3,3-Sigmatropic Rearrangements Involving N−O Bond-Cleavage of Enehydroxylamine Derivatives

Lucinda V. Reis,[a][‡] Ana M. Lobo,*[a] Sundaresan Prabhakar,*[a] and Mariana P. Duarte[a]

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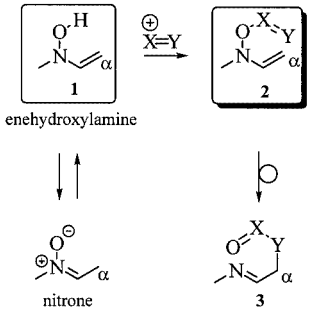
Enehydroxylamines, derived from carbocyclic and heterocyclic 1,3-dioxo compounds, react with a variety of unsaturated electrophiles to give, in good to excellent yields, substances that in general undergo 3,3-sigmatropic rearrangements either spontaneously or upon heating. In those cases in which such reactions failed, addition of sodium hydride was found to induce the transformation. A study of the rearrangement by use of deuterium-labelled compounds showed that no crossover occurs, indicating the intramolecular nature of the process. The method provides 2,3- or 3,4-disubstituted cyclohexenones, 5,6-disubstituted barbiturates and the corresponding fused pyrrole and imidazolinone derivatives.

Introduction

Enehydroxylamines **1**, which are tautomers of nitrones, are compounds with interesting chemical and biological properties, acting as 5-lipoxygenase and IL-1 inhibitors,[1] due to the presence of two adjacent functional groups: a weak N−O bond and an enamine nitrogen atom.[2] Of special relevance is the possible involvement of derivatives **2** in 3,3-sigmatropic rearrangements,[3] in which the N−O bond is cleaved, and the departing group is introduced at the adjacent α-carbon atom to give **3** in a thermodynamically driven process (Scheme 1).



Scheme 1

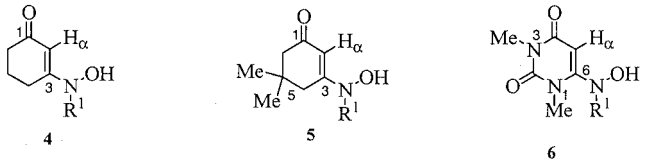
The seminal disclosure of the generation of such rearranging *O*-acyl-*N*-alkenylhydroxylamine systems in situ by quaternisation of *O*-acyl oximes containing one α-hydrogen atom, followed by base treatment, was made by House[4] more than 30 years ago. Other workers have applied the same methodology for the preparation of α-acyloxyimines,[5] α-amido ketones,[6] α-amino acids,[7] oxazolinones,[8] imidazoles,[9] furans,[10] and pyrroles.[11]

Since it was thought that the full synthetic potential of the cyclic enehydroxylamines had been left largely underexploited, we examined their chemistry from the standpoint of their 3,3-sigmatropic rearrangements. In this paper we give a full account of our work involving rearrangement of derivatives of *N*-alkylenehydroxylamine **2**, and extending it to amidic *N*-hydroxy-1,3-dicarbonyl compounds derived from barbituric acid, and show the usefulness of the process for the production of 2,3- and 3,4-heterodisubstituted cyclohexen-1-ones, fused pyrrolocyclohexenones, and 5,6-uracil derivatives. A brief preliminary communication of part of this work has already appeared.[12]

Results and Discussion

Compounds of types **4**, **5**, and **6** were readily obtainable in reasonable to good yields from the corresponding cyclohexane-1,3-diones or 6-chloro-1,3-dimethylbarbituric acid[13] and the appropriate *N*-substituted hydroxylamines, essentially by published methods[14] (see Exp. Sect.) (Table 1). A slight modification of the reported procedure, involving the prior liberation of the free hydroxylamines from their salts, was found to facilitate the isolation of the products, and hence improve the yields. However, only poor yields were obtained with *N*-isopropyl- and *N*-cyclohexylhydroxylamines.

[a] Departamento de Química, CQFB/REQUIMTE, Faculdade de Ciências e Tecnologia, Universidade Nova de Lisboa, and SINTOR-UNINOVA,
2829 Monte da Caparica, Portugal
Fax: (internat.) + 351-212948550
E-mail: aml@fct.unl.pt
[‡] Present address: Departamento de Química, Universidade de Trás-os-Montes e Alto Douro,
Apartado 202, 5001-911 Vila Real Codex, Portugal
Fax: (internat.) + 351-259350480
E-mail: lvrfisco@utad.pt



4-6	a	b	c	d
R^1	Me	CH_2Ph	*i*Pr	cyclohexyl

Table 1. Enehydroxylamines **4**−**6**: yields and diagnostic spectroscopic data

	R^1	Yield[a] [%]	$\tilde{\nu}$[b] [cm^{-1}]	$\delta_{H\alpha}$[c] [ppm]
4a	Me	70	1550	5.46
4b	CH_2Ph	87	1555	5.69
4c	*i*Pr	24	1550	5.78
4d	C_6H_{11} (cyclohexyl)	23	1540	5.16
5a	Me[d]	80	1590	5.52
5b	CH_2Ph	68	1538	5.68
6a	Me	80	1650	5.70
6b	CH_2Ph	55	1613	5.76

[a] Isolated yields. [b] KBr phase. [c]$CDCl_3$ solution. [d] Ref.[14]

The infrared spectra of the enehydroxylamines reported here indicated extensive electronic delocalisation (Table 1), as is observed for *N*-alkylenaminones of similar structures.[15,16] The ^1H NMR spectra of these compounds contained, inter alia, the characteristic one-proton singlet in the olefinic region (the α-proton in **4**, **5**, and **6**) at $\delta \approx 5.8-5.2$ ppm (Table 1). Consistent with the delocalised structures, deuterium exchange at C-2 occurred readily on shaking a $CDCl_3$ solution of the compounds with D_2O.

Reactions of Enehydroxylamines with Electrophiles

Reactions with Methanesulfonyl Chloride, *N*,*N*-Dimethylthiocarbamoyl Chloride and 1-Fluoro-2,4-dinitrobenzene

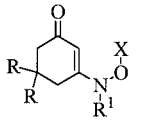
With a satisfactory method for the preparation of **4**−**6** at hand, their reactions with a variety of electrophiles were studied. Table 2 lists reactions with $MeSO_2Cl$, $Me_2NC(S)Cl$, 1-fluoro-2,4-dinitrobenzene, methyl propiolate, and dimethyl acetylenedicarboxylate, which directly provided products **3** of a 3,3-sigmatropic rearrangement, according to the general Scheme 1.

When, for example, enehydroxylamines **4a**, **4b**, and **5a** were treated with equimolar amounts of the powerful electrophile methanesulfonyl chloride in the presence of Hünig's base at 0 °C to room temp., the corresponding rearranged products **8a**, **8b**, and **8c** were obtained in yields ranging from 84 to 93% (Table 2, Entries 1, 2, and 3, and Scheme 2, *a*). For compound **6a**, however, the yield of the rearranged product **10a** dropped to 41% and a product identified as **10a′** was isolated in 48% yield. While **10a** was the expected product of a 3,3-sigmatropic rearrangement, compound **10a′** may have arisen from attack of the anion, liberated from the electrophile, at the adjacent carbon atom C-2 prior to the rearrangement (Scheme 2, *b*), or through the decomposition of an earlier intermediate (represented in Scheme 2, *c*). This difference in behaviour of compounds of type **6** was to be a constant theme with most of the reactions studied involving electrophiles bearing an halogen anion as the initially departing group.

Table 2. Treatment of **4**−**6** with electrophiles

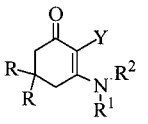
Entry	Starting material (SM)	Electrophile (E)	Ratio SM/E	Conditions	Time *t* [h]	Products (yield[a] [%]) [3,3]-Rearrang.	Others
1	**4a**	$MeSO_2Cl$	1:1	A[b]	1.5	**8a** (87)	−
2	**4b**	$MeSO_2Cl$	1:1	A	0.7	**8b** (84)	−
3	**5a**	$MeSO_2Cl$	1:1	A	3	**8c** (93)	−
4	**6a**	$MeSO_2Cl$	1:1	A	1	**10a** (41)	**10a′** (48)
5	**4a**	$Me_2NC(S)Cl$	1:3	B[c]	24	**8d** (53)	−
6	**5a**	$Me_2NC(S)Cl$	1:3	B	4.5	**8e** (63)	−
7	**6a**	$Me_2NC(S)Cl$	1:3	B	72	N.R.	−
8	**4a**	$Me_2NC(S)Cl$	1:3	C[d]	3.5	**8d′** (63)	−
9	**5a**	$Me_2NC(S)Cl$	1:3	C	4	**8e′** (84)	−
10	**6a**	$Me_2NC(S)Cl$	1:3	C	4.5	**10b** (30)	**10b′** (55)
11	**5a**	1-F-2,4-$(O_2N)_2C_6H_3$	1:1.3	D[e]	2	**11** (89)	−
12	**6a**	1-F-2,4-$(O_2N)_2C_6H_3$	1:1.3	D	2.5	**12** (73)	−
13	**4a**	$HCCCO_2Me$	1:1	E[f]	48	**13a** (82)	**14a** (77)
14	**5a**	$HCCCO_2Me$	1:1	E	96	**13b** (76)	**14b** (74)
15	**6a**	$HCCCO_2Me$	1:1	E	144	N.R.	−
16	**4a**	MeO_2CCCCO_2Me	1:1	E	40	**13c** (69)	**14c** (90)
17	**5a**	MeO_2CCCCO_2Me	1:1	E	40	**13d** (70)	**14d** (88)
18	**6a**	MeO_2CCCCO_2Me	1:1	E	144	N.R.	−

[a] Isolated yields. [b] Et*i*Pr_2N (1 equiv.), THF, 0 °C → room temp. [c] Et_3N (3 equiv.), THF, 0 °C → room temp. [d] NaH (2 equiv.), THF, 0 °C → room temp. [e] NaH (1.2 equiv.), THF, 0 °C → room temp. [f] Et*i*Pr_2N (1 equiv.), THF, 0 °C → room temp.; for **14a/b**: reflux **13a/b** in toluene; for **14c/d**: reflux **13c/d** in toluene/cat. *p*-TSA.



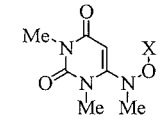
7

a: R = H R^1 = Me X = SO_2Me
b: R = H R^1 = CH_2Ph X = SO_2Me
c: R = R^1 = Me X = SO_2Me
d: R = H R^1 = Me X = $C(S)NMe_2$
e: R = R^1 = Me X = $C(S)NMe_2$
f: R = H R^1 = Me X = C(O)Ph
g: R = H R^1 = CH_2Ph X = C(O)Ph
h: R = R^1 = Me X = C(O)Ph
i: R = Me R^1 = CH_2Ph X = C(O)Ph
j: R = R^1 = Me X = $P(O)(OEt)_2$
k: R = H R^1 = Me X = C(O)NHPh
l: R = R^1 = Me X = C(O)NHPh



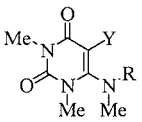
8

a: R = H R^1 = Me R^2 = H Y = OSO_2Me
b: R = H R^1 = CH_2Ph R^2 = H Y = OSO_2Me
c: R = R^1 = Me R^2 = H Y = OSO_2Me
d: R = H R^1 = Me R^2 = H Y = $SC(O)NMe_2$
d': R = H R^1 = Me R^2 = $C(S)NMe_2$ Y = $SC(O)NMe_2$
e: R = R^1 = Me R^2 = H Y = $SC(O)NMe_2$
e': R = R^1 = Me R^2 = $C(S)NMe_2$ Y = $SC(O)NMe_2$
f: R = H R^1 = Me R^2 = H Y = OC(O)Ph
g: R = H R^1 = CH_2Ph R^2 = H Y = OC(O)Ph
h: R = R^1 = Me R^2 = H Y = OC(O)Ph
i: R = Me R^1 = CH_2Ph R^2 = H Y = OC(O)Ph
j: R = R^1 = Me R^2 = H Y = $OP(O)(OEt)_2$
k: R = H R^1 = Me R^2 = C(O)NHPh Y = NHPh



9

a: X = SO_2Me
b: X = $C(S)NMe_2$
c: X = C(O)Ph
d: X = $P(O)(OEt)_2$
e: X = C(O)NHPh

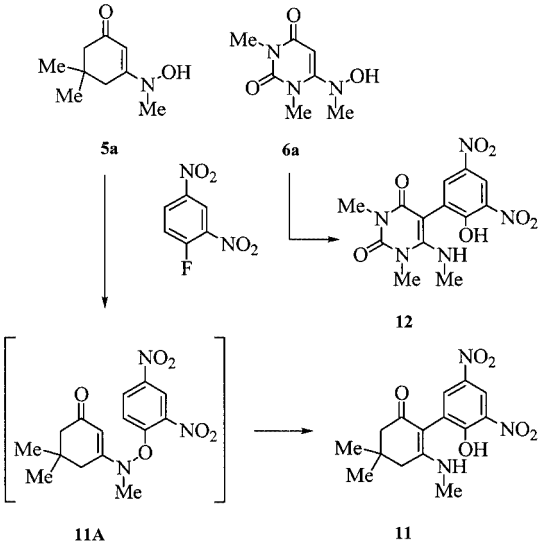


10

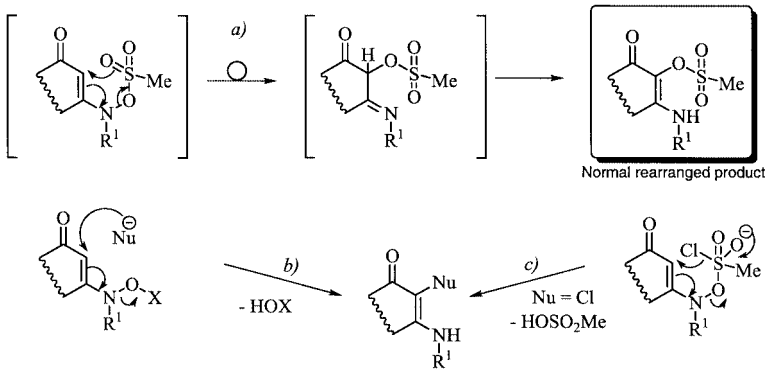
a: R = H Y = OSO_2Me
a': R = H Y = Cl
a'': R = H Y = Br
b: R = $C(S)NMe_2$ Y = $SC(O)NMe_2$
b': R = H Y = H
c: R = H Y = OC(O)Ph
d: R = H Y = $OP(O)(OEt)_2$
e: R = H Y = NHPh
e': R = C(O)NHPh Y = NHPh

For treatment with *N*,*N*-dimethylthiocarbamoyl chloride (1 equiv.) − a softer electrophile − in the presence of triethylamine, compounds **4a** and **4b** gave the corresponding **8d** (53%) and **8e** (63%), while **6a** failed to react. A threefold increase in the ratio of the electrophile to the enehydroxylamines, coupled with substitution of the Et_3N by NaH, improved the yields of the products **8d′** (63%) and **8e′** (84%) and resulted in the rearrangement of a product derived from **6a** to yield **10b** (30%). In this last reaction, however, the major compound was the *N*-deoxy compound **10b′** (55%) (Table 2, Entry 10).

A C-2−C-Ar bond, produced by a 3,3-shift, could also be established with a remarkable ease, as demonstrated by treatment of **5a** with 1-fluoro-2,4-dinitrobenzene in the presence of NaH (1.3 equiv.). The product, phenol **11**, presumably formed via the diethyl ether **11A**, was obtained in high yield (89%, Scheme 3). Similarly, **6a** yielded the barbiturate derivative **12** (73%), a type of compound otherwise difficult to obtain.



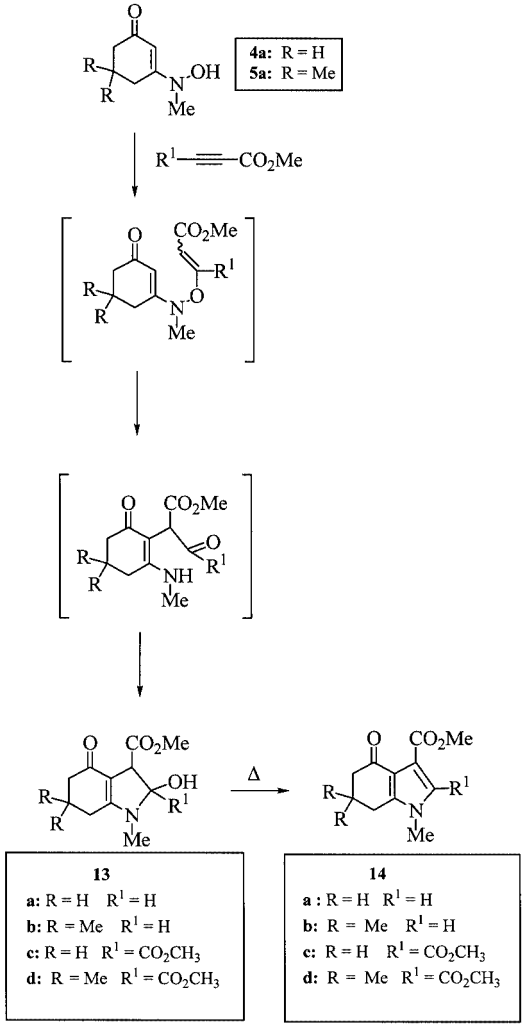
Scheme 3



Scheme 2

4-Oxo-4,5,6,7-tetrahydroindoles

4-Oxo-4,5,6,7-tetrahydroindoles derivatives have often served as key intermediates[17] for the preparation of important 4-substituted indoles. Treatment of **4a**, **5a**, and **6a** with methyl propiolate and dimethyl acetylenedicarboxylate was therefore examined as a means to achieve such an end. Accordingly, when equimolar amounts of **4a**, Hünig's base and methyl propiolate were allowed to stand at room temp., a smooth reaction ensued (Table 2, Entry 13, Scheme 4). The carbinol amine **13a**, isolated in 82% yield, was readily dehydrated in toluene under reflux to afford the synthetically useful pyrrolecarboxylate **14a** (77%). In an analogous manner, **5a** gave − via the intermediate **13b** (76%) − **14b** (74%). For the more reluctant **13c** and **13d** a catalytic amount of *p*-toluenesulfonic acid proved essential for high yields in the dehydration to the corresponding **14c** and **14d**.



Scheme 4

Imidazolinones

A system incorporating a cyano group linked to the *N*-hydroxy group of the hydroxylamines was examined with a view to achieve a short synthesis of *N*-monosubstituted imidazolones fused to a carboxylic ring. Indeed, **4a**, on treatment with BrCN in the presence of Et_3N, furnished the desired product **15a**, albeit in a modest yield (36%, Table 3, Entry 1, Scheme 5). With DABCO as the base, however, a vastly improved yield of the same compound (81%) was obtained (Entry 2). Other enehydroxylamines with bulky alkyl substituents at the nitrogen atom, such as isopropyl (**4c**) or cyclohexyl (**4d**), were found to give poorer yields or no reaction (Entries 4, 32%; Entry 5, no reaction).

When applied to **6a**, the procedure also did not provide the analogous imidazolinone. Instead, the spectral and analytical data of the only compound isolated (in 7.5% yield) from a very complex mixture pointed to 5-bromo-1,3-dimethyl-6-(methylamino)uracil (**10a′′**). Clearly, the mixture of DABCO and BrCN was acting as a brominating agent in this instance. It is known that the species formed from BrCN and 4-(dimethylamino)pyridine exists essentially as *N*-cyano-4-(dimethylamino)pyridinium bromide (CAP).[18] Use of this reagent for treatment of **6a** in stoichiometric quantities provided a mixture of the *N*-cyanated and the non-cyanated imidazolinones. With an excess of this reagent, however, the cyanamide **16a** could be obtained in high yield (79%, Table 3, Entry 11, Scheme 6). Reactions with other enehydroxylamines took a similar course.

Of relevance in this context is the unique ability of this reagent to convert the sulfo nitrone **17** into the *N*-cyanoimidazolone **18** in high yield. Alternative combinations of BrCN[19] with other bases exclusively afforded the α-bromo nitrone **19** (Scheme 7).

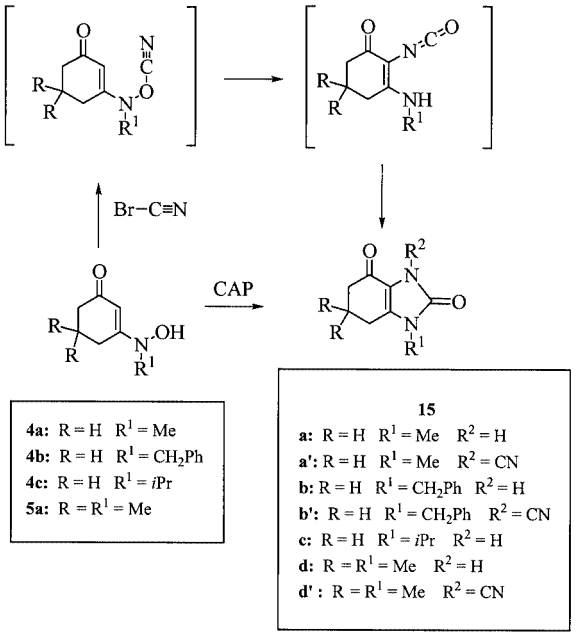
Reactions with Benzoyl Chloride and Diethyl Chlorophosphate

While the reactions between enehydroxylamines and the electrophiles discussed so far had given the rearranged products *directly*, treatment of **4a** with benzoyl chloride, on the other hand, enabled the *unrearranged* **7f** to be isolated in 92% yield. This compound was then induced to proceed to **8f** (90%) by heating it in toluene at reflux (Table 4, Entry 1). Similarly **4b**, **5a**, and **5b** gave **8g**, **8h**, and **8i** in excellent yields. Compound **6a** similarly gave **9c**, but the rearranged product **10c** spontaneously cyclised upon heating to give the bicyclic **20** (Entry 5, Scheme 8). This structure was assigned on the basis of the following facts: the product was found by mass spectrometry to be isomeric with **10c**, it lacked the IR absorption due to the carbonyl group of the enolic benzoate, the diagnostic NH−CH_3 *doublet* of **10c**, at δ = 2.98 ppm, now appeared as a *singlet*, and the low-field resonances (δ = 8.15−8.18 ppm) for the two aromatic H atoms *ortho* to the carbonyl group of the benzoate were also absent. The labile N−H resonance of **10c** at δ = 4.56 ppm was replaced in **20** by a signal, also exchangeable with D_2O, at δ = 6.17 ppm. Moreover, the compound's ^{13}C NMR spectrum in CD_2Cl_2 showed a quaternary carbon signal at δ = 126.9 ppm, which could be attributed to a tetrahedral carbon atom. Similar values of tetrahedral carbon atoms attached to two oxygen atoms, one nitrogen atom, and a phenyl group have been reported.[20]

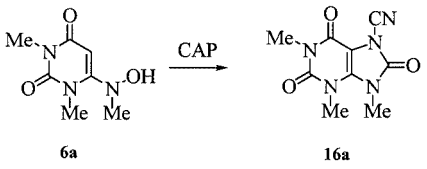
Table 3. Treatment of **4**−**6** with bromocyanogen and CAP

Entry	Starting material (SM)	Electrophile (E)	Ratio SM/E	Conditions	Time *t* [h]	Products (yield[a] [%])
1	**4a**	BrCN	1:1	A[b]	0.5	**15a** (36)
2	**4a**	BrCN	1:1.3	B[c]	2	**15a** (81)
3	**4b**	BrCN	1:1.5	B	1.0	**15b** (94)
4	**4c**	BrCN	1:1	A	0.5	**15c** (32)
5	**4d**	BrCN	1:1	A	30	N.R.
6	**5a**	BrCN	1:1.3	B	1	**15d** (83)
7	**6a**	BrCN	1:1	B	2	N.R.
8	**4a**	CAP	1:3	C[d]	28	**15a′** (80)
9	**4b**	CAP	1:3	C	24	**15b′** (83)
10	**5a**	CAP	1:3	C	24	**15d′** (89)
11	**6a**	CAP	1:3	C	48	**16a** (79)

[a] Isolated yields. [b] Et_3N (1 equiv.), THF, 0 °C → room temp. [c] DABCO (1.3 equiv.), THF, 0 °C → room temp. [d] Et*i*Pr_2N (1 equiv.), THF, 50 °C.

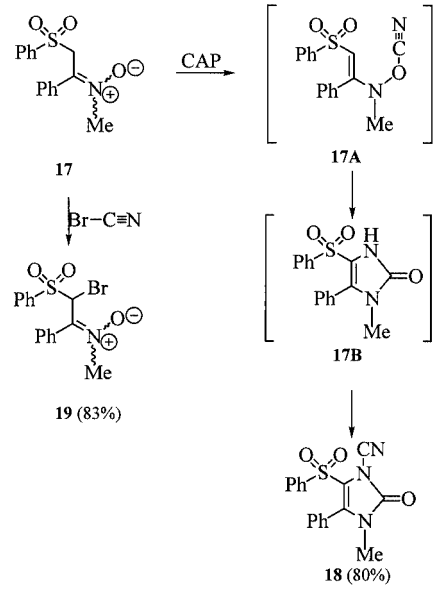


Scheme 5



Scheme 6

With diethyl chlorophosphate (Table 4, Entries 6 and 7), high-yield rearrangements converted **7j** and **9d** into **8j** and **10d**, respectively.



Scheme 7

Reactions with Phenyl Isocyanate

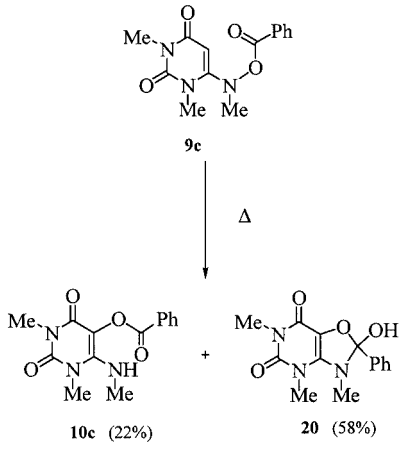
Unexpectedly, a class of closely related compounds failed to behave chemically in a similar manner on thermolysis (Scheme 9, Table 5). For instance, of the three structurally similar carbamate derivatives **7k**, **7l**, and **9e**, only the last underwent rearrangement in toluene at reflux, to provide the product, the *vic*-diamine **10e** (55%) and the derivative **10b′** (36%, Scheme 10, *a*).

However, the reluctance of **7k** to participate usefully in the rearrangement could be overcome if its anion was generated with NaH in THF and the resulting mixture was heated under reflux (Scheme 11). Acidic workup, followed by purification gave a product (49%) analysing as $C_{20}H_{21}N_3O_2$. Its ^1H NMR spectrum contained signals due to 10 aromatic protons, two NH resonances at δ = 7.53 and

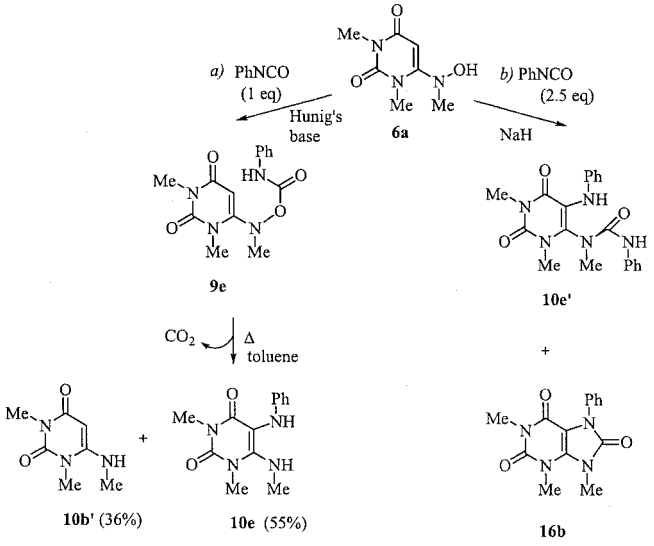
Table 4. Reactions of **4**−**6** with benzoyl chloride and diethyl chlorophosphate

Entry	Starting material (SM)	Electrophile (E)	Ratio SM/E	Conditions	Time *t* [h]	Products (yield[a] [%]) Before rearrang.	After rearrang.
1	**4a**	PhC(O)Cl	1:1	A[b]	1.5	**7f** (92)	**8f** (90)
2	**4b**	PhC(O)Cl	1:1	A	2	**7g** (88)	**8g** (90)
3	**5a**	PhC(O)Cl	1:1	A	1	**7h** (97)	**8h** (94)
4	**5b**	PhC(O)Cl	1:1	A	1	**7i** (97)	**8i** (85)
5	**6a**	PhC(O)Cl	1:1	A	1	**9c** (79)	**10c** (22), **20** (58)
6	**5a**	$(EtO)_2P(O)Cl$	1:1	B[c]	4	**7j** (86)	**8j** (77)
7	**6a**	$(EtO)_2P(O)Cl$	1:1	B	1.5	**9d** (86)	**10d** (78)

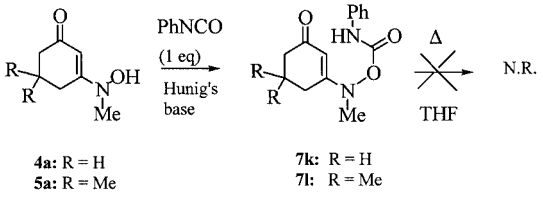
[a] Isolated yields. [b] Et*i*Pr_2N (1 equiv.), THF, 0 °C → room temp.; for **8**, **10**: reflux **7**, **9** in toluene. [c] NaH (1.2 equiv.), THF, 0 °C → room temp.; for **8**, **10**: reflux **7**, **9** intoluene.



Scheme 8



Scheme 10



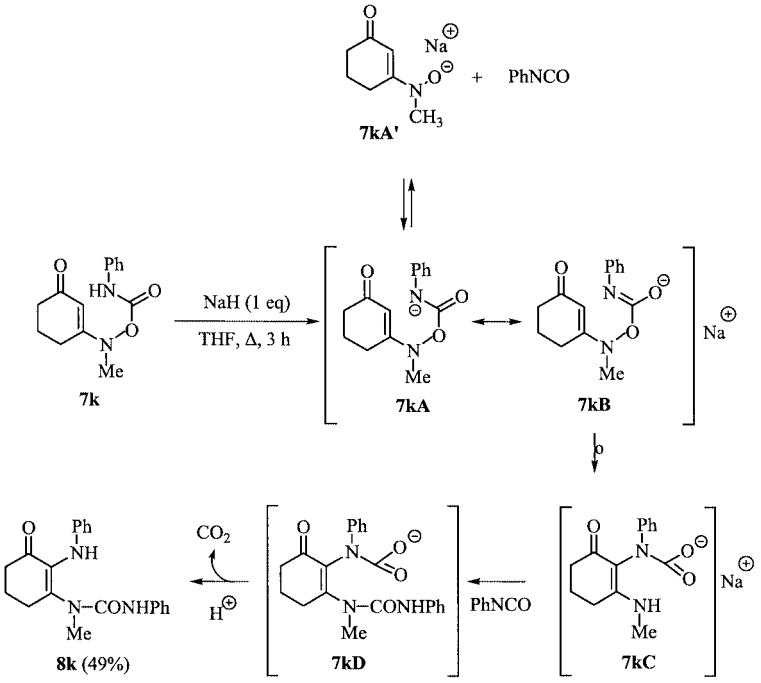
Scheme 9

6.70 ppm (each 1 H), and a *singlet* at δ = 3.10 (3 H) ppm. The absence of a signal due to the olefinic C-2 proton, in conjunction with the presence of IR absorptions at $\tilde{\nu}$ = 3210, 1670, and 1595 cm^{-1}, uniquely defined it as **8k**. It is a general feature of all compounds of type **8** (R^1 = Me; R^2 = H) in this study that they exhibit the N−CH_3 ^{1}H NMR signal either as a broad singlet or as a doublet ($J \approx$

Table 5. Treatment of **4**−**6** with phenyl isocyanate and rearrangement

Entry	Starting material (SM)	Electrophile (E)	Ratio SM/E	Conditions	Time *t* [h]	Products (yield[a] [%]) Before rearrang.	After rearrang.
1	**4a**	PhCNO	1:1	A[b]	2	**7k** (90)	–
2	**4a**	PhCNO	1:2.5	B[c]	3	–	**8k** (84)
3	**5a**	PhCNO	1:1	A	4	**7l** (85)	–
4	**5a**	PhCNO	1:2.5	B	1.25	–[d]	–
5	**6a**	PhCNO	1:1	A	2	**9e** (95)	**10e** (55), **10b′** (36)
6	**6a**	PhCNO	1:2.5	B	7	–	**10e′** (47), **16b** (51)

[a] Isolated yields. [b] Et*i*Pr_2N (1 equiv.), THF, 0 °C → room temp. [c] NaH (1.3 equiv.), THF, 0 °C → room temp. [d] Complex mixture.



Scheme 11

5 Hz), sharpening or collapsing to a singlet on addition of D_2O.

It is proposed that the sodium salt **7kA** undergoes two concurrent reactions on thermolysis, a rearrangement to **7kC** and a dissociation into PhNCO and the anion **7kA′**. It is the electrophile generated in this manner that reacts with the intermediate **7kC** to provide **7kD**, which subsequently undergoes decarboxylation to afford **8k**.

The fact that product **8k** was obtained in 84% yield when the above reaction was performed in the presence of an excess of electrophile (Table 5, Entry 2) is consistent with the above argument. For reasons not clearly understood, no useful products could be isolated from the dimedone derivative **7l**, although the heterocycle **6a** participated readily enough in a similar reaction to provide the rearranged **10e′**, which readily cyclised to the imidazolone **16b** (Entry 6 in Scheme 10, *b*, above).

The ready availability and the relative stability of the enehydroxylamine derivative **7k** prompted us to assess the possibility of generating a new enamine system, also capable of participating in a sigmatropic reaction. Accordingly, **7k** in THF was treated with KHMDS (3.3 equiv.) in the presence of excess TMSCl at −80 °C and the mixture was allowed to warm to room temp. Acidic workup, followed by purification of the resulting products furnished two compounds **21** and **22** in 54% and 14% yields, respectively (Scheme 12). The IR spectra of both compounds contained absorptions characteristic of the enamino system. Whilst the ^{1}H NMR spectra of both compounds exhibited the C-2 olefinic hydrogen atoms as singlets (1 H) with their expected δ values, significant differences in chemical shift were observed for the C-4 protons. In **21** the hydrogen atom referred to resonated as a triplet at δ = 5.44 (1 H) ppm (collapsing to a singlet on irradiation at δ ≈ 2.2 ppm), while in **22** it appeared as a multiplet centred at higher field (δ = 4.27 ppm). This information, coupled with their exact [M$^+$], permitted unequivocal attribution of the structures shown.

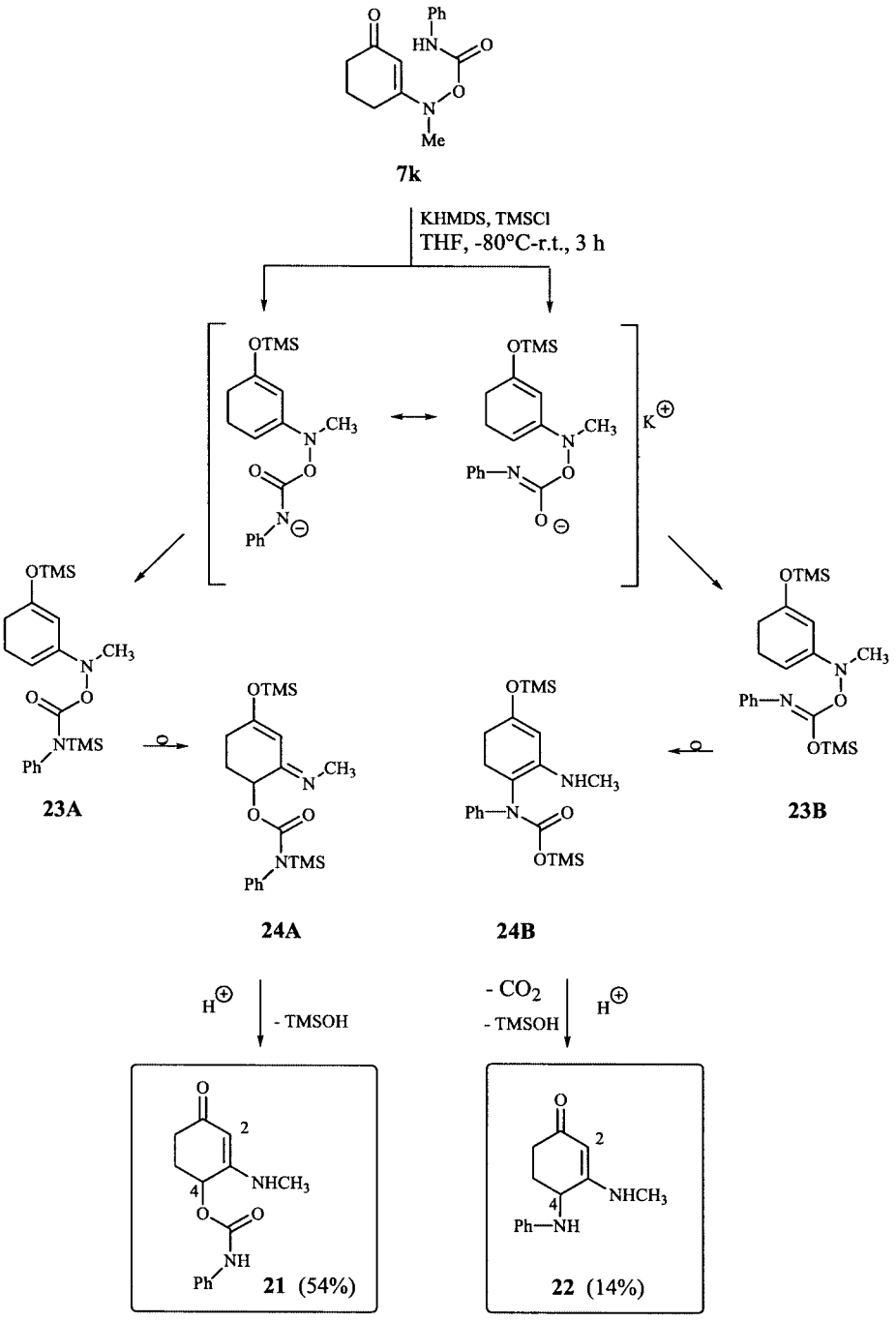
A mechanism that can be proposed for the above changes presupposes that the starting material is wholly converted into a mixture of *N*,*O*-disilylated derivatives **23A** and **23B**. Both of these would, on rearrangement, give rise to the corresponding silyl ethers of **24A** and **24B**, from which **21** and **22** are obtained on workup.

An analogous change in the site of attack (C-4 vs. C-2) was observed for the benzoate **7f**, which, when subjected to similar conditions (TBDMSCl instead of TMSCl), furnished the benzoate **25** in 29% yield (Scheme 13). Interestingly, however, when a mixture containing **7f**, prepared in situ from **4a**, PhC(O)Cl (1 equiv.) and a slight excess of NaH (1.3 equiv.) at 0 °C in THF, was heated to reflux (4 h) the two isomeric benzoates **8f** and **25** were isolated in almost equal proportions (46% and 47% yields, respectively).

A cursory examination of the reactions between **5a** and bromonitrile oxide and between **5a** and (diethylamino)sulfur trifluoride (DAST) identified only the 5-bromo and the 5-fluoro cyclic derivatives **26a** and **26b**, respectively, from the complex mixtures (Scheme 14).

The Intramolecularity of the Rearrangement

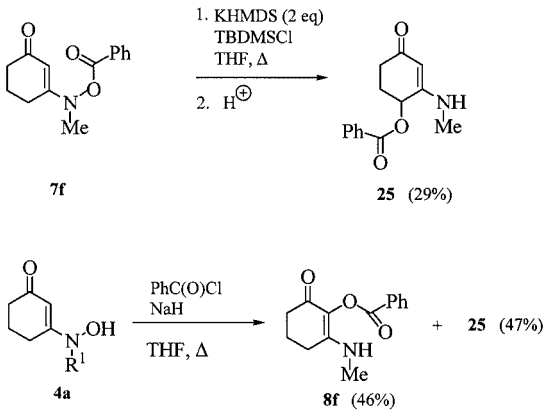
The clean thermal reactions of the deuterium-labelled derivative **7g-*d*$_5$** and **7i** were selected for mechanistic study (Scheme 15). The rearrangement of **7g-*d*$_5$** was conducted in toluene at 100 °C in the presence of an equimolar amount of compound **7i**. This experiment gave only the two prod-



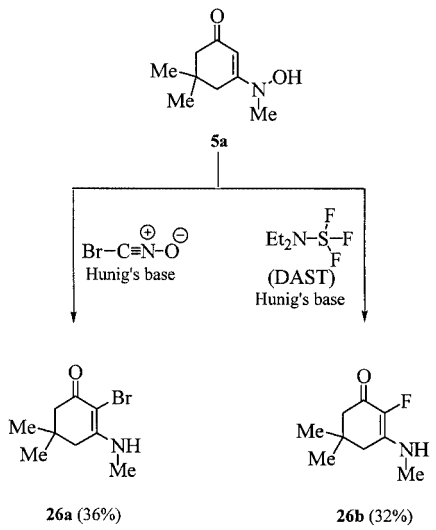
Scheme 12

ucts **A** and **B**. Their mass spectra were compared with those of authentic **8g**, **8g-d_5**, **8i**, and **8i-d_5** (Table 6).

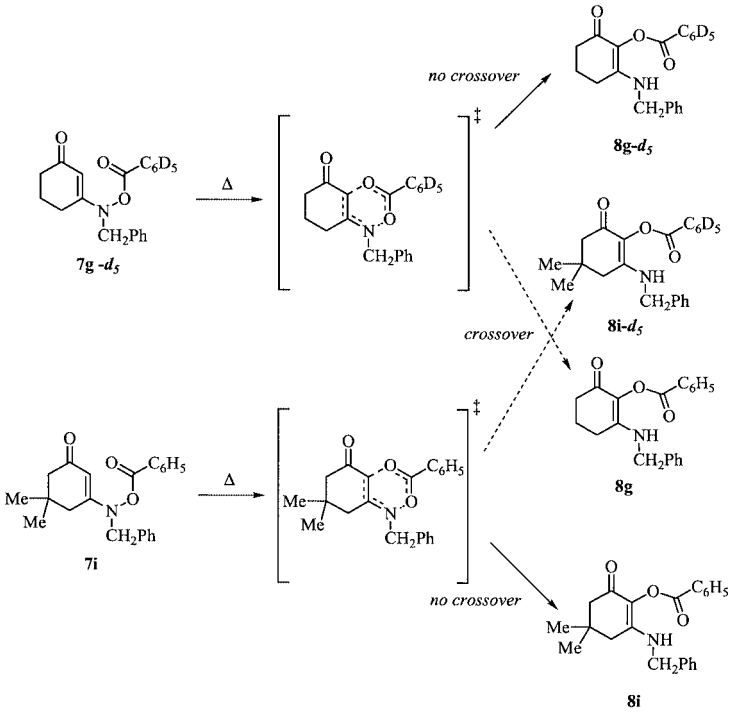
The rearrangement could in principle take place either intramolecularly (synchronously, or via a diradical or an intimate ion-pair)[21] or intermolecularly, in which case the appearance of *crossover* products would be expected. As can easily be deduced from the results, the mass spectra of compounds **A** and **B** correspond to those of authentic **8i** and **8g-d_5**, respectively; that is, *no crossover products* were observed, indicating an intramolecular rearrangement. The relative independence of the kinetic rate constant of the solvents employed while conducting the rearrangement of **7g** in toluene ($\varepsilon = 2.4$) and DMSO ($\varepsilon = 48.8$) at 373 K, ($k_{obsd.} = 3.7\pm0.4\cdot10^{-4}$ s^{-1} and $1.5\pm0.2\cdot10^{-4}$ s^{-1}, respectively), is consistent with a non-ionic transition state.[22] However, our data do not allow us to conclude whether the rearrangement proceeds through a concerted mechanism or a non-concerted one.[23]



Scheme 13



Scheme 14



Scheme 15

Table 6. Mass spectrometric data for **8g**, **8g-d_5**, **8i**, **8i-d_5**, **A**, and **B** (Scheme 15)

8g		**8g-d_5**		**8i**		**8i-d_5**		**A**		**B**	
m/z	(%)	*m/z*	(%)	*m/z*	(%)	*m/z*	(%)	*m/z*	(%)	*m/z*	(%)
321	(18.4)	326	(16.2)	349	(24.8)	354	(19.3)	349	(19.6)	326	(16.4)
216	(28.6)	216	(26.1)	244	(52.8)	244	(46.6)	244	(43.9)	216	(26.5)
188	(9.6)	188	(8.5)	216	(16.6)	216	(13.3)	216	(13.7)	188	(9.7)
105	(100.0)	110	(100.0)	105	(100.0)	110	(100.0)	105	(100.0)	110	(100.0)
91	(55.6)	91	(53.0)	91	(85.1)	91	(76.1)	91	(78.2)	91	(60.0)
77	(20.6)	82	(23.1)	77	(20.0)	82	(23.0)	77	(21.5)	82	(23.1)

Conclusions

O-Acyl and related derivatives of enehydroxylamines, often postulated as reactive intermediates, have been isolated and their chemistry studied. It has been shown that compounds with this functionality serve as starting materials for the facile preparation not only of polyfunctional cyclohexanes, namely 2,3- or 3,4-disubstituted cyclohexenones, but also of heterocycles such as hydroindoles, 5,6-disubstituted uracils, and uric acid derivatives. Evidence for the intramolecular nature of the rearrangement of *O*-benzoyl derivatives of carbocyclic enehydroxylamines is provided.

Experimental Section

General: Melting points were determined with a Reichert Thermovar apparatus and are uncorrected. IR spectra were measured with Perkin−Elmer 598 or 298 spectrophotometers. ^{1}H and ^{13}C NMR spectra were recorded with a Varian Unity 300, unless stated otherwise (Bruker ARX 400 spectrometer) with TMS as internal standard and solutions in $CDCl_3$. EI-MS spectra were recorded with AEI MS-9, Kratos MS 25 RF, or Fisons TRIO 2000 spectrometers at 70 eV, and HR-MS data were determined with an AutoSpecQ spectrometer at Imperial College of Science, Technology and Medicine, London. Elemental analyses were performed at the National Institute of Industrial Engineering and Technology, Lisbon, and at the Imperial College of Science, Technology and Medicine, London. Thin layer chromatography (TLC) was performed on Merck GF_{254} silica gel plates. Column chromatography was carried out on Merck 60 silica gel (230−400 mesh). All solvents were purified by standard procedures and anhydrous solvents were dried and freshly distilled.

Synthesis of Enehydroxylamines

General Procedure A: The *N*-alkylhydroxylamine hydrochloride (1 equiv.) and triethylamine (2 equiv.) were added at room temp. under N_2 to a vigorously stirred suspension of 1,3-dione (1 equiv.) in toluene. The progress of the reaction was monitored by TLC (silica; EtOAc/MeOH, 95:5). The toluene solution was then decanted and the resulting residue was purified by PTLC (silica; EtOAc/MeOH, 95:5). **General Procedure B:** The *N*-alkylhydroxylamine hydrochloride (1.5 equiv.) was slowly added to a solution of triethylamine (1.5 equiv.) in toluene, and the resulting dispersion was vigorously stirred overnight under N_2 at room temperature. Triethylammonium chloride was then removed by filtration and washed several times with toluene. A solution of the 1,3-dione (1 equiv.) in the same solvent was slowly added to the filtrate solutions, and the mixture was stirred at room temp. The toluene solution was then decanted and the resulting solid was recrystallised from an appropriate solvent.

Compound 4a: Treatment of *N*-methylhydroxylamine hydrochloride (1.67 g, 20.0 mmol) with cyclohexane-1,3-dione (1.50 g, 13.4 mmol) in toluene (120 mL) as described in General Procedure B (6 h) gave **4a** as colourless crystals (1.32 g, 70%). M.p. 126−128 °C (EtOAc/MeOH). IR (KBr): $\tilde{\nu}$ = 3000−2200, 1550 cm^{-1}. ^{1}H NMR: δ = 1.91−1.99 (*m*, 2 H, 5-CH_2), 2.26 (t, *J* = 6.4 Hz, 2 H, 4- or 6-CH_2), 2.50 (t, *J* = 6.3 Hz, 2 H, 6- or 4-CH_2), 3.35 (s, 3 H, NCH_3), 5.46 (s, 1 H, 2-H, D_2O exchange), 7.62 (br. s,1 H, OH, D_2O exchange) ppm. ^{13}C NMR: δ = 21.6, 25.8, 34.4, 40.7 (NCH_3), 94.6 (C-2), 165.1 (C-3), 195.3 (C-1) ppm. EI-MS: *m*/*z* (%) = 141 (84.6) [M$^+$], 125 (25.6), 113 (100.0). HR-MS: $C_7H_{11}NO_2$: calcd. 141.078979; found 141.079164. Treatment of *N*-methylhydroxylamine hydrochloride (746 mg, 8.93 mmol) with cyclohexane-1,3-dione (1.00 g, 8.93 mmol) in toluene (15 mL) as described in General Procedure A (30 min) gave **4a** (201 mg) in only 16%.

Compound 4b: Treatment of *N*-benzylhydroxylamine hydrochloride (1.00 g, 6.3 mmol) with cyclohexane-1,3-dione (471 mg, 4.2 mmol) in toluene (50 mL) as described in General Procedure B (6 h) gave **4b** as colourless crystals (93 mg, 87%). M.p. 113−115 °C (EtOAc/petroleum ether). IR (KBr): $\tilde{\nu}$ = 3100−3200, 1555 cm^{-1}. ^{1}H NMR: δ = 1.86−1.93 (m, 2 H, 5-CH_2), 2.21 (t, *J* = 6.3 Hz, 2 H, 4- or 6-CH_2), 2.48 (t, *J* = 6.3 Hz, 2 H, 6- or 4-CH_2), 4.76 (s, 2 H, CH_2Ph), 5.69 (s, 1 H, 2-H, D_2O exchange), 7.26−7.36 (m, 5 H, ArH), 9.53 (br. s, 1 H, OH, D_2O exchange) ppm. ^{13}C NMR: δ = 21.6, 25.6, 34.3, 56.8 (NCH_2Ph), 95.4 (C-2), 127.1, 127.1, 127.7, 128.6, 128.6, 135.3, 165.4 (C-3), 196.0 (C-1) ppm. EI-MS: *m*/*z* (%) = 217 (3.1) [M$^+$], 201 (24.6), 173 (18.7), 144 (27.2), 91 (100.0). HR-MS: $C_{13}H_{15}NO_2$: calcd. 217.110279; found 217.111588. Treatment of *N*-benzylhydroxylamine hydrochloride (286 mg, 1.79 mmol) with cyclohexane-1,3-dione (201 mg, 1.79 mmol) in toluene (5 mL) as described in General Procedure A (7 h) gave **4b** (54.4 mg) in only 14% yield.

Compound 4c: Treatment of *N*-isopropylhydroxylamine hydrochloride (200 mg, 1.8 mmol) with cyclohexane-1,3-dione (200 mg, 1.8 mmol) in toluene (3 mL) as described in General Procedure A (7 h) afforded **4c** as a colourless oil (73 mg, 24%). IR (neat): $\tilde{\nu}$ = 3200−2500, 1550 cm^{-1}. ^{1}H NMR: δ = 1.30 (d, *J* = 6.3 Hz, 6 H, CH_3), 1.94−1.99 (m, 2 H, 5-CH_2), 2.27 (t, *J* = 6.3 Hz, 2 H, 4- or 6-CH_2), 2.46 (t, *J* = 6.3 Hz, 2 H, 6- or 4-CH_2), 4.07−4.14 [m, 1 H, NC*H*(CH_3)$_2$], 5.33 (br. s, 1 H, OH, D_2O exchange), 5.78 (s, 1 H, s, 2-H, D_2O exchange) ppm. EI-MS: *m*/*z* (%) = 169 (60.1) [M$^+$], 127 (40.6), 126 (47.4), 99 (87.7), 96 (100.0). HR-MS: $C_9H_{15}NO_2$: calcd. 169.110279; found 169.110400.

Compound 4d: Treatment of *N*-cyclohexylhydroxylamine hydrochloride (290 mg, 1.91 mmol) with cyclohexane-1,3-dione (214 mg, 1.91 mmol) in toluene (5 mL) as described in General Procedure A (47 h) yielded **4d** as colourless crystals (91.8 mg, 23%). M.p. 156−157 °C (Et_2O/$CHCl_3$). IR (KBr): $\tilde{\nu}$ =3245, 1540 cm^{-1}. ^{1}H NMR: δ = 1.10−1.40 (m, 5 H), 1.61−1.78 (m, 3 H), 1.92−2.02 (m, 4 H), 2.30−2.34 (m, 4 H), 3.20−3.30 (m, 1 H), 4.69 (br. s, 1 H, OH, D_2O exchange), 5.16 (s, 1 H, 2-H) ppm. EI-MS: *m*/*z* (%) = 193 (32.4), 112 (100.0). FAB-MS (glycerol): *m*/*z* (%) = 210 (7.3) [M$^+$ + H], 194 (100.0) [M$^+$ + H − O]. HR-MS: $C_{12}H_{19}NO_2$: calcd. 209.141549; found 209.144118.

Compound 5a: Treatment of *N*-methylhydroxylamine hydrochloride (448 mg, 5.36 mmol) with 5,5-dimethylcyclohexane-1,3-dione (500 mg, 3.57 mmol) in toluene (40 mL) as described in General Procedure B (2 h) afforded **5a** as colourless crystals (483 mg, 80%). M.p. 158−160 °C ($CHCl_3$/*n*-hexane) (158−160 °C)[14]. IR (KBr): $\tilde{\nu}$ = 3100−2500, 1590, 1500 cm^{-1}. ^{1}H NMR: δ = 1.06 (s, 6 H, 5-CH_3), 2.12 (s, 2 H, 4- or 6-CH_2), 2.30 (s, 2 H, 6- or 4-CH_2), 3.35 (s, 3 H, NCH_3), 4.77 (br. s, 1 H, OH, D_2O exchange), 5.52 (s, 1 H, 2-H, D_2O exchange) ppm. FAB-MS (glycerol): *m*/*z* (%) = 170 (100.0) [M$^+$ + H].

Compound 5b: Treatment of *N*-benzylhydroxylamine hydrochloride (1000 mg, 6.27 mmol) with 5,5-dimethylcyclohexane-1,3-dione (585 mg, 4.17 mmol) in toluene (80 mL) as described in General Procedure B (6 h) afforded **5b** as colourless crystals (686 mg, 68%). M.p. 142−143 °C ($CHCl_3$/*n*-hexane). IR (KBr): $\tilde{\nu}$ = 3433, 1538, 1494 cm^{-1}. ^{1}H NMR (400 MHz): δ = 1.00 (s, 6 H, 5-CH_3), 2.08 (s, 2 H, 4- or 6-CH_2), 2.31 (s, 2 H, 6- or 4-CH_2), 4.77 (s, 2 H,

NCH_2Ph), 5.68 (s, 1 H, 2-H), 7.25−7.38 (m, 5 H, ArH) ppm. EI-MS: *m*/*z* (%) = 245 (8) [M^+], 144 (10), 91 (100.0). HR-MS: $C_{15}H_{19}NO_2$: calcd. 245.141579; found 245.141380.

Compounds 6a and 10b′: $NaHCO_3$ (4.20 g, 50 mmol) was added to a solution of *N*-methylhydroxylamine hydrochloride (2.99 g, 35.8 mmol) in ethanol (51 mL), and the resulting mixture was vigorously stirred at room temp. After 30 min, a solution of 6-chloro-1,3-dimethyluracil[13] (2.50 g, 14.3 mmol) in the same solvent (50 mL) was added, and the mixture was heated under reflux for 3 h. The mixture was then cooled and filtered, and the resulting solid was washed several times with ethanol. The combined filtrates were concentrated to dryness under reduced pressure and the residual oil was purified by CC (silica; EtOAc with gradual addition of MeOH) to give **10b′** (266 mg, 11%) followed by **6a** (2.12 g, 80%), both as colourless needles. Physical data for **6a**: M.p. 152−154 °C (dec.) (EtOH). IR (KBr): $\tilde{\nu}$ = 3120, 1700, 1650 cm^{-1}. ^1H NMR: δ = 3.01 (s, 3 H, NCH_3), 3.33 (s, 3 H, NCH_3), 3.42 (s, 3 H, NCH_3), 5.70 (s, 1 H, 5-H, D_2O exchange), 5.98 (br. s, 1 H, OH, D_2O exchange) ppm. ^{13}C NMR: δ = 28.0, 32.8, 44.5, 86.6, 152.4, 160.7 (C=O), 163.9 (C=O) ppm. EI-MS: *m*/*z* (%) = 169 (100.0) [M^+ − O]. FAB-MS (4-NBA): *m*/*z* = 186 (100.0) [M^+ + H]. $C_7H_{11}N_3O_3$: calcd. C 45.40, H 5.99, N 22.69; found C 45.62, H 5.87, N 22.41. Physical data for **10b′**: M.p. 248−249 °C (EtOH) [244−245 °C[13] (H_2O)]. IR (KBr): $\tilde{\nu}$ = 3300, 1710, 1650 cm^{-1}. ^1H NMR: δ = 2.86 (d, *J* = 4.8 Hz, 3 H, $NHCH_3$, collapses to s on irradiation at 4.57), 3.22 (s, 3 H, NCH_3), 3.40 (s, 3 H, NCH_3), 4.57 (br. s, 1 H, NH), 4.86 (s, 1 H, 5-H) ppm. EI-MS: *m*/*z* (%) = 169 (64.1) [M^+], 82 (100.0).

Compound 6b and 6-(Benzylamino)-1,3-dimethyluracil: By a procedure similar to the previous one, compounds **6b** (55%) and 6-(benzylamino)-1,3-dimethyluracil (12%) were obtained when *N*-benzylhydroxylamine hydrochloride was used. Physical data for **6b**: M.p. 175−177 °C ($CHCl_3$/*n*-hexane). IR (KBr): $\tilde{\nu}$ = 3185, 1709, 1613 cm^{-1}. ^1H NMR: δ = 3.28 (s, 3 H, NCH_3), 3.44 (s, 3 H, NCH_3), 4.18 (s, 2 H, NCH_2Ph), 5.76 (s, 1 H, 5-H, D_2O exchange), 6.98 (br. s, 1 H, OH, D_2O exchange), 7.34−7.39 (m, 5 H, ArH) ppm. ^{13}C NMR: δ = 28.0, 32.2, 61.0, 88.8, 128.2, 128.7, 128.8, 134.7, 152.4, 159.6 (C=O), 163.4 (C=O) ppm. EI-MS: *m*/*z* (%) = 261 (1.5) [M^+], 245 (13.4), 91 (100.0). HR-MS: $C_{13}H_{15}N_3O_3$: calcd. 261.110487; found 261.111342. Physical data for 6-(benzylamino)-1,3-dimethyluracil: M.p. 158−159 °C (MeOH/petroleum ether). IR (KBr): $\tilde{\nu}$ = 3241, 1698, 1626 cm^{-1}. ^1H NMR: δ = 3.28 (s, 3 H, NCH_3), 3.41 (s, 3 H, NCH_3), 4.24 (d, *J* = 4.8 Hz, 2 H, NCH_2Ph), 4.86 (s, 1 H, 5-H, D_2O exchange), 5.16 (br. s, 1 H, NH, D_2O exchange), 7.28−7.38 (m, 5 H, ArH) ppm. EI-MS: *m*/*z* (%) = 245 (29.1) [M^+], 91 (100.0). HR-MS: $C_{13}H_{15}N_3O_2$: calcd. 245.116083; found 245.116427.

Treatment of Enehydroxylamines with Methanesulfonyl Chloride. General Procedure: *N*,*N*-Diisopropylethylamine (1 equiv.) and methanesulfonyl chloride (1 equiv.) were added under N_2 to a stirred, ice-cooled suspension of enehydroxylamine (1 equiv.) in anhydrous THF. After 40 min, the mixture was allowed to stand at room temp. until the reaction was complete. The organic salt was removed by filtration and washed with anhydrous THF. The combined organic filtrates were concentrated under reduced pressure, and the resulting residue was dissolved in a mixture of diethyl ether and dichloromethane (1:1) and washed with water. The aqueous layer, after separation by decantation, was extracted several times with diethyl ether and the combined organic layers were dried with anhydrous sodium sulfate. Solvent removal under reduced pressure furnished a residue, which was recrystallised.

Compound 8a: Treatment of **4a** (200 mg, 1.42 mmol) with methanesulfonyl chloride (163 mg, 1.42 mmol) in anhydrous THF (10 mL), as described above (1 h 30 min), gave **8a** (270 mg, 87%) as colourless crystals. M.p. 147−148 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3375, 1580, 1355, 1180 cm^{-1}. ^1H NMR: δ = 1.98−2.06 (m, 2 H, 5-CH_2), 2.42 (t, *J* = 6.6 Hz, 2 H, 4- or 6-CH_2), 2.61 (t, *J* = 6.3 Hz, 2 H, 6- or 4-CH_2), 2.98 (d, *J* = 4.8 Hz, 3 H, $NHCH_3$, collapses to s on irradiation at 5.61), 3.41 (s, 3 H, SCH_3), 5.61 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS: *m*/*z* (%) = 219 (10.4) [M^+], 140 (52.3), 112 (100.0). HR-MS: $C_8H_{13}NO_4S$: calcd. 219.056530; found 219.057511.

Compound 8b: Treatment of **4b** (100 mg, 0.46 mmol) with methanesulfonyl chloride (52.7 mg, 0.46 mmol) in anhydrous THF (3 mL), as described above (40 min), gave **8b** (114 mg, 84%) as colourless prisms. M.p. 127−128 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3380, 1635, 1575, 1330, 1165 cm^{-1}. ^1H NMR: δ = 1.90−1.98 (m, 2 H, 5-CH_2), 2.36 (t, *J* = 6.4 Hz, 2 H, 4- or 6-CH_2), 2.57 (t, *J* = 6.0 Hz, 2 H, 6- or 4-CH_2), 3.35 (s, 3 H, SCH_3), 4.49 (d, *J* = 6.3 Hz, 2 H, $NHCH_2Ph$, collapses to s on irradiation at 5.97), 5.97 (br. s, 1 H, NH), 7.27−7.41 (m, 5 H, ArH) ppm. EI-MS: *m*/*z* (%) = 295 (2.1) [M^+], 216 (25.2), 188 (11.9), 91 (100.0). HR-MS: $C_{14}H_{17}NO_4S$: calcd. 295.087830; found 295.087588.

Compound 8c: Treatment of **5a** (100 mg, 0.59 mmol) with methanesulfonyl chloride (67.6 mg, 0.59 mmol) in anhydrous THF (5 mL), as described above (3 h), afforded **8c** (135 mg, 93%) as colourless prisms. M.p. 141−142 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 3385, 1590, 1355, 1180 cm^{-1}. ^1H NMR: δ = 1.14 (s, 6 H, 5-CH_3), 2.30 (s, 2 H, 4- or 6-CH_2), 2.45 (s, 2 H, 6- or 4-CH_2), 2.97 (d, *J* = 5.4 Hz, 3 H, $NHCH_3$, collapses to s on irradiation at 5.55), 3.43 (s, 3 H, SCH_3), 5.55 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS *m*/*z* (%) = 247 (53.0), 168 (62.5), 140 (27.0), 139 (53.0), 56 (100.0). $C_{10}H_{17}NO_4S$ (247.3): calcd. C 48.56, H 6.93, N 5.56; found C 48.44, H 6.99, N 5.54.

Compound 10a and Compound 10a′: Treatment of **6a** (163 mg, 0.88 mmol) with methanesulfonyl chloride (101 mg, 0.88 mmol) in anhydrous THF (8 mL), as described above (1 h), and separation of the resulting residue by PTLC (silica; EtOAc/petroleum ether, 1:1) gave **10a** (94.8 mg, 41%) followed by **10a′** (85.8 mg, 48%), both as colourless crystals. Physical data for **10a**: M.p. 148−149 °C ($CHCl_3/Et_2O$). IR (KBr): $\tilde{\nu}$ = 3425, 1700, 1640, 1615, 1550, 1335, 1170 cm^{-1}. ^1H NMR: δ = 3.16 (d, *J* = 5.4 Hz, 3 H, $NHCH_3$, collapses to s on irradiation at 4.40), 3.17 (s, 3 H, NCH_3), 3.46 (s, 3 H, SCH_3), 3.48 (s, 3 H, NCH_3), 4.40 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS: *m*/*z* (%) = 263 (5.9) [M^+], 184 (53.5), 183 (36.7), 156 (36.7), 55 (100.0). $C_{18}H_{13}N_3O_5S$: calcd. C 36.50, H 4.89, N 15.91; found C 36.70, H 4.89, N 15.92. Physical data for **10a′**: M.p. 192−193 °C (EtOAc/$CHCl_3$) (190−192 °C)[24]. IR (KBr): $\tilde{\nu}$ = 3370, 1700, 1635 cm^{-1}. ^1H NMR: δ = 3.00 (d, *J* = 5.7 Hz, 3 H, $NHCH_3$, collapses to s on irradiation at 4.50), 3.38 (s, 3 H, NCH_3), 3.50 (s, 3 H, NCH_3), 4.50 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS: *m*/*z* (%) = 203/205 (100.0/32.6) [M^+/M^+ + 2], 168 (6.6), 167 (13.2).

Treatment of Enehydroxylamines with *N*,*N*-Dimethylthiocarbamoyl Chloride. General Procedure A: Triethylamine (3 equiv.) and a solution of *N*,*N*-dimethylthiocarbamoyl chloride (3 equiv.) in anhydrous THF were added under N_2 to a stirred, ice-cooled suspension of enehydroxylamine (1 equiv.) in the same solvent. After the reaction was complete, the organic salt was removed by filtration and washed several times with anhydrous THF. The combined filtrates were concentrated at reduced pressure and the residue was purified by PTLC (silica; EtOAc/MeOH, 95:5). **General Procedure B:** A 60%

dispersion of sodium hydride in mineral oil (2 equiv.) was added under N_2 to a stirred, ice-cooled suspension of enehydroxylamine (1 equiv.) in anhydrous THF. After 1 h, a solution of *N*,*N*-dimethylthiocarbamoyl chloride (3 equiv.) in the same solvent was added. When the reaction was complete, the solvent was removed under reduced pressure and a mixture of water and diethyl ether was added to the residue. The aqueous layer was separated by decantation and extracted several times with diethyl ether, and the combined organic layers were dried with anhydrous sodium sulfate. Solvent removal at reduced pressure left a yellow solid, which was purified by PTLC (silica; EtOAc/MeOH, 95:5).

Compound 8d: Treatment of **4a** (100 mg, 0.71 mmol) with *N*,*N*-dimethyl-thiocarbamoyl chloride (263 mg, 2.13 mmol) in anhydrous THF (3 mL) as described in General Procedure A (24 h) afforded **8d** (86.0 mg, 53%) as a colourless oil. IR (KBr): $\tilde{\nu}$ = 3300, 1660, 1560 cm^{-1}. ^1H NMR: δ = 2.02−2.10 (m, 2 H, 5-CH_2), 2.50 (t, *J* = 6.4 Hz, 2 H, 4- or 6-CH_2), 2.64 (t, *J* = 6.3 Hz, 2 H, 6- or 4-CH_2), 2.96 (s, 3 H, NCH_3), 3.00 (d, *J* = 5.1 Hz, 3 H, NHCH_3, collapses to s on irradiation at 6.26), 3.15 (s, 3 H, NCH_3), 6.26 (br. s, 1 H, NH) ppm. EI-MS: *m*/*z* (%) = 228 (8.8) [M^+], 183 (15.7), 156 (7.8), 72 (100.0). HR-MS: $C_{10}H_{16}N_2O_2S$: calcd. 228.093250; found 228.093492.

Compound 8e: Treatment of **5a** (100 mg, 0.59 mmol) with *N*,*N*-dimethylthiocarbamoyl chloride (220 mg, 1.78 mmol) in anhydrous THF (3 mL) as described in General Procedure A (4 h 30 min) gave **8e** (95.2 mg, 63%) as colourless crystals. M.p. 116−117 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3380, 1670, 1630, 1570 cm^{-1}. ^1H NMR: δ = 1.17 (s, 6 H, 5-CH_3), 2.38 (s, 2 H, 4- or 6-CH_2), 2.46 (s, 2 H, 6- or 4-CH_2), 2.96 (s, 3 H, NCH_3), 2.99 (d, *J* = 5.4 Hz, 3 H, NHCH_3, collapses to s on irradiation at 6.24), 3.15 (s, 3 H, NCH_3), 6.24 (br. s, 1 H, NH) ppm. EI-MS: *m*/*z* (%) = 211 (100.0) [M^+ − $HN(CH_3)_2$], 196 (27.3), 182 (26.6), 155 (78.1). $C_{12}H_{20}N_2O_2S$ (256.4): calcd. C 56.22, H 7.86, N 10.93; found C 56.25, H 7.93, N 10.74.

Compound 8d′: Treatment of **4a** (100 mg, 0.71 mmol) with *N*,*N*-dimethylthiocarbamoyl chloride (263 mg, 2.13 mmol) in anhydrous THF (4 mL) as described in General Procedure B (3 h 30 min) afforded **8d′** (141 mg, 63%) as colourless crystals. M.p. 133−134 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1670, 1570 cm^{-1}. ^1H NMR: δ = 2.10−2.18 (m, 2 H, 5-CH_2), 2.62 (t, *J* = 6.6 Hz, 2 H, 4- or 6-CH_2), 2.74 (t, *J* = 6.3 Hz, 2 H, 6- or 4-CH_2), 2.86 [s, 6 H, $N(CH_3)_2$], 3.19 (s, 3 H, NCH_3), 3.48 [s, 6 H, $N(CH_3)_2$] ppm. EI-MS: *m*/*z* (%) = 315 (50.0) [M^+], 271 (27.5), 270 (24.0), 243 (100.0), 211 (94.0). $C_{13}H_{21}N_3O_2S_2$ (315.5): calcd. C 49.50, H 6.71, N 13.32; found C 49.52, H 6.73, N 13.23.

Compound 8e′: Treatment of **5a** (100 mg, 0.59 mmol) with *N*,*N*-dimethylthiocarbamoyl chloride (219 mg, 1.77 mmol) in anhydrous THF (5 mL) as described in General Procedure B (4 h) afforded **8e′** (170 mg, 84%) as colourless crystals. M.p. 125−126 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1690, 1650 cm^{-1}. ^1H NMR: δ = 1.18 (s, 6 H, 5-CH_3), 2.51 (s, 2 H, 4- or 6-CH_2), 2.56 (s, 2 H, 6- or 4-CH_2), 2.87 [s, 6 H, $N(CH_3)_2$], 3.19 (s, 3 H, NCH_3), 3.48 [s, 6 H, $N(CH_3)_2$] ppm. EI-MS: *m*/*z* (%) = 343 (80.5) [M^+], 299 (21.7), 271 (75.2), 239 (78.9), 72 (100.0). $C_{15}H_{25}N_3O_2S_2$ (343.5): calcd. C 52.45, H 7.34, N 12.23; found C 52.49, H 7.41, N 12.13.

Compounds 10b and 10b′: Treatment of **6a** (100 mg, 0.54 mmol) with *N*,*N*-dimethylthiocarbamoyl chloride (200 mg, 1.62 mmol) in anhydrous THF (3 mL) as described in General Procedure B (4 h 30 min) gave **10b** (58.2 mg, 30%) and **10b′** (50.2 mg, 55%), both as colourless crystals. Physical data for **10b**: M.p. 215−216 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1710, 1660, 1580, 1440, 1380 cm^{-1}. ^1H NMR: δ = 2.77 (s, 6 H, CH_3), 3.02 (s, 3 H, CH_3), 3.43 (s, 3 H, CH_3), 3.47 (s, 3 H, CH_3), 3.49 (s, 3 H, CH_3), 3.53 (s, 3 H, CH_3) ppm. FAB-MS (glycerol): *m*/*z* (%) = 360 (100.0) [M^+ + H]. $C_{13}H_{21}N_5O_3S_2$ (359.5): calcd. C 43.44, H 5.89, N 19.48; found C 43.74, H 6.12, N 19.57.

Treatment of Enehydroxylamines with 1-Fluoro-2,4-dinitrobenzene. Compound 11: A 60% dispersion of sodium hydride in mineral oil (40.6 mg, 1.69 mmol) was added under N_2 and protected from light to a stirred, ice-cooled suspension of **5a** (220 mg, 1.3 mmol) in anhydrous THF (6 mL), followed 1 h later by 1-fluoro-2,4-dinitrobenzene (315 mg, 1.69 mmol). After 1 h, the solvent was removed under reduced pressure and the remaining residue was dissolved in water and extracted with ethyl acetate. The aqueous layer, after separation by decantation, was neutralised with aqueous HCl (5%) and extracted several times with ethyl acetate. The combined organic layers were dried with anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the resulting residue was recrystallised to give **11** (388 mg, 89%) as yellow crystals. M.p. > 308 °C (EtOH/Et_2O). IR (KBr): $\tilde{\nu}$ = 3300, 1600, 1540, 1395, 1345 cm^{-1}. ^1H NMR: δ = 1.20 (s, 6 H, 5-CH_3), 2.33 (s, 2 H, 4- or 6-CH_2), 2.49 (s, 2 H, 6- or 4-CH_2), 2.91 (d, *J* = 4.8 Hz, 3 H, NHCH_3, collapses to s on irradiation at 5.09), 3.46 (s, 1 H, OH, D_2O exchange), 5.09 (br. s, 1 H, NH, D_2O exchange), 8.24 (d, *J* = 3.0 Hz, 1 H, ArH), 8.93 (d, *J* = 3.0 Hz, 1 H, ArH) ppm. FAB-MS (glycerol): *m*/*z* (%) = 336 (100.0) [M^+ + H]. HR-MS (FAB): $C_{15}H_{18}N_3O_6$: calcd. 336.119561; found 336.119026 [M^+ + H].

Compound 12: Treatment of **6a** (215 mg, 1.16 mmol) with 1-fluoro-2,4-dinitrobenzene (280 mg, 1.50 mmol) in anhydrous THF (6 mL) as described above (2 h 40 min) gave, after recrystallisation of the resulting residue, **12** (297 mg, 73%) as yellow crystals. M.p. 208−210 °C (dec.) (CH_2Cl_2/EtOH). IR (KBr): $\tilde{\nu}$ = 3360, 1700, 1600, 1550, 1340 cm^{-1}. ^1H NMR: δ = 2.60 (d, *J* = 4.8 Hz, 3 H, NHCH_3, collapses to s on irradiation at 4.30), 3.38 (s, 3 H, NCH_3), 3.56 (s, 3 H, NCH_3), 4.30 (br. s, 1 H, NH, D_2O exchange), 8.45 (d, *J* = 2.4 Hz, 1 H, ArH), 9.05 (d, *J* = 2.4 Hz, 1 H, ArH), 11.46 (br. s, 1 H, OH, D_2O exchange) ppm. FAB-MS (glycerol): *m*/*z* (%) = 352 (100.0) [M^+ + H]. $C_{13}H_{13}N_5O_7$ (351.3): calcd. C 44.46, H 3.73, N 19.94; found C 44.73, H 3.57, N 19.94.

Treatment of Enehydroxylamines with Methyl Propiolate or Dimethyl Acetylenedicarboxylate. General Procedure: *N*,*N*-Diisopropylethylamine (1 equiv.) was added under N_2 to a stirred, ice-cooled suspension of enehydroxylamine (1 equiv.) in anhydrous THF, followed 30 min later by dropwise addition of methyl propiolate or dimethyl acetylenedicarboxylate (1 equiv.). When the reaction was complete, the solvent was removed under reduced pressure and the resulting residue was washed with diethyl ether and purified by PTLC or recrystallisation.

Compound 13a: Treatment of **4a** (150 mg, 1.06 mmol) with methyl propiolate (89.0 mg, 1.06 mmol) in anhydrous THF (4 mL) as described in the General Procedure (48 h) and purification of the resulting residue by PTLC (silica; EtOAc/MeOH, 98:2) gave **13a** (196 mg, 82%) as a colourless oil. IR (KBr): $\tilde{\nu}$ = 3400−2700, 1740, 1600, 1550, 1520 cm^{-1}. ^1H NMR: δ = 1.99−2.06 (m, 2 H, 6-CH_2), 2.14−2.50 (m, 4 H, 5- and 7-CH_2), 3.03 (s, 3 H, NCH_3), 3.70 (s, 3 H, OCH_3), 3.74 (br. s, 1 H, 3-H), 5.28 (d, *J* = 2.7 Hz, 1 H, 2-H), 6.40 (br. s, 1 H, OH, D_2O exchange) ppm. FAB-MS (4-NBA): *m*/*z* (%) = 226 (100.0) [M^+ + H], 208 (18.2) [M^+ + H − H_2O], 166 (55.6). HR-MS (CI, ammonia): $C_{11}H_{16}NO_4$: calcd. 226.107933; found 226.109193 [M^+ + H].

Compound 14a: A solution of **13a** (95.0 mg, 0.42 mmol) in toluene was heated under reflux (5 h 30 min) and the reaction mixture was

worked up as described above to afford **14a** (66.9 mg, 77%) as colourless crystals. M.p. 167−168 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 1720, 1660 cm^{-1}. ^1H NMR: δ = 2.08−2.17 (m, 2 H, 6-CH_2), 2.43 (d, *J* = 6.9 Hz, 1 H, 7-H′), 2.44 (d, *J* = 7.5 Hz, 1 H, 7-H), 2.72 (m, 2 H, 5-CH_2) 3.55 (s, 3 H, NCH_3 or OCH_3), 3.76 (s, 3 H, OCH_3 or NCH_3), 7.19 (s, 1 H, 2-H) ppm. EI-MS: *m/z* (%) = 207 (43.9) [M^+], 179 (48.5), 176 (19.7), 121 (100.0). $C_{11}H_{13}NO_3$ (207.2): calcd. C 63.76, H 6.32, N 6.76; found C 63.72, H 6.19, N 6.71.

Compound 13b: Treatment of **5a** (100 mg, 0.59 mmol) with methyl propiolate (50.0 mg, 0.59 mmol) in anhydrous THF (4 mL) as described above (96 h) afforded, after recrystallisation from EtOAc, **13b** (113 mg, 76%) as colourless crystals. M.p. 147−149 °C (dec.) (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 3300−2600, 1740, 1590, 1550, 1510 cm^{-1}. ^1H NMR: δ = 1.09 (s, 3 H, 6-CH_3), 1.12 (s, 3 H, 6-CH_3), 2.16 (s, 2 H, CH_2), 2.26 (s, 2 H, CH_2), 3.01 (s, 3 H, NCH_3), 3.70 (s, 3 H, OCH_3), 3.76 (br. s, 1 H, 3-H), 4.84 (br. s, 1 H, OH, D_2O exchange), 5.26 (d, *J* = 1.8 Hz, 1 H, 2-H) ppm. EI-MS: *m/z* (%) = 253 (10.4) [M^+], 235 (40.7) [$M^+ - H_2O$], 221 (21.2), 194 (46.7), 179 (100.0). $C_{13}H_{19}NO_4$ (253.3): calcd. C 61.64, H 7.56, N 5.53; found C 61.48, H 7.41, N 5.46.

Compound 14b: A solution of **13b** (100 mg, 0.4 mmol) in toluene was heated under reflux for 7 h 30 min. Solvent removal at reduced pressure and purification of the resulting residue by PTLC (silica, EtOAc/MeOH, 95:5) gave **14b** (69.6 mg, 74%), as colourless crystals. M.p. 142−143 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 1730, 1660 cm^{-1}. ^1H NMR, [D_6]acetone: δ = 1.09 (s, 6 H, 6-CH_3), 2.27 (s, 2 H, CH_2), 2.72 (s, 2 H, CH_2), 3.67 (s, 3 H, NCH_3 or OCH_3), 3.69 (s, 3 H, OCH_3 or NCH_3), 7.33 (s, 1 H, 2-H) ppm. EI-MS: *m/z* (%) = 235 (41.2) [M^+], 220 (3.2), 204 (17.7), 179 (100.0). $C_{13}H_{17}NO_3$ (235.2): calcd. C 66.36, H 7.28, N 5.95; found C 66.34, H 7.29, N 5.98.

Compound 13c: Treatment of **4a** (300 mg, 2.1 mmol) with dimethyl acetylenedicarboxylate (300 mg, 2.1 mmol) in anhydrous THF (10 mL) as described in the General Procedure (40 h) afforded **13c** (410 mg, 69%) as colourless crystals. M.p. 163−165 °C (dec.) (Et_2O/MeOH). IR (KBr): $\tilde{\nu}$ = 3260−2600, 1750, 1550, 1500 cm^{-1}. ^1H NMR: δ = 2.07−2.16 (m, 2 H, 6-CH_2), 2.25−2.58 (m, 4 H, 5 and 7-CH_2), 2.82 (s, 3 H, NCH_3), 3.68 (s, 3 H, OCH_3), 3.83 (s, 3 H, OCH_3), 4.10 (s, 1 H, 3-H), 4.81 (br. s, 1 H, OH, D_2O exchange) ppm. EI-MS: *m/z* (%) = 283 (81.0) [M^+], 265 (38.0) [$M^+ - H_2O$], 251 (18.6), 224 (61.2), 164 (100.0). HR-MS (CI, ammonia): $C_{13}H_{18}NO_6$: calcd. 284.113413; found 284.112759 [M^+ + H].

Compound 14c: A solution of **13c** (127 mg, 0.45 mmol) and *p*-toluenesulfonic acid (8.56 mg, 0.045 mmol) in toluene was heated at reflux for 1 h 30 min. Solvent removal under reduced pressure and recrystallisation from Et_2O/CH_2Cl_2, afforded **14c** (107 mg, 90%) as colourless crystals. M.p. 127−128 °C. IR (KBr): $\tilde{\nu}$ = 1740, 1710, 1670 cm^{-1}. ^1H NMR: δ = 2.14−2.23 (m, 2 H, CH_2), 2.49 (d, *J* = 6.9 Hz, 1 H, 7-H′), 2.51 (d, *J* = 6.9 Hz, 1 H, 7-H), 2.79 (m, 2 H, CH_2), 3.82 (s, 3 H, OCH_3 or NCH_3), 3.84 (s, 3 H, OCH_3 or NCH_3), 3.95 (s, 3 H, NCH_3 or OCH_3) ppm. EI-MS: *m/z* (%) = 265 (86.4) [M^+], 237 (100.0), 234 (72.7), 179 (31.8). HR-MS (CI, ammonia): $C_{16}H_{14}NO_5$: calcd. 266.105528; found 266.104713 [M^+ + H].

Compound 13d: Treatment of **5a** (372 mg, 2.2 mmol) with dimethyl acetylenedicarboxylate (313 mg, 2.2 mmol) in anhydrous THF (10 mL) as described in the General Procedure (40 h) afforded **13d** (479 mg, 70%) as colourless crystals. M.p. 160−162 °C (dec.) (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3000−2500, 1750, 1590, 1550, 1500 cm^{-1}. ^1H NMR: δ = 1.11 (s, 3 H, 6-CH_3), 1.16 (s, 3 H, 6-CH_3), 2.23 (d, *J* = 4.2 Hz, 2 H, CH_2), 2.29 (d, *J* = 8.4 Hz, 2 H, CH_2), 2.82 (s, 3 H, NCH_3), 3.76 (s, 3 H, OCH_3), 3.89 (s, 3 H, OCH_3), 4.19 (s, 1 H, 3-H), 4.72 (s, 1 H, OH, D_2O exchange) ppm. FAB-MS (glycerol): *m/z* (%) = 312 (100.0) [M^+ + H]. HR-MS (CI, ammonia): $C_{15}H_{22}NO_6$: calcd. 312.144713; found 312.145444 [M^+ + H].

Compound 14d: A solution of **13d** (146 mg, 0.47 mmol) and *p*-toluenesulfonic acid (8.94 mg, 0.047 mmol) in toluene was heated under reflux for 1 h. Solvent removal at reduced pressure and purification of the resulting residue by PTLC (silica; EtOAc) afforded **14d** (121 mg, 88%) as colourless crystals. M.p. 146−147 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1730, 1715, 1675, 1490 cm^{-1}. ^1H NMR: δ = 1.14 (s, 6 H, 6-CH_3), 2.37 (s, 2 H, 7-CH_2), 2.64 (s, 2 H, 5-CH_2), 3.82 (s, 3 H, OCH_3 or NCH_3), 3.83 (s, 3 H, OCH_3 or NCH_3), 3.94 (s, 3 H, NCH_3 or OCH_3) ppm. FAB-MS (glycerol): *m/z* (%) = 294 (33.3) [M^+ + H]. $C_{15}H_{19}NO_5$ (293.3): calcd. C 61.42, H 6.53, N 4.78; found C 61.45, H 6.40, N 4.76.

Treatment of Enehydroxylamines with Bromocyanogen. General Procedure A: Bromocyanogen (1 equiv.) was added under N_2 to a stirred suspension of enehydroxylamine (1 equiv.) and triethylamine (1 equiv.) in anhydrous THF. After the reaction was complete, the solvent was removed under reduced pressure and the remainder solid was dissolved in dichloromethane. This solution was washed with water and dried with anhydrous sodium sulfate, and the solvent was removed under reduced pressure. The dark residues obtained were purified by PTLC (silica, EtOAc). **General Procedure B:** Bromocyanogen (1.3−1.5 equiv.) was added under N_2 to a stirred, ice-cooled suspension of enehydroxylamine (1 equiv.) and DABCO (1.3−1.5 equiv.) in anhydrous THF. After the reaction was complete, the solvent was removed under reduced pressure, and dichloromethane and water were added to the residual solid. The aqueous layer, after separation by decantation, was extracted with dichloromethane and/or ethyl acetate. The combined organic layers were dried with anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the resulting residue was recrystallised from an appropriate solvent.

Compound 15a: Treatment of **4a** (63.5 mg, 0.45 mmol) with BrCN (47.7 mg, 0.45 mmol) in anhydrous THF (3 mL) as described in General Procedure A (30 min) gave **15a** (26.9 mg, 36%) as colourless crystals. M.p. 241−242 °C (dec.) (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3230, 1725, 1690, 1625 cm^{-1}. ^1H NMR: δ = 2.15−2.24 (m, 2 H, CH_2), 2.50 (t, *J* = 6.6 Hz, 2 H, CH_2), 2.67 (t, *J* = 6.0 Hz, 2 H, CH_2), 3.28 (s, 3 H, NCH_3), 8.72 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS: *m/z* (%) = 166 (100.0) [M^+], 137 (61.0), 110 (26.3) . HR-MS: $C_8H_{10}N_2O_2$: calcd. 166.074228; found 166.073808. Treatment of **4a** (353 mg, 2.5 mmol) with BrCN (344 mg, 3.25 mmol) in anhydrous THF (15 mL) as described in General Procedure B (2 h) afforded **15a** (336 mg, 81%).

Compound 15b: Treatment of **4b** (1.00 g, 4.61 mmol) with BrCN (732 mg, 6.91 mmol) in THF (25 mL) as described in General Procedure B (1 h) afforded **15b** (1.05 g, 94%) as white needles. M.p. 184−185 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 3100, 1715, 1655 cm^{-1}. ^1H NMR: δ = 2.04−2.13 (m, 2 H, CH_2), 2.43 (t, *J* = 6.0 Hz, 2 H, CH_2), 2.53 (t, *J* = 6.9 Hz, 2 H, CH_2), 4.90 (s, 2 H, NCH_2Ph), 7.25−7.40 (m, 5 H, ArH), 10.20 (br. s, 1 H, NH, D_2O exchange) ppm. ^{13}C NMR: δ = 21.1, 22.9, 36.7, 45.2 (NCH_2Ph), 128.3, 127.6, 128.2, 129.2, 136.7, 141.2, 154.2 (C=O), 185.8 (C=O) ppm. EI-MS: *m/z* (%) = 242 (100.0) [M^+], 151 (2.37), 91 (43.6). HR-MS: $C_{14}H_{14}N_2O_2$: calcd. 242.105528; found 242.103999.

Compound 15c: Treatment of **4c** (65.9 mg, 0.39 mmol) with BrCN (41.3 mg, 0.39 mmol) in THF (3 mL) as described in General Procedure A (30 min) afforded **15c** (24.2 mg, 32%) as colourless crystals. M.p. 246−247 °C (dec.) (EtOAc/petroleum ether). IR (KBr):

$\tilde{\nu}$ = 3200, 1730, 1695, 1650 cm^{-1}. ^1H NMR: δ = 1.47 [d, 6 H, *J* = 6.9 Hz, $CH(CH_3)_2$, collapses to s on irradiation at the frequency of $CH(CH_3)_2$], 2.14−2.23 (m, 2 H, CH_2), 2.48 (t, *J* = 6.6 Hz, 2 H, CH_2), 2.77 (t, *J* = 6.3 Hz, 2 H, CH_2), 4.47 [m, 1 H, $CH(CH_3)_2$, collapses to s on irradiation at the frequency of $CH(CH_3)_2$], 8.57 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS: *m*/*z* (%) = 194 (50.5) [M^+], 152 (100.0). HR-MS: $C_{10}H_{14}N_2O_2$: calcd. 194.105528; found 194.106569.

Compound 15d: Treatment of **5a** (514 mg, 3.04 mmol) with BrCN (418 mg, 3.95 mmol) in THF (20 mL) as described in General Procedure B (1 h) yielded **15d** (489 mg, 83%) as white needles. M.p. 236−238 °C (dec.) (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3100, 1695, 1655 cm^{-1}. ^1H NMR: δ = 1.17 (s, 6 H, CH_3), 2.37 (s, 2 H, CH_2), 2.53 (s, 2 H, CH_2), 3.26 (s, 3 H, NCH_3), 9.05 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS: *m*/*z* (%) = 194 (100.0) [M^+], 179 (17.9), 138 (24.2), 110 (44.7). $C_{10}H_{14}N_2O_2$ (194.2): calcd. C 61.84, H 7.27, N 14.42; found C 61.90, H 7.10, N 14.40.

Treatment of Enehydroxylamines with *N*-Cyano-4-(dimethylamino)-pyridinium Bromide (CAP). General Procedure: Cyanogen bromide (1 equiv.) was added under N_2 to a stirred, ice-cooled solution of 4-DMAP (1 equiv.) in anhydrous THF. After 30 min, a solution of enehydroxylamine (0.3 equiv.) and *N*,*N*-diisopropylethylamine (0.3 equiv.) in the same solvent was added to the freshly prepared CAP, and the mixture was heated at 50 °C until the reaction was complete. The solvent was then removed under reduced pressure, and water and dichloromethane were added to the remaining residue. The aqueous layer, after separation by decantation, was extracted several times with dichloromethane, and the combined organic layers were dried with anhydrous sodium sulfate. Solvent removal under reduced pressure furnished a residue, which was recrystallised.

Compound 15a′: Treatment of CAP (486 mg, 2.13 mmol) in anhydrous THF (5.0 mL) with a solution of **4a** (100 mg, 0.71 mmol) in the same solvent, as described in the General Procedure (28 h) gave **15a′** (108 mg, 80%) as colourless prisms. M.p. 204−205 °C (EtOAc). IR (KBr): $\tilde{\nu}$ = 2230, 1760, 1670 cm^{-1}. ^1H NMR: δ = 2.20 (m, 2 H, CH_2), 2.54 (t, *J* = 6.6 Hz, 2 H, CH_2), 2.75 (t, *J* = 6.0 Hz, 2 H, CH_2), 3.32 (s, 3 H, NCH_3) ppm. EI-MS: *m*/*z* (%) = 191 (100.0) [M^+], 176 (16.4), 163 (86.8), 135 (63.8). $C_9H_9N_3O_2$ (191.2): calcd. C 56.54, H 4.74, N 21.98; found C 56.45, H 4.72, N 22.06.

Compound 15b′: Treatment of CAP (315 mg, 1.38 mmol) in anhydrous THF (7.0 mL) with **4b** (100 mg, 0.46 mmol), as described in the General Procedure (24 h), yielded **15b′** (102 mg, 83%) as colourless prisms. M.p. 160−161 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 2240, 1750, 1655 cm^{-1}. ^1H NMR: δ = 2.08−2.16 (m, 2 H, CH_2), 2.48 (t, *J* = 6.6 Hz, 2 H, CH_2), 2.57 (t, *J* = 6.0 Hz, 2 H, CH_2), 4.87 (s, 2 H, NCH_2Ph), 7.26−7.29 (m, 2 H, ArH), 7.36−7.43 (m, 3 H, ArH) ppm. EI-MS: *m*/*z* (%) = 267 (12.1) [M^+], 242 (5.4), 91 (100.0). HR-MS: $C_{15}H_{13}N_3O_2$: calcd. 267.100777; found 267.099921.

Compound 15d′: Treatment of CAP (406 mg, 1.78 mmol) in anhydrous THF (8.0 mL) with **5a** (100 mg, 0.59 mmol), as described above (24 h), afforded **15d′** (115 mg, 89%) as colourless crystals. M.p. 184−185 °C (CH_2Cl_2/EtOAc). IR (KBr): $\tilde{\nu}$ = 2250, 1750, 1670 cm^{-1}. ^1H NMR: δ = 1.20 (s, 6 H, CH_3), 2.43 (s, 2 H, CH_2), 2.57 (s, 2 H, CH_2), 3.30 (s, 3 H, NCH_3) ppm. EI-MS: *m*/*z* (%) = 219 (100.0) [M^+], 204 (57.7), 191 (23.8), 163 (64.0), 135 (55.0). $C_{11}H_{13}N_3O_2$ (219.2): calcd. C 60.26, H 5.95, N 19.17; found C 59.94, H 5.97, N 19.05.

Compound 16a: CAP (370 mg, 1.62 mmol) in anhydrous THF (7.0 mL) was treated with **6a** (100 mg, 0.54 mmol), as described in the General Procedure (48 h). The reaction mixture was filtered, and water and chloroform were added to the remaining residue. After separation of the resulting solid by filtration, washing with cool water and recrystallisation yielded **16a** (100 mg, 79%), as colourless crystals. M.p. 307−308 °C (dec.) (CH_3CN). IR (KBr): $\tilde{\nu}$ = 2260, 1775, 1765, 1710, 1700, 1670 cm^{-1}. ^1H NMR [D_3]acetonitrile: δ = 3.27 (s, 3 H, NCH_3), 3.55 (s, 3 H, NCH_3); 3.62 (s, 3 H, NCH_3) ppm. FAB-MS (4-NBA): *m*/*z* (%) = 236 (100.0) [M^+ + H]. HR-MS (CI, ammonia): $C_9H_{10}N_5O_3$: calcd. 236.078364; found 236.078536 [M^+ + H].

Compound 17: *N*-Methylhydroxylamine hydrochloride (1077 mg, 12.9 mmol) and sodium acetate (1058 mg, 12.9 mmol) were added to a solution of 1-phenyl-2-(phenylsulfonyl)ethanone[25] (560 mg, 2.15 mmol) in ethanol (2 mL), and the resulting mixture was heated at 40 °C for 8 d. The reaction mixture was then diluted with water and neutralised with $NaHCO_3$. The aqueous layer, after separation by decantation, was extracted several times with dichloromethane. The combined organic layers were dried with anhydrous magnesium sulfate and the solvent was removed at reduced pressure to give **17** (510 mg, 82%) as colourless crystals. M.p. 139−140 °C (CH_2Cl_2/MeOH). IR (KBr): $\tilde{\nu}$ = 1550, 1320, 1145 cm^{-1}. ^1H NMR: δ = 3.61 (s, 3 H, NCH_3), 4.83 (s, 2 H, 2-CH_2), 7.35−7.56 (m, 7 H, Ar-H), 7.62−7.67 (m, 1 H, Ar-H), 7.98−8.01 (m, 2 H, Ar-H) ppm. EI-MS: *m*/*z* (%) = 289 (1.6) [M^+], 273 (7.6) [M^+ − O], 149 (61.0) [M^+ − SO_2Ph + H], 148 (38.5) [M^+ − SO_2Ph], 103 (100.0) [$PhCN^+$]. $C_{15}H_{15}NO_3S$ (289.4): calcd. C 62.27, H 5.23, N 4.84; found C 62.32, H 5.34, N 4.89.

Compound 18: CAP (192.4 mg, 1.04 mmol) in anhydrous THF (1.0 mL) was treated with a solution of **17** (40.5 mg, 0.35 mmol) and *N*,*N*-diisopropylethylamine (0.35 mmol) in the same solvent (1.5 mL), as described in the General Procedure (24 h). The reaction mixture was filtered and the residual solid was washed several times with diethyl ether. Removal of solvent from the combined diethyl ether solutions at reduced pressure afforded **18** (95 mg, 80%) as colourless crystals. M.p. 177−178 °C (EtOH). IR (KBr): $\tilde{\nu}$ = 2270, 1750, 1370, 1160 cm^{-1}. ^1H NMR: δ = 3.03 (s, 3 H, NCH_3), 7.34−7.37 (m, 2 H, Ar-H), 7.54−7.67 (m, 6 H, Ar-H), 7.75−7.78 (m, 2 H, Ar-H) ppm. ^{13}C NMR: δ = 29.6, 102.5, 116.0, 124.2, 127.8, 128.9, 129.6, 129.9, 131.4, 134.5, 135.9, 140.0, 150.1 ppm. FAB-MS (4-NBA): *m*/*z* (%) = 340 (100.0) [M^+ + H], 339 (66.1) [M^+], 314 (6.5) [M^+ + H − CN], 173 (28.3) [M^+ + H − CN − SO_2Ph]. $C_{17}H_{13}N_3O_3S$ (339.4): calcd. C 60.55, H 3.79, N 12.27; found C 60.37, H 3.83, N 12.28.

Compound 19: *N*,*N*-Diisopropylethylamine (0.28 mmol) and BrCN (14.8 mg, 0.14 mmol) were added under N_2 to a stirred, ice-cooled solution of **17** (40.5 mg, 0.14 mmol) in anhydrous THF (5 mL). After 1 h, the solvent was removed at reduced pressure and the remaining residue was extracted several times with diethyl ether. The combined ethereal solutions were concentrated to dryness to yield **19** (42.8 mg, 83%) as white crystals. M.p. 130−131 °C ($Et_2O/CHCl_3$). IR (KBr): $\tilde{\nu}$ = 1585, 1530, 1335, 1160 cm^{-1}. ^1H NMR: δ = 3.59 (s, 3 H, NCH_3), 7.00 (s, 1 H, 2-H), 7.50−7.60 (m, 7 H, Ar-H), 7.70 (br. t, *J* = 7.2 Hz, 1 H, Ar-H), 7.97 (d, *J* = 7.8 Hz, 2 H, Ar-H) ppm. EI-MS: *m*/*z* (%) = 367/369 (0.1/0.1) [M^+/M^+ + 2], 351/353 (0.2/0.2) [(M^+ − O)/(M^+ + 2 − O)], 141 (21.8) [$PhSO_2^+$], 118 (19.5) [M^+ − $CHBrSO_2Ph$], 77 (100.0) [Ph^+]. HR-MS: $C_{15}H_{14}{}^{81}BrNO_3S$: calcd. 368.985730; found 368.987268. $C_{15}H_{14}{}^{79}BrNO_3S$: calcd. 366.987776; found 366.987639.

Treatment of Enehydroxylamines with Benzoyl Chloride. General Procedure: *N*,*N*-Diisopropylethylamine (1 equiv.) and benzoyl

chloride (1 equiv.) were added under N_2 to a stirred, ice-cooled suspension of enehydroxylamine (1 equiv.) in anhydrous THF. After the reaction was complete, the organic salt was removed by filtration and washed with anhydrous THF. The filtrate was concentrated to dryness, and the resulting residue was dissolved in a mixture of diethyl ether and dichloromethane (1:2) and washed with water. The aqueous layer, after separation by decantation, was extracted several times with diethyl ether, and the combined organic layers were dried with anhydrous sodium sulfate. Solvent removal under reduced pressure gave a residue, which was recrystallised.

Compound 7f: Treatment of **4a** (700 mg, 4.96 mmol) and benzoyl chloride (697 mg, 4.96 mmol) in anhydrous THF (10 mL) as described in the General Procedure (1 h 30 min) afforded **7f** (1.12 g, 92%) as colourless crystals. M.p. 71−73 °C ($CHCl_3/Et_2O$). IR (KBr): $\tilde{\nu}$ = 1755, 1640, 1570 cm^{-1}. ^1H NMR: δ = 2.00−2.09 (m, 2 H, 5-CH_2), 2.34 (t, *J* = 6.6 Hz, 2 H, 4- or 6-CH_2), 2.50 (t, *J* = 6.2 Hz, 2 H, 6- or 4-CH_2), 3.34 (s, 3 H, NCH_3), 5.42 (s, 1 H, 2-H), 7.51 (t, *J* = 7.6 Hz, 2 H, ArH), 7.64−7.69 (m, 1 H, ArH), 8.06−8.09 (m, 2 H, ArH) ppm. EI-MS: *m*/*z* (%) = 245 (2.7) [M^+], 125 (26.9), 122 (31.2), 105 (100.0). $C_{14}H_{15}NO_3$ (245.3): calcd. C 68.56, H 6.16, N 5.71; found C 68.65, H 6.18, N 5.65.

Compound 7g: Treatment of **4b** (100 mg, 0.46 mmol) and benzoyl chloride (65.0 mg, 0.46 mmol) in anhydrous THF (3 mL) as described in the General Procedure (2 h) afforded **7g** (130 mg, 88%) as a colourless oil. IR (neat): $\tilde{\nu}$ = 1760, 1640, 1580 cm^{-1}. ^1H NMR: δ = 2.01−2.10 (m, 2 H, 5-CH_2), 2.34 (t, *J* = 6.3 Hz, 2 H, 4- or 6-CH_2), 2.57 (t, *J* = 6.7 Hz, 2 H, 6- or 4-CH_2), 4.84 (s, 2 H, NCH_2Ph), 5.49 (s, 1 H, 2-H), 7.27−7.35 (m, 5 H, ArH), 7.45 (t, *J* = 7.7 Hz, 2 H, ArH), 7.60−7.65 (m, 1 H, ArH), 7.95−7.98 (m, 2 H, ArH) ppm. EI-MS: *m*/*z* (%) = 321 (100.0) [M^+], 199 (47.5), 122 (35.6), 105 (68.8), 91 (46.3). HR-MS: $C_{20}H_{19}NO_3$: calcd. 321.136494; found 321.137472.

Compound 7g-*d*$_5$: Treatment of **4b** (400 mg, 1.84 mmol) and [D_5]benzoyl chloride (268 mg, 1.84 mmol) in anhydrous THF (8 mL) as described above (2 h) afforded **7g-*d*$_5$** (545 mg, 91%) as a colourless oil. IR (neat): $\tilde{\nu}$ = 1762, 1708, 1566 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$): δ = 1.99−2.05 (m, 2 H, 5-CH_2), 2.32 (t, *J* = 6.4 Hz, 2 H, 4- or 6-CH_2), 2.54 (t, *J* = 6.4 Hz, 2 H, 6- or 4-CH_2), 4.83 (s, 2 H, NCH_2Ph), 5.49 (s, 1 H, 2-H), 7.27−7.33 (m, 5 H, ArH) ppm.

Compound 7h: Treatment of **5a** (100 mg, 0.59 mmol) and benzoyl chloride (83.0 mg, 0.59 mmol) in anhydrous THF (3 mL) as described in the General Procedure (1 h) gave **7h** (156 mg, 97%) as colourless needles. M.p. 111−112 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 1750, 1640, 1590 cm^{-1}. ^1H NMR: δ = 1.10 (s, 6 H, 5-CH_3), 2.21 (s, 2 H, 4- or 6-CH_2), 2.33 (s, 2 H, 6- or 4-CH_2), 3.33 (s, 3 H, NCH_3), 5.42 (s, 1 H, 2-H), 7.49−7.54 (m, 2 H, ArH), 7.64−7.69 (m, 1 H, ArH), 8.06−8.09 (m, 2 H, ArH) ppm. EI-MS: *m*/*z* (%) = 273 (4.1) [M^+], 153 (20.0), 138 (20.0), 122 (10.3), 105 (100.0). HR-MS: $C_{16}H_{19}NO_3$: calcd. 273.136494; found 273.135677.

Compound 7i: Treatment of **5b** (500 mg, 2.06 mmol) and benzoyl chloride (290 mg, 2.09 mmol) in anhydrous THF (8 mL) as described in the General Procedure (1 h) gave **7i** (700 mg, 97%) as a colourless oil. IR (neat): $\tilde{\nu}$ = 1760, 1639, 1579 cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ = 1.08 (s, 6 H, 5-CH_3), 2.20 (s, 2 H, 4- or 6-CH_2), 2.39 (s, 2 H, 6- or 4-CH_2), 4.83 (s, 2 H, NCH_2Ph), 5.47 (s, 1 H, 2-H), 7.28−7.37 (m, 5 H, ArH), 7.45 (t, *J* = 7.8 Hz, 2 H, ArH), 7.61 (t, *J* = 7.6 Hz, 1 H, ArH), 7.96 (d, *J* = 7.8 Hz, 2 H, ArH) ppm. EI-MS: *m*/*z* (%) = 349 (6) [M^+], 144 (14), 122 (10.3), 105 (100.0). HR-MS: $C_{22}H_{23}NO_3$: calcd. 349.167794; found 349.167624.

Compound 7i-*d*$_5$: Treatment of **5b** (46 mg, 0.19 mmol) and [D_5]benzoyl chloride (27.6 mg, 0.19 mmol) in anhydrous THF (1.5 mL) as described in the General Procedure (1 h) gave **7i-*d*$_5$** (68 mg, 99%) as a colourless oil. ^1H NMR (400 MHz): δ = 1.08 (s, 6 H, 5-CH_3), 2.21 (s, 2 H, 4- or 6-CH_2), 2.39 (s, 2 H, 6- or 4-CH_2), 4.84 (s, 2 H, NCH_2Ph), 5.49 (s, 1 H, 2-H), 7.30−7.37 (m, 5 H, ArH) ppm.

Compound 9c: Treatment of **6a** (100 mg, 0.54 mmol) and benzoyl chloride (75.9 mg, 0.54 mmol) in anhydrous THF (3 mL) as described in the General Procedure (1 h) yielded **9c** (123 mg, 79%) as colourless crystals. M.p. 138−140 °C (dec.) (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1755, 1705, 1650, 1475, 1450 cm^{-1}. ^1H NMR: δ = 3.22 (s, 3 H, NCH_3), 3.36 (s, 3 H, NCH_3), 3.42 (s, 3 H, NCH_3), 5.76 (s, 1 H, 5-H), 7.47−7.52 (m, 2 H, ArH), 7.63−7.68 (m, 1 H, ArH), 7.99−8.02 (m, 2 H, ArH) ppm. ^{13}C NMR: δ = 28.1, 31.7, 42.8, 89.7, 127.0, 128.8, 129.6, 134.3, 152.1, 157.3 (C=O), 162.6 (C=O), 163.5 (C=O) ppm. FAB-MS (glycerol): *m*/*z* (%) = 290 (100.0) [M^+ + H]. $C_{14}H_{15}N_3O_4$ (289.3): calcd. C 58.13, H 5.23, N 14.53; found C 57.95, H 5.27, N 14.46.

Rearrangement of *O*-Benzoylenehydroxylamines

Compound 8f: A solution of **7f** (100 mg, 0.41 mmol) in toluene was heated under reflux until all starting material was consumed (5 h). Solvent removal under reduced pressure and purification of the resulting residue by PTLC (silica; EtOAc/*n*-hexane, 1:1) gave **8f** (90.0 mg, 90%) as a colourless oil. IR (KBr): $\tilde{\nu}$ = 3300, 1730, 1570 cm^{-1}. ^1H NMR: δ = 1.98−2.07 (m, 2 H, 5-CH_2), 2.41 (t, *J* = 6.6 Hz, 2 H, 4- or 6-CH_2), 2.55 (t, *J* = 6.0 Hz, 2 H, 6- or 4-CH_2), 2.88 (d, *J* = 5.4 Hz, 3 H, NHCH_3, collapses to s on irradiation at 5.15), 5.15 (br. s, 1 H, NH, D_2O exchange), 7.46−7.48 (m, 2 H, ArH), 7.56−7.62 (m, 1 H, ArH), 8.15−8.18 (m, 2 H, ArH) ppm. EI-MS: *m*/*z* (%) = 245 (20.5) [M^+], 140 (7.1), 112 (12.0), 105 (100.0). HR-MS: $C_{14}H_{15}NO_3$: calcd. 245.105194; found 245.105726.

Compound 8g: A solution of **7g** (38.5 mg, 0.12 mmol) in toluene was heated under reflux for 2 h. Reaction workup as described above gave **8g** (35.0 mg, 90%) as colourless crystals. M.p. 114−115 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3220, 1730, 1590, 1540 cm^{-1}. ^1H NMR: δ = 2.03−2.08 (m, 2 H, 5-CH_2), 2.49 (t, *J* = 6.4 Hz, 2 H, 4- or 6-CH_2), 2.62 (t, *J* = 6.0 Hz, 2 H, 6- or 4-CH_2), 4.45 (d, *J* = 6.0 Hz, 2 H, NHCH_2Ph, collapses to s on irradiation at 5.43), 5.43 (br. s, 1 H, NH, D_2O exchange), 7.23−7.38 (m, 5 H, ArH), 7.44−7.49 (m, 2 H, ArH), 7.57−7.60 (m, 1 H, ArH), 8.16−8.17 (m, 2 H, ArH) ppm. EI-MS: See Table 6. HR-MS: $C_{20}H_{19}NO_3$: calcd. 321.136494; found 321.139207.

Compound 8g-*d*$_5$: A solution of **7g-*d*$_5$** gave, as above, **8g-*d*$_5$**, as colourless crystals. M.p. 114−115.5 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3455, 1733, 1588, 1543 cm^{-1}. ^1H NMR (400 MHz): δ = 2.01−2.07 (m, 2 H, 5-CH_2), 2.47 (t, *J* = 6.4 Hz, 2 H, 4- or 6-CH_2), 2.60 (t, *J* = 6.0 Hz, 2 H, 6- or 4-CH_2), 4.44 (d, *J* = 6.0 Hz, 2 H, NHCH_2Ph, collapses to s on irradiation at 5.24), 5.24 (br. s, 1 H, NH, D_2O exchange), 7.23−7.31 (m, 3 H, ArH), 7.36 (d, *J* = 7.2 Hz, 2 H, ArH) ppm. EI-MS: See Table 6.

Compound 8h: A solution of **7h** (112 mg, 0.41 mmol) in toluene was heated under reflux for 5 h 15 min. Reaction workup as described above furnished **8h** (105 mg, 94%) as a colourless oil. IR (KBr): $\tilde{\nu}$ = 3300, 1740, 1590 cm^{-1}. ^1H NMR: δ = 1.17 (s, 6 H, 5-CH_3), 2.29 (s, 2 H, 4- or 6-CH_2), 2.39 (s, 2 H, 6- or 4-CH_2), 2.87 (d, *J* = 5.4 Hz, 3 H, NHCH_3, collapses to s on irradiation at 5.10), 5.10 (br. s, 1 H, NH, exchangeable D_2O), 7.46 (t, *J* = 7.8 Hz, 2 H, ArH), 7.59 (t, *J* = 7.7 Hz, 1 H, ArH), 8.17 (d, *J* = 6.9 Hz, 2 H, ArH) ppm. EI-MS: *m*/*z* (%) = 273 (62.3) [M^+], 258 (42.0), 168

(40.6), 140 (46.4), 105 (100.0). HR-MS: $C_{16}H_{19}NO_3$: calcd. 273.136494; found 273.136657.

Compound 8i: A solution of **7i** (40.0 mg, 0.11 mmol) in toluene was heated under reflux for 6 h. Reaction workup as described above gave **8i** (32.8 mg, 85%) as colourless crystals. M.p. 195−196 °C (*n*-hexane/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3314, 1737, 1592, 1544 cm^{-1}. ^1H NMR (400 MHz): δ = 1.14 (s, 6 H, 5-CH_3), 2.34 (s, 2 H, 4- or 6-CH_2), 2.44 (s, 2 H, 6- or 4-CH_2), 4.43 (d, *J* = 6.0 Hz, 2 H, N*C*H_2Ph), 5.24 (br. s, 1 H, NH, D_2O exchange), 7.22−7.38 (m, 5 H, Ar), 7.45 (t, *J* = 7.6 Hz, 2 H, ArH), 7.58 (t, *J* = 7.4 Hz, 1 H, ArH), 8.17 (d, *J* = 7.6 Hz, 2 H, ArH) ppm. EI-MS: See Table 6. HR-MS: $C_{20}H_{19}NO_3$: calcd. 349.167794; found 349.168242.

Compound 8i-*d*$_5$: A solution of **7i-*d*$_5$** gave, as above, **8i-*d*$_5$**, as colourless crystals. M.p. 196−198 °C (*n*-hexane/$CHCl_3$). IR (KBr): $\tilde{\nu}$ = 3314, 1736, 1592, 1543 cm^{-1}. ^1H NMR (400 MHz): δ = 1.14 (s, 6 H, 5-CH_3), 2.34 (s, 2 H, 4- or 6-CH_2), 2.44 (s, 2 H, 6- or 4-CH_2), 4.43 (d, *J* = 6.0 Hz, 2 H, N*C*H_2Ph), 5.23 (br. s, 1 H, NH, D_2O exchange), 7.23−7.38 (m, 5 H, ArH) ppm. EI-MS: See Table 6.

Compounds 10c and 20: A solution of **9c** (49.0 mg, 0.17 mmol) in toluene was heated under reflux for 7 h. Reaction workup as described above gave **10c** (10.8 mg, 22%) as colourless crystals, followed by **20** (28.5 mg, 58%) as white needles. Physical data for **10c**: M.p. 191−192 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 3330, 1750, 1700, 1620, 1540 cm^{-1}. ^1H NMR: δ = 2.98 (d, *J* = 5.1 Hz, 3 H, NHC*H*$_3$, collapses to s on irradiation at 4.56), 3.33 (s, 3 H, NCH_3), 3.42 (s, 3 H, NCH_3), 4.56 (br. s, 1 H, N*H*CH_3), 7.49 (t, *J* = 8.0 Hz, 2 H, ArH), 7.62 (t, *J* = 7.2 Hz, 1 H, ArH), 8.15−8.18 (m, 2 H, ArH) ppm. FAB-MS (glycerol): *m*/*z* (%) = 290 (100.0) [M^+ + H]. HR MS (CI, ammonia): $C_{14}H_{15}N_3O_4$: calcd. 290.114081; found 290.114446 [M^+ + H]. Physical data for **20**: M.p. 158−160 °C (dec.) ($CH_2Cl_2Et_2O$). IR (KBr): $\tilde{\nu}$ = 3340, 1710, 1650 cm^{-1}. ^1H NMR: δ = 3.29 (s, 3 H, NCH_3), 3.33 (s, 3 H, NCH_3), 3.39 (s, 3 H, NCH_3), 6.17 (br. s, 1 H, OH, D_2O exchange), 7.27−7.33 (m, 2 H, ArH), 7.34−7.45 (m, 3 H, ArH) ppm. ^{13}C NMR (CD_2Cl_2) (quaternary carbon atoms): δ = 126.9, 131.8, 134.3, 149.0, 159.9 (C=O), 170.4 (C=O) ppm. FAB-MS (glycerol): *m*/*z* (%) = 290 (100.0) [M^+ + H]. $C_{14}H_{15}N_3O_4$ (289.3): calcd. C 58.13, H 5.23, N 14.53; found C 58.10, H 5.24, N 14.80. When a solution of **9c** (70.0 mg, 0.24 mmol) in toluene was heated under reflux for 15 h 30 min and worked up as described above, **10c** and **20** were obtained in 15 and 81% yields, respectively.

Compound 25: 1,1,1,3,3,3-Hexamethyldisilazane (HMDS, 1.22 mmol) was added under N_2 to a stirred 35% dispersion of potassium hydride in mineral oil (1.22 mmol, washed free of oil with anhydrous THF) in THF (2 mL), and the mixture was kept at room temp., protected from light, for 4 h. The resulting suspension was added slowly under N_2 to a vigorously stirred solution of **7f** (100.6 mg, 0.41 mmol) and *tert*-butyldimethylsilyl chloride (TBDMSCl, 2.04 mmol) in anhydrous THF (2 mL), cooled to −80 °C and protected from light. When the addition was complete, the temperature was slowly raised to room temp. and, after 2 h, the solvent was removed at reduced pressure. The resulting residue was redissolved in a mixture of ethyl acetate and water and the aqueous layer, after separation by decantation, was extracted several times with ethyl acetate. The combined organic layers were dried with anhydrous sodium sulfate and the solvent was removed at reduced pressure to leave a residue, which was separated by PTLC (silica; EtOAc) to give **25** (29.2 mg, 29%) as colourless crystals. M.p. 121−122 °C (Et_2O). IR (KBr): $\tilde{\nu}$ = 3240, 1720, 1615, 1580, 1530 cm^{-1}. ^1H NMR: δ = 2.17−2.51 (m, 3 H), 2.61−2.75 (m, 1 H), 2.79 (d, *J* = 5.1 Hz, 3 H, NHC*H*$_3$, collapses to s on irradiation at 5.41 and with D_2O), 5.14 (s, 1 H, 2-H), 5.41 (br. s, 1 H, NH, D_2O exchange), 5.73 (m, 1 H, 4-H), 7.46−7.51 (m, 2 H, Ar-H), 7.60−7.66 (m, 1 H, Ar-H), 8.04−8.07 (m, 2 H, Ar-H) ppm. EI-MS: *m*/*z* (%) = 245 (18.1) [M^+], 140 (12.2) [M^+ − COPh], 105 (100.0) [$COPh^+$]. HR-MS (EI): $C_{14}H_{15}NO_3$ (245.3): calcd. 245.105194; found 245.105395.

Treatment of Enehydroxylamines with Diethyl Chlorophosphate

Compound 7j: A 60% dispersion of sodium hydride in mineral oil (134.1 mg, 1.42 mmol) was added under N_2 to a stirred, ice-cooled suspension of **5a** (200 mg, 1.18 mmol) in anhydrous THF (4 mL), protected from light, followed 30 min later by diethyl chlorophosphate (204 mg, 1.18 mmol). After 4 h, the solvent was removed under reduced pressure and a mixture of dichloromethane and water was added to the residue. The aqueous layer, after separation by decantation, was extracted with dichloromethane and ethyl acetate and the combined organic layers were dried with anhydrous sodium sulfate. Solvent removal under reduced pressure and purification of the resulting residue by PTLC (silica; EtOAc/MeOH, 99:1) yielded **7j** (310 mg, 86%) as a yellow oil. IR (neat): $\tilde{\nu}$ = 1650, 1600, 1370, 1280, 1170, 1040 cm^{-1}. ^1H NMR: δ = 1.16 (s, 6 H, 5-CH_3), 1.36 (t, *J* = 7.0 Hz, 6 H, OCH_2CH_3), 2.22 (s, 2 H, 4- or 6-CH_2), 2.30 (s, 2 H, 6- or 4-CH_2), 3.24 (s, 3 H, NCH_3), 4.17−4.29 (m, 4 H, OCH_2CH_3), 5.67 (s, 1 H, 2-H) ppm. FAB-MS (glycerol): *m*/*z* (%) = 306 (100.0) [M^+ + H]. HR-MS (CI, ammonia): $C_{13}H_{25}NO_5P$: calcd. 306.147037; found 306.148643 [M^+ + H].

Compound 9d: Treatment of **6a** (200 mg, 1.08 mmol) with diethyl chlorophosphate (186 mg, 1.08 mmol) in anhydrous THF (4 mL) as described above (1 h 30 min) afforded **9d** (298 mg, 86%) as a colourless oil. IR (neat): $\tilde{\nu}$ = 1710, 1660, 1485, 1450, 1275, 1160, 1030 cm^{-1}. ^1H NMR: δ = 1.36 (t, *J* = 7.2 Hz, 6 H, OCH_2CH_3, collapses to s on irradiation at 4.2), 3.11 (s, 3 H, NCH_3), 3.34 (s, 3 H, NCH_3), 3.42 (s, 3 H, NCH_3), 4.14−4.25 (m, 4 H, OCH_2CH_3), 5.88 (s, 1 H, 5-H) ppm. FAB-MS (glycerol): *m*/*z* (%) = 322 (100.0) [M^+ + H]. HR-MS (CI, ammonia): $C_{11}H_{21}N_3O_6P$: calcd. 322.116799; found 322.116061 [M^+ + H].

Rearrangement of *O*-(Diethoxyphosphoryl)enehydroxylamines

Compound 8j: A solution of **7j** (104 mg, 0.34 mmol) in toluene was heated under reflux for 15 min. Solvent removal under reduced pressure and purification of the remaining residue by PTLC (silica; EtOAc/MeOH, 95:5) yielded **8j** (80.1 mg, 77%) as a colourless oil. IR (KBr): $\tilde{\nu}$ = 3400, 1580, 1270, 1155, 1040 cm^{-1}. ^1H NMR: δ = 1.12 (s, 6 H, 5-CH_3), 1.35 (t, *J* = 7.2 Hz, 6 H, OCH_2CH_3, collapses to s on irradiation at 4.3), 2.27 (s, 2 H, 4- or 6-CH_2), 2.41 (d, *J* = 1.8 Hz, 2 H, 6- or 4-CH_2), 2.94 (d, *J* = 5.1 Hz, 3 H, $NHCH_3$, collapses to s on irradiation at 5.94), 4.24−4.34 (m, 4 H, OCH_2CH_3), 5.94 (br. s, 1 H, NH) ppm. FAB-MS (glycerol): *m*/*z* (%) = 306 (100.0) [M^+ + H]. HR-MS (CI, ammonia): $C_{13}H_{25}NO_5P$: calcd. 306.147037; found 306.147492 [M^+ + H].

Compound 10d: A solution of **9d** (57.8 mg, 0.18 mmol) in toluene was heated under reflux for 1 h. Solvent removal at reduced pressure and recrystallisation of the resulting residue afforded **10d** (45.1 mg, 78%) as colourless crystals. M.p. 119−120 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 3300, 1710, 1620, 1610, 1250, 1160, 1030 cm^{-1}. ^1H NMR: δ = 1.37 (t, *J* = 7.2 Hz, 6 H, OCH_2CH_3, collapses to s on irradiation at 4.32), 2.98 (d, *J* = 5.1 Hz, 3 H, NHC*H*$_3$ collapses to s on irradiation at 5.08), 3.34 (s, 3 H, NCH_3), 3.43 (s, 3 H, NCH_3), 4.27−4.37 (m, 4 H, OCH_2CH_3), 5.08 (m, 1 H, NH). FAB-MS (glycerol): *m*/*z* (%) = 322 (100.0) [M^+ + H]. $C_{11}H_{20}N_3O_6P$ (321.3): calcd. C 41.12, H 6.27, N 13.08; found C 41.32, H 6.09, N 13.02.

Treatment of Enehydroxylamines with Phenyl Isocyanate. General Procedure A: *N*,*N*-Diisopropylethylamine (1 equiv.) was added under N_2 to a stirred, ice-cooled suspension of enehydroxylamine (1 equiv.) in anhydrous THF, followed by the slow addition of phenyl isocyanate (1 equiv.). After the reaction was complete, the solvent was removed under reduced pressure and the residue was recrystallised. **General Procedure B:** A 60% dispersion of sodium hydride in mineral oil (1.3 equiv.) was added under N_2 to a stirred, ice-cooled suspension of enehydroxylamine (1 equiv.) in anhydrous THF. After hydrogen evolution had ceased, phenyl isocyanate (2.5 equiv.) was added, and the mixture was kept at room temperature for 1 h and then heated at reflux until the reaction was completed. Solvent was removed under reduced pressure and the resulting residue was redissolved in water, acidified to pH ≈ 5 with a 5% aqueous solution of HCl and extracted several times with ethyl acetate and diethyl ether. After drying of the combined organic layers with anhydrous sodium sulfate and solvent removal under reduced pressure, a residue was obtained and purified by recrystallisation or PTLC.

Compound 7k: Treatment of **4a** (300 mg, 2.13 mmol) with phenyl isocyanate (254 mg, 2.13 mmol) in anhydrous THF (7 mL) as described in General Procedure A (2 h) gave **7k** (498 mg, 90%) as colourless crystals. M.p. 126−129 °C (dec.) (EtOAc). IR (KBr): $\tilde{\nu}$ = 3245, 1765, 1610, 1580 cm^{-1}. ^1H NMR: δ = 2.01−2.09 (m, 2 H, 5-CH_2), 2.35 (t, *J* = 6.6 Hz, 2 H, 4- or 6-CH_2), 2.49 (t, *J* = 6.3 Hz, 2 H, 6- or 4-CH_2), 3.30 (s, 3 H, NCH_3), 5.42 (s, 1 H, 2-H), 7.10−7.16 (m, 1 H, ArH), 7.31−7.36 (m, 2 H, ArH), 7.40−7.43 (m, 3 H, ArH + NH) ppm. FAB-MS (4-NBA): *m*/*z* (%) = 261 (74.4) [M^+ + H], 142 (100.0) ppm. $C_{14}H_{16}N_2O_3$ (260.3): calcd. C 64.60, H 6.20, N 10.76; found C 64.85, H 6.15, N 10.84.

Compound 8k: Treatment of **4a** (180 mg, 1.28 mmol) with phenyl isocyanate (379 mg, 3.18 mmol) in anhydrous THF (6 mL) as described in General Procedure B (3 h) afforded **8k** (360 mg, 84%) as colourless crystals. M.p. 217−218 °C (EtOAc/MeOH). IR (KBr): $\tilde{\nu}$ = 3210, 1670, 1595, 1565 cm^{-1}. ^1H NMR: δ = 1.99−2.05 (m, 2 H, 5-CH_2), 2.50−2.53 (m, 2 H, 4- or 6-CH_2), 2.66 (t, *J* = 6.3 Hz, 2 H, 6- or 4-CH_2), 3.10 (s, 3 H, NCH_3), 6.70 (br. s, 1 H, NH, D_2O exchange), 6.97−7.03 (m, 1 H, ArH), 7.10−7.14 (m, 2 H, ArH), 7.21−7.43 (m, 7 H, ArH), 7.53 (br. s, 1 H, NH, D_2O exchange) ppm. FAB-MS (4-NBA): *m*/*z* (%) = 336 (24.3) [M^+ + H], 243 (100.0). $C_{20}H_{21}N_3O_2$ (335.4): calcd. C 71.66, H 6.26, N 12.53; found C 71.57, H 6.30, N 12.56. Alternatively, a 60% dispersion of sodium hydride in mineral oil (4.56 mg, 0.19 mmol) was added under N_2 to a stirred solution of **7k** (50.0 mg, 0.19 mmol) in anhydrous THF (4 mL), protected from light. After hydrogen evolution had ceased, the reaction mixture was heated under reflux until all starting material was consumed. The solvent was then removed under reduced pressure and a mixture of diethyl ether and water (1:1) was added to the resulting residue. The aqueous layer, after separation by decantation, was acidified to pH ≈ 5 with aqueous HCl (5%) and extracted several times with dichloromethane and ethyl acetate. After drying of the combined organic layers with anhydrous sodium sulfate, solvent removal under reduced pressure and recrystallisation of the resulting residue from EtOAc/MeOH, **8k** (31.2 mg, 49%) was obtained.

Compound 7l: Treatment of **5a** (380 mg, 2.25 mmol) with phenyl isocyanate (268 mg, 2.25 mmol) in anhydrous THF (5 mL) as described in General Procedure A (4 h) afforded **7l** (551 mg, 85%) as colourless crystals. M.p. 130−132 °C (dec.) (Et_2O). IR (KBr): $\tilde{\nu}$ = 3240, 1770, 1615, 1585 cm^{-1}. ^1H NMR: δ = 1.11 (s, 6 H, 5-CH_3), 2.22 (s, 2 H, 4- or 6-CH_2), 2.32 (s, 2 H, 6- or 4-CH_2), 3.30 (s, 3 H, NCH_3), 5.43 (s, 1 H, 2-H), 7.08−7.12 (m, 1 H, ArH), 7.28−7.33 (m, 2 H, ArH), 7.42−7.44 (m, 2 H, Ar-H), 7.55 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS: *m*/*z* (%) = 169 (1.9) [M^+ − CONPh], 151 (20.6), 119 (100.0), 91 (47.9). FAB-MS (glycerol): *m*/*z* (%) = 289 (100.0) [M^+ + H]. $C_{16}H_{20}N_2O_3$ (288.3): calcd. C 66.65, H 6.99, N 9.72; found C 66.72, H 7.08, N 9.70.

Compound 9e: Treatment of **6a** (100 mg, 0.54 mmol) with phenyl isocyanate (64.3 mg, 0.54 mmol) in anhydrous THF (3 mL) as described in General Procedure A (2 h) yielded **9e** (156 mg, 95%) as colourless crystals. M.p. 150−151 °C (dec.) (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3340, 1770, 1700, 1650, 1650 cm^{-1}. ^1H NMR: δ = 3.14 (s, 3 H, NCH_3), 3.35 (s, 3 H, NCH_3), 3.44 (s, 3 H, NCH_3), 5.65 (s, 1 H, 5-H), 7.11−7.16 (m, 1 H, ArH), 7.32−7.37 (m, 2 H, ArH), 7.45−7.48 (m, 2 H, ArH), 7.83 (br. s, 1 H, NH, D_2O exchange) ppm. FAB-MS (4-NBA): *m*/*z* (%) = 305 (100.0) [M^+ + H], 186 (24.0), 185 (45.0), 169 (78.0). $C_{14}H_{16}N_4O_4$ (304.3): calcd. C 55.26, H 5.30, N 18.41; found C 55.16, H 5.35, N 18.45.

Compounds 10e and 10b′: A solution of **9e** (30.4 mg, 0.1 mmol) in toluene was heated under reflux until all starting material was consumed (1 h). Solvent removal at reduced pressure and purification of the resulting residue by PTLC (silica; EtOAc/MeOH, 95:5) gave **10e** (14.3 mg, 55%), followed by **10b′** (6.1 mg, 36%) (as above), both as colourless crystals. Physical data for **10e**: M.p. 197−198 °C (dec.) ($CHCl_3$/MeOH). IR (KBr): $\tilde{\nu}$ = 3360, 3300, 1685, 1625, 1600, 1550 cm^{-1}. ^1H NMR: δ = 2.93 (br. s, 3 H, NHC*H*$_3$, collapses to a sharp s on irradiation at the frequency of N*H*CH_3), 3.34 (s, 3 H, NCH_3), 3.52 (s, 3 H, NCH_3), 4.79 (br. s, 1 H, N*H*CH_3), 6.63−6.66 (m, 2 H, ArH), 6.78−6.83 (m, 1 H, ArH), 7.16−7.21 (m, 3 H, ArH + NH) ppm. FAB-MS (4-NBA): *m*/*z* (%) = 261 (88.2) [M^+ + H], 260 (100.0) [M^+]. HR-MS (CI, ammonia): $C_{13}H_{17}N_4O_2$: calcd. 261.135151; found 261.136036 [M^+ + H].

Compounds 10e′ and 16b: Treatment of **6a** (100 mg, 0.54 mmol) with phenyl isocyanate (161 mg, 1.35 mmol) in anhydrous THF (4 mL) as described in General Procedure B (7 h) and purification of the resulting residue by PTLC (silica; EtOAc/petroleum ether, 1:1) afforded **10e′** (94.9 mg, 47%) and **16b** (78.8 mg, 51%), both as colourless crystals. Physical data for **10e′**: M.p. 212−217 °C (dec.) (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 3340, 3230, 1710, 1670, 1640 cm^{-1}. ^1H NMR [D$_6$]acetone: δ = 2.95 (s, 3 H, NCH_3), 3.20 (s, 3 H, NCH_3), 3.25 (s, 3 H, NCH_3), 6.87−6.93 (m, 1 H, ArH), 7.07−7.21 (m, 5 H, ArH), 7.30−7.36 (m, 2 H, ArH), 7.40−7.43 (m, 2 H, ArH), 7.92 (br. s, 1 H, NH, D_2O exchange), 8.23 (br. s, 1 H, NH, D_2O exchange) ppm. FAB-MS (glycerol): *m*/*z* (%) = 380 (100.0) [M^+ + H]. $C_{20}H_{21}N_5O_3$: calcd. C 63.31, H 5.58, N 18.46; found C 63.37, H 5.67, N 18.47. Physical data for **16b**: M.p. 270 °C (Et_2O/CH_2Cl_2). IR (KBr): $\tilde{\nu}$ = 1740, 1730, 1690, 1670, 1540 cm^{-1}. ^1H NMR: δ = 2.99 (s, 3 H, NCH_3), 3.41 (s, 3 H, NCH_3), 3.65 (s, 3 H, NCH_3), 7.35−7.38 (m, 2 H, ArH), 7.54−7.57 (m, 3 H, ArH) ppm. FAB-MS (glycerol): *m*/*z* (%) = 287 (100.0) [M^+ + H]. HR-MS (CI, ammonia): $C_{14}H_{15}N_4O_3$: calcd. 287.114416; found 287.114306 [M^+ + H].

Compounds 21 and 22: 1,1,1,3,3,3-Hexamethyldisilazane (HMDS, 1025 mg, 6.35 mmol) was added to a 35% dispersion of potassium hydride in mineral oil (255 mg, 6.35 mmol, washed free of oil with anhydrous THF) in anhydrous THF (20 mL) and vigorously stirred under N_2. When hydrogen evolution had ceased (3 h), the mixture was cooled to −80 °C and a solution of **7k** (500 mg, 1.92 mmol) in the same solvent (25 mL) and TMSCl (1.04 g, 9.6 mmol) were slowly added. When the addition was complete, the temperature of the reaction mixture was slowly raised to room temp. After 3 h, the solvent was removed under reduced pressure and the residue was dissolved in a mixture of diethyl ether and aqueous $NaHCO_3$. The

aqueous layer, after separation by decantation, was extracted with diethyl ether and ethyl acetate and the combined organic layers were dried with anhydrous sodium sulfate. Solvent removal at reduced pressure and recrystallisation of the remaining residue yielded **21** (270 mg, 54%) as colourless crystals. M.p. 195−196 °C (Et_2O/MeOH). IR (KBr): $\tilde{\nu}$ = 3390, 1715, 1595, 1565 cm^{-1}. ^1H NMR: δ = 2.11−2.41 (m, 3 H, 5-CH_2 and 6-H), 2.56−2.65 (m, 1 H, 6-H′), 2.78 (d, J = 5.1 Hz, 3 H, NHCH_3 collapses to s on irradiation at 5.71), 5.10 (s, 1 H, 2-H), 5.44 (t, 1 H, $J_{ax,eq} = J_{eq,eq}$ = 4.2 Hz, 4-H, collapses to s on irradiation at ca. 2.2), 5.71 (br. s, 1 H, NHCH_3, D_2O exchange), 7.07−7.13 (m, 1 H, ArH), 7.27−7.36 (m, 2 H, ArH), 7.46−7.49 (m, 2 H, ArH), 8.06 (br. s, 1 H, NH, D_2O exchange) ppm. EI-MS: m/z (%) = 260 (2.5) [M^+], 141 (29.2), 119 (100.0), 91 (50.8). HR-MS: $C_{14}H_{16}N_2O_3$: calcd. 260.116093; found 260.115026. Purification of the mother liquors from recrystallisation of **21** by PTLC (silica; EtOAc) afforded **22** (14%), as colourless crystals. M.p. 170−172 °C (EtOAc/MeOH). IR (KBr): $\tilde{\nu}$ = 3370, 3300, 1610, 1560, 1510 cm^{-1}. ^1H NMR: δ = 1.93−2.10 (m, 1 H), 2.21−2.29 (m, 1 H), 2.42−2.49 (m, 2 H), 2.81 (d, J = 4.8 Hz, 3 H, NHCH_3, collapses to s on irradiation at 5.87), 3.49 (m, 1 H, NH, D_2O exchange), 4.23−4.30 (m, 1 H, 4-H, $J_{ax,ax}$ = 12.0, $J_{ax,eq}$ = 4.0 Hz, 4-H collapses to dd with D_2O), 5.14 (s, 1 H, 2-H), 5.87 (br. s, 1 H, NHCH_3, D_2O exchange), 6.71−6.74 (m, 2 H, ArH), 6.83−6.88 (m, 1 H, ArH), 7.21−7.27 (m, 2 H, ArH) ppm. EI-MS: m/z (%) = 216 (100.0) [M^+], 188 (23.2), 187 (24.1), 97 (43.0), 93 (58.9). HR-MS: $C_{13}H_{16}N_2O$: calcd. 216.126263; found 216.126923.

Treatment of Enehydroxylamine with Bromonitrile Oxide

Compound 26a: K_2CO_3 (300 mg, 3.0 mmol) was added with vigorous stirring to an ice-cooled mixture of **5a** (101 mg, 0.6 mmol), THF (6 mL) and H_2O (0.6 mL), followed by a solution of dibromoformaldoxime[26,27](365 mg, 1.8 mmol) in THF (1.5 mL). After 2 h, the inorganic solid was removed by filtration and washed with diethyl ether and ethyl acetate. The combined filtrates were dried with anhydrous sodium sulfate, the solvent was removed under reduced pressure, and the resulting residue was purified by PTLC (silica; EtOAc/MeOH, 9:1) to give **26a** (50.1 mg, 36%), as colourless crystals. M.p. 177−179 °C (MeOH/C_6H_6). IR (KBr): $\tilde{\nu}$ = 3300, 1580 cm^{-1}. ^1H NMR: δ = 1.11 (s, 6 H, 5-CH_3), 2.40 (s, 2 H, 4- or 6-CH_2), 2.44 (s, 2 H, 6- or 4-CH_2), 3.02 (d, J = 5.4 Hz, 3 H, NHCH_3, collapses to s on irradiation at 5.71), 5.71 (br. s, 1 H, NHCH$_3$, D_2O exchange) ppm. FAB-MS (glycerol): m/z (%) = 234/232 (100.0/100.0) [M^+ + H/M'^+ + H]. HR-MS (CI, ammonia): $C_9H_{15}{}^{81}BrNO$: calcd. 234.031654; found 234.029234 [M^+ + H]. $C_9H_{15}{}^{79}BrNO$: calcd. 232.033700; found 232.031193 [M'^+ + H].

Treatment of Enehydroxylamine with (Diethylamino)sulfur Trifluoride (DAST)

Compound 26b: *N*,*N*-Diisopropylethylamine (76.3 mg, 0.59 mmol) was added under N_2 to a stirred, ice-cooled suspension of **5a** (100 mg, 0.59 mmol), protected from light, followed by careful addition of DAST (95.1 mg, 0.59 mmol). After 2 h, the solvent was removed under reduced pressure and the resulting residue was purified by PTLC (silica; EtOAc/MeOH, 97:3) to give **26b** (32.3 mg, 32%), as colourless crystals. M.p. 124−125 °C (CH_2Cl_2/Et_2O). IR (KBr): $\tilde{\nu}$ = 3220, 1610, 1540, 1385, 1370 cm^{-1}. ^1H NMR: δ = 1.23 (s, 6 H, 5-CH_3), 2.28 (d, J = 2.7 Hz, 2 H, 4- or 6-CH_2), 2.39 (d, J = 4.2 Hz, 2 H, 6- or 4-CH_2), 2.97 (d, J = 4.8 Hz, 3 H, NHCH_3, collapses to s on irradiation at the frequency of NH), 5.02 (br. s, 1 H, NH) ppm. EI-MS: m/z (%) = 171 (100.0) [M^+], 156 (43.5), 128 (39.6), 114 (21.9), 73 (34.4). HR-MS: $C_9H_{14}FNO$: calcd. 171.105942; found 171.106261.

Kinetic Method: A solution (0.5−1.5 mL) of the enehydroxylamine derivative (0.08−0.1 M) in [D_8]toluene or [D_6]DMSO was heated in the ^1H NMR probe at the required temperature (80−100 ± 0.1 °C range) and the first-order reaction corresponding to the disappearance of the starting material was monitored by integration of relevant signals: for **7g** at δ = 4.43 (CH_2Ph) or δ = 5.60 (2-H); for **7i** at δ = 4.42 (CH_2Ph) or δ = 5.60 (2-H) ppm.

Rearrangements of 7i and 7g-d_5: A toluene solution (2 mL) containing compounds **7i** (101.0 mg, 0.29 mmol) and **7g-d_5** (167.6 mg, 0.33 mmol) was heated at 100 °C until total disappearance of the starting materials (7 h 30 min; TLC monitoring: silica; EtOAc). The solvent was removed under reduced pressure and the only two products formed − **A** and **B** − were isolated by PTLC. Their mass spectra were then taken and, by comparison with the mass spectra of authentic **8g**, **8g-d_5**, **8i** and **8i-d_5** (see Table 6), **A** was found to be identical with **8i** and **B** with **8g-d_5**.

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