DOI: 10.1002/ejoc.201000376

Preparation of Imino Lactones by Electrophilic Cyclization of β,γ-Unsaturated Hydroxamates: Formation of 3-Cyanoprop-2-en-1-ones through Fragmentation Reactions

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Keywords: Nitriles / Lactams / Lactones / Bromonium ions / Electrophilic cyclization

Treatment of γ-disubstituted β,γ-unsaturated hydroxamates with bis(collidine)bromine(I) hexafluorophosphate led mainly to the formation of cyclic bromo imidates – the thermodynamic products. Unsaturated cyclic imidates were then obtained by treatment with triethylamine. With γ-aryl β,γ-unsaturated hydroxamates, the corresponding cyclic bromo imidates were also obtained. On treatment with triethylamine, however, these compounds led to the formation of 3-cyanoprop-2-en-1-ones in good yields through fragmentation reactions.

Introduction

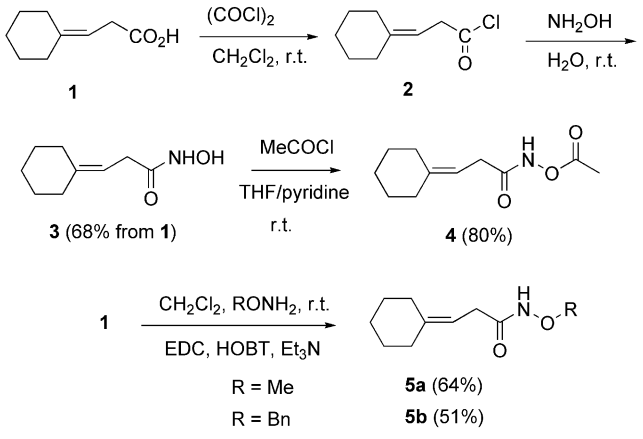
Electrophilic cyclization of unsaturated amides has been reported to lead to the formation either of imino lactones (or the corresponding immonium salts) or of lactams, depending on the structures of the amides, the substituents on the nitrogen and (or) the natures of the electrophiles.[1] Our research into the reactivity of bis(collidine)bromine(I) hexafluorophosphate[2] led us to examine the case of unsaturated hydroxamates. Their reaction behaviour with electrophiles has been briefly reported on in the literature. With bromine or *N*-bromosuccinimide the formation of lactams was observed,[3] whereas with selenium reagents, on the other hand, mixtures of γ-butyrolactams and immonium salts were generally obtained.[4] These immonium salts rearranged to the thermodynamically more stable lactams on heating.

We recently reported the synthesis of enantiomerically pure γ-butyrolactones through diastereoselective halolactonization of β,γ-unsaturated acids.[5] These results prompted us to study the possible application of this cyclization methodology for the preparation of optically pure γ-butyrolactams. Indeed, there are still no efficient syntheses of optically γ-butyrolactams possessing a tetrasubstituted C atom in α position to the N atom.[6]

Results and Discussion

a) Reactivities of γ-Disubstituted β,γ-Unsaturated Hydroxamates

We first decided to examine the reactivity of γ-disubstituted β,γ-unsaturated hydroxamates. These compounds were prepared from the corresponding acids either by treatment of the corresponding acid chlorides with hydroxyl- or *O*-alkylhydroxylamines or by direct treatment of the acids with the *O*-alkylhydroxylamines. We first examined the reactivities of the hydroxamic acid **3** and the hydroxamates **4**, **5a** and **5b**, obtained from 3-cyclohexylidenepropanoic acid (**1**).[7] These compounds were prepared as reported in Scheme 1. The hydroxamate **4** was obtained by treatment of 3-cyclohexylidenepropanoyl chloride (**2**) with aqueous hydroxylamine, followed by acylation with acetyl chloride. The hydroxamates **5a** and **5b** were formed by coupling of the acid function of compound **1** with the corresponding *O*-alkylhydroxylamines by a reported method.[8] These compounds were easily characterized by their NMR and IR spectra. Table 1 lists the results of their treatment with bis(collidine)bromine(I) hexafluorophosphate. No reaction was observed with the hydroxamic acid **3**, although decomposition of the bromo reagent due to the high acidity of this compound was observed. To avoid this drawback, hy-



Scheme 1. Preparation of the hydroxamates **4**, **5a** and **5b**.

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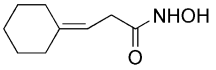
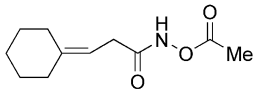
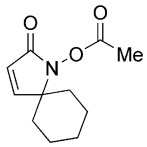
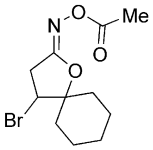
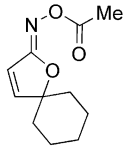
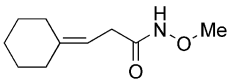
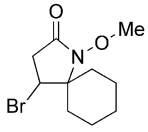
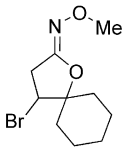
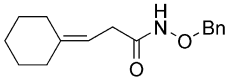
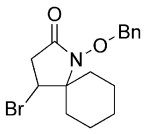
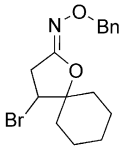
Table 1. Treatment of the hydroxamic acid **3** and the hydroxamates **4**, **5a** and **5b** with bis(collidine)bromine(I) hexafluorophosphate.

Entry	Reactant	Reaction conditions	Products (yield, %)			
a	 **3**	CH_2Cl_2, r.t., 1h	no reaction			
b	 **4**	CH_2Cl_2, r.t., 1h	 12[b] **6**	+  29[b] **7**	+  59[b] **8**	(85)[a]
c	**4**	toluene, –20 °C, 2h		100[b] **7**		(77)[a]
d	 **5a**	CH_2Cl_2, r.t., 1h	 23[b] **9**	+  77[b] **10**		(65)[a]
e	**5a**	toluene, r.t., 1h	12[b] **9**	88[b] **10**		(67)[a]
f	**5a**	toluene, –20 °C, 2h		100[b] **10**		(68)[a]
g	**5a**	$CHCl_3$, r.t., 1h	16[b] **9**	84[b] **10**		(63)[a]
h	**5a**	pentane, r.t., 1h	12[b] **9**	88[b] **10**		(60)[a]
i	 **5b**	CH_2Cl_2, r.t., 1h	 28[b] **11**	+  72[b] **12**		(92)[a]

[a] Global yield. [b] Proportion (^{1}H NMR) of the products in the crude reaction mixture (%).

droxamates were examined. With the hydroxamate **4** (Entry b), in dichloromethane at room temperature a mixture of three products was obtained: one lactam (compound **6**) and two cyclic imidates (compounds **7** and **8**). The unsaturated compounds **6** and **8** were probably formed by elimination of HBr from the initially formed bromo products. The structures of these different compounds were established from their NMR and IR spectra, and the structure of the unsaturated cyclic imidate **8** was confirmed from its single-crystal X-ray data (Figure 1).

More interestingly, in toluene at –20 °C only the cyclic bromo imidate **7** was isolated (Entry c). This bromo compound **7** appeared to be unstable, and partial elimination of HBr could be observed during its purification over silica. After standing at room temperature, rearrangement of the compound **6** into the cyclic imidate **8** was observed.

Mixtures of bromo lactams and cyclic bromo imidates were also observed from the *N*-methoxy hydroxamate **5a** and the *N*-benzyloxy hydroxamate **5b** when the cyclizations were carried out in dichloromethane at room temperature (Table 1, Entries d, i). With these cyclic imidates **10** and **12**, no HBr elimination was observed in dichloromethane. Rearrangement of the bromo lactams **9** and **11** into the cyclic bromo imidates and/or unsaturated cyclic imidates was observed during purification or on standing at room temperature. Our study shows only small variation – probably due to the electronic effects of the substituents – in the *N*- and

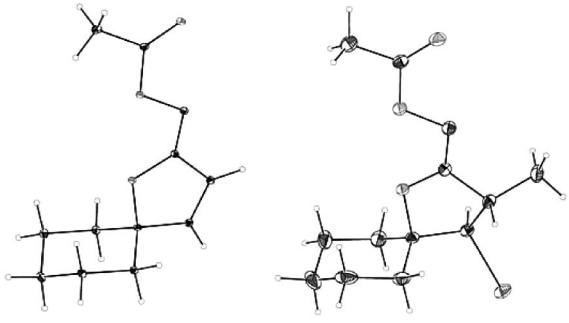
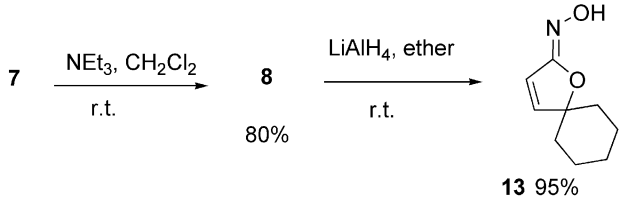


Figure 1. ORTEP drawing of the unsaturated imino lactone **8** and the bromo imino lactone **41**.

O-cyclization ratios as a function of the group on the nitrogen atom (Entries b, d and i).

We also examined the reactivity of hydroxamate **5a** in chloroform, toluene and pentane. Formation of the bromo imino lactone **10** was mainly observed. Lowering the temperature of the reaction enhanced its selectivity (Entries e, f). Otherwise, heating of the unsaturated lactam **6** in chloroform for 30 min led to its quantitative transformation into the cyclic imidate **8**. Such rearrangements have been reported in the literature, and in some cases have been shown to be equilibria.[9] The reverse transformation reaction has also been reported.[4] These results indicated that this rearrangement is related to the relative thermodynamic stabilities of the *N*-alkoxylactam and of the cyclic imidate. This relative stability seems to be influenced by the heteroatom attached to the carbon β to the carbonyl or imine group.

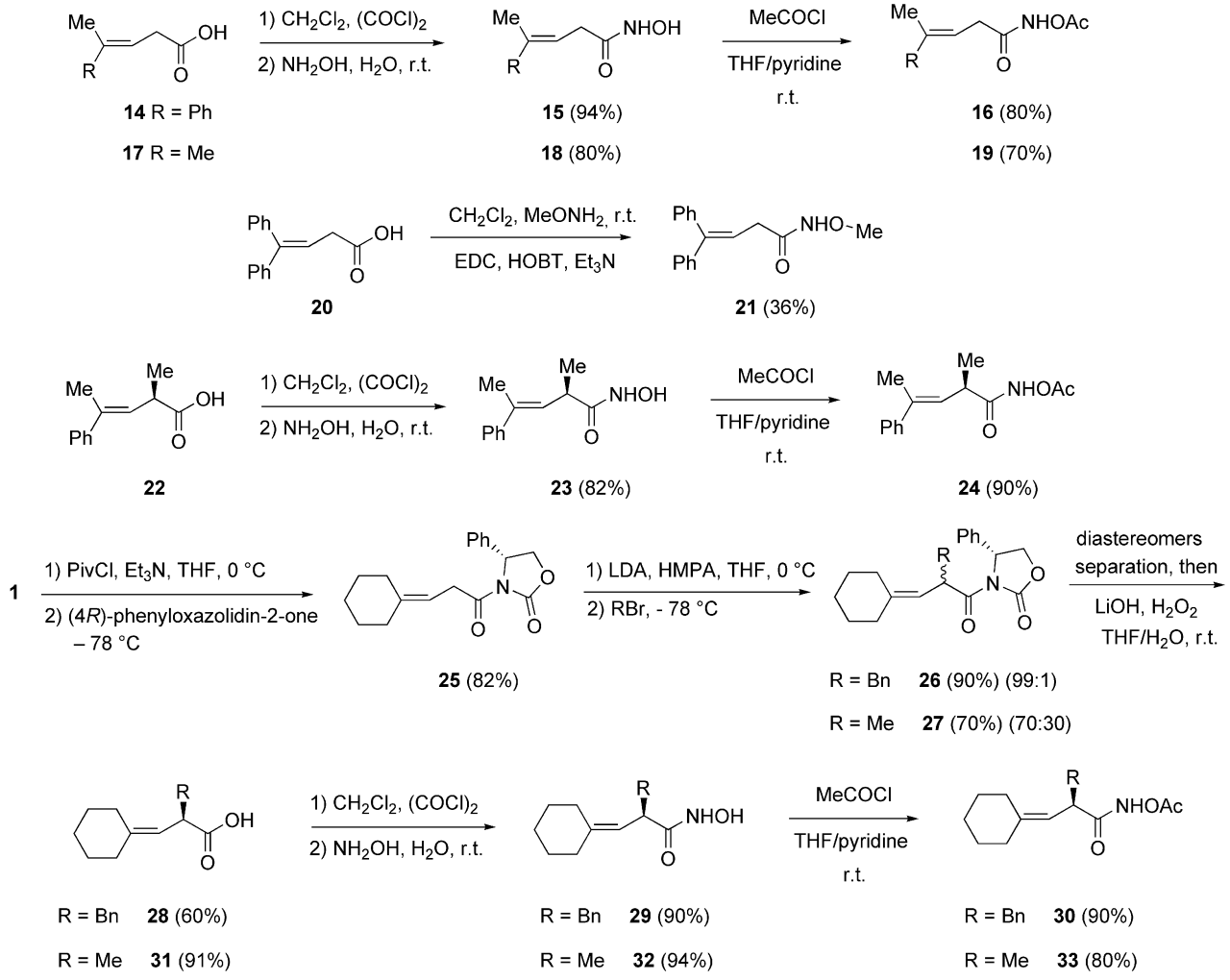
Treatment of the cyclic bromo imidate **7** with triethylamine in dichloromethane led to the formation of the unsaturated cyclic imidate **8**. Treatment of this in turn with lithium aluminium hydride led to the formation of the oxime **13** (Scheme 2).



Scheme 2. Preparation of the oxime **13**.

In a next step, we examined the behaviour of hydroxamates possessing various substituents on the C=C bond or substituted on the carbon α to the hydroxamate function. These compounds were prepared as shown in Scheme 3, either by direct treatment of the acid with alkoxyamine (compound **21**), or by treatment of the corresponding acid chloride with hydroxylamine, followed by acylation of the hydroxamic acid (compounds **16**, **19**, **24**, **30** and **33**). The preparation of the optically active hydroxamates **24**, **30** and **33** was carried out from the corresponding optically active acids by the Evans methodology, as previously reported.[5]

Subsequent treatment of these hydroxamates with bis-(collidine)bromine(I) hexafluorophosphate were then car-

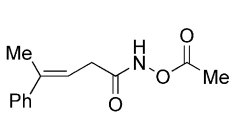
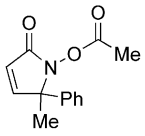
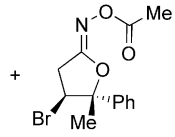
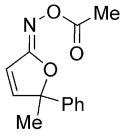
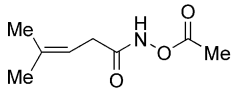
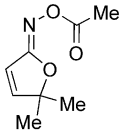
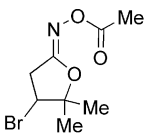
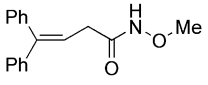
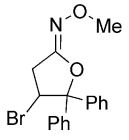
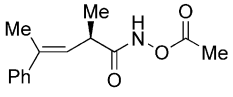
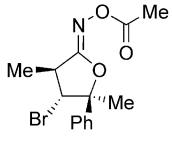
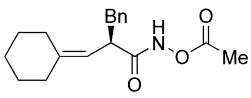
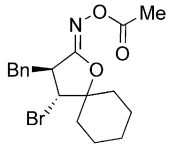
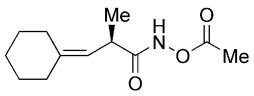
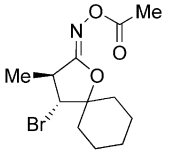


Scheme 3. Preparation of the hydroxamates **16**, **19**, **21**, **24**, **30** and **33**.

ried out as reported in the cases of compounds **4**, **5a** and **5b**. Our results are reported in Table 2. In all cases cyclizations occurred in satisfactory yields. Except in the case of the hydroxamate **16** in dichloromethane (Entry a), only cyclic imidates were formed under the studied conditions. In toluene at –20 °C, the exclusive formation of cyclic bromo imidates was observed in the cases of hydroxamates **16**, **19** and **21** (Table 2, Entries b, d and e). When a substituent was present α to the hydroxamate function (Entries f–h), only the bromo imidates **40**, **41** and **42** were isolated, even at room temperature in dichloromethane. This result indicates that the formation of lactams is disfavoured relative to the formation of imino lactones due to the steric hindrance introduced by the substituent α to the amide function.

As in the cases of unsaturated acids,[5] these cyclizations were diastereoselective. The structures of the different compounds were determined from their NMR, IR and mass spectra. The stereochemistry assigned to the cyclic bromo imidate **40** was also based on our previous results relating to the diastereoselective bromocyclization of (2*R*,4*E*)-2-methyl-5-phenylhex-4-enoic acid (**22**) in the presence of bis(collidine)bromine(I) hexafluorophosphate as electrophile.[5] The structure of the cyclic bromo imidate **42** was confirmed by its single-crystal X-ray data (Figure 1).

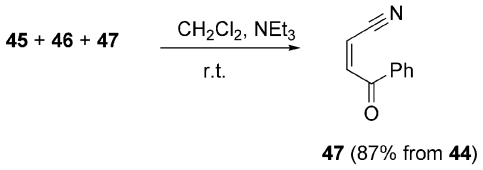
Table 2. Treatment of the hydroxamates **16**, **19**, **21**, **24**, **30** and **33** with bis(collidine)bromine(I) hexafluorophosphate.

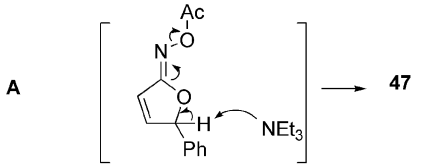
Entry	Reactant	Reaction conditions	Product(s) (yield, %)			
			 +	 +		
a	**16**	CH_2Cl_2, r.t., 1h	<2[b] **34**	>49[b] **35**	>49[b] **36**	(85)[a]
b	**16**	toluene, –20 °C, 1h		100[b] **35**		(66)[a]
			 +			
c	**19**	CH_2Cl_2, r.t., 1h	10[b] **37**	90[b] **38**		(65)[a]
d	**19**	toluene, –20 °C, 1h		100[b] **38**		(70)[a]
						
e	**21**	toluene, –20 °C, 1h	100[b] **39**			(62)[a]
						
f	**24**	CH_2Cl_2, r.t., 1h	100[b] **40**			(75)[a]
						
g	**30**	CH_2Cl_2, r.t., 1h	100[b] **41**			(75)[a]
						
h	**33**	CH_2Cl_2, r.t., 1h	100[b] **42**			(65)[a]

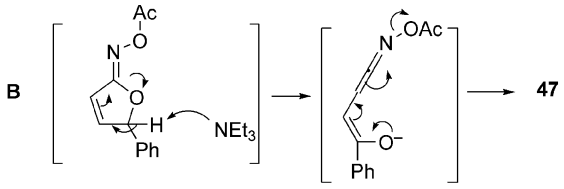
[a] Global yield after purification by liquid chromatography. [b] Proportion (^{1}H NMR) of the products in the crude reaction mixture (%).

b) Reactivities of γ-Aryl β,γ-Unsaturated Hydroxamates

The different examples reported in Tables 1 and 2 led us to reexamine the case previously reported by Miller, in which the formation of a mixture of two diastereoisomeric bromo lactams was claimed for the reaction between a hydroxamate derived from *trans*-styrylacetic acid and bromine.[3b] The hydroxamate **44** (Scheme 4) was prepared in two steps in good yield from the commercially available *trans*-styrylacetic acid, by treatment of the acid chloride with hydroxylamine, followed by acetylation. Treatment of this compound with bis(collidine)bromine(I) hexafluorophosphate in dichloromethane at room temperature led to the formation of a mixture of the bromo imine **45**, the stereochemistry of which can be reasonably postulated to be *trans*, the HBr elimination product **46** and the unsaturated β-cyano-α,β-enone **47**. No lactam derivatives were detected. Significant degradation of these products was observed during their attempted purification over silica gel. These products were characterized from their spectroscopic data. To avoid the yield loss during their purification, the crude reaction product was treated with one equivalent of triethylamine. Contrary to our expectations, the unsaturated imino lactone **46** was not isolated, but (*Z*)-4-oxo-4-phenylbut-2-enenitrile (**47**) was obtained as a unique product in high yield. This compound was characterized from its NMR and IR spectra and by comparison of its spectra with those reported in the literature.[10,11] Compound **47** was also formed on starting from (*E*)-*N*-(benzyloxy)-4-phenylbut-3-enamide. Its formation can be explained by a Beckman fragmentation.[12] Two different mechanisms can be proposed: either a concerted mechanism (**A**, Scheme 5), or the intermediate formation of a ketenimine followed by acetoxy elimination (**B**, Scheme 5).[13] Literature results relating to the Beckman fragmentation prompted us to favour the first mechanism. A similar reaction leading to the formation of 2-bromocyclohexanone and acetonitrile has been reported.[14] The abstraction of the mobile hydrogen α to the oxygen atom seems to be the key step of this reaction. Indeed, we did not observe this fragmentation on successive treatment of hydroxamate, formed from (3*E*)-hex-3-enoic acid, with bis(collidine)bromine(I) hexafluorophosphate and triethylamine.

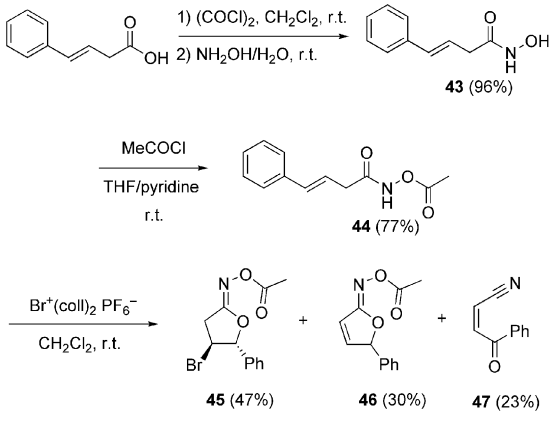




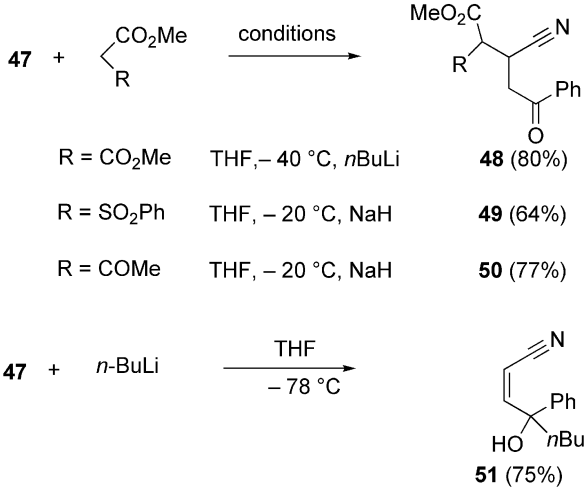


Scheme 5. Proposed mechanisms for the formation of **47**.

The reactivities of compound **47** and its *E* isomer have been briefly reported on in the literature.[11,15] In addition, we found that Michael additions were observed in good yields with soft carbanions formed from dimethyl malonate, β-keto ester and methyl (phenylsulfonyl)acetate (Scheme 6). The regiospecificities of these additions were deduced from the NMR spectra of the compounds and were consistent with previously published results.[11,15] With butyllithium, addition at the ketone function of **47** was observed and alcohol **51** was obtained. With other lithium derivatives (MeLi, *t*BuLi) and with Grignard reagents, complex reaction mixtures were observed [formation of alcohols and (or)



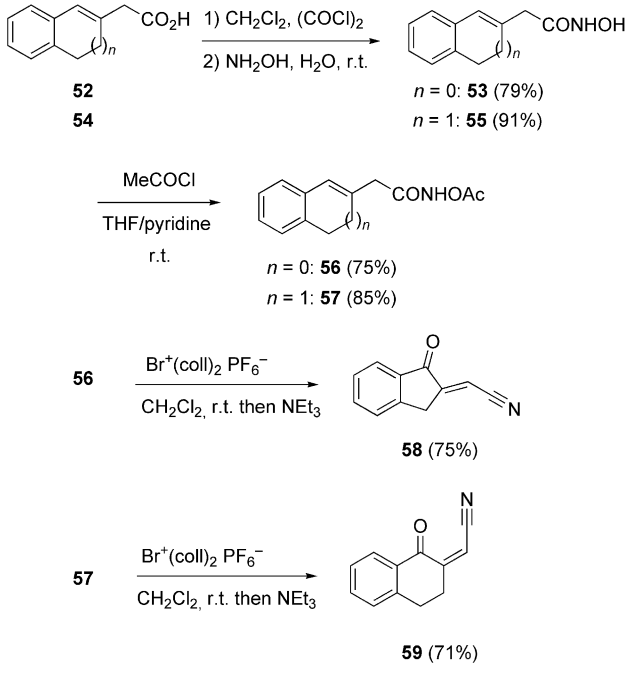
Scheme 4. Preparation of hydroxamate **44** and treatment with bis(collidine)bromine(I) hexafluorophosphate.



Scheme 6. Reactivity of the unsaturated nitrile **47**.

Michael products and probably products corresponding to the addition on the nitrile function].

We then studied the scope of this fragmentation. As indicated above, the presence of an aryl group in the γ-position seemed necessary to increase the mobility of the hydrogen α to the oxygen atom. The hydroxamates **56** and **57** were prepared as shown in Scheme 7 by hydroxy amidation and acylation of the corresponding known acids. Their reactions with bis(collidine)bromine(I) hexafluorophosphate led to the formation of the corresponding unstable cyclic imidates, which could not be purified by liquid chromatography over silica gel, so the crude reaction products were treated with triethylamine to lead to the formation of compounds **58**[15] and **59**.[16] The structures of these compounds were determined from their NMR and IR spectra and by comparison with those reported in the literature. For compound **59** the stereochemistry of the C=C bond was *Z*, whereas for compound **58** the *E* stereochemistry was observed. This latter result is probably due to the isomerization of the C=C bond in the reaction mixture. There are precedents in the literature concerning the low stability of (*Z*)-α-alkylidenecyclopentanones, and their isomerization into the corresponding *E* isomers.[17] Compounds **47** (see the Exp. Section) and **59** were unstable and were easily isomerized to their *E* isomers through the action of light, heat or nucleophiles.



Scheme 7. Preparation of the unsaturated nitriles **58** and **59**.

Conclusions

Treatment of β,γ-unsaturated hydroxamates with bis(collidine)bromine(I) hexafluorophosphate led mainly to the formation of cyclic bromo imidates rather than the bromo lactams expected from literature results.[3,4] These cyclic imidates, which are the thermodynamic reaction products, can be isolated when the unsaturated hydroxamates are γ-disubstituted. In the case of γ-aryl β,γ-unsaturated hydroxamates the cyclic bromo imidates were unstable, and their subsequent treatment with triethylamine led to the formation of 3-cyanoprop-2-en-1-ones through fragmentation reactions. These results lead us to comment on the results of Miller et al. concerning the reaction of (3*E*)-*N*-(benzyloxycarbonyl)-4-phenylbut-3-enamide in the presence of NBS, which was reported lo lead to a mixture of the two diastereomers of the bromo lactam.[3b] Under our conditions this substrate gave the same result as that found with hydroxamate **44**. This suggests that Miller et al. in fact obtained a mixture of a bromo lactam (minor compound) and a cyclic bromo imidate (major compound).

Experimental Section

General: All reactions were carried out under argon. Purification of products was carried out by normal-phase flash chromatography. 3-Cyclohexylidenepropanoic acid (**1**, 81%)[7] and bis(collidine)bromine(I) hexafluorophosphate[18] were prepared as reported previously.

3-Cyclohexylidene-*N*-hydroxypropanamide (3): Oxalyl chloride (1.75 equiv., 2.275 mmol, 0.2 mL) was added dropwise to a CH_2Cl_2 solution (5 mL) of 3-cyclohexylidenepropanoic acid (**1**, 200 mg, 1.3 mmol) cooled to 0 °C. The solution was stirred overnight at room temp. and was then concentrated under vacuum. An aqueous solution of hydroxyamine (7 equiv., 4.5 mL of a 2.5 M solution prepared from an equimolar mixture of $N^+H_3OH\ Cl^-$ and NaOH) was added to the acid chloride **2**. There was formation of a white solid, which was isolated by filtration. The filtrate was extracted twice with CH_2Cl_2 (10 mL). The organic phases were dried ($MgSO_4$), and concentrated under vacuum. The residue was added to the previous solid. 0.148 g (68%). ^{1}H NMR ($CDCl_3$; 300 MHz): δ = 9.00 (br. s, 2 H, –N*HOH*), 5.17 (s, 1 H, C=C*H*–), 2.97 (s, 2 H, –CH_2–CON), 2.11 [br. s, 4 H, 2×(CH_2)C=], 1.41 [br. s, 6 H, 3×(CH_2) cyclohexyl] ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 170.2, 145.7, 111.5, 36.9, 31.9, 29.1, 28.7, 27.3, 26.5 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3054, 2987, 2305, 1421, 1265, 896 cm^{-1}. LRMS: *m*/*z* = 170.0 [M + H]$^+$, 187.2 [M + NH_4]$^+$. HRMS (ESI): calcd. for $C_{18}H_{30}N_2NaO_4$ (dimer): 361.2103; found 361.2098.

***N*-(Acetoxy)-3-cyclohexylidenepropanamide (4):** Pyridine (1.06 equiv., 30 μL) was added over 10 min to a THF solution (10 mL) of hydroxamic acid **2** (66 mg, 0.39 mmol), cooled to 0 °C. The solution was stirred for 20 min at room temp., and acetyl chloride (1.06 equiv., 40 μL) was added dropwise. After the system had been kept for 2 h at room temp., diethyl ether (5 mL) was added and the homogeneous organic solution was washed successively with water (5 mL), aqueous HCl solution (0.5 M, 5 mL) and saturated NaCl solution (5 mL). The organic phase was dried ($MgSO_4$) and concentrated under vacuum to give a colourless oil (66 mg, 80%), which was used without further purification for the next step. ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 8.99 (br. s, 1 H, –N*H*–), 5.28 (t, $^3J_{H,H}$ = 7.5 Hz, 1 H, C=C*H*–), 3.04 (d, $^3J_{H,H}$ = 7.5 Hz, 2 H, –CH_2–CON), 2.25 [s, 3 H, O–(C=O)–CH_3], 2.18 [br. s, 4 H, 2(CH_2)C=], 1.59 [br. s, 6 H, 3×(CH_2) cyclohexyl] ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 168.7, 168.5, 145.7, 111.2, 36.8, 32.1, 29.0, 28.7, 28.4, 28.2, 18.1 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3054.5, 2987.1, 2305.8, 1792.0, 1712.4, 1421.8, 1267.0, 896.0, 753 cm^{-1}. LRMS: *m*/*z* = 212.0 [M + H]$^+$, 229.0 [M + NH_4]$^+$. HRMS: calcd. for $C_{11}H_{17}NNaO_3$: 234.1106 [M + Na]$^+$; found 234.1106.

3-Cyclohexylidene-*N*-methoxypropanamide (5a): Triethylamine (1.2 mL, 8.7 mmol) was added to a dichloromethane solution (50 mL) of cyclohexylidenepropanoic acid **1** (262 mg, 1.7 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide (498 mg, 2.6 mmol), hydroxybenzotriazole (280 mg, 2 mmol) and *O*-methylhydroxylamine hydrochloride (171 mg, 2 mmol) and the mixture was stirred for 4 d at room temp. The solution was then washed with an aqueous saturated solution of $NaHCO_3$ (20 mL), aqueous HCl solution (1 M, 20 mL) and saturated NaCl solution (10 mL). After concentration under vacuum, the residue was purified by liquid chromatography over silica gel (elution: diethyl ether) to give pure **5a** (200 mg, 64%). ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 9.80 (br. s, 1 H, –N*H*–), 5.17 (t, $^3J_{H,H}$ = 7.0 Hz, 1 H, C=C*H*–), 3.68 (s, 3 H, OCH_3), 2.88 (d, $^3J_{H,H}$ = 7.0 Hz, 2 H, –CH_2–CON), 2.06 [br. s, 4 H, 2 × (CH_2)C=], 1.48 [br. s, 6 H, 3 × (CH_2) cyclohexyl] ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 169.5, 144.3, 112.2, 63.8, 36.8, 32.0, 28.7, 28.1, 27.4, 26.4 ppm. LRMS: *m*/*z* = 184.0 [M + H]$^+$. HRMS: calcd. for $C_{10}H_{17}NNaO_2$: 206.1157; found 206.1156.

***N*-(Benzyloxy)-3-cyclohexylidenepropanamide (5b):** This compound was prepared by the method reported for the preparation of compound **5a**. From 1.19 g (7.71 mmol) of acid **1** we isolated 1.02 g (51%) of hydroxamate **5b**. ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 9.00 (s, 1 H, –N*H*–), 7.35–7.31 (m, 5 H, Ph), 5.14 (t, $^3J_{H,H}$ = 7.0 Hz, 1 H, C=C*H*–), 4.87 (s, 2 H, O-CH_2-Ph), 2.87 (d, $^3J_{H,H}$ = 7.0 Hz, 2 H, –CH_2–CON), 2.05 [br. s, 4 H, 2 × (CH_2)C=], 1.48 [br. s, 6 H, 3 × (CH_2) cyclohexyl] ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 169.2, 144.7, 135.2, 129.0, 128.3, 112.0, 77.8, 36.7, 28.6, 28.1, 28.1, 27.3, 26.4 ppm. IR (film): $\tilde{\nu}$ = 3435, 2928, 1655, 1448, 749, 697 cm^{-1}. LRMS: *m*/*z* = 260.1 [M + H]$^+$, 277.1 [M + NH_4]$^+$. HRMS: calcd. for $C_{16}H_{22}NO_2$: 260.1645; found 260.1657.

Treatment of Hydroxamate 4 with Bis(collidine)bromine(I) Hexafluorophosphate

a) In Dichloromethane at Room Temp.: Bis(collidine)bromine(I) hexafluorophosphate[18] (0.66 mmol, 307 mg) was added to a dichloromethane solution (10 mL) of the hydroxamate **4** (127 mg, 0.6 mmol). After 2 h at room temp., the solvent was removed under vacuum. The NMR spectra of the residue show the presence of three products (compounds **6**–**8**; see Table 1). After purification by liquid chromatography over silica gel only two products were isolated: the cyclic bromo imidate **7** (73 mg) and the unsaturated cyclic imidate **8** (33 mg).

1-(Acetoxy)-1-azaspiro[4.5]dec-3-en-2-one (6): (From the crude reaction mixture) ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 6.90 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, =C*H*-C=O), 6.5 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, –C*H*=CH-C=O), 2.10 [s, 3 H, O–(C=O)–CH_3], 1.80–1.30 (m, 10H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 168.2, 161.2, 152.6, 115.2, 94.5, 35.2 (2 C), 29.7, 24.7, 23.0, 18.7 ppm.

(2*Z*)-4-Bromo-1-oxaspiro[4.5]decan-2-one *O*-Acetyloxime (7): Oil. ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 4.30 (dd, $^3J_{H,H}$ = 3.0 and 7.0 Hz, 1 H, –C*H*Br–), 3.50 (dd, $^3J_{H,H}$ = 7.0 and 18.0 Hz, 1 H, –C*H*-C=N), 3.00 (dd, $^3J_{H,H}$ = 3.0 and 18.0 Hz, 1 H, –C*H*-C=N), 2.05 [s, 3 H, O–(C=O)–CH_3], 1.83–1.43 (m, 10 H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 168.3, 161.7, 92.4, 50.8, 38.4, 34.5, 24.7, 23.0, 22.5, 22.0, 19.4 ppm.

(2*Z*)-1-Oxaspiro[4.5]dec-3-en-2-one *O*-Acetyloxime (8): White solid. M.p. 106.7 °C. ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 6.84 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, =C*H*-C=O), 6.08 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, –C*H*=CH-C=O), 2.08 (s, 3 H, O-C=O-CH_3), 1.83–1.43 (m, 10 H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 90 MHz) δ: 168.6, 165.1, 149.6, 119.4, 96.6, 35.2 (2 C), 29.7, 24.7, 22.9, 19.5 ppm. LRMS: *m*/*z* = 210.1, BRMS [M + H]$^+$, 227.1. HRMS: calcd. for $C_{11}H_{16}NO_3$: 210.1130 [M + H]$^+$; found 210.1128.

b) In Toluene at –20 °C: Bis(collidine)bromine(I) hexafluorophosphate[15] (0.66 mmol, 307 mg) was added to a toluene solution (10 mL) of hydroxamate **4** (127 mg, 0.6 mmol), cooled to –20 °C. After 2 h at –20 °C, the solution was allowed to warm to room temp. and the solvent was removed under vacuum. The crude reaction mixture was purified by liquid chromatography over silica gel to give compound **7** (133 mg, 77%).

c) Preparation of (2*Z*)-1-Oxaspiro[4.5]dec-3-en-2-one *O*-Acetyloxime (8): After treatment of the hydroxamate **4** with bis(collidine)-bromine(I) hexafluorophosphate as indicated in paragraph a), triethylamine (1.12 mmol) was added to the crude reaction mixture. After 1 h at room temp., the solution was concentrated under vacuum, and the residue was purified by liquid chromatography over silica gel to give compound **8** (109 mg, 80%).

Treatment of the Hydroxamate 5a with Bis(collidine)bromine(I) Hexafluorophosphate: The reactions were carried out in dichloromethane and in toluene as reported for the hydroxamate **4**, starting from **5a** (0.6 mmol, 110 mg). In dichloromethane, compounds **9** and **10** were characterized from the crude reaction mixture (102 mg, 65%). Compound **9**, however, was not isolated after liquid chromatography over silica gel, due to its transformation into a mixture of compound **10** and **(2*Z*)-1-oxaspiro[4.5]dec-3-en-2-one *O*-methyloxime**, the HBr elimination product. In toluene at –20 °C, only compound **10** was formed (115 mg of crude reaction product, 68%, Table 1).

4-Bromo-1-methoxy-1-azaspiro[4.5]dec-3-en-2-one (9): Crude reaction mixture: ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 4.24 (dd, *J* = 4.4 and 7.3 Hz, 1 H, –C*H*Br), 3.70 (s, 3 H, OCH_3), 3.45 [dd, *J* = 7.0 and 18.8 Hz, 1 H, –C*H*–(C=O)–], 3.20 [dd, *J* = 4.4 and 18.7, 1 H, –C*H*–(C=O)–], 1.93–1.45 (m, 10H, cyclohexyl) ppm.

(2*Z*)-4-Bromo-1-oxaspiro[4.5]decan-2-one *O*-Methyloxime (10): Oil. ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 4.33 (dd, $^3J_{H,H}$ = 6.7 and 3.5 Hz, 1 H, –C*H*Br), 3.78 (s, 3 H, OCH_3), 3.40 (dd, $^3J_{H,H}$ = 17.5 and 6.7 Hz, 1 H, C*H*-C=N), 2.99 (dd, $^3J_{H,H}$ = 17.5 and 3.5 Hz, 1 H, C*H*-C=N), 1.93–1.45 (m, 10 H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 152.4, 90.4, 62.3, 51.4, 38.0, 34.7, 34.6, 24.8, 23.2, 22.6 ppm. HRMS: calcd. for $C_{10}H_{17}BrNO_2$: 262.0443 [M + H]$^+$; found 262.0445.

(2Z)-1-Oxaspiro[4.5]dec-3-en-2-one *O*-Methyloxime: ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 6.78 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, =C*H*-C=N), 6.07 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, C*H*=CH-C=N), 3.77 (s, 3 H, OCH_3), 1.98–1.25 (m, 10 H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 160.6, 146.4, 119.4, 87.2, 62.5, 35.0, 34.7, 24.8, 23.1, 22.6 ppm.

Treatment of Hydroxamate 5b with Bis(collidine)bromine(I) Hexafluorophosphate: The reaction was carried out in dichloromethane as reported for the hydroxamate **4**. From hydroxamate **5b** (166 mg, 0.6 mmol) we isolated a mixture of compounds **11** and **12** (186 mg, 92%). Compound **11** was not isolated after liquid chromatography over silica gel, due to its transformation into a mixture of compound **12** (Table 1) and **(2*Z*)-1-oxaspiro[4.5]dec-3-en-2-one *O*-benzyloxime**, the HBr elimination product.

1-Benzyloxy-4-bromo-1-azaspiro[4.5]dec-3-en-2-one (11): Crude reaction mixture: ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 7.41–7.28 (m, 5 H, Ph), 4.96 (s, 2 H, O–CH_2Ph), 4.20 (dd, $^3J_{H,H}$ = 4.7 and 7.3 Hz, 1 H, –C*H*Br), 3.47 (dd, $^3J_{H,H}$ = 7.3 and 18.8 Hz, 1 H, –C*H*-C=O), 3.22 (dd, $^3J_{H,H}$ = 4.7 and 18.8 Hz, 1 H, –C*H*-C=O), 1.83–1.43 (m, 10H, cyclohexyl) ppm.

(2*Z*)-4-Bromo-1-oxaspiro[4.5]decan-2-one *O*-Benzyloxime (12): ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 7.41–7.28 (m, 5 H, Ph), 5.02 (s, 2 H, O–CH_2Ph), 4.32 (dd, $^3J_{H,H}$ = 3.5 and 6.7 Hz, 1 H, –C*H*Br),

3.39 (dd, $^3J_{H,H}$ = 6.7 and 17.5 Hz, 1 H, –C*H*-C=N), 3.00 (dd, $^3J_{H,H}$ = 3.5 and 17.5 Hz, 1 H, C*H*-C=N), 1.83–1.43 (m, 10 H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 155.1, 138.2, 128.1 (2 C), 127.8 (2 C), 127.7, 90.2, 75.8, 51.3, 38.0, 35.6, 34.5, 24.7, 23.1, 22.1 ppm. HRMS: calcd. for $C_{16}H_{21}BrNO_2$: 338.0756 [M + H]$^+$; found 338.0759.

(2*Z*)-1-Oxaspiro[4.5]dec-3-en-2-one *O*-Benzyloxime: ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 7,44–7.26 (m, 5 H, Ph), 6.75 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, =C*H*-C=N), 6.01 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, –C*H*=CH-C=N), 5.07 (s, 2 H, O–CH_2Ph), 1.85–1.51 (m, 10 H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 160.3, 145.6, 138.3, 128.1, 127.9, 127.4, 119.6, 94.9, 76.0, 35.6, 24.8, 23.1 ppm. IR (film): $\tilde{\nu}$ = 3062 2981 2869 1759 1652 1453 1275 1052 698 cm^{-1}. HRMS: calcd. for $C_{16}H_{20}NO_2$: 258.1494 [M + H]$^+$; found 258.1495.

(2*Z*)-1-Oxaspiro[4.5]dec-3-en-2-one Oxime (13): An ethereal solution (8 mL) of $LiAlH_4$ (9.4 mg) was added dropwise to a diethyl ether solution (10 mL) of the acetyloxime **8** (50 mg, 0.24 mmol). After the system had been kept for one night at room temp., solid hydrated Na_2SO_4 was added. The mixture was stirred for two hours at room temp. and was then filtered through Celite. The filtrate was concentrated under vacuum and the residue was purified by liquid chromatography over silica gel to give the oxime **13** as an oil (38 mg, 95%). ^{1}H NMR ($CDCl_3$, 360 MHz) δ: 8.18 (br. s, 1 H, –O*H*), 6.74 [d, $^3J_{H,H}$ = 6.0 Hz, 1 H, –C*H*=CH–(C=N)–], 6.07 [d, $^3J_{H,H}$ = 6.0 Hz, 1 H, –CH=C*H*–(C=N)–], 1.83–1.43 (m, 10 H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 161.3, 146.1, 119.4, 94.9, 35.6 (2 C), 24.8, 23.0 (2 C) ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3247.0 3135.5 2934.8 2860.3 1670.1 1449.4 1286.8 1241.4 979.0 cm^{-1}. HRMS: calcd. for $C_9H_{14}NO_2$: 168.1025 [M + H]$^+$; found 168.1025.

(3*E*)-*N*-Hydroxy-4-phenylpent-3-enamide (15): The procedure used for the preparation of the hydroxamic acid **3** was used. From (*E*)-4-phenylpent-3-enoic acid (**14**,[19] 1.76 g, 10 mmol), the hydroxamic acid **15** (1.80 g, 94%) was obtained as a white solid (m.p. 112 °C, MeOH). ^{1}H NMR (CD_3OD, 250 MHz): δ = 7.36–7.18 (m, 5 H, Ph), 5.86 (t, $^3J_{H,H}$ = 6.5 Hz, 1 H, C=C*H*–), 3.05 [d, $^3J_{H,H}$ = 6.5 Hz, 2 H, –CH_2(C=O)–], 2.02 (s, 3 H, –CH_3) ppm. ^{13}C NMR (CD_3OD, 62.9 MHz) δ : = 171.1, 144.2, 139.6, 129.1, 128.0 (2 C), 126.6 (2 C), 120.6, 33.9, 16.2 ppm. IR (MeOH): $\tilde{\nu}$ = 3369, 3056, 2944, 2832, 1644 cm^{-1}. HRMS: calcd. for $C_{11}H_{13}NNaO_2$: 214.0844 [M + Na]$^+$; found 214.0845.

(3*E*)-*N*-(Acetoxy)-4-phenylpent-3-enamide (16): The procedure used for the preparation of hydroxamate **4** was used. From the hydroxamic acid **15** (1.53 g, 8 mmol), the hydroxamate **16** (1.49 g, 80%) was obtained as an oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 9.07 (br. s, 1 H, –N*H*–), 7.42–7.24 (m, 5 H, Ph), 5.91 (t, $^3J_{H,H}$ = 7.5 Hz, 1 H, C=C*H*–), 3.28 [d, $^3J_{H,H}$ = 7.5 Hz, 2 H, –CH_2(C=O)–], 2.22 [s, 3 H, O–(C=O)–CH_3], 2.11 (s, 3 H, –CH_3) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 169.2, 168.6, 142.4, 139.7, 128.1 (2 C), 127.2 (2 C), 125.6, 117.9, 33.2, 18.0, 16.1 ppm. IR (film): $\tilde{\nu}$ = 3155, 2985, 1793, 1709 cm^{-1}. HRMS: calcd. for $C_{13}H_{15}NNaO_3$: 256.0950 [M + Na]$^+$; found 256.0944.

***N*-Hydroxy-4-methylpent-3-enamide (18):** The procedure reported for the preparation of the hydroxamic acid **3** was used. From 4-methylpent-3-enoic acid **1** (**7**, 1.03 g, 9 mmol), the hydroxamic acid **18** (1.16 g, 80%) was obtained as a white solid (m.p. 69 °C, Et_2O). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 8.60–8.10 (br. s, 2 H, –N*HOH*), 5.23 (tt, $^3J_{H,H}$ = 1.0 and 7.5 Hz, 1 H, C=C*H*–), 2.98 [d, $^3J_{H,H}$ = 7.5 Hz, 2 H, –CH_2(C=O)–], 1.77 (s, 3 H, =CCH_3–), 1.66 (s, 3 H, =CCH_3–) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.3, 137.8, 115.1, 32.7, 25.6, 17.8 ppm.

***N*-(Acetoxy)-4-methylpent-3-enamide (19):** The procedure reported for the preparation of the hydroxamate **4** was used. From the hydroxamic acid **18** (1.03 g, 8 mmol), the hydroxamate **19** (0.96 g, 70%) was obtained as an oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 9.94 (br. s, 1 H, –N*H*–), 5.22 (tt, $^3J_{H,H}$ = 1.0 and 7.5 Hz, 1 H, C=C*H*–), 2.94 [d, $^3J_{H,H}$ = 7.5 Hz, 2 H, –CH_2(C=O)–], 2.13 [s, 3 H, O–(C=O)–CH_3], 1.69 (s, 3 H, =CCH_3–), 1.60 (s, 3 H, =CCH_3–) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 168.4 (2 C), 137.2, 114.8, 32.6, 25.4, 18.0, 17.7 ppm. IR (film): $\tilde{\nu}$ = 3145, 2969, 1793, 1655, 1533, 1427, 1373, 1189, 1048, 979, 856 cm^{-1}. HRMS: calcd. for $C_8H_{14}NO_3$: 172.0974 [M + H]$^+$; found 172.0976.

***N*-Methoxy-4,4-diphenylbut-3-enamide (21):** The procedure reported for the preparation of compound **5a** was used. From 4,4-diphenylbut-3-enoic acid (**20**, 1.90 g, 8 mmol), the hydroxamate **21** (0.77 g, 36%) was obtained as a white solid (m.p. 110 °C, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 8.68 (br. s, 1 H, –N*H*–), 7.43–7.20 (m, 10 H, 2 × Ph), 6.26 (t, $^3J_{H,H}$ = 7.4 Hz, 1 H, C=C*H*–), 3.74 (br. s, 3 H, OCH_3), 2.99 [br. s, 2 H, –CH_2(C=O)–] ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 168.7, 145.5, 141.5, 139.0, 129.7 (2 C), 128.5 (2 C), 128.2 (2 C), 127.6 (2 C), 127.4 (2 C), 119.9, 64.4, 30.1 ppm.

(2*R*,4*E*)-*N*-Hydroxy-2-methyl-5-phenylhex-4-enamide (23): The procedure reported for the preparation of the hydroxamate **4** was used. From (2*R*,4*E*)-2-methyl-5-phenylhex-4-enoic acid (**22**,[5] 0.50 g, 2.45 mmol), the hydroxamate **23** (0.44 g, 82%) was obtained as an oil. ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 9.24 (br. s, 2 H, –N*HOH*), 7.43–7.22 (m, 5 H, Ph), 5.77 (d, $^3J_{H,H}$ = 8.6 Hz, 1 H, C=C*H*–), 3.39 (m, 1 H, –C*H*CH$_3$–), 2.10 (s, 3 H, =CCH_3–), 1.33 (d, $^3J_{H,H}$ = 6.5 Hz, 3 H, –CHCH_3–) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.5, 142.5, 138.0, 128.6 (2 C), 127.2, 125.9 (2 C), 125.7, 38.0, 18.0, 16.0 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3202, 2925, 1658, 1450, 1016, 759 cm^{-1}. LRMS: *m*/*z* = 206.2 [M + H]$^+$, 223.2 [M + NH_4]$^+$.

(2*R*,4*E*)-*N*-(Acetoxy)-2-methyl-5-phenylhex-4-enamide (24): The procedure reported for the preparation of the hydroxamate **4** was used. From the hydroxamic acid **23** (0.548 g, 2.5 mmol), the hydroxamate **24** (0.588 g, 90%) was obtained as a white solid (m.p. 122–123 °C, Et_2O). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 9.27 (br. s, 1 H, –N*H*–), 7.44–7.26 (m, 5 H, Ph), 5.83 (d, $^3J_{H,H}$ = 9.2 Hz, 1 H, C=C*H*–), 3.52 (m, 1 H, –C*H*CH$_3$–), 2.23 [s, 3 H, –O(CO)CH_3], 2.15 (s, 3 H, =CCH_3–), 1.42 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, –CHCH_3–) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 168.8 (2 C), 142.4, 138.6, 128.3 (2 C), 127.4, 126.9 (2 C), 125.8, 38.5, 18.2, 17.7, 16.2 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3139, 2960, 1794, 1656, 1179, 1021, 849, 755, 696 cm^{-1}. HRMS: calcd. for $C_{14}H_{18}NO_3$: 248.1287 [M + H]$^+$; found 248.1288.

(4*R*)-3-(3-Cyclohexylidenepropanoyl)-4-phenyl-1,3-oxazolidin-2-one (25): Triethylamine (121 mg, 1.2 mmol) and pivaloyl chloride (144 mg, 1.2 mmol) were added successively at –78 °C to a THF solution (20 mL) of 3-cyclohexylidenepropanoic acid (**1**, 0.154 g, 1 mmol). After 15 min at this temperature, the solution was allowed to warm to 0 °C for 45 min and was then cooled again at –78 °C. In a second flask, *n*-butyllithium (1 mmol, 1.6 M hexane solution) was added to a THF solution (3.5 mL) of (*R*)-4-phenyloxazolidin-2-one[20] (163.2 mg, 1 mmol) cooled to –78 °C. The solution from the first flask was cannulated at –78 °C into the oxazolidine solution. After 20 min at –78 °C, the resulting mixture was allowed to warm to room temperature for 2 h. A saturated aqueous solution (30 mL) of ammonium chloride was added, and the aqueous phase was extracted with dichloromethane (3 × 20 mL). After drying ($MgSO_4$), the organic phase was concentrated under vacuum, and the residue was purified by liquid chromatography over silica gel (pentane/Et_2O). The oxazolidine **25** (245 mg, 82%) was obtained

as white crystals (m.p. 67 °C, CH_2Cl_2). $[\alpha]_D$ = –102.4 (c = 0.167, MeOH). ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 7.40–7.20 (m, 5 H, Ph), 5.36 (dd, $^3J_{H,H}$ = 3.8 and 10.5 Hz, 1 H, –C*H*PhN), 5.27 (dd, $^3J_{H,H}$ = 7.0 Hz, 1 H, C=C*H*–), 4.70 [t, $^3J_{H,H}$ = 8.8 Hz, 1 H, CCH_2O(CO)–], 4.29 [dd, $^3J_{H,H}$ = 3.8 and 8.8 Hz, 1 H, CCH_2O(CO)–], 3.67 [d, $^3J_{H,H}$ = 7.0 Hz, 2 H, –CH_2(CO)N–], 2.10 [br. s, 4 H, 2× –CH_2C=(cyclohexyl)], 1.50 [m, 6 H, 3×CH_2 (cyclohexyl)] ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 171.3, 153.7, 144.4, 139.1, 129.4 (2 C), 129.1, 126.0 (2 C), 111.4, 70.0, 57.6, 37.0, 34.3, 29.1, 28.4, 27.5, 26.7 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 2928.6, 2853.3, 1782.2, 1706.7, 1385.5, 1327.7, 1202.2, 705.0 cm^{-1}. HRMS: calcd. for $C_{18}H_{21}NNaO_3$: 322.1419 [M + Na]$^+$; found 322.1414.

(4*R*)-3-[(2*R*)-2-Benzyl-3-cyclohexylidenepropanoyl]-4-phenyl-1,3-oxazolidin-2-one (26): Diisopropylamine (0.54 mL, 3.86 mmol, 1.2 equiv.), *n*-butyllithium (2.4 mL of a 1.6 M hexane solution, 1.2 equiv.) and HMPA (0.8 mL) were added to THF (10 mL), cooled to 0 °C. After 30 min at this temperature, the solution was cooled to –78 °C and a THF solution (10 mL) of oxazolidine **25** (0.963 g, 3.22 mmol, 1 equiv.) was added over 10 min. After 1 h at –78 °C, the solution was allowed to warm to –50 °C for 50 min and then to –15 °C. A saturated aqueous solution of ammonium chloride (20 mL) was added and the mixture was concentrated under vacuum. The resulting aqueous phase was extracted with diethyl ether (3× 5 mL). The organic phases were then washed with HCl (0.5 M, 5 mL), water (5 mL) and saturated NaCl (5 mL). After drying ($MgSO_4$), the solution was concentrated under vacuum, and the residue was purified by liquid chromatography over silica gel (ether/pentane 40–60) to give compound **26** (0.800 g, 64%). The crude reaction product, before chromatography, showed a 99:1 ratio of the two diastereomers. The minor isomer was not isolated after chromatography. White crystals, m.p. 83 °C (Et_2O). $[\alpha]_D$ = –12.9 (c = 0.029, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 7.40–7.29 (m, 10 H, 2×Ph), 5.43 (dd, $^3J_{H,H}$ = 3.6 and 8.6 Hz, –C*H*PhN), 5.15 (m, 2 H, C=C*H*- and –C*H*CH$_2$Ph), 4.66 [t, $^3J_{H,H}$ = 8.8 Hz, 1 H, CC*H*HO(CO)–], 4.22 [dd, $^3J_{H,H}$ = 3.6 and 8.8 Hz, 1 H, CCH*H*O(CO)–], 3.10 (m, 1 H, –C*H*HPh), 2.60 (m, 1 H, –CH*H*Ph), 2.07 [m, 4 H, 2× –CH_2C=(cyclohexyl)], 1.40 [m, 6 H, 3×CH_2 (cyclohexyl)] ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 174.4, 153.2, 144.2, 139.0, 139.0, 138.5, 129.5 (2 C), 129.0 (2 C), 128.1, 128.4, 126.1, 125.6 (2 C), 117.9, 69.7, 57.8, 43.5, 39.8, 37.1, 29.4, 28.4, 27.3, 26.6 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 2928, 2853, 1781, 1702, 1384, 1196, 1104, 700 cm^{-1}. HRMS: calcd. for $C_{25}H_{28}NO_3$: 390.2069 [M + H]$^+$; found 390.2071.

(4*R*)-3-[(2*R*)-3-Cyclohexylidene-2-methylpropanoyl]-4-phenyl-1,3-oxazolidin-2-one (27): This reaction was carried out as reported for the preparation of compound **26**, with methyl iodide as alkylation agent. From compound **25** (1.10 g, 3.34 mmol), a mixture of two diastereomers (70:30, 0.732 g, 70%) was obtained. Only the major diastereomer (2*R*) was characterized after chromatography over silica gel. $[\alpha]_D$ = –14.0 (c = 0.043, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 7.40–7.29 (m, 5 H, Ph), 5.40 (dd, $^3J_{H,H}$ = 3.6 and 8.6 Hz, 1 H, –C*H*PhN), 5.19 (d, $^3J_{H,H}$ = 9.3 Hz, 1 H, C=C*H*–), 4.74 [dq, $^3J_{H,H}$ = 6.9 and 13.8 Hz, 1 H, CCH_2O(CO)–], 4.64 (q, $^3J_{H,H}$ = 8.7 Hz, 1 H, –C*H*CH$_3$), 4.21 [dd, $^3J_{H,H}$ = 3.6 and 8.7 Hz, 1 H, CCH_2O(CO)–], 2.20 [m, 2 H, –CH_2C=(cyclohexyl)], 2.18 [br. s, 2 H, –CH_2C=(cyclohexyl)], 1.53 [br. s, 6 H, 3×CH_2 (cyclohexyl)], 1.17 (d, J = 6.9 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 175.5, 153.3, 142.3, 139.4, 129.1 (2 C), 128.6 (2 C), 125.7, 119.9, 69.8, 57.8, 37.1, 36.4, 29.3, 28.5, 27.9, 26.8, 19.1 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 2925, 2842, 1785, 1698, 1456, 1309, 1236, 703 cm^{-1}. HRMS: calcd. for $C_{19}H_{23}NNaO_3$: 336.1576 [M + Na]$^+$; found 336.1574.

(2*R*)-2-Benzyl-3-cyclohexylidenepropanoic Acid (28): Hydrogen peroxide (0.68 mL of a 33% solution, 7.8 mmol, 6 equiv.) was added dropwise to oxazolidine **26** (0.410 g, 1.3 mmol) in solution in a THF/H_2O mixture (12 and 4 mL, respectively) cooled to 0 °C, followed by LiOH (0.138 g, 3.35 mmol, 2.5 equiv.). After the system had been stirred at this temperature for 3.5 h, Na_2SO_3 (10 mL of a 1.3 M solution) was added and the mixture was stirred for 30 min. After concentration under vacuum, the aqueous phase was extracted with dichloromethane (3×10 mL) and acidified (pH 1) with 1 M HCl. The acidic phase was extracted with dichloromethane (3×10 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated under vacuum to give the acid **28** (0.154 g, 60%), which was used without further purification. $[\alpha]_D$ = –109.4 (c = 0.059, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 11.66 (s, 1 H, CO_2H), 7.32 (m, 5 H, Ph), 5.21 (d, $^3J_{H,H}$ = 9.7 Hz, 1 H, C=C*H*–), 3.66 (m, 1 H, –C*H*CH$_2$Ph), 3.20 (dd, $^3J_{H,H}$ = 6.5 and 13.5 Hz, 1 H, –CH_2Ph), 2.80 (dd, $^3J_{H,H}$ = 8.3 Hz, 1 H, and 13.5, –CH_2Ph), 2.09 [m, 4 H, 2×–CH_2C=(cyclohexyl)], 1.55 [m, 6 H, 3×CH_2 (cyclohexyl)] ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 180.9, 144.1, 138.7, 129.2 (2 C), 128.2 (2 C), 126.2, 117.6, 45.8, 38.8, 37.1, 29.1, 28.3, 27.2, 26.5 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3030, 2931, 2855, 1705, 1448, 1265, 909, 739, 701 cm^{-1}. HRMS: calcd. for $C_{16}H_{24}NO_2$: 262.1807 [M + NH_4]$^+$; found 262.1809.

(2*R*)-2-Benzyl-3-cyclohexylidene-*N*-hydroxypropanamide (29): The procedure reported for the preparation of the hydroxamic acid **3** was used. From (2*R*)-2-benzyl-3-cyclohexylidenepropanoic acid (**28**, 0.140 g, 0.573 mmol), the hydroxamic acid **29** (0.134 g, 90%) was obtained as a white solid. ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 8.40 (br. s, 2 H, –N*H*O*H*), 7.22 (m, 5 H, Ph), 5.11 (d, $^3J_{H,H}$ = 9.5 Hz, 1 H, C=C*H*–), 3.35 (m, 1 H, –C*H*CH$_2$Ph), 3.20 (dd, $^3J_{H,H}$ = 5.5 and 13.5 Hz, 1 H, –CH_2Ph), 2.70 (dd, $^3J_{H,H}$ = 8.7 Hz, 1 H, and 13.4, –CH_2Ph), 2.33 [m, 4 H, 2× –CH_2C=(cyclohexyl)], 1.40 [m, 6 H, 3×CH_2 (cyclohexyl)] ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 170.2, 145.2, 139.0, 129.3 (2 C), 128.2 (2 C), 126.3, 117.3, 44.2, 38.6, 37.2, 29.2, 28.3, 27.3, 26.5 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3345, 2924, 2851, 16.77, 1619, 1446, 1023, 700 cm^{-1}. HRMS: calcd. for $C_{16}H_{25}N_2O_2$: 277.1916 [M + NH_4]$^+$; found 277.1919.

(2*R*)-*N*-(Acetoxy)-2-benzyl-3-cyclohexylidenepropanamide (30): The procedure reported for the preparation of the hydroxamate **4** was used. From the hydroxamic acid **29** (0.120 g,0.463 mmol), the hydroxamate **30** (0.140 g, 90%) was obtained as an oil. $[\alpha]_D$ = –83.0 (c = 0.0324, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 8.40 (br. s, 1 H, –N*H*–), 7.22 (m, 5 H, Ph), 5.11 (d, $^3J_{H,H}$ = 9.5 Hz, 1 H, C=C*H*–), 3.35 (m, 1 H, –C*H*CH$_2$Ph), 3.20 (dd, $^3J_{H,H}$ = 5.5 and 13.4 Hz, 1 H, –CH_2Ph), 2.70 (dd, $^3J_{H,H}$ = 8.7 Hz and 13.4, 1 H, –CH_2Ph), 2.23 [s, 3 H, –O(CO)–CH_3], 2.00 [m, 4 H, 2× –CH_2C=(cyclohexyl)], 1.40 [m, 6 H, 3×CH_2 (cyclohexyl)] ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 168.5 (2 C), 145.2, 139.0, 129.2 (2 C), 128.2 (2 C), 126.2, 117.3, 44.5, 38.4, 37.1, 29.1, 28.2, 27.2, 26.4, 18.2 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3170 3929 2853 1797 1667 1448 1367 1177 1030 690 cm^{-1}. HRMS: calcd. for $C_{18}H_{27}N_2O_3$: 319.2022 [M + NH_4]$^+$; found 319.2028.

(2*R*)-3-Cyclohexylidene-2-methylpropanoic Acid (31): This compound was obtained by the method reported for the preparation of acid **28**. From the oxazolidine **27** (0.52 g), the acid **31** (0.254 g, 91%) was isolated. $[\alpha]_D$ = –138.6 (c = 0.060, CH_2Cl_2). ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 12.09 (s, 1 H, CO_2H), 5.09 (d, $^3J_{H,H}$ = 9.1 Hz, 1 H, C=C*H*–), 3.38 (qd, $^3J_{H,H}$ = 7.0 and 9.0 Hz, 1 H, –C*H*CH$_3$), 2.11 [d, $^3J_{H,H}$ = 19.2 Hz, 4 H, 2×-CH_2C=(cyclohexyl)], 1.53 [br. s, 6 H, 3×CH_2 (cyclohexyl)], 1.21 (d, $^3J_{H,H}$ = 7.0 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 182.4, 142.6, 119.8, 37.8, 36.9, 29.1, 28.3, 27.6, 26.6, 18.1 ppm. IR (CH_2Cl_2): $\tilde{\nu}$

= 2931, 2854, 1708, 1448, 1415, 1287, 1237, 1220, 934 cm^{-1}. HRMS: calcd. for $C_{10}H_{17}O_2$: 169.1229 $[M + H]^+$; found 169.1230.

(2*R*)-3-Cyclohexylidene-*N*-hydroxy-2-methylpropanamide (32): This compound was prepared by the procedure reported for the formation of the hydroxamic acid **3**. From the acid **31** (0.168 g, 1.31 mmol), the hydroxamic acid **32** (0.225 g, 94%) was obtained as a white solid. $[\alpha]_D$ = –58.5 (*c* = 0.220, CH_2Cl_2). ^1H NMR ($CDCl_3$, 300 MHz): δ = 8.42 (br. s, 2 H, –N*H*O*H*), 5.06 (d, $^3J_{H,H}$ = 8.8 Hz, 1 H, C=C*H*–), 3.20 (m, 1 H, –C*H*CH_3–), 2.11 [br. s, 4 H, 2× –CH_2C=(cyclohexyl)], 1.41 [br. s, 6 H, 3×CH_2 (cyclohexyl)], 1.25 (d, $^3J_{H,H}$ = 5.9 Hz, 3 H, CHCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 173.3, 144.0, 119.6, 37.0, 36.5, 29.2, 28.4, 27.7, 26.6, 18.3 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3191, 2928, 2853, 1629, 1533, 1270, 957 cm^{-1}. HRMS: calcd. for $C_{10}H_{18}NO_2$: 184.1338 $[M + H]^+$; found 184.1338.

(2*R*)-*N*-(Acetoxy)-3-cyclohexylidene-2-methylpropanamide (33): This compound was prepared by the procedure reported for the formation of the hydroxamate **4**. From compound **32** (0.150 g), the hydroxamate **33** (0.147 g, 80%) was obtained. $[\alpha]_D$ = –93.7 (*c* = 0.088, CH_2Cl_2). ^1H NMR ($CDCl_3$, 360 MHz): δ = 9.10 (br. s, 1 H, –N*H*–), 5.10 (d, *J* = 9.0 Hz, 1 H, C=C*H*–), 3.04 (dq, $^3J_{H,H}$ = 6.7 and 9.0 Hz, 1 H, –C*H*Me–), 2.18 [s, 3 H, –O(CO)CH_3], 2.00 [br. s, 4 H, 2× –CH_2C=(cyclohexyl)], 1.54 [br. s, 6 H, 3×CH_2 (cyclohexyl)], 1.28 (d, $^3J_{H,H}$ = 9.0 Hz, 3 H, –CHCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.7 (2 C), 144.3, 119.6, 37.0 (2 C), 29.2, 28.3, 27.6, 26.5, 18.3, 17.9 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3583, 3183, 2930, 2853, 1797, 1674, 1448, 1369, 1178, 1024, 850 cm^{-1}. HRMS: calcd. for $C_{12}H_{19}NNaO_3$: 248.1263 $[M + Na]^+$; found 248.1263.

Treatment of Hydroxamate 16 with Bis(collidine)bromine(I) Hexafluorophosphate: This reaction was carried out in dichloromethane as reported for the treatment of the hydroxamate **4**. From the hydroxamate **16** (233 mg, 1 mmol) we obtained a mixture (265 mg) composed of products **35** and **36** (50:50), together with a small amount (<2%) of compound **34**, which could not be characterized (Table 2).

(2*Z*,4*S,5*R**)-4-Bromo-5-methyl-5-phenyldihydrofuran-2(3*H*)-one *O*-Acetyloxime (35):** ^1H NMR ($CDCl_3$, 360 MHz): δ = 7.42–7.31 (m, 5 H, Ph), 4.68 (dd, $^3J_{H,H}$ = 2.8 and 6.0 Hz, 1 H, –C*H*Br–), 3.26 [dd, $^3J_{H,H}$ = 6.0 and 17.6 Hz, 1 H, –CH_2(C=N)–], 3.11 [dd, $^3J_{H,H}$ = 2.8 and 17.6 Hz, 1 H, –CH_2(C=N)–], 2.25 [s, 3 H, CH_3–(CO)-O–], 1.91 (s, 3 H, –OCPhCH_3) ppm. ^{13}C NMR ($CDCl_3$, 90 MHz): δ = 168.3, 161.7, 140.9, 129.1 (2 C), 128.6 (2 C), 124.1, 93.5, 53.1, 38.3, 27.5, 19.5 ppm. HRMS: calcd. for $C_{13}H_{14}BrNNaO_3$: 334.0055 $[M + Na]^+$; found 334.0052.

(2*Z*)-5-Methyl-5-phenyl-2(5*H*)-furanone *O*-Acetyloxime (36): White solid. ^1H NMR ($CDCl_3$, 360 MHz): δ = 7.41–7.37 (m, 5 H, Ph), 7.00 (d, $^3J_{H,H}$ = 6.0 Hz, 1 H, cmePh–C*H*=), 6.29 [d, $^3J_{H,H}$ = 6.0 Hz, 1 H, =C*H*–(C=N)O–], 2.23 [s, 3 H, CH_3–(CO)O–], 1.89 (s, 3 H, –OCPhCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.5, 165.0, 150.0, 139.4, 128.8 (2 C), 128.5 (2 C), 125.9, 119.0, 96.3, 26.0, 19.5 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3155, 3091, 3066, 2987, 1762, 1654 cm^{-1}. HRMS: calcd. for $C_{13}H_{14}NO_3$: 232.0974 $[M + H]^+$; found 232.1337.

Treatment of the Hydroxamate 19 with Bis(collidine)bromine(I) Hexafluorophosphate: These reactions were carried out in dichloromethane and in toluene as reported in the case of the hydroxamate **4**. In dichloromethane, from the hydroxamate **19** (171 mg, 1 mmol), compound **37** (150 mg) and compound **38** (12 mg) were obtained after chromatography. In toluene at –20 °C, compound **38** (175 mg) was isolated.

(2*Z*)-5,5-Dimethyl-2(5*H*)furanone *O*-Acetyloxime (37): Oil. ^1H NMR ($CDCl_3$, 360 MHz): δ = 6.77 (d, $^3J_{H,H}$ = 8 Hz, 1 H, CMe_2-C*H*=), 6.16 [d, $^3J_{H,H}$ = 8.0 Hz, 1 H, =C*H*–(C=N)O–], 2.18 [s, 3 H, CH_3–(CO)O–], 1.52 (s, 6 H, –OCMe_2) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.4, 165.0, 150.7, 119.1, 94.5, 25.9, 23.2, 19.5 ppm. HRMS: calcd. for $C_8H_{12}NO_3$: 170.0817 $[M + H]^+$; found 170.0817.

(2*Z*)-4-Bromo-5,5-dimethyldihydrofuran-2(3*H*)-one *O*-Acetyloxime (38): Oil. ^1H NMR ($CDCl_3$, 360 MHz): δ = 4.22 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, –C*H*Br–), 3.43 [dd, $^3J_{H,H}$ = 7.2 and 18.0 Hz, 1 H, –CH_2(C=N)–], 3.11 [dd, $^3J_{H,H}$ = 7.2 and 18.0 Hz, 1 H, –CH_2(C=N)–], 2.11 [s, 3 H, CH_3–(CO)O–], 1.54 (s, 3 H, –OCCH_3CH_3), 1.50 (s, 3 H, –OCCH_3CH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.0, 161.2, 91.1, 49.8, 37.7, 25.5, 25.0, 19.2 ppm. HRMS: calcd. for $C_8H_{13}BrNO_3$: 250.0079 $[M + H]^+$; found 250.0078.

Treatment of the Hydroxamate 21 with Bis(collidine)bromine(I) Hexafluorophosphate: This reaction was carried out in toluene at –20 °C as reported in the case of the hydroxamate **4**. From the hydroxamate **21** (267 mg), the cyclic bromo imidate **39** (215 mg) was obtained.

(2*Z*)-4-Bromo-5,5-diphenyldihydrofuran-2(3*H*)-one *O*-Methyloxime (39): ^1H NMR ($CDCl_3$, 360 MHz): δ = 7.59–7.28 (m, 10 H, 2×Ph), 5.30 (dd, *J* = 2.7 and 5.5 Hz, 1 H, –C*H*Br–), 3.94 (s, 3 H, –OCH_3), 3.20 double AB System: 3.23 [part A, dd, *J* = 5.5 and 17.0, 1 H, –CH_2–(C=N)O-, part B, dd, *J* = 2.7 and 17.0 Hz, 1 H, –CH_2–(C=N)O–] ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 153.9, 141.0, 140.8, 129.0 (2 C), 128.4 (2 C), 127.9 (2 C), 127.8 (2 C), 125.9, 125.2, 94.5, 62.6, 51.9, 38.4 ppm. HRMS: calcd. for $C_{17}H_{17}BrNO_2$: 346.0443 $[M + H]^+$; found 346.0444.

Treatment of the Hydroxamate 24 with Bis(collidine)bromine(I) Hexafluorophosphate: This reaction was carried out in dichloromethane as reported in the case of the hydroxamate **4**. From the hydroxamate **24** (247 mg), the cyclic bromo imidate **40** (245 mg) was obtained.

(2*Z*,3*S*,4*R*,5*S*)-4-Bromo-3,5-dimethyl-5-phenyldihydro-2(3*H*)-furanone *O*-Acetyloxime (40): $[\alpha]_D$ = –1.80 (*c* = 0.875, CH_2Cl_2). ^1H NMR ($CDCl_3$, 360 MHz): δ = 7.56–7.37 (m, 5 H, Ph), 4.00 (d, $^3J_{H,H}$ = 10.5 Hz, 1 H, –C*H*Br–), 3.36 (dq, $^3J_{H,H}$ = 6.7 and 10.5 Hz, 1 H, –C*H*Me), 2.21 [s, 3 H, CH_3–(CO)O–], 1.87 (s, 3 H, –CPhCH_3), 1.41 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, –CHCH_3) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.2, 163.7, 141.6, 128.7 (2 C), 128.4 (2 C), 124.1, 90.5, 58.0, 43.8, 24.7, 19.4, 13.9 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 2983, 1771, 1671, 1448, 1204, 1047, 984, 700 cm^{-1}. HRMS: calcd. for $C_{14}H_{16}BrNNaO_3$ $[M + Na]^+$: 348.0204; found 348.0211.

Treatment of the Hydroxamate 30 with Bis(collidine)bromine(I) Hexafluorophosphate: This reaction was carried out in dichloromethane as reported in the case of the hydroxamate **4**. From the hydroxamate **30** (151 mg), the product **41** (143 mg) was isolated.

(2*Z*,3*S*,4*R*)-3-Benzyl-4-bromo-1-oxaspiro[4.5]decan-2-one *O*-Acetyloxime (41): $[\alpha]_D$ = –45.7 (*c* = 0.165, CH_2Cl_2). ^1H NMR ($CDCl_3$, 250 MHz): δ = 7.22 (m, 5 H, Ph), 3.50 (m, 2 H, –C*H*Br- and -C*H*CH_2Ph–), 3.28 (dd, $^3J_{H,H}$ = 4.5 and 14.3 Hz, 1 H, –CH_2Ph), 3.10 (dd, $^3J_{H,H}$ = 5.2 and 14.3 Hz, 1 H, –CH_2Ph), 2.15 [s, 3 H, CH_3–(CO)O–], 1.40 (m, 10 H, cyclohexyl) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.3, 162.4, 136.0, 130.1 (2 C), 128.4 (2 C), 127.0, 89.7, 53.0, 48.3, 34.4, 33.1, 31.6, 24.8, 22.2, 21.6, 19.4 ppm. IR (CH_2Cl_2): $\tilde{\nu}$ = 3507, 2936, 2865, 1768, 1667, 1450, 1366, 1199, 1017, 794, 703 cm^{-1}. HRMS: calcd. for $C_{18}H_{23}BrNO_3$: 380.0861 $[M + H]^+$; found 380.0863.

Treatment of the Hydroxamate 33 with Bis(collidine)bromine(I) Hexafluorophosphate: This reaction was carried out in dichloro-

methane as reported in the case of the hydroxamate **4**. From the hydroxamate **33** (112 mg), the cyclic bromo imidate **42** (98 mg) was isolated.

(2*Z*,3*S*,4*R*)-4-Bromo-3-methyl-1-oxaspiro[4.5]decan-2-one *O*-Acetyloxime (42): $[\alpha]_D$ = –1.84 (*c* = 0.075, MeOH). ^{1}H NMR ($CDCl_3$, 360 MHz): δ= = 3.60 (d, $^3J_{H,H}$ = 11.3 Hz, 1 H, –C*H*Br–), 3.20 (dq, $^3J_{H,H}$ = 6.7 Hz and 11.3, 1 H, –C*H*Me), 2.17 [s, 3 H, C*H*$_3$–(CO)-O–], 1,96–1.54 (m, 10 H, cyclohexyl), 1.41 (d, $^3J_{H,H}$ = 6.7 Hz, 3 H, –CHC*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 168.4, 164.3, 89.8, 57.3, 42.6, 34.5, 31.9, 24.9, 22.2, 21.5, 19.4, 14.0 ppm. HRMS: calcd. for $C_{12}H_{19}BrNO_3$: 304.0548 [M + H]$^+$; found 304.0549.

(*E*)-*N*-Hydroxy-4-phenylbut-3-enamide (43): This compound was prepared by the procedure reported for the preparation of the hydroxamic acid **3**. From commercially available (*E*)-4-phenylbut-3-enoic acid (1.62 g, 10 mmol) we isolated compound **43** (1.70 g, 96%) as a white solid (m.p. 135–137 °C, MeOH). ^{1}H NMR (CD_3OD, 250 MHz): δ = 7.33–7.11 (m, 5 H, Ph), 6.47 (d, $^3J_{H,H}$ = 16.0 Hz, 1 H, Ph–C*H*=CH), 6.23 (dt, $^3J_{H,H}$ = 7.0 and 16.0 Hz, 1 H, Ph–CH=C*H*–), 2.97 (d, *J* = 7.0 Hz, 2 H, C*H*$_2$–CON) ppm. ^{13}C NMR (CD_3OD, 62.9 MHz): δ = 169.6, 136.9, 133.4, 128.4 (2 C), 127.2 (2 C), 126.0, 122.0, 36.6 ppm. IR (CD_3OD): ṽ = 3344 3031 1650 cm^{-1}. HRMS: calcd. for $C_{10}H_{11}NNaO_2$: 200.0687 [M + Na]$^+$; found 200.0690.

(3*E*)-*N*-(Acetoxy)-4-phenylbut-3-enamide (44): This compound was obtained by the procedure reported for the preparation of compound **4**. From the hydroxamic acid **43** (1.1 g), compound **44** (1.05 g, 77%) was isolated as a white solid (m.p. 131–133 °C, Et_2O). ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 9.0 (br. s, 1 H, –N*H*–), 7.38–7.25 (m, 5 H, Ph), 6.59 (d, $^3J_{H,H}$ = 15.8 Hz, 1 H, Ph–C*H*=CH), 6.29 (dt, $^3J_{H,H}$ = 15.8 and 7.4 Hz, 1 H, Ph–CH=C*H*–), 3.25 (d, $^3J_{H,H}$ = 7.3 Hz, 2 H, C*H*$_2$–CON), 2.22 [s, 3 H, C*H*$_3$–(CO)O–] ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 169.3, 168.7, 136.3, 135.0, 128.6 (2 C), 127.9 (2 C), 126.3, 120.4, 37.5, 18.2 ppm. IR (CH_2Cl_2): ṽ = 3148, 2964, 1792, 1662 cm^{-1}. HRMS: calcd. for $C_{12}H_{13}NNaO_3$: 242.0793 [M + Na]$^+$; found 242.0803.

Treatment of the Hydroxamate 44 with Bis(collidine)bromine(I) Hexafluorophosphate: This reaction was carried out in dichloromethane as reported in the case of hydroxamate **4**. The ^{1}H NMR spectrum of the crude reaction mixture showed the presence of three products: the cyclic bromo imidate **45** (47%), the unsaturated cyclic imidate **46** (30%) and the β-cyano-α,β-enone **47** (23%). Purification of this mixture by liquid chromatography over silica gel led to intensive degradation. Only small amounts of compounds **46** and **47** were isolated.

(2*Z*)-4-Bromo-5-phenyldihydrofuran-2(3*H*)-one *O*-Acetyloxime (45): Oil. ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.37–7.20 (m, 5 H, Ph), 5.66 (d, $^3J_{H,H}$ = 4.8 Hz, 1 H, –C*H*Ph–), 4.29 (ddd, *J* = 4.8, 5.8 and 7.0 Hz, 1 H, –C*H*Br–), 3.40 [dd, $^3J_{H,H}$ = 17.5 and 7.0 Hz, 1 H, –C*H*$_2$(C=N)O–], 3.12 [dd, $^3J_{H,H}$ = 17.5 and 5.8 Hz, 1 H, –C*H*$_2$(C=N)O–], 2.17 [s, 3 H, C*H*$_3$–(C=O)O–] ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 168.0, 162.2, 135.1, 129.5 (2 C), 129.1 (2 C), 125.4, 92.3, 46.1, 37.0, 19.3 ppm. IR (film): ṽ = 2902, 1767, 1679 cm^{-1}. HRMS: calcd. for $C_{12}H_{12}BrNNaO_3$: 319.9898 [M + Na]$^+$; found 319.9899.

(2*Z*)-5-Phenyl-2(5*H*)-furanone *O*-Acetyloxime (46): ^{1}H NMR ($CDCl_3$, 250 MHz): δ = 7.37–7.20 (m, 5 H, Ph), 7.04 [d, $^3J_{H,H}$ = 5.7 Hz, 1 H, –C*H*=CH(C=N)O–], 6.34 [d, $^3J_{H,H}$ = 5.7 Hz, 1 H, =C*H*(C=N)O–], 6.29 (br. s, 1 H, –C*H*Ph–), 2.15 [s, 3 H, C*H*$_3$–(C=O)O–] ppm.

(*Z*)-4-Oxo-4-phenylbut-2-enenitrile (47): After treatment of the hydroxamate **44** (200 mg, 0.91 mmol) with bis(collidine)bromine(I) hexafluorophosphate, triethylamine (2 equiv.) was added to the reaction mixture. After stirring for 2 h at room temp., the mixture was concentrated under vacuum, and the residue was purified by liquid chromatography over silica gel to give compound **47**[10] (125 mg, 87%) as a white solid (m.p. 77 °C, CH_2Cl_2). Heating at reflux for three days in toluene caused isomerization to give the *E* isomer (m.p. 72 °C). The isomerization of the pure product was also observed in 5 weeks at room temp. ^{1}H NMR ($CDCl_3$, 360 MHz): δ = 7.97 (d, *J* = 7.2 Hz, 2 H, phenyl), 7.64 (d, $^3J_{H,H}$ = 11.5 Hz, 1 H, PhC*H*=), 7.63 (m, 1 H, phenyl), 7.54 (t, $^3J_{H,H}$ = 7.2 Hz, 2 H, phenyl), 6.00 (d, $^3J_{H,H}$ = 11.5 Hz, 1 H, =C*H*-CN) ppm. For the *E* isomer, the vinylic protons were at 7.97 and 6.57 (d, *J* = 20 Hz) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 186.6, 141.7, 135.4, 134.2, 128.9 (2 C), 128.6 (2 C), 115.4, 108.8 ppm. IR (CH_2Cl_2): ṽ = 3084, 3054, 2965, 2928, 1671, 1603, 1579, 908, 732 cm^{-1}. HRMS: calcd. for $C_{10}H_7NNaO$: 180.0425 [M + Na]$^+$; found 180.0427.

Dimethyl 2-(1-Cyano-3-oxo-3-phenylpropyl)malonate (48): *n*-Butyllithium (0.375 mL of a 1.6 M solution in hexanes, 0.60 mmol) was added dropwise at –40 °C to a THF solution (5 mL) of dimethyl malonate (76 μL, 0.66 mmol). After 30 min, a THF solution (1 mL) of (*Z*)-4-oxo-4-phenylbut-2-enenitrile (**47**, 0.095 g, 0.60 mmol) was added dropwise and the temperature was maintained at –40 °C for 1 h. A saturated aqueous solution of NH_4Cl (5 mL) was added. After separation, the aqueous phase was extracted with diethyl ether (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated under vacuum. The residue was purified by liquid chromatography over silica gel, to give compound **48** as an oil (140 mg, 80%). ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.93 (d, $^3J_{H,H}$ = 8.4 Hz, 2 H, phenyl), 7.60 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, phenyl), 7.47 (t, $^3J_{H,H}$ = 7.2 Hz, 2 H, phenyl), 3.97–3.90 [m, 2 H, –C*H*CN and CH(CO$_2$Me)$_2$–], 3.80 (s, 3 H, –OC*H*$_3$), 3.79 (s, 3 H, –OCH$_3$), 3.54–3.50 [m, *2* H, CH$_2$–(CO)Ph] ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 194.5, 166.6, 166.5, 135.3, 133.9, 128.7 (2 C), 127.9 (2 C), 118.8, 53.2 (2 C), 51.4, 38.1, 25.8 ppm. IR (CH_2Cl_2): ṽ = 2957, 2249, 1741, 1739, 1687, 1598, 1449, 1437 cm^{-1}. HRMS: calcd. for $C_{15}H_{19}N_2O_5$: 307.1294 [M + NH_4]$^+$; found 307.1297.

Methyl 3-Cyano-5-oxo-5-phenyl-2-(phenylsulfonyl)pentanoate (49): Methyl (phenylsulfonyl)acetate (0.058 mL, 0.35 mmol) was added dropwise at room temp. to a suspension of sodium hydride (17 mg of a 50% dispersion in mineral oil, 0.35 mmol) in dry THF (3 mL). After 30 min, the solution was cooled to –20 °C, a THF solution (1 mL) of (*Z*)-4-oxo-4-phenylbut-2-enenitrile (**47**, 50 mg, 0.31 mmol) was added dropwise, and the temperature was maintained at –20 °C for 1 h. A saturated aqueous solution of NH_4Cl (5 mL) was added. After separation, the aqueous phase was extracted with diethyl ether (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated under vacuum. The residue was purified by liquid chromatography over silica gel, to give compound **49** as a mixture of two diastereomers (60:40, 76 mg, 64%). Major diastereomer (from the crude reaction mixture): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.99–7.49 (m, 10 H, 2 × Ph), 4.65 (d, $^3J_{H,H}$ = 6.9 Hz, 1 H, –C*H*SO$_2$PhCO$_2$Me), 4.17–4.12 (m, 1 H, –C*H*CN–), 3.91–3.60 [m, 2 H, –C*H*$_2$(CO)Ph], 3.64 (s, 3 H, –OC*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 194.3, 163.9, 134.9, 134.0, 129.3, 129.1, 128.7 (2 C), 128.0 (2 C), 117.5, 68.8, 53.3, 38.1, 25.3 ppm. HRMS: calcd. for $C_{19}H_{21}N_2O_5S$: 389.1171 [M + NH_4]$^+$; found 389.1175. Minor diastereomer (from the crude reaction mixture): ^{1}H NMR ($CDCl_3$, 300 MHz): δ = 7.99–7.49 (m, 10 H, 2 × Ph), 4.61 (d, $^3J_{H,H}$ = 6.9 Hz, 1 H, –C*H*SO$_2$PhCO$_2$Me), 4.17–4.12 (m, 1 H, –C*H*CN–), 3.91–3.60 [m, 2 H, –C*H*$_2$(CO)Ph], 3.84 (s, 3 H, –OC*H*$_3$) ppm. ^{13}C NMR ($CDCl_3$, 100 MHz): δ =

194.5, 163.7, 134.9, 134.0, 129.3, 129.1, 128.7 (2 C), 128.0 (2 C), 117.7, 68.6, 53.4, 37.9, 25.1 ppm. IR (film, mixture of the two diastereomers): $\tilde{\nu}$ = 2955, 2251, 1747, 1686, 1598, 1449, 1329, 1151, 1082, 911, 732 cm^{-1}.

Methyl 2-Acetyl-3-cyano-5-oxo-5-phenylpentanoate (50): Methyl 3-oxobutanoate (41 mg, 0.35 mmol) was added dropwise at room temp. to a suspension of sodium hydride (17 mg of a 50% dispersion in mineral oil, 0.35 mmol) in dry THF (3 mL). After 30 min, the solution was cooled to –20 °C, a THF solution (1 mL) of (*Z*)-4-oxo-4-phenylbut-2-enenitrile (**47**, 50 mg, 0.31 mmol) was added dropwise, and the temperature was maintained at –20 °C for 1 h. A saturated aqueous solution of NH_4Cl (5 mL) was added. After separation, the aqueous phase was extracted with diethyl ether (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated under vacuum. The residue was purified by liquid chromatography over silica gel, to give compound **50** as a mixture of two diastereomers (50:50, 74 mg, 77%). ^1H NMR ($CDCl_3$, 250 MHz, mixture): δ = 7.94 (d, $^3J_{H,H}$ = 8.7 Hz, 2 H, Ph), 7.62 (t, $^3J_{H,H}$ = 7.2 Hz, 1 H, Ph), 7.49 (t, $^3J_{H,H}$ = 7.2 Hz, 2 H, Ph), 4.11 (m, 1 H, –C*H*CN–), 3.95–3.84 [m, 1 H, –C*H*(COMe)CO_2Me], 3.84 and 3.81 (2 × s, 3 H, –OCH_3), 3.50–3.45 [m, 2 H, –CH_2(CO)Ph], 2.39 and 2.36 [2 × s, 3 H, –(CO)CH_3] ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz, mixture): δ = 199.3, 199.1, 194.9, 194.8, 166.8 (2 diast.), 135.4 (2 diast.), 133.9 (2 diast.), 128.7 (2 C for the 2 diast.), 127.9 (2 C for the 2 diast.), 119.3 (2 diast.), 58.5, 58.2, 53.2 (2 diast.), 38.0, 37.9, 30.0, 29.7, 25.0 (2 diast.) ppm. IR (film, mixture): $\tilde{\nu}$ = 2957, 2247, 1744, 1720, 1637, 1597, 1449, 1360, 1247, 1219, 1159, 913, 755, 690 cm^{-1}. HRMS: calcd. for $C_{15}H_{19}N_2O_4$: 291.1345 [M + NH_4]$^+$; found 291.1346.

(*Z*)-4-Hydroxy-4-phenyloct-2-enenitrile (51): *n*-Butyllithium (0.30 mL of 1.6 M solution in hexanes, 0.478 mmol) was added dropwise at –78 °C to a THF solution (5 mL) of (*Z*)-4-oxo-4-phenylbut-2-enenitrile (**47**, 0.050 g, 0.32 mmol). After the system had been kept for 1 h at this temperature, a saturated aqueous solution of NH_4Cl (5 mL) was added. After separation, the aqueous phase was extracted with diethyl ether (3 × 5 mL) and the combined organic phases were dried ($MgSO_4$) and concentrated under vacuum. The residue was purified by liquid chromatography over silica gel, to give the alcohol **51** as an oil (52 mg, 75%). ^1H NMR ($CDCl_3$, 360 MHz, mixture): δ = 7.44–7.31 (m, 5 H, Ph), 6.96 (d, $^3J_{H,H}$ = 16.2 Hz, 1 H, NC–CH=C*H*–), 5.77 (d, $^3J_{H,H}$ = 16.2 Hz, 1 H, NC–C*H*=CH–), 2.08 (br. s, 1 H, –O*H*), 2.00–1.94 (m, 2 H, HO–C–CH_2–), 1.38–1.23 (m, 4 H, –CH_2–CH_2–), 0.91 (t, $^3J_{H,H}$ = 6.8 Hz, 3 H, –CH_3) ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 159.0, 142.9, 128.7 (2 C), 127.8 (2 C), 125.0, 117.8, 97.8, 72.7, 41.0, 25.4, 22.8, 13.9 ppm. HRMS: calcd. for $C_{14}H_{17}NNaO$: 238.1208 [M + Na]$^+$; found 238.1211.

***N*-Hydroxy-2-(1*H*-inden-2-yl)acetamide (53):** This compound was prepared by the procedure reported for the preparation of the hydroxamic acid **3** from 2-(1*H*-inden-2-yl)acetic acid (**56**, 348 mg).[21] Yield 300 mg (79%). White pasty solid. ^1H NMR (CD_3OD, 250 MHz): δ = 7.35–7.05 (m, 4 H, aromatic), 6.70 (br. s, 1 H, C*H*=), 4.97 [br. s, 2 H, –CH_2– (ring)], 3.41 [br. s, 2 H, –CH_2–(C=O)–] ppm. ^{13}C NMR (CD_3OD, 62.9 MHz): δ = 171.1, 147.0, 145.5, 144.3, 131.5, 128.1, 126.2, 125.2, 122.2, 42.8, 37.2 ppm. HRMS: calcd. for $C_{11}H_{11}NNaO_2$: 212.0682 [M + Na]$^+$; found 212.0683.

2-(1,2-Dihydronaphthalen-3-yl)-*N*-hydroxyacetamide (55): This compound was prepared by the procedure reported for the preparation of the hydroxamic acid **3**, from the acid **54**[21] (1.88 g). The hydroxamic acid **55** (1.85 g, 91%) was isolated as a white solid (m.p. 180 °C, CH_2Cl_2). ^1H NMR ($CDCl_3$, 250 MHz): δ = 8.60–8.20 (br. s, 1 H, –N*H*–), 7.25–7.00 (m, 4 H, aromatic), 6.42 (s, 1 H, –C*H*=), 3.16 [br. s, 2 H, –CH_2–(CO)N], 2.87 (t, $^3J_{H,H}$ = 7.8 Hz, 2 H, –CH_2–C_{ar}), 2.35 (t, $^3J_{H,H}$ = 7.8 Hz, 2 H, –CH_2-CH_2-C=), 1.80 (br. s, 1 H, –O*H*) ppm. ^{13}C NMR (CD_3OD, 62.9 MHz): δ = 170.2, 135.8, 135.5, 135.4, 126.8, 126.5, 126.1, 125.6, 125.5, 42.1, 28.8, 27.9 ppm. HRMS: calcd. for $C_{12}H_{13}NNaO_2$: 226.0844 [M + Na]$^+$; found 226.0849.

***N*-Acetoxy-2-(1*H*-inden-2-yl)acetamide (56):** This compound was obtained by the procedure reported for the preparation of compound **4**. From the hydroxamic acid **53** (378 mg, 2 mmol), compound **56** (347 mg, 75%) was isolated as a white solid (m.p. 95 °C, CH_2Cl_2). ^1H NMR ($CDCl_3$, 250 MHz): δ = 9.20 (br. s, 1 H, –N*H*–), 7.50–7.10 (m, 4 H, aromatic), 6.80 (br. s, 1 H, C*H*=), 3.54 [s, 2 H, –CH_2– (ring)], 3.49 [s, 2 H, –CH_2–(C=O)–], 2.23 [s, 3 H, CH_3–(CO)O–] ppm. ^{13}C NMR ($CDCl_3$, 62.9 MHz): δ = 168.7 (2 C), 144.5, 143.4, 140.2, 131.2, 126.5, 124.8, 123.7, 120.8, 41.3, 36.2, 18.3 ppm. HRMS: calcd. for $C_{13}H_{13}NNaO_3$: 254.0793 [M + Na]$^+$; found 254.0798.

2-(Acetoxy)-2-(3,4-dihydronaphthalen-2-yl)acetamide (57): This compound was obtained by the procedure reported for the preparation of compound **4**. From the hydroxamic acid **55** (1.10 g), the hydroxamate **57** (1.13 g , 85%) was obtained as a white solid (m.p. 115 °C, CH_2Cl_2). ^1H NMR ($CDCl_3$, 250 MHz): δ = 9.00 (br. s, 1 H, –N*H*–), 7.20–7.00 (m, 4 H, aromatic), 6.48 (s, 1 H, –C*H*=), 3.26 [s, 2 H, –CH_2–(CO)N], 2.90 (t, $^3J_{H,H}$ = 7.8 Hz, 2 H, –CH_2–C_{ar}), 2.41 (t, $^3J_{H,H}$ = 7.8 Hz, 2 H, –CH_2–CH_2–C=), 2.26 [s, 3 H, –O(CO)-CH_3] ppm. ^{13}C NMR ([D$_6$]DMSO, 62.9 MHz): δ = 169.0, 167.4, 136.4, 135.4, 134.4, 127.6, 127.1, 126.9, 125.9, 125.7, 41.1, 27.7, 27.1, 18.5 ppm. HRMS: calcd. for $C_{14}H_{15}NNaO_3$: 268.0950 [M + Na]$^+$; found 268.0948.

(*E*)-2-[1-Oxo-1*H*-inden-2(3*H*)-ylidene]acetonitrile (58): This compound was prepared by the procedure reported for the preparation of compound **47** (45 mg, 75%). White solid, m.p. 138 °C (CH_2Cl_2) (ref.[16] m.p. 138 °C); see also ref.[15]

(*Z*)-2-[3,4-Dihydro-1-oxonaphthalen-2(1*H*)-ylidene]acetonitrile (59): This compound was prepared by the procedure reported for the preparation of compound **47** (120 mg, 74%). White solid, m.p. 88–89 °C (CH_2Cl_2); see also ref.[16]

X-ray Crystallography: Data were collected with a Kappa X8 APEX II Bruker diffractometer with use of graphite-monochromated

Table 3. Crystallographic data for compounds **8** and **41**.

	41	**8**
Empirical formula	$C_{12}H_{18}BrNO_3$	$C_{11}H_{15}NO_3$
Formula wt. [g/mol]	304.17	209.24
Temp. [K]	290(2)	100(1)
Wavelength [Å]	0.71073	0.71073
Crystal system	monoclinic	monoclinic
Space group	*P*21	*P*21/*n*
a [Å]	9.0816(12)	9.6440(17)
b [Å]	7.3831(9)	10.170(2)
c [Å]	10.7751(12)	11.373(2)
β [°]	93.856(6)	97.480(4)
Cell volume [Å^3]	720.84(15)	1106.0(4)
Z	2	4
Density (calcd.)	1.401	1.257
Absor. coeff. [mm^{-1}]	2.848	0.091
Reflections collected	16986	13119
Independent reflections	4401 (R_{int} = 3.72%)	4199 (R_{int} = 3.50%)
Final *R* indices [$I > 2\sigma(I)$]	0.0375	0.0452
Final *wR* indices [$I > 2\sigma(I)$]	0.0756	0.1161
Goodness of fit	1.038	1.034
Flack parameter	0.025(12)	–

Mo-K_α radiation (λ = 0.71073 Å) (Table 3). The temperature of the crystal was maintained at the selected value (100 K) by means of a 700 series Cryostream cooling device to within an accuracy of ±1 K. The data were corrected for Lorentz polarization and absorption effects. The structures were solved by direct methods with SHELXS-97[22] and refined against F^2 by full-matrix least-squares techniques with SHELXL-97[23] with anisotropic displacement parameters for all non-hydrogen atoms. Hydrogen atoms were located on a difference Fourier map and introduced into the calculations as a riding model with isotropic thermal parameters. All calculations were performed by use of the crystal structure crystallographic software package WINGX.[24] The absolute configuration of compound **41** was determined by refining the Flack[25] parameter with use of a large number of Friedel's pairs.

CCDC-756240 (for **8**) and -756241 (for **41**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from the Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_ request/cif.

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Received: March 18, 2010
Published Online: September 7, 2010

