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A ring-fission/C–C bond cleavage reaction with an *N*-alkyl-*N*-methyl-*N*-[(5-phenyl-1,2,4-oxadiazol-3-yl)methyl]amine

Christine Jäger,[a] Christian Laggner,[a] Kurt Mereiter[b] and Wolfgang Holzer[a,*]

[a]*Institute of Pharmaceutical Chemistry, University of Vienna, Pharmaziezentrum, Althanstraße 14, A-1090 Vienna, Austria*
[b]*Institute of Chemical Technology and Analytics, Technical University of Vienna, Getreidemarkt 9/164, A-1060 Vienna, Austria*

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Abstract—The reaction of *N*-(3,4-dichlorophenethyl)-*N*-methylamine (**1**) with 3-chloromethyl-5-phenyl-1,2,4-oxadiazole (**2**) was investigated. Employment of an equimolar amount of **1** and **2** in the presence of potassium carbonate led to the expected tertiary amine **3** (*N*-[(3,4-dichlorophenyl)ethyl]-*N*-methyl-*N*-[(5-phenyl-1,2,4-oxadiazol-3-yl)methyl]amine), whereas an excess of **1** and prolonged reaction time resulted in ring fission of the oxadiazole system in **3** and finally in the formation of *N*′-benzoyl-*N*-[(3,4-dichlorophenyl)ethyl]-*N*-methylguanidine (**4**) and *N*,*N*′-bis[(3,4-dichlorophenyl)ethyl]-*N*,*N*′-dimethylmethanediamine (**5**). The structures of products **3**–**5** were determined by means of ^{1}H and ^{13}C NMR-spectroscopy, mass spectrometry and IR-spectroscopy, for **3** (as picrate) and **4** also X-ray structure analysis was employed. A possible mechanism of the reaction pathway leading to compounds **4** and **5** is proposed. © 2002 Elsevier Science Ltd. All rights reserved.

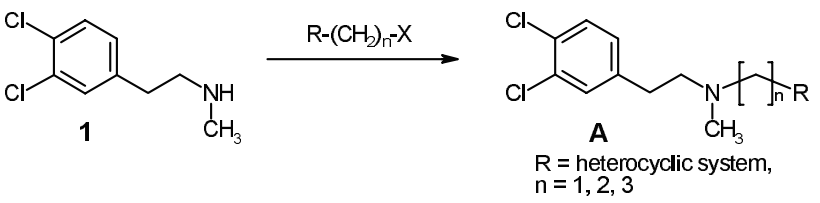
1. Introduction

In the course of a project directed to the synthesis of potential new sigma-receptor-ligands[1a–e] of type **A**, we were interested in compounds containing an oxadiazole ring as heterocyclic partial structure R (Scheme 1). The synthesis of compound **A** usually was carried out via alkylation of *N*-(3,4-dichlorophenethyl)-*N*-methylamine (**1**) with appropriate chloro- or bromoalkyl substituted hetarenes[2] (Scheme 1). Thus, we investigated the reaction of **1** with 3-chloromethyl-5-phenyl-1,2,4-oxadiazole (**2**) in order to obtain the corresponding oxadiazole derivative of type **A** (*n*=1, R=5-phenyl-1,2,4-oxadiazol-3-yl).

2. Results and discussion

TLC-monitoring the reaction of **2** with two equivalents of amine **1** in toluene/DMF according to a procedure described in Ref. 3 showed—besides educt **1**—the gradual formation of an initial reaction product. However, with time a second product occurred and became more and more intensive. After 24 h of reflux, the reaction was stopped and the two reaction products were separated by column chromatography affording as the minor component a yellowish oil and as the main component a colorless solid, which was further purified by recrystallisation. NMR-spectroscopic investigations together with MS data and CHN analysis revealed the oil to be the desired tertiary amine of type **A**, namely *N*-[(3,4-dichlorophenyl)ethyl]-*N*-methyl-*N*-[(5-phenyl-1,2,4-oxadiazol-3-yl)methyl]amine (**3**) (Scheme 2), which was obtained in 24% yield.

From the mass spectrum (using chemical ionisation) of the main component **4**, showing a parent peak of *m*/*z*=350/352/354 (100/63/13% relative intensity), that should originate from the $M^{+}+1$ ion, and from the result of the combustion analysis an elemental composition $C_{17}H_{17}Cl_2N_3O$ was deduced (42% yield). For compound **4** this means a formal loss of one carbon atom and the loss of one double-bond equivalent compared to the expected amine product **3**. The NMR spectra of **4** revealed the



Scheme 1.

Keywords: 1,2,4-oxadiazole; ring opening; C–C bond cleavage; X-ray structure analysis.
* Corresponding author. Tel.: +43-1-4277-55123; fax: +43-1-4277-9551; e-mail: holzer@merian.pch.univie.ac.at

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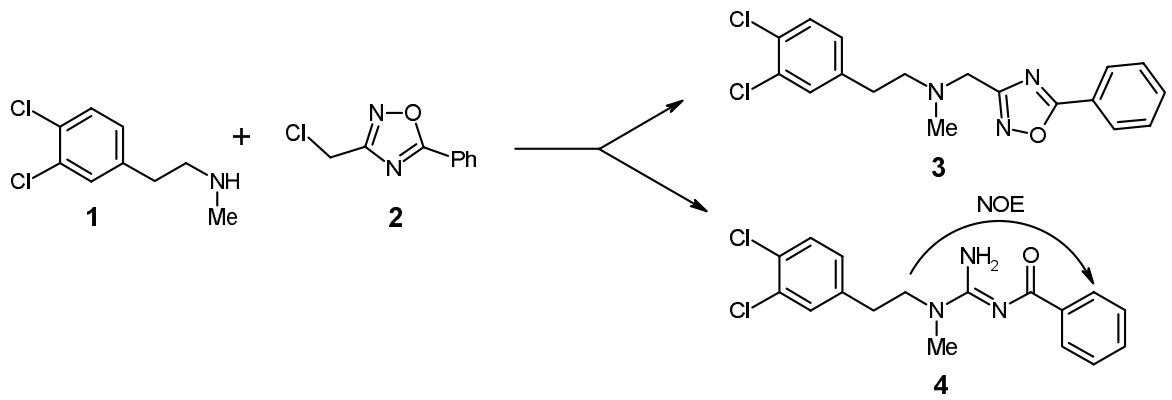
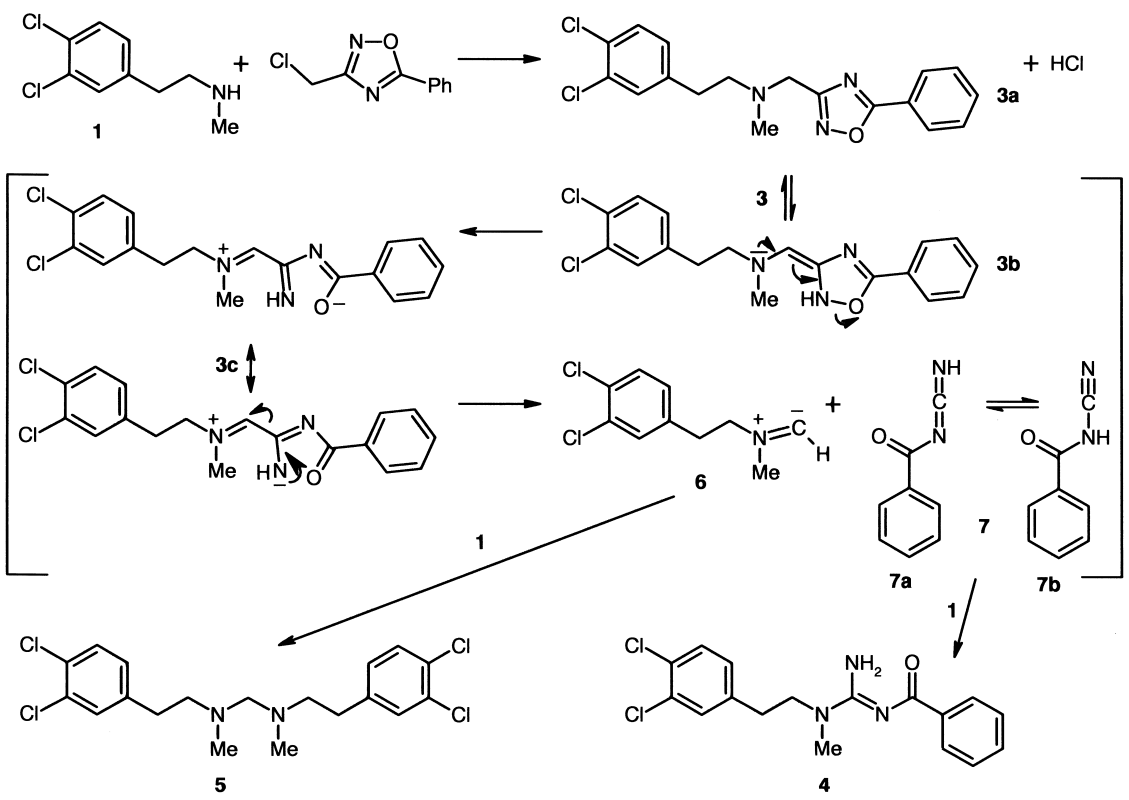


Scheme 2.



Scheme 3. Possible mechanism for the formation of **4** and **5**.

existence of a phenyl ring, an *N*-methyl group and an intact 3,4-dichlorophenethyl group, but not that of an isolated methylene fragment as included in **3**. A remarkable difference in the ^{13}C NMR spectra of **3** and **4** concerned the phenyl C-1 signal, which in **4** was shifted nearly 15 ppm downfield (δ 138.9, in $CDCl_3$) compared to the corresponding signal in **3** (δ 124.1). All these findings provided a strong hint for the absence of an 1,2,4-oxadiazole system in compound **4**. Ultimately, an unambiguous determination of the structure of **4** was achieved by X-ray diffraction analysis, which revealed this reaction product to contain a substituted guanidine moiety (Scheme 2, Fig. 2), obviously resulting from ring opening of the 1,2,4-oxadiazole moiety. Evidence for the bent 'U-turn' structure of **4** found in the solid state was also obtained in solution, as a relatively strong NOE appeared on the signal due to H-2,6 of COPh upon irradiation of the N(Me)CH_2 resonance, indicating spatial closeness of the involved nuclei (Scheme 2, NOE indicated by an arrow).

A possible reaction mechanism for the formation of guanidine derivative **4** from the initial substitution product **3** is outlined in Scheme 3.[†] It includes ring fission of the 1,2,4-oxadiazole system in **3** via cleavage of the weak O–N bond[4] and subsequent C–C bond cleavage in **3c** to afford the reactive intermediates **6** and **7**. Subsequently, **7** reacts with excess amine **1** to afford guanidine derivative **4**, whereas iminium ylide **6** stabilizes upon addition to excess **1** under formation of diamine **5**. The proposed mechanism is supported by the following findings from the literature. O–N Bond cleavage is known to occur with different

[†] Reaction mechanism according to a proposal of Professor A. Eschenmoser, see also acknowledgement.

5-substituted and 3,5-disubstituted 1,2,4-oxadiazoles under alkaline conditions.[5–7] Interestingly, such a ring opening process was even observed upon attempted transesterification of ethyl 5-phenyl-1,2,4-oxadiazole-3-carboxylate by treatment with 2-diethylaminoethanol, this was found to result in the formation of *N*-benzoylcyanamide (**7b**).[8] Nevertheless, to the best of our knowledge no C–C bond cleavages comparable to the fission of **3c** into **6** and **7** have been described in the literature. On the other hand, the transformation of **7** into **4** seems to be plausible as well, since reactions of *N*-benzoylcyanamide (**7b**) with amines are known to result in the formation of *N*-benzoylguanidines.[9–11] However, according to the proposed mechanism, also diamine **5** should be finally formed. This, in fact, could be unambiguously detected by means of NMR spectroscopy when monitoring the reaction of three equivalents of **1** with one equivalent of **2** in a mixture of benzene-d_6–DMSO-d_6 (5:1), particularly via observation of the characteristic N–CH_2–N signal occuring at δ (ppm) ~81 in the ^{13}C NMR spectrum.[12] Moreover, also mass spectrometry (FAB) of the reaction mixture showed the presence of **5**. The structure of diamine **5** was verified by an independent synthesis, i.e. reaction of **1** with formaldehyde according to Refs.[13,14] The similar chromatographic behavior of **5** and **1** (TLC on silica gel) is the obvious reason why the presence of **5** in the original reaction mixture was not noticed.

In contrast, upon employment of equimolar amounts of **1** and **2** (solvent: acetonitrile, addition of K_2CO_3 as HCl-acceptor) the desired tertiary amine (**3**) was obtained as the sole reaction product in 70% yield.

Full and unambiguous assignment of all proton and carbon resonances in the NMR-spectra of compounds **1**–**5** was achieved by a combination of different NMR techniques, such as NOE-difference,[15] APT,[16] gated decoupled ^{13}C NMR, HMQC,[17] long-range INEPT experiments with selective excitation,[18] and 1D-TOCSY.[19]

2.1. X-Ray diffraction analysis

In order to ascertain the chemical structures of **3** and **4**, X-ray single-crystal structure determinations were carried out. Compound **3** was available only in thin needles unsuitable for X-ray analysis and all attempts failed to improve this by recrystallization from various standard solvents where seeding with crystals was always needed to prevent the formation of oil. Hence, **3** was converted into the corresponding picrate **3p** (see Section 3) and suitable crystals were then obtained from hot ethanol. Technical details of the X-ray diffraction study and selected geometric parameters of **3p** are given in Section 3. A view of the solid state structure is shown in Fig. 1. The tertiary nitrogen atom N1 (crystallographic atom designation) is protonated in **3p** and forms a strong but notably bent hydrogen bond to the phenolate oxygen O2 of the picrate, N1···O2=2.627 Å, N1–H1*n*···O2=156°. The 5-phenyl-1,2,4-oxadiazole moiety forms an essentially planar bicyclic aromatic system. Bond lengths and angles in the 1,2,4-oxadiazole ring of **3p** are in good agreement with a few related compounds[20–23] and point to a cyclodiene-like behavior with C11–N3=1.304 Å and N2–C12=1.302 Å as the formal double bonds and C11–N2=1.374 Å shortened by delocalization. Like in other 1,2,4-oxadiazoles the ring bond O1–N3=1.414 Å is relatively long and weak whereas O1–C12=1.344 Å is short and strong.

Compound **4** demanded also some efforts to obtain crystals suitable for X-ray diffraction work. Slow recrystallization from methanol finally produced the required material. Technical details of the structure determination are given in Section 3. A view of the solid state structure is shown in Fig. 2. The compound crystallizes with a triclinic lattice that contains two chemically identical but crystallographically independent molecules distinguished by unprimed and primed atom labels (Fig. 2). Although the two molecules agree basically in conformation they show in detail gradual differences that end up in clearly different non-bonding distances of C15–Cl2=8.04 Å for the first and 9.02 Å for the second molecule. The core of the two molecules is an almost flat *N*,*N*-dialkyl-*N*′-acylguanidine moiety that is stabilized by delocalization causing bonds C10–N1, C10–N2, C10–N3, and C11–N2 to measure all about 1.35 Å. A concomitant lengthening of the C11–O double bond to 1.26 Å (ideal value 1.22 Å) and a strong intramolecular hydrogen bond N3–H3n···O of N···O=2.62 Å are observed. Two intermolecular N3···O hydrogen bonds of

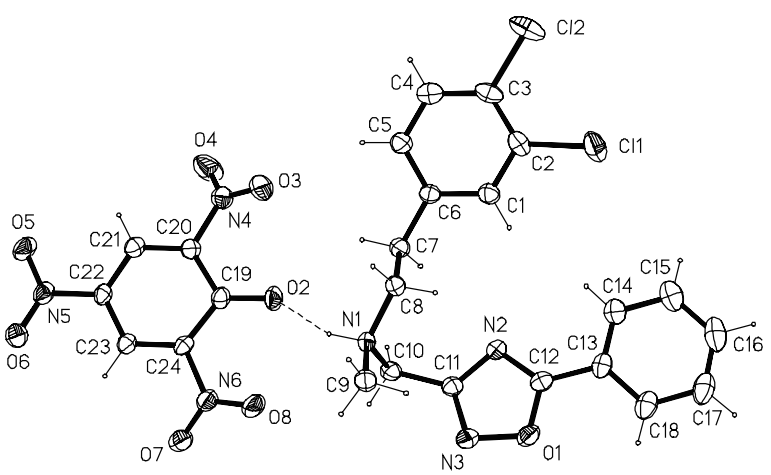


Figure 1. Asymmetric unit of the solid state structure of **3p** showing 20% thermal ellipsoids and the crystallographic atom designation.

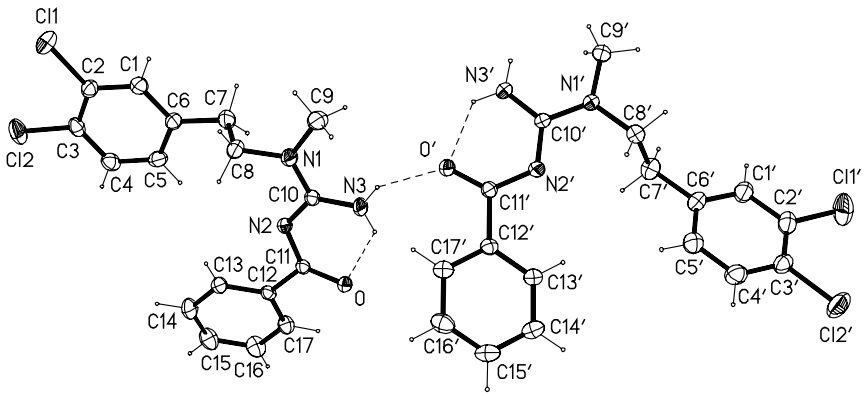


Figure 2. Asymmetric unit of the solid state structure of **4** showing 20% thermal ellipsoids and the crystallographic atom designation.

about 2.86 Å link the two independent molecules in an alternating chain parallel to the *a*-axis of the unit cell. In both molecules, the benzoyl benzene ring is inclined to the carboxyguanidine plane by 18–19°, obviously due to repulsion between N2 and O and the phenyl ortho hydrogen atoms. Comparable features were found in *N*-[bis(cyclohexylamino)methylene]benzamide.[24]

3. Experimental

3.1. General

Melting points were determined on a Reichert–Kofler hot-stage microscope and are uncorrected. The IR spectra were recorded on an ATI Mattson Genesis Series FTIR™ spectrophotometer. Mass spectra were recorded either on a Shimadzu QP5050 (EI, 70 eV), a Shimadzu GCMS-QP1000 EX instrument (chemical isonisation, isobutane, temperature of the ion source 180°C, heating rate 80°C/min, 8.10^{-5} Torr) or on a Finnigan MAT 900S (FAB, matrix: glycerine). The NMR spectra were recorded on a Varian UnityPlus 300 spectrometer (299.95 MHz for ^{1}H, 75.43 MHz for ^{13}C) at 28°C. The chemical shifts are reported in parts per million (ppm); the center of the solvent signal was used as an internal standard, which was related to TMS with δ 7.26 (^{1}H, $CDCl_3$), δ 2.49 (^{1}H, DMSO-d_6), δ 7.16 (^{1}H, benzene-d_6), δ 77.0 (^{13}C, $CDCl_3$), δ 39.5 (^{13}C, DMSO-d_6), δ 128.0 (^{13}C, benzene-d_6). Column chromatographic separations were performed on Merck Kieselgel 60 (70–230 mesh). 3-Chloromethyl-5-phenyl-1,2,4-oxadiazole (**2**) is commercially available (Maybridge Chemical Company, UK), the yields given below are not optimized.

3.1.1. *N*-[(3,4-Dichlorophenyl)ethyl]-*N*-methylamine (1).[25] ^{1}H NMR ($CDCl_3$): δ 7.31 (d, $^{3}J_{5,6}$=8.4 Hz, 1H, Ph H-5,), 7.27 (d, $^{4}J_{2,6}$=2.1 Hz, 1H, Ph H-2), 7.01 (dd, $^{3}J_{5,6}$=8.4 Hz, $^{4}J_{2,6}$=2.1 Hz, 1H, Ph H-6), 2.79 (m, 2H, N–CH_2–CH_2), 2.72 (m, 2H, N–CH_2–CH_2), 2.41 (s, 3H, NCH_3); ^{13}C NMR ($CDCl_3$): δ 140.4 (Ph C-1), 132.2 (Ph C-3), 130.5 (Ph C-2), 130.2 (Ph C-5), 130.0 (Ph C-4), 128.1 (Ph C-6), 52.6 (N–CH_2–CH_2), 36.2 (NCH_3, ^{1}J=133.2 Hz), 35.5 (N–CH_2–CH_2).

3.1.2. 3-Chloromethyl-5-phenyl-1,2,4-oxadiazole (2). ^{1}H NMR ($CDCl_3$): δ 8.15 (m, 2H, Ph H-2,6), 7.62 (m, 1H, Ph H-4), 7.54 (m, 2H, Ph H-3,5), 4.67 (s, 2H, CH_2); ^{13}C NMR ($CDCl_3$): δ 176.7 (oxadiazole C-5, $^{3}J_{C5,Ph\text{-}2,6}$=5.2 Hz), 167.7 (oxadiazole C-3, $^{2}J_{C3,CH2}$=4.4 Hz), 133.1 (Ph C-4), 129.2 (Ph C-3,5), 128.2 (Ph C-2,6), 123.7 (Ph C-1), 34.6 (CH_2, ^{1}J=153.6 Hz).

3.1.3. Reaction of 1 and 2 in equimolar ratio: synthesis of *N*-[(3,4-dichlorophenyl)ethyl]-*N*-methyl-*N*-[(5-phenyl-1,2,4-oxadiazol-3-yl)methyl]amine (3). To a solution of 3-chloromethyl-5-phenyl-1,2,4-oxadiazole (**2**, 973 mg, 5 mmol) and *N*-(3,4-dichlorophenethyl)-*N*-methylamine (**1**, 1.021 g, 5 mmol) in acetonitrile (15 mL) was added K_2CO_3 (5.52 g, 40 mmol) and the mixture was heated at reflux overnight. After filtration, the precipitate was extracted with acetonitrile and the combined filtrates were evaporated in vacuo. The remaining brown oil (2.100 g) was purified by column chromatography (eluent: light petroleum–ethyl acetate, 2:1) to afford **3** (1.268 g, 70%) as a yellowish oil, which solidified in the refrigerator after several months; ^{1}H NMR ($CDCl_3$): δ 8.15 (m, 2H, oxadiazole-*Ph* H-2,6), 7.59 (m, 1H, oxadiazole-*Ph*, H-4), 7.52 (m, 2H, oxadiazole-*Ph* H-3,5), 7.32 (d, $^{4}J_{2,6}$=2.1 Hz, 1H, dichloroPh H-2), 7.31 (d, $^{3}J_{5,6}$=8.2 Hz, 1H, dichloroPh H-5), 7.04 (dd, $^{3}J_{5,6}$=8.2 Hz, $^{4}J_{2,6}$=2.1 Hz, 1H, dichloroPh H-6), 3.84 (s, 2H, oxadiazole-CH_2), 2.82 (m, 2H, N–CH_2–CH_2), 2.76 (m, 2H, N–CH_2–CH_2), 2.46 (s, 3H, NCH_3); ^{13}C NMR ($CDCl_3$): δ 175.8 (oxadiazole C-5), 168.0 (oxadiazole C-3, $^{2}J_{C\text{-}3,CH2}$=5.4 Hz), 140.4 (dichloroPh C-1), 132.7 (oxadiazole-*Ph* C-4), 132.2 (dichloroPh C-3), 130.7 (dichloroPh C-2), 130.2 (dichloroPh C-5), 130.0 (dichloroPh C-4), 129.0 (oxadiazole-*Ph* C-3,5), 128.2 (oxadiazole-*Ph* C-2,6 and dichloroPh C-6), 124.1 (oxadiazole-*Ph* C-1), 57.9 (N–*C*H_2–CH_2), 51.5 (oxadiazole-*C*H_2, ^{1}J=136.5 Hz), 42.4 (NCH_3, ^{1}J=133.9 Hz), 32.9 (N–CH_2–*C*H_2); MS (CI): *m*/*z* (%) 362/364/366 (M^++1, 100/63/9), 365 (12), 363 (19), 218 (13), 216 (17), 204 (12), 202 (83). Anal. calcd for $C_{18}H_{17}Cl_2N_3O$: C, 59.68; H, 4.73; N, 11.60. Found: C, 59.91; H, 4.63; N 11.64.

3.1.4. Reaction of 2 equiv. of 1 with 1 equiv. of 2.[26] A solution of **1** (2.042 g, 10 mmol) and **2** (973 mg, 5 mmol) in toluene (10 mL) and DMF (2 mL) was heated to reflux for 24 h, in which time the color of the solution continuously got darker and a colorless precipitate was formed. After cooling, the mixture was poured onto water (20 mL), the organic phase was separated and the aqueous phase was extracted three times with ethyl acetate. The combined organic phases were washed twice with saturated brine,

dried (Na_2SO_4) and evaporated in vacuo. The residue (2.24 g) was subjected to column chromatography (eluent: gradient starting from light petroleum–ethyl acetate, 2:1 to pure ethyl acetate) to afford **3** (428 mg, 24%, faster eluted component) as an oil and **4** (728 mg, 42%) as a colorless solid which was recrystallized from ethanol-water to give needles of mp 134°C. *N′*-Benzoyl-*N*-[(3,4-dichlorophenyl)-ethyl]-*N*-methylguanidine (**4**) had ^{1}H NMR ($CDCl_3$): δ 8.2–7.0 (br s, 2H, NH_2), 8.21 (m, 2H, COPh H-2,6), 7.46–7.38 (m, 3H, COPh H-3,4,5), 7.35 (d, $^4J_{2,6}$=2.1 Hz, 1H, dichloroPh H-2), 7.35 (d, $^3J_{5,6}$=8.2 Hz, 1H, dichloroPh H-5), 7.05 (dd, $^3J_{5,6}$=8.2 Hz, $^4J_{2,6}$=2.1 Hz, 1H, dichloroPh H-6), 3.82 (t, ^3J=7.2 Hz, 2H, N–CH_2–CH_2), 2.92 (t, ^3J=7.2 Hz, 2H, N–CH_2–CH_2), 2.90 (s, 3H, NCH_3); ^{1}H NMR (DMSO-d_6): δ 11.0–8.4 (br s, 2H, NH_2), 8.07 (m, 2H, COPh H-2,6), 7.58 (s, 1H, dichloroPh H-2), 7.46–7.35 (m, 3H, COPh H-3,4,5), 7.31 (d, $^3J_{5,6}$=8.1 Hz, 1H, dichloroPh H-5), 7.26 (d, $^3J_{5,6}$=8.1 Hz, 1H, dichloroPh H-6), 3.78 (br s, 2H, N–CH_2–CH_2), 2.97 (s, 3H, NCH_3), 2.88 (t, ^3J=7.5 Hz, 2H, N–CH_2–CH_2); ^{13}C NMR ($CDCl_3$): δ 176.7 (C=O), 160.6 (C=N), 139.1 (dichloroPh C-1), 138.9 (COPh C-1), 132.5 (dichloroPh C-3), 130.9 (COPh C-4), 130.7 (dichloroPh C-2), 130.5 (dichloroPh C-4 and C-5), 128.9 (COPh C-2,6), 128.2 (dichloroPh C-6), 127.7 (COPh C-3,5), 51.5 (N–CH_2–CH_2), 35.0 (NCH_3), 33.5 (N–CH_2–CH_2); ^{13}C NMR (DMSO-d_6): δ 174.5 (C=O), 160.5 (C=N), 140.3 (dichloroPh C-1), 139.3 (COPh C-1), 130.8 (dichloroPh C-3), 130.8 (COPh C-4), 130.4 (dichloroPh C-2), 130.3 (dichloroPh C-5), 129.2 (dichloroPh C-6), 128.8 (dichloroPh C-4), 128.4 (COPh C-2,6), 127.6 (COPh C-3,5), 49.8 (N–CH_2–CH_2), 34.6 (NCH_3), 32.4 (N–CH_2–CH_2); IR (KBr): 3293, 3156 (NH), 1638 (C=O) cm^{-1}; MS (CI): *m/z* (%) 350/352/354 (M^++1, 100/63/13), 353 (13), 351 (24), 316 (23). Anal. calcd for $C_{17}H_{17}Cl_2N_3O$: C, 58.30; H, 4.89; N, 12.00. Found: C, 58.47; H, 4.64; N, 11.96.

3.1.5. *N,N′*-Bis[(3,4-dichlorophenyl)ethyl]-*N,N′*-dimethylmethanediamine (5). To a mixture of **1** (2.04 g, 10 mmol) and conc. HCl (0.5 mL, 5 mmol) in MeOH (10 mL) was added dropwise a solution of aqueous formaldehyde (37%, 0.41 mL, 5 mmol) in MeOH (10 mL) at 0°C. The mixture was then stirred at rt for 15 h and poured onto saturated Na_2CO_3 solution (100 mL). After extraction with Et_2O (4×50 mL), the combined organic phases were washed with water and saturated NaCl solution, dried over anhydrous K_2CO_3 and evaporated under reduced pressure. The residue was subjected to Kugelrohr distillation (250°C/0.15 Torr) to afford **5** (1.317 g, 63%) as a colorless oil; ^{1}H NMR ($CDCl_3$): δ 7.31 (d, $^3J_{H\text{-}5,H\text{-}6}$=8.2 Hz, 1H, Ph H-5), 7.28 (d, $^4J_{2,6}$=2.1 Hz, 1H, Ph H-2), 6.98 (dd, $^3J_{5,6}$=8.2 Hz, $^4J_{2,6}$=2.1 Hz, 1H, Ph H-6), 2.92 (s, 2H, N–CH_2–N), 2.67 (m, 2H, N–CH_2–CH_2), 2.59 (m, 2H, N–CH_2–CH_2), 2.23 (s, 3H, NCH_3); ^{1}H NMR (benzene-d_6): δ 7.09 (d, $^4J_{2,6}$=2.1 Hz, 1H, Ph H-2,), 7.06 (d, $^3J_{5,6}$=8.1 Hz, 1H, Ph H-5), 6.55 (dd, $^3J_{5,6}$=8.1 Hz, $^4J_{2,6}$=2.1 Hz, 1H, Ph H-6), 2.61 (s, 2H, N–CH_2–N), 2.32 (s, 4H, N–CH_2–CH_2), 2.03 (s, 3H, NCH_3); ^{13}C NMR ($CDCl_3$): δ 141.1 (Ph C-1), 132.0 (Ph C-3), 130.6 (Ph C-2), 130.0 (Ph C-5), 129.7 (Ph C-4), 128.2 (Ph C-6), 80.8 (N–CH_2–N), 56.2 (N–CH_2–CH_2), 40.4 (NCH_3), 32.8 (N–CH_2–CH_2); ^{13}C NMR (benzene-d_6): δ 141.5 (Ph C-1), 132.4 (Ph C-3), 131.0 (Ph C-2), 130.3 (Ph C-5), 130.1 (Ph C-4), 128.5 (Ph C-6), 81.1 (N–CH_2–N), 56.1 (N–CH_2–CH_2), 40.1 (NCH_3), 33.0 (N–CH_2–CH_2); MS (EI): *m/z* (%) 217 (24), 216 (100), 215 (17), 173 (28); MS (FAB): *m/z* (%) 418 (M^+, 29), 216 (100), 173 (23). Anal. calcd for $C_{19}H_{22}C_{l4}N_2$: C, 54.31; H, 5.28; N, 6.67. Found: C, 54.57; H, 5.04; N, 6.46.

3.2. X-Ray structure determination of 3 in the form of its picrate 3p

Crystal data of **3p**: $C_{24}H_{20}Cl_2N_6O_8$, M_r=591.36, monoclinic, space group $P2_1/c$ (no. 14), a=12.059(4) Å, b=23.481(8) Å, c=10.065(3) Å, β=112.31(1)°, V=2636.6(15) Å^3, Z=4, D_x=1.490 g cm^{-3}, λ=0.71073 Å, μ=0.307 mm^{-1}, T=295 K. To a solution of **3** in ethanol was added slowly under stirring an equimolar amount of picric acid in ethanol. The fine-grained yellow precipitate was recrystallized from hot ethanol. A yellow blade of 0.40×0.12×0.06 mm was used for X-ray data collection with a Bruker Smart CCD diffractometer (CCD area detector, platform type 3-circle goniometer) and Mo Kα radiation (sealed X-ray tube, graphite monochromator). Intensity data with $2\theta \leq 25°$ were harvested over an entire sphere of the reciprocal space (four hemicircles of 0.3°/30 s ω-scan frames) using the SMART[27] and SAINT[28] program packages; corrections for absorption with program SADABS;[29] 26648 reflections collected, 4631 independent, R_{int}=0.079. The structure was solved with direct methods and was then refined on F^2 with program SHELXL97.[30] Hydrogen atoms were located from a different Fourier map and refined riding with the atoms to which they were bonded. The final refinement varied 369 parameters and converged at $R1$=0.056 ($I>2\sigma(I)$, 2457 data) and $R1$=0.130/$wR2$=0.127 (all 4631 data). A view of the asymmetric unit of the structure is shown in Fig. 1. Selected bond lengths (Å; esds 0.004–0.007 Å): Cl1–C2 1.727, Cl2–C3 1.737, O1–C12 1.344, O1–N3 1.414, N1–C9 1.499, N1–C10 1.503, N1–C8 1.505, N2–C12 1.302, N2–C11 1.372, N3–C11 1.304, C1–C2 1.386, C1–C6 1.386, C2–C3 1.378, C3–C4 1.377, C4–C5 1.372, C5–C6 1.390, C6–C7 1.513, C7–C8 1.511, C10–C11 1.494, C12–C13 1.465, C13–C14 1.373, C13–C18 1.393, C14–C15 1.384, C15–C16 1.374, C16–C17 1.365, C17–C18 1.383, O2–C19 1.245, O3–N4 1.211, O4–N4 1.206, O5–N5 1.233, O6–N5 1.217, O7–N6 1.218, O8–N6 1.216, N4–C20 1.468, N5–C22 1.452, N6–C24 1.455, C19–C24 1.436, C19–C20 1.449, C20–C21 1.364, C21–C22 1.381, C22–C23 1.372, C23–C24 1.373.[31]

3.3. X-Ray structure determination of 4

Crystal data of **4**: $C_{17}H_{17}Cl_2N_3O$, M_r=350.24, triclinic, space group P-1 (no. 2), a=9.174(4) Å, b=10.910(4) Å, c=17.914(8) Å, α=78.72(2)°, β=87.66(2)°, γ=89.27(2)°, V=1756.9(13) Å^3, Z=4, D_x=1.324 Mg/m^3, λ=0.71073 Å, μ=0.376 mm^{-1}, T=296 K. A colorless plate of 0.40×0.32×0.04 mm was used for X-ray data collection with a Bruker Smart CCD diffractometer (see above). Intensity data with $2\theta \leq 25°$ harvested over the entire sphere of the reciprocal space (5 hemicircles of 0.3°/26 s ω-scan frames); corrections for absorption with program SADABS;[29] 22633 reflections collected, 5947 independent, R_{int}=0.045. Structure solution with direct methods, refinement on F^2 with program SHELXL97.[30] Hydrogen atoms were located from a difference Fourier map and refined

riding with the atoms to which they were bonded. The final refinement varied 422 parameters and converged at $R1=0.055$ ($I>2\sigma(I)$, 3865 data) and $R1=0.130$/$wR2=0.127$ (all 5947 data). The structure contains two independent molecules as shown in Fig. 2. Selected bond lengths for 1st/2nd molecule (Å; esds 0.004–0.006 Å): Cl1–C2 1.730/1.722, Cl2–C3 1.742/1.754, O1–C11 1.257/1.251, N1–C8 1.469/1.482, N1–C9 1.463/1.457, N1–C10 1.362/1.358, N2–C10 1.341/1.347, N2–C11 1.352/1.347, N3–C10 1.336/1.329, C1–C6 1.385/1.367, C1–C2 1.403/1.419, C2–C3 1.378/1.358, C3–C4 1.388/1.370, C4–C5 1.386/1.369, C5–C6 1.383/1.418, C6–C7 1.522/1.525, C7–C8 1.531/1.504, C11–C12 1.508/1.515, C12–C13 1.386/1.388, C12–C17 1.397/1.391, C13–C14 1.389/1.384, C14–C15 1.390/1.391, C15–C16 1.370/1.373, C16–C17 1.388/1.404.[31]

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