Controlled Release of Volatile Aldehydes and Ketones from Dynamic Mixtures Generated by Reversible Hydrazone Formation

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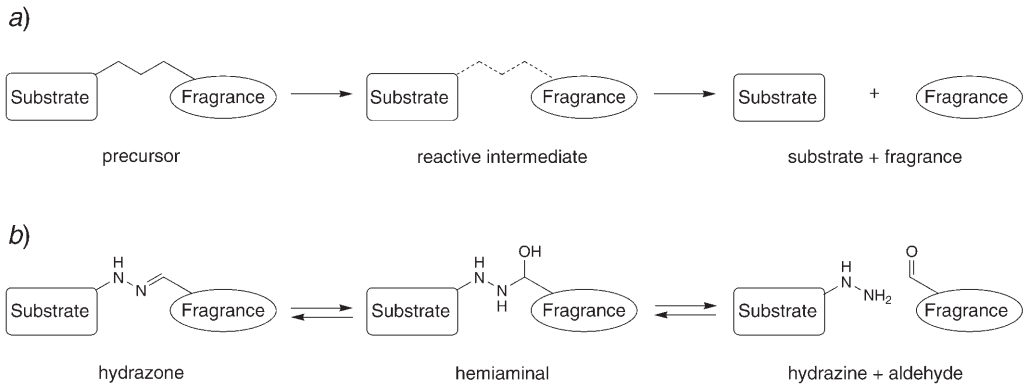
Delivery systems generated by reversible hydrazone formation from hydrazine derivatives (see *Fig. 1*) and carbonyl compounds in H_2O efficiently increase the long-lastingness of volatile aldehydes and ketones ($R^1R^2C{=}O$) in various perfumery applications. The hydrazones are usually obtained in an (*E*) configuration at the imine double bond (NHN=C) and, in the case of aliphatic acylhydrazones $R'CO{-}NH{-}N{=}CR^1R^2$ (R' = alkyl), as *syn* and *anti* conformers with respect to the amide bond (CO–NHN). An average free-energy barrier of *ca.* 78 kJ/mol was determined for the amide-bond rotation by variable-temperature ^{1}H-NMR measurements (*Fig. 2*). In the presence of H_2O, the hydrazone formation is entirely reversible, reaching an equilibrium composed of the hydrazine derivative, the carbonyl compound, and the corresponding hydrazone. Kinetic measurements carried out by UV/VIS spectroscopy showed that the same equilibrium was reached for the formation and hydrolysis of the hydrazone. Rate constants are strongly pH-dependent and increase with decreasing pH (*Table 1*). The influence of the hydrazine structure on the rate constants is less pronounced than the pH effect, and the presence of surfactants reduces the rate of equilibration (*Tables 1* and *3*). The full reversibility of the hydrazone formation allows to prepare dynamic mixtures by simple addition of a hydrazine derivative to several carbonyl compounds. Dynamic headspace analysis on dry cotton showed that the presence of a hydrazine derivative significantly increased the headspace concentrations of the different carbonyl compounds as compared to the reference sample without hydrazine (*Table 4*). The release of the volatiles was found to be efficient for fragrances with high vapor pressures and low H_2O solubility. Furthermore, a special long-lasting effect was obtained for the release of ketones. The simplicity of generating dynamic mixtures combined with the high efficiency for the release of volatiles makes these systems particularly interesting for practical applications and will certainly influence the development of delivery systems in other areas such as the pharmaceutical or agrochemical industry.

1. Introduction. – The efficient performance of biologically active substances such as pharmaceuticals, agrochemicals, or flavors and fragrances mainly depends on the long-lastingness of action at the target site. Fragrances, for example, have to be deposited onto a wide range of surfaces from which they have to evaporate in order to be perceived. As a consequence of their volatility, the duration of perception is often quite short. Furthermore, many fragrance ingredients, in particular aldehydes, are unstable and undergo degradation before their use in application. As the performance of perfumed consumer articles is often judged on the duration of fragrance perception, the development of efficient delivery systems for highly volatile compounds has become an important domain of research within the flavor and fragrance industry. In

contrast to encapsulation techniques, where the liberation of the active molecule is mainly based on diffusion out of an entrapping matrix (see, *e.g.*, [1]), chemical delivery systems, also termed 'profragrances' or 'properfumes', release small molecules in the targeted application by cleavage of a covalent bond of a suitably designed precursor molecule (*Scheme 1*,*a*) [2]. Reaction conditions that are defined by various applications of functional perfumery, and which may, therefore, serve as triggers for the chemical release of flavors and fragrances from their corresponding precursors, are limited to oxidation, the action of enzymes or light, and hydrolysis or change of pH [2][3].

Scheme 1. *Comparison of the Controlled Release of Fragrances* a) *from 'Classical' Profragrances and* b) *from a Dynamic Mixture Obtained by Reversible Hydrazone Formation*



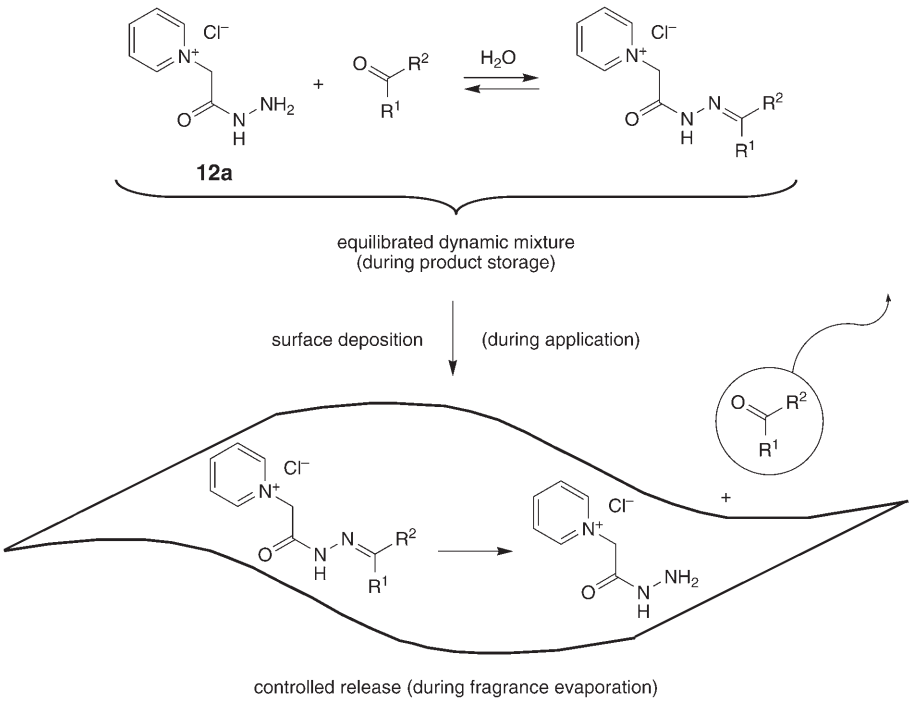
Similarly to previously reported fragrance precursors [2], hydrazones may at first view be considered as 'classical' profragrances (*Scheme 1*,*b*). In the presence of H_2O, they hydrolyze *via* an intermediate hemiaminal ('carbinolamine') to form a hydrazine derivative together with an aldehyde or a ketone [4][5]. At acidic pH, hydrazones are generally more stable than imines (*Schiff* bases) [4], the latter having been previously developed as fragrance precursors [6]. However, the major difference as compared to previous profragrances is the fact that the hydrolysis and the formation of hydrazones (and of *Schiff* bases in general) are reversible, forming an equilibrium between hydrazone, hydrazine, and the free aldehyde or ketone [5][7].

Reversible covalent reactions have recently been developed in combinatorial chemistry for the generation of dynamic libraries (see, *e.g.*, [8–12]). Their successful use in drug discovery (see, *e.g.*, [12]) prompted us to investigate the potential of dynamic mixtures obtained by reversible reaction of volatile aldehydes and ketones with hydrazine derivatives for the controlled release of fragrances [13] (parts of this publication are the subject of a patent application [14]). In contrast to pharmaceutical applications where the hydrazone itself is usually the targeted active species, the use of dynamic mixtures as fragrance-delivery systems requires the full reversibility of the reaction in order to recover the active molecule from the intermediate hydrazone.

Flavor- and fragrance-delivery systems based on reversible reactions leading to a dynamic mixture are expected to have several practical advantages. First of all, the profragrances do not have to be prepared separately, since they are automatically formed *in situ* by simple addition of the hydrazine derivative to a mixture of aldehydes and ketones as for example during product formulation (*Scheme 2*). Furthermore, one single hydrazine derivative can simultaneously form a multitude of different fragrance precursors when added to a mixture of aldehydes or ketones. The stability of the precursors themselves is not considered to be a problem [2], because an equilibrium mixture of a hydrazine, the free aldehyde or ketone, and the corresponding hydrazone is reached depending on external conditions such as temperature, concentration, or pH. The same equilibrium mixture should, therefore, be obtained either from the hydrazone or from a mixture of the corresponding hydrazine derivative and a carbonyl compound. As long as the fragrance is not lost through evaporation (*e.g.*, during storage), the dynamic mixture is expected to be stable and can be deposited as such onto the targeted surface of the perfumery application. Once deposited on the surface, evaporation then slowly shifts the equilibrium towards hydrolysis of the corresponding hydrazone, and thus gives rise to a long-lasting fragrance perception (*Scheme 2*) [13][14].

The goal of this work was to investigate the release of volatile aldehydes and ketones from dynamic mixtures in aqueous media by studying the equilibration at

Scheme 2. *Principle of the Controlled Release of Carbonyl Compounds from an Equilibrated Dynamic Mixture After Surface Deposition*



acidic pH as a function of the hydrazine structure and in the presence or absence of surfactants. The performance of the fragrance-delivery system is then evaluated by dynamic headspace analysis (see, *e.g.*, [15]) in practical applications of functional perfumery by using cotton as the model surface.

2. Results and Discussion. – 2.1. *Synthesis and Structures of Hydrazines and Hydrazones.* Numerous hydrazine derivatives are commercially available or can easily be prepared in a few reaction steps (see, *e.g.*, [16]). Particularly interesting in the context of the present studies are acylhydrazines (= hydrazides; $R'CO-NH-NH_2$), as these compounds incorporate a peptide bond together with the imine-forming hydrazine functionality [17]. For our studies, we used alkyl- or arylhydrazines **1a** and **2a**, sulfonylhydrazine (= sulfonic acid hydrazide) **3a**, as well as a series of different hydrazides such as semicarbazide (= hydrazinecarboxamide) **4a**, hydrazinecarboxylate **5a**, furoyl- and arylhydrazides (= furan- and arenecarboxylic acid hydrazides) **6a**–**8a**, alkylhydrazides (= alkanoic acid hydrazides) **9a** and **10a**, and the *Girard T* (**11a**) or *P* (**12a**) reagents [18] (*Fig. 1*). Hydrazides **13a** and **14a** as well as polymeric hydrazides **15a** and **16a** were prepared from their respective methyl esters by treatment with hydrazine hydrate [19][20]. The corresponding hydrazones of benzaldehyde **1b**–**13b**

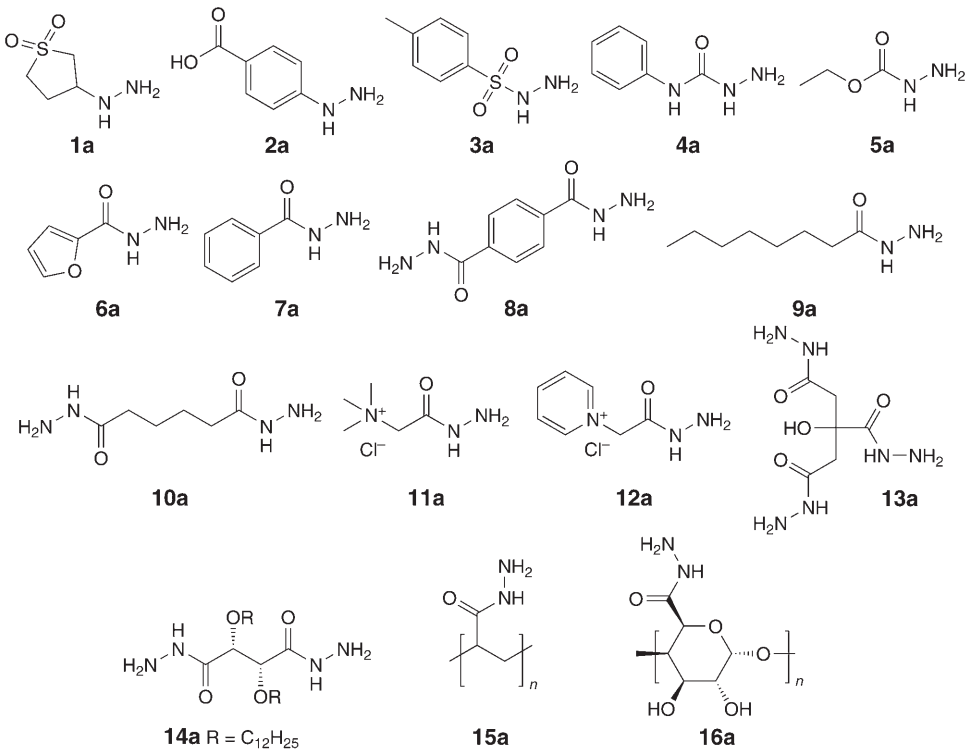
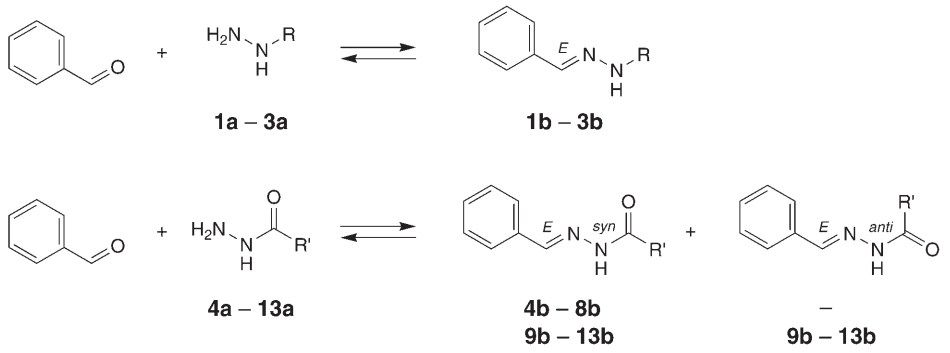


Fig. 1. *Structures of hydrazine derivatives* **1a**–**16a**. The corresponding hydrazones **1b**–**13b** of benzaldehyde (PhCHO) were prepared according to *Scheme 3*.

Scheme 3. *Reversible Formation and Respective Conformations of Different Hydrazone Derivatives.* For R and R′, see *Fig. 1.*



(*Scheme 3*) were prepared in one step by heating the hydrazine derivatives with a slight excess of benzaldehyde in heptane, toluene or, as in most of the cases, in MeOH or EtOH (for the compounds discussed in this work, see, *e.g.*, [21]; for the general synthesis of hydrazones, see also [22]). The products generally crystallized on cooling to room temperature, and could thus easily be isolated. Although most of the compounds described in this work have already been previously reported [21][23], surprisingly, they often have only been partially characterized. In particular, the formation of different conformational or configurational isomers was only rarely mentioned [24–27]).

All synthesized compounds were analyzed by NMR spectroscopy. One- (^{1}H,^{13}C) and two-dimensional, homo- (COSY, NOESY) and heteronuclear (^{1}H,^{13}C-HSQC, ^{1}H,^{13}C-HMBC) NMR experiments were recorded to determine the conformation and configuration of the products. All hydrazones were obtained with an (*E*) configuration at the imine double bond (NHN=C). Hydrazones **2b** and **3b** as well as acylhydrazones **4b**–**8b** were isolated as the pure *syn* isomers (*Scheme 3*), whereas both *syn* and *anti* isomerization with respect to the amide-bond conformation (CO–NHN) was observed for the aliphatic acylhydrazones **9b**–**13b** (R′ = alkyl in *Scheme 3*). In agreement with the literature [24–26], the ratio of the different conformers is solvent-dependent [24][25], with the *anti* conformation being generally the predominant form in DMSO.

The *syn* and *anti* amide-bond conformers can easily be distinguished by their chemical shifts in the ^{1}H- and ^{13}C-NMR spectra. As the exchange between the two isomers is slow on the NMR time scale, they both give separate sets of signals in the spectra. For example, in DMSO, we observe an upfield shift for the imine H-atom (NHN=C*H*) of the *anti* conformer (δ 8.0–8.3) and a downfield shift for the *syn* isomer (δ 8.2–8.5). In the ^{13}C-NMR spectra, the resonances of the amide carbonyl groups (R′*C*O–NHN) of the *anti* conformer are shifted downfield by *ca.* 5 ppm (δ 166–174) and the imine groups (NHN=*C*H) are shifted upfield by *ca.* 3 ppm (δ 142–146), whereas the signals of the corresponding *syn* conformers are observed at δ 161–168 and 146–148, respectively.

Variable-temperature ^{1}H-NMR measurements were carried out to study the *syn*/*anti* isomerism in more detail. Hydrazone **11b** is formed with a *syn*/*anti* ratio of *ca.* 1:1.8

in (D_6)DMSO. By increasing the temperature, a coalescence of several resonances can be observed, notably at δ 12.5 (NH), 8.4 (NHN=C*H*), and 4.7 (CH_2), at 397.1, 387.3, and 392.2 K, respectively (*Fig. 2*). This results in an average free-energy barrier for the amide-bond rotation of $\Delta G = 79.1$ kJ/mol for the *anti* → *syn* isomerization and $\Delta G^{\neq} = 77.2$ kJ/mol for the *syn* → *anti* isomerization [28], which is in the same order of magnitude as the ones previously reported for a similar system [25]. A recently reported X-ray solid-state molecular structure of the hydrazone formed from **11a** and isobutyraldehyde showed that the imine double bond has an (*E*) configuration and the amide bond is in an *anti* conformation [29].

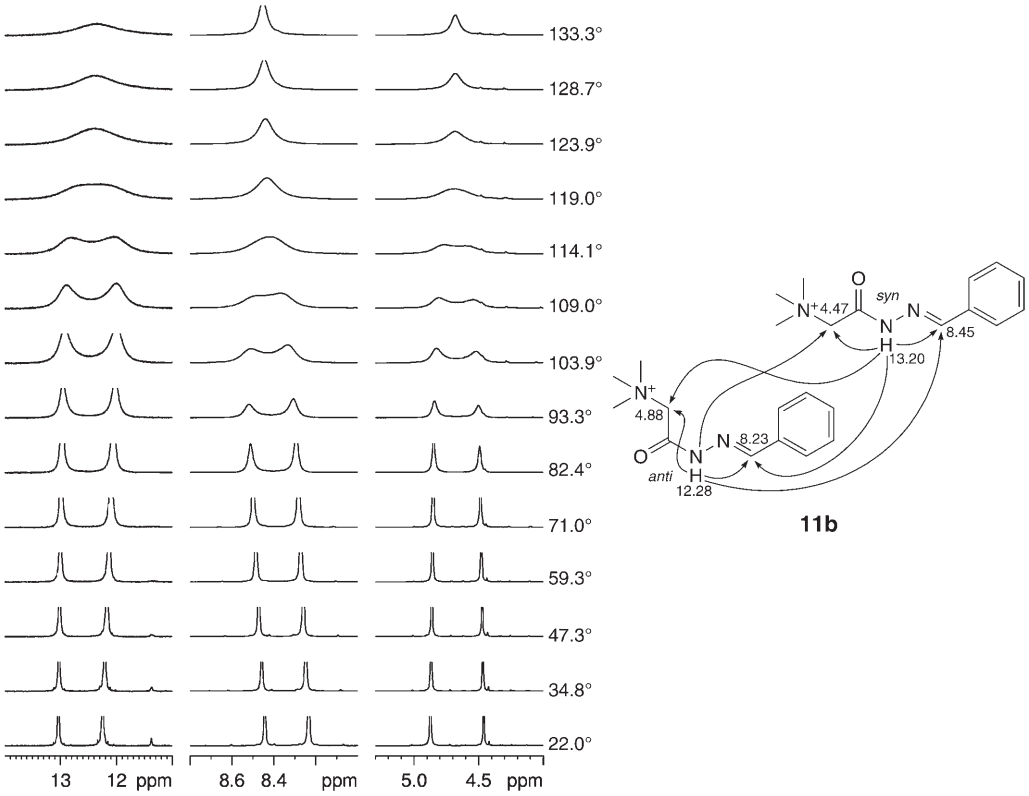


Fig. 2. *Temperature-dependent ^{1}H-NMR spectra and observed NOEs* (at r.t.) *for the* syn/anti *isomers of* **11b** *in (D_6)DMSO*

The chemical exchange between *syn* and *anti* conformers can be directly observed in the NOESY plot (data not shown). In addition to the expected NOE peaks for the individual isomers, exchange peaks between corresponding positions in both *syn* and *anti* isomers were found with a different sign than that of the real NOEs (*Fig. 2*). Apparently, the chemical exchange between the *syn* and *anti* conformers is fast enough to allow substantial chemical exchange in the mixing time of the NOESY experiment (800 ms). This corroborates our initial assignments of the isomers as *syn* and *anti*

rotamers of the amide moiety rather than as configurational isomers with respect to the C=N bond.

Aliphatic bis-acylhydrazones $R^1R^2C{=}N{-}NH{-}COR'CO{-}NH{-}N{=}CR^1R^2$ ($R' =$ alkyl) give rise to a mixture of the three possible conformational isomers. In the case of **10b**, the *syn*/*anti* isomer was found to be the predominant conformer, followed by the *anti*/*anti* and *syn*/*syn* conformers, respectively. This structural assignment was confirmed by NOE and HMBC measurements, and is in agreement with literature data reported for analogous structures [26].

The structural assignment of tris-acylhydrazone **13b** was more complicated. In the presence of two different C=O and C=N bonds, up to six different isomers, *i.e.*, **A**–**F**, resulting from the combinations of all possible *syn*/*anti* conformations of the amide bonds can potentially be formed (*Fig. 3*). Two-dimensional NMR spectroscopy

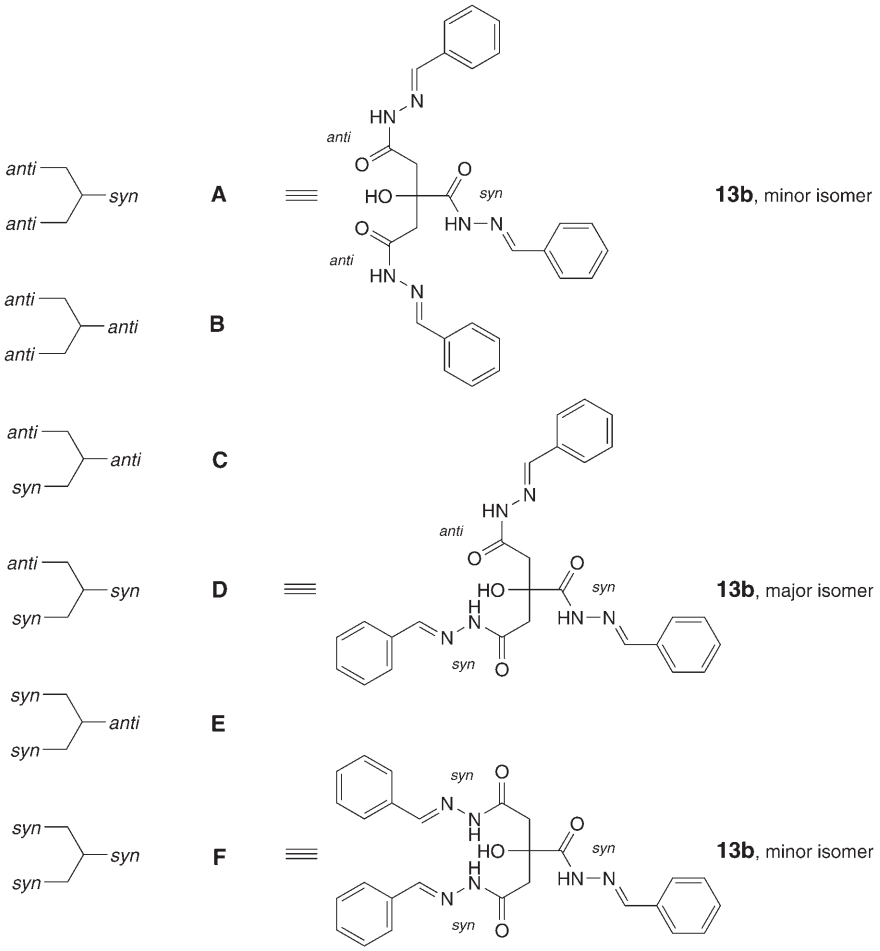


Fig. 3. *Structures of the three isomers* **A**, **D**, *and* **F** *obtained, out of six possible isomers, in a ratio of* ca. *1:2:1*

revealed a 1:2:1 mixture of conformers **A**, **D**, and **F**, all of which are in the *syn* conformation with respect to the amide bond connected to the quaternary C-atom in **13b** (*Fig. 3*).

The preparation and structural assignment of hydrazones **3c**, **6c**, **7c**, **7d**, and **10c** (*Fig. 4*) were similar to the corresponding benzaldehyde derivatives. In the case of bisacylhydrazone **10c**, the *anti*/*anti* conformer was obtained as the major isomer.

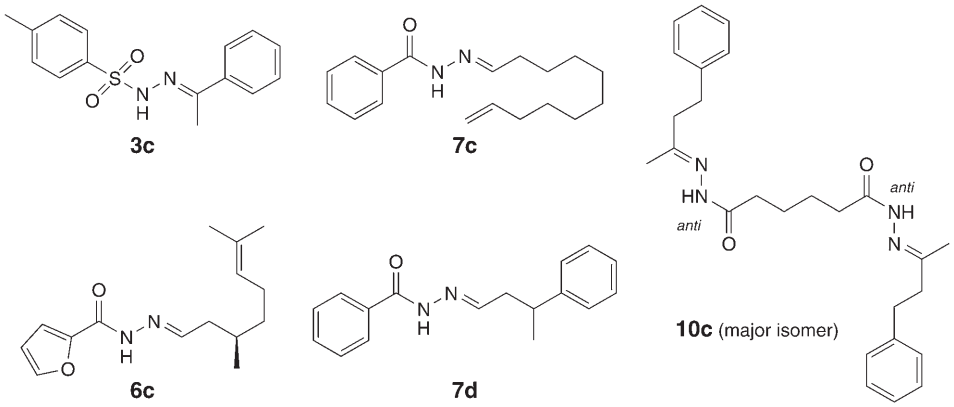


Fig. 4. *Structures of hydrazones* **3c**, **6c**, **7c**, **7d**, *and* **10c**

2.2. *Kinetics of Hydrazone Formation and Hydrolysis.* The reaction of carbonyl compounds with hydrazine derivatives has been investigated by several research groups, exemplified by semicarbazides (= hydrazinecarboxamides) [5][7][30–33]. The formation of semicarbazones (= alkylidenehydrazinecarboxamides) is general acid-catalyzed [34], with the addition step being less sensitive to acid catalysis than the dehydration step. In many cases, the rate decreases at lower pH, which indicates a change in the rate-determining step. General base catalysis was observed for the dehydration of hemiaminals obtained from ethyl carbazates (= ethyl hydrazinecarboxylates), hydrazides, thiosemicarbazides (= hydrazinecarbothioamides) or arenesulfonic acid hydrazides with lower basicity than semicarbazides [7].

Comparison of the reaction of (+)-(*S*)-carvone with phenylhydrazine, hydroxylamine, and semicarbazide indicated that all three proceed by the same mechanism, and an increase of the rate constants was observed by moving from the former to the latter [35]. In a series of pharmaceutically active hydrazine derivatives, hydrazides were found to react faster with pyridoxal 5′-phosphate (= 3-hydroxy-2-methyl-5-[(phosphonooxy)methyl]pyridine-4-carboxaldehyde) than alkyl- and arylhydrazines [36].

In the reaction of *Girard T* reagent (**11a**) with benzaldehydes or naphthalenecarboxaldehydes, the change of the rate-determining step was determined to be at a pH of *ca*. 4 [37]. Whereas a change in the rate-determining step from neutral to acidic conditions was also observed for the hydrolysis of *Girard T* hydrazones derived from aliphatic carbonyl compounds, this was not the case for the hydrolysis of aromatic *Girard T* hydrazones [38]. The hydrolysis of hydrazones was found to be pseudo-first-order, especially if an excess of hydrazine was used, and the measured rate constants decreased with increasing pH. At very low pH, as for example in the presence of HCl,

the reaction proceeded almost to completion [39], whereas under slightly acidic conditions (pH > 3.5 or 4), no hydrolysis was observed [36].

Rate constants were generally determined spectrophotometrically [7][30–32][34–37][39][40], but also titrations [33] or polarographic methods [38][41] have been reported. The measurements were carried out over a broad range of pH in H_2O or H_2O/alcohol solutions and under a variety of conditions where parameters such as product concentration, temperature, or ionic strength were changed.

As a first approach to evaluate the potential of dynamic mixtures for the controlled release of volatile aldehydes and ketones, we investigated the reaction rates involved in the equilibration of a single hydrazine derivative with one fragrance aldehyde or ketone in buffered solution at acidic pH. Kinetic measurements were performed by UV/VIS spectroscopy in a buffered aqueous solution (H_2O/EtOH 2:1 (*v*/*v*)) at pH 2.47 (phosphoric acid buffer) and 4.48 (citric acid buffer). The reactions were carried out at a product concentration of *ca.* $1.7 \cdot 10^{-5}$ M with benzaldehyde as the model carbonyl compound [13]. For compounds with two or three hydrazine units within the same molecule (see **8a**, **10a**, and **13a**), the aldehyde concentration was increased to correspond to a molar equivalent of available hydrazine functionalities. UV/VIS Spectra were recorded at constant time intervals between 240 and 450 nm, and the reactions were investigated at equimolar concentrations in both directions. Within the experimental error, the same equilibrium states were reached either from a mixture of the aldehyde and a hydrazine derivative, or by hydrolysis of the corresponding hydrazone [13], as shown in *Scheme 4* for the reaction between benzaldehyde and hexanedioic acid 1,6-dihydrazide (adipic acid dihydrazide; **10a**). The rate constants and half-lifes determined for the reaction of benzaldehyde with hydrazine derivatives **1a**–**14a** are summarized in *Table 1*.

Good linear fits of the data points ($r^2 > 0.99$) were generally obtained by plotting the logarithm of the difference of the end absorption (A_e, corresponding in our case to the absorption measured once the equilibrium is reached) and the absorption at time *t* (A_t) against time (infinity time method), thus indicating pseudo-first-order kinetics under the given reaction conditions [42]. Since the end absorption can not always be accurately measured, the rate constants were determined by plotting the logarithm of the difference of absorption at time $t + \Delta t$ and time *t* (*i.e.*, $\log (A_{t+\Delta t} - A_t)$) against time (*Guggenheim* method) [43], or by plotting the absorption at time *t* (A_t) against the absorption at time $t + \Delta t$ ($A_{t+\Delta t}$) (*Kezdy–Mangelsdorf–Swinbourne* method) [44]. Since almost identical values were obtained in both cases, we only considered the data obtained from the *Guggenheim* method[1]). With $\Delta t = 1$ h (pH 2.47) or $\Delta t = 7.5$ h (pH 4.48), the rate constants listed in *Table 1* were obtained from the change of absorption measured at 290 nm.

The determination of the kinetic rate constants for the formation and hydrolysis of hydrazones allows a study of the influence of various parameters such as pH, molecular

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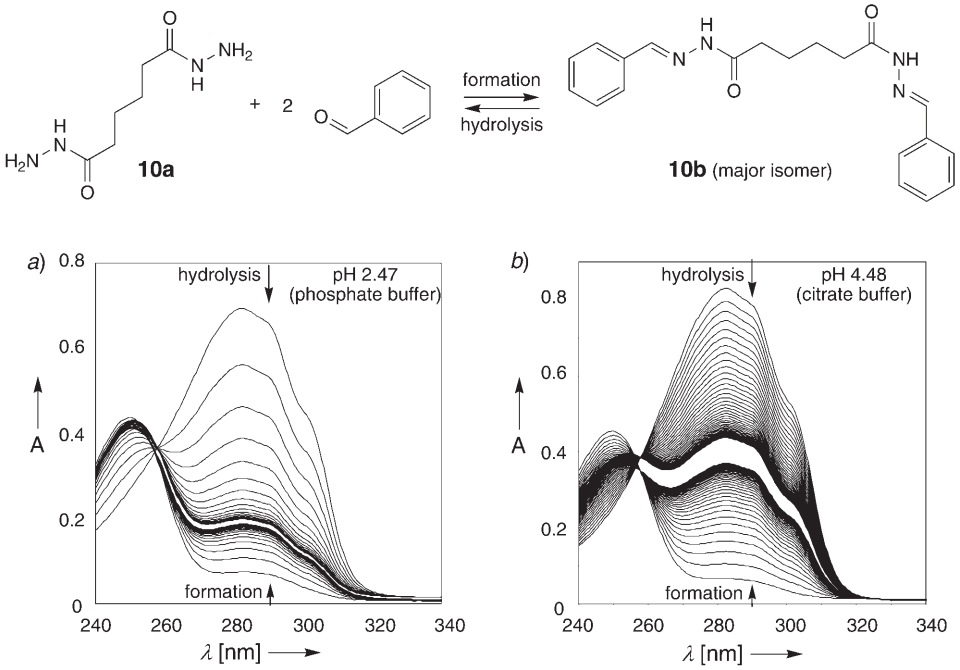
[1]) As a general trend, the *Guggenheim* method gave higher correlation coefficients for fast reactions with $t_{1/2} < \Delta t$. In the case of slower reactions with $t_{1/2} \geq \Delta t$, higher correlation coefficients were obtained with the *Kezdy–Mangelsdorf–Swinbourne* method. As an example, the latter method gave rate constants of $0.78 \cdot 10^{-4}$ s^{-1} and $0.37 \cdot 10^{-4}$ s^{-1} for the formation and hydrolysis of **3b** at pH 2.47, resp., with a correlation coefficient > 0.99.

Scheme 4. *Equilibria Obtained for the Reversible Formation and Hydrolysis of Dihydrazone* **10b** *Followed by UV/VIS Spectroscopy in Buffered Aqueous Solution* (H_2O/EtOH 2 : 1, 25°) *at* a) *pH 2.47 and* b) *pH 4.48*



structure, and concentration. Our measurements (*Table 1*) show that, under acidic conditions and in accordance with previous data [5][7][11][13], the rate constants increase with decreasing pH. This effect is more pronounced for the formation and hydrolysis of acylhydrazones **6b**–**12b**, where a pH drop of two units increases the rate by a factor of 16–55. In the case of alkylhydrazone **1b**, sulfonylhydrazone **3b**, semicarbazone **4b**, or carboxylate-substituted hydrazone **5b**, the rate constants change only by a factor of 3 to 8. In general, the hydrolysis of the hydrazones is slower than their formation, particularly for the rates measured at pH 4.48. At lower pH (2.47), this difference is less pronounced, and in the case of acylhydrazones **6b**–**12b**, the rates for the formation and hydrolysis of the hydrazones, and thus the half-lifes to reach the equilibrium, are almost identical. At a given pH, the equilibration rates for the reaction of different hydrazine derivatives with benzaldehyde are generally comparable. It is interesting to note that, at pH 2.47, the variation between the smallest (formation of sulfonylhydrazone **3b**) and highest rate constants (formation of bis-acylhydrazones **8b** or **10b**) is more pronounced (factor 14–16) than at pH 4.48 (factor 3), where all reactions are considerably slower, and where the formation of acylhydrazone **11b** is the slowest reaction, and the formation of alkylhydrazone **1b** is the fastest (*Table 1*). The formation or hydrolysis of arylhydrazones such as **2b** are exceptions in that their rate constants are too small to be accurately determined by the present method. At both pH, 2.47 and 4.48, dihydrazides **8a** and **10a** react faster with benzaldehyde than their

Table 1. *Observed Pseudo-First-Order Kinetic Rate Constants and Half-Lifes to Reach the Equilibrium for the Formation and Hydrolysis of Hydrazones* **1b**–**14b** *at pH 2.47 and 4.48*. Reactions were carried out at a product concentration of *ca*. $1.7 \cdot 10^{-5}$ M in H_2O/EtOH 2 : 1 at 25° and analyzed by UV/VIS spectroscopy at 290 nm. All data are average values of at least two measurements with standard deviations smaller than $2.5 \cdot 10^{-5}$ s^{-1} (pH 2.47) or $2.5 \cdot 10^{-6}$ s^{-1} (pH 4.48). Variations with respect to [13] are due to additional measurements.

Formation of hydrazone	pH 2.47		pH 4.48		Hydrolysis of hydrazone	pH 2.47		pH 4.48	
	$k_{obs} \cdot 10^4$ [s^{-1}]	$t_{1/2}$ [h]	$k_{obs} \cdot 10^4$ [s^{-1}]	$t_{1/2}$ [h]		$k_{obs} \cdot 10^4$ [s^{-1}]	$t_{1/2}$ [h]	$k_{obs} \cdot 10^4$ [s^{-1}]	$t_{1/2}$ [h]
1b	2.22[a])	0.87	0.77	2.50					
3b	0.76[b])	2.53	0.20[c])	9.63	**3b**	0.36[d])	5.35	0.08[e])	24.07
4b	1.30	1.48	0.39	4.94	**4b**	0.75	2.57	0.11[c])	17.50
5b	2.72	0.71	0.51	3.78	**5b**	2.23	0.86	0.29	6.64
6b	6.10	0.32	0.29	6.64	**6b**	6.43	0.30	0.18	10.70
7b	9.88	0.19	0.41	4.70	**7b**	10.66	0.18	0.30	6.42
8b	12.13	0.16	0.50	3.85	**8b**	11.35[f])	0.17	–[g])	
9b	7.64	0.25	0.44	4.38	**9b**	7.37	0.26	0.28	6.88
10b	10.60[h])	0.18	0.66	2.92	**10b**	10.95[i])	0.18	0.43	4.48
11b	5.53[j])	0.35	0.15	12.84	**11b**	5.98	0.32	0.11[k])	17.50
12b	5.48	0.35	0.16	12.03	**12b**	4.95	0.39	0.09[c])	21.39
					13b	9.09[l])	0.21	0.47	4.10
14b	1.05[c])	1.83	0.21[m])	9.17					

[a]) $r^2 > 0.89$. [b]) $r^2 > 0.89$, $\Delta t = 1.3$ h, see *Footnote 1*. [c]) $r^2 > 0.98$. [d]) $r^2 > 0.98$, $\Delta t = 3.8$ h at 270 nm, see *Footnote 1*. [e]) $r^2 > 0.98$, first point taken after 32 min, $\Delta t = 15$ h at 270 nm. [f]) $\pm 8.5 \cdot 10^{-5}$ s^{-1}. [g]) Partial precipitation of **8b** was observed. [h]) $\pm 6.7 \cdot 10^{-5}$ s^{-1}. [i]) $\pm 3.7 \cdot 10^{-5}$ s^{-1}. [j]) Baseline drift, $r^2 > 0.99$. [k]) $\Delta t = 15$ h. [l]) $r^2 \approx 0.98$, slight deviation from linearity. [m]) $r^2 > 0.97$.

corresponding monohydrazides **7a** and **9a**; however, the distance between two hydrazide functions in dihydrazides has only a slight influence on the rate of hydrazone formation. The rate constant measured for the reaction between benzaldehyde and dodecanedioic acid 1,12-dihydrazide ($k_{obs} = 0.58 \cdot 10^{-4}$ s^{-1}) at pH 4.48 is only slightly smaller than the one measured for its lower homologue **10a** ($k_{obs} = 0.66 \cdot 10^{-4}$ s^{-1}).

During the hydrolysis of bis-acylhydrazone **8b** at pH 4.48, the formation of a white precipitate was observed. ^{1}H-NMR Analysis in (D_6)DMSO indicated the presence of unreacted **8b** which, as a consequence of its low solubility in the buffer solution, seems to aggregate under the reaction conditions. A baseline drift was observed for the formation of **14b** which also may be attributed to a slow aggregation of the hydrazone in aqueous media.

As the equilibration between different aldehydes (benzaldehyde, vanillin (=4-hydroxy-3-methoxybenzaldehyde), and cinnamaldehyde (=(2*E*)-3-phenylpropanal)) with several hydrazides, *i.e.*, with **6a**, **7a**, and **11a**, has already been discussed [13], this aspect will not be further detailed here. Nevertheless, it should be noted that the equilibria formed between hydrazine derivatives, ketones, and their corresponding hydrazones often lie almost completely on the side of the unreacted ketones, with the hydrolysis of the hydrazone being quite fast. Indeed, because the UV/VIS spectrum for the reaction of acetophenone (=1-phenylethanone) with **3a** remained almost unchanged, the rate constants could not be accurately determined. However, the

hydrolysis of the corresponding hydrazone **3c** proceeded smoothly, and rate constants of $1.47 \cdot 10^{-4}$ s^{-1} (pH 2.47) and $0.97 \cdot 10^{-5}$ s^{-1} (pH 4.48) were measured at 270 nm.

The dependence of aldehyde concentration on the rate constants was investigated for the formation of aromatic and aliphatic acylhydrazones **7b**–**10b** as shown in *Table 2*. Keeping the hydrazide concentration constant and varying the benzaldehyde concentration to 0.5, 1, or 2 equiv. with respect to the hydrazide functions resulted, in all cases, in an increase of the respective rate constants. At equimolar hydrazide concentration, the bis-acylhydrazones **8b** and **10b**, formed with 2 equiv. of benzaldehyde, were found to be generated faster than the corresponding mono-acylhydrazones **7b** and **9b**, formed with 1 equiv. of benzaldehyde. The influence of the concentration on the rate constants is nevertheless less important than the other factors discussed above. In all cases, a few-fold increase in aldehyde concentration (going from 0.5 equiv. to 2 equiv. per hydrazide function) corresponds to a 32–47% increase in rate constant.

Table 2. *Concentration-Dependent Pseudo-First-Order Kinetic Rate Constants and Half-Lifes to Reach Equilibrium for the Formation of Hydrazones* **7b**–**10b** *at pH 2.47, Analyzed by UV/VIS Spectroscopy at 290 nm*. For the values corresponding to 1 equiv. of benzaldehyde, see *Table 1.*

Formation of hydrazone	0.5 equiv. of benzaldehyde[a])		2 equiv. of benzaldehyde[a])	
	$k_{obs} \cdot 10^4$ [s^{-1}]	$t_{1/2}$ [h]	$k_{obs} \cdot 10^4$ [s^{-1}]	$t_{1/2}$ [h]
7b	8.90	0.21	11.77	0.16
8b	9.44	0.20	13.90	0.14
9b	6.35	0.30	8.54	0.23
10b	9.62	0.20	13.01	0.15

[a]) With respect to the hydrazide functions.

We also investigated the influence of a nonionic surfactant on the equilibration of the system. Surfactants are present in almost all practical applications of functional perfumery and, besides solubilizing the fragrance molecules in an aqueous environment, also serve as the active cleaning or softening agent of the particular application. As cationic surfactants such as tetraalkylammonium derivatives or quaternized triethanolamine (=2,2′,2″-nitrilotris[ethanol]) esters of fatty acids (TEA-esterquats) [45] form milky emulsions even at very low concentrations, we investigated the formation and hydrolysis of the aromatic and aliphatic acylhydrazones **7b**–**10b** with benzaldehyde in the presence of a nonionic surfactant (*Table 3*). The corresponding phosphate buffer solution in H_2O/EtOH 2:1 was prepared as described above by adding *Triton® X-100* as an additional ingredient. A total of 0.1 weight-% of surfactant in the final buffer solution shifted the pH to a value of 2.51 (instead of 2.47 without surfactant). Due to the slight absorption of the surfactant at 290 nm, the data in *Table 3* were acquired at 300 nm.

As one might expect, the equilibration of the products is slowed down in the presence of the surfactant. However, the influence of the surfactant seems to be strongly dependent on the structure of the hydrazones. Furthermore, both forward and reverse steps of the equilibration are not (always) equally affected. Whereas the rate for the hydrolysis of the aromatic bis-acylhydrazone **8b** remains almost unchanged in the presence of 0.1% of *Triton® X-100* in the solution, the rate for product formation

Table 3. *Observed Pseudo-First-Order Kinetic Rate Constants and Half-Lifes to Reach Equilibrium for the Formation and Hydrolysis of Hydrazones* **7b** – **10b** *at pH 2.51 in the Presence of 0.1%* (wt.) *of* Triton® X-100 *as a Nonionic Surfactant Analyzed by UV/VIS Spectroscopy at 300 nm.* For the absence of surfactant, see *Table 1.*

Formation of hydrazone	pH 2.51		Hydrolysis of hydrazone	pH 2.51	
	$k_{obs} \cdot 10^4$ [s^{-1}]	$t_{1/2}$ [h]		$k_{obs} \cdot 10^4$ [s^{-1}]	$t_{1/2}$ [h]
7b	8.74	0.22	**6b**	8.63	0.22
8b	10.01	0.19	**7b**	11.07	0.17
9b	4.10	0.47	**9b**	3.69	0.52
10b	9.56	0.20	**10b**	8.35	0.23

was slowed down by 18%. In the presence of the surfactant, the rate of formation of **10b** was reduced by 10%, and the rate of hydrolysis by 24%. The rate constants measured for the formation and hydrolysis of mono-acylhydrazones **7b** and **9b** were affected by a similar amount corresponding to a decrease of the rate constants by 12% and 19% (**7b**), and 46% and 50% (**9b**). The presence of the surfactant influences the equilibration of the system, and in particular at high surfactant concentrations, the rates of equilibration of the dynamic mixtures are slowed down considerably.

Being aware that the pH value of the environment and the presence of surfactant are probably the most important factors that influence the rate constants for the equilibration of hydrazones, and that both parameters are defined by the desired practical applications, we suppose that the actual structure of the hydrazine/hydrazone is of minor importance under more realistic application conditions. Therefore, we expect that the delivery of volatile aldehydes and ketones should proceed in a similar fashion for different hydrazine derivatives. It should, furthermore, be noted that the time of the hydrazine/hydrazone equilibration is not really important for practical applications, because the dynamic mixtures being prepared during product formulation have enough time to equilibrate during the storage of the final consumer article prior to its use. More important are the evaporation kinetics of the different fragrance aldehydes and ketones after deposition of the dynamic mixture onto the target surface, once the equilibrium is reached. This issue is addressed in the following section by dynamic headspace analysis of the released volatiles on dry cotton surfaces.

2.3. *Controlled Release of Volatiles from Cotton Surfaces.* In a typical washing cycle, fragrances are deposited on the target surface together with the surfactants contained in the product formulation. Cationic surfactants, which are used as fabric-softening agents [45], are particularly efficient with respect to deposition onto cotton (see, *e.g.*, [46]) and thus play an important role in the transport of apolar organic molecules such as fragrances from an aqueous environment onto textiles [47]. The fabric-softening process is usually the last step of a washing cycle, which means that the fragrances are most efficiently deposited onto the fabric during this step. Due to their relatively simple formulation (they consist of *ca.* 15% of a cationic surfactant in H_2O, and contain up to 1% of perfume, small amounts of $CaCl_2$, and optionally a dye), fabric softeners are an ideal starting point to study the controlled release of volatiles from dynamic mixtures.

To simulate a fabric-softening process and to be able to evaluate the release of volatile aldehydes or ketones from a dynamic mixture under more realistic conditions, a

relatively simple laboratory procedure was developed. As a first step, the hydrazine derivative and an equimolar amount of one or several fragrance aldehydes and ketones were added to an emulsion of a TEA-esterquat in H_2O (pH *ca.* 3.1) which was then left equilibrating for 5 days to set up the dynamic mixture. The sample was then diluted with H_2O which increases the pH of the emulsion by about one unit (pH *ca.* 4.0–4.2) and slows down the re-equilibration. Then a small cotton square (*ca.* 12 × 12 cm) was added, which was manually stirred for 3 min and left standing for 2 min to allow the deposition of the dynamic mixture and the surfactant on the cotton surface. After wringing out, and air-drying overnight, the amount of volatiles evaporating from the fabric surface was analyzed by dynamic headspace analysis. For headspace analyses, the dry cotton square was placed into a closed sampling cell and exposed to a constant flow of air which was passed through a filter of activated charcoal and then through a saturated salt solution to control the humidity of the air [48]. The volatiles were trapped at constant time intervals in a cartridge containing a polymeric adsorbant (*Tenax®*) and, after thermal desorption, analyzed by gas chromatography (GC). All analyses were compared to a reference sample composed of the same volatiles but without the hydrazine derivative, which was prepared and analyzed under the same conditions. As long as the individual volatiles are separated by GC, fragrance mixtures can easily be analyzed and quantitative data for each component of the mixture can be obtained.

To verify the concept of dynamic mixtures for controlling the release of volatile aldehydes and ketones by reversible hydrazone formation, we chose hydrazide **12a** (*Girard P* reagent) which, as a consequence of its positive charge, was expected to be preferentially deposited on the cotton surface together with the cationic surfactant. Two sets of three samples were thus prepared by adding either benzaldehyde alone, benzaldehyde and **12a**, or the corresponding acylhydrazone **12b** to the TEA-esterquat emulsion. One set of samples was immediately diluted without equilibration and exposed to the cotton square directly after the preparation, the other set was left standing for 5 days to equilibrate before being diluted and being brought into contact with the cotton square. *Fig. 5,a*, and *Table 4* show the benzaldehyde headspace-concentration measurements for the set of the nonequilibrated samples. As one might expect, the sample containing hydrazone **12b** behaves as a classical profragrance

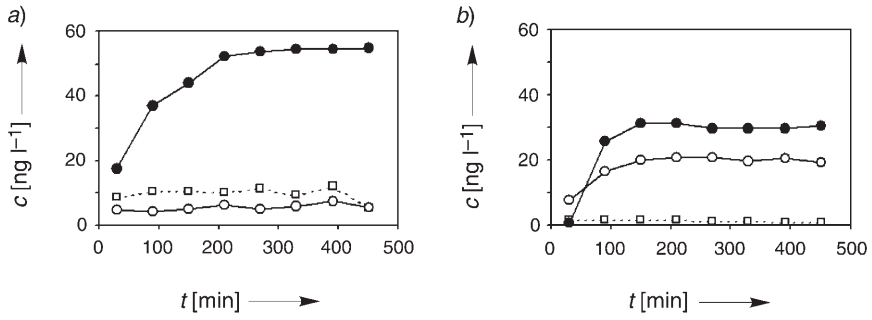


Fig. 5. *Headspace concentrations of benzaldehyde on dry cotton measured* a) *without equilibration and* b) *after equilibration for 5 d of a dynamic mixture of* **12a** *and benzaldehyde* (—○—), **12b** (—●—), *or pure benzaldehyde* (···□···)

delivery system [2] which releases benzaldehyde at higher amounts than the sample containing the free aldehyde. As the mixture of benzaldehyde and **12a** had no time to equilibrate, it behaves just as the reference sample giving rise to almost the same headspace concentrations as the sample containing the unmodified benzaldehyde.

Pre-equilibration of the system in the TEA-esterquat emulsion before washing the cotton square changes the situation, as illustrated in *Fig. 5*, *b*. The sample with acylhydrazone **12b** still releases higher amounts of benzaldehyde than the reference with the free aldehyde. However, this time the mixture of **12a** and benzaldehyde gives rise to almost the same headspace concentrations as the sample with the hydrazone **12b**, thus indicating that the same dynamic mixture and thus the same composition of the equilibrium was obtained in both cases. It is interesting to note that the performance of **12b** is higher in the fresh sample than in the equilibrated sample. This may be explained by the fact that, in the latter case, a certain amount of the hydrazone is hydrolyzed, and that the fragrance is then less efficiently deposited in its free form than when it is bound to the cationic hydrazide.

Dynamic headspace analysis is the ideal tool to investigate the performance of dynamic mixtures. As long as the different volatile constituents of the mixture can be separated by GC, quantitative headspace concentrations for each compound in the mixture can be determined simultaneously in one single experiment. For the following measurements, several fragrance aldehydes and ketones (see *Table 4*) were equilibrated together with a hydrazide derivative in the concentrated TEA-esterquat formulation and deposited onto small cotton squares as described above. The experiment was repeated three times to estimate the error of the headspace sampling.

Table 4 and *Fig. 6* show the average individual headspace concentrations measured on dry fabric for an equimolar mixture of furan-2-carboxaldehyde (= furfural), 2,4,6-trimethylcyclohex-3-ene-1-carboxaldehyde (mixture of stereoisomers), (±)-*exo*-tricyclo[5.2.1.$0^{2,6}$]decane-8-*exo*-carboxaldehyde (= *rel*-(3a*R*,4*R*,5*S*,7*R*,7a*R*)-octahydro-4,7-methano-1*H*-indene-5-carboxaldehyde = *Vertral*®), 1-(4-methylphenyl)ethanone (= 4-methylacetophenone), (±)-5-methylheptan-3-one and 2-pentylcyclopentanone (= delphone) that was equilibrated in the presence or absence of hexanedioic acid dihydrazide (**10a**). The data show that, in the presence of **10a**, higher headspace concentrations were determined for all the constituents of the dynamic mixture as compared to the reference sample without **10a** (*Table 4*, *Fig. 6*). In some cases, none of the carbonyl compound was detected in the reference sample, whereas the presence of the hydrazide still gave detectable amounts of the aldehydes or ketones after 1 day. At the end of the experiment, the presence of **10a** increased the headspace concentration of the fragrances between 1.5 (furfural) and 350 times (delphone) (*Fig. 6*). Despite the fact that the equilibrium between hydrazine derivatives and ketones seems to be mostly on the side of the unreacted compounds, a particular long-lasting effect was generally observed for the release of ketones. Similar results were obtained for a mixture of fragrances in the presence or absence of **13a** (*Table 4*).

To determine the increase in headspace concentration in the case where no aldehyde or ketone was left in the reference sample, we estimated its concentration at the detection threshold of *ca.* 0.05 ng l^{-1}. The error bars in *Fig. 6* indicate that the measurements were quite reproducible, despite some larger variations for higher

Table 4. *Vapor Pressures, log* $P_{o/w}$ *Values and Time-Dependent Headspace Concentrations of the Different Aldehydes and Ketones Released from Dynamic Mixtures Determined on Dry Cotton with Respect to the Reference Sample* (in parentheses)

Hydrazide or hydrazone (conditions)/ volatile	Vapor pressure [Pa][a])	log $P_{o/w}$[a])	Time-dependent headspace concentrations of the released volatiles compared to the reference sample (in parentheses) [ng l^{-1} air] on dry cotton							
			30 min	90 min	150 min	210 min	270 min	330 min	390 min	450 min
12a (non equilibrated)[b])/ benzaldehyde	134.6	1.71	4.6 (8.7)	4.3 (10.5)	5.1 (10.3)	6.1 (10.0)	5.3 (11.3)	6.0 (9.5)	7.3 (12.3)	5.6 (5.6)
12b (non equilibrated)[b])/ benzaldehyde			17.4	37.0	44.0	52.1	53.7	54.5	54.4	54.8
12a (equilibrated)[b])/benzaldehyde			7.7 (1.5)	16.4 (1.4)	19.9 (1.4)	20.9 (1.5)	20.8 (1.3)	19.7 (1.2)	20.4 (0.9)	19.0 (0.8)
12b (equilibrated)[b])/benzaldehyde			1.0	25.9	31.3	31.0	29.7	29.8	29.8	30.2
10a (equilibrated)[c]) with										
furfural	309.3	0.83	0.6 (1.0)	1.0 (1.1)	1.3 (0.9)	1.6 (1.1)	1.6 (1.0)	1.7 (1.2)	1.6 (1.1)	1.4 (0.9)
2,4,6-trimethylcyclo-hex-3-ene-1-carboxaldehyde	23.3	3.27	0.4 (0.0)	0.9 (0.0)	1.1 (0.0)	1.2 (0.0)	1.2 (0.0)	1.1 (0.0)	1.2 (0.0)	1.2 (0.0)
Vertral®	7.9	2.52	8.6 (0.4)	21.4 (0.9)	30.7 (1.2)	33.9 (1.2)	33.1 (1.0)	30.4 (0.9)	27.5 (0.8)	24.7 (0.8)
4-methylacetophenone	11.3	2.10	0.2 (0.0)	0.7 (0.0)	1.1 (0.0)	1.5 (0.0)	1.7 (0.0)	1.8 (0.0)	1.8 (0.0)	1.9 (0.0)
5-methylheptan-3-one	458.6	2.15	3.2 (0.3)	4.4 (0.2)	4.6 (0.1)	4.3 (0.1)	3.8 (0.1)	3.5 (0.2)	3.1 (0.2)	2.8 (0.2)
delphone	17.6	3.02	2.8 (0.0)	10.2 (0.0)	16.2 (0.0)	19.0 (0.0)	19.7 (0.0)	19.9 (0.0)	19.7 (0.0)	19.4 (0.0)
13a (equilibrated, humidity of air at *ca.* 75%)[d]) with										
furfural	309.3	0.83	9.2 (2.0)	13.6 (4.0)	21.8 (5.6)	19.2 (4.4)	18.8 (5.4)	17.8 (4.1)	15.5 (3.3)	13.1 (2.5)
undec-10-enal	8.7	4.12	10.6 (1.4)	11.7 (2.6)	13.4 (3.2)	15.0 (3.6)	15.3 (3.9)	16.0 (3.2)	16.0 (3.5)	16.4 (3.5)
citronellal	37.3	3.53	2.6 (0.0)	3.2 (0.0)	4.0 (0.0)	4.2 (0.0)	4.8 (0.0)	4.1 (0.0)	3.9 (0.0)	4.3 (0.0)
benzaldehyde	134.6	1.71	47.0 (7.4)	54.7 (7.9)	66.4 (9.4)	60.7 (9.0)	59.7 (10.0)	58.1 (9.3)	54.2 (9.9)	51.8 (9.8)
4-methylacetophenone	11.3	2.10	23.2 (0.0)	42.6 (0.5)	55.0 (0.0)	61.5 (0.7)	64.4 (0.8)	66.8 (0.0)	64.9 (0.0)	63.2 (0.0)
delphone	17.6	3.02	45.6 (0.0)	67.1 (0.0)	75.3 (0.0)	74.6 (0.0)	73.7 (0.0)	71.0 (0.0)	66.9 (0.0)	63.0 (0.0)
13a (equilibrated, humidity of air at *ca.* 33%)[d]) with										
furfural	309.3	0.83	8.3 (3.7)	14.7 (7.0)	20.9 (7.0)	20.4 (7.2)	18.7 (4.4)	19.0 (3.5)	17.7 (2.3)	17.2 (3.6)
undec-10-enal	8.7	4.12	11.6 (2.8)	13.9 (5.3)	14.8 (7.0)	17.6 (8.1)	15.7 (8.4)	17.0 (1.0)	17.0 (7.9)	17.3 (8.4)
citronellal	37.3	3.53	2.5 (0.0)	3.2 (0.0)	3.6 (0.0)	4.6 (0.0)	4.1 (0.0)	4.0 (0.0)	4.3 (0.0)	5.1 (0.0)
benzaldehyde	134.6	1.71	33.8 (3.8)	46.8 (5.9)	54.6 (5.0)	53.9 (5.2)	53.0 (8.1)	52.4 (7.6)	51.5 (7.8)	50.3 (6.5)
4-methylacetophenone	11.3	2.10	15.3 (1.2)	32.7 (1.3)	43.2 (0.0)	49.4 (0.0)	52.5 (0.0)	54.8 (0.0)	59.0 (0.0)	59.8 (0.0)
delphone	17.6	3.02	32.9 (0.0)	64.6 (0.0)	72.5 (0.0)	73.7 (0.0)	71.1 (0.0)	67.8 (0.0)	67.0 (0.0)	64.2 (0.0)

Table 4 (cont.)

Hydrazide or Hydrazone/volatile	Vapor pressure [Pa][a])	log $P_{o/w}$[a])	Time-dependent headspace concentrations of the released volatiles compared to the reference sample (in parentheses) [ng l^{-1} air] on dry cotton							
			30 min	90 min	150 min	210 min	270 min	330 min	390 min	450 min
15a[e]) with										
4-ethylbenzaldehyde	16.6	2.75	0.3 (0.0)	0.8 (0.0)	0.9 (0.0)	0.9 (0.0)	1.0 (0.0)	1.1 (0.0)	0.9 (0.0)	1.0 (0.0)
Triplal®	46.9	2.85	20.2 (27.8)	24.2 (22.2)	22.7 (16.8)	19.4 (13.2)	16.6 (12.1)	17.6 (11.8)	14.8 (10.4)	15.5 (9.9)
5-methylheptan-3-one	458.6	2.15	4.3 (1.3)	6.2 (3.0)	6.1 (3.4)	4.6 (1.0)	4.4 (0.8)	4.5 (0.7)	4.0 (0.6)	3.9 (0.6)
(+)-carvone	17.3	3.07	0.1 (0.0)	0.3 (0.0)	0.5 (0.0)	0.5 (0.0)	0.5 (0.0)	0.6 (0.0)	0.5 (0.0)	0.6 (0.0)
2-methyldecanal	14.5	4.18	3.8 (0.4)	7.1 (0.9)	8.8 (1.6)	8.9 (1.5)	8.1 (1.4)	9.4 (1.2)	8.2 (1.1)	9.2 (1.0)
methoxymelonal	37.2	2.32	1.3 (0.0)	4.0 (0.5)	5.6 (1.1)	5.8 (1.5)	5.9 (1.7)	6.7 (1.4)	6.4 (1.5)	7.0 (1.2)
2b/benzaldehyde[f])	134.6	1.71	2.8 (0.1)	4.0 (0.6)	4.7 (0.2)	5.4 (0.2)	5.9 (0.5)	6.7 (0.5)	5.4 (0.6)	4.6 (0.5)
3c/acetophenone[f])	43.5	1.67	1.7 (0.3)	5.2 (0.5)	5.6 (0.4)	5.4 (0.4)	5.4 (0.3)	5.5 (0.4)	5.3 (0.3)	5.0 (0.4)
6c/citronellal[f])	37.3	3.53	5.3 (0.2)	11.8 (0.3)	14.3 (0.3)	17.0 (0.2)	17.3 (0.2)	17.0 (0.2)	17.3 (0.1)	16.3 (0.1)
7c/undec-10-enal[f])	8.7	4.12	2.2 (0.8)	5.0 (3.2)	5.6 (5.9)	7.2 (6.2)	7.9 (5.7)	7.8 (5.3)	8.3 (4.5)	8.4 (3.8)
7d/*Trifernal*®[f])	11.4	2.45	2.2 (1.0)	3.3 (1.2)	3.7 (1.6)	4.8 (1.7)	5.2 (1.4)	5.0 (1.4)	5.5 (1.2)	5.5 (1.2)
10c/4-phenylbutan-2-one[f])	8.7	1.96	1.8 (0.1)	10.3 (0.4)	14.8 (0.7)	15.7 (0.8)	16.0 (0.7)	16.0 (0.6)	15.9 (0.5)	15.0 (0.5)

[a]) Values calculated with the EPIwin v 3.10 program (*US Environmental Protection Agency*, 2000). [b]) Average values of two measurements, see *Fig. 5*. [c]) Average values of three measurements, see *Fig. 6*. [d]) Data from a single measurement, see *Fig. 7*. [e]) Data from a single measurement, see *Fig. 8*. [f]) Data from a single measurement, see *Fig. 9*.

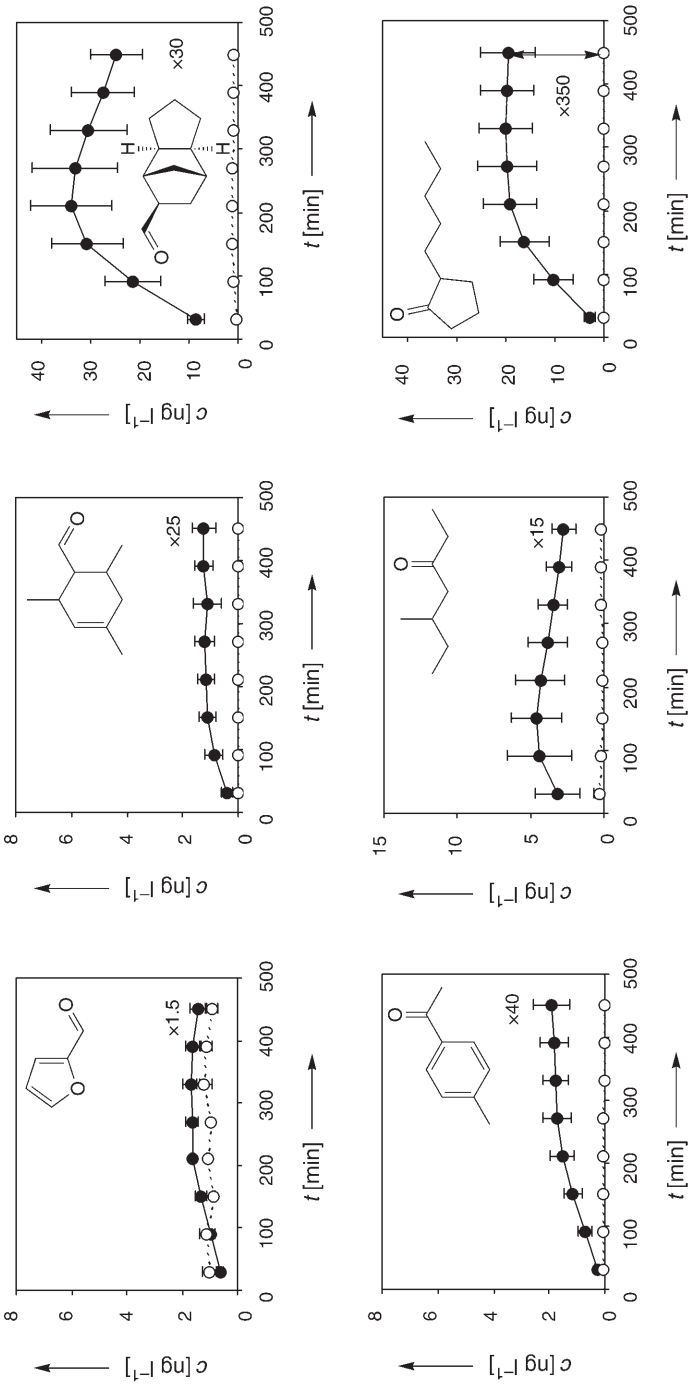


Fig. 6. *Headspace concentrations measured on dry cotton for the evaporation of an equilibrated dynamic mixture of fragrance aldehydes and ketones in the presence (—●—) or absence (---○---) of dihydrazide* **10a**

headspace concentrations, which are due to a certain inherent imprecision of the method (typically *ca.* 5–10%).

Our measurements show that the release of the volatiles is particularly efficient for fragrances with high vapor pressures (typically above 5.0 Pa), although this relationship is not linear [13][14]. Other parameters such as the water solubility of the fragrance molecule, expressed by the octanol/water partition coefficient (log $P_{o/w}$) [49], and the efficiency of surface deposition of the respective volatiles seem to play an important role [47]. For example, furfural has with 309.3 Pa a relatively high vapor pressure but is, with a log $P_{o/w}$ value of 0.83, also the most H_2O-soluble compound of the series (*Table 4*). It is therefore expected that a considerable amount of furfural remains dissolved in the aqueous emulsion and thus reduces its efficiency of release into the gas phase.

Interestingly, the headspace concentrations of the aldehydes and ketones measured on dry fabric in the presence of the hydrazine were found to increase at the beginning of the experiment, and to reach a constant value after 150–300 min (*Figs. 5* and *6*). In some cases, the headspace concentrations decreased again after passing through a maximum. As this initial increase in concentration could be a result of the air humidity which wets the dry fabric and triggers the fragrance release by hydrolysis of the hydrazones, we studied the influence of ambient humidity on fragrance release. The experiment carried out with a mixture of fragrance aldehydes and ketones in the presence of **13a** was thus repeated by replacing the saturated NaCl solution (which was used to obtain a constant air humidity of *ca.* 75%) by a saturated $MgCl_2$ solution, resulting in a lower humidity of *ca.* 33% [48]. *Table 4* and *Fig. 7* display the headspace concentrations measured for a mixture of furfural, undec-10-enal, (+)-3,7-dimethyloct-6-enal (=citronellal), benzaldehyde, 4-methylacetophenone, and delphone in the presence of **13a** on dry fabric exposed to these different air humidities. The data (single measurement) represented with solid lines correspond to the higher humidity (*ca.* 75%), those drawn with dashed lines to the lower humidity (*ca.* 33%). The results were found to be quite reproducible; repetition of the two measurements confirmed the headspace concentrations depicted in *Fig. 7* (error bars not shown), and only for the release of delphone, we observed a quite large deviation of the two curves (data not shown).

The headspace concentrations depicted in *Fig. 7* clearly show that the air humidity does not significantly influence the fragrance release. This is very important for the practical application of the present delivery systems since it indicates that even a low ambient humidity is sufficient to trigger the desired fragrance release, or that there is at least enough residual H_2O on dry cotton to allow the re-equilibration of the system. The observed increase in headspace concentration at the beginning of the experiment thus seems to be a general effect due to the equilibration of the headspace cell, and is not an effect of the air humidity.

The hydrazine derivatives, as well as the aldehydes or ketones to be released, cover a wide range of structures. *Fig. 8* and *Table 4* shows the headspace concentrations obtained for a mixture of 4-ethylbenzaldehyde, 2,4-dimethylcyclohex-3-ene-1-carboxaldehyde (= *Triplal*®) (mixture of stereoisomers), (±)-5-methylheptan-3-one, and some sterically hindered α-substituted aldehydes and ketones such as (+)-(*S*)-*p*-mentha-1(6),8-dien-2-one (=(+)-carvone), (±)-2-methyldecanal, and (±)-6-methoxy-2,6-dimethylheptanal (=methoxymelonal) in the presence or absence of polyhydrazide

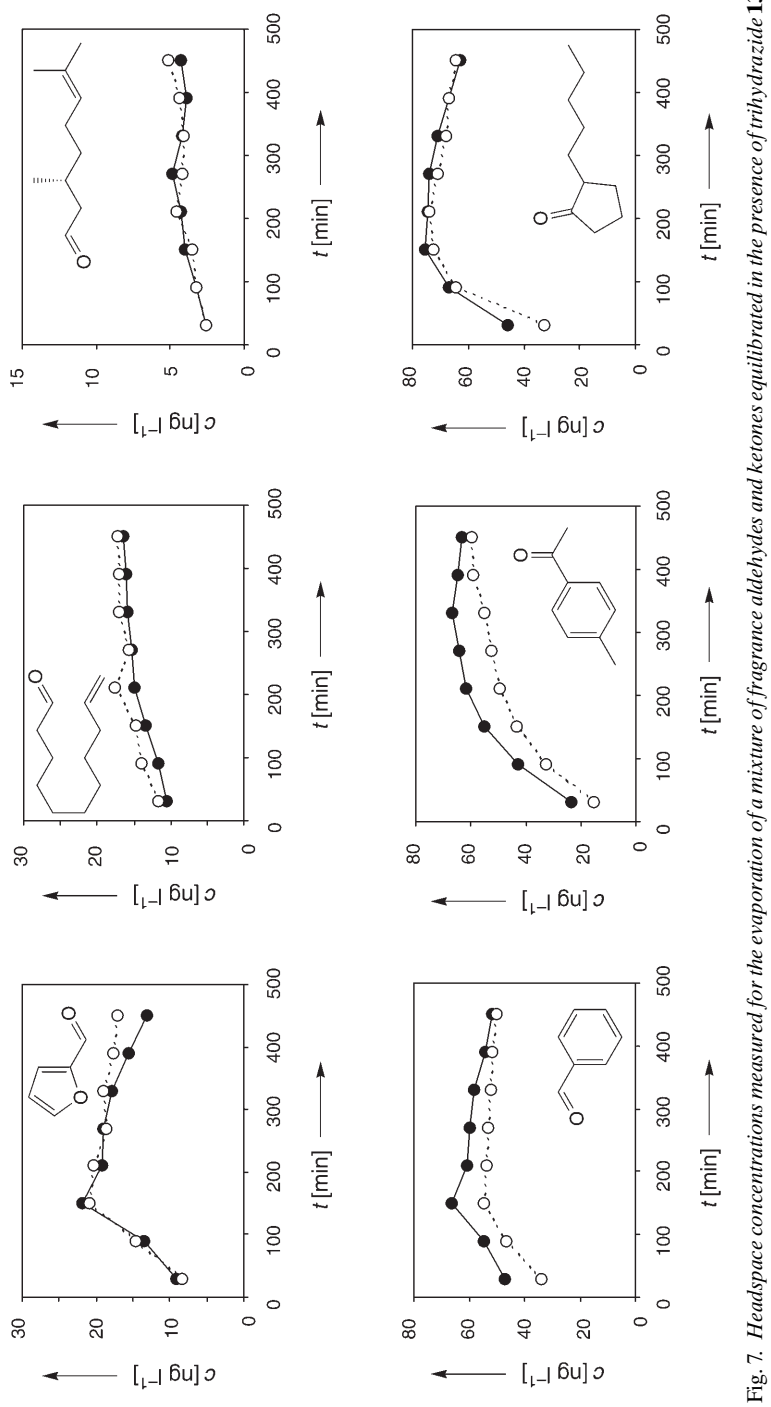


Fig. 7. *Headspace concentrations measured for the evaporation of a mixture of fragrance aldehydes and ketones equilibrated in the presence of trihydrazide* **13a** *and exposed to* ca. *75% (—●—) or* ca. *33% (---○---) of humidity*

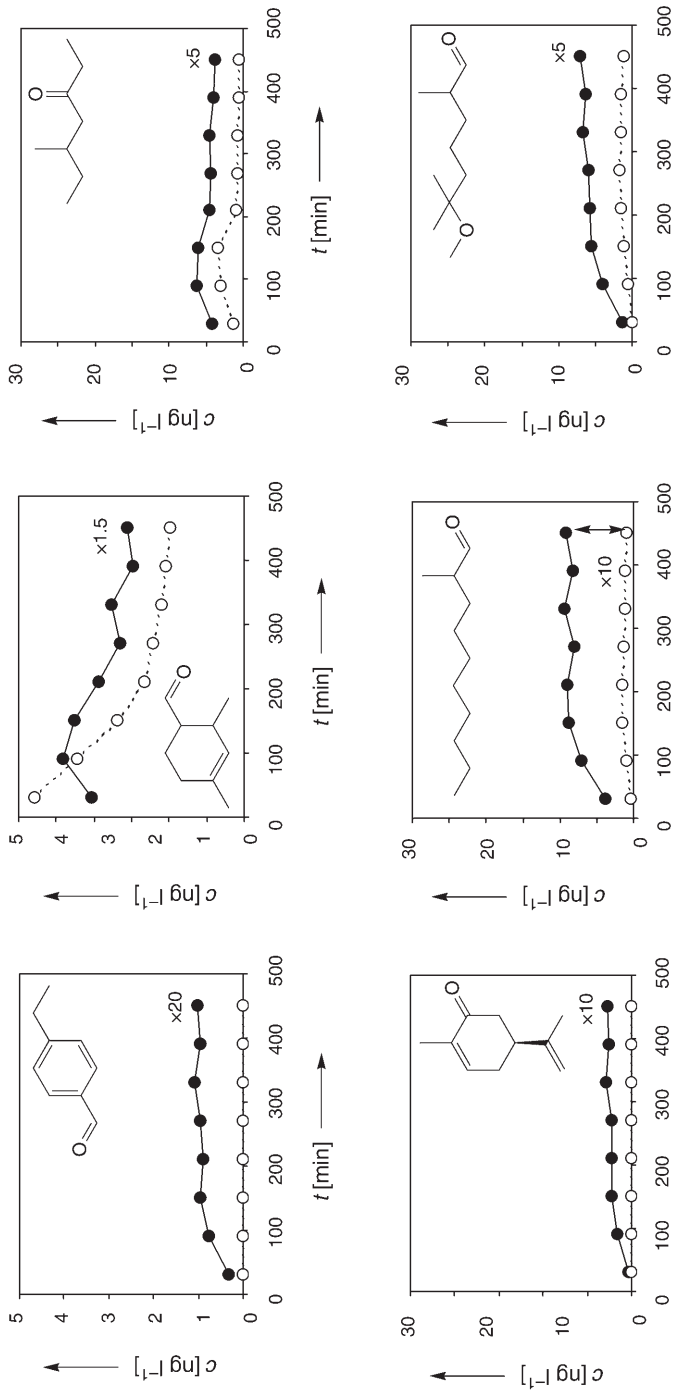


Fig. 8. *Headspace concentrations measured on dry cotton for the evaporation of an equilibrated dynamic mixture of fragrance aldehydes and ketones in the presence (—●—) or absence (- - -○- - -) of polymer* **15a**

15a. As was observed for the release of monomeric hydrazides **10a**, **12a**, and **13a** described above, the headspace concentrations of all six fragrance aldehydes and ketones in the mixture were considerably higher in the presence of **15a** than in its absence. However, the total difference is less pronounced in the sample with the polyhydrazide (where the headspace concentrations increased by a factor of 1.5 to 20, *Fig. 8*) as compared to those where a monomeric hydrazide was used (and an increase between 1.5 and 350 times was observed for example in the presence of **10a**, *Fig. 6*). This less pronounced difference may be attributed to the comparable log $P_{o/w}$ of the more hydrophobic six fragrance molecules released in the presence of **15a** (all values are comprised between *ca.* 2 and 4, *Table 4*) as well as to a stabilizing effect of the hydrazone profragrance unit within the polymer backbone. This stabilizing effect decreases the efficiency of the fragrance release and was previously observed for other types of polymeric profragrance-delivery systems [2][6][50].

As discussed above, dynamic mixtures can also be generated by equilibrating the corresponding hydrazones in an acidic aqueous environment as shown in the following experiment. An equimolar mixture of hydrazones **2b**, **3c**, **6c**, **7c**, **7d**, and **10c**, releasing benzaldehyde, acetophenone, citronellal, undec-10-enal, (±)-3-phenylbutanal (= *Trifernal*®), and 4-phenylbutan-2-one, respectively, was equilibrated in the TEA-esterquat emulsion as described above, and compared to the corresponding amount of aldehyde and ketone as the reference (*Fig. 9* and *Table 4*). The data show that significantly higher headspace concentrations of the corresponding volatiles were obtained in the sample of the hydrazones in comparison to the reference. This was even the case for hydrazone **2b**, which was found to hydrolyze so slowly that, as described above, the corresponding rate constants in buffered solution could not be determined accurately.

3. Conclusions. – Our results show that delivery systems generated by reversible covalent-bond formation between aldehydes and ketones with hydrazine derivatives are very efficient for controlling the release of volatile carbonyl compounds in various practical applications in perfumery. Hydrazine derivatives are commercially available or can easily be prepared from methyl or ethyl esters by reaction with hydrazine hydrate. The corresponding hydrazones are obtained by heating the hydrazine derivatives with aldehydes or ketones in various solvents. The hydrazones are generally isolated with an (*E*) configuration at the imine double bond (NHN=C) and, in the case of aliphatic acylhydrazones $R'CO-NH-N=CR^1R^2$ (R' = alkyl), with a *syn* and *anti* conformation with respect to the amide bond (CO–NHN). The ratio of the two conformers is solvent-dependent, and the *anti* isomer is usually the predominant form in DMSO. Variable-temperature ^{1}H-NMR measurements showed that the average free-energy barrier for the amide-bond rotation of aliphatic acylhydrazones is *ca.* 78 kJ/mol.

In the presence of H_2O, hydrazone formation is reversible, reaching an equilibrium consisting of a dynamic mixture between the hydrazine derivative, the carbonyl compound, and the corresponding hydrazone. Kinetic measurements carried out by UV/VIS spectroscopy for the reaction of benzaldehyde with different hydrazine derivatives, *i.e.*, with **3a**–**12a**, and the hydrolysis of the corresponding hydrazones showed that, within experimental error, the same equilibrium is reached. The measured rate constants are strongly pH-dependent and increase with decreasing pH. The

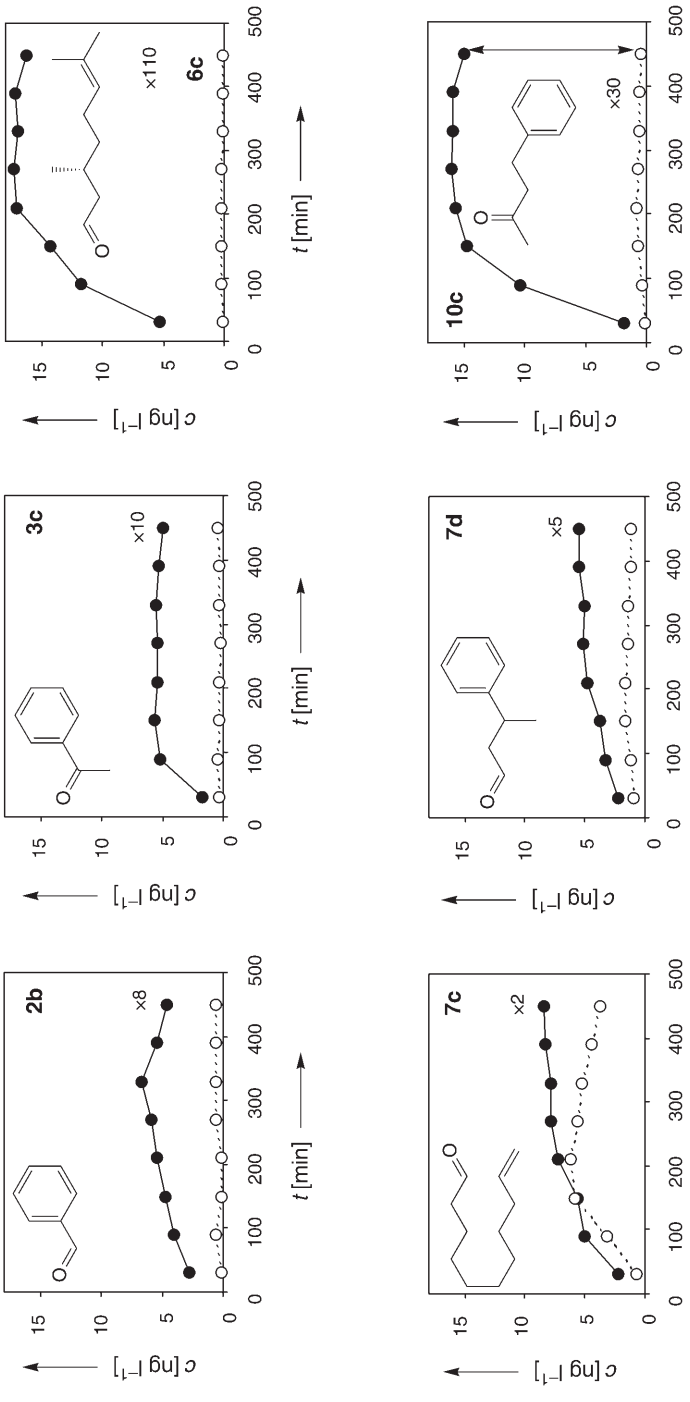


Fig. 9. *Headspace concentrations measured on dry cotton for the evaporation of a mixture of fragrance aldehydes and ketones from an equilibrated dynamic mixture of precursors* **2b**, **3c**, **6c**, **7c**, **7d**, *and* **10c** (—●—) *with respect to the corresponding mixture of aldehydes and ketones as reference sample* (- - -○- - -)

hydrolysis of the hydrazones is slower than their formation, and this difference is less pronounced at lower pH. The influence of the hydrazine structures on the rate constants for the equilibrium formation is less pronounced than the effect of the pH, and the equilibration between hydrazine derivatives and ketones is almost completely on the side of the unreacted compounds. Increasing the concentration of the carbonyl compound with respect to the amount of the hydrazine results in a constant increase of the rate constants, and the presence of surfactants reduces the rate of equilibration.

The full reversibility of the hydrazone formation allows the preparation of dynamic mixtures by simple addition of a hydrazine derivative to one or several carbonyl compounds. The state of the equilibrium is dependent only on external conditions such as temperature, concentration, or pH. The dynamic mixtures are deposited as such on the target surface, and the evaporation of the volatile aldehydes and ketones shifts the equilibrium towards the free hydrazine, thus resulting in an increased long-lastingness of fragrance perception. Dynamic headspace analysis, after deposition of the dynamic mixtures together with a cationic surfactant on cotton, showed that the presence of a hydrazine derivative considerably increases the headspace concentrations of the different carbonyl compounds in the mixture with respect to the reference sample without hydrazine. The set-up of the dynamic mixture in a fabric-softener product application requires a certain equilibration time. Nonequilibrated mixtures do not have the desired effect, although in practical applications the time of product storage is sufficient to equilibrate dynamic mixtures. The release of the volatiles is very efficient for fragrances with high vapor pressures and low water solubility. Furthermore, a particular long-lasting effect is generally obtained for the release of ketones, although the equilibrium between hydrazine derivatives and ketones is mostly on the side of the unreacted compounds. The fact that all carbonyl compounds in a mixture are affected by the presence of a hydrazine derivative makes dynamic mixtures particularly powerful for the controlled release of fragrances.

The simultaneous modulation of the evaporation properties of several different molecules positions the effect of dynamic mixtures based on reversible covalent-bond formation between encapsulating systems (where different chemical functionalities are physically retained) and classical profragrances (where usually one compound is released by covalent-bond cleavage). The ease of generation of dynamic mixtures (by adding one ingredient to a mixture of active compounds) combined with the high efficiency for the release of these compounds makes these systems particularly interesting for practical applications, and will certainly generate further research activity on this topic. Besides its impact for the flavor and fragrance industry, we expect that the concept of reversible covalent bond-formation will also influence the development of delivery systems in other areas such as the pharmaceutical or agrochemical industry.

We thank Dr. *Olivier Haefliger* for measuring ESI-mass spectra, *Maude Gaillard* and *Romain Bieri* for their assistance in the synthesis of hydrazones and the determination of kinetic rate constants, *Walter Thommen* and Dr. *Horst Sommer* for NMR measurements, Dr. *Jean-Yves de Saint Laumer* for calculating vapor pressures and log $P_{o/w}$ values, as well as Dr. *Roger Snowden* for constructive comments on the manuscript. We are grateful to Prof. *James H. Davis Jr.* for communicating to us the cited hydrazone crystal structure prior to publication.

Experimental Part

General. Commercially available reagents and solvents were used without further purification if not stated otherwise. Reactions were carried out in standard glassware under N_2 or Ar, and yields are not optimized. Demineralized H_2O was obtained from a *Millipore-Synergy-185* water purifier. Dynamic headspace measurements: *Perkin-Elmer TurboMatrix-ATD* desorber coupled to a *Carlo-Erba MFC-500* gas chromatograph; *J&W Scientific DB1* capillary column (30 m, i.d. 0.45 mm, film 0.42 μm); FID detector; two-step temp. gradient starting from 70° to 130° at 3°/min and then going to 260° at 25°/min; injection temp. 240°, detector temp. 260°. M.p.: *Büchi B540* melting-point instrument; heating rate 1°/min; uncorrected. UV/VIS Spectra: *Perkin-Elmer Lambda-14* or *Lambda-35* spectrometer; λ in nm (ε). IR Spectra: *Perkin-Elmer 1600 FTIR* or *Spectrum-One* instrument, $\tilde{\nu}$ in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Bruker 400-MHz-DPX* or *500-MHz-Avance* spectrometer; at 25°; δ in ppm downfield from Me_4Si as internal standard, J in Hz; standard pulse sequences and parameters for 1D spectra and for 2D, gradient-selected COSY, NOESY, ^1H,^{13}C-HSQC, and ^1H,^{13}C-HMBC experiments; variable-temperature measurements at 500 MHz, with a sample of ethylene glycol for external calibration of the temp. GC/EI-MS: *Hewlett-Packard HP-5890* or *-6890* GC system equipped with a *Supelco SPB-1* capillary column (30 m, 0.25 mm i.d.); at 70° for 10 min, then to 260° (10°/min); He flow *ca.* 1 ml/min; system coupled with a *HP-MSD-5972* or *-5973* quadrupole mass spectrometer; electron energy *ca.* 70 eV; in m/z (rel. int. in % of the base peak). LC/ESI-MS: *Agilent 1100* LC/MS system equipped with a *Waters Nova-Pak C18* (60 Å, 4 μ; 2.1 × 150 mm i.d.) or a *Macherey-Nagel Nucleosil-C2* (2.0 × 250 mm i.d.) column; 0.5 ml/min of a gradient H_2O/MeCN (both containing 0.1% of formic acid); system coupled to a *G1946D* mass spectrometer; ionization source with the following parameters: drying-gas flow 12 l/min, nebulizer pressure 40 psig, drying-gas temp. 350°, capillary voltage 4000 V (pos.); for direct infusion (200 μl/min), drying-gas flow 10 l/min, nebulizer pressure 20 psig; in m/z (rel. int. in % of the base peak). APCI-MS = Atmospheric-pressure chemical-ionization MS.

2-Hydroxypropane-1,2,3-tricarboxylic Acid 1,2,3-Trihydrazide (**13a**) [19]. A mixture of trimethyl 2-hydroxypropane-1,2,3-tricarboxylate (citric acid trimethyl ester; 1.00 g, 4.3 mmol) and hydrazine hydrate (51% in H_2O; 1 ml (= 1.07 g), 17.1 mmol, 4 equiv.) in EtOH (20 ml) was heated under reflux overnight (→ white precipitate after a few minutes). After cooling to r.t., the mixture was filtered and the residue dried under vacuum: 0.85 g (85%) of **13a**. White solid. M.p. 160.2–162.0°. UV/VIS (H_2O): 283 (sh, 500). IR (neat): 3352*m*, 3315*w*, 3283*m*, 3219*m*, 3076*m*, 2938*w*, 2868*w*, 1653*s*, 1638*m*, 1590*s*, 1522*s*, 1474*m*, 1442*m*, 1419*m*, 1374*m*, 1310*m*, 1273*m*, 1243*m*, 1214*m*, 1144*m*, 1098*s*, 1031*s*, 986*s*, 947*m*, 916*m*, 861*w*, 814*m*, 790*m*, 759*m*, 735*m*, 670*s*. ^1H-NMR (400 MHz, (D_6)DMSO): 9.09 (br. *s*, 2 H); 8.90 (br. *s*, 1 H); 6.15 (br. *s*, 1 H); 4.21 (br. *s*, 6 H); 2.47 (*AB*, J = 14.3, 5.1, 4 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 172.38 (*s*); 168.93 (*s*); 74.50 (*s*); 40.64 (*t*). ESI-MS: 492 (6), 491 (35, $[2M + Na]^+$), 470 (8), 469 (47, $[2M + H]^+$), 257 (6, $[M + Na]^+$), 236 (10), 235 (100, $[M + H]^+$), 64 (7), 59 (3).

*(+)-(2*R*,3*R*)-2,3-Bis(dodecyloxy)-*N*^{1},*N*^{1},*N*^{4},*N*^{4}-tetramethylbutanediamide.* NaH (3.60 g, 60% suspension; 90.0 mmol) was washed with pentane (3 ×) before DMF (150 ml) and (+)-(2*R*,3*R*)-2,3-dihydroxy-*N*^{1},*N*^{1},*N*^{4},*N*^{4}-tetramethylbutanediamide (9.2 g, 45.0 mmol) were added (→ thicker suspension and generation of H_2). The mixture was stirred at r.t. for 90 min, then a soln. of 1-iodododecane (28.0 g, 94.5 mmol, 2.1 equiv.) in DMF (50 ml) was added. The mixture was stirred for another 2 h at r.t. and then heated at 80° overnight. After cooling to r.t., the mixture was extracted with Et_2O (4 ×), the extract washed with H_2O (2 ×), dried (Na_2SO_4), and concentrated. Column chromatography (SiO_2, CH_2Cl_2/acetone 3:1) gave 5.93 g (28%) of a pale-yellow solid. $[\alpha]_D = +49.9$ ($c = 0.07$, $CHCl_3$). IR (neat): 2954*w*, 2916*s*, 2871*w*, 2848*s*, 1637*s*, 1504*m*, 1467*m*, 1417*m*, 1396*m*, 1388*m*, 1344*w*, 1298*w*, 1254*m*, 1206*w*, 1119*s*, 1094*s*, 1076*s*, 1051*m*, 1001*w*, 972*w*, 953*w*, 912*w*, 890*w*, 864*w*, 849*m*, 720*m*. ^1H-NMR (400 MHz, $CDCl_3$): 4.69 (*s*, 2 H); 3.61–3.48 (*m*, 4 H); 3.17 (*s*, 6 H); 2.92 (*s*, 6 H); 1.63–1.51 (*m*, 4 H); 1.37–1.19 (*m*, 36 H); 0.88 (*t*, J = 6.9, 6 H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 169.87 (*s*); 77.27 (*d*); 69.88 (*t*); 37.25 (*q*); 35.79 (*q*); 31.94 (*t*); 30.04 (*t*); 29.71 (*t*); 29.67 (*t*, 3 ×); 29.50 (*t*); 29.38 (*t*); 26.12 (*t*); 22.70 (*t*); 14.13 (*q*). ESI-MS: 543 (7), 542 (37), 541 (100, $[M + H]^+$), 50 (6).

*(+)-(2*R*,3*R*)-2,3-Bis(dodecyloxy)butanedioic Acid.* A suspension of (+)-(2*R*,3*R*)-2,3-bis(dodecyloxy)-*N*^{1},*N*^{1},*N*^{4},*N*^{4}-tetramethylbutanediamide (6.63 g, 12.3 mmol), 36% HCl soln. (110 ml) and H_2O (55 ml) was heated under reflux for 4 d. After cooling to r.t., the mixture was extracted with CH_2Cl_2

(3×), dried (Na_2SO_4), and concentrated: 6.03 g (quant.) of the butanedioic acid. $[\alpha]_D = +20.6$ ($c = 0.08$, $CHCl_3$). IR (neat): 3298*w* (br.), 3115*w* (br.), 3044*w* (br.), 2955*m*, 2917*s*, 2871*w*, 2850*m*, 2627*w* (br.), 1747*s*, 1467*m*, 1425*w*, 1379*w*, 1325*m*, 1304*m*, 1259*m*, 1198*m*, 1136*m*, 1119*m*, 1103*s*, 1090*s*, 1032*m*, 1015*m*, 913*w*, 893*w*, 876*w*, 832*m*, 809*w*, 788*m*, 733*m*, 720*m*, 670*m*, 611*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.39 (*s*, 2 H); 3.82–3.65 (*m*, 2 H); 3.56–3.40 (*m*, 2 H); 1.67–1.52 (*m*, 4 H); 1.37–1.19 (*m*, 36 H); 0.88 (*t*, $J = 6.9$, 6 H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 172.81 (*s*); 79.45 (*d*); 73.49 (*t*); 31.94 (*t*); 29.67 (*t*, 2×); 29.62 (*t*); 29.54 (*t*); 29.37 (*t*); 29.33 (*t*, 2×); 25.76 (*t*); 22.70 (*t*); 14.12 (*q*). ESI-MS: 516 (11), 515 (34), 487 (6), 486 (31, M^-), 485 (100, $[M-1]^-$).

*(+)-Dimethyl (2*R*,3*R*)-2,3-Bis(dodecyloxy)butanedioate.* Conc. sulfuric acid (55 drops = *ca.* 1 ml) was added to a soln. of (2*R*,3*R*)-2,3-bis(dodecyloxy)butanedioic acid (4.18 g, 8.6 mmol) in MeOH (275 ml). The mixture was heated under reflux overnight. After cooling to r.t., the mixture was concentrated and then added to H_2O (700 ml) at 0°. The precipitate was filtered off: 3.98 g (90%) of a white solid. M.p. 40.0–40.9°. $[\alpha]_D = +32.9$ ($c = 0.08$, $CHCl_3$). IR (neat): 3001*w*, 2970*w*, 2912*s*, 2867*w*, 2847*s*, 1745*s*, 1709*w*, 1471*m*, 1431*m*, 1397*w*, 1385*w*, 1361*w*, 1349*w*, 1278*m*, 1219*s*, 1183*m*, 1167*s*, 1151*m*, 1108*s*, 1066*w*, 1043*m*, 1026*m*, 999*m*, 947*w*, 938*m*, 895*w*, 874*w*, 838*w*, 821*w*, 760*w*, 715*m*, 707*m*, 664*w*. ^{1}H-NMR (400 MHz, $CDCl_3$): 4.31 (*s*, 2 H); 3.81–3.74 (*m*, 2 H); 3.77 (*s*, 6 H); 3.33–3.25 (*m*, 2 H); 1.64–1.45 (*m*, 4 H); 1.37–1.16 (*m*, 36 H); 0.88 (*t*, $J = 6.9$, 6 H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 170.12 (*s*); 80.13 (*d*); 72.47 (*t*); 52.04 (*q*); 31.94 (*t*); 29.68 (*t*); 29.65 (*t*, 3×); 29.41 (*t*, 2×); 29.37 (*t*); 25.92 (*t*); 22.71 (*t*); 14.12 (*q*). ESI-MS: 741 (3), 740 (10), 739 (20), 661 (3), 615 (3), 614 (8), 575 (7), 574 (19), 561 (3), 560 (9), 542 (6), 541 (18), 538 (8), 537 (22), 533 (3), 532 (8), 517 (6), 516 (32), 515 (100, $[M + H]^+$), 449 (4), 64 (4).

*(+)-(2*R*,3*R*)-2,3-Bis(dodecyloxy)butanedioic Acid 1,4-Dihydrazide* (**14a**). As described for **13a**, with (+)-dimethyl (2*R*,3*R*)-2,3-bis(dodecyloxy)butanedioate (5.00 g, 9.7 mmol), hydrazine hydrate (51% in H_2O; 2.37 ml (= 2.44 g), 38.9 mmol) and EtOH (650 ml): 2.76 g (55%) of **14a**. White solid. M.p. 113.1–117.8°. $[\alpha]_D = +43.3$ ($c = 0.08$, $CHCl_3$). IR (neat): 3271*m*, 3214*w*, 3178*w*, 3062*w*, 2954*w*, 2914*s*, 2871*w*, 2849*s*, 1748*w*, 1687*m*, 1663*s*, 1640*m*, 1533*m*, 1468*m*, 1432*w*, 1414*w*, 1376*w*, 1333*w*, 1294*w*, 1280*w*, 1261*w*, 1222*w*, 1154*w*, 1118*s*, 1102*s*, 1095*w*, 1042*w*, 1028*w*, 1013*w*, 992*m*, 980*m*, 961*w*, 907*w*, 890*w*, 858*w*, 795*m*, 783*w*, 764*w*, 718*m*, 674*m*, 655*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 7.82 (*s*, 2 H); 4.34 (*s*, 2 H); 3.87 (br. *s*, 4 H); 3.57–3.48 (*m*, 2 H); 3.47–3.37 (*m*, 2 H); 1.62–1.45 (*m*, 4 H); 1.37–1.18 (*m*, 36 H); 0.88 (*t*, $J = 6.9$, 6 H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 170.22 (*s*); 80.70 (*d*); 73.51 (*t*); 31.93 (*t*); 29.66 (*t*, 4×); 29.59 (*t*); 29.37 (*t*, 2×); 25.93 (*t*); 22.70 (*t*); 14.13 (*q*). ESI-MS: 537 (5), 517 (6), 515 (32, $[M+2]^+$), 515 (100, $[M+1]^+$).

(±)-Poly(prop-2-enoic Acid Hydrazide) (**15a**). Commercially available poly(methyl prop-2-enoate) in toluene (M_w 30700, M_n 10600) was concentrated. Hydrazine hydrate (51% in H_2O; 68 ml (= 69.90 g), 1112.4 mmol, 13.7 equiv.) was added to 7.00 g (81.3 mmol) of the polymer, and the mixture was heated at 80° for 5 h. After cooling to r.t., the mixture was poured into MeOH (700 ml) and the white precipitate filtered. The solid was suspended in CH_2Cl_2 (1×) and Et_2O (2×) (under sonication) to remove remaining MeOH: 3.52 g (50%) of **15a**. White solid. IR (neat): 3259*m* (br.), 3052*m*, 2931*m*, 2162*w*, 1980*w*, 1614*s* (br.), 1531*s*, 1447*m*, 1385*m*, 1336*w*, 1297*m*, 1266*w*, 1178*w*, 1125*w*, 983*s* (br.), 882*w*, 610*s* (br.). ^{1}H-NMR (400 MHz, D_2O): 2.5–1.0 (*m*, 3 H). ^{13}C-NMR (100.6 MHz, D_2O): 177.84 (*s*); 43.42 (*d*); 37.38 (br. *t*).

α-D-Galactopyranuronic Acid Hydrazide (1→4)-Homopolymer (=(1→4)-α-D-Galactopyranuronan Hydrazide; **16a**). Pectin (from apples; 20.00 g) was suspended in H_2O (250 ml) and stirred mechanically for 1 h, before hydrazine hydrate (51% in H_2O; 17.6 ml (= 18.09 g)) was added during 5 min (→ dark brown). The mixture was stirred at r.t. for 3 h, then at 30° for another 140 h (6 d). The crude product was washed with toluene. After decantation of the toluene, the remaining product was dried under reduced pressure and lyophilized overnight: 21.5 g of **16a**. Grey solid. IR (neat): 3274*m* (br.), 3199*m* (br.), 2926*m* (br.), 1594*m* (br.), 1529*m*, 1406*m* (br.), 1329*m* (br.), 1236*w* (br.), 1138*m*, 1095*s*, 1073*s*, 1008*s*, 950*s*, 886*m*, 849*w*, 831*m*, 760*m*, 629*s*, 616*w*.

*4-[(2*E*)-2-(Phenylmethylene)hydrazinyl]benzoic Acid* (**2b**). A mixture of **2a** (3.00 g, 19.7 mmol) and benzaldehyde (3.14 g, 29.6 mmol, 1.5 equiv.) in EtOH (50 ml) was heated under reflux for 3 h. After cooling to r.t., the mixture was filtered, and the residue washed with EtOH and dried at 0.21 mbar: 2.14 g (45%) of **2b**. Pale-yellow solid. M.p. 231.5–232.8°. UV/VIS (EtOH): 365 (sh, 41400), 353 (47800), 308 (sh, 13100), 297 (sh, 11200), 278 (8500), 236 (18700), 229 (sh, 16400), 203 (sh, 29500), 201 (31600). IR (neat): 3318*m*, 3052*w*, 3028*w*, 2969*m*, 2953*m*, 2878*m*, 2819*m*, 2713*w*, 2646*m*, 2537*m* (br.), 2301*w*, 1867*w*,

1804*w*, 1743*w*, 1664*s*, 1603*s*, 1595*s*, 1571*m*, 1528*s*, 1495*m*, 1426*s*, 1414*m*, 1361*m*, 1312*s*, 1288*s*, 1266*s*, 1164*s*, 1130*s*, 1122*s*, 1097*s*, 1068*m*, 1029*w*, 1007*w*, 978*w*, 945*m*, 928*s*, 842*s*, 783*w*, 769*s*, 750*s*, 689*s*, 664*m*, 651*m*, 625*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 12.31 (br. *s*, 1 H); 10.82 (*s*, 1 H); 7.96 (*s*, 1 H); 7.83 (*d*, *J* = 8.7, 2 H); 7.70 (*d*, *J* = 7.7, 2 H); 7.41 (*t*, *J* = 7.7, 2 H); 7.34 (*t*, *J* = 7.4, 1 H); 7.12 (*d*, *J* = 8.7, 2 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 167.20 (*s*); 148.72 (*s*); 138.88 (*d*); 135.19 (*s*); 131.11 (*d*); 128.60 (*d*); 128.45 (*d*); 125.94 (*d*); 120.28 (*s*); 111.10 (*d*). ESI-MS: 487 (5), 304 (8), 263 (6), 242 (16, $[M+2]^+$), 241 (100, $[M+1]^+$).

*4-Methylbenzenesulfonic Acid (2*E*)-2-(Phenylmethylene)hydrazide* (**3b**) [21a–g][23a]. As described for **2b**, with **3a** (3.00 g, 16.1 mmol), benzaldehyde (1.5 equiv.), and EtOH (38 ml). Recrystallization of the filtrate gave a total of 3.59 g (81%) of **3b**. White solid. M.p. 130.9–139.0° ([21a]: 129–131°). UV/VIS (EtOH): 331 (sh, 1700), 297 (sh, 11300), 288 (sh, 16900), 278 (20600), 272 (sh, 20200), 266 (sh, 18400), 259 (sh, 14900), 221 (sh, 22900), 215 (sh, 27000), 205 (sh, 33400), 202 (35900). IR (neat): 3223*m*, 3085*w*, 3068*w*, 3033*w*, 2989*w*, 2915*w*, 2866*w*, 2745*w*, 2258*w*, 2162*w*, 1948*w*, 1930*w*, 1890*w*, 1799*w*, 1665*w*, 1613*w*, 1596*m*, 1576*w*, 1495*m*, 1451*m* 1437*m* 1378*w*, 1365*m*, 1325*m*, 1311*m*, 1291*m*, 1226*m*, 1187*m*, 1159*s*, 1121*w*, 1107*w*, 1093*m*, 1078*w*, 1042*s*, 1021*m*, 1002*w*, 977*w*, 957*s*, 907*m*, 872*w*, 854*w*, 835*m*, 814*s*, 750*s*, 703*m*, 685*s*, 664*s*, 646*s*, 618*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.47 (*s*, 1 H); 7.93 (*s*, 1 H); 7.79 (*d*, *J* = 8.7, 2 H); 7.60–7.53 (*m*, 1 H); 7.45–7.35 (*m*, 5 H); 2.35 (*s*, 3 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 146.88 (*d*); 143.35 (*s*); 136.08 (*s*); 133.59 (*s*); 129.97 (*d*); 129.57 (*d*); 128.69 (*d*); 127.15 (*d*); 126.66 (*d*); 20.90 (*q*). EI-MS: 274 (11, M^+), 208 (3), 207 (12), 180 (5), 179 (5), 178 (4), 171 (5), 165 (4), 155 (6), 140 (3), 139 (7), 125 (3), 124 (27), 123 (7), 121 (4), 120 (3), 119 (31), 118 (33), 108 (4), 107 (7), 106 (37), 105 (41), 104 (13), 103 (30), 102 (3), 93 (5), 92 (54), 91 (100), 90 (89), 89 (35), 79 (7), 78 (14), 77 (48), 76 (14), 75 (6), 74 (7), 69 (3), 66 (4), 65 (40), 64 (12), 63 (18), 62 (7), 61 (3), 53 (3), 52 (8), 51 (27), 50 (17), 48 (3), 45 (5), 44 (8), 41 (3), 39 (16), 38 (4), 37 (3), 29 (4), 27 (3).

*4-Methylbenzenesulfonic Acid (2*E*)-2-(1-Phenylethylidene)hydrazide* (**3c**) [21f–i]. As described for **2b**, with **3a** (3.00 g, 16.1 mmol), acetophenone (1.5 equiv.), and EtOH (45 ml) for 4 h: 2.84 g (62%) of **3c**. White solid. M.p. 147.4–151.3° ([21h]: 148–149°). UV/VIS (EtOH): 276 (sh, 10900), 270 (sh, 12200), 264 (12500), 258 (sh, 12000), 229 (sh, 15400), 220 (sh, 19500), 214 (sh, 21000), 202 (29100). IR (neat): 3222*m*, 3056*w*, 2922*w*, 2593*w*, 2323*w*, 2165*w*, 1979*w*, 1921*w*, 1810*w*, 1761*w*, 1682*w*, 1657*w*, 1596*m*, 1571*w*, 1494*m*, 1445*m*, 1400*m*, 1335*s*, 1314*m*, 1298*s*, 1211*w*, 1186*m*, 1160*s*, 1120*w*, 1108*w*, 1082*m*, 1047*s*, 1027*m*, 1021*w*, 1000*w*, 961*w*, 815*m*, 801*m*, 762*m*, 751*s*, 702*w*, 692*s*, 667*s*, 629*s*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 10.51 (*s*, 1 H); 7.82 (*d*, *J* = 8.2, 2 H); 7.66–7.59 (*m*, 2 H); 7.41 (*d*, *J* = 8.2, 2 H); 7.39–7.33 (*m*, 3 H); 2.36 (*s*, 3 H); 2.18 (*s*, 3 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 153.04 (*s*); 143.23 (*s*); 137.32 (*s*); 136.16 (*s*); 129.35 (*d*); 129.26 (*d*); 128.25 (*d*); 127.47 (*d*); 125.85 (*d*); 20.91 (*q*); 14.17 (*q*). EI-MS: 288 (1, M^+), 207 (3), 133 (13), 132 (5), 124 (10), 123 (4), 121 (4), 120 (21), 119 (7), 118 (4), 106 (6), 105 (67), 104 (100), 103 (44), 102 (17), 92 (16), 91 (22), 89 (5), 79 (5), 78 (40), 77 (70), 76 (10), 75 (6), 74 (9), 65 (10), 64 (3), 63 (10), 62 (5), 52 (9), 51 (35), 50 (18), 44 (5), 43 (7), 39 (10), 38 (3), 27 (3).

*Benzaldehyde (*E*)-*N*-Phenylsemicarbazone* (=*(2*E*)-N-Phenyl-2-(phenylmethylene)hydrazinecarboxamide*; **4b**) [21j][23b]. As described for **2b**, with **4a** (3.00 g, 19.8 mmol), benzaldehyde (1.5 equiv.), and EtOH (45 ml). Recrystallization of the filtrate gave a total of 4.13 g (87%) of **4b**. White solid. M.p. 178.9° ([23b]: 180–181°). UV/VIS (EtOH): 309 (sh, 18800), 294 (27300), 287 (sh, 25900), 276 (sh, 19600), 239 (sh, 20100), 232 (22700), 222 (sh, 20200), 202 (34200). IR (neat): 3368*m*, 3193*m*, 3082*m*, 3028*m*, 2952*m*, 2862*m*, 2530*w*, 2271*w*, 2027*w*, 1951*w*, 1874*w*, 1807*w*, 1680*s*, 1593*s*, 1573*w*, 1533*s*, 1497*s*, 1444*s*, 1361*m*, 1332*m*, 1319*w*, 1309*m*, 1297*m*, 1281*m*, 1228*m*, 1177*m*, 1140*s*, 1082*w*, 1071*m*, 1032*m*, 1010*w*, 991*w*, 965*w*, 944*s*, 910*w*, 895*m*, 872*m*, 859*w*, 842*w*, 744*s*, 719*m*, 685*s*, 606*s*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 10.75 (*s*, 1 H); 8.90 (*s*, 1 H); 7.96 (*s*, 1 H); 7.88–7.82 (*m*, 2 H); 7.67 (*d*, *J* = 7.7, 2 H); 7.48–7.36 (*m*, 3 H); 7.30 (*t*, *J* = 7.9, 2 H); 7.02 (*t*, *J* = 7.4, 1 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 152.96 (*s*); 140.68 (*d*); 138.97 (*s*); 134.29 (*s*); 129.31 (*d*); 128.49 (*d*); 128.33 (*d*); 126.93 (*d*); 122.38 (*d*); 119.80 (*d*). ESI-MS: 502 (6), 501 (17), 486 (3), 485 (9), 386 (8), 262 (6), 241 (17, $[M+2]^+$), 240 (100, $[M+1]^+$).

*Ethyl (2*E*)-2-(Phenylmethylene)hydrazinecarboxylate* (**5b**) [21k]. As described for **2b**, with **5a** (3.00 g, 28.8 mmol), benzaldehyde (1.5 equiv.), and EtOH (85 ml): 4.82 g (87%) of **5b**. White solid. M.p. 140.2–140.7° ([21k]: 138–139°). UV/VIS (EtOH): 332 (sh, 300), 298 (sh, 12600), 290 (sh, 18900), 279 (24400), 272 (sh, 23300), 221 (sh, 14500), 216 (19400), 211 (19200), 207 (18700). IR (neat): 3178*m*, 3153*w*, 3052*m*, 2984*m*, 2940*w*, 2905*w*, 2870*w*, 2804*w*, 2285*w*, 1963*w*, 1908*w*, 1710*m*, 1690*s*, 1601*m*, 1553*s*,

1489*m*, 1476*m*, 1447*m*, 1388*w*, 1369*m*, 1357*m*, 1331*w*, 1315*w*, 1244*s*, 1223*s*, 1176*w*, 1156*w*, 1146*m*, 1108*w*, 1073*m*, 1045*s*, 1014*s*, 973*w*, 955*m*, 916*w*, 879*m*, 867*m*, 844*w*, 760*s*, 692*s*, 651*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.11 (*s*, 1 H); 8.03 (*s*, 1 H); 7.66–7.59 (*m*, 2 H); 7.46–7.35 (*m*, 3 H); 4.15 (*q*, *J* = 7.0, 2 H); 1.24 (*t*, *J* = 6.9, 3 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 153.38 (*s*); 143.68 (*d*); 134.33 (*s*); 129.43 (*d*); 128.66 (*d*); 126.50 (*d*); 60.40 (*t*); 14.46 (*q*). EI-MS: 192 (10, M^+), 146 (6), 120 (3), 119 (14), 118 (7), 106 (6), 105 (11), 104 (30), 103 (100), 93 (5), 92 (15), 91 (6), 90 (39), 89 (34), 78 (5), 77 (21), 76 (30), 75 (9), 74 (6), 65 (10), 64 (6), 63 (13), 62 (13), 61 (4), 52 (6), 51 (18), 50 (17), 46 (6), 45 (18), 44 (26), 43 (12), 42 (3), 39 (8), 38 (4), 37 (3), 31 (19), 30 (3), 29 (20), 27 (9), 26 (4).

*Furan-2-carboxylic Acid (2*E*)-2-(Phenylmethylene)hydrazide* (**6b**) [21l][21m]. As described for **2b**, with **6a** (3.00 g, 23.8 mmol), benzaldehyde (1.5 equiv.), and EtOH (50 ml): 4.74 g (92%) of **6b**. White solid. M.p. 225.8–226.4° ([21l]: 232–234°). UV/VIS (EtOH): 359 (sh, 1300), 304 (33800), 256 (sh, 11800), 225 (sh, 15900), 218 (sh, 18900), 213 (18800), 205 (sh, 21400), 202 (22900). IR (neat): 3158*w*, 3138*w*, 3105*m*, 3029*w*, 2997*w*, 2823*w*, 1682*w*, 1638*s*, 1601*m*, 1586*s*, 1537*m*, 1488*w*, 1473*m*, 1445*w*, 1380*w*, 1356*s*, 1315*w*, 1289*s*, 1232*m*, 1226*m*, 1174*m*, 1154*w*, 1132*m*, 1083*m*, 1074*w*, 1060*m*, 1016*s*, 974*w*, 962*m*, 949*w*, 921*w*, 900*w*, 883*w*, 874*s*, 856*w*, 844*w*, 829*m*, 765w, 751*s*, 695*s*, 646*w*, 619*w*, 603*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.86 (*s*, 1 H); 8.48 (*s*, 1 H); 7.96 (*s*, 1 H); 7.79–7.68 (*m*, 2 H); 7.52–7.41 (*m*, 3 H); 7.33 (*s*, 1 H); 6.72 (*s*, 1 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 154.15 (*s*); 147.78 (*d*); 146.56 (*s*); 145.77 (*d*); 134.17 (*s*); 130.00 (*d*); 128.77 (*d*); 126.99 (*d*); 114.86 (*d*); 112.00 (*d*). EI-MS: 214 (3, M^+), 112 (6), 111 (86), 106 (3), 105 (7), 104 (12), 103 (79), 96 (6), 95 (100), 94 (4), 93 (6), 92 (5), 90 (5), 89 (9), 77 (11), 76 (26), 75 (7), 74 (4), 67 (3), 65 (8), 64 (6), 63 (6), 55 (3), 52 (5), 51 (12), 50 (13), 44 (5), 39 (22), 38 (8), 37 (5).

*Furan-2-carboxylic Acid (2*E*)-2-[(3*R*)-3,7-Dimethyloct-6-en-1-ylidene]hydrazide* (**6c**). A mixture of **6a** (1.50 g, 11.9 mmol) and (*R*)-citronellal (2.74 g, 17.7 mmol, 1.5 equiv.) in EtOH (30 ml) was heated under reflux for 2 h. After cooling to r.t., the mixture was concentrated and the excess of citronellal removed by bulb-to-bulb distillation at 120°/0.39 mbar: 2.03 g (55%) of **6c**. Highly viscous yellow oil containing small amounts of an unknown impurity. UV/VIS (EtOH): 330 (sh, 420), 267 (27300), 251 (sh, 20700), 241 (sh, 15400), 232 (sh, 11000), 211 (sh, 11500), 202 (14300). IR (neat): 3201*m*, 3127*w*, 3105*w*, 3043*m*, 2959*m*, 2910*m*, 2868*w*, 2850*w*, 2726*w*, 1662*s*, 1642*s*, 1622*s*, 1589*s*, 1570*s*, 1536*s*, 1471*s*, 1454*w*, 1391*w*, 1373*w*, 1362*m*, 1297*s*, 1241*m*, 1233*m*, 1193*m*, 1184*w*, 1136*m*, 1080*m*, 1038*w*, 1020*m*, 983*w*, 946*m*, 885*m*, 848*m*, 832*m*, 795*w*, 759*m*, 692*m*. ^{1}H-NMR (400 MHz, $CDCl_3$): 9.49 (*s*, 1 H); 7.59 (*t*, *J* = 5.1, 1 H); 7.45 (*s*, 1 H); 7.26 (br. *s*, 1 H); 6.54–6.49 (*m*, 1 H); 5.07 (*t*, *J* = 7.2, 1 H); 2.47–2.35 (*m*, 1 H); 2.32–2.18 (*m*, 1 H); 2.13–2.09 (*m*, 2 H); 1.82–1.71 (*m*, 1 H); 1.68 (*s*, 3 H); 1.60 (*s*, 3 H); 1.48–1.33 (*m*, 1 H); 1.33–1.18 (*m*, 1 H); 0.95 (*d*, *J* = 6.7, 3 H). ^{13}C-NMR (100.6 MHz, $CDCl_3$): 154.48 (*s*); 152.21 (*d*); 146.70 (*s*); 144.29 (*d*); 131.58 (*s*); 124.28 (*d*); 115.81 (*d*); 112.33 (*d*); 39.45 (*t*); 36.86 (*t*); 31.20 (*d*); 25.71 (*q*); 25.44 (*t*); 19.54 (*q*); 17.68 (*q*). EI-MS: 263 (3, $[M+1]^+$), 262 (18, M^+), 260 (5), 247 (3), 245 (10), 180 (6), 179 (18), 168 (10), 167 (83), 152 (10), 151 (5), 150 (3), 139 (6), 138 (3), 137 (11), 136 (19), 123 (5), 122 (7), 121 (11), 112 (19), 111 (14), 110 (3), 109 (8), 108 (7), 107 (3), 96 (9), 95 (100), 94 (10), 93 (6), 83 (3), 82 (5), 81 (12), 79 (4), 71 (3), 70 (4), 69 (19), 68 (6), 67 (11), 56 (5), 55 (11), 53 (5), 43 (4), 42 (3), 41 (20), 39 (13), 29 (3).

*Benzoic Acid (2*E*)-2-(Phenylmethylene)hydrazide* (**7b**) [21n–p][23c][24a]. As described for **2b**, with **7a** (3.00 g, 22.0 mmol), benzaldehyde (1.5 equiv.), and EtOH (50 ml): 4.18 g (85%) of **7b**. White solid. M.p. 208.4–209.0° ([21n]: 207°). UV/VIS (EtOH): 299 (28600), 294 (sh, 28500), 281 (sh, 22600), 224 (sh, 17500), 219 (18900), 205 (sh, 25900), 202 (29700). IR (neat): 3177*m*, 3152*w*, 3059*m*, 3028*m*, 2836*w*, 1960*w*, 1820*w*, 1638*s*, 1600*m*, 1576*m*, 1551*s*, 1486*m*, 1446*m*, 1362*m*, 1322*w*, 1304*m*, 1284*s*, 1251*w*, 1227*w*, 1185*w*, 1172*w*, 1161*w*, 1140*m*, 1105*w*, 1078*m*, 1057*m*, 1021*m*, 1000*w*, 986*w*, 970*m*, 932*w*, 912*m*, 842*m*, 799*m*, 760*m*, 690*s*, 669*s*, 644*m*, 616*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.90 (*s*, 1 H); 8.51 (*s*, 1 H); 7.96 (*d*, *J* = 7.7, 2 H); 7.76 (*d*, *J* = 6.1, 2 H); 7.66–7.37 (*m*, 6 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 163.09 (*s*); 147.73 (*d*); 134.28 (*s*); 133.38 (*s*); 131.67 (*d*); 129.99 (*d*); 128.76 (*d*); 128.39 (*d*); 127.55 (*d*); 127.02 (*d*). EI-MS: 224 (3, M^+), 122 (3), 121 (33), 106 (10), 105 (100), 104 (12), 103 (81), 89 (5), 78 (6), 77 (52), 76 (29), 75 (8), 74 (5), 65 (4), 63 (5), 52 (5), 51 (20), 50 (15), 44 (4), 39 (5), 38 (3).

*Benzoic Acid (2*E*)-2-(Undec-10-en-1-ylidene)hydrazide* (**7c**). A mixture of **7a** (1.50 g, 11.0 mmol) and undec-10-enal (2.80 g, 16.5 mmol, 1.5 equiv.) in EtOH (28 ml) was heated under reflux for 2 h. After cooling to r.t., the mixture was concentrated, and the residue washed with hexane and dried at 0.20 mbar:

2.78 g (88%) of **7c**. White solid. M.p. 58.5–59.4°. UV/VIS (EtOH): 250 (23500), 239 (sh, 20500), 229 (sh, 18200), 204 (sh, 31100), 203 (32700). IR (neat): 3251*m*, 3062*m*, 2995*w*, 2973*w*, 2926*m*, 2878*w*, 2847*m*, 1820*w*, 1768*w*, 1649*s*, 1624*s*, 1601*w*, 1579*m*, 1538*s*, 1490*m*, 1462*m*, 1445*w*, 1431*w*, 1416*w*, 1367*s*, 1300*m*, 1281*s*, 1238*w*, 1202*w*, 1182*w*, 1150*m*, 1128*w*, 1112*w*, 1077*m*, 1041*m*, 1027*w*, 998*m*, 987*m*, 956*m*, 925*w*, 903*s*, 868*m*, 846*w*, 837*w*, 795*m*, 776*w*, 743*w*, 724*m*, 690*s*, 661*s*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.40 (*s*, 1 H); 7.84 (*d*, *J* = 7.7, 2 H); 7.74 (*t*, *J* = 5.3, 1 H); 7.56 (*t*, *J* = 7.2, 1 H); 7.49 (*t*, *J* = 7.4, 2 H); 5.86–5.73 (*m*, 1 H); 5.04–4.89 (*m*, 2 H); 2.25 (*q*, *J* = 6.5, 2 H); 2.01 (*q*, *J* = 6.8, 2 H); 1.55–1.42 (*m*, 2 H); 1.41–1.15 (*m*, 10 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 162.65 (*s*); 152.19 (*d*); 138.72 (*d*); 133.53 (*s*); 131.39 (*d*); 128.27 (*d*); 127.38 (*d*); 114.53 (*t*); 33.09 (*t*); 31.90 (*t*); 28.69 (*t*, 2×); 28.56 (*t*); 28.40 (*t*); 28.18 (*t*); 25.95 (*t*). APCI-MS: 575 (4), 574 (18), 573 (43, $[2M+1]^+$), 289 (4), 288 (24), 287 (100, $[M+1]^+$), 137 (3).

*Benzoic Acid (2*E*)-2-(3-Phenylbutylidene)hydrazide* (**7d**). A mixture of **7a** (1.50 g, 11.0 mmol) and (±)-3-phenylbutanal (= *Trifernal*®; 2.45 g, 16.5 mmol, 1.5 equiv.) in EtOH (28 ml) was heated under reflux for 2 h. After cooling to r.t., the mixture was concentrated. The residue was washed with EtOH and then with hexane and finally dried at 0.17 mbar: 2.04 g (70%) of **7d**. White solid. M.p. 105.4–107.5°. UV/VIS (EtOH): 253 (20200), 238 (sh, 17000), 230 (sh, 16200). IR (neat): 3275*m*, 3079*w*, 3060*w*, 3025*w*, 2955*m*, 2926*w*, 2867*w*, 2826*w*, 1939*w*, 1722*w*, 1648*s*, 1625*m*, 1601*m*, 1579*m*, 1547*s*, 1492*m*, 1452*m*, 1447*m*, 1424*w*, 1374*m*, 1321*w*, 1302*w*, 1280*m*, 1266*m*, 1202*w*, 1185*w*, 1158*w*, 1136*m*, 1110*w*, 1090*w*, 1072*m*, 1045*m*, 1026*m*, 1000*w*, 971*m*, 924*w*, 901*m*, 862*m*, 794*m*, 759*s*, 744*w*, 717*m*, 697*s*, 687*s*, 676*s*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.43 (*s*, 1 H); 7.84 (*d*, *J* = 7.2, 2 H); 7.65 (*t*, *J* = 5.4, 1 H); 7.55 (*t*, *J* = 7.2, 1 H); 7.48 (*t*, *J* = 7.4, 2 H); 7.37–7.26 (*m*, 4 H); 7.24–7.17 (*m*, 1 H); 3.09–2.96 (*m*, 1 H); 2.65–2.48 (*m*, 2 H); 1.26 (*d*, *J* = 7.2, 3 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 162.63 (*s*); 150.90 (*d*); 145.89 (*s*); 133.39 (*s*); 131.43 (*d*); 128.35 (*d*); 128.25 (*d*); 127.40 (*d*); 126.82 (*d*); 126.08 (*d*); 40.11 (*t*); 37.25 (*d*); 21.88 (*q*). APCI-MS: 535 (4), 534 (23), 533 (59, $[2M+1]^+$), 322 (4), 268 (19), 267 (100, $[M+1]^+$).

*Benzene-1,4-dicarboxylic Acid 1,4-Bis[(2*E*)-2-(phenylmethylene)hydrazide]* (**8b**) [19][21q]. As described for **2b**, with **8a** (2.00 g, 10.3 mmol), benzaldehyde (2 equiv.), and EtOH (40 ml) for 3.5 h: 2.94 g (77%) of **8b**. White solid. M.p. >300°. UV/VIS (EtOH): 310 (46400), 292 (sh, 36900), 245 (sh, 18200), 226 (sh, 24000), 219 (sh, 26800), 204 (42500). IR (neat): 3255*m*, 3060*w*, 3030*w*, 2824*w*, 1811*w*, 1761*w*, 1644*s*, 1603*m*, 1578*w*, 1546*s*, 1505*w*, 1489*m*, 1447*m*, 1405*w*, 1364*m*, 1311*m*, 1280*s*, 1230*w*, 1189*w*, 1173*w*, 1150*m*, 1120*m*, 1077*w*, 1055*m*, 1019*m*, 1000*w*, 987*w*, 962*m*, 912*m*, 874*w*, 859*m*, 842*m*, 786*w*, 754*s*, 731*m*, 719*w*, 690*s*, 651*s*, 632*s*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 12.03 (*s*, 2 H); 8.52 (*s*, 2 H); 8.17–8.00 (*m*, 4 H); 7.82–7.71 (*m*, 4 H); 7.59–7.37 (*m*, 6 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 162.28 (*s*); 148.23 (*d*); 136.00 (*s*); 134.14 (*s*); 130.11 (*d*); 128.78 (*d*); 127.69 (*d*); 127.06 (*d*). ESI-MS: 764 (7), 763 (15), 373 (4), 372 (24), 371 (100, $[M+1]^+$), 186 (3).

*Octanoic Acid (2*E*)-2-(Phenylmethylene)hydrazide* (**9b**). As described for **2b**, with **9a** (4.35 g at 80%, 22.0 mmol), benzaldehyde (1.5 equiv.), and EtOH (50 ml): 5.15 g (94%) of **9b**. White solid consisting of two isomers (*anti*/*syn ca*. 1.5:1). M.p. 68.0–70.0°. UV/VIS (EtOH): 300 (sh, 14300), 287 (sh, 21500), 283 (22200), 223 (sh, 12400), 218 (15900), 213 (sh, 14100), 207 (sh, 11900). IR (neat): 3182*w*, 3083*w*, 3065*w*, 3031*w*, 2960*w*, 2947*m*, 2921*m*, 2859*w*, 2848*m*, 1946*w*, 1886*w*, 1806*w*, 1698*w*, 1665*s*, 1622*w*, 1612*m*, 1604*m*, 1575*w*, 1519*w*, 1499*w*, 1487*w*, 1469*m*, 1454*w*, 1438*m*, 1425*m*, 1391*s*, 1350*m*, 1325*m*, 1309*m*, 1295*m*, 1268*m*, 1230*m*, 1187*w*, 1177*w*, 1143*m*, 1121*w*, 1105*m*, 1071*m*, 1031*m*, 1002*m*, 987*w*, 969*w*, 944*m*, 924*m*, 913*m*, 892*w*, 832*w*, 790*m*, 752*m*, 725*m*, 718*m*, 687*s*, 658*m*, 620*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): major isomer (*anti*): 11.22 (*s*, 1 H); 7.99 (*s*, 1 H); 7.72–7.61 (*m*, 2 H); 7.48–7.36 (*m*, 3 H); 2.62 (*t*, *J* = 7.4, 2 H); 1.65–1.53 (*m*, 2 H); 1.39–1.18 (*m*, 8 H); 0.85 (*t*, *J* = 6.9, 3 H); minor isomer (*syn*): 11.33 (*s*, 1 H); 8.19 (*s*, 1 H); 7.72–7.61 (*m*, 2 H); 7.48–7.36 (*m*, 3 H); 2.20 (*t*, *J* = 7.4, 2 H); 1.65–1.53 (*m*, 2 H); 1.39–1.18 (*m*, 8 H); 0.87 (*t*, *J* = 6.7, 3 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): major isomer (*anti*): 174.35 (*s*); 142.26 (*d*); 134.36 (*s*); 129.52 (*d*); 128.71 (*d*); 126.51 (*d*); 31.84 (*t*); 31.14 (*t*); 28.71 (*t*); 28.45 (*t*); 24.26 (*t*); 22.04 (*t*); 13.87 (*q*); minor isomer (*syn*): 168.61 (*s*); 145.64 (*d*); 134.40 (*s*); 129.74 (*d*); 128.68 (*d*); 126.87 (*d*); 34.20 (*t*); 31.14 (*t*); 28.61 (*t*); 28.44 (*t*); 24.99 (*t*); 22.04 (*t*); 13.87 (*q*). EI-MS: 246 (4, M^+), 162 (8), 143 (7), 131 (5), 127 (7), 121 (13), 120 (100), 119 (34), 114 (6), 105 (3), 104 (17), 103 (6), 100 (7), 93 (14), 92 (12), 91 (6), 90 (9), 89 (14), 86 (10), 78 (4), 77 (23), 76 (4), 73 (4), 72 (30), 69 (3), 67 (3), 66 (3), 65 (15), 64 (3), 63 (5), 60 (4), 59 (93), 57 (64), 56 (3), 55 (19), 51 (9), 50 (3), 44 (4), 43 (35), 42 (8), 41 (35), 39 (11), 29 (16), 27 (9).

*Hexanedioic Acid 1,6-Bis[(2*E*)-2-(phenylmethylene)hydrazide]* (**10b**) [21r]. As described for **2b**, with **10a** (4.00 g, 22.9 mmol), benzaldehyde (3 equiv.), and EtOH (95 ml) for 4 h: 7.86 g (98%) of **10b**. White solid as a mixture of three isomers (*anti*/*syn* to *anti*/*anti* to *syn*/*syn ca.* 1.4:1.1:1). M.p. 226.6–228.4° ([21r]: 215°). UV/VIS (EtOH): 300 (sh, 30000), 290 (sh, 44100), 283 (46000), 274 (sh, 40500), 224 (sh, 26700), 218 (34400), 213 (sh, 31300), 207 (sh, 27400). IR (neat): 3308*w*, 3180*m*, 3027*m*, 2959*w*, 2946*w*, 2857*w*, 1660*s*, 1664*s*, 1607*m*, 1566*s*, 1500*w*, 1487*m*, 1459*w*, 1449*m*, 1437*w*, 1402*s*, 1375*m*, 1369*m*, 1356*m*, 1310*m*, 1302*m*, 1291*w*, 1278*s*, 1259*m*, 1238*m*, 1221*m*, 1174*w*, 1145*m*, 1132*m*, 1095*w*, 1068*m*, 1054*w*, 1044*w*, 1013*m*, 986*m*, 957*m*, 948*m*, 920*w*, 891*m*, 878*w*, 868*w*, 835*w*, 792*w*, 777*m*, 753*s*, 739*s*, 688*s*, 666*w*, 653*m*, 644*w*, 614*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): major isomer (*anti*/*syn*): 11.37 (*s*, 1 H); 11.24 (*s*, 1 H); 8.18 (*s*, 1 H); 7.99 (*s*, 1 H); 7.80–7.57 (*m*, 4 H); 7.52–7.32 (*m*, 6 H); 2.77–2.60 (*m*, 2 H); 2.32–2.18 (*m*, 2 H); 1.76–1.66 (*m*, 4 H); *anti*/*anti* isomer: 11.24 (*s*, 2 H); 7.99 (*s*, 2 H); 7.80–7.57 (*m*, 4 H); 7.52–7.32 (*m*, 6 H); 2.77–2.60 (*m*, 4 H); 1.76–1.66 (*m*, 4 H); minor isomer (*syn*/*syn*): 11.37 (*s*, 2 H); 8.18 (*s*, 2 H); 7.80–7.57 (*m*, 4 H); 7.52–7.32 (*m*, 6 H); 2.32–2.18 (*m*, 4 H); 1.76–1.66 (*m*, 4 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): major isomer (*anti*/*syn*): 174.10 (*s*); 168.41 (*s*); 145.66 (*d*); 142.36 (*d*); 134.30 (*s*); 134.26 (*s*); 129.73 (*d*); 129.49 (*d*); 128.67 (*d*, 2×); 126.84 (*d*); 126.49 (*d*); 33.99 (*t*); 31.60 (*t*); 24.73 (*t*); 23.82 (*t*); *anti*/*anti* isomer: 174.16 (*s*); 142.31 (*d*); 134.26 (*s*); 129.49 (*d*); 128.67 (*d*); 126.84 (*d*); 31.60 (*t*); 23.92 (*t*); minor isomer (*syn*/*syn*): 168.38 (*s*); 145.66 (*d*); 134.30 (*s*); 129.73 (*d*); 128.67 (*d*); 126.49 (*d*); 33.99 (*t*); 24.68 (*t*). ESI-MS: 724 (4), 723 (8, $[2M+Na]^+$), 373 (3), 353 (3), 352 (24), 351 (100, $[M+1]^+$).

*Hexanedioic Acid 1,6-Bis[(2*E*)-2-(1-methyl-3-phenylpropylidene)hydrazide]* (**10c**). As described for **2b**, with **10a** (1.50 g, 8.6 mmol), 4-phenylbutan-2-one (3 equiv.), and EtOH (22 ml) for 4 h: 2.94 g (79%) of **10c**. White solid as one major isomer together with small amounts of other isomers. M.p. 152.8–154.7°. UV/VIS (EtOH): 268 (9400), 235 (11700), 218 (sh, 11800), 208 (14800), 204 (sh, 14000). IR (neat): 3235*w*, 3202*w*, 3176*w*, 3024*m*, 3000*w*, 2924*m*, 2866*w*, 2824*w*, 1679*m*, 1656*s*, 1634*m*, 1603*w*, 1546*s*, 1494*m*, 1453*m*, 1440*w*, 1417*m*, 1373*m*, 1343*m*, 1314*w*, 1295*w*, 1254*m*, 1220*m*, 1199*m*, 1137*m*, 1104*m*, 1078*m*, 1059*w*, 1029*m*, 1015*m*, 994*m*, 951*w*, 913*w*, 896*w*, 869*w*, 846*w*, 824*w*, 801*w*, 749*m*, 701*s*, 627*m*. ^{1}H-NMR (400 MHz, $CDCl_3$; major isomer): 8.95 (*s*, 2 H); 7.35–7.24 (*m*, 4 H); 7.24–7.15 (*m*, 6 H); 2.92–2.82 (*m*, 4 H); 2.71–2.61 (*m*, 4 H); 2.60–2.49 (*m*, 4 H); 1.82 (*s*, 6 H); 1.75–1.66 (*m*, 4 H). ^{13}C-NMR (100.6 MHz, $CDCl_3$; major isomer): 175.91 (*s*); 150.84 (*s*); 141.25 (*d*); 128.37 (*d*); 128.31 (*d*); 125.98 (*d*); 40.40 (*t*); 32.45 (*t*); 32.07 (*t*); 23.72 (*t*); 15.56 (*q*). ESI-MS: 679 (9), 671 (5), 462 (4), 458 (6), 457 (19), 437 (5), 436 (31, $[M+2]^+$), 435 (100, $[M+1]^+$), 305 (3), 245 (3).

N,N,N-*Trimethyl-2-oxo-2-[(2*E*)-2-(phenylmethylene)hydrazinyl]ethanaminium Chloride (1:1)* (**11b**) [38c]. A mixture of **11a** (*Girard T* reagent; 3.00 g, 17.9 mmol) and benzaldehyde (1.5 equiv.) in EtOH (50 ml) was heated under reflux for 4 h. After cooling to r.t., Et_2O was added and the precipitate filtered: 3.88 g (83%) of **11b**. White solid consisting of two isomers (*anti*/*syn ca.* 1.8:1). M.p. 169.6–170.4°. UV/VIS (EtOH): 300 (sh, 14700), 289 (sh, 21800), 283 (22800), 275 (sh, 21100), 224 (sh, 12600), 218 (15800), 212 (sh, 13900), 206 (sh, 11500). IR (neat): 3675*w*, 3440*w*, 3389*w*, 3195*w*, 2965*w*, 2938*m*, 2900*w*, 2823*w*, 1688*s*, 1608*m*, 1582*m*, 1486*m*, 1460*m*, 1447*m*, 1412*m*, 1369*w*, 1356*w*, 1319*m*, 1304*m*, 1290*m*, 1274*m*, 1235*m*, 1172*w*, 1128*m*, 1084*w*, 1067*m*, 1018*w*, 1003*w*, 989*m*, 968*w*, 949*m*, 924*m*, 878*m*, 847*m*, 781*w*, 756*m*, 721*m*, 692*s*, 685*s*, 646*m*, 624*m*, 611*m*. ^{1}H-NMR (400 MHz, (D_6)DMSO): major isomer (*anti*): 12.28 (br. *s*, 1 H); 8.23 (*s*, 1 H); 7.86–7.63 (*m*, 2 H); 7.58–7.35 (*m*, 3 H); 4.88 (*s*, 2 H); 3.37 (*s*, 3 H); minor isomer (*syn*): 13.20 (br. *s*, 1 H); 8.45 (*s*, 1 H); 7.86–7.63 (*m*, 2 H); 7.58–7.35 (*m*, 3 H); 4.47 (*s*, 2 H); 3.33 (*s*, 3 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): major isomer (*anti*): 165.31 (*s*); 145.29 (*d*); 133.47 (*s*); 130.25 (*d*); 128.71 (*d*); 127.03 (*d*); 62.14 (*t*); 53.12 (*q*); minor isomer (*syn*): 159.76 (*s*); 148.61 (*d*); 133.59 (*s*); 130.41 (*d*); 128.80 (*d*); 127.14 (*d*); 63.23 (*t*); 53.33 (*q*). ESI-MS: 440 (4), 439 (14), 221 (14, $[M+1]^+$), 220 (100, M^+).

*1-{2-Oxo-2-[(2*E*)-2-(phenylmethylene)hydrazinyl]ethyl}pyridinium Chloride (1:1)* (**12b**). As described for **2b**, with **12a** (*Girard P* reagent; 3.00 g, 16.0 mmol), benzaldehyde (1.5 equiv.), and EtOH (45 ml). Recrystallization of the filtrate and drying under high vacuum gave a total of 4.28 g (97%) of **12b**. White solid consisting of two isomers (*anti*/*syn ca.* 4:1) and still containing some EtOH. M.p. 257.3–260.0°. UV/VIS (EtOH): 299 (sh, 15500), 289 (sh, 23300), 281 (25400), 275 (sh, 24600), 268 (sh, 22800), 223 (sh, 15800), 217 (20000), 213 (sh, 19000), 206 (sh, 17400). IR (neat): 3564*w*, 3326*m* (br.), 3126*w*, 3039*m*, 2983*w*, 2962*w*, 2936*m*, 2849*m*, 2780*m*, 2733*w*, 2162*w*, 1856*w*, 1778*w*, 1734*w*, 1697*s*, 1633*s*, 1574*w*, 1484*s*, 1447*w*, 1421*m*, 1387*s*, 1350*m*, 1313*m*, 1297*m*, 1274*s*, 1218*m*, 1199*m*, 1174*w*, 1158*w*, 1131*w*, 1113*m*,

1104*m*, 1088*w*, 1071*w*, 1055*w*, 1044*m*, 1025*w*, 998*w*, 971*w*, 949*m*, 924*w*, 887*m*, 850*m*, 801*m*, 771*s*, 757*s*, 692*s*, 646*m*, 616*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): major isomer (*anti*): 12.38 (*s*, 1 H); 9.14 (*d*, *J* = 5.1, 2 H); 8.71 (*t*, *J* = 7.7, 1 H); 8.32–8.20 (*m*, 2 H); 8.26 (*s*, 1 H); 7.80–7.73 (*m*, 2 H); 7.53–7.42 (*m*, 3 H); 6.11 (*s*, 2 H); minor isomer (*syn*): 13.18 (*s*, 1 H); 9.14 (*d*, *J* = 5.1, 2 H); 8.74–8.66 (*m*, 1 H); 8.46 (*s*, 1 H); 8.32–8.20 (*m*, 2 H); 7.73–7.67 (*m*, 2 H); 7.53–7.42 (*m*, 3 H); 5.74 (*s*, 2 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): major isomer (*anti*): 166.40 (*s*); 146.40 (*d*); 146.12 (*d*); 145.05 (*d*); 133.63 (*s*); 130.20 (*d*); 128.79 (*d*); 127.43 (*d*); 126.90 (*d*); 61.33 (*t*); minor isomer (*syn*): 161.28 (*s*); 147.88 (*d*); 146.26 (*d*); 146.12 (*d*); 133.78 (*s*); 130.20 (*d*); 128.79 (*d*); 127.43 (*d*); 127.04 (*d*); 60.85 (*t*). ESI-MS: 241 (16, $[M+1]^+$), 240 (100, M^+).

*2-Hydroxypropane-1,2,3-tricarboxylic Acid 1,2,3-Tris[(2*E*)-2-(phenylmethylene)hydrazide]* (**13b**) [19]. As described for **2b**, with **13a** (3.00 g, 12.8 mmol), benzaldehyde (4.5 equiv.), and EtOH (200 ml): 6.32 g (97%) of **13b**. White solid as a mixture of three isomers **A**/**D**/**F** in a ratio of *ca.* 1:2:1 (see *Fig. 3*). M.p. 202.9–203.2° ([19]: 213°). UV/VIS (EtOH): 301 (sh, 50600), 291 (68900), 284 (68800), 223 (sh, 40100), 219 (50100), 213 (sh, 45000), 207 (sh, 38700). IR (neat): 3418*w*, 3259*w*, 3060*w*, 3031*w*, 2963*w*, 2930*w*, 1655*s*, 1618*w*, 1608*w*, 1574*m*, 1530*m*, 1498*w*, 1487*w*, 1447*w*, 1439*w*, 1424*w*, 1396*m*, 1368*m*, 1355*w*, 1328*w*, 1312*w*, 1295*w*, 1281*w*, 1263*w*, 1239*m*, 1179*w*, 1139*m*, 1095*w*, 1082*w*, 1057*m*, 1026*w*, 1006*w*, 996*w*, 986*w*, 949*m*, 893*m*, 873*w*, 842*w*, 812*m*, 751*s*, 688*s*, 640*m*, 624*w*. ^{1}H-NMR (400 MHz, (D_6)DMSO): 11.58 (*s*, 1 H); 11.45 (*s*, 1 H); 11.28, 11.26, 11.24 (3*s*, 1 H); 8.49, 8.46, 8.45 (3*s*, 1 H); 8.20, 8.18 (2*s*, 1 H); 8.01, 8.00 (2*s*, 1 H); 7.76–7.55 (*m*, 6 H); 7.49–7.32 (*m*, 9 H); 6.15, 6.02, 5.86 (3*s*, 1 H); 3.42–3.25 (*m*, 2 H); 2.91, 2.87 (2*d*, *J* = 8.2, 7.7, 1 H); 2.80, 2.76 (2*s*, 1 H). ^{13}C-NMR (100.6 MHz, (D_6)DMSO): 171.68 (*s*); 171.52 (*s*), 170.35 (*s*); 170.21 (*s*); 170.01 (*s*); 166.05 (*s*); 165.89 (*s*); 147.77 (*d*); 147.49 (*d*); 147.27 (*d*); 146.53 (*d*), 146.44 (*d*); 143.14 (*d*); 143.10 (*d*); 134.40 (*s*); 134.34 (*s*); 134.31 (*s*); 134.10 (*s*); 134.07 (*s*); 134.01 (*s*); 129.95 (*d*); 129.86 (*d*); 129.74 (*d*); 129.65 (*d*); 129.63 (*d*); 128.68 (*d*); 128.63 (*d*); 128.59 (*d*); 126.94 (*d*); 126.89 (*d*); 126.83 (*d*); 126.78 (*d*); 126.70 (*d*); 126.68 (*d*); 74.98 (*s*); 74.76 (*s*); 74.70 (*s*); 42.75 (*t*); 42.38 (*t*); 40.02 (*t*); 39.74 (*t*). ESI-MS: 1549 (3), 1273 (9), 1025 (7), 1024 (10), 1021 (3), 1020 (7), 1019 (12), 775 (6), 587 (6), 526 (7), 501 (3), 500 (18), 499 (56, $[M+1]^+$), 481 (3), 381 (3), 380 (24), 379 (100), 297 (5).

Citric Acid Buffer Stock Solution. A citric acid buffer stock soln. (0.15M, *I* = 0.1) was prepared by dissolving anh. NaOH pellets (0.65 g), NaCl (0.62 g), and anh. citric acid (2.58 g) in demineralized H_2O (160.02 g) and abs. EtOH (31.45 g (=40 ml)). To determine the pH of the soln., the buffer stock soln. (10 ml) was diluted with EtOH (2 ml) (→ H_2O/EtOH 2:1 (*v*/*v*) which is the composition used for the kinetic measurements), and the pH value was measured with a *Mettler-Toledo MP220* pH meter and an *InLab 410* Ag/AgCl glass electrode: pH 4.48 (±0.027) at 25.0° (±0.31) (after 2 point calibration at pH 7.00 and 4.01).

Phosphoric Acid Buffer Stock Solutions. A phosphoric acid buffer stock soln. (0.15M, *I* = 0.1) was prepared as described above with orthophosphoric acid (H_3PO_4; 1.97 g), monobasic KH_2PO_4 (1.37 g), NaCl (0.60 g), demineralized H_2O (160.01 g), and abs. EtOH (31.45 g) (=40 ml)). After dilution of the buffer stock soln. (10 ml) with EtOH (2 ml) (→ H_2O/EtOH 2:1 (*v*/*v*)), a pH of 2.47 (±0.039) was measured at 25.0° (±0.35).

Similarly, a nonionic surfactant-containing phosphoric acid buffer stock soln. was obtained with *Triton® X-100* (2.28 g) as additional ingredient. After dilution of the buffer stock soln. (10 ml) with EtOH (2 ml) (→ H_2O/EtOH 2:1 (*v*/*v*)), a pH of 2.51 (±0.010) was measured at 25.0° (±0.19).

Kinetic Measurements. All UV/VIS measurements were carried out in quartz cuvettes (1 cm) by adding either hydrazine derivative (0.2 ml) and aldehyde (0.2 ml) (both at $2.0 \cdot 10^{-4}$ M in EtOH) or, alternatively, by adding, the corresponding hydrazone (0.4 ml; at $1.0 \cdot 10^{-4}$ M in EtOH) to the above described buffer stock soln. (2 ml) to give a final product concentration of $1.7 \cdot 10^{-5}$ M in H_2O/EtOH 2:1 (*v*/*v*). UV/VIS Spectra were recorded at constant time intervals between 240 and 450 nm at a scan rate of 960 nm/min. The first spectrum was recorded 2 min after addition of the compounds to the buffer soln., the following spectra were taken every 5 min at pH 2.47, and every 30 min at pH 4.48. The rate constants were determined from the change of absorption measured at 290 nm, with $\Delta t = 1$ h (pH 2.47) or $\Delta t =$ 7.5 h (pH 4.48). The pH values recorded after the kinetic measurements were generally found to remain within the exper. error given above.

Dynamic Headspace Analysis. To a TEA-esterquat emulsion (1.80 g), composed of a TEA-esterquat (*Stepantex®*) (16.5%), $CaCl_2$ (0.2%), and H_2O (83.3%) (all by weight), was added EtOH (1 ml) containing the fragrance molecules (each at 0.04M), and H_2O (1 ml) containing the hydrazine derivative

(at a molar equivalent of hydrazine functions with respect to the total amount of fragrance) or pure H_2O (1 ml; reference). The vial was closed and the mixture left equilibrating for 5 d. Then it was dispersed in a beaker with tap H_2O (600 ml), and a cotton square was added (cotton-test cloth Nr. 221 from *Eidgenössische Materialprüfanstalt* (*EMPA*); pre-washed with an unperfumed detergent powder and cut to *ca.* 12 × 12 cm squares). The cotton square was stirred manually for 3 min, left standing for 2 min, and wrung out by hand while ensuring a constant amount of residual H_2O (weighing). It was then left to dry overnight at r.t., put into a home-made headspace sampling cell (160 ml) thermostatted at 25°, and exposed to a constant air flow of *ca.* 200 ml/min. The air was filtered through active charcoal and passed through a sat. NaCl soln. (to ensure a constant air humidity of *ca.* 75%) or, alternatively, through a sat. $MgCl_2$ soln. (to obtain a humidity of *ca.* 33%) [48]. During 15 min, the system was left equilibrating, then the volatiles were adsorbed during 15 min onto a clean *Tenax*® cartridge. The sampling was repeated every hour (7 times). The cartridges were desorbed thermally and analyzed by GC (FID). Headspace concentrations (in ng/l of air) were obtained by external standard calibration of the corresponding fragrance aldehydes and ketones with EtOH solns. at five different concentrations. Each calibration soln. (0.1 µl) was injected onto *Tenax*® cartridges, which were immediately desorbed under the same conditions as those obtained from the headspace sampling. Due to the relatively low headspace concentrations of aldehydes and ketones in some cases, the calibration curves were generally forced through the origin.

For the experiment with the hydrazones, a soln. (1 ml) of a mixture of **2b**, **3c**, **6c**, **7c**, **7d**, and **10c** (each at 0.041M, **10c** at 0.021M) in EtOH was added to the TEA-esterquat emulsion (1.80 g). As reference sample, a soln. (1 ml) of a mixture of the corresponding aldehydes and ketones (each at 0.041M) in EtOH added to the TEA-esterquat emulsion (1.80 g) was used. The samples were equilibrated for 5 d, then prepared, and analyzed as described above.

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