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Synthesis and mass spectrometric fragmentation pattern of 6-(4-chlorophenyl)-*N*-aryl-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amines

https://doi.org/10.1515/hc-2018-0082
Received May 23, 2018; accepted August 14, 2018; previously published online September 18, 2018

Abstract: The mass spectrometric fragmentation of 6-(4-chlorophenyl)-*N*-aryl-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amines was studied under fast-atom bombardment (FAB) conditions. To simplify the interpretation of the mass spectra, a number of new 4*H*-1,3,5-oxadiazine derivatives containing polyisotopic elements (Cl and Br) in the arylamine substituent were synthesized. It was shown that fragmentation occurs in two main patterns.

Keywords: 1,3,5-oxadiazonium cation; FAB; fragmentation; 4*H*-1,3,5-oxadiazine; mass spectra.

Introduction

Derivatives of 1,3,5-oxadiazines are of interest in medical chemistry, pharmaceutical industry and agriculture [1, 2]. Effective antibacterial and antifungal agents have been found among the representatives of this class of compounds [3–10]. The antitumor drug 'synthazin' has been developed [11–13]. A large number of pesticides have been synthesized as well [14–17].

For the synthesis of 4*H*-1,3,5-oxadiazine derivatives, the [4+2] cycloaddition reactions [16, 18–25] are most often used, in addition to the intramolecular cyclization of bisamidals [26–28] and certain thioureas [29]. In studies on the synthesis of 1,3,5-oxadiazines, the structure of the products was confirmed mainly by ^{1}H NMR, ^{13}C NMR and IR spectroscopy, and in some cases by X-ray diffraction analysis [20, 29, 30]. MS data were used primarily to confirm the molecular weight of synthesized compounds [9, 10, 25, 29]. Only in two reports [23, 24] the fragmentation patterns of 2-(dialkylamino)-6-phenyl-4*H*-1,3,5-oxadiazin-4-ones and 2-aryl-6-(2-aryl-4,4-*bis*(trifluoromethyl)-5,6-dihydro-4*H*-1,3-oxazin-5-yl)-4,4-*bis*(trifluoromethyl)-4*H*-1,3,5-oxadiazines have been suggested. This work is devoted to the determination of the fragmentation pattern of 6-(4-chlorophenyl)-*N*-aryl-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amines **4**, the synthetic chemistry of which was developed earlier [29].

Results and discussion

Compounds **4** were prepared by the dehydrosulfation reaction of *N*-amidoalkylated thioureas **3** [31] which are the products of the addition reaction of aromatic amines **2** to 4-chloro-*N*-(2,2,2-trichloro-1-isothiocyanatoethyl) benzamide **1** [32] with dicyclohexylcarbodiimide (DCC) (Scheme 1). In addition to compounds **4a–e**, **4g**, **4l** and **4n** synthesized previously, a series of new derivatives of 4*H*-1,3,5-oxadiazines **4f**, **4h–k** and **4m** were prepared. These compounds contain polyisotopic elements (Cl and Br) in the arylamine substituent, which greatly simplifies interpretation of their mass spectra.

The structure of the products was confirmed by spectral studies. For example, in the IR spectra of compounds **4**, intense absorption bands related to symmetric and antisymmetric stretching vibrations of the N=C-O-C=N group are observed in the region of 1732–1717 cm^{-1} and 1653–1645 cm^{-1} [33]. In the ^{1}H NMR spectra of these compounds, the signal of the methine proton (5.8–5.6 ppm) adjacent to the trichloromethyl group is manifested as a singlet, while for their precursors **3** the corresponding signal is in the form of a double-doublet (7.5–7.2 ppm). The proton of the amino group in compounds **4** appears in the region of 10.1–9.0 ppm in the form of a singlet, which confirms ring closure with the participation of both amide and thiourea fragments. In the ^{13}C NMR spectra of

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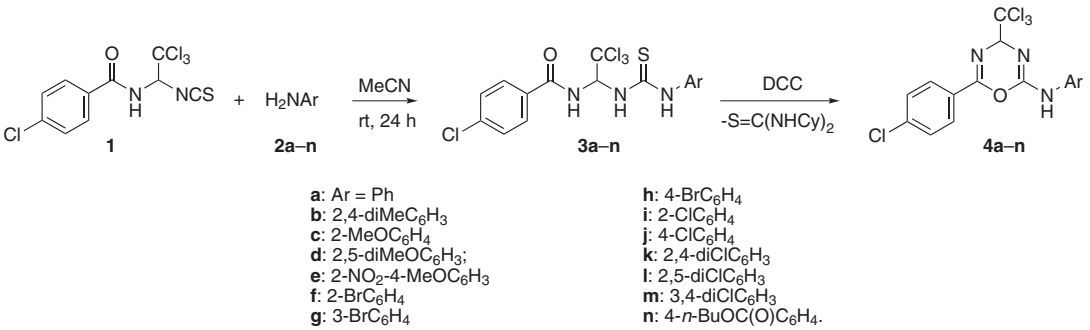


Scheme 1 Synthesis of 4*H*-1,3,5-oxadiazine derivatives **4**.

compounds **4** in the region of 152–145 ppm, carbon signals of two imino groups are observed, with no signals for C=S (182–180 ppm) and C=O (165–164 ppm) carbons that are characteristic for the starting thioureas **3**.

The EI-MS for many compounds **4** are not informative because the peak intensity for the molecular ion does not exceed 1% of the base peak and, for some compounds, the peak of the molecular ion is not observed at all. The absence of a molecular ion peak in the EI mass spectra of many 1,3,5-oxadiazine derivatives has been previously noted [3]. Accordingly, in this study the mass spectra were recorded in a fast-atom bombardment (FAB) mode. In these mass spectra, with the exception of compound **4d**, the molecular ion is manifested by the protonated form $[MH]^+$. Protonation is also characteristic for some fragment ions. The presence of polyisotopic elements (Cl and Br) in 4*H*-1,3,5-oxadiazines **4** in the arylamine substituent greatly facilitates interpretation of the mass spectra. At the beginning of this work, elimination of the HCl (pathway A) or $CHCl_3$ (B) molecule, as well as cleavage of the oxadiazine ring (C) or (D), could be predicted (Figure 1). It turned out that the elimination of the HCl molecule for the molecular ion of 1,3,5-oxadiazines **4** is not preferred and intensity of the peaks $[MH-36]^+$ in most cases does not exceed 5% of the base peak. Moreover, for compounds **4d**, **4e** and **4n** these peaks are not observed at all. Only for compounds **4f** and **4h**, the intensity of this peak is about 10%. Elimination of the chloroform molecule was observed for all compounds, probably because of the thermodynamic stability of the aromatic 1,3,5-oxadiazonium cation $[MH-118]^+$ formed (Scheme 2). The intensity of the peaks $[M-118]^+$, in some cases reaches 25–30%, and for the compound **4n** it is 53%. Most likely, the fragmentation pathway B proceeds under thermodynamic control. The second stage of the decomposition pathway B is the elimination of HCN and ArNHCN. The resulting two isotopic cations $[p\text{-}ClC_6H_4CO]^+$ are characterized by high intensity peaks. At the third stage, the elimination of the CO molecule from the cations $[p\text{-}ClC_6H_4CO]^+$ is observed. Thereafter, the isotopic cations $[p\text{-}ClC_6H_4]^+$ undergo fragmentation according to the classical scheme for the corresponding aromatic compounds.

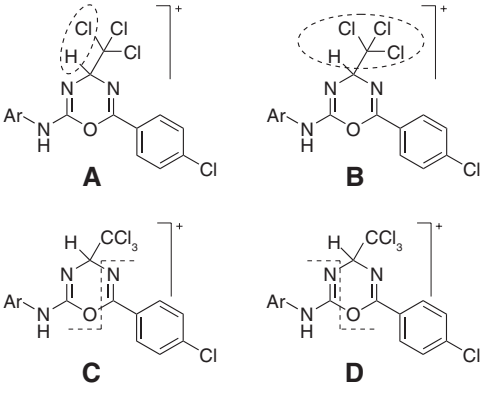
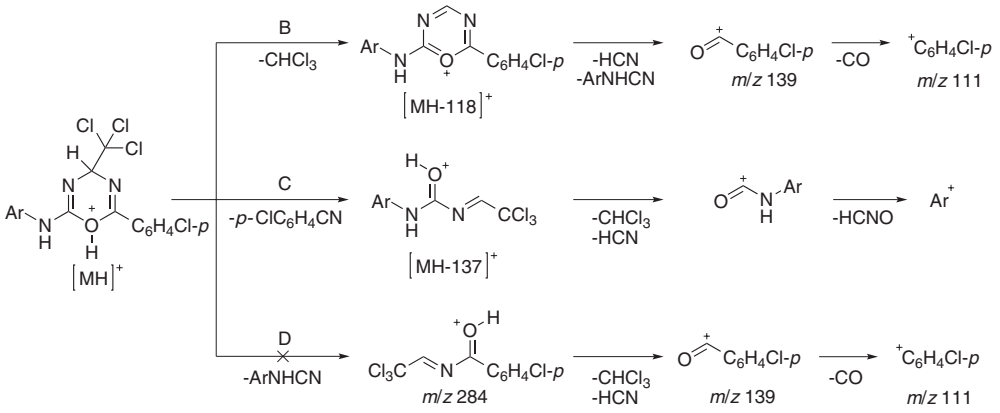


Figure 1 Possible fragmentation pattern of 4*H*-1,3,5-oxadiazines **4**.

The fragmentation pathway C is the most characteristic (Scheme 2). Obviously, the process takes place under kinetic control with the rupture of the weakest bonds. The intensities of the $[MH-p\text{-}ClC_6H_4CN]^+$ peaks range from 10% to 50% of the base peak, and for compound **4c** this peak amounts to 100%. Elimination of the ArCN fragment in the mass spectra of 4*H*-1,3,5-oxadiazine derivatives has been observed earlier [23, 24]. In the second stage of the decomposition pathway C, the molecules of chloroform and hydrogen cyanide are eliminated. The peak for the resultant ion $[OCNHAr]^+$ is of high intensity and for compound **4b** it reaches 100%. In the third stage of the cleavage, the molecule of HNCO is eliminated, after which the $[Ar]^+$ ion formed undergoes fragmentation according to the classical scheme for the corresponding aromatic compounds. It is noteworthy that the thermal decomposition of 4*H*-1,3,5-oxadiazines occurs according to a similar scheme [34]. Fragmentation pathway D was not observed. This is probably due to the greater stability



Scheme 2 Fragmentation patterns B, C and the hypothetical pathway D of 4*H*-1,3,5-oxadiazines **4**.

of the resulting (*E*)-1-aryl-3-(2,2,2-trichloroethylidene)urea (pathway C) than the stability of the anticipated molecule of (*E*)-4-chloro-*N*-(2,2,2-trichloroethylidene)benzamide (pathway D).

Conclusion

Several 4*H*-1,3,5-oxadiazine derivatives were synthesized and their fragmentation under FAB conditions was studied. The most characteristic fragmentation pattern involves fragmentation of the 1,3,5-oxadiazine ring followed by cleavage of the resulting (*E*)-1-aryl-3-(2,2,2-trichloroethylidene)urea.

Experimental

IR spectra were recorded in KBr pellets using a Spectrum BX II spectrometer. FAB mass spectra were recorded on a VG7070 instrument. Desorption of ions from the samples in *meta*-nitrobenzyl alcohol or 3-mercaptopropane-1,2-diol was carried out with a beam of argon atoms having an energy of 8 keV. ^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were recorded for solutions in DMSO-d_6 on a Varian VXR-400 spectrometer. EA was performed on a LECO CHNS-900 instrument. Control of the reactions and the purity of compounds were performed by thin layer chromatography (TLC) on Silufol UV-254 plates eluting with chloroform/acetone (3:1).

General procedure for the synthesis of new substituted thioureas 3f, 3h–k and 3m

The isothiocyanate **1** (3.44 g, 0.01 mol), prepared according to the method reported in [32], was dissolved in 15–18 mL of acetonitrile. Then, the solution was stirred vigorously and treated portion-wise, to avoid overheating, for 7–10 min, with 0.01 mol of the appropriate amine **2**. After the stirring was stopped, the mixture was left at room temperature for 24 h. The resultant precipitate was filtered off, washed with acetonitrile (2×3 mL), dried for 24 h at room temperature and then for 5 h at 100°C. Product **3** was crystallized from MeCN.

***N*-(1-(3-(2-Bromophenyl)thioureido)-2,2,2-trichloroethyl)-4-chlorobenzamide (3f)** Pale yellow solid; yield 87% (4.49 g); mp 211–213°C; R_f 0.74; IR: ν_{max} 3282, 3235, 3068, 3052 (NH), 2944, 2853 (CH), 1657 (C=O), 1594, 1537, 1507, 1482, 1331, 1297, 1136, 1014, 903, 821, 804, 725, 633, 590 cm^{-1}; ^{1}H NMR: δ 10.16 (s, 1H, NH), 9.40 (d, J=7.3 Hz, 1H, NH), 8.20 (br. s, 1H, NH), 7.91–7.89 (m, 2H, $H_{arom.}$), 7.71–7.69 (m, 1H, $H_{arom.}$), 7.63–7.61 (m, 2H, $H_{arom.}$), 7.56–7.52 (m, 2H, $H_{arom.}$), 7.42–7.39 (m, 1H, $H_{arom.}$), 7.22 (dd, J=7.8, 7.3 Hz, 1H, CH); ^{13}C NMR: δ 182.2 (C=S), 164.7 (C=O), 137.0, 136.8, 132.6, 131.9, 130.1, 129.5, 128.5, 128.3, 127.8, 120.6, 101.6 (CCl_3), 70.5 (CH); FAB-MS: *m/z* (%) 514 (4) [MH]$^+$. Anal. Calcd for $C_{16}H_{12}BrCl_4N_3OS$ (516.06): C, 37.24; H, 2.34; Br, 15.48; Cl, 27.48; N, 8.14; S, 6.21. Found: C, 37.26; H, 2.36; Br, 15.50; Cl, 27.50; N, 8.15; S, 6.19.

***N*-(1-(3-(4-Bromophenyl)thioureido)-2,2,2-trichloroethyl)-4-chlorobenzamide (3h)** Pale yellow solid; yield 84% (4.33 g); mp 210–212°C; R_f 0.66; IR: ν_{max} 3279, 3199 (NH), 3093, 3063, 3002, 2944, 2852, 2777 (CH), 1637 (C=O), 1596, 1537, 1505, 1485, 1396, 1332, 1273, 1136, 1068, 1013, 897, 800, 723, 650, 602, 500 cm^{-1}; ^{1}H NMR: δ 10.57 (s, 1H, NH), 9.25 (d, J=7.3 Hz, 1H, NH), 8.08 (d, J=9.8 Hz, 1H, NH), 7.89–7.87 (m, 2H, $H_{arom.}$), 7.62–7.47 (m, 7H, 6$H_{arom.}$+CH); ^{13}C NMR: δ 180.4 (C=S), 164.6 (C=O), 137.8, 136.8, 131.8, 131.6, 129.4, 128.5, 125.1, 117.0, 101.5 (CCl_3), 70.1 (CH); FAB-MS: *m/z* (%) 515 (2) [M+2H]$^+$. Anal. Calcd for $C_{16}H_{12}BrCl_4N_3OS$ (516.06): C, 37.24; H, 2.34; Br, 15.48; Cl, 27.48; N, 8.14; S, 6.21. Found: C, 37.21; H, 2.31; Br, 15.45; Cl, 27.51; N, 8.18; S, 6.18.

4-Chloro-*N*-(2,2,2-trichloro-1-(3-(2-chlorophenyl)thioureido)ethyl)benzamide (3i) Pale yellow solid; yield 85% (4.01 g); mp 214–216°C; R_f 0.67; IR: ν_{max} 3289, 3238, 3053 (NH), 2943, 2813 (CH), 1659 (C=O), 1594, 1538, 1505, 1480, 1331, 1296, 1132, 1014, 903, 802, 733, 665, 601, 499 cm^{-1}; ^{1}H NMR: δ 10.18 (s, 1H, NH), 9.35 (s, 1H, NH), 8.23 (d, J=7.3 Hz, 1H, NH), 7.91–7.89 (m, 2H, $H_{arom.}$), 7.63–7.53 (m, 5H, $H_{arom.}$), 7.38–7.27 (m, 2H, $H_{arom.}$+CH); ^{13}C NMR: δ 182.1 (C=S), 164.7 (C=O), 136.8, 135.6, 131.9, 129.6, 129.5, 129.5, 129.4, 128.5, 127.8, 127.2, 101.6 (CCl_3), 70.5 (CH); FAB-MS: *m/z* (%) 470 (9), [MH]$^+$. Anal. Calcd for $C_{16}H_{12}Cl_5N_3OS$ (471.60): C, 40.75; H, 2.56; Cl, 37.58; N, 8.91; S, 6.80. Found: C, 40.71; H, 2.53; Cl, 37.61; N, 8.95; S, 6.78.

4-Chloro-*N*-(2,2,2-trichloro-1-(3-(4-chlorophenyl)thioureido) ethyl)benzamide (3j) Pale yellow solid; yield 88% (4.15 g); mp 207–209°C; R_f 0.61; IR: ν_{max} 3281, 3196, 3093, 3064 (NH), 3003, 2945, 2850, 2779 (CH), 1637 (C=O), 1596, 1505, 1485, 1330, 1273, 1137, 1092, 1014, 898, 800, 725, 656, 605 cm^{-1}; ^1H NMR: δ 10.62 (s, 1H, NH), 9.27 (d, J = 6.4 Hz, 1H, NH), 8.10 (d, J = 8.8 Hz, 1H, NH), 7.90–7.88 (m, 2H, $H_{arom.}$), 7.61–7.50 (m, 5H, $H_{arom.}$), 7.45–7.42 (m, 2H, $H_{arom.}$ + CH); ^{13}C NMR: δ 180.5 (C=S), 164.6 (C=O), 137.4, 136.9, 131.8, 129.4, 128.9, 128.6, 128.5, 124.8, 101.6 (CCl_3), 70.1 (CH); FAB-MS: *m/z* (%) 470 (6), $[MH]^+$. Anal. Calcd for $C_{16}H_{12}Cl_5N_3OS$ (471.60): C, 40.75; H, 2.56; Cl, 37.58; N, 8.91; S, 6.80. Found: C, 40.77; H, 2.54; Cl, 37.60; N, 8.94; S, 6.79.

4-Chloro-*N*-(2,2,2-trichloro-1-(3-(2,4-dichlorophenyl)thioureido) ethyl)benzamide (3k) Pale yellow solid; yield 87% (4.40 g); mp 212–214°C; R_f 0.72; IR: ν_{max} 3412, 3291, 3245 (NH), 3092, 2943 (CH), 1651 (C=O), 1595, 1531, 1482, 1330, 1297, 1138, 1099, 1015, 803 cm^{-1}; ^1H NMR: δ 10.23 (s, 1H, NH), 9.40 (d, J = 8.8 Hz, 1H, NH), 8.37 (d, J = 8.6 Hz, 1H, NH), 7.91–7.89 (m, 2H, $H_{arom.}$), 7.72–7.67 (m, 2H, $H_{arom.}$), 7.62–7.60 (m, 2H, $H_{arom.}$), 7.52 (dd, J = 8.8, 8.6 Hz, 1H, CH), 7.45–7.43 (m, 1H, $H_{arom.}$); ^{13}C NMR: δ 182.2 (C=S), 164.8 (C=O), 136.8, 134.9, 131.9, 131.0, 130.7, 130.3, 129.5, 128.9, 128.5, 127.3, 101.5 (CCl_3), 70.5 (CH); FAB-MS: *m/z* (%) 504 (3), $[MH]^+$. Anal. Calcd for $C_{16}H_{11}Cl_6N_3OS$ (506.04): C, 37.98; H, 2.19; Cl, 42.03; N, 8.30; S, 6.34. Found: C, 37.95; H, 2.20; Cl, 42.07; N, 8.34; S, 6.30.

4-Chloro-*N*-(2,2,2-trichloro-1-(3-(3,4-dichlorophenyl)thioureido) ethyl)benzamide (3m) Pale yellow solid; yield 80% (4.05 g); mp 211–213°C; R_f 0.68; IR: ν_{max} 3280, 3212, 3089 (NH), 2940, 2852, 2760 (CH), 1646 (C=O), 1595, 1503, 1329, 1298, 1145, 1121, 1014, 932, 835, 719, 655 cm^{-1}; ^1H NMR: δ 10.70 (s, 1H, NH), 9.26 (d, J = 7.3 Hz, 1H, NH), 8.21 (d, J = 9.3 Hz, 1H, NH), 7.99 (s, 1H, $H_{arom.}$), 7.90–7.88 (m, 2H, $H_{arom.}$), 7.64–7.60 (m, 3H, $H_{arom.}$), 7.52–7.43 (m, 2H, $H_{arom.}$ + CH); ^{13}C NMR: δ 180.5 (C=S), 164.6 (C=O), 138.7, 136.9, 131.7, 130.7, 130.5, 129.4, 128.5, 126.5, 124.2, 122.9, 101.4 (CCl_3), 70.0 (CH); FAB-MS: *m/z* (%) 504 (16), $[MH]^+$. Anal. Calcd for $C_{16}H_{11}Cl_6N_3OS$ (506.04): C, 37.98; H, 2.19; Cl, 42.03; N, 8.30; S, 6.34. Found: C, 38.01; H, 2.16; Cl, 42.04; N, 8.31; S, 6.29.

General procedure for the synthesis of new 4*H*-1,3,5-oxadiazines 4f, 4h–k and 4m

DCC (1.13 g, 5.5 mmol) was added to a thiourea **3** (5 mmol) in acetonitrile (20 mL), and the mixture was heated under reflux for 50–60 min. As the reaction progressed, the precipitate of thiourea **3** gradually dissolved, and the solution turned yellow due to formation of dicyclohexylthiourea. After completion, the solution was filtered while hot, and the filtrate was left at room temperature for 24 h. The precipitated crystals were filtered off and washed with acetonitrile (2×5 mL), then dried and crystallized from the appropriate solvent indicated below.

6-(4-Chlorophenyl)-*N*-phenyl-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4a) FAB-MS: *m/z* (%) 402 (27) $[MH]^+$, 366 (4) $[MH-36]^+$, 284 (25) $[MH-118]^+$, 265 (43) $[MH-137]^+$, 148 (50), 139 (100) $[p\text{-}ClC_6H_4CO]^+$, 120 (64) $[C_6H_4NHCO]^+$, 111 (18) $[p\text{-}ClC_6H_4]^+$, 107 (30), 89 (34), 65 (16), 55 (8), 50 (18).

6-(4-Chlorophenyl)-*N*-(2,4-dimethylphenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4b) FAB-MS: *m/z* (%) 430 (14) $[MH]^+$, 394 (2) $[MH-36]^+$, 312 (9) $[MH-118]^+$, 293 (49) $[MH-137]^+$, 165 (8), 147 (100) $[2,4\text{-}diCH_3C_6H_3NHCO]^+$, 139 (55) $[p\text{-}ClC_6H_4CO]^+$, 120 (49), 111 (12) $[p\text{-}ClC_6H_4]^+$, 106 (31) $[2,4\text{-}diCH_3C_6H_3]^+$, 88 (31), 76 (54), 65 (8).

6-(4-Chlorophenyl)-*N*-(2-methoxyphenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4c) FAB-MS: *m/z* (%) 432 (22) $[MH]^+$, 396 (3) $[MH-36]^+$, 313 (21) $[MH-118]^+$, 295 (100) $[MH-137]^+$, 195 (12), 167 (11), 150 (59) $[2\text{-}CH_3OC_6H_4NHCO]^+$, 139 (75) $[p\text{-}ClC_6H_4]^+$, 123 (38), 106 (80) $[CH_3OC_6H_4]^+$, 88 (51), 76 (41), 61 (43).

6-(4-Chlorophenyl)-*N*-(2,5-dimethoxyphenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4d) FAB-MS: *m/z* (%) 461 (14) $[M]^+$, 343 $[M-118]^+$, 324 (100) $[M-137]^+$, 180 (67) $[2,5\text{-}diCH_3OC_6H_3NHCO]^+$, 165 (46), 148 (28), 137 (90) $[2,4\text{-}diCH_3OC_6H_3]^+$, 124 (25), 120 (29), 115 (10), 107 (56), 95 (17), 89 (50), 77 (49), 69 (13), 63 (29), 55 (17), 51 (39).

6-(4-Chlorophenyl)-*N*-(4-methoxy-2-nitrophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4e) FAB-MS: *m/z* (%) 477 (10) $[MH]^+$, 359 (6) $[MH-118]^+$, 340 (29) $[MH-137]^+$, 307 (78), 280 (20), 274 (14), 259 (8), 243 (10), 226 (14), 195 (17) $[2\text{-}NO_2\text{-}4\text{-}CH_3OC_6H_3NHCO]^+$, 166 (21), 152 (40) $[2\text{-}NO_2\text{-}4\text{-}CH_3OC_6H_3]^+$, 139 (100) $[p\text{-}ClC_6H_4CO]^+$, 120 (54), 111 (19) $[p\text{-}ClC_6H_4]^+$, 107 (90), 89 (88), 77 (80), 62 (52), 50 (17).

***N*-(2-Bromophenyl)-6-(4-chlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4f)** Pale yellow crystals; yield 40% (0.96 g); mp 148–150°C (from MeCN); R_f 0.62. IR: ν_{max} 3435, 3384, 3281 (NH), 3089, 3066, 2952, 2891, 2855 (CH), 1732 (-N=C-O-C=N-), 1653 (C=N), 1594, 1535, 1439, 1400, 1318, 1288, 1210, 1135, 1086, 1012, 824, 772, 751, 728, 700, 665, 615, 514 cm^{-1}; ^1H NMR: δ 9.17 (s, 1H, NH), 8.07–8.06 (m, 2H, $H_{arom.}$), 7.87 (m, 1H, $H_{arom.}$), 7.69–7.66 (m, 3H, $H_{arom.}$), 7.42–7.38 (m, 1H, $H_{arom.}$), 7.14–7.11 (m, 1H, $H_{arom.}$), 5.62 (s, 1H, CH). ^{13}C NMR: δ 152.2 (C=N), 146.3 (C=N), 137.6, 132.7, 129.8, 129.0, 128.9, 128.0, 127.9, 126.3, 126.1, 117.1, 103.0 (CCl_3), 79.3 (CH); FAB-MS: *m/z* (%) 480 (10) $[M+H]^+$, 444 (12) $[MH-36]^+$, 362 (5) $[MH-118]^+$, 343 (21) $[MH-137]^+$, 311 (17), 286 (10), 242 (21), 215 (75), 200 (55), 181 (61), 165 (40), 148 (100), 139 (89) $[p\text{-}ClC_6H_4CO]^+$, 123 (32), 105 (48), 89 (67), 79 (48), 75 (54). Anal. Calcd for $C_{16}H_{10}BrCl_4N_3O$ (481.98): C, 39.87; H, 2.09; Br, 16.58; Cl, 29.42; N, 8.72. Found: C, 39.85; H, 2.10; Br, 16.60; Cl, 29.41; N, 8.75.

***N*-(3-Bromophenyl)-6-(4-chlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4g)** FAB-MS: *m/z* (%) 480 (25) $[MH]^+$, 444 (4) $[MH-36]^+$, 362 (25) $[MH-118]^+$, 343 (27) $[MH-137]^+$, 249 (8), 234 (7), 198 (35) $[3\text{-}BrC_6H_4NHCO]^+$, 171 (10), 165 (11), 146 (58), 139 (100) $[p\text{-}ClC_6H_4CO]^+$, 124 (13), 120 (22), 115 (7), 106 (27), 89 (45), 76 (37), 67 (9), 61 (21), 52 (19).

***N*-(4-Bromophenyl)-6-(4-chlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4h)** White crystals; yield 53% (1.28 g); mp 172–174°C (from MeCN); R_f 0.87; IR: ν_{max} 3418, 3247 (NH), 3097, 2911, 2885, 2856 (CH), 1717 (N=C-O-C=N), 1646 (C=N), 1595, 1537, 1489, 1400, 1326, 1287, 1250, 1213, 1131, 1090, 823, 798, 770, 731, 603, 492 cm^{-1}; ^1H NMR: δ 9.92 (s, 1H, NH), 8.05–8.03 (m, 2H, $H_{arom.}$), 7.71–7.67 (m, 4H, $H_{arom.}$), 7.52–7.50 (m, 2H, $H_{arom.}$), 5.71 (s, 1H, CH); ^{13}C NMR: δ 152.2 (C=N), 145.0 (C=N), 138.2, 137.2, 128.9, 128.8, 128.0, 120.8, 117.3, 103.0 (CCl_3), 79.3 (CH); FAB-MS: *m/z* (%) 480 (9) $[M+H]^+$, 446 (9) $[MH-36]^+$, 362 (6) $[MH-118]^+$, 343 (16) $[MH-137]^+$, 307 (19), 242 (38), 215 (76), 200 (49), 181 (70), 165 (43), 157 (87), 147 (61), 139 (100), 123 (42), 109 (64), 89 (89), 75 (55), 60 (79). Anal. Calcd for $C_{16}H_{10}BrCl_4N_3O$ (481.98): C, 39.87; H, 2.09; Br, 16.58; Cl, 29.42; N, 8.72. Found: C, 39.84; H, 2.11; Br, 16.62; Cl, 29.45; N, 8.74.

***N*-(2-Chlorophenyl)-6-(4-chlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4i)** White crystals; yield 68% (1.49 g); mp 135–137°C (from MeCN); R_f 0.69. IR: ν_{max} 3402, 3285 (NH), 3190, 3096, 2929, 2898, 2853 (CH), 1729 (-N=C-O-C=N-), 1651 (C=N), 1596, 1536, 1488, 1443, 1316, 1211, 1135, 1089, 1013, 838, 749, 700, 503 cm^{-1}; ^1H NMR: δ 9.00 (br. s, 1H, NH), 8.07 (d, J = 7.8 Hz, 2H, $H_{arom.}$), 7.95 (m, 1H, $H_{arom.}$), 7.63 (d, J = 7.8 Hz, 2H, $H_{arom.}$), 7.51–7.49 (m, 1H, $H_{arom.}$), 7.37–7.33 (m, 1H, $H_{arom.}$), 7.19–7.16 (m, 1H, $H_{arom.}$) 5.63 (s, 1H, CH); ^{13}C NMR: δ 152.3 (C=N), 146.0 (C=N), 137.6, 134.4, 129.5, 129.1, 128.8, 128.0, 127.3, 125.5, 125.3, 124.8, 103.0 (CCl_3), 79.3 (CH); FAB-MS: *m/z* (%) 436 (8) $[MH]^+$, 400 (3) $[MH-36]^+$, 318 (7) $[MH-118]^+$, 299 (17) $[MH-137]^+$, 186 (14), 139 (100) [*p*-$ClC_6H_4CO]^+$, 98 (32), 83 (43), 54 (36). Anal. Calcd for $C_{16}H_{10}Cl_5N_3O$ (437.53): C, 43.92; H, 2.30; Cl, 40.51; N, 9.60. Found: C, 43.89; H, 2.32; Cl, 40.55; N, 9.63.

***N*,6-*bis*(4-Chlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4j)** White crystals; yield 38% (0.83 g); mp 151–153°C (from MeCN); R_f 0.73; IR: ν_{max} 3419, 3281 (NH), 3189, 3093, 2929, 2880 (CH), 1723 (-N=C-O-C=N-), 1645 (C=N), 1597, 1537, 1492, 1402, 1322, 1286, 1132, 1088, 1013, 826, 770, 731, 703, 606, 494 cm^{-1}; ^1H NMR: δ 9.91 (s, 1H, NH), 8.04 (d, J = 8.3 Hz, 2H, $H_{arom.}$), 7.74–7.68 (m, 4H, $H_{arom.}$), 7.38 (d, J = 8.8 Hz, 2H, $H_{arom.}$), 5.71 (s, 1H, CH); ^{13}C NMR: δ 152.3 (C=N), 145.0 (C=N), 137.6, 137.3, 128.9, 128.8, 128.5, 128.1, 126.1, 120.0, 103.0 (CCl_3), 79.3 (CH); FAB-MS: *m/z* (%) 436 (9) $[M+H]^+$, 400 (3) $[MH-36]^+$, 318 (4) $[MH-118]^+$, 299 (13) $[MH-137]^+$, 208 (10), 186 (20), 139 (100) [*p*-$ClC_6H_4CO]^+$, 125 (17), 98 (36), 83 (42), 54 (36). Anal. Calcd for $C_{16}H_{10}Cl_5N_3O$ (437.53): C, 43.92; H, 2.30; Cl, 40.51; N, 9.60. Found: C, 43.94; H, 2.28; Cl, 40.49; N, 9.62.

6-(4-Chlorophenyl)-*N*-(2,4-dichlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4k) White crystals; yield 52% (1.23 g); mp 164–166°C (from EtOH); R_f 0.89; IR: ν_{max} 3412, 3279 (NH), 3093, 2974, 2916 (CH), 1724 (N=C-O-C=N), 1645 (C=N), 1594, 1527, 1390, 1336, 1292, 1212, 1134, 1091, 1012, 805, 730 cm^{-1}; ^1H NMR: δ 9.36 (s, 1H, NH), 8.11 (d, J = 7.3 Hz, 2H, $H_{arom.}$), 7.94–7.92 (m, 1H, $H_{arom.}$), 7.69–7.67 (m, 3H, $H_{arom.}$), 7.47–7.67 (m, 1H, $H_{arom.}$), 5.66 (s, 1H, CH); ^{13}C NMR: δ 152.1 (C=N), 146.1 (C=N), 137.7, 133.6, 129.8, 129.1, 128.9, 128.4, 127.9, 127.4, 126.3, 125.7 (arom.), 102.8 (CCl_3), 79.2 (CH). FAB-MS: *m/z* (I, %) 470 (2) $[MH]^+$, 434 (5) $[MH-36]^+$, 352 (5) $[MH-118]^+$, 333 (6) $[MH-137]^+$, 215 (43), 187 (30) [2,4-diCl-$C_6H_3NHCO]^+$, 179 (26), 163 (16), 145 (76) $[C_6H_3Cl_2]^+$, 139 (100) [*p*-$ClC_6H_4CO]^+$, 123 (33), 109 (51), 89 (44), 75 (24), 60 (47). Anal. Calcd for $C_{16}H_9Cl_6N_3O$ (471.97): C, 40.72; H, 1.92; Cl, 45.07; N, 8.90. Found: C, 40.69; H, 1.90; Cl, 45.11; N, 8.94.

6-(4-Chlorophenyl)-*N*-(2,5-dichlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4l) FAB-MS: *m/z* (%) 470 (14) $[MH]^+$, 434 (3) $[MH-36]^+$, 368 (9), 352 (30) $[MH-118]^+$, 333 (22) $[MH-137]^+$, 317 (10), 299 (10), 280 (14), 226 (10), 206 (10), 188 (26) [2,4-diCl-$C_6H_3NHCO]^+$, 160 (24), 145 (74) $[C_6H_3Cl_2]^+$, 139 (100) [*p*-$ClC_6H_4CO]^+$, 124 (30), 120 (39), 115 (18), 111 (16) [*p*-$ClC_6H_4]^+$, 107 (84), 89 (93), 77 (86), 62 (46), 51 (18).

6-(4-Chlorophenyl)-*N*-(3,4-dichlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-amine (4m) White crystals; yield 67% (1.58 g); mp 159–161°C (from MeCN); R_f 0.89. IR: ν_{max} 3415, 3285 (NH), 3185, 3102, 2926, 2877 (CH), 1723 (N=C-O-C=N), 1649 (C=N), 1588, 1531, 1476, 1395, 1315, 1128, 1089, 1013, 810, 730, 610 cm^{-1}; ^1H NMR: δ 10.09 (s, 1H, NH), 8.23 (s, 1H, $H_{arom.}$), 8.03 (d, J = 8.3 Hz, 2H, $H_{arom.}$), 7.69 (d, J = 8.3 Hz, 2H, $H_{arom.}$), 7.58–7.56 (m, 1H, $H_{arom.}$), 7.52–7.50 (m, 1H, $H_{arom.}$), 5.75 (s, 1H, CH); ^{13}C NMR: δ 152.1 (C=N), 144.9 (C=N), 138.4, 137.7, 131.0, 130.5, 129.0, 128.8, 127.9, 123.8, 119.8, 118.5, 102.8 (CCl_3), 79.2 (CH); FAB-MS: *m/z* (%) 470 (7) $[MH]^+$, 434 (4) $[MH-36]^+$, 352 (5) $[MH-118]^+$, 333 (18) $[MH-137]^+$, 299 (17), 232 (9), 215 (14), 187 (28) [2,4-diCl-$C_6H_3NHCO]^+$, 161 (19), 145 (95) $[C_6H_3Cl_2]^+$, 139 (100) [*p*-$ClC_6H_4CO]^+$, 112 (42), 91 (72), 79 (70), 56 (45). Anal. Calcd for $C_{16}H_9Cl_6N_3O$ (471.97): C, 40.72; H, 1.92; Cl, 45.07; N, 8.90. Found: C, 40.74; H, 1.94; Cl, 45.05; N, 8.95.

Butyl 4-((6-(4-chlorophenyl)-4-(trichloromethyl)-4*H*-1,3,5-oxadiazin-2-yl)amino)benzoate (4n) FAB-MS: *m/z* (%) 502 (22) $[MH]^+$, 384 (53) $[MH-118]^+$, 369 (9) $[MH-137]^+$, 329 (11), 238 (50), 220 (73) [*n*-BuOC(O)$C_6H_4NHCO]^+$, 193 (30), 181 (20), 164 (79), 146 (63), 139 (100) [*p*-$ClC_6H_4CO]^+$, 120 (84), 115 (21), 111 (18), 107 (74), 89 (88), 76 (66), 62 (51), 55 (53).

Supplementary material (online only)

FAB spectra

Acknowledgments: The authors thank Dr. Alexandr V. Mazepa (A. V. Bogatsky Physico-Chemical Institute, Odessa, Ukraine) for assistance in the mass spectrometric studies.

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Supplementary Material: The online version of this article offers supplementary material (https://doi.org/10.1515/hc-2018-0082).