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# 1,2-Reduction of α,β-unsaturated hydrazones using dimethylamine–borane/*p*-toluenesulfonic acid: an easy route to allyl hydrazines

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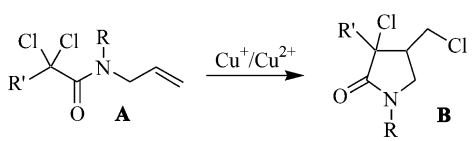
**Abstract**—α,β-Unsaturated hydrazones can be easily converted into *N*-allyl hydrazines by reaction with dimethylamine–borane/*p*-toluenesulfonic acid under mild reaction conditions. The reduction works well for *N*′-allylhydrazides but *N*′-allyl-*N*,*N*-dimethylhydrazines are rapidly reoxidised by air and so need to be manipulated under an inert atmosphere prior to *N*′-acylation. Competitive conjugate reduction can also be observed and the regioselectivity of the dimethylamine–borane attack is determined by steric and/or electronic factors. The procedure is also effective for the C=N reduction of unconjugated hydrazones. 

## 1. Introduction

(Pyrrolidin-2-ones γ-lactams) are a class of heterocyclic compounds frequently found in molecules, of natural or anthropic origin, endowed with interesting biological properties.[1] Owing to their great value in medicinal chemistry, the synthesis of these substances have received considerable attention by researchers, an interest that still continues to bloom.[2]

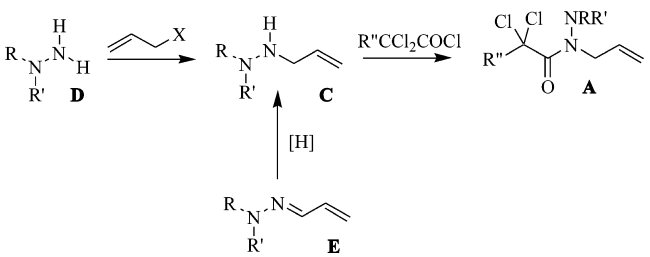
Among the many approaches developed for their preparation, the halogen atom transfer radical cyclization of *N*-allyl α-perchloroamides **A** (HATRC), promoted e.g. by the redox couple $Cu^{+}/Cu^{2+}$, stands out for versatility, efficiency and convenience (Scheme 1).[3] To be effective, the transformation of dichloroamide **A** into the γ-lactam **B** requires a 'cyclization adjuvant', typically a benzyl group (R=Bzl), bound to the amide nitrogen atom.[4] Several bioactive pyrrolidin-2-ones, however, are devoid of any substituent at the N-1 position[5] and, unfortunately, *N*-benzyl groups can be difficult to remove from amides.[6] To overcome this problem, we recently pioneered cyclization




**Scheme 1.**

auxiliaries of the type $R{=}NR^1R^2$, which exploited the well-known weakness of the heteroatom–heteroatom connection to encourage facile 'deprotection'.[7] This strategy proved successful and N–N bond cleavage of lactams **B** with R=dimethylamino or R=benzoylamino, was smoothly achieved with Raney-Ni† in ethanol/water at 100–110°C.[7,8]

While the parent amides **A** are easily formed by acylation of *N*-allyl hydrazines **C**, the preparation of **C** is not a routine operation owing to the lack of suitable synthetic procedures. The commonly used methods of allylation of hydrazines **D**, as described by Konig[9] and Tiecco,[10] (Scheme 2) are tedious and somewhat inefficient, affording often frustratingly low yields. Another major drawback of this approach rests in the limited number of allylating reagents, which restricts the number of accessible hydrazines. To widen our research on the deprotection of *N*-amino-pyrrolidin-2-ones, we have investigated a more versatile




**Scheme 2.**

*Keywords*: reduction; hydrazones; hydrazines; boron and compounds.

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† The dimethylamino protection can be also cleaved by magnesium monoperoxy phtalate.[27]

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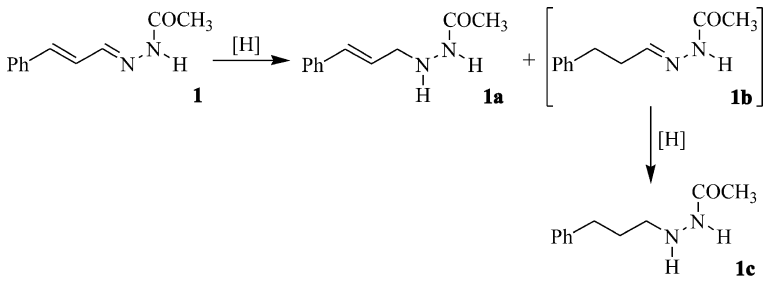



**Scheme 3.**

**Table 1**. Reduction of cinnamaldehyde acetylhydrazone **1**

| Entry | Reductant | *t* (h) | *T* (°C) | Conversion (%)[a] | Products | |
|---|---|---|---|---|---|---|
| | | | | | **1a** (%)[a] | **1c** (%)[a] |
| 1[b] | PB | 0.2 | 0 | 100 | 83 | 15 |
| 2[b] | DMAB | 0.2 | 0 | 100 | 93 | 3 |
| 3[b] | TMAB | 0.2 | 0 | 86 | 54 | 6 |
| 4[c] | $NaBH_4$ | 20 | 0 | 0 | – | – |
| 5[c] | $NaBH_4$ | 20 | 60 | 0 | – | – |

Substrate (1 mmol); THF (2.5 ml) and MeOH (2.5 ml).
[a] GC values.
[b] Borane–amine complex (1.6 mmol), $HCl_{MeOH}$ 3.6N (5 ml).
[c] $NaBH_4$ (1.6 mmol).

and easier route to *N*-allylhydrazines of type **C**. This work has shown that **C** can be efficiently prepared by 1,2-reduction of α,β-unsaturated hydrazones **E** using dimethylamine–borane under acid conditions (Scheme 2). As discussed below, the procedure is both simple and efficient and also works satisfactorily in large-scale preparations.

## 2. Results and discussion

The starting α,β-unsaturated hydrazones, which are commonly used as building blocks for the assembly of pyrazoles,[11–13] are widespread and easily prepared. Recently, these compounds have also been profitably employed as heterodienic components in Diels–Alder cycloadditions.[14–17] The synthetic value of enhydrazones stimulated the development of many procedures for their preparation.[18–23] Among these, certainly the most direct route involves the hydrazono-de-oxo-bisubstitution reaction which occurs between hydrazine derivatives and conjugated carbonyl compounds.[12,24–26] The Michael-type addition, a side reaction which afflicts the condensation reaction between amines and enketones,[28,29] is not such a prevalent side-reaction with hydrazines and so several conjugated hydrazones of this type can be prepared.[30–32]

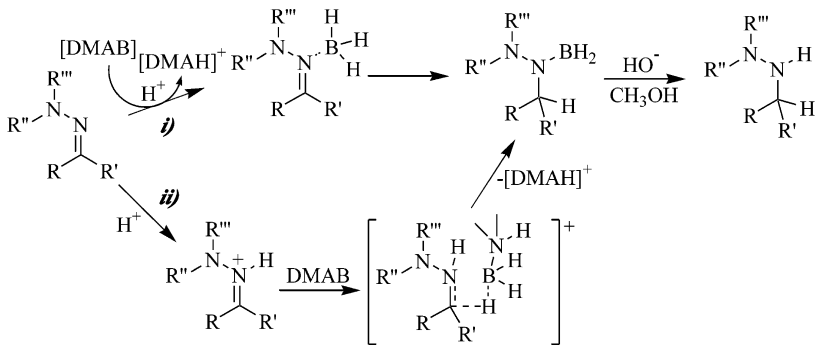
Whilst the deoxygenation of unsaturated carbonyl compounds through reduction of the intermediate tosylhydrazones has been thoroughly investigated,[33,34] the conversion of enhydrazones into the respective allyl hydrazines has, to our knowledge, never been comprehensively investigated. As far we are aware, this transformation has only surfaced in rare examples using $LiAlH_4$,[35] DuPhos-Rh/$H_2$[24] or pyridine–borane/$H^+$ (PB)[36] as reducing agents. The procedure using PB/$H^+$, which avoids the use of a dangerous gas and anhydrous solvents, is certainly the most convenient approach in terms of safety and practicality.

Amino-borane complexes have attracted the interest of many synthetic organic chemists. Their stability, tolerance to acids, solubility in many solvents and reducing power have resulted in numerous laboratory and industrial applications.[37–39] One of the most valuable and promising being the reduction of the C=N double bond to form C–N.[37,40–42] A large variety of amines have been used to prepare amino-boranes and a number of these reagents are now commercially available. PB is, however, somewhat expensive and, moreover, commercial solutions contain an excess of pyridine which reduces the appeal of the reagent. Two particularly more attractive substitutes are the dimethylamine–borane complex (DMAB) and the triethylamine–borane complex (TEAB). These solid complexes are economical, safe, soluble in both protic and aprotic solvents and hence suitable for large-scale preparations.

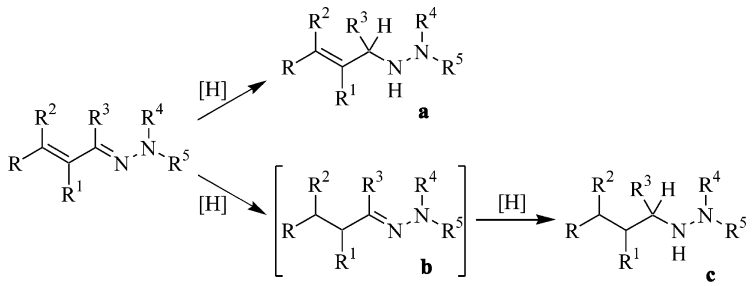
To evaluate the effectiveness of DMAB, TEAB and the standard hydride donor $NaBH_4$, versus PB, we initially chose cinnamaldehyde acetylhydrazone **1** as a reference substrate (Scheme 3). The reducing agents were tested under the optimum conditions reported by Kikugawa for the reduction of tosylhydrazones with PB and alcoholic HCl.[36]

The use of DMAB showed the most promise, delivering the 1,2-reduction product **1a** (Scheme 3, Table 1) with the highest yield and the best selectivity. The side-product **1c**, which resulted from conjugate attack, was only formed in 3% yield.[43] Interestingly, $NaBH_4$ did not react with **1**, even under forcing conditions (Table 1, entries 4 and 5). This may be explained by the fact that hydrazones, among the C=N-containing functional groups, exhibit the highest electron density on the iminic carbon[44] and should, therefore, be less prone to attack by hydride donors. Indeed *N*,*N*-dialkylhydrazones have been exploited as nucleophilic reagents.[45] In contrast, reduction using amino-borane complexes work well although this requires the presence of a strong acid. Under these conditions, the C=N double bond is protonated, which enhances the susceptibility towards attack by nucleophiles.[40,46]

According to the role played by $H^+$, two mechanisms can be proposed for the reduction of imines with amino-boranes in acidic media.[47] In one case (Scheme 4, path *i*) protonation could promote the release of borane from DMAB, which could lead to coordination of $BH_3$ with the imine nitrogen. Intramolecular hydride transfer would complete the reaction. Alternatively, the Schiff base could be protonated,



**Scheme 4.**



| | R | $R^1$ | $R^2$ | $R^3$ | $R^4$ | $R^5$ |
|---|---|---|---|---|---|---|
| **1** | Ph | H | H | H | H | $COCH_3$ |
| **2** | Propyl | H | H | H | H | $COCH_3$ |
| **3** | Propyl | H | H | H | H | COPh |
| **4** | $CH_3$ | H | H | H | H | COPh |
| **5** | $CH_3$ | H | $CH_3$ | H | H | COPh |
| **6** | Ph | H | H | $CH_3$ | H | $COCH_3$ |
| **7** | Ph | H | H | Ph | H | COPh |
| **8** | H | H | $CH_2CH_2CH_2$ | | H | $COCH_3$ |
| **9** | $CH_3$ | H | $CH_2CH_2CH_2$ | | H | COPh |
| **10** | $CH_2(CH_2)_2CH_2$ | | H | H | $CH_3$ | $CH_3$ |
| **11** | Ph | H | H | H | $CH_3$ | $CH_3$ |
| **12** | Propyl | H | H | H | $CH_3$ | $CH_3$ |

**Scheme 5.**

making the iminium carbon atom more susceptible to hydride transfer from DMAB (Scheme 4, path *ii*). The second route was the one favoured by Billman and McDowell in the reduction of imines,[47] and the related reduction of hydrazones could follow the same mechanism. It must be stressed, however, that borane can reduce hydrazones in the presence of a proton carrier,[48–50] but considering the different behaviour exhibited by PB, TEAB and DMAB in the reduction of **1** (Table 1), it is unlikely that these reagents behave as simple $BH_3$ carriers and so simple hydride transfer from borane can be well ruled out. A recent article by Mayr did support path *ii* reporting that amino-boranes behave indeed as true hydride donors, with strength comparable to $NaBH_3CN$, towards positively charged electrophiles.[51]

Unfortunately, reduction with DMAB required the preparation of titrated solutions of hydrochloric acid in methanol. The reactions also required high dilution (i.e. 10 ml of solvent per mmol of substrate) and this made the procedure unattractive for large-scale preparations. Therefore, we looked for a more effective method for achieving the requisite acidity and our attention turned to the use of acetic acid or 37% aqueous HCl. Although DMAB/acetic acid gave excellent results in the reduction of Schiff bases[46] the same combination, in our hands,‡ was disappointing affording unsatisfactory conversions and yields. Aqueous hydrochloric acid appeared to be more promising: in fact, reduction of **1** (1 mmol) with DMAB (1.6 mmol) and 37% aqueous HCl (2.3 ml) in $CH_2Cl_2$ (2 ml) gave the same result as when using methanolic HCl; both protocols affording **1a** in excellent yield (95%). The procedure, however, turned out to be unsuitable for reactions on a larger scale. While 1 mmol of **2** (Scheme 5) provided **2a** in good yield (72%) and acceptable selectivity (**2a**/**2c**, 4.80:1), the outcome when using 15 mmol of **2** was definitely worse (**2a**, 60% and **2a**/**2c**, 2.85:1). The reason for the deterioration is likely to be due to the presence of two immiscible liquid phases in the reaction mixture, which prevents homogenisation and this

‡ Using various amounts of acetic acid.

**Table 2**. Reduction of α,β-unsaturated hydrazones by DMAB/PTS

| Entry | Hydarazone | DMAB (mmol) | *t* (h) | Conversion (%)[a] | **a**+**c** (%)[b] | **a**/**c**[c] |
|---|---|---|---|---|---|---|
| 1 | **1** | 1.6 | 0.5 | 100 | 96 | ∞ |
| 2 | **2** | 1.6 | 0.5 | 100 | 97(89)[d] | 5.93(5.85)[d] |
| 3 | **3** | 1.6 | 1 | 100 | 95 | 10.88 |
| 4 | **4** | 1.6 | 0.7 | 100 | 93 | 5.20 |
| 5 | **5** | 1.6 | 0.7 | 100 | 98 | ∞ |
| 6 | **6** | 1.6 | 0.7 | 100 | 92 | ∞ |
| 7 | **7** | 2 | 0.75 | 96 | 90 | ∞ |
| 8 | **8** | 2 | 0.7 | 100 | 85 | 0 |
| 9 | **9** | 2 | 1 | 75 | 70 | 0.43 |
| 10[e] | **10** | 1.6 | 3 | 80 | 55 | 12.75 |
| 11[e,f] | **10** | 1.6 | 3 | 97 | 77 | 8.63 |
| 12[e,f] | **11** | 1.6 | 3 | 93 | 61 | ∞ |
| 13[e,f] | **12** | 1.6 | 3 | 100 | 66(70)[g] | 8.43(7.75)[g] |

Substrate (1 mmol); PTS (6 mmol); $CH_2Cl_2$ (3.5 ml) and MeOH (0.5 ml).
[a] GC values.
[b] Determined on isolated material.
[c] Ratios calculated by $^1$H NMR spectroscopy.
[d] The results in parentheses are obtained when using 15 mmol of **2**.
[e] Reaction performed under argon, and products isolated after trichloroacetylation.
[f] Diethyl ether (4 ml) and anhydrous PTS were used.
[g] The results in parentheses are obtained when using 25 mmol of **12**.

may be particularly acute when using large volumes of solvents.

In an attempt to develop a practical method suitable for multigram preparations, we thought that *p*-toluenesulfonic acid (PTS) could be an expedient proton donor to couple with DMAB. This strong organic acid is solid, cheap and soluble in many solvents. The commercial PTS, however, is supplied in the monohydrated form, and its complete solubilization in the reaction mixture required dilution of the reaction solvent ($CH_2Cl_2$) with a small amount of methanol ($CH_2Cl_2$/$CH_3OH$, 7:1).

A number of reactions were tried using this solvent system to investigate the reduction of **2** using DMAB/PTS. The best selectivity for **2a** over **2c** (5.93:1) and the highest yields of the allyl hydrazine **2a** (83%) were obtained, under satisfactory dilution conditions (i.e. 4 ml of solvent per mmol of substrate) when using 6 equiv. of PTS and 1.6 equiv. of amino-borane (Table 2, entry 2). We were also pleased to observe that the use of DMAB/PTS was equally effective on large-scale runs (e.g. **2a**, 76% and **2a**/**2c**, 5.85:1; Table 2, entry 2).

It is evident from the stoichiometry of the reaction that DMAB provides only one equivalent of hydride for the reduction and that an excess of the reducing agent was required to compensate for its decomposition because of the strong acidity of reaction medium. Efforts to activate the DMAB under neutral conditions through Pd/C, according to Couturier's method,[39] were attempted but unfortunately failed since the saturated hydrazone was the main product observed in all the attempted trials (i.e. this resulted in 3,4- rather than 1,2-reduction).

The scope and generality of the 1,2-reduction (type **a** products) of various unsaturated acylhydrazones using DMAB/PTS was then examined (Table 2). The reaction often suffered from some competitive conjugate reduction (type **c** products), the regiochemical outcome of which being governed, as expected for Michael-type acceptors,[52] by steric and/or electronic factors. For example, as the size of the γ substituents(s) (R or $R^2$) increased (Scheme 5, Table 2) so more attack at the imine carbon atom resulted to the point that with 3-methyl-crotonaldehyde *N*-benzoyl hydrazone (**5**), the 1,2-addition product became exclusive (Table 2, entries 3–5).

On the other hand, bulky substituents linked to the imine α-carbon atom diverted the attack towards the conjugated γ-position. This was indeed the case with hydrazone **8**, and even with **9**, where substitution at the γ-position could not prevent conjugate addition by DMAB (Table 2, entries 8 and 9). However, when a phenyl group was introduced at the γ-position, 1,2-reduction practically became the sole reaction with unsaturated hydrazones prepared from either ketones (Table 2, entries 6 and 7) or aldehydes (Table 2, entry 1). This may be explained by the conjugation between the aromatic ring and the 1-azadienic system, which is expected to increase the activation energy for the unwanted C=C reduction.

Since it was reported that the nature of the amino groups linked to the imine nitrogen could affect the regioselectivity of the nucleophilic addition to 1-azadienic arrangements,[53] we also studied the reduction of the unsaturated dimethylhydrazones **10**–**12** (Scheme 5) with DMAB/PTS. Unfortunately, attempted reduction of each of these substrates was unsuccessful and only unreacted starting material was isolated in each case. The failure, originally thought to be due to no reaction, was actually due to the astonishing propensity of *N*′,*N*′-dimethyl-allylhydrazines **10a**, **11a** and **12a** (Scheme 5) to be reoxidised by air; a shortcoming that even precluded their isolation from the reaction mixture. Reduction was thus performed under argon and the crude products were immediately *N*-acylated under an inert atmosphere.

Using this new protocol (Table 2, entry 10), the conversions, albeit high, were only partial. Moreover, in the presence of hydrated PTS, the dimethylhydrazones proved to be susceptible to hydrolysis and significant amounts (8–13%) of allyl esters were formed which hindered product isolation. To overcome these drawbacks, we resorted to using anhydrous *p*-toluenesulfonic acid.

With satisfaction we noted that DMAB/anhydrous PTS in diethyl ether worked well, minimizing the side reactions and affording the acylated allyl hydrazines **10a**, **11a** and **12a** in good yields (Table 2, entries 11–13). The regioselectivities were similar to those observed for the corresponding conjugated acylhydrazones (Table 2, entries 2, 3 and 13). Therefore, the electronic effects of the nitrogen substituents $R^4$ and $R^5$ have little effect on the regioselectivity presumably because, in all cases, the DMAB reacts with similar iminium ions.

Finally, for the unequivocal characterization of the side products **2**–**4c**, **10c** and **12c**, formed by over-reduction of the parent α,β-unsaturated hydrazones, we investigated their preparation by reaction of hydrazones **2b**-**4b**, **10b** and

**Table 3**. Reduction of hydrazones **b** by DMAB/PTS

| Entry | Hydrazone | DMAB (mmol) | *t* (h) | Conversion (%)[a] | **c** (%)[b] |
|---|---|---|---|---|---|
| 1 | **2b** | 1.6 | 0.7 | 100 | 86 |
| 2 | **3b** | 1.6 | 0.7 | 100 | 91 |
| 3 | **4b** | 1.6 | 0.7 | 100 | 95 |
| 4[c,d,e] | **10b** | 1.6 | 1 | 100 | 85 |
| 5[c,d,e] | **12b** | 1.6 | 1 | 100 | 83 |

Substrate (1 mmol); PTS (6 mmol); $CH_2Cl_2$ (3.5 ml) and MeOH (0.5 ml).
[a] GC values.
[b] Determined on isolated material.
[c] Reaction performed under argon (trichloroacetylated products).
[d] Anhydrous PTS was used.
[e] Using diethyl ether (4 ml) as the solvent.

**12b** with DMAB/PTS.[54] As expected, and without any modification of the reaction protocol, the targeted hydrazines **c** were smoothly obtained (Table 3). The *N*,*N*-dimethyl hydrazines **10c** and **12c** were more stable to oxidation (by air) than the corresponding hydrazines **10a** and **12a**, although the reduction of **10b** and **12b** was performed under an inert atmosphere and the reaction products were promptly acylated.

## 3. Conclusion

In connection with our studies aimed at developing easy removable cyclization auxiliaries for preparation of unprotected pyrrolidin-2-ones through the rearrangement of *N*-allyl α-perchloroamides, we required a versatile, efficient and practical route to *N*-allylhydrazines. This work has demonstrated a proficient approach to these compounds by 1,2-reduction of enhydrazones using DMAB/PTS. In some cases, competitive conjugate reduction was observed. The regioselectivity of the attack rests on the substitution pattern of the α-(C-2) and γ-(C-4) carbon atoms, but is unaffected by the nature of the amino group bound to the imine nitrogen. This versatile process, using readily available starting materials, offers an effective route to substituted hydrazines on both at small and large scale. The procedure is also effective for the reduction of unconjugated hydrazones.

## 4. Experimental

### 4.1. General

$^1$H NMR, IR and MS spectra were recorded respectively on Bruker DPX200, Philips PU 9716 and HP 5890 GC–HP 5989A MS Engine. HRMS for compounds **2a**, **3a**, **4a** and **12a** were recorded on a Fisons Instruments VG Analytical Autospec Spectrometer. Reagents were standard grade commercial products, purchased from Aldrich or Fluka, and used without further purification. *N*-Benzoyl hydrazones of chalcone (**7**), 3-methylcyclohexenone (**9**) and *N*-acetyl hydrazones of *trans*-2-hexenal (**2**), benzylidenacetone (**6**) and 2-cyclohexenone (**8**) were prepared according to the procedure reported by Feid-Allah,[12] whereas *N*-benzoyl hydrazones of crotonaldehyde (**4**) and 3-methyl-crotonaldehyde (**5**) were obtained following the protocol described by Burk.[24] Dried PTS was obtained by azeotropic distillation of a solution of monohydrated *p*-toluenesulfonic acid in toluene with a Dean–Stark apparatus.[55]

**4.1.1. Preparation of cinnamaldehyde acetylhydrazone (1).** In a single-necked round-bottom flask (100 ml) acetohydrazide (3.70 g, 50 mmol) and cinnamaldehyde (6.61 g, 50 mmol) were successively added to $CH_2Cl_2$ (80 ml). The stirred solution, after 1 h at room temperature, was cooled to precipitate the cinnamaldehyde acetylhydrazone. The crude product was filtered off and purified by recrystallization from $CH_2Cl_2$. White solid, mp 164–165°C. $^1$H NMR ($CDCl_3$): $\delta$ 2.35 (s, 3H), 6.86–6.95 (m, 2H), 7.10–7.74 (m, 6H). IR (KBr) 1673 (C=O) cm$^{-1}$. MS (EI, *m*/*z*): 188 (15, M$^+$), 145 (63), 129 (100), 115 (22), 43 (26). Anal. calcd for $C_{11}H_{12}N_2O$: C, 70.19; H, 6.43; N, 14.88. Found: C, 70.1; H, 6.5; N, 14.7. The hexanal *N*-acetyl hydrazone (**2b**), hexanal *N*-benzoyl hydrazone (**3b**) and butanal *N*-benzoyl hydrazone (**4b**) were secured following the same procedure.

**4.1.2. Preparation of cinnamaldehyde dimethylhydrazone (11).** In a single-necked round-bottom flask (100 ml) *N*,*N*-dimethylhydrazine (3.61 g, 60 mmol) and cinnamaldehyde (6.61 g, 50 mmol) were successively added, at room temperature, to a suspension of $MgSO_4$ (5 g) in $CH_2Cl_2$ (80 ml). After stirring overnight, the mixture was filtered. The crude product, obtained after evaporation of solvent and unreacted hydrazine did not require any further purification. Liquid, bp 143–145°C/7 mm Hg. $^1$H NMR ($CDCl_3$): $\delta$ 2.97 (s, 6H), 6.64 (d, *J*=15.7 Hz, 1H), 6.98 (dd, *J*=8.8, 15.7 Hz, 1H), 7.18 (d, *J*=8.8 Hz, 1H), 7.21–7.49 (m, 5H). IR (film) 1553 (C=N) cm$^{-1}$. MS (EI, *m*/*z*): 174 (100, M$^+$), 159 (9), 130 (35), 115 (23), 104 (17). Anal. calcd for $C_{11}H_{14}N_2$: C, 75.82; H, 8.10; N, 16.08. Found: C, 75.9; H, 7.9; N, 16.2. The dimethylhydrazones of 1-cyclohexen-1-carboxaldehyde (**10**), *trans*-2-hexenal (**12**), 1-cyclohexanecarboxaldehyde (**10b**) and hexanal (**12b**), were prepared following the same procedure.

### 4.2. General procedure for the 1,2-reduction of α,β-unsaturated acylhydrazones with DMAB/PTS

In a double-necked round-bottom flask (25 ml), fitted with a reflux condenser were added DMAB (0.094 g, 1.6 mmol) and cinnamaldehyde acetohydrazone **1** (0.188 g, 1 mmol) and the apparatus was thermostatted at 0°C. Then, $CH_2Cl_2$ (2 ml) and a solution of PTS monohydrate (1.141 g, 6 mmol) in $CH_2Cl_2$/$CH_3OH$, 3:1 (2 ml), previously cooled to 0°C, were introduced (gas evolves) while stirring. After 0.5 h, $Na_2CO_3$ (10% w/v, 6 ml) and $CH_3OH$ (2 ml) were added and the mixture refluxed for a further 0.5 h to cleave any residual boron–nitrogen bond. The organic phase was then separated and the aqueous phase extracted with $CH_2Cl_2$. The combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography of the crude product on silica gel, using a petroleum ether (bp 40–60°C)/diethyl ether gradient, gave 0.183 g of **1a** (96%).

**4.2.1. *N*′-Cinnamyl-acetohydrazide (1a).** Solid, mp 90–91°C. $^1$H NMR ($CDCl_3$): $\delta$ 1.90 (s, 3H), 3.57 (d, *J*=6.5 Hz, 2H), 4.70 (s, 1H), 6.20 (dt, *J*=6.5, 15.9 Hz, 1H), 6.52 (d, *J*=15.9 Hz, 1H), 7.12–7.38 (m, 5H), 8.1 (s, 1H). IR (KBr) 1641 (C=O) cm$^{-1}$. MS (EI, *m*/*z*): 190 (1, M$^+$), 132 (24),

130 (55), 117 (100), 115 (50), 91 (17), 43 (10). Anal. calcd for $C_{11}H_{14}N_2O$: C, 69.45; H, 7.42; N, 14.72. Found: C, 69.5; H, 7.3; N, 14.7.

**4.2.2. *N′*-(*trans*-2-Hexenyl)-acetohydrazide (2a).** According to the general procedure the *trans*-2-hexenal acetohydrazone **2** (0.154 g, 1 mmol) was converted to an inseparable mixture of **2a** (0.130 g, 83%) and **2c** (0.022 g, 14%). When this reaction was scaled up and carried out using 2.31 g of **2** (15 mmol), 2.087 g of a 85/15 mixture of **2a** (76%) and **2c** (13%) were secured. Solid. $^1$H NMR ($CDCl_3$): $\delta$ 0.80 (t, $J$=7.3 Hz, 3H), 1.28 (m, 2H), 1.72–2.08 (m, 2H), 1.85 (s, 3H), 3.28 (d, $J$=6.2 Hz, 2H), 4.36 (bs, 1H), 5.22–5.68 (m, 2H), 8.72 (bs, 1H). IR (KBr) 1649 (C=O) cm$^{-1}$. MS (EI, *m/z*): 156 (4, $M^+$), 113 (11), 98 (100), 83 (21), 60 (39), 55 (74), 43 (38). HRMS. Calcd for $C_8H_{17}N_2O$ ($M+H^+$): 157.1341. Found: 157.1342.

**4.2.3. *N′*-(*trans*-2-Hexenyl)-benzoylhydrazide (3a).** According to the general procedure the *trans*-2-hexenal benzoylhydrazone **3** (0.216 g, 1 mmol) was converted to an inseparable mixture of **3a** (0.189 g, 87%) and **3c** (0.018 g, 8%). Solid. $^1$H NMR ($CDCl_3$): $\delta$ 0.92 (t, $J$=7.3 Hz, 3H), 1.36–1.55 (m, 2H), 2.05 (q, $J$=6.9 Hz, 2H), 3.53 (d, $J$=6.2 Hz, 2H), 5.47–5.85 (m, 2H), 7.39–7.85 (5H, m). IR (KBr) 1627 (C=O) cm$^{-1}$. MS (EI, *m/z*): 218 (2, $M^+$), 175 (2), 122 (21), 105 (100), 98 (40), 77 (52). HRMS. Calcd for $C_{13}H_{19}N_2O$ ($M+H^+$): 219.1497. Found: 219.1497.

**4.2.4. *N′*-(2-Butenyl)-benzoylhydrazide (4a).** According to the general procedure, the crotonaldehyde benzoylhydrazone **4** (0.188 g, 1 mmol) was converted to an inseparable mixture of **4a** (0.148 g, 78%) and **4c** (0.029 g, 15%). Solid. $^1$H NMR ($CDCl_3$): $\delta$ 1.69 (dd, $J$=1.1, 6.0 Hz, 3H), 3.49 (d, $J$=6.4 Hz, 2H), 5.41–5.84 (m, 2H), 7.38–7.82 (m, 5H). IR (KBr) 1633 (C=O) cm$^{-1}$. MS (EI, *m/z*): 190 (2, $M^+$), 149 (4), 122 (27), 105 (100), 77 (37), 70 (41). HRMS. Calcd for $C_{11}H_{15}N_2O$ ($M+H^+$): 191.1184. Found: 191.1186.

**4.2.5. *N′*-(3-Methyl-2-butenyl)-benzoylhydrazide (5a).** According to the general procedure, the 3-methyl-2-butenal benzoylhydrazone **5** (0.202 g, 1 mmol) was converted to **5a** (0.200 g, 98%). Solid, mp 47–48°C. $^1$H NMR ($CDCl_3$): $\delta$ 1.67 (s, 3H), 1.73 (s, 3H), 3.55 (d, $J$=7.2 Hz, 2H), 5.30 (t, $J$=7.2 Hz, 1H), 7.41–7.83 (m, 5H). IR (KBr) 1628 (C=O) cm$^{-1}$. MS (EI, *m/z*): 204 (2, $M^+$), 189 (2), 136 (14), 122 (27), 105 (100), 84 (49), 77 (33), 69 (30). Anal. calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.89; N, 13.71. Found: C, 70.8; H, 7.7; N, 13.5.

**4.2.6. *N′*-(3-Phenyl-1-methyl-propenyl)-acetohydrazide (6a).** According to the general procedure the benzylidenacetone acetohydrazone **6** (0.202 g, 1 mmol) was converted to **6a** (0.188 g, 92%). Solid, mp 75–76°C. $^1$H NMR ($CDCl_3$): $\delta$ 1.28 (d, $J$=6.5 Hz, 3H), 1.92 (s, 3H), 3.71 (m, 1H), 6.09 (dd, $J$=8.0, 15.9 Hz, 1H), 6.53 (d, $J$=15.9 Hz, 1H), 7.18–7.43 (m, 5H). IR (KBr) 1648 (C=O) cm$^{-1}$. MS (EI, *m/z*): 204 (1, $M^+$), 144 (11), 131 (100), 116 (9), 115 (9), 91 (28). Anal. calcd for $C_{12}H_{16}N_2O$: C, 70.56; H, 7.89; N, 13.71. Found: C, 70.7; H, 8.0; N, 13.9.

**4.2.7. *N′*-(1,3-Diphenyl-propenyl)-benzoylhydrazide (7a).** According to the general procedure, but using 2 mmol of DMAB, the chalcone benzoylhydrazone **7** (0.326 g, 1 mmol) was converted to **7a** (0.295 g, 90%). Solid, mp 109–111°C. $^1$H NMR ($CDCl_3$): $\delta$ 4.90 (d, $J$=7.9 Hz, 1H), 6.42 (dd, $J$=7.9, 15.8 Hz, 1H), 6.74 (d, $J$=15.8 Hz, 1H), 7.13–7.71 (m, 15H). IR (KBr) 1642 (C=O) cm$^{-1}$. MS (EI, *m/z*): 328 (1, $M^+$), 194 (14), 193 (100), 178 (9), 115 (44), 105 (12), 91 (11), 77 (13). Anal. calcd for $C_{22}H_{20}N_2O$: C, 80.46; H, 6.14; N, 8.53. Found: C, 80.7; H, 6.0; N, 8.3.

**4.2.8. *N′*-Cyclohexyl-acetohydrazide (8c).** According to the general procedure, the 2-cyclohexenone acetohydrazone **8** (0.152 g, 1 mmol) was converted to **8c** (0.132 g, 85%). Solid, mp 62–64°C. $^1$H NMR ($CDCl_3$): $\delta$ 0.90–1.90 (m, 10H), 1.94 (s, 3H), 2.77 (m, 1H). IR (KBr) 1641 (C=O) cm$^{-1}$. MS (EI, *m/z*): 156 (8, $M^+$), 113 (60), 98 (75), 83 (34), 71 (49), 60 (100), 55 (67), 43 (38). Anal. calcd for $C_8H_{16}N_2O$: C, 61.51; H, 10.32; N, 17.93. Found: C, 61.4; H, 10.5; N, 17.7.

**4.2.9. *N′*-(3-Methyl-2-cyclohexenyl)-benzoylhydrazide (9a).** According to the general procedure, the 3-methyl-2-cyclohexenone benzoylhydrazone **9** (0.228 g, 1 mmol) was converted to **9a** (0.049 g, 21%). Solid, mp 127–129°C. $^1$H NMR ($CDCl_3$): $\delta$ 1.30–2.10 (m, 6H), 1.71 (s, 3H), 3.57 (m, 1H), 5.47 (m, 1H), 7.36–7.85 (m, 5H). IR (KBr) 1638 (C=O) cm$^{-1}$. MS (EI, *m/z*): 230 (2, $M^+$), 137 (16), 122 (14), 110 (16), 105 (30), 95 (100), 77 (18). Anal. calcd for $C_{14}H_{18}N_2O$: C, 73.01; H, 7.88; N, 12.16. Found: C, 73.2; H, 8.0; N, 12.1. From the crude product, 0.114 g of *N′*-(3-methyl-cyclohexyl)-benzoylhydrazide **9c** (49%) was also recovered. Solid, mp 133–135°C. $^1$H NMR ($CDCl_3$): $\delta$ 0.94 (d, $J$=6.5 Hz, 3H), 1.00–2.02 (m, 8H), 2.92 (m, 1H), 7.39–7.81 (m, 5H). IR (KBr) 1641 (C=O) cm$^{-1}$. MS (EI, *m/z*): 232 (5, $M^+$), 189 (11), 122 (100), 112 (63), 105 (94), 77 (27). Anal. calcd for $C_{14}H_{20}N_2O$: C, 72.38; H, 8.68; N, 12.06. Found: C, 73.5; H, 8.8; N, 12.0.

### 4.3. General procedure for the 1,2-reduction of α,β-unsaturated *N,N*-dimethylhydrazones with DMAB/PTS

DMAB (0.094 g, 1.6 mmol) and 1-cyclohexen-1-carboxaldehyde *N,N*-dimethylhydrazone **10** (0.152 g, 1 mmol) were weighed in a screw capped Schlenk tube equipped with a perforable septum; then, under argon and at 0°C, diethyl ether (2 ml) and a solution of PTS anhydrous (1.033 g, 6 mmol) in diethyl ether (2 ml), both cooled to 0°C, were added. After 3 h, the reaction mixture was quenched with $Na_2CO_3$ (10% w/v, 6 ml), always keeping the inert atmosphere. The organic phase (ether) was cannulated into another Schlenk tube, evaporated and restored as $CH_2Cl_2$ (2 ml). After cooling at 0°C, triethylamine (1.2 mmol) and trichloroacetyl chloride (1.1 mmol) were introduced. The mixture, after overnight stirring, was diluted with NaOH (5% w/v, 6 ml), and extracted with $CH_2Cl_2$. The combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography of the crude product on silica gel, using a petroleum ether (bp 40–60°C)/diethyl ether gradient, gave 0.230 g of a 89/11 mixture of trichloroacetylated **10a** (69%) and **10c** (8%).

**4.3.1. *N*-[(1-Cyclohexenyl)-methyl]-*N′*,*N′*-dimethylhydrazine (10a), trichloroacetylated.** Oil. $^1$H NMR ($CDCl_3$): $\delta$ 1.50–1.77 (m, 4H), 1.92–2.14 (m, 4H), 2.64 (s, 6H), 4.00 (s, 2H), 5.61 (m, 1H). IR (film) 1687 (C=O) cm$^{-1}$. MS (EI, *m/z*): 298 (1, M$^+$), 204 (50), 169 (53), 153 (10), 133 (10), 41 (100). HRMS. Calcd for $C_{11}H_{18}Cl_3N_2O$ (M+H$^+$): 299.0485. Found: 299.0485.

**4.3.2. *N*-Cinnamyl-*N′*,*N′*-dimethylhydrazine (11a), trichloroacetylated.** Following the general procedure, the cinnamaldehyde dimethylhydrazone (**11**) (0.174 g, 1 mmol) was converted to 0.196 g of trichloroacetylated **11a** (61%). Solid, mp 72–74°C. $^1$H NMR ($CDCl_3$): $\delta$ 2.69 (s, 6H), 4.23 (dd, *J*=1.2, 6.4 Hz, 2H), 6.34 (dt, *J*=6.4, 15.9 Hz, 1H), 6.67 (dt, *J*=1.2, 15.9 Hz, 1H), 7.21–7.47 (m, 5H). IR (KBr) 1682 (C=O) cm$^{-1}$. MS (EI, *m/z*): 320 (M$^+$, 1), 276 (2), 117 (100), 91 (8). Anal. calcd for $C_{13}H_{15}Cl_3N_2O$: C, 48.55; H, 4.70; N, 8.71. Found: C, 48.7; H, 4.8; N, 8.5.

**4.3.3. *N*-(*trans*-2-Hexenyl)-*N′*,*N′*-dimethylhydrazine (12a), trichloroacetylated.** Following the general procedure, the *trans*-2-hexenal dimethylhydrazone (**12**) (0.140 g, 1 mmol) was converted to 0.191 g of a 89/11 mixture of trichloroacetylated **12a** (59%) and **12c** (7%). When this reaction was scaled-up and carried out using 3.50 g of **12** (25 mmol), 5.035 g of a 88/12 mixture of **12a** (62%) and **12c** (8%) were secured. Oil. $^1$H NMR ($CDCl_3$): $\delta$ 0.92 (t, *J*=7.5 Hz, 3H), 1.26–1.54 (m, 2H), 2.05 (q, *J*=7.1 Hz, 2H), 2.64 (s, 6H), 4.01 (d, *J*=5.9 Hz, 2H), 5.59–5.85 (m, 2H). IR (film) 1688 (C=O) cm$^{-1}$. MS (EI, *m/z*): 286 (M$^+$, 2), 204 (100), 96 (100), 141 (35), 86 (30), 55 (77). HRMS. Calcd for $C_{10}H_{18}Cl_3N_2O$ (M+H$^+$): 287.0485. Found: 287.0480.

### 4.4. General procedure for the reduction of unconjugated acylhydrazones with DMAB/PTS

In a double-necked round-bottom flask (25 ml), fitted with a reflux condenser were added DMAB (0.094 g, 1.6 mmol) and hexanal acetohydrazone **2b** (0.156 g, 1 mmol) and the apparatus was thermostatted at 0°C. Then $CH_2Cl_2$ (2 ml) and a solution of PTS monohydrate (1.141, 6 mmol) in $CH_2Cl_2$/$CH_3OH$, 3:1 (2 ml), previously cooled to 0°C, were introduced (gas evolves) while stirring. After 0.5 h, $Na_2CO_3$ (10% w/v, 6 ml) and $CH_3OH$ (2 ml) were added and the mixture refluxed for a further 0.5 h to cleave any residual boron–nitrogen bond. The organic phase was then separated and the aqueous phase extracted with $CH_2Cl_2$. The combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography of the crude product on silica gel, using a petroleum ether (bp 40–60°C)/diethyl ether gradient, gave 0.136 g of **2c** (86%).

**4.4.1. *N′*-Hexyl-acetohydrazide (2c).** Oil. $^1$H NMR ($CDCl_3$): $\delta$ 0.82 (t, *J*=7.3 Hz, 3H), 1.02–1.64 (m, 8H), 1.88 (s, 3H), 2.75 (t, *J*=6.2 Hz, 2H). IR (film) 1648 (C=O) cm$^{-1}$. MS (EI, *m/z*): 158 (4, M$^+$), 116 (18), 100 (55), 87 (71), 60 (33), 45 (100). Anal. calcd for $C_8H_{18}N_2O$: C, 59.96; H, 12.58; N, 17.48. Found: C, 59.9; H, 12.6; N, 17.6.

**4.4.2. *N′*-Hexyl-benzoylhydrazide (3c).** According to the general procedure, the hexanal benzoylhydrazone **3b** (0.218 g, 1 mmol) was converted to **3c** (0.200 g, 91%). Solid, mp 57–60°C. $^1$H NMR ($CDCl_3$): $\delta$ 0.90 (t, *J*=6.4 Hz, 3H), 1.16–1.68 (m, 8H), 2.95 (t, *J*=7.2 Hz, 2H), 7.38–7.81 (5H, m). IR (KBr) 1627 (C=O) cm$^{-1}$. MS (EI, *m/z*): 220 (4, M$^+$), 149 (40), 122 (35), 105 (100), 100 (53), 77 (30). Anal. calcd for $C_{13}H_{20}N_2O$: C, 72.19; H, 7.46; N, 12.95. Found: C, 72.3; H, 7.7; N, 13.1.

**4.4.3. *N′*-Butyl-benzoylhydrazide (4c).** According to the general procedure, the butanal benzoylhydrazone **4b** (0.190 g, 1 mmol) was converted to **4c** (0.182 g, 95%). Oil. $^1$H NMR ($CDCl_3$): $\delta$ 0.96 (t, *J*=6.7 Hz, 3H), 1.30–1.68 (m, 4H), 2.96 (t, *J*=7.0 Hz, 2H), 7.34–7.78 (m, 5H). IR (film) 1627 (C=O) cm$^{-1}$. MS (EI, *m/z*): 192 (3, M$^+$), 149 (22), 122 (27), 105 (100), 77 (35), 72 (32). Anal. calcd for $C_{11}H_{16}N_2O$: C, 67.31; H, 10.27; N, 14.27. Found: C, 67.1; H, 10.1; N, 14.1.

### 4.5. General procedure for the reduction of unconjugated *N*,*N*-dimethylhydrazones with DMAB/PTS

DMAB (0.094 g, 1.6 mmol) and cyclohexanecarboxaldehyde *N*,*N*-dimethylhydrazone **10b** (0.154 g, 1 mmol) were weighed in a screw capped Schlenk tube equipped with a perforable septum; then, under argon and at 0°C, diethyl ether (2 ml) and a solution of PTS anhydrous (1.033, 6 mmol) in diethyl ether (2 ml), both cooled to 0°C, were added. After 3 h, the reaction mixture was quenched with $Na_2CO_3$ (10% w/v, 6 ml), always keeping the inert atmosphere. The organic phase (ether) was cannulated into another Schlenk tube, evaporated and restored as $CH_2Cl_2$ (2 ml). After cooling at 0°C, triethylamine (1.2 mmol) and trichloroacetyl chloride (1.1 mmol) were introduced. The mixture, after overnight stirring, was diluted with NaOH (5% w/v, 6 ml), and extracted with $CH_2Cl_2$. The combined organic layers were dried over $MgSO_4$ and concentrated. Column chromatography of the crude product on silica gel, using a petroleum ether (bp 40–60°C)/diethyl ether gradient, gave 0.255 g of trichloroacetylated **10c** (85%).

**4.5.1. *N*-[(Cyclohexyl)-methyl]-*N′*,*N′*-dimethylhydrazine (10c), trichloroacetylated.** Oil. $^1$H NMR ($CDCl_3$): $\delta$ 0.80–1.98 (m, 11H), 2.55 (s, 6H), 3.57 (d, *J*=7.4 Hz, 2H). IR (film) 1687 (C=O) cm$^{-1}$. MS (EI, *m/z*): 300 (3, M$^+$), 265 (1), 169 (3), 155 (100), 83 (6), 73 (39), 55 (13). Anal. calcd for $C_{11}H_{19}Cl_3N_2O$: C, 43.80; H, 6.35; N, 9.29. Found: C, 43.9; H, 6.5; N, 9.1.

**4.5.2. *N*-Hexyl-*N′*,*N′*-dimethylhydrazine (12c), trichloroacetylated.** According to the previous procedure, hexanal *N*,*N*-dimethylhydrazone **12b** (0.142 g, 1 mmol) was converted to **12c** (0.240 g, 83%). Oil. $^1$H NMR ($CDCl_3$): $\delta$ 0.88 (t, *J*=7.3 Hz, 3H), 1.18–1.40 (m, 6H), 1.66 (m, 2H), 2.58 (s, 6H), 3.31 (m, 2H). IR (film) 1686 (C=O) cm$^{-1}$. MS (EI, *m/z*): 288 (M$^+$, 7), 253 (4), 144 (27), 143 (100), 98 (37). Anal. calcd for $C_{10}H_{19}Cl_3N_2O$: C, 41.47; H, 6.61; N, 9.67. Found: C, 41.4; H, 6.5; N, 9.5.

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