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A new 'one-pot' synthesis of hydrazides by reduction of hydrazones

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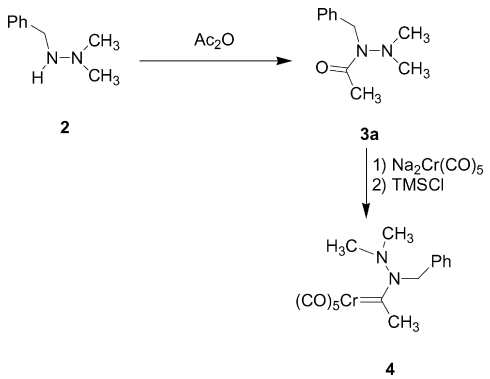
Abstract—A new, high-yielding methodology for reducing hydrazones to hydrazines is described, which allows the synthesis of different mono-, di- and trisubstituted hydrazines. Moreover, the reduction step can be followed by an in situ reaction with a carboxylic acid making possible a 'one-pot' synthesis of trisubstituted hydrazides. The method is relatively general and, in principle, suitable for industrial applications.

1. Introduction

Hydrazines and hydrazides are important precursors for the synthesis of heterocycles, pharmaceuticals, agrochemicals, polymers, dyestuffs and photography products,[1] which is why the lack of an efficient and general synthetic route for the preparation of substituted hydrazines still stimulates research in this area.[2] Of the previously reported methods of hydrazine synthesis, the reduction of hydrazones[2e,3] is the most interesting because of its simplicity and the great diversity allowed by the large number of available aldehydes and ketones.



Scheme 1.

However, the ease of this method greatly depends on the electronic and steric properties of the hydrazone, and on how the reduction is carried out. Our interest in seeking a versatile and general method of hydrazide and hydrazine synthesis was related to another research project concerning the synthesis of Fischer-type hydrazino carbene complexes, a new class whose synthesis and reactivity have been established in our laboratory.[4] For example, carbene complex **4** was synthesised from the hydrazide **3a** obtained by acylating the parent hydrazine **2** (Scheme 1). Hydrazine **2** has previous been prepared[5] in high yield (80%) by means of the benzylation of *N*,*N*-dimethylhydrazine, but this synthetic method is not general because the reaction conditions are very harsh (NaOH at 280–320°C) and the yields vary widely when even small changes are made to the structure of **2**.

2. Results and discussion

In the search of a more versatile method of preparing differently substituted hydrazines for use in the synthesis of carbene complexes, we tried some published reduction protocols. Hydrazone **1a** was thus reduced using BH_3·THF[3d] and Et_3SiH[3a] in CF_3COOH, and the hydrazine was acylated in situ in order to avoid its easy oxidation to the parent hydrazone (Scheme 2). Hydrazide **3a** was recovered in rather low overall yields (26 and 40% respectively).

The presence of an acid in the reaction medium (as in the case of Et_3SiH/CF_3COOH[3a]) plays an important role in improving the reduction because protonation of the

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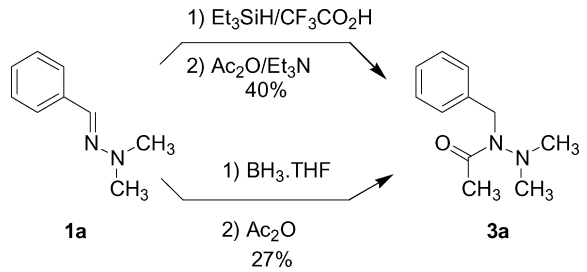
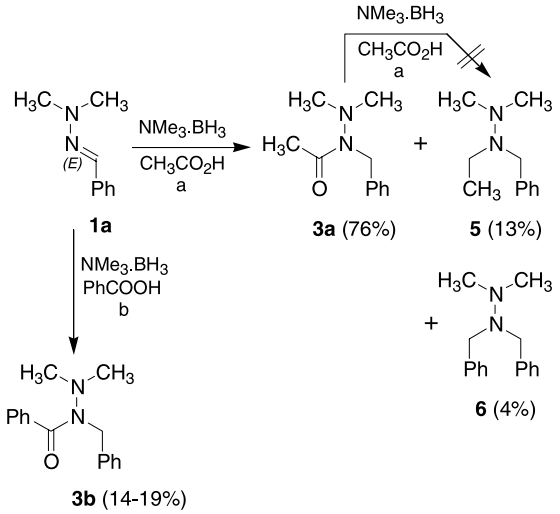


Scheme 2. First attempts to synthesise hydrazide **3a**.



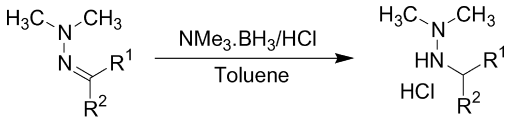
Reaction conditions and yields: a) $NMe_3.BH_3$ (1.3 equiv); reflux for 5 hours; b) $NMe_3.BH_3$ (1.3 equiv.), $PhCO_2H$ (3 equiv.) in refluxing xylene: yield 17%; $PhCO_2H$ (10 equiv.) in refluxing toluene: yield 14%; $PhCO_2H$ (6 equiv.) without solvent at 150°C: yield 19%.

Scheme 3. Reductive acylation of hydrazone **1a**.

hydrazone activates the C=N bond to the attack of nucleophiles. We therefore considered the use of amine–borane complexes,[6,7] which are stable in acid medium, as hydrazone reducing agents. Hydrazone **1a** was used as a model compound (Scheme 3). The use of AcOH as solvent (path a) gave hydrazide **3a** in 76% yield, but the presence of the two tetralkyl hydrazines **5** and **6** as by-products required the chromatographic purification of the reaction mixture. Hydrazine **5** does not arise from reduction of hydrazide **3a**[8] but may originate from the reduction of acetic acid to an aldehyde equivalent,[9] which reacts with hydrazine **2** to give the corresponding hydrazonium ion[9b] whose reduction affords hydrazine **5**. Furthermore, this method was not generally applicable because, when PhCOOH was used under different reaction conditions (including those reported for the benzoylation of imines[7]), the yield of hydrazide **3b** did not exceed 19%.

In order to improve the selectivity of the reduction step, we considered using a strong acid in order to protonate the hydrazone completely. In this way, the reduction of hydrazones **1a–i** in toluene and gaseous HCl led to the exclusive formation of the corresponding *N*,*N*-dimethyl-*N'*-substituted hydrazine hydrochlorides **2a–i** (Table 1) in very high yields.[10] The reaction is fast (about 30 min) and the work-up very easy: the hydrazine hydrochloride salts are obtained as pure compounds after filtration from the

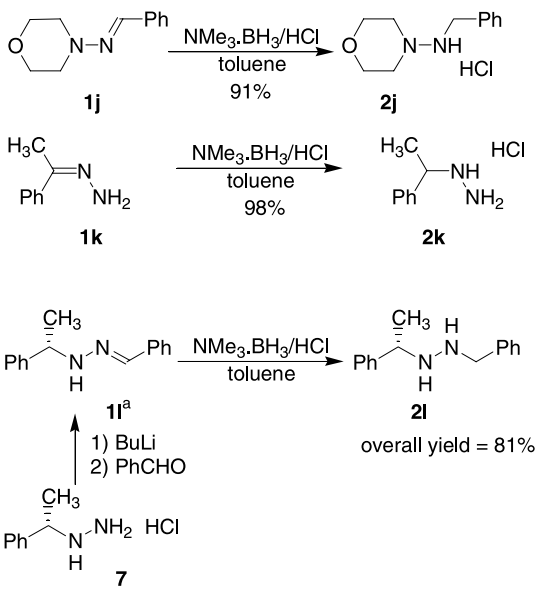
Table 1. Reduction of hydrazones by $NMe_3{\cdot}BH_3$/HCl



Entry	R^1	R^2	Hydrazine	Yield (%)
1	Ph	H	**2a**	97
2	Ph	Me	**2b**	94
3	4-Me_2NPh	H	**2c**	97
4	4-O_2NPh	H	**2d**	96
5	3-Thienyl	H	**2e**	98
6	3-Pyridyl	H	**2f**	98
7	1-Naphthyl	H	**2g**	92
8	Ethyl	H	**2h**	96
9	2-Ph-ethyl	Me	**2i**	82

reaction mixture and washing with toluene. Moreover, hydrazine hydrochlorides are completely stable against oxidation and much safer to handle.

The reduction proved to be generally applicable as a number of different aldehydes and ketones (Table 1) with different steric and electronic properties could be used. The reaction was also successful in the case of different nitrogen substituted hydrazones (Scheme 4):[11] hydrazones **1j–l** all gave the corresponding hydrazine hydrochlorides **2j–l** in high chemical yields.

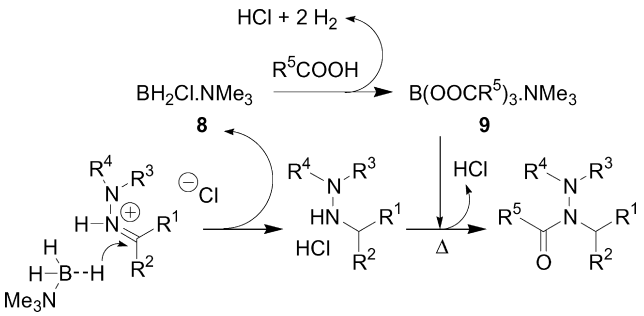


2j-l in high chemical yields.

Reaction conditions: 1 equiv. of $NMe_3.BH_3$. (a) hydrazone **1l** is unstable and was used at once.

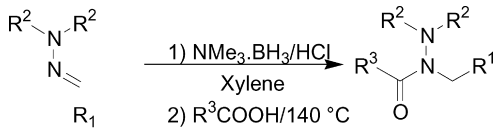
Scheme 4. Reduction of differently *N*-substituted hydrazones.

The hypothesized mechanism by which hydrazones are reduced and acylated to hydrazides is reported in Scheme 5. It is known that the amine–borane reduction of imines implies hydride transfer to the protonated species to be reduced.[12]



Scheme 5. Mechanism of reduction and acylation of hydrazones.

Table 2. One-pot synthesis of hydrazides from hydrazones

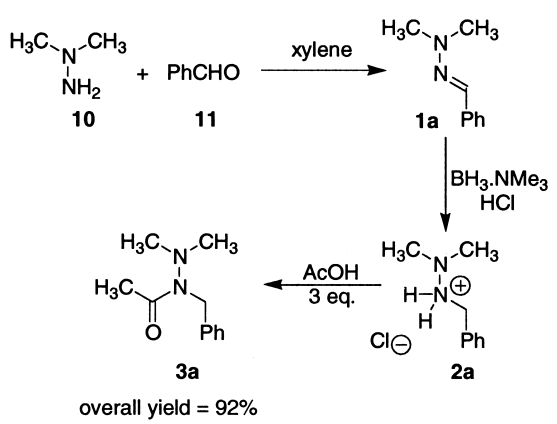


Hydrazone	R^1	NR^2_2	R^3	Hydrazide	Yield (%)
1a	Ph	NMe_2	Me	**3a**	95
1a	Ph	NMe_2	Ph	**3b**	81
1a	Ph	NMe_2	Et	**3c**	88
1d	4-O_2NPh	NMe_2	Me	**3d**	91
1e	3-Thienyl	NMe_2	2-Cl-Ph	**3e**	62
1f	3-Pyridyl	NMe_2	Me	**3f**	60
1g	1-Naphthyl	NMe_2	Me	**3g**	80
1h	Ethyl	NMe_2	2,6-diCl-Ph	**3h**	25
1j	Ph	Morpholinyl	Me	**3i**	90

Reaction conditions: 1 equiv. of $NMe_3{\cdot}BH_3$. After reduction, 3 equiv. of carboxylic acid and heating for 2.5 h.

It is likely that the same mechanism operates in the case of hydrazones (Scheme 5). Thus, the transfer of a hydride from the borane to the protonated hydrazones[13] generates chloroborane **8**.

We thought that the addition of a carboxylic acid to the reaction would generate acyloxyborane **9**, which is a known acylating agent.[14] Our idea was to exploit compound **9** in order to obtain in situ hydrazine acylation and so, after the reduction step, 3 equiv. of the appropriate carboxylic acid were added and the reaction was stirred overnight in order to convert any reducing species such as **8** to the acyloxyborane **9** before the heating step[15] (see experimental details). During heating, gaseous HCl is generated and must be removed from the reaction medium in order to complete the reaction.[16] We tested this reaction protocol using various hydrazones (Table 2) as well as different carboxylic acids: the yields were high except for hydrazides **3f** (some byproducts were formed during the reaction), **3e** and **3h** (probably because of steric hindrance of the two ortho-substituted benzoic acids).



Scheme 6. One-pot synthesis of hydrazide **3a**

As hydrazones can be synthesised in a xylene solution using a Marcusson apparatus, it is possible to run the reduction and acylation without isolating intermediate hydrazones and hydrazines. In this way, hydrazide **3a** was synthesised at multigram scale (Scheme 6).

The work-up was very easy: after concentration under reduced pressure, the crude product was distilled and the hydrazide was obtained in high yield and purity.

3. Conclusion

We here describe a new and efficient method of reducing hydrazones to hydrazines, in which we considered six aromatic aldehydes, one aliphatic aldehyde and two ketones, all of which gave the corresponding trisubstituted hydrazines. Furthermore, using the same procedure, we prepared one mono- and one disubstituted hydrazine. Moreover, hydrazides **3a**–**i** can be directly obtained from hydrazones **1a**–**j** by adding a carboxylic acid to the reaction after the reduction step. The overall procedure can be carried out as a 'one-pot multi-step' synthesis with a low environmental impact. The advantages of the method are: (i) high yields; (ii) few by-products; (iii) easy purification; (iv) the use of solvents and reagents available in bulk, which would be compatible with an industrial processes; and (v) short reaction times.

4. Experimental

Reagents obtained from commercial sources were used without further purification. Hydrazone **1b** was prepared as reported in the literature.[17] Before use, THF was dried by distillation over sodium wires/benzophenone, and the butyllithium solutions were titrated with 1,3-diphenyl-2-propanone tosylhydrazone. In order to monitor the progress of the reactions, thin layer chromatography (TLC) was performed using precoated Merck silica gel 60 F254 plates after eluting the indicated solvents, and the results visualised using a 254 nm UV lamp. Vacuum chromatography was performed using Merck silica gel 60, 230–400 mesh. Melting points were determined by means of a Büchi 510 apparatus, and are uncorrected. The ^{1}H NMR (300 MHz, $CDCl_3$) and ^{13}C NMR (75 MHz, $CDCl_3$) spectra were recorded on a Bruker AC 300 and Bruker AMX 300. The IR spectra were recorded on a Perkin–Elmer FT-IR 1725X. The high-resolution EI mass spectra were recorded on a Vg Analytical 7070 EQ.

4.1. General procedure and characterisation of hydrazones 1a, 1c–g and 1i,j

Aldehyde (1 equiv.) was added to *N*,*N*-dimethylhydrazine **10** (1 equiv. or more) under magnetic stirring and ice bath cooling. Toluene or xylene was added and the solution was refluxed in a Marcusson apparatus until the theoretical amount of water was generated. The solvent was removed in vacuo and the crude product purified by means of distillation or crystallisation.

4.1.1. *N′*-Benzylidene-*N*,*N*-dimethyl-hydrazine (1a). *N*,*N*-dimethylhydrazine **10**: 2.35 g, 42 mmol, 1 equiv.; benzaldehyde **11**: 4.38 g, 41 mmol, 1 equiv.; toluene 34 mL. The crude product was purified by distillation: 6.06 g of hydrazone **1a** was obtained; yield 99%. Data for **1a**: colourless oil; bp:[18] 121–122°C/18 mmHg. ^{1}H NMR ($CDCl_3$, 300 MHz)[18] δ (ppm) 7.57 (2H, d, $J_{ortho-meta}$=7.2 Hz, $H_{arom.\ ortho}$), 7.32 (2H, t, $J_{meta-ortho}$=7.2 Hz, $H_{arom.\ meta}$), 7.25 (1H, s, CHN), 7.22 (1H, t, $J_{para-meta}$=7.2 Hz, $H_{arom.\ para}$), 2.94 (6H, s, NMe_2); IR/FT[18] (neat) ν (cm^{-1}) 1591 (ν C=N); 1562 (ν C=C); 1471, 1445 ($\delta_{as.}$ CH_3); 755 (γ $CH_{arom.}$); 695(δ $CH_{arom.}$).

4.1.2. 4-(Dimethyl-hydrazonomethyl)-phenyl]-dimethyl-amine (1c). *N*,*N*-dimethylhydrazine **10**: 5.54 g, 92.1 mmol, 7 mL, 2 equiv.; *p*-NMe_2-benzaldehyde **12**: 6.87 g, 46 mmol, 1 equiv.; toluene: 37 mL. The crude product was purified by crystallisation: 8.37 g of hydrazone **1c** was obtained; yield 95%. Data for **1c**: white solid; mp 65–67°C (toluene). ^{1}H NMR (CCl_4, internal reference C_6D_6, 300 MHz) δ (ppm) 7.54 (2H, d, *J*=8.8 Hz, $H_{arom.}$), 7.33 (1H, s, CHN), 6.78 (2H, d, *J*=8.8 Hz, $H_{arom.}$), 3.18 (6H, s, $ArNMe_2$), 3.06 (6H, s, $NNMe_2$); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 150.2 (CH=N), 135.5 (C–NMe_2), 126.8 ($C_{arom.}$), 125.2 (*C*–CH=N), 112.2 ($C_{arom.}$), 43.2 (ArN*Me*$_2$), 40.4 (NN*Me*$_2$); IR/FT (nujol) ν (cm^{-1}) 1608 (ν C=N); 731 (γ $CH_{arom.}$); 695 (δ $CH_{arom.}$).

4.1.3. *N*,*N*-Dimethyl-*N′*-(4-nitro-benzylidene)-hydrazine (1d). *N*,*N*-dimethylhydrazine **10**: 3 mL, 39.4 mmol, 1 equiv.; *p*-NO_2-benzaldehyde **13**: 5.94 g, 39.3 mmol, 1 equiv.; toluene: 30 mL. The crude product was purified by crystallisation: 7.28 g of hydrazone **1d** was obtained; yield 96%. Data for **1d**: orange solid; mp[19] 111°C (toluene). ^{1}H NMR[20] ($CDCl_3$, 300 MHz) δ (ppm) 8.15 (2H, d, *J*=8.9 Hz, $H_{arom.}$), 7.61 (2H, d, *J*=8.8 Hz, $H_{arom.}$), 7.09 (1H, s, CHN), 3.09 (6H, s, $NNMe_2$); IR/FT (nujol) ν (cm^{-1}) 1594 (ν C=N); 1544 (ν ArC–C); 1502 ($\nu_{asym.}$ NO_2); 1328 ($\nu_{sym.}$ NO_2); 755 (γ $CH_{arom.}$); 696 (δ $CH_{arom.}$).

4.1.4. *N*,*N*-Dimethyl-*N′*-thiophen-3-ylmethylene-hydrazine (1e). *N*,*N*-dimethylhydrazine **10**: 2.7 mL, 35.5 mmol, 1.19 equiv.; thiophene-3-carbaldehyde **14**: 3.35 g, 29.9 mmol, 1 equiv.; toluene: 15 mL. The crude product was purified by distillation: 3.90 g of hydrazone **1e** was obtained; yield 85%. Data for **1e**: yellow oil; bp: 72°C/0.78 mmHg. ^{1}H NMR (CCl_4, internal reference C_6D_6, 300 MHz) δ (ppm) 7.6–7.2 (3H, m, $H_{arom.}$), 7.40 (1H, s, CHN), 3.09 (6H, s, $NNMe_2$); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 140.3 (*C*–CH=N), 128.8 (CH=N), 125.8, 125.2, 121.3 ($C_{arom.}$), 42.8 (NN*Me*$_2$); IR/FT (neat) ν (cm^{-1}) 1582 (ν C=N); 1519 (ν ArC–C); 776 (γ $CH_{arom.}$).

4.1.5. *N*,*N*-Dimethyl-*N′*-pyridin-3-ylmethylene-hydrazine (1f). *N*,*N*-dimethylhydrazine **10**: 4.4 mL, 57.8 mmol, 1 equiv.; pyridine-3-carbaldehyde **15**: 6.16 g, 57.5 mmol, 1 equiv.; toluene: 46 mL. The crude product was purified by distillation: 8.14 g of hydrazone **1f** was obtained; yield 95%. Data for **1f**: yellow oil. ^{1}H NMR (CCl_4, internal reference C_6D_6, 300 MHz)[21] δ (ppm) 8.78 (1H, d, *J*=1.6 Hz, $H_{arom.2}$), 8.56 (1H, dd, *J*=4.7 Hz, *J*=1.6 Hz, $H_{arom.6}$), 8.07 (1H, dt, *J*=7.9 Hz, *J*=1.6 Hz, $H_{arom.4}$), 7.36 (1H, dd, *J*=7.9 Hz, *J*=4.7 Hz, $H_{arom.5}$), 7.30 (1H, s, CHN), 3.21 (6H, s, $NNMe_2$); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 147.5, 147.2 ($C_{arom.2,6}$), 132.5 ($C_{arom.3}$), 131.2 (CH=N), 127.3 ($C_{arom.4}$), 123.0 ($C_{arom.5}$), 42.1 (NN*Me*$_2$); IR/FT (neat)[22] ν (cm^{-1}) 1585 (ν C=N); 1556 (ν ArC–C); 711 (γ $CH_{arom.}$); 663 (δ $CH_{arom.}$).

4.1.6. *N*,*N*-Dimethyl-*N′*-naphthalen-1-ylmethylene-hydrazine (1g). *N*,*N*-dimethylhydrazine **10**: 3.7 mL, 48.6 mmol, 1.2 equiv.; naphthalene-1-carbaldehyde **16**: 6.29 g, 40.3 mmol, 1 equiv.; toluene: 36 mL. The crude product was purified by distillation: 7.51 g of hydrazone **1g** was obtained; yield 94%. Data for **1g** yellow oil; bp: 120–121 °C/0.1 mmHg. ^{1}H NMR (CCl_4, internal reference C_6D_6, 300 MHz) δ (ppm) 8.75–7.4 (7H, m, $H_{arom.}$), 7.98 (1H, s, CHN), 3.25 (6H, s, $NNMe_2$); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 134.7, 133.1 ($C_{arom.\ quat.}$), 131.2 (CH=N), 129.3, 128.3, 126.7, 126.3, 126.2, 124.9, 124.7 ($C_{arom.}$), 43.3 (NN*Me*$_2$); IR/FT (neat) ν (cm^{-1}) 1592 (ν C=N); 1557 (ν ArC–C); 775 (γ $CH_{arom.}$).

4.1.7. *N*,*N*-Dimethyl-*N′*-(1-methyl-3-phenyl-propyl-idene)-hydrazine (1i). *N*,*N*-dimethylhydrazine **10**: 1.7 mL, 22.3 mmol, 1.3 equiv.; 4-phenyl-butan-2-one **17**: 2.55 g, 17.2 mmol, 1 equiv.; PTSA: 10 mg; toluene: 18 mL. The solution was refluxed in a Marcusson apparatus for 13 h. The crude product was purified by distillation: 2.81 g of hydrazone **1i** was obtained as a mixture of two isomers; yield 85.8%. Data for **1i** yellow oil; bp: 60–63°C/1.5 mmHg. ^{1}H NMR[23] (CCl_4, internal reference C_6D_6, 300 MHz) δ (ppm) 7.5–7.2 (5H, m, $H_{arom.}$), 3.1–2.9 (2H, m, CH_2Ph), 2.8–2.6 (2H, m, CH_2C=N), 2.55 (6H, s, major. isomer, $NNMe_2$), 2.52 (6H, s, min. isomer, $NNMe_2$), 2.09 (3H, s, Me); IR/FT (neat) ν (cm^{-1}) 1639 (ν C=N); 747 (γ $CH_{arom.}$); 699 (δ $CH_{arom.}$).

4.1.8. Benzylidene-morpholin-4-yl-amine (1j). *N*-amino-morpholine **18**: 1.59 mL, 16.6 mmol, 1 equiv.; benzaldehyde **11**: 1.74 g, 16.5 mmol, 1 equiv.; toluene: 10 mL. The crude product was purified by crystallisation: 3.04 g of hydrazone **1j** was obtained; yield 97%. Data for **1j**: white solid; mp: 89°C (EtOH). ^{1}H NMR (CCl_4, internal reference C_6D_6, 300 MHz) δ (ppm) 7.8–7.3 (5H, m, $H_{arom.}$), 7.67 (1H, s, CHN), 4.0 (4H, m, OCH_2) 3.3 (4H, m, NCH_2); IR/FT (neat) ν (cm^{-1}) 1604 (ν C=N); 1495 (ν ArC–C); 730 (γ $CH_{arom.}$); 694 (δ $CH_{arom.}$).

4.2. Synthesis of *N*,*N*-dimethyl-*N′*-propylidene-hydrazine (1h)

Propionaldehyde **19** (7.3 mL, 0.1 mol, 1 equiv.) was added to *N*,*N*-dimethylhydrazine **10** (7.6 mL, 0.1 mol, 1 equiv.), under magnetic stirring and ice bath cooling; after 1 h, KOH was added until saturation. The organic layer was separated

and purified by means of distillation with CaH_2; 9.11 g of hydrazone **1h** was obtained; yield 91%. Data for **1h**: colourless oil; bp:[24] 112°C. ^{1}H NMR (CCl_4, internal reference C_6D_6, 300 MHz)[21] δ (ppm) 6.65 (1H, t, J=5.37 Hz, CHN), 2.70 (6H, s, $NNMe_2$), 2.3–2.1 (2H, m, CH_2), 1.05 (3H, t, J=7.5 Hz, CH_3CH_2); IR/FT[25] (neat) ν (cm^{-1}) 2782 (ν NMe_2); 1613 (ν C=N); 1471, 1445 (δ_{as} CH_3).

4.3. Synthesis of (*S*)-*N*-benzylidene-*N'*-(1-phenyl-ethyl)-hydrazine (1l)

A solution of *n*-BuLi in hexane (1.46 M, 30 mL, 43.8 mmol) was added to a slurry of (1-phenyl-ethyl)-hydrazine hydrochloride **7**[26] (7.46 g, 43.2 mmol, 1 equiv.) in 26 mL of dry THF, cooled with an ice bath under a nitrogen atmosphere. The ice bath was removed and, after 30 min, benzaldehyde **11** (4.59 g, 43.2 mmol, 1 equiv.), dry THF (11 mL) and dry $MgSO_4$ were added. After 3 h, the slurry was filtered and the solvent removed in vacuo: 9.70 g of hydrazone **1l** was obtained; quantitative yield. Hydrazone **1l** is unstable and was used at once in the reduction reaction. Data for **1l**: colourless oil. ^{1}H NMR[27] ($CDCl_3$, 300 MHz) δ (ppm) 7.5–7.2 (5H, m, $H_{arom.}$), 7.52 (1H, s, CHN), 4.55 (1H, q, J=6.7 Hz, $CHCH_3$); 1.56 (3H, d, J=6.7 Hz, $CHCH_3$); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 164.9 (CH=N), 136.7, 131.7 ($C_{arom.\ quat.}$), 132.7–128.3 (C_{arom}), 61.6 ($CHCH_3$), 18.6 ($CHCH_3$); IR/FT (neat) ν (cm^{-1}) 3386 (ν NH); 1584 (ν C=N); 1571 (ν C=C); 755 (γ $CH_{arom.}$); 698 (δ $CH_{arom.}$).

4.4. Synthesis of (1-phenyl-ethylidene)-hydrazine (1k)

Acetophenone **21** (2.30 g, 19.1 mmol, 1 equiv.) was added to hydrazine monohydrate **20** (10 mL, 0.21 mol, 10.8 equiv.) under magnetic stirring. Toluene (15 mL) was added, and the solution refluxed in a Marcusson apparatus, under a nitrogen atmosphere for 2 h. The solvent was removed in vacuo and 40 mL of water were added; the mixture was extracted with CH_2Cl_2 (3×30 mL). The organic layers were collected and dried over Na_2SO_4, and the solvent was removed in vacuo: 2.57 g of hydrazone **1k** was obtained (stored at −20°C); quantitative yield. Data for **1k**: colourless oil. ^{1}H NMR ($CDCl_3$, 300 MHz)[28] δ (ppm) 7.7–7.25 (5H, m, $H_{arom.}$), 5.34 (2H, broad s, NH_2), 2.14 (3H, s, CH_3); IR/FT (neat)[28] ν (cm^{-1}) 3387, 3304, 3215 (ν NH_2); 3057 (ν_{as} and ν_{sim} CH_3, ν CH_{arom}); 1955, 1890, 1811 (overtones of γ $CH_{arom.}$); 1635, 1592 (ν C=N); 1572 (ν C=C); 1495, 1445 (δ_{as} CH_3); 762 (γ $CH_{arom.}$); 696 (δ $CH_{arom.}$).

4.5. General procedure and characterisation of hydrazines 2

A solution of hydrazone **1** (1 equiv.) and $NMe_3{\cdot}BH_3$ (1 equiv.) in toluene (16 mL for 0.01 mol of hydrazone) was saturated with HCl for about 30 min. The slurry of hydrazine hydrochloride **2** was filtered on a ceramic septum and washed with toluene to give the hydrazine hydrochloride as the only product and in high yield.

4.5.1. *N'*-Benzyl-*N*,*N*-dimethyl-hydrazine hydrochloride (2a). Hydrazone **1a**: 2.54 g, 17.2 mmol, 1 equiv.; trimethylamine-borane: 1.25 g, 17.2 mmol, 1 equiv.; toluene: 25 mL; 3.11 g of hydrazine hydrochloride **2a** was obtained; yield 97%. Data for **2a** white solid; mp: 133–135°C (EtOH/toluene). Anal. Calcd for $C_9H_{15}ClN_2$: C, 57.90; H, 8.10; N, 15.01. Found: C, 57.58; H, 7.84; N, 14.75. ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.91 (2H, s broad, NH_2), 7.5–7.25 (5H, m, $H_{arom.}$), 4.25 (2H, s, CH_2), 2.94 (6H, s, $NNMe_2$); ^{13}C NMR DEPT (CF_3COOD, 75 MHz) δ (ppm) 134.9 ($C_{arom.\ quat.}$), 130.7 (C_{arom}), 52.6 (CH_2), 46.5 (NMe_2); IR/FT (nujol) ν (cm^{-1}) 3146 (ν NH); 850 (ν N–N); 754 (γ $CH_{arom.}$); 699 (δ $CH_{arom.}$).

4.5.2. *N*,*N*-Dimethyl-*N'*-(1-phenyl-ethyl)-hydrazine hydrochloride (2b). Hydrazone **1b**: 1.69 g, 10.4 mmol, 1 equiv.; trimethylamine-borane: 0.759 g, 10.4 mmol, 1 equiv.; toluene: 15 mL; 1.96 g of hydrazine hydrochloride **2b** was obtained; yield 94%. Data for **2b** white solid; mp: 157–158°C (EtOH/toluene). Anal. Calcd for $C_{10}H_{17}ClN_2$: C, 59.84; H, 8.54; N, 13.96. Found: C, 59.51; H, 8.73; N, 14.25. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 7.6–7.4 (5H, m, $H_{arom.}$), 4.47 (1H, q, J=6.5 Hz, CH), 3.01 (6H, s, $NNMe_2$), 1.44 (3H, d, J=6.5 Hz, CH_3); ^{13}C NMR DEPT (CF_3COOD, 75 MHz) δ (ppm) 136.9 ($C_{arom.\ quat.}$), 131.3, 130.3, 128.4 (C_{arom}), 58.9 (CH), 47.5 (NMe_2), 22.1 (CH_3); IR/FT (nujol) ν (cm^{-1}) 3179 (ν NH); 883 (ν N–N); 759 (γ $CH_{arom.}$); 702 (δ $CH_{arom.}$).

4.5.3. [4-(*N'*,*N'*-Dimethyl-hydrazinomethyl)-phenyl]-dimethyl-amine dihydrochloride (2c). Hydrazone **1c**: 2.02 g, 10.5 mmol, 1 equiv.; trimethylamine-borane: 0.763 g, 10.5 mmol, 1 equiv.; toluene: 15 mL; 2.70 g of hydrazine dihydrochloride **2c** was obtained; yield 97%. Data for **2c**: white solid; m.p[29]: 158–161°C (EtOH/toluene). Anal. Calcd for $C_{11}H_{21}Cl_2N_3$: C, 49.63; H, 7.95; N, 15.78 Found: C, 49.93; H, 8.17; N, 15.42. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 7.66 (4H, s, $H_{arom.}$), 4.28 (2H, s, CH_2), 3.31 (6H, s, NMe_2), 3.12 (6H, s, NMe_2); IR/FT (nujol) ν (cm^{-1}) 3172 (ν NH); 785 (γ $CH_{arom.}$); 713 (δ $CH_{arom.}$).

4.5.4. *N*,*N*-Dimethyl-*N'*-(4-nitro-benzyl)-hydrazine hydrochloride (2d). Hydrazone **1d**: 2.006 g, 10.4 mmol, 1 equiv.; trimethylamine-borane: 0.759 g, 10.4 mmol, 1 equiv.; toluene: 15 mL; 2.291 g of hydrazine hydrochloride **2d** was obtained; yield 96%. Data for **2d**: yellow solid; mp: 180–181°C (EtOH). Anal. Calcd for $C_9H_{14}ClN_3O_2$: C, 46.66; H, 6.09; N, 18.14. Found: C, 46.76; H, 6.48; N, 18.37. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 8.27 (2H, d, J=8.7 Hz, $H_{arom.\ ortho\ NO2}$), 7.67 (2H, d, J=8.7 Hz, $H_{arom.\ meta\ NO2}$), 4.34 (2H, s, CH_2), 3.13 (6H, s, NMe_2); ^{13}C NMR DEPT (CF_3COOD, 75 MHz) δ (ppm) 151.4 (C–NO_2), 146.0 ($C_{arom.\ quat.}$), 133.4, 127.8 (C_{arom}), 53.9 (CH_2), 49.3 (NMe_2); IR/FT (nujol) ν (cm^{-1}) 3167 (ν NH); 1606 (ν ArC–C); 1529 ($\nu_{asym.}$ NO_2); 1359 ($\nu_{sym.}$ NO_2); 854 (ν N–N); 742 (γ $CH_{arom.}$); 692 (δ $CH_{arom.}$).

4.5.5. *N*,*N*-Dimethyl-*N'*-thiophen-3-ylmethyl-hydrazine hydrochloride (2e). Hydrazone **1e**: 0.98 g, 6.3 mmol, 1 equiv.; trimethylamine-borane: 0.476 g, 6.5 mmol, 1 equiv.; toluene: 8 mL; 1.19 g of hydrazine hydrochloride **2e** was obtained; yield 98%. Data for **2e**: white solid; mp: 107–109°C (EtOH). Anal. Calcd for $C_7H^{13}ClN_2S$: C, 43.63; H, 6.80; N, 14.54. Found: C, 43.31; H, 7.01; N, 14.23. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 7.5–7.0 (3H, m, $H_{arom.}$), 4.18 (2H, s, CH_2), 2.97 (6H, s, NMe_2); ^{13}C NMR DEPT (D_2O, 75 MHz) δ

(ppm) 131.5 ($C_{arom.\ quat.}$), 127.7, 127.5, 125.6 (C_{arom}), 44.6 (CH_2), 44.3 (NMe_2); IR/FT (nujol) ν(cm^{-1}) 3152 (νNH); 895 (ν N–N); 782 (γ $CH_{arom.}$); 693 (δ $CH_{arom.}$).

4.5.6. *N*,*N*-Dimethyl-*N′*-pyridin-3-ylmethyl-hydrazine dihydrochloride (2f). Hydrazone **1f**: 1.73 g, 11.6 mmol, 1 equiv.; trimethylamine-borane: 0.827 g, 11.3 mmol, 1 equiv.; toluene: 16 mL; 2.55 g of hydrazine dihydrochloride **2f** was obtained; yield 98%. Data for **2f** white solid; mp: 158–161°C (EtOH). Anal. Calcd for $C_8H_{15}Cl_2N_3$: C, 42.87; H, 6.75; N, 18.75. Found: C, 42.49; H, 6.94; N, 18.39. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 8.73 (1H, s, $H_{arom.2}$), 8.63 (1H, d, J=5.8 Hz, $H_{arom.6}$), 8.54 (1H, d, J=8.2 Hz, $H_{arom.4}$), 7.96 (1H, dd, J=5.8 Hz, J=8.2 Hz, $H_{arom.5}$), 4.33 (2H, s, CH_2), 3.02 (6H, s, NMe_2); ^{13}C NMR DEPT (D_2O, 75 MHz) δ (ppm) 154.0 ($C_{arom.\ quat.}$), 149.6, 143.4, 130.1 (C_{arom}), 48.7 (CH_2), 47.4 (NMe_2).

4.5.7. *N*,*N*-Dimethyl-*N′*-naphthalen-1-ylmethyl-hydrazine hydrochloride (2g). Hydrazone **1g**: 1.08 g, 5.4 mmol, 1 equiv.; trimethylamine-borane: 0.410 g, 5.6 mmol, 1 equiv.; toluene: 8 mL; 1.18 g of hydrazine hydrochloride **2f** was obtained; yield 92%. Data for **2g** white solid; mp: 173–174°C (EtOH). Anal. Calcd for $C_{13}H_{17}ClN_2$: C, 65.95; H, 7.24; N, 11.83. Found: C, 65.57; H, 7.14; N, 11.51. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 8.2–7.2 (7H, m, H_{arom}), 4.48 (2H, s, CH_2), 2.99 (6H, s, NMe_2); ^{13}C NMR DEPT (D_2O, 75 MHz) δ (ppm) 151.4, 135.8, 133.3 ($C_{arom.\ quat.}$), 131.0, 130.6, 129.1, 128.6, 127.9, 125.5 (C_{arom}), 49.8 (CH_2), 46.6 (NMe_2); IR/FT (nujol) ν (cm^{-1}) 3199 (ν NH); 888 (ν N–N).

4.5.8. *N*,*N*-Dimethyl-*N′*-propyl-hydrazine hydrochloride (2h). Hydrazone **1h**: 1.03 g, 10.2 mmol, 1 equiv.; trimethylamine-borane: 0.748 g, 10.2 mmol, 1 equiv.; toluene: 15 mL; 1.36 g of hydrazine hydrochloride **2h** was obtained; yield 96%. Data for **2h** white solid; mp: 66–68°C (toluene). Anal. Calcd for $C_5H_{15}ClN_2$: C, 43.32; H, 10.91; N, 20.21. Found: C, 43.51; H, 10.58; N, 19.96. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 3.05 (2H, t, J=7.45, NCH_2), 2.95 (6H, s, NMe_2), 1.59 (2H, sest, J=7.45, NCH_2CH_2), 0.97 (3H, t, J=7.45, CH_2CH_3); ^{13}C NMR DEPT (D_2O, 75 MHz) δ (ppm) 50.4 (NCH_2), 46.5 (NMe_2), 21.7 (NCH_2CH_2), 13.2 (CH_2CH_3); IR/FT (nujol) ν(cm^{-1}) 3161 (νNH); 866 (νN–N).

4.5.9. *N*,*N*-Dimethyl-*N′*-(1-methyl-3-phenyl-propyl)-hydrazine hydrochloride (2i). Hydrazone **1i**: 0.81 g, 4.2 mmol, 1 equiv.; trimethylamine-borane: 0.306 g, 4.2 mmol, 1 equiv.; toluene: 6 mL; 0.789 g of hydrazine hydrochloride **2i** was obtained; yield 82%. Data for **2i** white solid; mp: 122–124°C (toluene/pentane). Anal. Calcd for $C_{12}H_{21}ClN_2$: C, 63.00; H, 9.25; N, 12.25. Found: C, 62.65; H, 9.49; N, 12.22. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 7.4–7.2 (5H, m, H_{arom}), 1.8–1.6 (1H, m, NCH), 2.79 (6H, s, NMe_2), 3.0–2.5 (8H, m, $PhCH_2$ and NMe_2), 2.1–1.6 (2H, m, $CHCH_2$), 1.26 (3H, d, J=6.3 Hz, CH_3); ^{13}C NMR DEPT (D_2O, 75 MHz) δ (ppm) 141.2 ($C_{arom.\ quat.}$), 128.7, 128.4, 126.3 (C_{arom}), 51.5 (NCH), 44.2 (NMe_2), 33.9, 30.7 (CH_2CH_2), 15.8 (CH_3); IR/FT (nujol) ν (cm^{-1}) 3192 (ν NH); 739 (γ $CH_{arom.}$); 700 (δ $CH_{arom.}$).

4.5.10. Benzyl-morpholin-4-yl-amine hydrochloride (2j). Hydrazone **1j**: 0.93 g, 4.9 mmol, 1 equiv.; trimethylamine-borane: 0.356 g, 4.9 mmol, 1 equiv.; toluene: 6 mL; 1.01 g of hydrazine hydrochloride **2j** was obtained; yield 91%. Data for **2j** white solid; mp:[30] 245°C (EtOH). Anal. Calcd for $C_{11}H_{17}ClN_2O$: C, 57.76; H, 7.49; N, 12.25. Found: C, 57.42; H, 7.34; N, 11.92. ^{1}H NMR (D_2O, 300 MHz) δ (ppm) 7.7–7.4 (5H, m, H_{arom}), 4.38 (2H, s, CH_2Ph), 4.1–3.7 (4H, m, OCH_2), 3.4–3.1 (4H, m, NCH_2); ^{13}C NMR DEPT (D_2O, 75 MHz) δ (ppm) 130.3 ($C_{arom.\ quat.}$), 130.1, 129.5, 129.1 (C_{arom}), 65.1 (CH_2Ph), 52.6 (OCH_2), 49.4 (NCH_2); IR/FT (nujol) ν(cm^{-1}) 3166 (νNH); 1499 (νArC–C); 859 (νN–N); 745 (γ $CH_{arom.}$); 694 (δ $CH_{arom.}$).

4.5.11. *N*-benzyl-*N′*-(1-phenyl-ethyl)-hydrazine hydrochloride (2l). Hydrazone **1l**: 1.73 g, 7.7 mmol, 1 equiv.; trimethylamine-borane: 0.567 g, 7.7 mmol, 1 equiv.; toluene: 16 mL; 1.65 g of hydrazine hydrochloride **2l** was obtained; yield 81%. Data for **2l**: white solid; mp: 167°C (MeOH/Et_2O). Anal. Calcd for $C_{15}H_{19}ClN_2$: C, 68.50; H, 7.30; N, 10.70. Found: C, 68.40; H, 6.99; N, 10.34. ($\alpha(^{25}_{D}$=−52.7 (c=2 g/100 mL $CHCl_3$). ^{1}H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.60–7.50 (2H, s broad, NH_2), 7.45–7.20 (11H, m, NH+$H_{arom.}$), 4.30 (1H, q, J=6.7 Hz, $CHPh$), 4.12 (1H, d, J=12.4 Hz, CH_2Ph), 4.14 (1H, d, J=12.4 Hz, CH_2Ph), 1.55 (3H, d, J=6.7 Hz, CH_3).

4.5.12. (1-Phenyl-ethyl)-hydrazine hydrochloride (2k). Hydrazone **1k**: 2.53 g, 18.8 mmol, 1 equiv.; trimethylamine-borane: 1.38 g, 18.8 mmol, 1 equiv.; toluene: 25 mL; 3.06 g of hydrazine hydrochloride **2k** was obtained; yield 94%. Data for **2k**: colourless vitreous oil. ^{1}H NMR[26] (D_2O, 300 MHz) δ (ppm) 7.48 (5H, m, $H_{arom.}$), 4.39 (1H, q, J=6.86 Hz, CH), 1.60 (3H, d, J=6.86 Hz, CH_3); IR/FT (neat) ν (cm^{-1}) 3285, 3171 (ν NH); 2055, 1947, 1816 (overtones of γ $CH_{arom.}$); 1571 (νC=C); 848 (νN–N); 764 (γ $CH_{arom.}$); 699 (δ $CH_{arom.}$).

4.6. First attempts to synthesise hydrazide 3a

4.6.1. Reduction of hydrazone 1a with BH_3·THF. Under a nitrogen atmosphere, a 1 M solution of complex BH_3·THF in THF (22 mL, 22 mmol, 2.5 equiv.) was dropped in a solution of hydrazone **1a** (1.30 g, 8.7 mmol, 1 equiv.) in 50 mL of dry THF. After 10 min, the reaction was quenched with 1 mL of acetic acid, and Ac_2O (4 mL, 40 mmol, 4.6 equiv.) was added. The reaction mixture was heated under reflux for 30 min. The organic solution was washed with a saturated solution of sodium bicarbonate, and the aqueous solution extracted with CH_2Cl_2 (3×20 mL). The organic layers were collected and dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product was purified by means of flash chromatography over silica gel (30 g); eluent: Et_2O/ETP=3/7; 0.446 g of hydrazide **3a** was obtained; yield 26.5%.

4.6.2. Reduction of hydrazone 1a with Et_3SiH/CF_3-COOH. Under a nitrogen atmosphere, Et_3SiH (2.66 mL, 17 mmol, 2 equiv.) was added to a solution of hydrazone **1a** (1.24 g, 8.4 mmol, 1 equiv.) in 13 mL of CF_3COOH: the reaction mixture was heated under reflux for 4 h. The solvent was removed in vacuo; 10 mL of dry Et_3N, 20 mg of DMAP and 5 mL of Ac_2O were added, and the solution was stirred overnight. The solvent was removed in vacuo and the crude product diluted with 50 mL of CH_2Cl_2; the

organic solution was washed with a saturated solution of sodium bicarbonate and then dried over Na_2SO_4; the solvent was removed in vacuo. The crude product was purified by means of flash chromatography over silica gel (30 g); eluent: CH_2Cl_2; 0.67 g of hydrazide **3a** was obtained; yield 40%.

4.6.3. Reduction of hydrazone 1a with $Me_3N{\cdot}BH_3$ in CH_3COOH. Under a nitrogen atmosphere, $Me_3N{\cdot}BH_3$ (2.60 g, 35.7 mmol, 1.3 equiv.) was added to a solution of hydrazone **1a** (3.96 g, 26.7 mmol, 1 equiv.) in 30 mL of CH_3COOH: the reaction mixture was heated under reflux for 5 h. The solvent was removed in vacuo and the crude product diluted with 30 mL of AcOEt; the organic solution was washed with a saturated solution of sodium bicarbonate; the aqueous solution was extracted with AcOEt (2×20 mL). The organic layers were collecteda nd dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product (5.337 g) was purified by means of flash chromatography over silica gel (50 g); eluent: Et_2O/ETP=1/1 for byproducts (hydrazines **5** and **6**[31]) and AcOEt for hydrazide **3a**; 1.98 g of hydrazide **3a** was obtained; yield 76%. Data for **5**: colourless oil; bp 120°C/0.3 mmHg. HRMS (EI) for $C_{11}H_{18}N_2$: $(M)^+$ calcd: 178.146998, found: 178.1478. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.5–7.1 (5H, m, $H_{arom.}$), 3.63 (2H, s, PhCH_2), 2.50 (2H, q, J=7 Hz, CH_2CH_3) 2.43 (6H, s, $NNMe_2$), 1.05 (3H, t, J=7 Hz, CH_2CH_3); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 140.2 ($C_{arom\cdot quat.}$), 128.1, 127.7, 126.2 ($C_{arom.}$), 51.7 (PhCH_2), 43.7 (CH_2CH_3), 39.2 ($NNMe_2$), 13.5 (CH_2CH_3); IR/FT (neat) ν (cm^{-1}) 1601, 1495 (ν ArC–C); 721 (γ $CH_{arom.}$); 697 (δ $CH_{arom.}$). MS (EI), m/z 178 (M^+); 150 ($M^+-C_2H_4$); 134 (M^+-NMe_2); 87 (M^+-PhCH_2); 91 ($C_7H_7^+$); 79 ($C_6H_7^+$); 65 ($C_5H_5^+$).

4.7. First attempts to synthesise hydrazide 3b

4.7.1. Reduction of hydrazone 1a with $Me_3N{\cdot}BH_3$ and 3 equiv. of PhCOOH in xylene. Under a nitrogen atmosphere, $Me_3N{\cdot}BH_3$ (0.32 g, 4.3 mmol, 1.3 equiv.) was added to a solution of hydrazone **1a** (0.47 g, 3.2 mmol, 1 equiv.) and PhCOOH (1.18, 9.6 mmol, 3 equiv.) in 10 mL of xylene: the reaction mixture was heated under reflux for 18 h. The organic solution was washed with a saturated solution of sodium bicarbonate (3×25 mL); the aqueous solution was extracted with Et_2O (1×20 mL). The organic layers were collected and dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product (0.76 g) was purified by means of flash chromatography over silica gel (30 g); eluent: Et_2O/ETP=1/1; 0.139 g of hydrazide **3b** was obtained; yield 17%.

4.7.2. Reduction of hydrazone 1a with $Me_3N{\cdot}BH_3$ and 10 equiv. of PhCOOH in xylene. Under a nitrogen atmosphere, $Me_3N{\cdot}BH_3$ (0.22 g, 3.1 mmol, 1.3 equiv.) was added to a solution of hydrazone **1a** (0.35 g, 2.4 mmol, 1 equiv.) and PhCOOH (2.88, 23.6 mmol, 10 equiv.) in 20 mL of toluene: the reaction mixture was heated under reflux for 13 h. The organic solution was washed with a saturated solution of sodium carbonate (1×25 mL) and then with a saturated solution of sodium bicarbonate (2×25 mL); the aqueous solution was extracted with Et_2O (1×20 mL). The organic layers were collected and dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product (0.55 g) was purified by means of flash chromatography over silica gel (30 g); eluent: Et_2O/ETP=1/1; 0.084 g of hydrazide **3b** was obtained; yield 14%.

4.7.3. Reduction of hydrazone 1a by $Me_3N{\cdot}BH_3$ and 6 equiv. of PhCOOH without solvent. Under a nitrogen atmosphere, a mixture of $Me_3N{\cdot}BH_3$ (0.33 g, 4.4 mmol, 1.3 equiv.), hydrazone **1a** (0.50 g, 3.4 mmol, 1 equiv.) and PhCOOH (2.50, 20.5 mmol, 6 equiv.) was heated at 140–150°C for 6 h. The crude mixture was diluted with 10 mL of AcOEt and the organic solution was washed with a saturated solution of sodium carbonate (1×25 mL) and then with a saturated solution of sodium bicarbonate (2×25 mL); the aqueous solution was extracted with Et_2O (1×20 mL). The organic layers were collected and dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product (0.986 g) was purified by means of flash chromatography over silica gel (30 g); eluent: Et_2O/ETP=1/1; 0.167 g of hydrazide **3b** was obtained; yield 19%.

4.8. General procedure and characterisation of hydrazides 3

A solution of hydrazone **1** (1 equiv.) and $NMe_3{\cdot}BH_3$ (1 equiv.) in xylene (15 mL for 0.01 mol of hydrazone) was saturated with HCl for about 30 min. Carboxylic acid (3 equiv.) was added, and the slurry was stirred overnight at room temperature. Under a nitrogen atmosphere, the reaction mixture was then heated under reflux (140°C) and the HCl trapped by a saturated solution of NaOH; the progress of the reactions was monitored by means of TLC. The organic solution was washed with a saturated solution of sodium bicarbonate until neutral pH; the aqueous solution was extracted with ethyl acetate (2×20 mL). The organic layers were collected and dried over Na_2SO_4, and the solvent was removed in vacuo. The crude product was purified by means of distillation or chromatography.

4.8.1. Acetic acid *N*-benzyl-*N′*,*N′*-dimethyl-hydrazide (3a). Hydrazone **1a**: 5.82 g, 39.3 mmol, 1 equiv.; trimethylamine-borane: 2.91 g, 39.8 mmol, 1 equiv.; xylene: 60 mL; acetic acid: 6.8 mL, 118.9 mmol, 3 equiv.; the reaction mixture was heated under reflux for 2 h. The crude product was purified by means of distillation: 7.114 g of hydrazide **3a** was obtained; yield 95%.

One-pot synthesis of hydrazide **3a**. Dimethyl hydrazine **10**: 30 mL, 0.39 mol, 1 equiv.; benzaldehyde **11**: 40.9 g, 0.39 mol, 1 equiv.; xylene: 500 mL; after the synthesis of hydrazone **1a**: trimethylamine-borane=28.29 g, 38.5 mol, 1 equiv.; after the synthesis of hydrazine **2a**: acetic acid=67 mL, 1.17 mol, 3 equiv.; the reaction mixture was heated under reflux for 2 h. The crude product was purified by means of distillation: 68.24 g of hydrazide **3a** was obtained; yield 92%. Data for **3a**: colourless oil; bp[32] 105°C/0.7 mmHg. HRMS (EI) for $C_{11}H_{16}ON_2$: $(M)^+$ calcd: 192.1262, found: 192.1270. ^1H NMR[33] ($CDCl_3$, 300 MHz) δ (ppm) 7.4–7.1 (5H, m, $H_{arom.}$), 4.60 (2H, s, CH_2), 2.46

(6H, s, $NNMe_2$), 2.23 (3H, s, $COCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 174.0 (CO), 139.0 ($C_{arom.\ quat.}$), 128.4, 127.4, 126.8 ($C_{arom.}$), 44.2 ($NNMe_2$), 41.3 (CH_2), 21.0 (CH_3CO); IR/FT (neat) ν (cm^{-1}) 1657 (ν C=O); 1604, 1496 (ν ArC–C); 715 (γ $CH_{arom.}$); 693 (δ $CH_{arom.}$). MS (EI), *m/z* 192 (M^+); 150 ($M^+-C_2H_2O$); 149 (M^+-CH_3CO); 106 ($M^+-C_2H_2O-NMe_2$); 101 (M^+-PhCH_2); 91 ($C_7H_7^+$); 79 ($C_6H_7^+$); 65 ($C_5H_5^+$).

4.8.2. Benzoic acid *N*-benzyl-*N′*,*N′*-dimethyl-hydrazide (3b). Hydrazone **1a**: 1.00 g, 6.8 mmol, 1 equiv.; trimethylamine-borane: 0.50 g, 6.8 mmol, 1 equiv.; xylene: 12 mL; benzoic acid: 2.48 g, 20.3 mmol, 3 equiv.; the reaction mixture was heated under reflux for 6 h. The crude product was purified by means of flash chromatography over silica gel (30 g); eluent: Et_2O/ETP=6/4; 1.39 g of hydrazide **3b** was obtained; yield 81%. Data for **3b**: white solid; mp[33] 61–62°C (Et_2O). ^1H NMR[33] ($CDCl_3$, 300 MHz) δ (ppm) 7.7–7.1 (10H, m, $H_{arom.}$), 4.73 (2H, s, CH_2), 2.48 (6H, s, $NNMe_2$); IR/FT (nujol) ν (cm^{-1}) 1641 (ν C=O).

4.8.3. Propionic acid *N*-benzyl-*N′*,*N′*-dimethyl-hydrazide (3c). Hydrazone **1a**: 2.04 g, 13.7 mmol, 1 equiv.; trimethylamine-borane: 0.99 g, 13.5 mmol, 1 equiv.; xylene: 25 mL; propionic acid: 3.1 mL, 41.2 mmol, 3 equiv.; the reaction mixture was heated under reflux for 2.5 h. The crude product was purified by means of distillation; 2.51 g of hydrazide **3c** was obtained; yield 88%. Data for **3c**[34]: colourless oil; bp 130°C/2.3 mmHg. HRMS (EI) for $C_{12}H_{18}ON_2$: $(M)^+$ calcd: 206.14191, found: 206.1410. ^1H NMR ($CDCl_3$, 300 MHz) δ (ppm) 7.3–7.2 (5H, m, $H_{arom.}$), 4.60 (2H, s, PhC*H*$_2$), 2.62 (2H, q, *J*=7.5 Hz, CH_2CO), 2.47 (6H, s, $NNMe_2$), 1.16 (3H, t, *J*=7.5 Hz, CH_3); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 175.7 (CO), 138.8 ($C_{arom.\ quat.}$), 127.5, 126.7, 125.9 ($C_{arom.}$), 43.5 ($NNMe_2$), 40.5 (NCH_2), 25.6 (*C*H_2CO), 8.8 (CH_3); IR/FT (neat) ν (cm^{-}1) 1661 (ν C=O); 1605, 1497 (ν ArC–C); 724 (γ $CH_{arom.}$); 694 (δ $CH_{arom.}$). MS (EI), *m/z* 206 (M^+); 149 (M^+-CH_3-CH_2CO); 115 (M^+-PhCH_2); 91 ($C_7H_7^+$); 77 ($C_6H_5^+$); 65 ($C_5H_5^+$).

4.8.4. Acetic acid *N′*,*N′*-dimethyl-*N*-(4-nitro-benzyl)-hydrazide (3d). Hydrazone **1d**: 2.01 g, 10.4 mmol, 1 equiv.; trimethylamine-borane: 0.76 g, 10.4 mmol, 1 equiv.; xylene: 15 mL; acetic acid: 1.8 mL, 31.5 mmol, 3 equiv.; the reaction mixture was heated under reflux for 2 h. The crude product was purified by means of flash chromatography over silica gel (15 g); eluent: Et_2O; 2.24 g of hydrazide **3d** was obtained; yield 91%. Data for **3d**: yellow solid; mp[35] 101–102°C (toluene/hexane). ^1H NMR[35] ($CDCl_3$, 300 MHz) δ (ppm) 8.13 (2H, d, *J*=8.6 Hz, $H_{arom.\ ortho\ NO2}$), 7.43 (2H, d, *J*=8.6 Hz, $H_{arom.\ meta\ NO2}$), 4.64 (2H, s, PhC*H*$_2$), 2.47 (6H, s, $NNMe_2$), 2.25 (3H, s, $COCH_3$); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 174.2 (CO), 147.3 ($C_{arom.\ quat.}$), 128.6, 123.9 (C_{arom}), 44.6 ($NNMe_2$), 41.4 (NCH_2), 21.4 (*C*H_3CO); IR/FT (nujol) ν (cm^{-1}) 1653 (ν C=O); 1603, 1492 (ν ArC–C); 1525 ($\nu_{asym.}$ NO_2); 1351 ($\nu_{sym.}$ NO_2); 729 (γ $CH_{arom.}$); 677 (δ $CH_{arom.}$).

4.8.5. 2-Chloro-benzoic acid *N′*,*N′*-dimethyl-*N*-thiophen-3-ylmethyl-hydrazide (3e). Hydrazone **1e**: 0.72 g, 4.6 mmol, 1 equiv.; trimethylamine-borane: 0.34 g, 4.6 mmol, 1 equiv.; xylene: 18 mL; 2-chloro-benzoic acid: 2.34 g, 13.9 mmol, 3 equiv.; the reaction mixture was heated under reflux for 9 h. The crude product was purified by means of flash chromatography over silica gel (15 g); eluent: Et_2O/ETP=1/1; 0.848 g of hydrazide **3e** was obtained; yield 62%. Data for **3e**: white solid; mp 109–110°C (Et_2O/pentane). Anal. Calcd for $C_{14}H_{15}ClN_2OS$: C, 57.04; H, 5.13; N, 9.50. Found: C, 56.78; H, 5.13; N, 9.19. ^1H NMR[36] (C_6D_6, 300 MHz) δ (ppm) 7.3–6.5 (7H, m, $H_{arom.}$), 4.54 (2H, s, rotamer *E*, CH_2), 4.01 (2H, s, rotamer *Z*, CH_2), 2.90 (6H, s, rotamer *Z*, $NNMe_2$), 2.01 (6H, s, rotamer *E*, $NNMe_2$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 170.0 (CO), 139.1, 138.1, 129.7 ($C_{arom.\ quat.}$), 129.1, 128.9, 127.8, 126.1, 125.6, 122.4 ($C_{arom.}$), 44.3 ($NNMe_2$), 37.1 (NCH_2); IR/FT (neat) ν (cm^{-1}) 1650 (ν C=O); 764 (γ $CH_{arom.}$).

4.8.6. Acetic acid *N′*,*N′*-dimethyl-*N*-pyridin-3-ylmethyl-hydrazide (3f). Hydrazone **1f**: 1.96 g, 13.1 mmol, 1 equiv.; trimethylamine-borane: 0.94 g, 12.9 mmol, 1 equiv.; xylene: 24 mL; acetic acid: 2.3 mL, 39.4 mmol, 3 equiv.; the reaction mixture was heated under reflux for 2 h. The crude product was purified by means of flash chromatography over silica gel (30 g); eluent: Et_2O/MeOH=9/1; 1.4715 g of hydrazide **3f** was obtained; yield 60%. Data for **3f**: colourless oil; bp: 108 °C/0.2 mmHg. HRMS (EI) for $C_{10}H_{15}ON_3$: $(M)^+$ calcd: 193.1244, found: 206.1238. ^1H NMR (CCl_4, internal reference C_6H_6, 300 MHz) δ (ppm) 8.7–8.5 (2H, m, $H_{arom.}$), 8.0–7.7 (1H, m, $H_{arom.}$), 7.5–7.2 (1H, m, $H_{arom.}$), 4.75 (2H, s, PyC*H*$_2$), 2.73 (6H, s, $NNMe_2$), 2.35 (3H, s, $COCH_3$); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 173.3 (CO), 148.8, 147.9, 135.4, 123.0 ($C_{arom.}$), 134.6 ($C_{arom.\ quat.}$), 43.8 ($NNMe_2$), 39.0 (NCH_2), 20.8 (*C*H_3CO); IR/FT (neat) ν (cm^{-1}) 1651 (ν C=O); 1592, 1479 (ν ArC–C); 723 (γ $CH_{arom.}$); 694 (δ $CH_{arom.}$). MS (EI), *m/z* 193 (M^+); 151 ($M^+-C_2H_2O$); 150 (M^+-CH_3CO); 107 ($M^+-C_2H_2O$ $-NMe_2$); 106 (M^+-CH_3CO – NMe_2); 92 ($C_6H_6N^+$).

4.8.7. Acetic acid *N′*,*N′*-dimethyl-*N*-naphthalen-1-ylmethyl-hydrazide (3g). Hydrazone **1g**: 2.43 g, 12.1 mmol, 1 equiv.; trimethylamine-borane: 0.89 g, 12.1 mmol, 1 equiv.; xylene: 23 mL; acetic acid: 2.1 mL, 36.8 mmol, 3 equiv.; the reaction mixture was heated under reflux for 2.5 h. The crude product was purified by means of flash chromatography over silica gel (30 g); eluent: Et_2O/ETP=6/4;: 2.362 g of hydrazide **3g** was obtained; yield 80%. Data for **3g**: white solid; mp 55–56°C (Et_2O/pentane). Anal. Calcd for $C_{15}H_{18}N_2O$: C, 74.45; H, 7.49; N, 11.56. Found: C, 74.17; H, 7.56; N, 11.26. ^1H NMR (CCl_4, internal reference C_6D_6, 300 MHz) δ (ppm) 8.5–7.4 (7H, m, $H_{arom.}$), 5.32 (2H, s, CH_2), 2.63 (6H, s, $NNMe_2$), 2.40 (3H, s, $COCH_3$); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 173.4 (CO), 133.4, 130.6 ($C_{arom.\ quat.}$), 128.5, 127.4, 125.9, 125.3, 124.8, 122.8 ($C_{arom.}$), 43.4 ($NNMe_2$), 39.1 (NCH_2), 21.1 (*C*H_3CO); IR/FT (nujol) ν (cm^{-1}) 1657 (ν C=O); 1599, 1495 (ν ArC–C).

4.8.8. 2,6-Dichloro-benzoic acid *N′*,*N′*-dimethyl-*N*-propyl-hydrazide (3h). Hydrazone **1h**: 0.735 g, 7.3 mmol, 1 equiv.; trimethylamine-borane: 0.535 g, 7.34 mmol, 1 equiv.; xylene: 11 mL; 2,6-dichloro-benzoic acid: 4.206 g, 3 equiv.; the reaction mixture was heated under reflux for 16 h. The crude product was purified by means of flash chromatography over silica gel (15 g);

eluent: Et_2O/ETP=2/8;: 0.42 g of hydrazide **3h** was obtained; yield 21%. Data for **3h**: white solid; mp 125–127°C (Et_2O/pentane). Anal. Calcd for $C_{12}H_{16}Cl_2N_2O$: C, 52.38; H, 5.86; N, 10.18. Found: C, 52.52; H, 6.06; N, 9.84. ^{1}H NMR[37] (CCl_4, internal reference C_6D_6, 300 MHz) δ (ppm) 7.6–7.3 (3H, m, $H_{arom.}$), 3.57 (2H, m, NCH_2), 3.14 (6H, s, rotamer *Z*, $NNMe_2$), 2.73 (6H, s, rotamer *E*, $NNMe_2$), 2.04 (2H, sest., J=7.4 Hz, rotamer *E*, CH_2CH_3), 1.86 (2H, sest., J=7.4 Hz, rotamer *Z*, CH_2CH_3), 1.24 (3H, t, J=7.4 Hz, rotamer *Z*, CH_2CH_3), 1.01 (3H, t, J=7.4 Hz, rotamer *E*, CH_2CH_3); ^{13}C NMR ($CDCl_3$, 75 MHz) δ (ppm) 166.5 (CO), 137.8, 130.7 ($C_{arom.\ quat.}$), 128.7, 127.4 ($C_{arom.}$), 44.5 ($NNMe_2$), 40.6 (NCH_2), 22.1 (CH_2CH_3), 11.6 (CH_2CH_3); IR/FT (neat) ν (cm^{-1}) 1641 (ν C=O); 1456 (ν ArC–C); 789 (γ $CH_{arom.}$).

4.8.9. *N*-Benzyl-*N*-morpholin-4-yl-acetamide (3i). Hydrazone **1j**: 1.05 g, 5.5 mmol, 1 equiv.; trimethylamine-borane: 0.40 g, 5.5 mmol, 1 equiv.; xylene: 12 mL; acetic acid: 0.94 mL, 16.4 mmol, 3 equiv.; the reaction mixture was heated under reflux for 6 h. The crude product was purified by means of flash chromatography over silica gel (30 g); eluent: Et_2O/ETP=6/4; 1.1691 g of hydrazide **3i** was obtained; yield 90%. Data for **3i**: white solid; mp 114–115°C (CH_2Cl_2/pentane). Anal. Calcd for $C_{13}H_{18}O_2N_2$: C, 66.64; H, 7.74; N, 11.96. Found: C, 66.97; H, 8.02; N, 11.61. ^{1}H NMR (CCl_4, internal reference C_6D_6, 300 MHz) δ (ppm) 7.5–7.3 (5H, m, $H_{arom.}$), 4.83 (2H, m, NCH_2), 3.94 (2H, dd, J_{gem}=11 Hz, $J_{vic\ eq,eq}$=3 Hz, OCH_{eq}), 3.72 (2H, td, J_{gem}=$J_{vic\ ax,eq}$=11 Hz, $J_{vic\ ax,ax}$=2 Hz, OCH_{ax}), 3.09 (2H, td, J_{gem}=$J_{vic\ eq,ax}$=11 Hz, $J_{vic\ eq,eq}$=3 Hz, NCH_{eq}), 2.74 (2H, dd, J_{gem}=11 Hz, $J_{vic\ ax,ax}$=2 Hz, NCH_{ax}), 2.39 (3H, s, $COCH_3$); ^{13}C NMR DEPT ($CDCl_3$, 75 MHz) δ (ppm) 175.3 (CO), 138.9 ($C_{arom.\ quat.}$), 128.3, 127.4, 126.8 ($C_{arom.}$), 66.8 (OCH_2), 52.8 (NCH_2), 42.2 ($PhCH_2$), 21.2 ($COCH_3$); IR/FT (neat) ν (cm^{-1}) 1652 (ν C=O); 1495 (ν ArC–C); 738 (γ $CH_{arom.}$); 702 (δ $CH_{arom.}$).

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