199-1204.
29. Atioğlu, Z., Akkurt, M., Shikhaliyev, N. Q., Suleymanova, G. T., Bagirova, K. N., & Toze, F. A. (2019). Crystal structure and Hirshfeld surface analysis of (E)-1-[2, 2-dichloro-1-(4-nitrophenyl) ethenyl]-2-(4-fluorophenyl) diazene. *Acta Crystallographica Section E: Crystallographic Communications*, *75*(2), 237-241.
30. Spackman, P. R., Turner, M. J., McKinnon, J. J., Wolff, S. K., Grimwood, D. J., Jayatilaka, D., & Spackman, M. A. (2021). CrystalExplorer: A program for Hirshfeld surface analysis, visualization and quantitative analysis of molecular crystals. *Journal of Applied Crystallography*, *54*(3), 1006-1011.