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α,β-Unsaturated Ketoximes Carrying a Terminal Pyridine or Quinoline Subunit as Building Blocks for Supramolecular Syntheses

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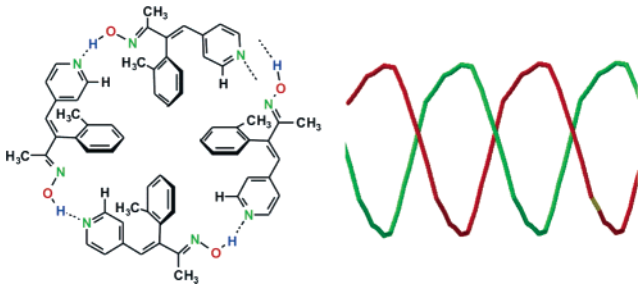

The crystal structures of a new series of α,β-unsaturated ketoximes, **8**−**14**, carrying the terminal 4-pyridinyl, 3-pyridinyl, or 4-quinolinyl subunit have been investigated by X-ray structural analysis. The dominating intermolecular interaction in all structures, except **11**, is the head−tail OH···N hydrogen bond between the oxime moiety and the nitrogen atom of the heterocyclic unit. This intermolecular interaction generates infinite chains, which are cross-linked by CH···O/N/Cl or CH···π interactions. Compound **10** has been shown to adopt a double-helical structure in the crystalline state. Compound **11** represents the only case where the unexpected head−head NOH···N(OH) hydrogen bonds determine the crystal packing. Both hydrogen-bonding and aromatic interactions stabilize the crystal structures of **8**−**14**.

Introduction

Recently, we have demonstrated the utility of α,β-unsaturated ketoximes carrying a terminal pyridine subunit (compounds of type **I**) as versatile building blocks for supramolecular syntheses.[1] X-ray structure analyses of ketoximes **1**−**7** revealed that their self-assembly is controlled by both hydrogen-bonding and aromatic interactions. The dominating hydrogen-bonding motif in all structures is the head−tail OH···N hydrogen bond between the oxime O−H moiety and the pyridine nitrogen atom. Compounds of type **I** possessing a suitably sized aromatic group as an R^1 subunit (formulas **1**−**4**) form predictably discrete cyclic tetrameric aggregates corresponding to the ring motif in Scheme 1a[1a,c] (in the case of compound **4**, the interactions between the oxime O−H moiety and the pyridine nitrogen atom are ethanol-mediated). The aromatic interactions, which stabilize all of the formed supermacrocycles, involve both the phenyl−phenyl and pyridine−phenyl interactions between the rings of the neighboring molecules. The steric demand of the aromatic R^1 group (as in the case of compound **5**, a para substituted phenyl ring) prevents the formation of discrete cyclic tetramers.[1c] Furthermore, the ketoximes in which the aromatic R^1 residue is replaced by an aliphatic group (compounds **6** and **7**) do not form the supramolecular cyclic structure because of the absence of edge−face interactions among aromatic groups projected into the "cavity" of the supermacrocycle. This type of compound prefers the formation of linear motifs (in the case of **6**, helically grown structures) with the molecules linked by OH···N−pyr hydrogen bonds (Scheme 1b).[1b,c]

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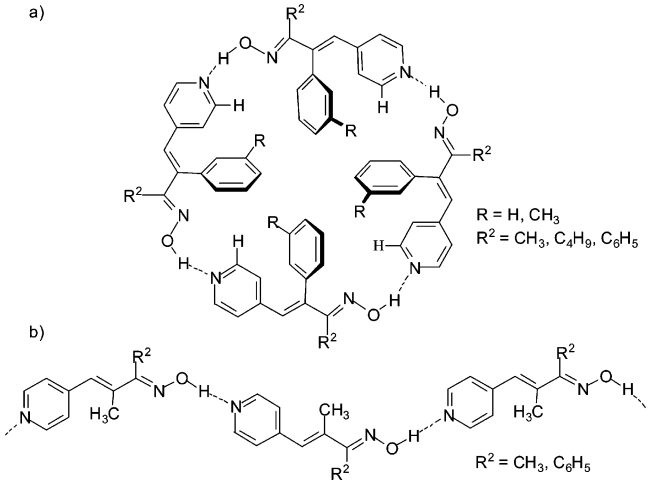
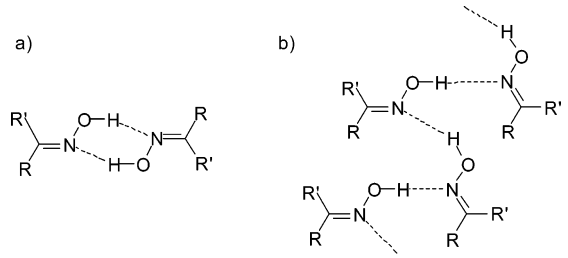
SCHEME 1. Schematic Structure of the Cyclic (a) and Linear Motif (b) in the Crystal Structures of 1−4 and 6 and 7, Respectively.[a]



[a] See ref 1.

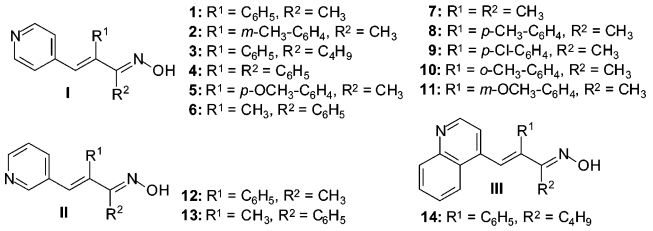
SCHEME 2. Common Hydrogen-Bonding Arrangements for the Oxime Group[a]



[a] In the absence of other hydrogen-bond donors and acceptors. Adapted from ref 2b.

The dominating head−tail OH···N hydrogen bond has also been observed in the crystal structures of other compounds displaying both oxime and pyridinyl moieties. For example, Aakeröy et al. have noted the potential of this motif for the determination of the crystal structures of oxime-substituted pyridines, such as aldoximepyridine, acetyloximepyridine, benzoyloximepyridine, and amidoximepyridine [py−C(R)NOH, where R = H, CH_3, C_6H_5, or NH_2].[2a] In the absence of other hydrogen bond donors and acceptors, the oxime−oxime OH···N hydrogen-bonded dimer (Scheme 2a) or catemeric motif (Scheme 2b) can be observed in the solid state, as shown recently for aromatic and aliphatic dioximes.[2b,3] It should be noted that oximes have received far less attention in supramolecular chemistry than other compounds such as carboxylic acids and amides.[4]

In this study, a new series of α,β-unsaturated ketoximes, **8**−**14**, carrying the terminal 4-pyridinyl, 3-pyridinyl, or 4-quinolinyl subunit (compounds of type **I**, **II**, and **III**) have been examined. The hydrogen-bonding motifs in the crystalline state have been analyzed to verify the generality of the oxime−OH···N−pyridine/quinoline hydrogen-bonding motif and to establish the suitability of this interaction for engineering molecular crystals.



Results and Discussion

Ketoximes **8**−**14** were obtained by oximation of the corresponding α,β-unsaturated ketones, which were prepared by condensation of pyridine-4-, pyridine-3-, or quinoline-4-carbaldehyde with 1-(*p*-methylphenyl)-2-propanone, 1-(*p*-chlorophenyl)-2-propanone, 1-(*o*-methylphenyl)-2-propanone, 1-(*m*-methoxyphenyl)-2-propanone, 1-phenyl-2-hexanone, or 1-(*p*-methylphenyl)-1-propanone. Crystals of **8**−**14** were obtained by slow evaporation of the solvent from ethanol solutions.

As expected, the dominating intermolecular interaction in all structures, except **11**, is the head−tail hydrogen bond from the oxime moiety to the nitrogen atom of the 3-pyridinyl, 4-pyridinyl, or 4-quinolinyl unit. Compound **11** represents the only case where the unexpected head−head NOH···N(OH) hydrogen bonds determine the crystal packing.

α,β-Unsaturated Ketoximes Carrying the Terminal 4-Pyridinyl Subunit (Compounds 8−11, Type I). A. Compound 8 (R^1 = 4-CH_3−C_6H_4, R^2 = CH_3). In the crystal structure of **8**, the oxime OH is engaged in an expected OH···N hydrogen bond to the pyridine nitrogen atom. This intermolecular interaction generates chains, which are cross-linked by weaker CH···O hydrogen bonds[5] (Figure 1). The oxime hydroxyl group forms cooperative hydrogen bonds through simultaneous participation as a donor and acceptor of hydrogen bonds (the hydrogen-bonding scheme is CH→OH→N−pyr). Similar to **5**, the steric demand of the para substituted phenyl group of **8** prevents the formation of discrete cyclic tetramers.

The OH···N distances are in the range 1.85−1.87 Å, with angles at the H atom of 164−174° (Table 1). The CH···O hydrogen bonds between the chains are formed through interactions of both the methyl group [−N=$C(CH_3)$−] and the pyr−CH_α unit with the oxime oxygen atom of the neighboring molecule (see Figure 1). The normalized distances of CH_3···OH and pyr−CH_α···OH hydrogen bonds are 2.31 and 2.59 Å (for details, see Table 1), respectively. There are also short CH···N interactions[6]

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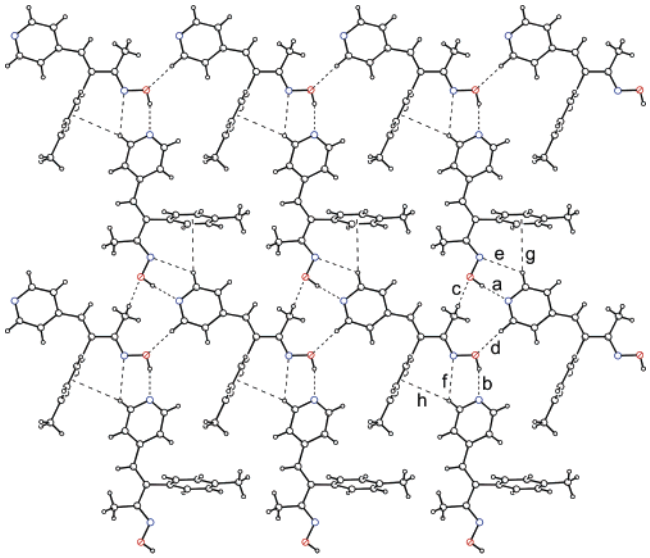

FIGURE 1. Crystal structure of **8** showing the OH···N−pyr (a and b), CH···OH (c and d), and CH···N−oxime (e and f) hydrogen bonds and the C−H···π(Ph) (g and h) interactions (for details, see Table 1).

involving the pyr−CH_α and the oxime nitrogen atom with distances of 2.72 Å (see Figure 1 and Table 1).

Within the chains, the pyridine and the phenyl ring of the adjacent molecules show edge−face orientations [pyr−CH_α···π(Ph)]; the interplanar angles between these rings alternate between 56.2 and 57.9°. The normalized pyr−CH···Ph(centroid) distances alternate between 3.13 and 3.23 Å (Table 1). Furthermore, the *p*-methylphenyl group participates in phenyl−CH_3···π(Ph) interactions[7] with the neighboring phenyl ring. The distance of the closest (Ph)CH_3···C_{Ph} contact is 3.22 Å (see Table 1), and the (Ph)CH_3···Ph(centroid) distance amounts to 3.78 Å [C−H···Ph(centroid) angle, 127.7°].

B. Compound 9 (R^1 = 4-Cl−C_6H_4, R^2 = CH_3). The crystal structure of **9** bears many common features with the preceding structure. Here again, the oxime OH is engaged in an expected OH···N hydrogen bond to the pyridine nitrogen atom. The OH···N−pyr distances amount to 1.78 Å (see Figure 2 and Table 1). Similar to **8**, the OH···N hydrogen bonds form chains that are cross-linked through CH···O hydrogen bonds involving the pyr−CH unit and the oxime oxygen atom (H···O, 2.46 Å; Table 1). Thus, the hydrogen-bonding scheme involving the oxime hydroxyl group is again CH→OH→N−pyr. The

TABLE 1. X−H···Y/X···Y Distances and X−H···Y Angles[a] in the Crystal Structures of 8−14

comp	XH···Y interactions	XH···Y (Å)	X···Y (Å)	X−H···Y angle (deg)	figure/ interaction
8	OH···N−pyr	1.85	2.73	173.8	Figure 1/a
		1.87	2.71	164.2	Figure 1/b
	=CCH_3···OH	2.31	3.37	169.0	Figure 1/c
	pyr−CH···OH	2.59	3.56	149.6	Figure 1/d
	pyr−CH···N−oxime	2.72	3.29	110.0	Figure 1/e
		2.72	3.25	113.0	Figure 1/f
	pyr−CH···Ph(centroid)	3.23	4.29	167.3[b]	Figure 1/g
		3.13	4.12	151.0[b]	Figure 1/h
	phenyl−CH_3···C_{Ph}	3.22	3.68	111.0	
9	OH···N−pyr	1.78	2.74	174.2	Figure 2/b
		1.78	2.75	164.3	Figure 2/a
	pyr−CH···OH	2.46	3.52	166.8	Figure 2/c
		2.80	3.64	134.3	Figure 2/d
	pyr−CH···N−oxime	2.74	3.35	115.8	Figure 2/e,f
	=CH···Cl	2.97	4.00	160.6	Figure 2/i
	pyr−CH···Ph(centroid)	3.22	4.19	149.4[b]	Figure 2/g
		3.27	4.24	150.0[b]	Figure 2/h
10	OH···N−pyr	1.87	2.73	172.7	Figure 4/a
	pyr−CH···N−oxime	2.59	3.26	119.6	Figure 4/b
	Ph−CH_3···OH	2.80	3.58	128.7	
	pyr−CH···C_{Ph}-6	2.90	3.95	165.2	
	pyr−CH···Ph(centroid)	3.40	4.33	144.6[b]	Figure 4/c
	4-C_{Ph}H···C_{Ph}-5	3.32	4.33	156.1	Figure 4/d
11	OH···N−oxime	1.96	2.82	144.7	Figure 5/a,b
	=CH···OCH_3	2.31	3.32	154.9	Figure 5/c
	6-C_{Ph}H···O−oxime	2.44	3.46	157.3	Figure 6/d
	5-C_{Ph}H···O−oxime	2.55	3.57	157.3	Figure 6/e
	OCH_3···N−pyr	2.45	3.47	156.2	Figure 6/f
12	OH···N−pyr	1.90	2.73	153.7	Figure 7/a,b
	2-C_{Ph}H···OH	2.41	3.44	157.9	Figure 7/c,d
13	OH···N−pyr	1.73	2.71	171.6	Figure 9/a
	2-CH···N−oxime	2.61	3.58	149.3	Figure 9/b
	pyr−CH···C_{Ph}	2.59	3.64	164.1	Figure 9/c
	pyr−CH···Ph(centroid)	2.91	3.76	136.4[b]	Figure 9/d
	4-C_{Ph}H···C_{Ph}-4	2.89	3.94	167.4	Figure 9/e
14	OH···N−quinoline	1.76	2.72	171.8	Figure 10/a
	CH_2···C_{Ph}-4	2.82	3.85	160.6	Figure 10/d
	quinoline-8-CH···Ph(centroid)	3.24	4.07	134.6[b]	Figure 10/b
	quinoline-7-CH···C_{Ph}-4	3.03	3.85	132.9	Figure 10/c

[a] Hydrogen bond criteria used: X−H···Y angle > 110°, H···Y ≤ sum of the van der Waals radii, C−H···π < 3.4 Å. [b] Y = ring midpoint.

CH···N interactions involving the pyr−CH_α and the oxime nitrogen atom have a distance of 2.74 Å (see Table 1).

There are also relatively short =CH···Cl contacts with a distance of 2.97 Å (C···Cl distance is 4.00 Å, C−H···Cl = 160.6°). The CH···Cl contact occurs near the sum of the van der Waals radii of H and Cl (2.95 or 3.0 Å as determined by Bondi[8a] and Pauling,[8b] respectively). The distance/angle criterion[9] indicates the hydrogen-bonding character of the CH···Cl interaction. Aakeröy et al. have demonstrated that the formation of CH···Cl hydrogen bonds is a universal phenomenon, which is not restricted to any specific category of compounds. The extensive occurrence of CH···Cl hydrogen bonds has been established through a systematic analysis of the Cambridge Crystallographic Database.[9]

Within the chains, the pyridine and the phenyl ring of the adjacent molecules adopt an edge−face geometry

(6) For examples of CH···N hydrogen bonds, see: (a) Mazik, M.; Bläser, D.; Boese, R. *Tetrahedron Lett.* **2000**, *41*, 5827−5831. (b) Mazik, M.; Bläser, D.; Boese, R. *Tetrahedron* **2001**, *57*, 5791−5797. (c) Thalladi, V. R.; Gehrke, A.; Boese, R. *New J. Chem.* **2000**, 463−470. (d) Thalladi, V. R.; Smolka, T.; Gehrke, A.; Boese, R.; Sustmann, R. *New J. Chem.* **2000**, *24,* 143−147. (e) Reddy, D. S.; Craig, D. C.; Desiraju, G. R. *J. Am. Chem. Soc.* **1996**, *118*, 4090. (f) Desiraju, G. R. *Crystal Engineering. The Design of Organic Solids*; Elsevier: Amsterdam, 1989; pp 166−167. (g) Taylor, R.; Kennard, O. *J. Am. Chem. Soc.* **1982**, *104*, 5063−5070.

(7) For a discussion on CH···π interactions, see: (a) Nishio, M.; Hirota, M.; Umezawa, Y. *The CH/π Interactions. Evidence, nature and consequences*; Wiley: New York, 1998. (b) Steiner, T.; Koellner, G. *J. Mol. Biol.* **2001**, *305,* 535−557. (c) Bazzicalupi, C.; Dapporto, P. *Struct. Chem.* **2004**, *15*, 259−268. (d) Novoa, J. J.; Mota, F. *Chem. Phys. Lett.* **2000**, *318,* 345−354.

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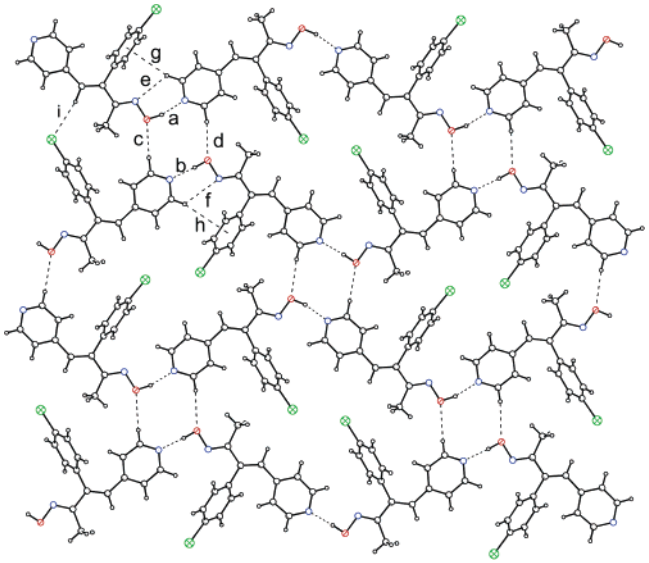

FIGURE 2. Crystal structure of **9** showing the OH···N−pyr (a and b), CH···OH (c and d), CH···N−oxime (e and f), and CH···Cl (i) bonds and the CH···π (g and h) interactions (for details, see Table 1; the Cl···Cl contact amounts to 3.58 Å).

(Figure 2). The pyr−CH_α···Ph(centroid) distance amounts to 3.22 Å (see Table 1), and the interplanar angle between the two aromatic rings is 89.5°. There are also interlayer offset face−face interactions between the phenyl rings with an average $\pi-\pi$ stacking distance of 3.38 Å; see Figure 3).

C. Compound 10 (R^1 = 2-CH_3−C_6H_4, R^2 = CH_3). The common feature of the crystal structure of **10** is the formation of the O−H···N−pyr hydrogen bonds as well as the pyridine−phenyl and phenyl−phenyl interactions between the neighbors. These interactions generate chains with a helical shape, as shown in Figure 4. Interestingly, the chains undergo dimerization into double-helical supramolecular architectures. Contrary to the meta substituted analogue **2**,[1c] the molecules of **10** do not form the expected cyclic aggregates depicted in Scheme 1a, although broadly similar intermolecular interactions are observed in both of the crystal structures (see Figure 4d).

The O−H···N−pyr bond length in the structure of **10** is 1.87 Å, and the pyr−CH_α···N−oxime contact has a distance of 2.59 Å (details are given in Table 1). The pyridine and the phenyl ring of the adjacent molecules adopt an edge−face orientation (see Figure 4c,d). The pyr−CH_α···Ph(centroid) distance amounts to 3.40 Å, and the distance of the closest pyr−CH_α···C_{Ph}(6-C_{Ph}) contact is 2.90 Å (Table 1). The interplanar angle between the two rings is 91.9°.

The ortho substituted phenyl rings of the neighbors participate in edge−face interactions (see Figure 4c,d).[10] The closest CH···C_{Ph} interaction is formed between the 4-CH and the 5-C of the adjacent rings and has a distance of 3.32 Å. The interplanar angle between the neighboring phenyl rings is alternating between 93.5 and 86.5°.

There are also relatively short CH···O interactions involving the (Ph)CH_3 and the oxime oxygen atom with a distance of 2.80 Å. The double helices are connected via offset face−face pyridine−pyridine interactions (with an average $\pi-\pi$ stacking distance of 3.5 Å).

Other hydrogen-bonding interactions have also been used to form double-helical architectures. For example, self-assembled helices from 2,2′-benzimidazoles have been reported by Sessler et al.[11] Adjacent 2,2′-benzimidazoles were found to be bound together in the solid state by pairs of NH···N hydrogen bonds, forming twisted ribbonlike columns which resemble double helices. The formation of supramolecular double helices by dimerization of helical oligopyridine−dicarboxamide strands has been described by Huc and Lehn et al.[12] Dimerization of single-helical strands with five or seven pyridine rings has been studied in solution and in the solid state. According to these studies, both aromatic stacking and hydrogen bonding contribute to the double-helical arrangement of the oligopyridine−dicarboxamide strand. The hydrogen-bonding interactions involve NH···N−pyr and NH···O=C hydrogen bonds. Some of the hydrogen-bonding motifs found in the crystal structures of the oligopyridine−dicarboxamides were also found in the crystals of the related compounds *N,N′*-bis(6-methylpyridin-2-yl)isophthalamide and *N,N′*-bis(6-aminopyridin-2-yl)isophthalamide.[13]

A double-helical assembly in inclusion crystals of fumaropimaric acid has been reported by Miyata et al.[14] In this case, each helix is retained by the cyclic hydrogen-bonding network involving a pair of OH···O=C hydrogen bonds (carboxylic acid dimer).

D. Compound 11 (R^1 = 3-OCH_3−C_6H_4, R^2 = CH_3). Among the examined crystal structures, the structure of **11** is the only one that does not include the typical head−tail hydrogen bond from the oxime moiety to the nitrogen atom of the heterocyclic unit. The characteristic feature of this crystal structure is the presence of a head−head NOH···N(OH) motif, which is typical for oximes lacking other hydrogen-bond donors and acceptors (see Scheme 2a).

The molecules of **11** exist in the solid state as oxime−OH···N−oxime (H···N = 1.96 Å) hydrogen-bonded dimers,[15] which are connected via CH···O hydrogen bonds between the =CH unit and the ether oxygen atom of the adjacent molecules (H···O = 2.31 Å), as shown in Figure 5. The dimers are furthermore linked with the dimers from the other layers by CH···O/N hydrogen bonds and π stacking interactions between the pyridine rings (with an average $\pi-\pi$ stacking distance of 3.5 Å), as illustrated in Figure 6. The CH···O/N hydrogen bonds involve the interactions between the phenyl 5-CH/6-CH and the oxime oxygen atom (6-CH_{Ph}···OH = 2.44 Å and 5-CH_{Ph}···OH = 2.55 Å; for details, see Table 1) and the

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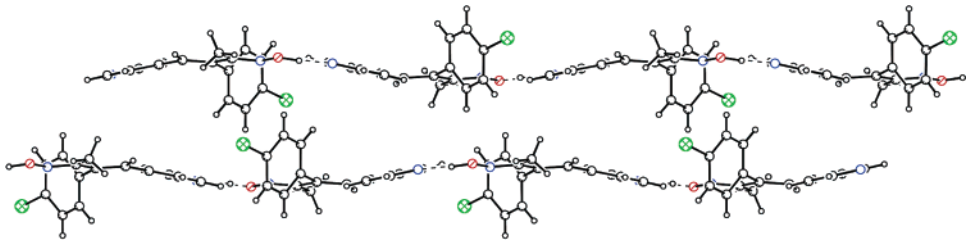


FIGURE 3. Crystal structure of **9** showing the phenyl−phenyl interactions between the chains from the adjacent sheets.

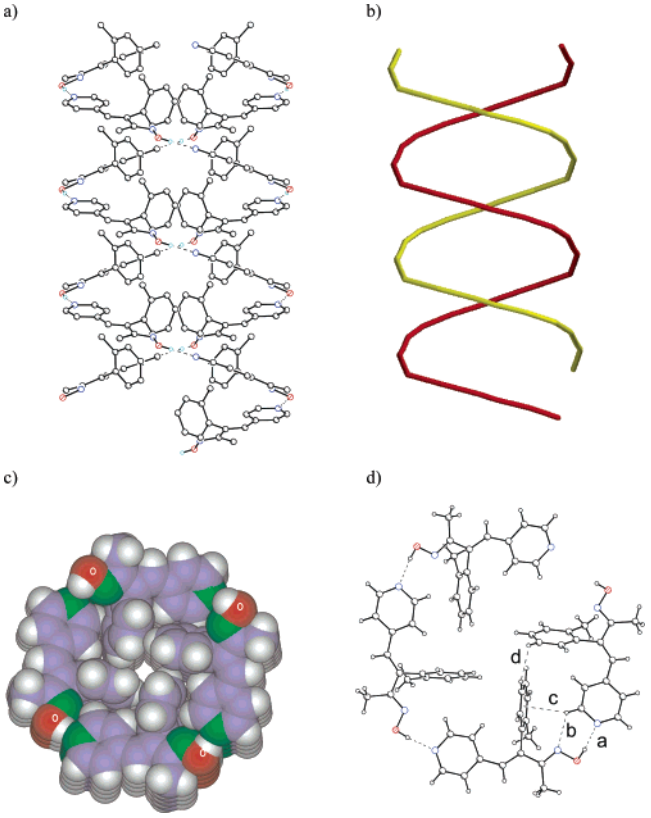


FIGURE 4. (a) Double helix in the crystal structure of **10** (non-hydrogen-bonded CH hydrogens are omitted for clarity). (b) Schematic representation of the double helix. (c) Space-filling representation of the double helix (top view). (d) OH···N−pyr (a), CH···N−oxime (b), and C−H···π interactions (pyridine−phenyl and phenyl−phenyl interactions are represented by c and d, respectively) between the adjacent molecules of **10** (see Table 1).

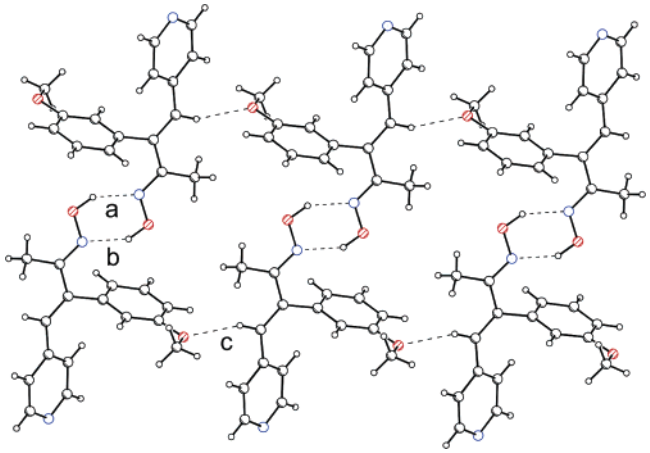


FIGURE 5. Crystal structure of **11** showing the O−H···N−oxime (a and b) and =C−H···OCH_3 (c) hydrogen bonds (bond lengths and angles are given in Table 1).

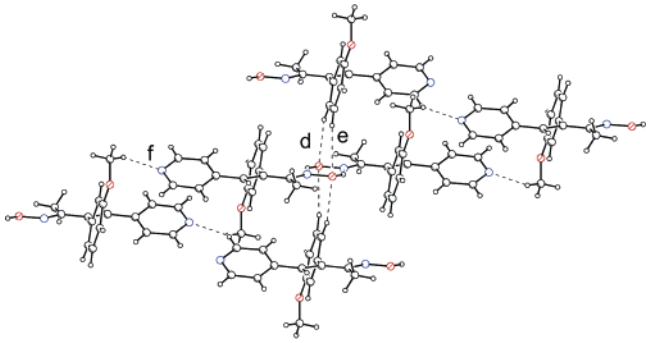


FIGURE 6. Crystal structure of **11** showing the interlayer interactions with the oxime−OH···N−oxime hydrogen-bonded dimer. The CH_{Ph}···O−oxime (d and e) and OCH_3···N−pyr (f) hydrogen bonds and face−face pyridine−pyridine interactions are shown (see Table 1).

interactions between the methoxy group and the pyridine nitrogen atom (OCH_3···N−pyr = 2.45 Å; Table 1).

α,β-Unsaturated Ketoximes Carrying the Terminal 3-Pyridine Subunit (Compounds 12 and 13, Type II). A. Compound 12 ($R^1 = C_6H_5$, $R^2 = CH_3$; 3-Pyridinyl Analogue of 1). Compound **12** forms a network held together by OH···N/CH···O hydrogen bonds and pyridine−phenyl/phenyl−phenyl interactions. The molecules of **12** interact through strong OH···N−pyr hydrogen bonds forming chains, which are pairwise bound via CH···O interactions. The resulting structure is shown in Figure 7. Each molecule of **12** forms four hydrogen bonds to three neighboring residues. The oxime hydroxyl participates in cooperative hydrogen bonds, forming simultaneous C−H···O and O−H···N hydrogen bonds (the hydrogen-bonding scheme is CH→OH→N−pyr). Within the chains, the molecules of **12** adopt a head−tail packing motif. Neighboring chains run antiparallel to each other.

The OH···N distance is 1.90 Å with an angle at the H atom of 153.7° (Table 1). The CH···O hydrogen bonds between the chains are formed through an interaction of the 2-CH_{Ph} unit with the oxime oxygen atom of the neighboring molecule (see Figure 7); the normalized distances of CH···OH hydrogen bonds are 2.41 Å (see Table 1).

Within the chains, the pyr−CH_α···Ph(centroid) distance amounts to 3.99 Å (C_{pyr}···Ph(centroid) distance = 5.06 Å, C−H···Ph(centroid) angle = 171.0°). The interplanar angle between the two rings is 80.2°. Within the double-chain architecture, the pyridine rings are lying

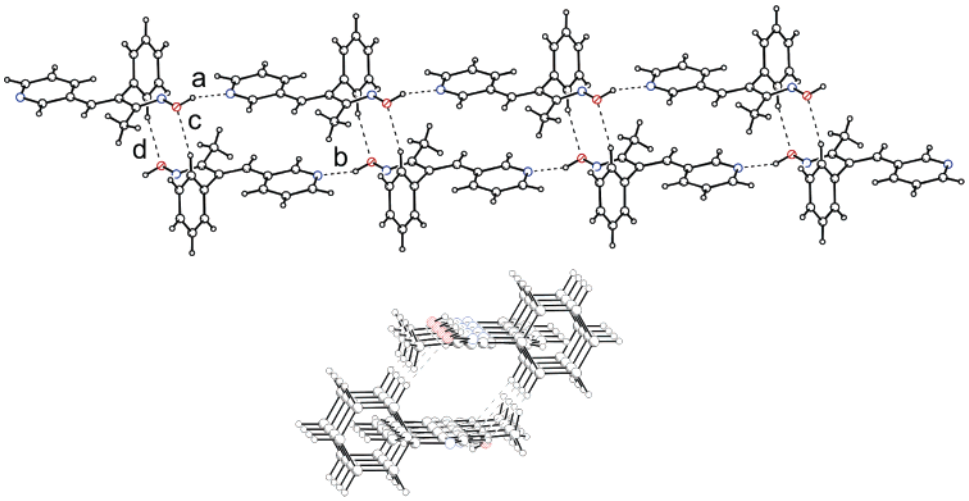


FIGURE 7. Crystal structure of **12** showing the O−H···N−pyr (a and b) and CH_{Ph}···OH (c and d) hydrogen bonds (see Table 1) and offset face−face pyridine−pyridine interactions (two different views).

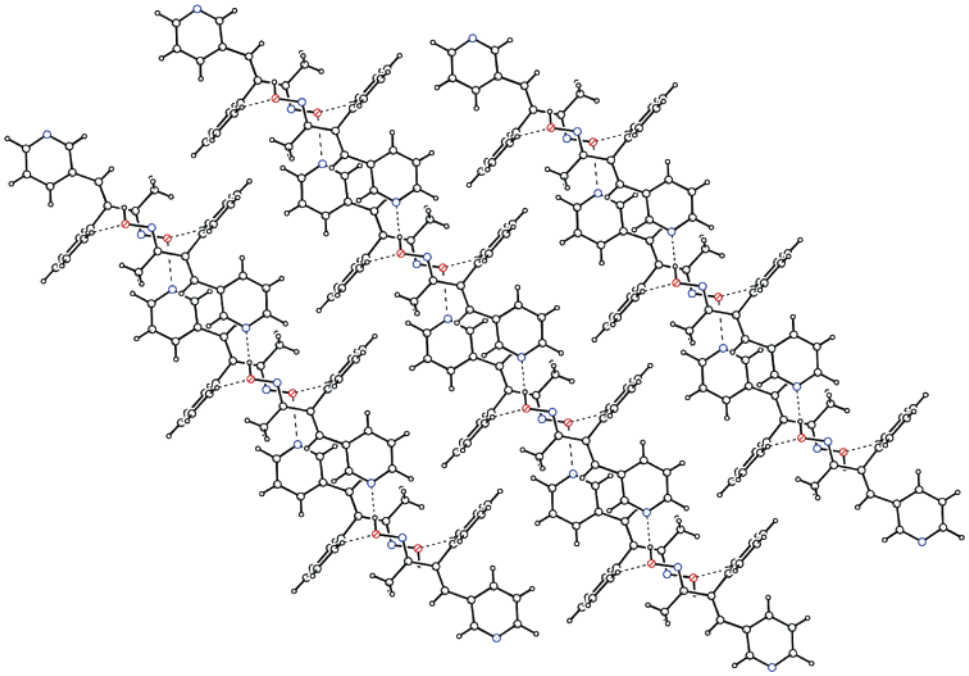


FIGURE 8. Crystal structure of **12** showing the offset phenyl−phenyl interactions between the double-chain architectures.

above one another in an offset face−face stacking arrangement (with a $\pi-\pi$ stacking distance of 3.47 Å). Between the double-chain arrangements, the offset face−face phenyl−phenyl interactions (with an average $\pi-\pi$ stacking distance of 3.48 Å) can be recognized, as shown in Figure 8.

B. Compound 13 ($R^1 = CH_3$, $R^2 = C_6H_5$; 3-Pyridinyl Analogue of 6). The molecules of **13** are arranged in infinite hydrogen-bonded chains with OH···N−pyr distances of 1.73 Å (see Figure 9 and Table 1). The molecules adopt a head−tail orientation (Figure 9, top). Within a sheet, the chains are in a parallel orientation, and the chains from adjacent sheets adopt an orthogonal orientation. The phenyl CH (ortho position) participates in CH···N(OH)= hydrogen bonds with the oxime nitrogen atom (interlayer interactions); the CH···N distances are 2.61 Å. The pyridine and the phenyl ring of the adjacent molecules (from neighboring sheets) adopt an edge−face geometry with a pyr−CH_α···Ph(centroid) distance of 2.91 Å; the closest pyr−CH···C_{Ph} interaction has a distance of 2.59 Å (see Table 1). The interplanar angle between the neighboring pyridine and phenyl rings is 72.7°. Furthermore, phenyl−phenyl interactions stabilize the crystal structure of **13**. The closest CH···C_{Ph} interaction is formed between the 4-CH and the 4-C of the adjacent rings (see Figure 9 bottom), and the H···C_{Ph} distance amounts to 2.89 Å.

α,β-Unsaturated Ketoxime Carrying a Terminal 4-Quinoline Subunit. A. Compound 14, Type III. The crystal structure of ketoxime **14** (4-quinolinyl analogue of **3**) provides a further example of the present type of control of molecular self-assembly via hydrogen-bonding and aromatic interactions. The predominant hydrogen-bond interaction is the head−tail OH···N hydrogen bond

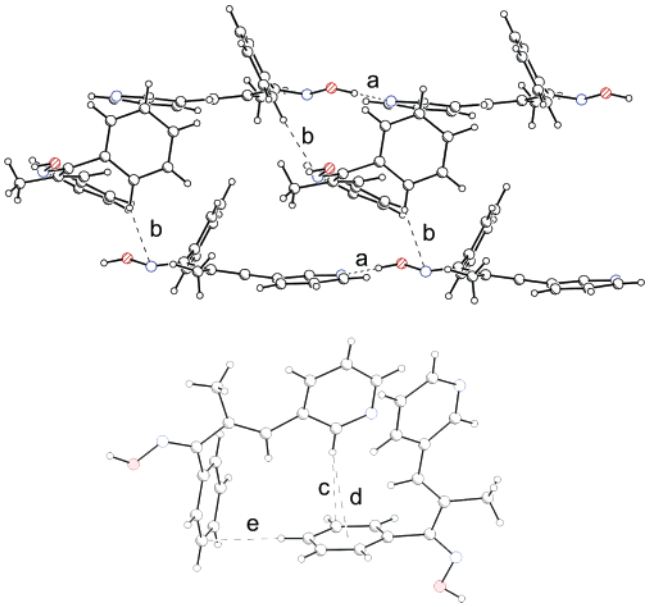


FIGURE 9. Crystal structure of **13** showing the O−H···N−pyr (a), C−H···N−oxime (b), and C−H···π(Ph) (c−e) interactions (for details, see Table 1).

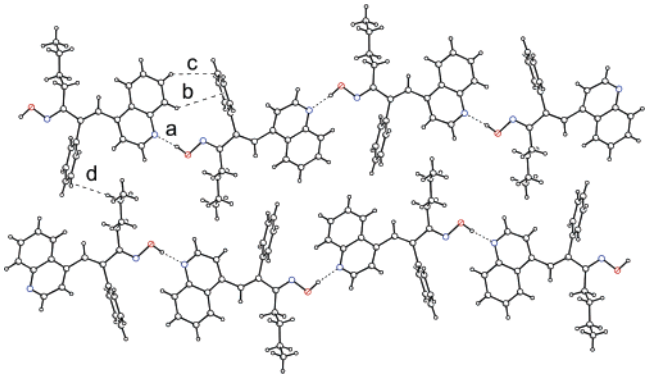


FIGURE 10. Crystal structure of **14** showing the O−H···N−guinoline (a) hydrogen bonds and C−H···Ph interactions (b−d; see Table 1).

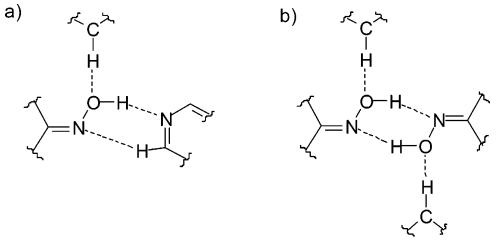
involving the oxime O−H and the quinoline nitrogen atom (Figure 10). This intermolecular interaction generates infinite chains. Neighboring chains run antiparallel to each other. The OH···N distance amounts to 1.76 Å with an angle at the H atom of 171.8° (Table 1).

The distance of the quinoline hydrogen atom (8-CH) to the center of the phenyl ring of the neighboring molecule amounts to 3.24 Å; the intermolecular distance of the closest quinoline−CH···Ph contact is 3.03 Å (see Table 1). The interplanar angle between the quinoline and the phenyl ring of adjacent molecules amounts to 70°.

In addition, the interchain interactions involve the CH···π(Ph) interactions between the *n*-butyl group and the phenyl ring (Figure 10). The 3-C(H)−H of the *n*-butyl group points at the 4-C atom of the phenyl ring (CH···C = 2.82 Å; Table 1).

The crystal structures of **8**−**14** show that all the molecules adopt the *E* configuration of the C=C and C=N bonds. Compounds **8**, **9**, **12**, and **13** crystallize with two independent molecules in the asymmetric unit (in the case of **13**, these molecules are rotamers), as shown in Figure S1 (Supporting Information). The pyridine 3-CH of **8**−**11**, the pyridine 4-CH of **12**, and the quinoline 3-CH of **14** participate in intramolecular CH···π interactions with the phenyl ring. The CH···π(Ph) distances are in the range 2.40−2.90 Å with angles at the H atom of 117−155°. The interplanar angles between the pyridine and the phenyl rings are in the range 60−110° (in the case of **10**, 90.9°).

SCHEME 3. Hydrogen-Bonding Arrangements for the Oxime Group in the Crystal Structures of 8−10, 12−14 (a), and 11 (b).



Conclusion

The results showed that α,*β*-unsaturated ketoximes carrying a terminal pyridine or quinoline subunit are versatile building blocks for supramolecular syntheses. The dominating intermolecular interaction in all structures, except **11**, is the head−tail hydrogen bond from the oxime moiety to the nitrogen atom of the 3-pyridinyl, 4-pyridinyl, or 4-quinolinyl unit. Compound **11** represents the only case where the unexpected head−head NOH···N(OH) hydrogen bonds determine the crystal packing.

The head−tail OH···N hydrogen bond generates, in the crystal structures of **8**, **9**, **12**, **13**, and **14**, infinite chains that are cross-linked by CH···O/N/Cl or CH···π interactions. In the case of compound **10**, the chains undergo dimerization into double-helical supramolecular architectures. Similar to the case for **5**, the steric demand of the para substituted phenyl group of **8** and **9** prevents the formation of discrete cyclic tetramers (which are typical for oximes possessing a suitably sized aromatic group as an R^1 subunit, such as formulas **1**−**4**). The molecules of **11** exist in the solid state as oxime−OH···N−oxime hydrogen-bonded dimers, which are further connected via CH···O/N hydrogen bonds. Thus, the C−H···O/N interactions[5,6] play an important role in the stabilization of the crystal structures of **8**−**14**. The oxime hydroxyl group forms cooperative hydrogen bonds through simultaneous participation as a donor and acceptor of hydrogen bonds. The typical hydrogen-bonding scheme involving an oxime OH group is CH→OH→N−het. Typical hydrogen-bonding motifs found in the crystals of **8**−**14** are shown in Scheme 3.

The CH···O interactions with the oxime oxygen have also been considered in drug design. For example, the complex between the human retinoic acid receptor hRAR and an oxime ihibitor[5h] is stabilized via CH···O hydrogen bonds between the oxime oxygen (the OH group acts as an H bond acceptor and donor) and relatively nonpolar amino acid side chains (Met272 and Ile275).[5a,5h]

The common feature of the crystal structures of **8**−**14** is also the formation of the pyridine/quinoline−phenyl and phenyl−phenyl interactions[10,16] between the neigh-

boring molecules. Thus, both the hydrogen-bonding and aromatic interactions stabilize all the crystal structures.

Experimental Section

Analytical thin-layer chromatography (TLC) was carried out on Kieselgel 60 F_{254} plates employing a methanol/chloroform 1:7 (v/v) or benzene/ethyl acetate 3:1 (v/v) mixture as the mobile phase. Chemical shifts are reported in ppm downfield from tetramethylsilyl (TMS) as an internal standard (solvent $CDCl_3$)

General Procedure for the Synthesis of 8−14. A mixture of the corresponding carbaldehyde (0.025 mol) and ketone (0.05 mol) in chloroform (150 mL) was saturated with gaseous hydrogen chloride (0.05 mol) at 0−5 °C. Then, the reaction mixture was kept at 25 °C for 48 h. Chloroform was evaporated, and the residue was washed several times with diethyl ether. The residual product was dried under vacuum. The crude hydrochlorides of the obtained α,β-unsaturated ketones were used for the oximation reactions without further purification. The mixture of pyridinyl- or quinolinyl-α,β-unsaturated ketone hydrochloride (0.025 mol), hydroxylamine hydrochloride (0.075 mol), and sodium hydroxide (0.05 mol) in aqueous ethanol (100 mL) was refluxed for 4 h and then poured into water (150 mL). The oxime formed was filtered off and crystallized from ethanol. Additionally, the water solution (after evaporation of ethanol) was extracted with chloroform. After the chloroform separation, the residual product was crystallized from ethanol.

3-(4-Methylphenyl)-4-(pyridin-4-yl)-3-buten-2-onoxime (8). Yield: 75%. Mp: 165−166 °C. ^{1}H NMR (500 MHz): δ 2.01 (s, 3H), 2.31 (s, 3H), 6.71 (dd, 2H, J = 6.3/1.5 Hz), 6.73 (s, 1H), 6.91 (d, 2H, J = 7.8 Hz), 7.08 (d, 2H, J = 7.8 Hz), 8.24 (dd, 2H, J = 6.3/1.5 Hz), 9.10 (s, 1H). ^{13}C NMR (125 MHz): δ 11.8, 21.8, 124.4, 127.9, 129.7, 129.9, 133.9, 138.3, 144.5, 144.7, 149.6, 158.6. HRMS: calcd for $C_{16}H_{16}N_2O$, 252.1263; found, 252.1257. Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.08; H, 6.43; N, 11.19. R_f = 0.56 (methanol/chloroform 1:7 v/v).

3-(4-Chlorophenyl)-4-(pyridin-4-yl)-3-buten-2-onoxime (9). Yield: 79%. Mp: 198−199 °C. ^{1}H NMR (500 MHz): δ 2.05 (s, 3H), 6.70 (d, 2H, J = 5.3 Hz), 6.78 (s, 1H), 6.98 (d, 2H, J = 8.2 Hz), 7.25 (d, 2H, J = 8.2 Hz), 8.26 (d, 2H, J = 5.3 Hz), 9.11 (s, 1H). ^{13}C NMR (125 MHz): δ 11.5, 124.3, 128.8, 129.5, 131.4, 134.5, 135.5, 143.1, 144.1, 149.9, 158.2. HRMS: calcd for $C_{15}H_{13}ClN_2O$, 272.0716; found, 272.0734. Anal. Calcd for $C_{15}H_{13}ClN_2O$: C, 66.05; H, 4.80; N, 10.31; Cl, 12.99. Found: C, 66.18; H, 4.95; N, 10.17; Cl, 12.79. R_f = 0.19 (benzene/ethyl acetate 3:1 v/v).

3-(2-Methylphenyl)-4-(pyridin-4-yl)-3-buten-2-onoxime (10). Yield: 53%. Mp: 144−145 °C. ^{1}H NMR (500 MHz): δ 2.03 (s, 3H), 2.13 (s, 3H), 6.67 (dd, 2H, J = 6.1/1.4 Hz), 6.85 (s, 1H), 6.95 (dd, 1H, J = 8.6/1.1 Hz), 7.16−7.22 (m, 2H), 7.26−7.29 (m, 1H), 8.27 (d, 2H, J = 6.1 Hz), 8.67 (s, 1H). ^{13}C NMR (125 MHz): δ 10.6, 19.4, 123.5, 126.4, 128.0, 128.4, 129.1, 130.5, 135.8, 136.4, 143.9, 144.2, 149.0, 157.3. HRMS: calcd for $C_{16}H_{16}N_2O$, 252.1263; found, 252.1266. Anal. Calcd for $C_{16}H_{16}N_2O$: C, 76.16; H, 6.39; N, 11.10. Found: C, 76.04; H, 6.47; N, 11.21. R_f = 0.50 (methanol/chloroform 1:7 v/v).

3-(3-Methoxyphenyl)-4-(pyridin-4-yl)-3-buten-2-onoxime (11). Yield: 40%. Mp: 168−169 °C. ^{1}H NMR (500 MHz): δ 2.11 (s, 3H), 3.75 (s, 3H), 6.66−6.80 (m, 6H), 7.27 (t, 1H, J = 7.7 Hz), 8.34 (dd, 2H, J = 6.2/1.5 Hz), 8.90 (s, 1H). ^{13}C NMR (125 MHz): δ 12.0, 56.0, 112.4, 113.9, 119.4, 123.1, 130.8, 129.9, 135.7, 142.0, 144.4, 150.1, 159.3, 159.9. HRMS: calcd for $C_{16}H_{16}N_2O_2$, 268.1212; found, 268.1219. Anal. Calcd for $C_{16}H_{16}N_2O_2$: C, 71.62; H, 6.01; N, 10.44. Found: C, 71.55; H, 6.13; N, 10.59. R_f = 0.59 (methanol/chloroform 1:7 v/v).

3-Phenyl-4-(pyridin-3-yl)-3-buten-2-onoxime (12). Yield: 80%. Mp: 155−156 °C. ^{1}H NMR (500 MHz): δ 2.14 (s, 3H), 6.91 (s, 1H), 6.97−6.99 (m, 1H), 7.01−7.03 (m, 1H), 7.14−7.15 (m, 2H), 7.37−7.39 (m, 3H), 8.31−8.33 (m, 2H), 8.86 (s, 1H). ^{13}C NMR (125 MHz): δ 11.6, 123.2, 127.3, 128.3, 129.3, 129.9, 132.5, 136.4, 137.3, 142.2, 148.4, 151.5, 158.6. HRMS: calcd for $C_{15}H_{14}N_2O$, 238.1106; found, 238.1108. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.52; H, 6.04; N, 11.87. R_f = 0.14 (benzene/ethyl acetate 3:1 v/v).

2-Methyl-1-phenyl-3-(pyridin-3-yl)-2-propen-1-onoxime (13). Yield: 83%. Mp: 145−146 °C. ^{1}H NMR (500 MHz): δ 2.20 (d, 3H, J = 1.3 Hz), 6.42 (q, 1H, J = 1.3 Hz), 7.30−7.33 (m, 1H), 7.36−7.38 (m, 3H), 7.64−7.66 (m, 2H), 7.73−7.75 (m, 1H), 8.50 (dd, 1H, J = 5.9/1.4 Hz), 8.66 (d, 1H, J = 1.4 Hz), 9.23 (s, 1H). ^{13}C NMR (125 MHz): δ 17.5, 123.3, 127.2, 127.8, 128.5, 129.5, 132.4, 134.5, 134.8, 136.3, 147.9, 150.1, 159.9. HRMS: calcd for $C_{15}H_{14}N_2O$, 238.1106; found, 238.1112. Anal. Calcd for $C_{15}H_{14}N_2O$: C, 75.61; H, 5.92; N, 11.76. Found: C, 75.49; H, 6.06; N, 11.90. R_f = 0.55 (methanol/chloroform 1:7 v/v).

2-Phenyl-1-(quinolin-4-yl)-1-hepten-3-onoxime (14). Yield: 65%. Mp: 169−170 °C. ^{1}H NMR (500 MHz): δ 0.96 (t, 3H, J = 7.2 Hz), 1.45 (m, 2H), 1.63 (m, 2H), 2.67 (t, 2H, J = 7.5 Hz), 6.81 (d, 1H, J = 4.4 Hz), 7.07 (d, 2H, J = 7.6 Hz), 7.20−7.22 (m, 3H), 7.43 (s, 1H), 7.62 (t, 1H), 7.74 (t, 1H), 8.09 (d, 1H, J = 8.2 Hz), 8.14 (d, 1H, J = 8.2 Hz), 8.57 (d, 1H, J = 4.4 Hz), 9.20 (s, 1H). ^{13}C NMR (125 MHz): δ 13.9, 22.9, 25.2, 28.5, 121.8, 124.07, 125.7, 126.8, 127.3, 128.3, 129.5, 129.7, 129.8, 136.4, 143.0, 143.8, 147.8, 149.4, 162.1. HRMS: calcd for $C_{22}H_{22}N_2O$, 330.1726; found, 330.1730. Anal. Calcd for $C_{22}H_{22}N_2O$: C, 79.97; H, 6.71; N, 8.48. Found: C, 79.84; H, 6.89; N, 8.61. R_f = 0.51 (methanol/chloroform 1:7 v/v).

X-ray Crystallographic Analysis. Crystallographic data for the structures reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC 238313 (**8**), 238314 (**9**), 238312 (**10**), 238315 (**11**), 238316 (**12**), 238317 (**13**), and 238318 (**14**). The coordinates can be obtained, on request, from the Director, Cambridge Crystallographic Data Centre, 12 Union Road, Cambridge, CB2 1EZ, UK (fax: +44-1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

X-ray data for compounds **8**−**14** are also given in the Supporting Information.

Acknowledgment. This work was supported by the Deutsche Forschungsgemeinschaft.

Supporting Information Available: X-ray data for compounds **8**−**14.** This material is available free of charge via the Internet at http://pubs.acs.org.

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(16) For a discussion on aromatic interactions in supramolecular chemistry and in biomolecules, see: (a) Hunter, C. A.; Lawson, K. R.; Perkins, J.; Urch, C. J. *J. Chem. Soc., Perkin Trans. 2* **2001**, 651−669. (b) Meyer, E. A.; Castellano, R. K.; Diederich, F. *Angew. Chem.* **2003**, *115,* 1244−1287.