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Derivatives of arylhydrazonic acids. Part 3: Stereochemical rearrangement of *Z*-oxanilo-*N*1-dialkyl-*N*2-arylamidrazones☆

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Abstract—Oxanilo-N^1-dialkyl-N^2-arylamidrazones have been prepared by nucleophilic substitution of the chloride function of appropriate hydrazonoyl chlorides. Relative stabilities of *Z*- and *E*-isomers, calculated with the RHF/6-31G* ab initio method, range between 0.7 and 2.1 kcal/mol. The *Z*-isomer is detected to be thermodynamically more stable for studied compounds. X-ray structure determination of 2-dimethylamino-*N*-phenyl-2-phenylhydrazonoacetamide revealed *E*- and *Z*-isomers (ratio 1:1) in the crystal. The different intra- and intermolecular hydrogen bond interactions, which are identified in solid state of compounds, are dissolved in polar solvents. All compounds were found to form *E*/*Z*-equilibrium in solution. In some cases *E*-isomers could be separated and fully characterized.
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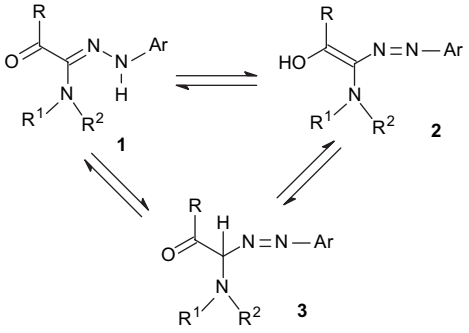
1. Introduction

Compounds with an open-chain or cyclic amidrazone structure represent a class of substances with various interesting biological activities. They have been found to be effective towards cholinesterase,[2] nucleoside hydrolase[3] or glycosidase.[4] Their antiinflammatory[5] and lipoxygenase or cyclooxygenase inhibiting properties[6] are already known.

Recently we reported about the synthesis of α-carbonyl substituted, open-chain amidrazones, which demonstrate inhibitory activity against soybean lipoxygenase-1 and human 5-lipoxygenase.[7] To correlate the biological activity with the structure of amidrazones, their exact structural elucidation is required. N^2-Arylsubstituted amidrazones with an α-carbonyl function can exist in the hydrazono (**1**), azo–enol (**2**) or azo (**3**) tautomeric form (see Scheme 1), each of which exhibits geometric isomerism. In literature, structure **1** is indicated to predominate.

Nearly all structures of N^2-arylamidrazones determined by X-ray diffraction analysis were found to be *Z*-configured.[8–10] The structure of *Z*- and *E*-isomers of *C*-phosphoryl substituted formamidrazones was reported by Buzykin.[11] Cunningham et al.[12] describe *E*/*Z*-N^2-aryl-N^1-dimethylethaneamidrazones, which bear at N^2 an additional methyl group. It was observed that uncatalyzed isomerization could be slowed by the presence of a disubstituted N^2-nitrogen. Since amidines are configurationally less stable, more attention has yet been given to isomerism of corresponding amidoximes,[13] imidates[14] and hydrazonates.[15]



Scheme 1. Tautomeric forms of α-carbonyl substituted amidrazones.

Starting from hydrazonoyl chlorides **4**, we have synthesized further derivatives of N^1-dialkyl-N^2-aryl substituted oxanilo-amidrazones **5**–**8**.

In the presence of a base in aprotic solvents hydrazonoyl chlorides react to form 1,3-dipolar ions. Kinetic studies demonstrated that base catalyzed dehydrochlorination of hydrazonoyl chlorides like **4** proceed in a fast step to the anion, which is followed by the slow abstraction of chloride to form nitrilimine. Studies referred to solvent mixture dioxane/water and triethylamine as base.[16] Furthermore, the nucleophile can substitute the chloride function. To explain

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mechanism of substitution at the carbon–nitrogen double bond, extensive investigations were undertaken by Rowe and Hegarty.[17–20] Preferably, *N*-disubstituted hydrazonoyl halides Aryl–C(X)=N–N(Me)Aryl **9** were studied, which cannot form nitrilimines under base conditions. Modes of reaction of the halide with a nucleophile are conceivable:

- S_N1 type slow scission of the carbon–halogen bond to yield an intermediate azocarbenium ion;
- direct (S_N2) displacement of halogen by a nucleophile.

Reaction in polar solvents like acetone/water or dioxane/water proceeds following the dissociative mechanism (S_N1, D_N+A_N).[18] In less polar solvents, an addition–elimination mechanism (S_N2, A_N+D_N) predominates. The rate determining step of S_N2 varies depending on solvent and base. With a strong base, the addition is discussed to be rate determining ($A_N^{\#}$)[14] whereas in most nonpolar solvent like benzene with secondary amines the elimination was noted to be the rate determining step ($S_N^{\#}$).[17]

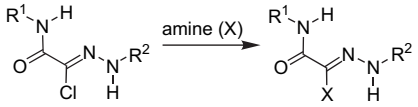
Considering that amidrazones **5–8** were prepared using dioxane as solvent, first step of reaction is assumed to lead to the abstraction of proton by base followed by an addition–elimination pathway. The stereospecifical formation of *Z*-isomers is explainable with both mechanisms. In case of S_N1, the nucleophile attacks the carbenium ion in trans position to the imino lone pair.[12] On the other hand following S_N2, the lone pair has such a configuration in the transition state that the stereospecifically trans elimination can occur.[18] All these data indicate, that the reaction of **4** with amines leads to *Z*-configured amidrazones.

Here we report for the first time on the separation and fully characterization of *E*-isomers besides *Z*-isomers of N^2-aryl-amidrazones.

2. Results and discussion

The preparation of hydrazonoyl chlorides **4** is well known because of their extensive use in 1,3-dipolar cycloaddition reactions. The synthesis of derivatives **4a–4j**, **4l**, **4m** and **4o–4q** is described in literature (lit. see Section 3). According to the reported procedures hydrazonoyl chlorides **4k** and **4n** were additionally prepared. The substitution pattern of compound **4** is shown in Table 1.

The structural assignment of **4** in solid state and in solution was reported.[21] Amidrazones **5–8** were obtained by reaction of oxanilo-1-arylhydrazono-1-chlorides **4** with dimethylamine, diisopropylamine, piperidine or morpholine (see Scheme 2). The substitution pattern of known (**5b**, **5d** and **7a**) and newly synthesized N^1-dialkyl-N^2-aryl substituted oxaniloamidrazones is summarized in Table 5. In accordance to literature data, the reaction of hydrazonoyl chlorides **4** with secondary amines results in isolation of *Z*-isomers. X-ray diffraction analysis of **7g** confirmed that the amidrazone moiety is *Z*-configured, see Figure 1. Essential bond lengths of **7g** are listed in Table 2. The N1–N2 bond length of 1.342(4) Å as well as C1–N2 and C1–N3 distances of 1.291(4) and 1.405(4) are well within the range that typically occurs in other amidrazone derivatives (1.30–1.37 Å for N1–N2, 1.28–1.30 Å for C1–N2 and 1.36–1.47 Å for C1–N3).[8–11] Two intramolecular hydrogen bonds N1–H1···N3 and N4–H2···N2 but no intermolecular hydrogen interactions were detected. The structure of the molecule in the crystal of **7g** with intramolecular hydrogen bonding is outlined in Figure 1.



4 **5-8**

Scheme 2. Synthesis of amidrazones.

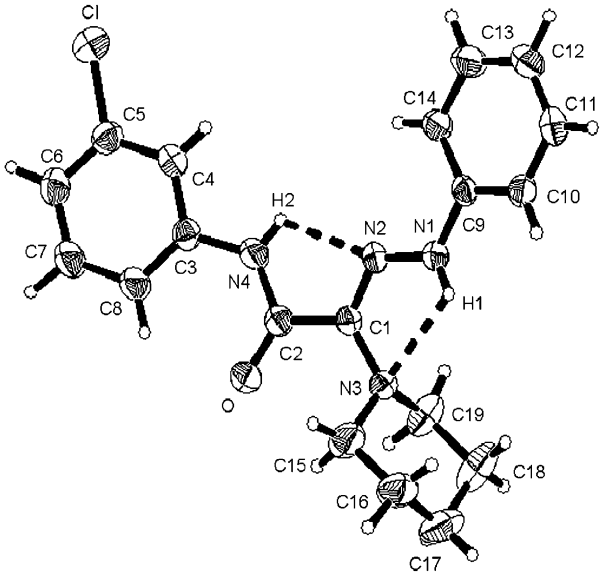


Figure 1. Molecular structure, atom numbering scheme (displacement ellipsoids with 50% probability) and intramolecular hydrogen bonds (dashed lines) of **7g**.

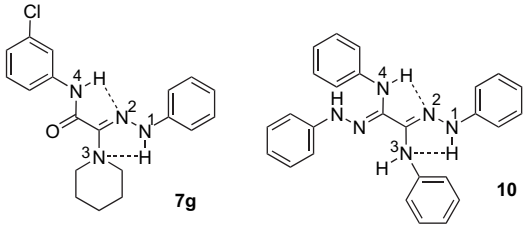
Table 1. Substitution pattern of starting hydrazonoyl chlorides $R^1NHCOC{=}N(Cl)NHR^2$ (**4**)

	R^1	R^2		R^1	R^2
4a	Ph	Ph	**4j**	3-Cl–C_6H_4	Ph
4b	Ph	3-CF_3–C_6H_4	**4k**	4-Cl–C_6H_4	Ph
4c	Ph	2-Cl–C_6H_4	**4l**	2-Cl–C_6H_4	2-Cl–C_6H_4
4d	Ph	4-Cl–C_6H_4	**4m**	2-Cl–C_6H_4	3-Cl–C_6H_4
4e	Ph	2-F–C_6H_4	**4n**	2-Cl–C_6H_4	4-Cl–C_6H_4
4f	Ph	3-F–C_6H_4	**4o**	3-Cl–C_6H_4	2-Cl–C_6H_4
4g	Ph	4-F–C_6H_4	**4p**	3-Cl–C_6H_4	3-Cl–C_6H_4
4h	3-CF_3–C_6H_4	Ph	**4q**	4-Cl–C_6H_4	4-Cl–C_6H_4
4i	2-Cl–C_6H_4	Ph			

Table 2. Characteristic bond length [Å] of the molecule structure of (*E*/*Z*)-**5a** and (*Z*)-**7g**

	(*Z*)-**5a**	(*E*)-**5a**	**7g**
	Molecule A	Molecule B	
N(1)–N(2)	1.351(2)	1.390(3)	1.342(4)
C(1)–N(2)	1.294(2)	1.286(3)	1.291(4)
C(1)–N(3)	1.395(2)	1.373(3)	1.405(4)
C(9)–N(1)	1.391(2)	1.396(3)	1.391(4)
C(1)–C(2)	1.496(3)	1.511(3)	1.491(4)

The formation of possible intramolecular hydrogen bonds as a result of very weak interactions is discussed for amidrazone derivative **10** by Harlow[10] as well (Scheme 3). The distances are comparable in both structures for N1–H1···N3 **7g**: 2.25(3) Å, **10**: 2.37(2) Å for N4–H2···N2 **7g**: 2.23(3) Å, **10**: 2.48(2) Å.



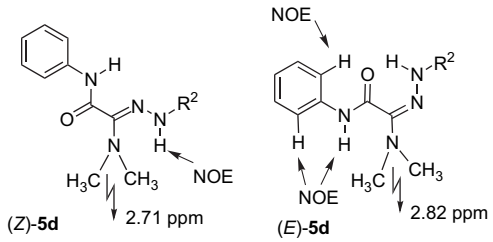
Scheme 3. Structures of *Z*-configured amidrazones **7g** and **10**.

However, purification of crude product of **7a** by careful recrystallization only from heptane led to isolation of different crystal forms. First nearly white crystals were obtained with melting point of 136–138 °C. Besides mixed crystals with melting points of nearly 125 °C, deep yellow, long and thin needles were collected (mp: 118–120 °C). All attempts to get crystals for X-ray diffraction analysis failed. Using TLC with solvent hexane/ether 7:3, two different compounds could be detected. The doubling of signals in ^{1}H and ^{13}C NMR spectra of mixed crystals and the adjustment of equilibrium in solution starting from one form point to the existence of tautomeric or isomeric forms of compound **7a**, see Scheme 1. From further amidrazone derivatives **5c** and **5d**, two different crystal forms could be isolated as well. It was observed by NMR that these different forms occur as pure isomer with less than 10% impurity of the other isomer.

The formation of different tautomeric forms according to Scheme 1 could be ruled out. Besides the signal of anilide proton, an additional lowfield signal was observed in ^{1}H NMR spectrum, which points to NH or OH moiety. Therefore, the azo form (structure **3** in Scheme 1, R=NHAryl) has been excluded. On the other hand, NOE was not observed between both lowfield signals, which is in contrast to enolic structure. In addition, ^{1}H NMR signal of enolic protons is usually found in the region of 13–14 ppm. However, all ^{1}H NMR studies were complicated by the presence of the two signals in the range of 8–10 ppm. Furthermore, mixtures of isomeric forms exhibit four signals. The assignment of different NH signals could only be realized with nearly pure isomers and from experience of appropriate hydrazonoyl chlorides.[21] All routine NMR experiments were run in DMSO, because in chloroform the isomers equilibrated fast.

NOE experiments with derivative **5d** revealed that the compound exists in (*Z*)-**5d** and (*E*)-**5d**, see Scheme 4. The irradiation in frequency of the methyl protons causes in *Z*-isomer an NOE to the hydrazone proton, whereas in the *E*-isomer an NOE was observed not only to the anilide proton but also to the aromatic *ortho*-protons.

Unfortunately, pure *E*-isomers form quiet long and extremely thin needles, which were not suitable for X-ray analysis. All effort to get crystals of *E*-isomer finished at most in isolation of crystals of *E*/*Z*-isomer mixture. X-ray structure determination of amidrazone derivative **5a** revealed *E*- and *Z*-isomer in the crystal ratio of 1:1. The molecular structure of *E*-isomer (molecule B) in the crystal of **5a** is shown in Figure 2. Besides the known intramolecular interactions in the *Z*-isomer, a hydrogen bond between the amide oxygen and the hydrazone proton is present in *E*-isomer (Fig. 3, molecule B). An additional intermolecular hydrogen bond is formed in the crystal of (*E*/*Z*)-**5a** between the carbonyl oxygen of *Z*-isomer (molecule A) and the amide proton of *E*-isomer (molecule B). Distances and angles of hydrogen bonds are listed in Table 3.



Scheme 4. Results of NOE experiments for *E*- and *Z*-isomer of amidrazone **5d**.

To prove the origin of *E*-isomer, crude products of different reaction mixtures were investigated by ^{1}H NMR. It could be noted that the mixtures contained variable amounts of *E*-isomers but not more than 50%, see Table 4. In some cases, *Z*- and *E*-isomers of compounds could be separated

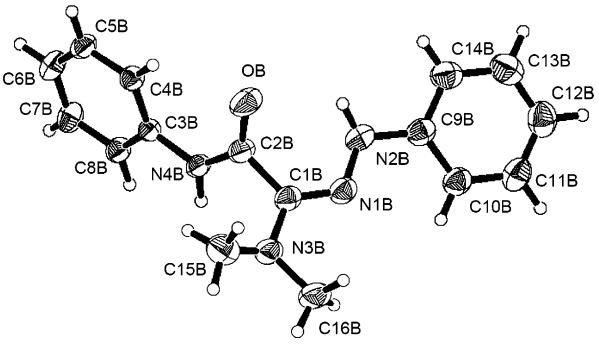


Figure 2. Molecular structure and atom numbering scheme of (*E*)-**5a** in molecule B (displacement ellipsoids with 50% probability).

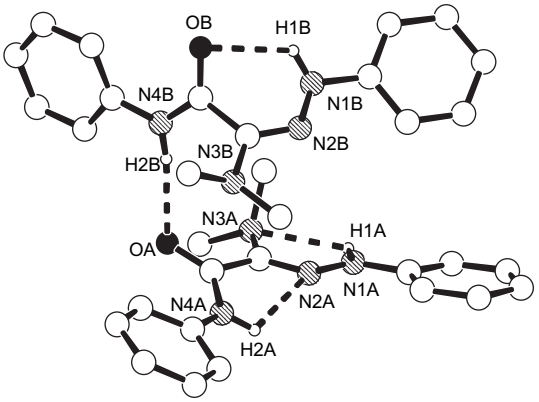


Figure 3. Intra- and intermolecular hydrogen bonding (dashed lines) in the crystal of (*E*/*Z*)-**5a**, molecule A: *Z*-isomer, molecule B: *E*-isomer.

Table 3. Potential intra- and intermolecular hydrogen bonds of the molecule structure of (*E*/*Z*)-**5a** and (*Z*)-**7g**

Type, D–H···A	D–H	H···A	D···A	D–H···A
Intramolecular				
(*Z*)-**5a** N1A–H1A···N3A	0.89(2)	2.34(2)	2.647(2)	100.4(15)
(*Z*)-**7g** N1–H1···N3	0.79(3)	2.25(3)	2.640(4)	111(3)
Intramolecular				
(*Z*)-**5a** N4A–H2A···N2A	0.87(2)	2.26(2)	2.670(2)	109.1(17)
(*Z*)-**7g** N4–H2···N2	0.81(4)	2.23(3)	2.634(4)	111(3)
Intramolecular				
(*E*)-**5a** N1B–H1B···OB	0.91(3)	2.37(3)	2.959(3)	122(2)
Intermolecular				
(*E*/*Z*)-**5a** N4B–H2B···OA	0.88(3)	2.08(3)	2.946(3)	171(2)

Distances (D–H, H···A, D···A) are given in Å, angles in °, D: donor, A: acceptor.

Table 4. Rate % of *E*-isomer of selected crude and recrystallized products of amidrazones $R^1NHCOC{=}N(X)NHR^2$ (**5–8**)

	R^1	R^2	Crude product	*Z*-Isomer	*E*-Isomer	Δ*E* (kcal/mol)
5a	H	H	38	21	50 (90[a])	1.269
5b	H	3-CF_3	16	5	70[a]	0.691
5e	H	4-F	46	<5	50	1.002
5h	2-Cl	2-Cl	<5	15	90	2.102
5l	3-Cl	3-Cl	<5	7	>95	0.879
5m	4-Cl	4-Cl	12	<5	85	1.084
7a	H	H	9	<5	85	1.189
7b	H	2-Cl	30	6	87	2.039
7f	2-Cl	H	<5	<5	n.i.[b]	1.313
8d	4-Cl	H	14	<5	n.i.[b]	1.102

[a] After SC-separation.
[b] Not isolated.

by fractionated crystallization or column chromatography, see Section 3. Besides the involved atoms and the substitution pattern at the phenyl rings the formation enthalpy depends on the specific configuration of the molecule. Ab initio calculations, carried out at the RHF 6-31G* level (see Section 3.1), demonstrate that the energy differences between the *Z*- and *E*-isomers range between 0.69 kcal/mol (compound **5b**) and 2.1 kcal/mol (compound **5h**). On the one hand, compounds with R^2=2-Cl (Table 4: **5h**, **7b**) were found to have higher energy differences between *Z*- and *E*-isomers, but on the other hand a relation of differences of the formation enthalpies and separation of isomers could not been detected. *Z*-Isomers are identified to be thermodynamically more stable for studied compounds. Melting points of *E*-isomer were observed at more than 10 °C lower temperatures like that of *Z*-isomers. Sometimes, *E*-isomers such as (*E*)-**7b** or (*E*)-**5a** transform to *Z*-isomer during heating process. Furthermore, separated *E*-isomers recrystallized from polar solvents as *E*/*Z*-mixtures.

In solution, intramolecular interactions seem to influence the stability of isomers. Maintaining and disrupting of intramolecular hydrogen bonding can be followed in ^{1}H NMR spectra. In accordance with earlier published data of hydrazonoyl chlorides **4**, the intra- and intermolecular interactions are disrupted in polar solvents. Compounds with NH···*ortho*-halogen hydrogen bonds display an independent NH signal.[21] In general, increasing polarity of solvent causes a downfield shift of NH signal of the more or less strong interactions N1–H1···N3 and N4–H2···N2 for about 1–2 ppm and an upfield shift of the strong intramolecular hydrogen bond N1–H1···O in *E*-isomer for about 3 ppm (cf.

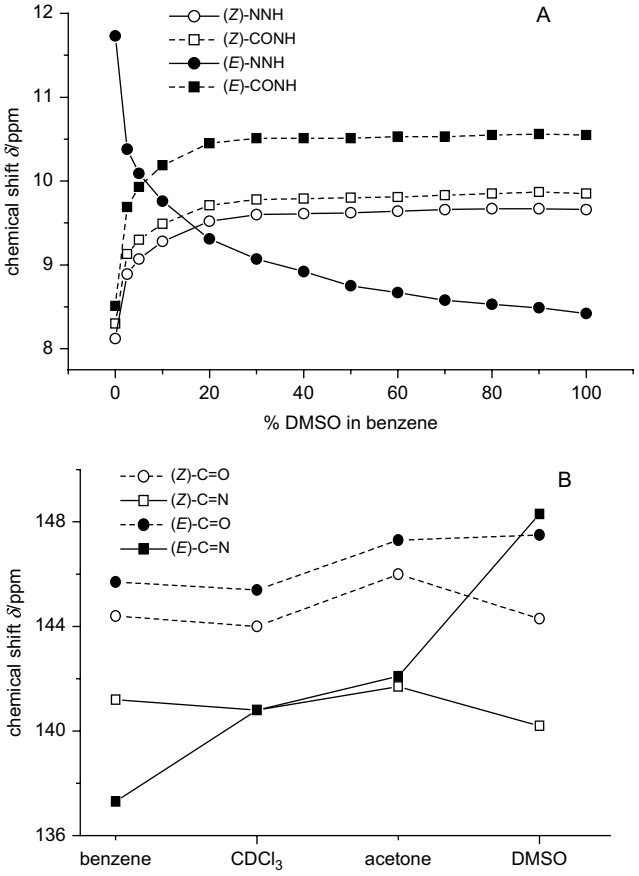


Figure 4. Dependence of the chemical shift δ **A**: of the NH of *Z*-isomer (open symbols) and NH of *E*-isomer (closed symbols) proton of compound **5d** on polarity of solvent; **B**: of C=O and C=N moiety of *Z*-isomer (open symbols) and NH of *E*-isomer (closed symbols) of compound **5d** on polarity of solvent.

Fig. 4A). The exceptional chemical shift of hydrazone proton in *E*-isomer indicates to an intensive intramolecular hydrogen bond in nonpolar solvent benzene.

The disruption of the strong intramolecular hydrogen bond N1–H1···O in *E*-isomer has a particular influence on the chemical environment of C atom of the amidrazone moiety, which is detected in ^{13}C NMR for C=N as well. The signal is shifted in dependence of polarity of solvent for about 10 ppm downfield. All the other signals remain unchanged (see Fig. 4B).

Intramolecular hydrogen bonds between NH proton and *ortho*-halogen substituent of appropriate phenyl ring were the only one, which could be detected in solution as well. In Table 5 compounds with *ortho*-substituted aryl moieties are highlighted. Signals in conjunction with amide structure (R^1) are profiled in bold character and with hydrazone moiety (R^2) in italic character. It is observed in ^{1}H NMR spectra that the *ortho*-halogen substituent of the aryl hydrazone structure (R^2) influences the chemical environment of corresponding proton but only in *Z*-isomer. On the other hand, *ortho*-chloro substituent of the arylamide function ($\mathbf{R^1}$) interacts with the amide proton in *Z*- and *E*-isomer as well, but it actually causes an interference with hydrazone proton in *E*-isomers. Even in ^{13}C NMR spectra the chemical shift of the signal of the hydrazone carbon reflects conspicuously the

Table 5. Substitution pattern of amidrazones $R^1NHCOC{=}N(X)NHR^2$ (**5**–**8**) and essential ^1H and ^{13}C NMR data of CONH and C=NNH moiety of *E*- and *Z*-isomers

No.	X	R^1	R^2	^1H NMR				^{13}C NMR			
				CONH		NNH		CO		C=N	
				Z	*E*	*Z*	*E*	*Z*	*E*	*Z*	*E*
5a	$N(CH_3)_2$	Ph	Ph	9.77	10.49	9.52	8.37	161.1	160.7	140.3	150.3
5b	$N(CH_3)_2$	Ph	3-CF_3–C_6H_4	9.96	10.60	9.81	8.56	160.5	160.7	141.5	153.0
5c	$N(CH_3)_2$	Ph	**2-Cl–C_6H_4**	10.00	10.70	**8.63**	8.46	160.1	160.1	**143.4**	150.8
5d	$N(CH_3)_2$	Ph	4-Cl–C_6H_4	9.84	10.55	9.65	8.41	161.0	161.0	140.9	152.2
5e	$N(CH_3)_2$	Ph	4-F–C_6H_4	9.78	10.47	9.56	8.20	160.6	160.4	141.0	151.4
5f	$N(CH_3)_2$	*2-Cl–C_6H_4*	Ph	9.84	*10.20*	9.56	*9.08*	160.2	n.d.	138.5	n.d.
5g	$N(CH_3)_2$	3-Cl–C_6H_4	Ph	9.94	10.70	9.62	8.44	161.2	n.d.	139.7	n.d.
5h	$N(CH_3)_2$	*2-Cl–C_6H_4*	**2-Cl–C_6H_4**	*9.63*	10.43	**8.74**	*9.01*	159.4	160.4	**141.8**	148.5
5i	$N(CH_3)_2$	*2-Cl–C_6H_4*	3-Cl–C_6H_4	9.93	*10.28*	9.63	*8.70*	160.0	n.d.	139.5	n.d.
5j	$N(CH_3)_2$	*2-Cl–C_6H_4*	4-Cl–C_6H_4	9.90	*10.25*	9.52	*8.83*	159.7	n.d.	138.9	n.d.
5k	$N(CH_3)_2$	3-Cl–C_6H_4	**2-Cl–C_6H_4**	10.13	10.83	**8.70**	8.51	160.2	n.d.	**143.5**	n.d.
5l	$N(CH_3)_2$	3-Cl–C_6H_4	3-Cl–C_6H_4	10.06	10.78	9.76	8.47	160.8	161.2	140.7	152.2
5m	$N(CH_3)_2$	4-Cl–C_6H_4	4-Cl–C_6H_4	9.97	10.69	9.70	8.42	160.8	160.9	140.4	151.6
6a	$N[CH_2CH(CH_3)_2]_2$	Ph	3-CF_3–C_6H_4	10.43	11.00	9.08	8.31	161.3	n.d.	141.1	n.d.
6b	$N[CH_2CH(CH_3)_2]_2$	*2-Cl–C_6H_4*	Ph	*9.66*	*9.94*	9.13	*8.91*	160.5	159.8	*138.0*	*140.6*
6c	$N[CH_2CH(CH_3)_2]_2$	4-Cl–C_6H_4	Ph	9.97	10.40	8.98	8.41	161.2	n.d.	139.5	n.d.
7a	$N(CH_2)_5$	Ph	Ph	9.79	10.35	9.05	8.73	161.1	160.7	140.2	148.2
7b	$N(CH_2)_5$	Ph	**2-Cl–C_6H_4**	9.96	10.46	**8.77**	8.81	160.1	160.2	**142.7**	148.8
7c	$N(CH_2)_5$	Ph	**2-F–C_6H_4**	9.93	10.41	**8.50**	8.41	160.0	160.2	**142.3**	150.1
7d	$N(CH_2)_5$	Ph	3-F–C_6H_4	9.88	10.47	9.21	8.67	160.5	160.4	140.7	149.8
7e	$N(CH_2)_5$	3-CF_3–C_6H_4	Ph	10.10	10.68	9.16	8.82	161.4	161.5	139.5	147.5
7f	$N(CH_2)_5$	*2-Cl–C_6H_4*	Ph	*9.52*	*10.00*	9.28	*10.42*	160.4	n.d.	*138.6*	n.d.
7g	$N(CH_2)_5$	3-Cl–C_6H_4	Ph	9.94	10.60	9.12	8.77	161.4	n.d.	139.7	n.d.
8a	$N(CH_2)_2O(CH_2)_2$	3-CF_3–C_6H_4	Ph	10.12	10.72	9.46	9.25	161.4	n.d.	137.7	n.d.
8b	$N(CH_2)_2O(CH_2)_2$	*2-Cl–C_6H_4*	Ph	*9.55*	*10.07*	9.59	*10.53*	160.3	159.5	*136.8*	*144.9*
8c	$N(CH_2)_2O(CH_2)_2$	3-Cl–C_6H_4	Ph	9.97	10.57	9.43	9.22	160.9	n.d.	137.6	n.d.
8d	$N(CH_2)_2O(CH_2)_2$	4-Cl–C_6H_4	Ph	9.94	10.53	9.39	9.14	161.1	n.d.	138.0	n.d.

δ (DMSO-d_6)/ppm; n.d.: not detected.

intramolecular association particularly between compounds **5h**, **6b** and **8b** (last two columns in Table 5).

In UV spectra the absorption with highest wavelength in both *Z*- and *E*-isomers is observed at about 350 nm with remarkably high intensity. This absorption is shifted to higher wavelength in the case of the *E*-isomer, possibly due to the different hydrogen bonding in both isomers, see Figure 5.

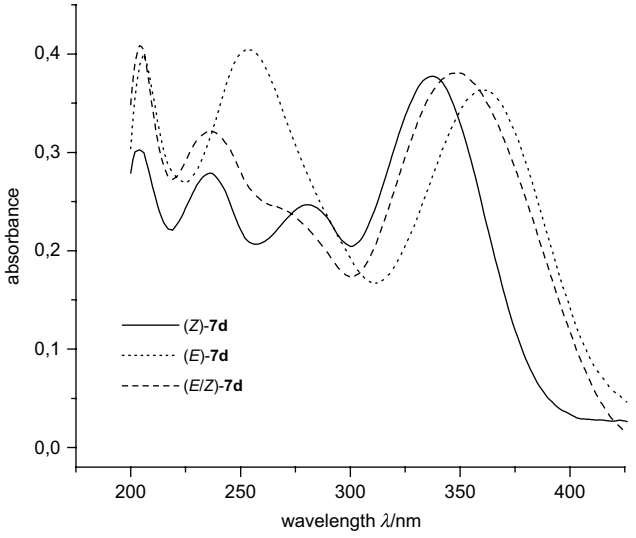


Figure 5. UV spectra of *Z*- and *E*-isomer of compound **7d** as well as of *E*/*Z*-isomer mixture.

In the case of the *E*-configuration, a further absorption band at about 250 nm with high intensity is observed. Due to the altered geometry in the *Z*-configuration, the energy differences between the excited singlet states diverge into two distinct values with higher distance, leading to the two observed absorption peaks at about 280 nm and 235 nm with lower intensity. In the experimentally measurable region up to the shortest wavelength of 200 nm yet another absorption band at about 215 nm is observed. The wavelength seems to be independent of the geometry of the molecule.

In conclusion, *E*-configured arylamidrazones **5**–**8** are formed from *Z*-isomers by rearrangement in solution. Presumably this process occurs whereas preparation and/or recrystallization from polar solvents. Nonpolar solvents like heptane favour the crystallization of *E*-isomers, the configuration of which is stabilized by intramolecular interaction N1–H1···O in such a nonpolar medium.

3. Experimental

3.1. General remarks

The quantum chemical calculations of the interesting compounds were carried out using the GAMESS program.[22] Optimized geometries and total energies of the *E*- and *Z*-isomers were calculated using the RHF/6-31G* ab initio method. The input structures for the individual compounds

were generated on the basis of the determined X-ray structures of **5a** and **7g** using the SYBYL6.9 program.[23]

Melting points were determined with a Kofler hot-stage apparatus and are uncorrected. NMR spectra were recorded on a Gemini 2000 and Gemini 200, operating at 399.96 MHz and 199.95 MHz for ^{1}H NMR and at 100.6 MHz and 50.3 MHz for ^{13}C NMR spectra. TMS was used as internal standard and routinely DMSO-d_6 as solvent. Chemical shifts are given in δ units and refer to the centre of the signal. Mass spectra were obtained with an AMD 402 of the firm AMD INTEDRA (70 eV); IR spectra were recorded on a Spectrum BX FT-IR from the firm Perkin Elmer. Probes were prepared in KBr. UV spectra were run on Spekol 1200 from the firm Carl Zeiss Jena GmbH using ethanol for solvent. TLC was routinely carried out with TLC aluminium sheets Silica gel 60 F_{254} of the firm Merck developed in the solvent chloroform/ether (7:3, v/v) and detected with ultraviolet light (254 nm). For separation of *E*/*Z*-isomers of amidrazones TLC sheets were developed in mixture of hexane/ether 7:3.

Crystallographic data (excluding structure factors) for the structures **5a** and **7g** in this paper have been deposited to the Cambridge Crystallographic Data Centre as supplementary publication numbers CCDC 254724 (**5a**) and CCDC 254724 (**7g**). Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge CB2 1EZ, UK [fax: +44 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].

3.2. Arylhydrazonoyl chlorides (4)

Compounds were obtained in accordance to Ref. 24 (**4a**), Ref. 21 (**4b**, **4e**, **4h**–**4j**, **4l**, **4m**, **4o** and **4p**), Ref. 25 (**4c** and **4d**), Ref. 1 (**4f** and **4g**) and Ref. 26 (**4q**).

3.2.1. *N*-Phenyl-2-[(4-chlorophenyl)amino]-2-oxoethanehydrazonoyl chloride (4k). According to lit.[21] **4k** is obtained from aniline (0.01 mol, 0.93 g) and 2-chloro-*N*-(4-chlorophenyl)-3-oxobutanamide (0.01 mol, 2.5 g) as yellow needles (2.1 g, 67%), mp 209–210 °C (from chloroform/heptane). IR (KBr) ν_{max}/cm^{-1}: 3380m, 3227m (NH ass.), 1865s (C=O, amide). ^{1}H NMR (DMSO-d_6) δ_H: 6.95–7.78 (9H, arom), 10.15 (1H, s, CONH, amide), 10.33 (1H, s, NNH, hydrazone). ^{13}C NMR (DMSO-d_6) δ_C: 114.9–143.0 (12C, arom), 118.0 (CN, hydrazone), 157.5 (CONH, amide); *m*/*z* 307 (M^+, 100%), 127 (100), 92 (55). Anal. Calcd for $C_{14}H_{11}Cl_2N_3O$ (308.2): C 54.6; H 3.6; Cl 23.0; N 13.6. Found: C 54.5; H 3.7; Cl 23.0; N 13.6.

3.2.2. *N*-(4-Chlorophenyl)-2-[(2-chlorophenyl)amino]-2-oxoethanehydrazonoyl chloride (4n). According to lit.[21] **4n** is obtained from 4-chloroaniline (0.01 mol, 1.3 g) and 2-chloro-*N*-(2-chlorophenyl)-3-oxobutanamide (0.01 mol, 2.5 g) (synthesized following lit.[27]) as pale yellow needles (1.2 g, 68%), mp 230–232 °C (from chloroform/ethyl acetate). IR (KBr) ν_{max}/cm^{-1}: 3358m, 3285m (NH ass.), 1793s (C=O, amide); ^{1}H NMR (DMSO-d_6) δ_H: 7.23–7.82 (8H, arom), 9.81 (1H, s, CONH, amide), 10.56 (1H, s, NNH, hydrazone). ^{13}C NMR (DMSO-d_6) δ_C: 116.1–141.6 (12C, arom), 118.1 (CN, hydrazone), 156.8 (CONH, amide). MS *m*/*z* 343 (M^+, 32%), 127 (100). Anal. Calcd for $C_{14}H_{10}Cl_3N_3O$ (342.6): C 49.1; H 2.9; Cl 31.0; N 12.3 Found: C 49.1; H 2.9; Cl 30.8; N 12.2.

3.3. Synthesis of substituted 2-amino-*N*-aryl-2-arylhydrazonoacetamides 5–8 (GP 1)

A solution of arylhydrazonoyl chloride **1** (5 mmol) in about 20 ml dioxane was added dropwise to 10 mmol dimethylamine (5 ml of 2 M solution in tetrahydrofuran), 5 mmol diisobutylamine (0.9 ml) and 5 mmol triethylamine (0.7 ml), 10 mmol piperidine (1.0 ml) or 10 mmol morpholine (0.9 ml), respectively, in a few millilitres of dioxane. After stirring at 40–45 °C for at least 12 h (control of reaction progress by TLC) the mixture was poured into 150 ml cold water. The solid was collected, washed with water, dried and recrystallized from the given solvent. The described *Z*-isomers as well as *E*-isomers are commonly impured with 1–15% of the corresponding isomer. Physical characteristics of prepared compounds are described in Table 6.

3.3.1. 2-Dimethylamino-*N*-phenyl-2-phenylhydrazonoacetamide (5a). The preparation from **4a** (1.4 g, 5 mmol) and dimethylamine following GP 1 gave the crude product **5a** as a mixture of 62% *Z*- and 38% *E*-isomer. Recrystallization from heptane led first to pale yellow crystals of *Z*-isomer (0.5 g, 35% yield) and then to yellow needles as an *E*/*Z*-mixture, which was recrystallized from heptane/chloroform and then from methanol to give yellow crystals as 1:1 mixture of (*Z*)- and (*E*)-**5a** for X-ray structure determination. Crystal structure analysis of **5a**: Crystal data. $C_{32}H_{36}N_8O_2$, M_r=564.69, monoclinic, a=11.770(4), b=15.400(4), c=17.362(6) Å, V=3077(2) Å^3, T=293(2) K, space group $P2_1/c$, Z=4, μ(Mo Kα)=0.080 mm^{-1}, =0.71073 Å, 28,673 reflections collected, 6001 unique (R_{int}=0.0943), which were used in all calculations. Final $wR(F^2)$ was 0.1382 (all data).

3.3.2. 2-Dimethylamino-*N*-phenyl-2-{[3-(trifluoromethyl)phenyl]hydrazono}acetamide (5b). The preparation from **4b** (1.7 g, 5 mmol) and dimethylamine following GP 1 gave the crude product **5b** as a mixture of 84% *Z*- and 16% *E*-isomer. Recrystallization from heptane led to pale yellow needles of *Z*-isomer, which was rapidly transformed to the *E*/*Z*-mixture within one day at room temperature. The isomers could be separated by column chromatography (heptane, heptane/ether). After a fraction with 70% (*E*)-**5b** as yellow oil (0.5 g, 29% yield), fractions with *E*/*Z*-mixture and (*Z*)-**5b** (0.2 g, 12% yield) were obtained.

3.3.3. 2-[2-(Chlorophenyl)hydrazono]-2-dimethylamino-*N*-phenylacetamide (5c). The preparation from **4c** (1.5 g, 5 mmol) and dimethylamine following GP 1 gave from heptane first (*Z*)-**5c** as white needles (0.9 g, 55% yield). The second crystallization fraction gave (*E*)-**5c** as thin yellow needles (0.1 g, 5% yield).

3.3.4. 2-[4-(Chlorophenyl)hydrazono]-2-dimethylamino-*N*-phenylacetamide (5d). The preparation from **4d** (1.5 g, 5 mmol) and dimethylamine following GP 1 gave from heptane first (*Z*)-**5d** as pale yellow crystals (0.3 g, 19% yield). After crystals with *E*/*Z*-mixtures, long yellow needles were obtained as (*E*)-**5d** (0.5 g, 30% yield).

3.3.5. 2-[4-(Fluorophenyl)hydrazono]-2-dimethylamino-*N*-phenylacetamide (5e). The preparation from **4g** (1.5 g, 5 mmol) and dimethylamine following GP 1 gave the crude product **5e** as a mixture of 55% *Z*- and 45% *E*-isomer.

Table 6. Physical characteristics of amidrazones **5–8**

Mp		Anal.		MS	UV (log ε)	IR NH; CO	^{1}H NMR	^{13}C NMR
		C	H					
Calcd for $C_{16}H_{18}N_4O$		68.1	6.4	M, 282				
(*Z*)-**5a**	112–114	68.0	6.5	282 (M^+, 100), 92 (55)	347 (4.23)	3372, 3330, 3296, 3241; 1661, 1648	2.69 (6H, s, $2CH_3$), 6.80–7.75 (10H arom)	40.2 (2C, $2CH_3$), 113.9–144.7 (12C arom)
(*E*)/(*Z*)-**5a** (1:1)	107–109	67.9	6.5	282 (M^+, 100), 161 (30)	348 (4.23)	3372, 3330; 1661, 1648	(*E*): 2.80 (6H, s, $2CH_3$), 6.61–7.70 (10H arom)	(*E*): 38.2 (2C, $2CH_3$), 112.6–147.7 (12C arom)
Calcd for $C_{17}H_{11}F_3N_3O$		58.3	4.9	M, 350				
(*Z*)-**5b**	74–78	58.2	4.9	350 (M^+, 100), 229 (46), 186 (35)	340 (3.96)	3392, 3297; 1663, 1655(sh)	2.71 (6H, s, $2CH_3$), 7.01–7.73 (9H arom)	40.1 (2C, $2CH_3$), 109.7–145.1 (12C arom), 124.5 (q, J=295 Hz, CF_3)
(*E*)-**5b**	64–66	58.1	5.1	350 (M^+, 100), 229 (57), 186 (46)	342 (4.11)	3289; 1667	2.85 (6H, s, $2CH_3$), 6.87–7.69 (9H arom)	37.7 (2C, $2CH_3$), 108.3–148.7 (12C arom)
Calcd for $C_{16}H_{17}ClN_4O$		60.7	5.4	M, 316				
(*Z*)-**5c**	133–135	60.7	5.4	316 (M^+, 100), 195 (40)	335 (4.11)	3289; 1656	2.75 (6H, s, $2CH_3$), 6.84–7.76 (9H arom)	40.1 (2C, $2CH_3$), 115.2–143.4 (12C arom)
(*E*)-**5c**	125–135	60.4	5.4	316 (M^+, 100), 195 (30)	359 (3.87)	3333, 3251; 1653	2.87 (6H, s, $2CH_3$), 6.69–7.73 (9H arom)	38.4 (2C, $2CH_3$), 113.3–142.5 (12C arom)
(*Z*)-**5d**	128–129	60.5	5.3	316 (M^+, 100), 195 (42), 125 (42)	344 (3.95)	3301, 3244; 1654(sh), 1649	2.71 (6H, s, $2CH_3$), 7.04–7.76 (9H arom)	40.2 (2C, $2CH_3$), 115.3–143.7 (12C arom)
(*E*)-**5d**	125–135	60.7	5.3	316 (M^+, 100), 195 (55), 125 (50).	360 (3.96)	3322, 3263; 1654	2.82 (6H, s, $2CH_3$), 6.64–7.71 (9H arom)	38.0 (2C, $2CH_3$), 114.1–152.0 (12C arom)
(*Z*)-**5f**	144–146	60.7	5.4	316 (M^+, 100), 161 (38)	351 (3.77)	3343, 3218; 1669, 1658	2.77 (6H, s, $2CH_3$), 6.84–8.27 (9H arom)	40.2 (2C, $2CH_3$), 113.6–144.2 (12C arom)
(*Z*)-**5g**	118–120	60.6	5.3	316 (M^+, 100), 161 (50)	346 (4.21)	3286; 1654	2.69 (6H, s, $2CH_3$), 6.64–7.94 (9H arom)	40.2 (2C, $2CH_3$), 114.0–144.5 (12C arom)
Calcd for $C_{16}H_{17}FN_4O$		64.0	5.7	M, 300				
(*Z*)-**5e**	107–109	64.1	5.7	300 (M^+, 100), 179 (38)	342 (4.20)	3401(w), 3298, 3267; 1673, 1660	2.69 (6H, s, $2CH_3$), 7.03–7.73 (9H arom)	40.1 (2C, $2CH_3$), 114.6–141.0 (11 C arom), 156.4 (1 C, d, J=235 Hz, arom *C*F)
(*E*)/(*Z*)-**5e** (1:1)	97–100	63.8	5.7	300 (M^+, 100), 179 (38), 109 (37)	347 (4.09)	3374, 3324, 3288; 1661, 1647	(*E*): 2.81 (6H, s, $2CH_3$), 6.91–7.75 (9H arom)	(*E*): 38.1 (2C, $2CH_3$), 113.5–144.7 (11C arom), 155.1 (1 C, d, J=231 Hz, arom *C*F)
Calcd for $C_{16}H_{16}Cl_2N_4O$		54.7	4.6	M, 350				
(*Z*)-**5h**	79–81	54.7	4.5	350 (M^+, 100), 195 (62)	343 (4.10)	3354; 1693	2.78 (6H, s, $2CH_3$), 6.89–8.06 (8H arom)	40.1 (2C, $2CH_3$), 114.6–139.3 (12C arom)
(*E*)-**5h**	103–105	54.5	4.6	350 (M^+, 100), 195 (75)	364 (3.98)	3282; 1685, 1660	2.86 (6H, s, $2CH_3$), 6.70–7.61 (8H arom)	39.1 (2C, $2CH_3$), 114.8–143.9 (12C arom)
(*Z*)-**5i**	127–129	54.4	4.5	350 (M^+, 100), 195 (62), 152 (45)	349 (3.89)	3345, 3242; 1674, 1665(sh)	2.77 (6H, s, $2CH_3$), 6.85–8.19 (8H arom)	40.2 (2C, $2CH_3$), 112.2–145.8 (12C arom)
(*Z*)-**5j**	139–141	54.7	4.6	350 (M^+, 100), 195 (100), 160 (60), 125 (100)	353 (4.23)	3379, 3364, 3247; 1670	2.73 (6H, s, $2CH_3$), 7.12–8.17 (8H arom)	40.2 (2C, $2CH_3$), 114.8–143.0 (12C arom)
(*Z*)-**5k**	147–149	54.7	4.6	350 (M^+, 100), 195 (42)	336 (4.23)	3295, 1659	2.75 (6H, s, $2CH_3$), 6.88–7.93 (8H arom)	40.0 (2C, $2CH_3$), 115.3–142.7 (12C arom)
(*Z*)-**5l**	146–148	54.8	4.5	350 (M^+, 100), 195 (42)	342 (4.33)	3295, 1659	2.69 (6H, s, $2CH_3$), 6.79–7.93 (8H arom)	40.3 (2C, $2CH_3$), 112.3–146.1 (12C arom)
(*E*)-**5l**	107–110	54.6	4.4	350 (M^+, 60), 195 (100), 160 (60), 152 (100), 125 (60)	359 (3.91)	3170; 1652	2.83 (6H, s, $2CH_3$), 6.59–7.91 (8H arom)	37.8 (2C, $2CH_3$), 111.2–149.6 (12C arom)
(*Z*)-**5m**	125–129	54.5	4.8	350 (M^+, 100), 195 (76), 160 (40), 125 (58)	347 (4.18)	3384, 3283; 1665(sh), 1655	2.69 (6H, s, $2CH_3$), 7.22–7.81 (8H arom)	40.2 (2C, $2CH_3$), 115.3–143.4 (12C arom)

Table 6. (*continued*)

	Mp	Anal.		MS	UV (log ε)	IR NH; CO	^{1}H NMR	^{13}C NMR
		C	H					
(*E*)-**5m**	106–112	54.6	4.6	350 (M^+, 100), 195 (85), 160 (52), 125 (79)	355 (4.05)	3412(br), 3300(br), 1654	2.81 (6H, s, $2CH_3$), 6.90–7.72 (8H arom)	38.0 (2C, $2CH_3$), 114.0–146.9 (12C arom)
Calcd for $C_{23}H_{29}F_3N_4O$		63.6	6.7	M, 434				
(*Z*)-**6a**	123–125	63.5	6.7	434 (M^+, 100), 93 (65)	337 (3.93)	3346, 3308; 1660	0.87 (12H, d, J=7 Hz, $4CH_3$), 1.74 (2H, m, 2CH, J=7 Hz), 2.93 (4H, d, $2CH_2$, J=7 Hz), 7.04–7.76 (9H arom)	20.5 (4C, $4CH_3$), 27.3 (2C, 2CH), 58.5 (2C, $2CH_2$), 110.0–145.4 (12C arom), 124.5 (q, CF_3, J=273 Hz)
Calcd for $C_{22}H_{29}ClN_4O$		65.9	7.3	M, 400				
(*Z*)-**6b**	49–51	65.6	7.3	400 (M^+, 100), 308 (30)	348 (3.91)	3368, 3313, 1687, 1677	0.86 (12H, d, J=7 Hz, $4CH_3$), 1.73 (2H, m, 2CH, J=7 Hz), 2.92 (4H, d, $2CH_2$, J=7 Hz), 6.84–8.20 (9H arom)	20.6 (4C, $4CH_3$), 27.2 (2C, 2CH), 58.8 (2C, $2CH_2$), 113.6–143.9 (12C arom)
(*Z*)-**6c**	88–90	65.7	7.2	400 (M^+, 100), 308 (25)	342 (4.24)	3374, 3360, 3305; 1678(sh), 1660	0.87 (12 H, d, J=7 Hz, $4CH_3$), 1.71 (2H, m, 2CH, J=7 Hz), 2.84 (4H, d, $2CH_2$, J=7 Hz), 6.82–7.82 (9H arom)	20.6 (4C, $4CH_3$), 27.2 (2C, 2CH), 59.0 (2C, $2CH_2$), 113.0–143.9 (12C arom)
Calcd for $C_{19}H_{22}N_4O$		70.8	6.9	M, 322				
(*Z*)-**7a**	136–138	70.7	6.9	322 (M^+, 90%), 84 (100)	342 (4.34)	3284; 1654	1.58 (m)[a], 1.67 (m)[b], 2.98 (m)[c], 6.81–7.74 (10H, arom)	23.9[d], 25.2[e], 48.5[f], 114.1–144.3 (12C arom)
(*E*)-**7a**	118–120	70.6	6.8	322 (M^+, 100), 84 (20)	358 (4.17)	3332, 3296; 1651	1.59 (s)[a,b], 3.14 (s)[c], 6.61–7.72 (10H arom)	24.0[d], 24.7[e], 47.6[f], 112.6–147.3 (12C arom)
Calcd for $C_{19}H_{21}ClN_4O$		63.9	5.9	M, 356				
(*Z*)-**7b**	194–196	63.9	5.9	356 (M^+, 90%), 84 (100)	337 (3.97)	3297, 3269, 3247; 1652	1.58 (d, J=5 Hz)[a], 1.65 (s)[b], 3.02 (t, J=5 Hz)[c], 6.88–7.77 (9H arom)	23.7[d], 26.1[e], 48.6[f], 115.1–139.2 (12C arom)
(*E*)-**7b**	>150 (transf.)			356 (M^+, 100), 230 (55), 84 (100)	355 (3.81)	3347, 3326; 1656	1.59[a], 1.64[b], 3.14 (t, J=5 Hz)[c], 6.70–7.73 (9H arom)	23.9[d], 24.5[e], 47.8[f], 113.2–142.2 (12C arom)
(*Z*)-**7f**	133–136	63.8	5.9	356 (M^+, 100), 84 (62)	350 (4.13)	3355, 3245; 1677	1.54 (d, J=5 Hz)[a], 1.67 (d, J 5)[b], 3.02 (t, J=5 Hz)[c], 6.84–8.21 (9H arom)	23.9[d], 25.3[e], 48.6[f], 115.3–145.4 (12C arom)
(*Z*)-**7g**	146–149	63.9	6.0	356 (M^+, 100), 84 (100)	344 (4.13)	3354, 3267; 1667	1.54 (s)[a], 1.68 (s)[b], 2.97 (t, J=5 Hz)[c], 6.81–7.92 (9H arom)	23.9[d], 25.3[e], 48.5[f], 114.2–144.1 (12C arom)
Calcd for $C_{19}H_{21}FN_4O$		67.0	6.2	M, 340				
(*Z*)-**7c**	148–150	67.0	6.2	340 (M^+, 91%), 84 (100)	336 (4.14)	3286; 1656	1.56 (t, J=4 Hz)[a], 1.61 (d, J 5)[b], 3.00 (t, J=5 Hz)[c], 6.84–7.75 (9H arom)	23.8[d], 25.9[e], 48.6[f], 115.0–151.3 (11C arom), 151.8 (d, 1C, J=239 Hz, arom *C*F)
(*Z*)-**7d**	135–137	67.1	6.3	340 (M^+, 75%), 84 (100)	337 (3.93)	3284; 1655	1.54 (d, J=4 Hz)[a], 1.69 (s)[b], 3.00 (t, J=5 Hz)[c], 6.56–7.76 (9H arom)	23.9[d], 25.1[e], 48.5[f], 100.4–140.7 (11C arom), 163.3 (d, 1C, J=241 Hz, arom *C*F)
(*E*)-**7d**	105–108	67.1	6.3	340 (M^+, 85%), 84 (100)	360 (3.95)	3339; 1653	1.58 (s)[a,b], 3.18 (s)[c], 6.35–7.70 (9H arom)	24.0[d], 24.6[e], 47.0[f], 98.6–149.8 (11 C arom), 162.9 (d, 1C, J=239 Hz, arom *C*F)
Calcd for $C_{20}H_{21}F_3N_4O$		61.5	5.4	390				
(*Z*)-**7e**	130–134	61.6	5.4	390 (M^+, 100), 84 (90)	342 (4.07)	3282; 1656	1.55 (s)[a], 1.68 (s)[b], 2.97 (d, J=5 Hz)[c], 6.81–8.04 (9H arom)	24.0[d], 25.3[e], 48.6[f], 114.1–143.9 (11C arom), 124.2 (q, CF_3, J=272 Hz)
Calcd for $C_{19}H_{19}F_3N_4O_2$		58.2	4.9	M, 392				
(*Z*)-**8a**	169–171	58.1	5.0	392 (M^+, 100), 91 (30), 86 (35)	342 (4.16)	3382, 3280; 1676(sh), 1658	3.04 (4H, t, $2NCH_2$, J=4.5 Hz), 3.78 (4H, t, J=4.5 Hz, $2OCH_2$), 6.84–8.22 (9H arom)	47.6 (2C, $2NCH_2$), 66.1 (2C, $2OCH_2$), 115.8–145.4 (11C arom), 125.7 (q, CF_3, J=273 Hz)

(*continued*)

Table 6. (*continued*)

	Mp	Anal.		MS	UV (log ε)	IR NH; CO	^{1}H NMR	^{13}C NMR
		C	H					
Calcd for $C_{18}H_{19}ClN_4O_2$		60.2	5.3	M, 358				
(*Z*)-**8b**	158–161	60.2	5.2	358 (M^+, 100), 91 (45), 86 (51)	349 (4.03)	3362, 3289; 1673	3.08 (4H, t, $2NCH_2$, J=4.5 Hz), 3.78 (4H, t, J=4.5 Hz, $2OCH_2$), 6.86–8.21 (9H arom)	47.6 (2C, $2NCH_2$), 66.1 (2C, $2OCH_2$), 114.0–143.8 (12C arom)
(*E*)-**8b**	139–142	60.3	5.1	358 (M^+, 100), 86 (45)	370 (4.13)	3308, 3246; 1660	3.05 (t, 4H, J=4.5 Hz, $2NCH_2$), 3.77 (t, 4H, J=4.5 Hz, $2OCH_2$), 6.76–8.00 (9H arom)	49.4 (2C, $2NCH_2$), 65.9 (2C, $2OCH_2$), 112.6–139.2 (12C arom)
(*Z*)-**8c**	161–163	60.1	5.4	358 (M^+, 100), 91 (35), 86 (52)	342 (4.11)	3360, 3284; 1665	3.04 (t, 4H, J=4.5 Hz, $2NCH_2$), 3.79 (t, 4H, J=4.5 Hz, $2OCH_2$), 6.83–7.95 (9H arom)	47.5 (2C, $2NCH_2$), 66.0 (2C, $2OCH_2$), 114.2–143.8 (12C arom)
(*Z*)-**8d**	213–215	60.2	5.4	358 (M^+, 100), 86 (45)	342 (3.72)	3281, 3263; 1673(sh), 1652	3.02 (t, 4H, J=4.5 Hz, $2NCH_2$), 3.76, 6.82–7.78 (9H arom)	47.6 (2C, $2NCH_2$), 66.1, 115.7–145.5 (12C arom)

Melting point mp/°C, elemental analysis Anal., mass spectrometry data (MS) *m*/*z* %, UV(EtOH) λ_{max}/nm, IR (KBr) ν_{max}/cm^{-1} and NMR (DMSO-d_6) δ/ppm.

[a] 2H, $NCH_2CH_2CH_2$–.
[b] 4H, $2NCH_2CH_2$–.
[c] 4H, $2NCH_2$–.
[d] 1C, $NCH_2CH_2CH_2$–.
[e] 2C, $2NCH_2CH_2$–.
[f] 2C, $2NCH_2$.

Recrystallization from heptane led first to pale yellow crystals of *Z*-isomer (0.4 g, 27% yield) and then to yellow crystals as 1:1 mixture of (*Z*)- and (*E*)-**5e** (0.9 g, 60% yield).

3.3.6. *N*-(2-Chlorophenyl)-2-dimethylamino-2-phenylhydrazonoacetamide (5f). The preparation from **4i** (1.5 g, 5 mmol) and dimethylamine following GP 1 gave from heptane first (*Z*)-**5f** (0.8 g, 51% yield) as yellow crystals and then an *E*/*Z*-mixture of **5f** (0.3 g, 19% yield).

3.3.7. *N*-(3-Chlorophenyl)-2-dimethylamino-2-phenylhydrazonoacetamide (5g). The preparation from **4j** (1.5 g, 5 mmol) and dimethylamine following GP 1 gave from heptane (*Z*)-**5g** (0.4 g, 25% yield) as pale yellow needles.

3.3.8. *N*-(2-Chlorophenyl)-2-[2-(chlorophenyl)hydrazono]-2-dimethylaminoacetamide (5h). The preparation from **4l** (1.7 g, 5 mmol) and dimethylamine following GP 1 gave the crude product **5h** as 100% of *Z*-isomer. Recrystallization from heptane led first to pale yellow crystals of (*Z*)-**5h** (0.9 g, 51% yield). The second crystallization fraction gave (*E*)-**5h** as yellow, plate-like crystals (0.1 g, 6% yield).

3.3.9. *N*-(2-Chlorophenyl)-2-[3-(chlorophenyl)hydrazono]-2-dimethylaminoacetamide (5i). The preparation from **4m** (1.7 g, 5 mmol) and dimethylamine following GP 1 gave from heptane (*Z*)-**5i** (0.8 g, 45% yield) as yellow, short needles.

3.3.10. *N*-(2-Chlorophenyl)-2-[4-(chlorophenyl)hydrazono]-2-dimethylaminoacetamide (5j). The preparation from **4n** (1.7 g, 5 mmol) and dimethylamine following GP 1 gave from heptane (*Z*)-**5j** as yellow crystals (1.0 g, 57% yield).

3.3.11. *N*-(3-Chlorophenyl)-2-[2-(chlorophenyl)hydrazono]-2-dimethylaminoacetamide (5k). The preparation from **4o** (1.7 g, 5 mmol) and dimethylamine following GP 1 gave from heptane (*Z*)-**5k** as yellowish-white needles (1.0 g, 57% yield).

3.3.12. *N*-(3-Chlorophenyl)-2-[3-(chlorophenyl)hydrazono]-2-dimethylaminoacetamide (5l). The preparation from **4p** (1.7 g, 5 mmol) and dimethylamine following GP 1 gave a crude product of a mixture of 97% (*Z*)-**5l** and 3% (*E*)-**5l**. From heptane/dioxane, first (*Z*)-**5l** crystallized as white needles (0.7 g, 40% yield), and then (*E*)-**5l** as a white amorphous solid (0.2 g, 11% yield). (2*E*)-**5l** dissolved in polar solvents with a quiet yellow colour and transformed to an 1:1 mixture of *E*/*Z*-isomers within one week at room temperature.

3.3.13. *N*-(4-Chlorophenyl)-2-[4-(chlorophenyl)hydrazono]-2-dimethylaminoacetamide (5m). The preparation from **4q** (1.7 g, 5 mmol) and dimethylamine following GP 1 gave a crude product of a mixture of 88% (*Z*)-**5m** and 12% (*E*)-**5m**. From heptane, first (*Z*)-**5m** crystallized as yellow crystals (0.4 g, 23% yield), then *E*/*Z*-mixtures (0.6 g, 34% yield) and at least (*E*)-**5m** as fine, dark yellow needles (0.1 g, 6% yield).

3.3.14. 2-Diisobutylamino-*N*-phenyl-2-{[3-(trifluoromethyl)phenyl]hydrazono}acetamide (6a). The preparation

from **4b** (1.7 g, 5 mmol), diisobutylamine and triethylamine following GP 1 gave from heptane (*Z*)-**6a** as pale yellow needles (0.9 g, 41% yield).

3.3.15. *N*-(2-Chlorophenyl)-2-diisobutylamino-2-phenylhydrazonoacetamide (6b). The preparation from **4i** (1.5 g, 5 mmol), diisobutylamine and triethylamine following GP 1 gave a crude product, which did not crystallize after pouring into the water. The oily product was separated by extraction with diethyl ether. The solvent was evaporated and the residue was crystallized from heptane to give (*Z*)-**6b** as pale yellow crystals (0.4 g, 24% yield).

3.3.16. *N*-(4-Chlorophenyl)-2-diisobutylamino-2-phenylhydrazonoacetamide (6c). The preparation from **4k** (1.5 g, 5 mmol), diisobutylamine and triethylamine following GP 1 gave from heptane (*Z*)-**6c** as pale yellow needles (0.9 g, 45% yield).

3.3.17. *N*-Phenyl-2-phenylhydrazono-2-piperidin-1-ylacetamide (7a). The preparation from **4a** (1.4 g, 5 mmol) and piperidine following GP 1 gave the crude product **7a** as a mixture of 90% *Z*- and 10% *E*-isomer. From heptane crystallized first (*Z*)-**7a** as white needles (0.9 g, 56% yield). The second crystallization fraction gave (*E*)-**7a** as thin and long yellow needles (50 mg, 3% yield). Recrystallization of **7a** from heptane/chloroform gave yellow crystals as 1:1 mixture of (*Z*)/(*E*)-**7a**, mp 125–132 °C according to Ref. 6.

3.3.18. 2-[2-(Chlorophenyl)hydrazono]-*N*-phenyl-2-piperidin-1-ylacetamide (7b). The preparation from **4c** (1.5 g, 5 mmol) and piperidine following GP 1 gave the crude product **7b** as a mixture of 80% *Z*- and 20% *E*-isomer. From heptane crystallized first (*Z*)-**7b** as white crystals (1.1 g, 61% yield). The second crystallization fraction gave (*E*)-**7b** as thin yellow needles (0.1 mg, 6% yield).

3.3.19. 2-[2-(Fluorophenyl)hydrazono]-*N*-phenyl-2-piperidin-1-ylacetamide (7c). The preparation from **4e** (1.5 g, 5 mmol) and piperidine following GP 1 gave from heptane (*Z*)-**7c** as whitish fine needles (1.4 g, 72% yield).

3.3.20. 2-[3-(Fluorophenyl)hydrazono]-*N*-phenyl-2-piperidin-1-ylacetamide (7d). The preparation from **4f** (1.5 g, 5 mmol) and piperidine following GP 1 gave from heptane first (*Z*)-**7d** (0.9 g, 53% yield) as pale yellow needles. In a second fraction, a mixture of isomers and at least (*E*)-**7d** crystallized from heptane as thin, yellow needles (85 mg, 5% yield).

3.3.21. 2-Phenylhydrazono-2-(piperidin-1-yl)-*N*-[3-(trifluoromethyl)phenyl]acetamide (7e). The preparation from **4h** (1.5 g, 5 mmol) and piperidine following GP 1 gave from heptane (*Z*)-**7e** as pale yellow needles (1.2 g, 62% yield).

3.3.22. *N*-(2-Chlorophenyl)-2-phenylhydrazono-2-piperidin-1-ylacetamide (7f). The preparation from **4i** (1.5 g, 5 mmol) and piperidine following GP 1 gave the crude product **7f** as a mixture of 97% *Z*- and 3% *E*-isomer. Recrystallization from heptane led to (*Z*)-**7f** as yellow crystals (0.8 g, 45% yield).

3.3.23. *N*-(3-Chlorophenyl)-2-phenylhydrazono-2-piperidin-1-ylacetamide (7g). The preparation from **4j** (1.5 g, 5 mmol) and piperidine following GP 1 gave from heptane (*Z*)-**7g** as yellow crystals (1.0 g, 56% yield). Crystal structure analysis of **7g**: Crystal data. $C_{19}H_{21}ClN_4O$, M=356.85, orthorhombic, a=11.860(1), b=15.138(5), c=20.643(3) Å, V=3706.2(13) Å^3, T=293(2) K, space group *Pcab*, Z=8, μ(Mo Kα)=0.220 mm^{-1}, 4658 reflections collected, 2415 unique (R_{int}=0.0272), which were used in all calculations. Final $wR(F^2)$ was 0.1122 (all data).

3.3.24. 2-(Morpholin-4-yl)-2-phenylhydrazono-*N*-[3-(trifluoromethyl)phenyl]acetamide (8a). The preparation from **4h** (1.4 g, 5 mmol) and morpholine following GP 1 gave from heptane (*Z*)-**8a** as white crystals (1.5 g, 76% yield).

3.3.25. *N*-(2-Chlorophenyl)-2-(morpholin-4-yl)-2-phenylhydrazonoacetamide (8b). The preparation from **4i** (1.5 g, 5 mmol) and morpholine following GP 1 gave from heptane first (*Z*)-**8b** as pale yellow needles (1.2 g, 67% yield). In a second fraction (*E*)-**8b** crystallized from heptane as thin, yellow needles (140 mg, 8% yield).

3.3.26. *N*-(3-Chlorophenyl)-2-(morpholin-4-yl)-2-phenylhydrazonoacetamide (8c). The preparation from **4j** (1.5 g, 5 mmol) and morpholine following GP 1 gave from heptane (2*Z*)-**8c** as yellow crystals (1.4 g, 78% yield).

3.3.27. *N*-(4-Chlorophenyl)-2-(morpholin-4-yl)-2-phenylhydrazonoacetamide (8d). The preparation from **4k** (1.5 g, 5 mmol) and morpholine following GP 1 gave the crude product **8d** as a mixture of 86% *Z*- and 14% *E*-isomer. Recrystallization from heptane/acetone led to (*Z*)-**8d** as pale yellow fine crystals (1.1 g, 61% yield).

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