^1H, ^{13}C, ^{15}N, 2D and Variable Temperature NMR Study of the Role of Hydrogen Bonding in the Structure and Conformation of Oxamide Derivatives

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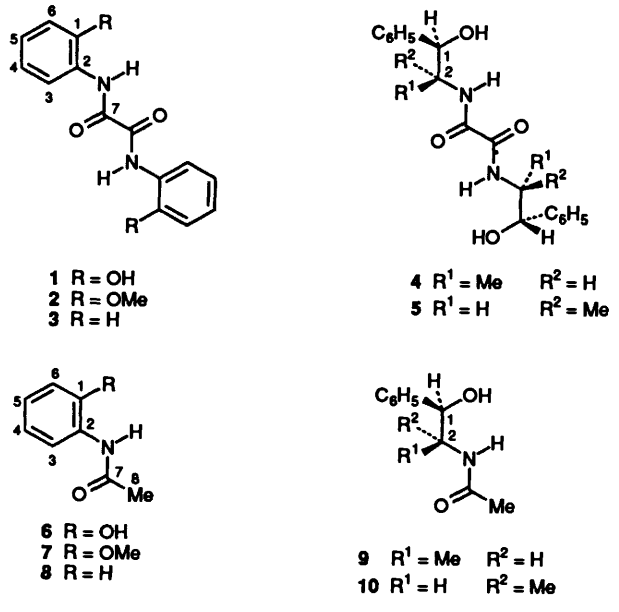
The structure and conformation of *N,N'*-bis[(2-hydroxy)phenyl]oxamide (**1**); *N,N'*-bis[(2-methoxy)-phenyl]oxamide (**2**); *N,N'*-bis(phenyl)oxamide (**3**); *N,N'*-bis[(1*R*,2*S*)-(−)-norephedrine]oxamide (**4**); *N,N'*-bis[(1*R*,2*R*)-(−)-norpseudoephedrine]oxamide (**5**); *N*-[(2-hydroxy)phenyl]methylamide (**6**); *N*-[(2-methoxy)phenyl]methylamide (**7**); *N*-phenylmethylamide (**8**); *N*-[(−)-norephedrine]-methylamide (**9**) and *N*-[(−)-norpseudoephedrine]methylamide (**10**) were unambiguously established by ^1H, ^{13}C, ^{15}N, 2D and variable temperature NMR spectroscopy. A careful NMR investigation of the conformational behaviour in these systems was relevant. It has been found that the dicarbonylic group in compounds **1–5** has a *trans* geometry, stabilized by intramolecular hydrogen bonding and that they possess a C_2 axis. Compounds **1** and **2** are planar and compounds **1**, **2**, **4** and **5** present the amidic proton coordinated by two oxygen atoms.

This paper describes our studies in the synthesis and structural investigation of several oxamides **1–5** (Scheme 1). Owing to



1 R = OH
2 R = OMe
3 R = H

4 R^1 = Me R^2 = H
5 R^1 = H R^2 = Me

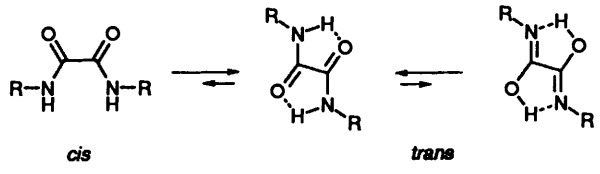
6 R = OH
7 R = OMe
8 R = H

9 R^1 = Me R^2 = H
10 R^1 = H R^2 = Me

Scheme 1

the varying functional groups in the molecules, several conformations and tautomers could be expected, as well as intramolecular hydrogen bonding. Hydrogen bonding and tautomerism are very widespread and understanding this phenomenon in simple model compounds may lead to the extrapolation of information to complex biomolecules such as peptides.[1-2] In order to understand the role of the phenol group (compounds **1–2**) or the hydroxy group (**4–5**) in the intramolecular hydrogen bonding in structures **1–5**, compounds **6–10** were synthesized.

It has therefore been necessary to do a detailed investigation of the structure of these compounds by ^1H, ^{13}C and ^{15}N NMR spectroscopy. The oxamide derivatives were prepared from the reaction of oxalyl chloride and the corresponding aromatic compounds (**1–3**), norephedrine (**4**) or norpseudoephedrine (**3**).



cis *trans*

Fig. 1 *cis* and *trans* conformers of oxamides

Results and Discussion

Compounds **1–5** may exist in two conformations, *cis* or *trans*, of the dicarbonylic function. The phenolamine or the ethanolamine moieties may also have a conformational preference. It was therefore interesting to study the conformation of these molecules and if the presence of hydrogen bonding could stabilize some of the possible conformers. A careful NMR investigation of the conformational behaviour in these systems was relevant. The syntheses of compounds **1–5** afforded in all cases only one structure that was attributed to the *trans*-conformer as we will show.

The synthesis of compound **1** has been reported previously,[3] but its structure was not supported by spectroscopic data. The *trans*-conformer may be stabilized by the two five-membered rings formed by hydrogen bonding. It has been found by molecular mechanics calculations[4] that for compound **1** the *trans* conformer is more stable than the *cis* by 9.96 kcal mol^{-1} * (Fig. 1). As we will discuss later, the NMR study confirmed that the *trans* conformer is the more stable.

The first fact to be checked was the presence of hydrogen bonding between the amidic proton and the β carbonyl group. We have registered the ^1H NMR spectra chemical shift of the N–H at different temperatures in order to correlate its shift with the temperature, Fig. 2, Table 1. It is accepted that the temperature dependence of N–H chemical shifts ($\Delta\delta/\Delta T$) in a proton accepting solvent ([$^2H_6$]DMSO) indicates the situation of a proton in intramolecular, intermolecular or in solvent interactions.[5,6] $\Delta\delta/\Delta T$ values higher than 4×10^{-3} ppm/K correspond to solvated N–H groups whereas lower values than 3×10^{-3} ppm/K are attributed to N–H groups involved in intramolecular bonding.[2] A decrease in entropic effects conse-

* 1 cal = 4.184 J.

Table 1 ^{1}H NMR Chemical shift-temperature dependence (ppm/K) in [$^2H_6$]DMSO for **1–10**[a]

Amide	$\Delta\delta/\Delta T$ (10^{-3}) N–H	O–H
1	−0.5	−6.5
2	−1.1	
3	−5.2	
4	−3.3	−4.1[b]
5	−2.5	−5.0[b]
6	−3.5	−4.8
7	−5.2	
8	−4.9	
9	−5.9	−5.1[b]
10	−5.4	−5.1[b]

[a] The data for compounds **1–10** were obtained over the temperature range of 303–423 K. Use of the δ-scale for chemical-shifts necessarily lead to negative values for the temperature gradients defined by $\Delta\delta/\Delta T$, ref. 2. [b] Range of 303–383 K.

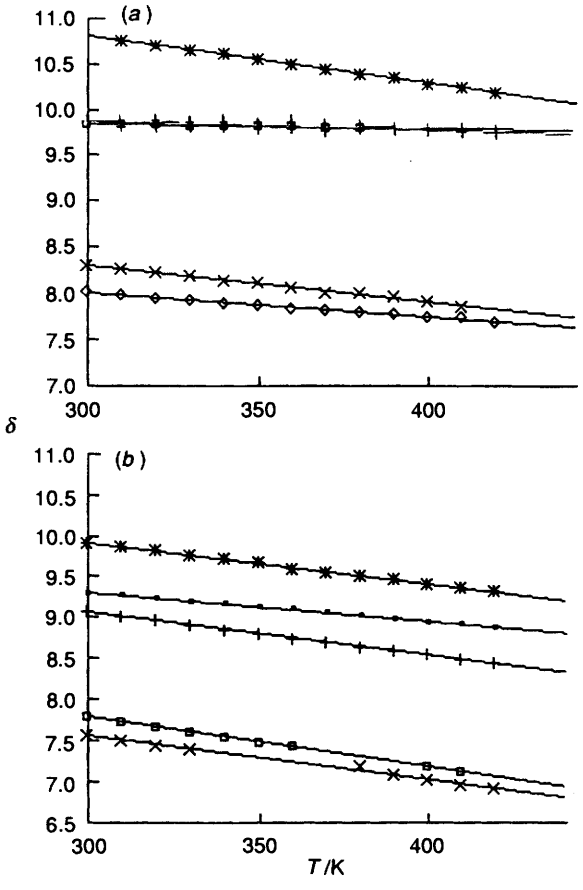


Fig. 2 Correlation of the ^{1}H NMR chemical shift of N–H with the temperature (K): (*a*) oximes **1–5**: **1**, —□—; **2**, —○—; **3**, —✱—; **4**, —×—; **5**, —◇—: (*b*) amides **6–10**: **6**, —■—; **7**, —+—; **8**, —✱—; **9**, —□—; **10**, —×—

quent upon solvent binding is more pronounced at higher temperatures.

In order to avoid a confusion in the assignment of the labile protons OH and NH (compounds **1** and **6**) ^{15}N/^{1}H heteronuclear correlation [2D (two-dimensional) HETCOR] experiments were carried out (Fig. 3).

The signals of the N–H protons of **1–3** and **6–8** were observed at 9.12–10.82 ppm; and the resonances of the labile phenolic protons of **1** and **6** at 10.43 and 9.62 ppm (Table 2); the phenolic and hydroxy protons exchange quickly with D_2O whereas the amidic protons exchange slowly.

All these experiments previously discussed informed us about

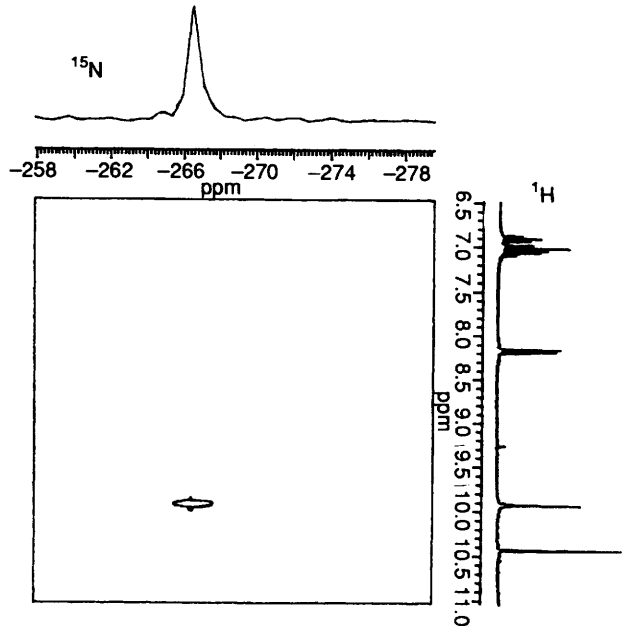


Fig. 3 ^{15}N/^{1}H Heteronuclear correlation (HETCOR) spectrum of compound **1**

the nature of the hydrogen bonding. A strong bonding for the N–H was found in compounds **1** and **2** (**1**; $\Delta\delta/\Delta T = -0.5 \times 10^{-3}$ and **2** -1.3×10^{-3}), and the big difference with compound **3** ($\Delta\delta/\Delta T = -5.2 \times 10^{-3}$) shows that not only the carbonyl is involved in the coordination but also the phenolic oxygen atom. A less strong but still important coordination was found for the N–H proton of the amino-alcohol derivatives **4** and **5** (**4**; $\Delta\delta/\Delta T = -3.3 \times 10^{-3}$ and **5** -2.5×10^{-3}). The *cis*-relationship between the substituents of the *erythro* compound **4** causes a destabilization of the hydrogen coordination by steric hindrance, a better arrangement is adopted in the *threo* molecule **5**.

For the monoamides, it was found that with the exception of compound **6** they do not form, as expected, significant intramolecular bonding. The moderately intramolecular hydrogen bonding found in **6** is attributed to a coordination between the phenolic oxygen to the amidic proton. The finding that compounds **1** and **6** form stronger hydrogen bonding than the *O*-methylated analogues **2** and **7** is explained using molecular mechanic calculations[4] data that show that the methyl group inhibits the oxygen coordination by steric hindrance.

Another important argument in favour of the *trans* conformation of the glyoxal group that discriminates the enol tautomers is the ^{15}N NMR data. The chemical shift for compounds **1**, **3–5** have normal values for an amide function ($\delta = -254$ to -266 ppm; Table 3). The coupling constants ^1J(NH) between 90 and 92 Hz show the residence of the proton at the nitrogen atom and precludes the existence of enolic tautomers. They also indicate a trigonal planar geometry for these nitrogen atoms.[7,8]

The ^{1}H NMR chemical shifts for all compounds are collected in Table 2. The proton spectra of compounds **1–3** and **6–8**, show a complex pattern for the aromatic protons because they have similar chemical shift values, with the exception of low field H-3 deshielded by the carbonyl group. A similar deshielding effect was reported in the literature for an *endo* conformer of an aromatic amide.[9] Examples of *exo* compounds are also found, see compounds **11** and **12**,[10] Fig. 4.

From the latter fact it can be deduced that the deshielded H-3 could be explained if the phenolic group was opposed to the carbonyl group in **1** and **2**, Fig. 5. In contrast amides **3**, **6–8** have averaged values (7.87, 7.69, 7.98, 7.62 ppm respectively) owing

Table 2 ^{1}H Chemical shifts δ and coupling constants (^3J, Hz)[a]

Compd.[b]	H-3	H-4	H-5	H-6	OH	NH	OMe	C(O)Me
1	8.13(d) (7.8)	6.89(d, d) (7.6, 7.8)	7.60(d, d) (7.6, 7.8)	7.00(d) (7.8)	10.43(s)	9.92(s)	—	
2	8.15(d) (7.9)	7.02(d, d) (7.0, 7.9)	7.21 (d, d) (7.0, 8.2)	7.15(d) (8.2)	—	9.96(s)	3.92	
3[c]	7.87(d) (8.8)	7.39(d, d) (8.8, 7.5)	7.16(t) (7.5)	7.87(d) (8.8)	—	10.82	—	
6	7.69(d) (7.9)	6.77(d, d) (7.9, 7.2)	6.95 (d, d) (7.9, 7.2)	6.89(d) (7.9)	9.62(s)	9.25(s)	—	2.12
7	7.98(d) (7.7)	6.89(d, d) (7.7, 6.8)	7.05 (d, d) (6.8, 8.2)	6.99(d) (8.2)		9.12(s)	3.81	2.10
8[c]	7.62(d) (7.7)	7.29(d, d) (7.7, 7.4)	7.02(t) (7.4)	7.62(d) (7.7)		9.93	—	2.06

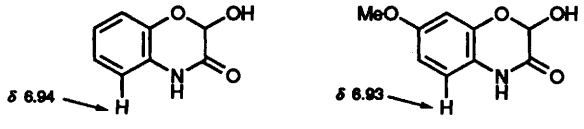
Compd.[b]	C-1-H	C-2-H	CH_3	$COCH_3$	C_6H_5	NH	OH
4	4.66(dd) (4.7, 4.5)	3.94(ddd) (4.6, 6.6, 8.9)	0.99(d) (6.6)		7.22–7.37(m)	8.30(d) (8.9)	5.55(d) (4.7)
5	4.61(d) (4.9)	3.94(ddc) (8.9, 6.8, 4.9)	1.05(d) (6.8)		7.25–7.38(m)	8.02(d) (8.9)	5.60(br)
9	4.65(dd) (4.4, 4.7)	3.97(ddd) (4.4, 6.7, 8.2)	0.92(d) (6.7)	1.80	7.17–7.35(m)	7.79(d) (8.2)	5.45(d) (4.7)
10	4.57(dd) (4.6, 4.4)	3.99(ddc) (8.2, 6.7, 4.6)	0.94(d) (6.8)	1.77	7.25–7.38(m)	7.56(d) (8.2)	5.43(d) (4.4)

[a] In [$^2H_6$]DMSO, relative to TMS as internal reference. [b] See Scheme 1 for atom numbers. [c] H-3 = H-1 and H-4 = H-6.

Table 3 ^{15}N Chemical shifts δ[a] and $^1J(^{15}N-H)$ coupling constants (Hz)

Compd.[b]	δ_N	^1J(N, H)
1	−266	92
3	−254	91
4	−258	91
5	−261	90
6	−253	91
7	−258	92
8	−246	91
9	−251	92
10	−254	92

[a] In [$^2H_6$]DMSO, relative to nitromethane as external reference. [b] Compound **2** was not soluble enough in order to record the spectrum.



11 **12**

Fig. 4 Model compounds for a *exo* conformation of aromatic amides and the ^{1}H NMR chemical shifts of H-3

to the rotation of the phenyl group. By analogy and from the data of the variable temperature experiments, described above, a similar structure may be proposed for the ethanolamine compounds **4** and **5**, Fig. 5.

The ^{13}C NMR chemical shifts of the amides **1–10** are listed in Table 4. The ^{13}C-NMR spectra of compounds **1–5** show half the total carbon atoms indicative of a symmetric molecule. The amidic carbon chemical shifts of **1–5** (156.9–159.0 ppm) that appear at higher field than the monoamides **6–10** (168.3–169.1 ppm) indicate that the nitrogen lone pair is delocalized over the π-system of the adjacent carbonyl bond.[8] The signals of C-1 atoms are observed in the range 147.2–149.5 ppm and those of the C-2 were at 124.5–139.4 ppm. C-2 and C-3 were assigned from the coupling with the amidic proton in a ^{13}C coupled spectrum. A 2D ^{13}C/^{1}H HETCOR experiment allowed us the unambiguous assignment of all carbon and proton atoms of **1**. Comparison of the chemical shift data of **1** and **6** with the other

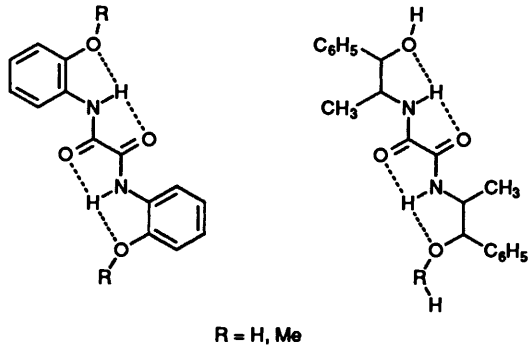


Fig. 5 Proposed preferred conformers for oximes **1–5**

aromatic compounds has been used to assign the NMR spectral data of **2**, **3**, **7** and **8**.

The C-2–CH_3 group of the norpseudoephedrine amides **5** and **10** appears at lower field than those groups of the norephedrine derivatives **4** and **9** owing to the fact that the methyl groups in the latter are under the shielding effect of the phenyl group.

From the ^{15}N NMR data of Table 3, it was found that the structure of the studied compounds has a systematic effect on the chemical shift. The phenolic substitution causes ^{15}N resonances of compounds **1** and **6** to appear at higher field (12 and 7 ppm) as compared to **3** and **8**. The ^{15}N signals of the oxamides (**1**, **3–5**) also appear at higher field than the corresponding amides. The *threo* compounds (**5** and **10**) present a similar trend compared with the *erythro* isomers.

In the IR spectra, the ν N–H compounds **1–10** is found between 3248–3403 cm^{-1} and the ν C=O between 1648–1680 cm^{-1} (Table 5). The mass spectra of aromatic compounds **1–3** shows as an important fragmentation the symmetric rupture through the glyoxal bond.

Conclusion

These above results clearly indicate the *trans* conformation of the oxamide group and the presence of an intramolecular hydrogen bonding that involves the infrequently reported

Table 4 ^{13}C Chemical shifts and ^{1}J(C, H) coupling constants[a]

Compd.[b]	C-1	C-2	C-3	C-4	C-5	C-6	C-7	OMe	C(O)Me
1	147.2	124.5	119.8	119.3	125.4	115.1	156.9	—	—
			(163.5)	(162.3)	(161.4)	(158.7)	—	—	—
2	149.2	125.4	119.9	120.6	125.7	111.3	157.1	55.8	—
			(165.2)	(163.1)	(161.9)	(159.7)	—	—	—
3	120.4	137.6	120.4	128.7	124.6	128.7	158.6	—	—
	(167.9)		(167.9)	(162.4)	(160.7)	(162.4)	—	—	—
6	147.9	126.4	122.4	119.0	124.7	116.0	169.1		23.5
			(157.9)	(161.7)	(160.2)	(159.4)	—	—	—
7	149.5	127.5	121.9	120.1	124.1	111.0	168.4	55.5	23.8
			(155.3)	(161.9)	(160.9)	(159.8)	—	—	—
8	119.0	139.4	119.0	128.6	122.9	128.6	168.3	—	24.0
	(159.7)		(159.7)	(158.6)	(163.0)	(158.6)	—	—	—
	C-1	C-2	CH_3	C=O	C_i	C_o	C_m	C_p	$COCH_3$
4	73.6	50.8	14.3	158.7	142.7	126.3	127.7	126.8	
5	73.9	51.0	17.4	159.0	143.0	126.3	127.9	127.1	
9	74.2	50.4	13.8	168.6	143.5	126.0	127.7	126.5	22.7
10	74.3	50.0	16.6	168.8	143.0	126.7	127.5	126.7	22.6

[a] In [$^2H_6$]DMSO, relative to TMS as internal reference. [b] See Scheme 1 for atom numbers.

Table 5 Solid state infrared frequencies (cm^{-1}, KBr) for amides **1–10**

Amide	νN–H	νC=O
1	3353	1658
2	3357	1680
3	3302	1667
4	3305	1655
5	3308	1650
6	3403	1658
7	3248	1658
8	3293	1662
9	3302	1648
10	3378	1664

coordination of two oxygen atoms to the same hydrogen atom. ^{15}N and variable temperature NMR are invaluable tools in establishing the structure and conformation of these molecules.

Experimental

Melting points were measured on a Gallenkamp apparatus and are uncorrected. The infrared spectra were taken in KBr discs using a Nicolet MX-1-FT infrared spectrometer. All the NMR spectra were obtained on a JEOL GXS-270 spectrometer in [$^2H_6$]DMSO solution. ^1H and ^{13}C NMR spectra were measured with TMS as internal reference. ^{15}N NMR spectra were obtained with neat nitromethane as a standard set to 0 ppm. All signals are upfield from nitromethane and hence chemical shifts are negative. ^{15}N spectra were recorded at 27.25 MHz using a multinuclear 5 mm probe and approximately 0.3 mmol of each compound was dissolved in 0.5 cm^3 of [$^2H_6$]DMSO (99% deuteriated, Aldrich, used directly without any further purification). The refocused INEPT pulse sequence was used to detect the ^{15}N signals. The values of t_D were set to 2.7 ms in cases where the average $^1J(^{15}N–^1H)$ value was 93 Hz [$t_D = \frac{1}{4}$, $^1J(^{15}N–^1H)$].[11] A spectral width of 16,400 Hz with a digital resolution of 0.5 Hz was used; the pulse delay was 5 s with an acquisition time of 0.999 s. The ^{15}N NMR spectrum of compound **2** has not been recorded due to its low solubility.

The $^{15}N/^1H$ HETCOR spectra were recorded using the following parameters: spectral width 1250 Hz in F_1 and 4000 Hz in F_2; acquisition time, 0.064 s; pulse intervals 1 and 2 set at 2.7 ms and 1.35 ms respectively [$\frac{1}{2}{}^1J(^{15}N–^1H)$ and $\frac{1}{4}J$]; relaxation delay 2 s; number of transients 32; number of increments 256. The Fourier transformations were carried out, using a trapezoidal function for F_1 and sine-bell function for F_2, in the absolute value mode with zero-filled in both dimensions.

The $^{13}C/^1H$ HETCOR spectra were measured as for $^{15}N/^1H$ but using a coupling constant of $^1J(^{13}C–^1H) = 160$ Hz.

For the INEPT, $^{13}C/^1H$ and $^{15}N/^1H$ HETCOR spectra the 90°-pulse for ^1H, ^{13}C and ^{15}N respectively was calibrated prior to acquisition. Variable temperature experiments were performed with a temperature controller to keep the temperature constant within 0.3 °C. A microprogram was used to change temperature automatically in fixed increments, with a delay of 5 min for the temperature stabilization. Each spectrum was obtained with 32 scans.

N,N′-*Bis*[(2-*hydroxy*)*phenyl*]*oxamide* (**1**).—*o*-Aminophenol (10 g, 91.74 mmol) in THF (50 cm^3) was treated dropwise under vigorous stirring with oxalyl chloride (5.82 g, 45.87 mmol, 0.5 eq.) at 25 °C. After stirring for an additional 1 h at 25 °C, the solid was removed and washed with 95% ethanol. Recrystallization from ethanol gave **1** (68%) as yellow needles; IR ν_{max}(KBr)/cm^{-1} 3353, 1658, 1613, 1595, 1537, 1459, 1342, 1288, 1230, 1192, 1096, 840, 746, 710, 574, 514 and 470; MS (EI) *m*/*z* M^+, 254 (18), 163 (5), 136 (25), 109 (100), 80 (33) (Found: C, 61.9; H, 4.45; N, 10.25. Calc. for $C_{14}H_{12}N_2O_4$: C, 61.76; H, 4.41; N, 10.29%); m.p. 282–284 °C.

N,N′-*Bis*[(2-*methoxy*)*phenyl*]*oxamide* (**2**).—*o*-Anisidine (5 g, 37.59 mmol) in THF (25 cm^3) was treated dropwise under vigorous stirring with oxalyl chloride (2.35 g, 18.79 mmol, 0.5 eq.) at 25 °C. After stirring for an additional 1 h at 25 °C, the solid was removed and washed with 95% ethanol to give **2** (69.0%) as white needles. IR ν_{max}(KBr)/cm^{-1} 3360, 1683, 1602, 1526, 1482, 1461, 1430, 1297, 1105, 1023, 753, 718, 517 and 490; MS (EI) *m*/*z* M^+, 300 (100), 269 (18), 150 (14), 135 (18), 123 (62), 108 (40), 80 (18) (Found: C, 63.8; H, 5.4; N, 9.3. Calc. for $C_{16}H_{16}N_2O_4$: C, 64.0; H, 5.36; N, 9.33%); m.p. 252–254 °C.

N,N′-*Bis*[*phenyl*]*oxamide* (**3**).—Aniline (5 g, 53.76 mmol) in THF (25 cm^3) was treated dropwise under vigorous stirring with oxalyl chloride (3.41 g, 26.88 mmol, 0.5 eq.) at 25 °C. After stirring for an additional 1 h at 25 °C, the reaction product **5** was obtained from the precipitate that was removed and washed with 95% ethanol. On drying it appears as white needles (64.0%). IR ν_{max}(KBr)/cm^{-1} 3306, 1668, 1595, 1523, 1488,

1317, 1232, 1160, 1075, 1026, 891, 866, 755, 731, 682, 529 and 482; MS (EI) *m/z* M^+, 240 (100), 120 (31), 93 (98), 77 (70) (Found, C, 70.15; H, 5.15; N, 11.5; Calc. for $C_{14}H_{12}N_2O_2$: C, 70.0; H, 5.02; N, 11.66%; m.p. 250–252 °C.

N,N'-*Bis*[(1R,2S)-(−)-*norephedrine*]*oxamide* (**4**).—Oxalyl chloride (16.85 mmol, 1.5 cm^3) in 25 cm^3 of CH_2Cl_2 was added dropwise under vigorous stirring to a solution containing 33.06 mmol (5 g) of norephedrine. After stirring for 2 h more at room temperature, 75 cm^3 of CH_2Cl_2 and 33.06 mmol (5 g) of norephedrine and 32.28 mmol (4.5 cm^3) triethylamine in CH_2Cl_2 were added over 20 min. After stirring for an additional 2 h at room temperature, 75 cm^3 of CH_2Cl_2 and 75 cm^3 of water were added and stirred 30 min. The organic phase was separated and dried. The solvent was removed under vacuum to give a white solid: 5.10 g (86.2%). IR ν_{max}(KBr)/ cm^{-1} 3380, 3305, 1655, 1510, 1451, 1201, 1000, 740 and 701. MS (EI) *m/z* $M^+ + H$, 357 (1), 250 (19), 118 (40), 115 (23), 79 (23), 77 (21) and 44 (100) (Found: C, 67.0; H, 60.75; N, 7.6. Calc. for $C_{20}H_{24}N_2O_4$: C, 67.40; H, 6.78; N, 7.85%); m.p. 179 °C.

N,N'-*Bis*[(1R,2R)-(−)-*norpseudoephedrine*]*oxamide* (**5**).—A procedure identical to that used to prepare **4** was followed, using norpseudoephedrine in place of norephedrine, to afford 4.66 g of **5** (79.30%). IR ν_{max}(KBr)/cm^{-1} 3398, 3308, 1650, 1514, 1453, 1198, 1044, 763 and 700. MS (EI) *m/z* 250 (37), 118 (51), 115 (30), 79 (37), 77 (32), 44 (100) (Found: C, 63.8; H, 6.2; N, 7.2. Calc. for $C_{20}H_{24}N_2O_4H_2O$, C, 64.15; H, 6.99; N, 7.47%); m.p. 166 °C.

N-[(2-*Hydroxy*)*phenyl*]*methylamide* (**6**).—Compound **6** was prepared as reported.[12] IR ν_{max}(KBr)/cm^{-1} 3403, 1658, 1587, 1539, 1446, 1397, 1287, 1103, 1037, 891, 767, 662, 572 and 456; MS (EI) *m/z* M^+, 151 (24), 109 (100), 91 (2), 80 (47) (Found: C, 63.6; H, 6.0; N, 9.3. Calc. for $C_8H_9N_1O_2$: C, 63.57; H, 5.99; N, 9.27%); m.p. 204–206 °C.

N-[(2-*Methoxy*)*phenyl*]*methylamide* (**7**).—Compound **7** was prepared as reported for **6**.[12] Spectroscopic data: IR ν_{max}-(KBr)/cm^{-1} 3248, 1652, 1540, 1496, 1459, 1437, 1371, 1322, 1252, 1118, 1030, 751, 662 and 527. MS (EI) *m/z* M^+, 165 (100), 123 (74), 108 (92), 92 (6), 80 (38), 65 (19), 43 (50); m.p. 84–85 °C.

N-[*Phenyl*]*methylamide* (**8**).—Compound **8** was prepared as reported for **6**.[12] Spectroscopic data: IR ν_{max}(KBr)/cm^{-1} 3293, 1662, 1598, 1557, 1500, 1431, 1368, 1325, 1262, 1040, 1012, 962, 906, 750, 681 and 537. MS (EI) *m/z* M^+, 135 (31), 93 (100), 77 (4), 52 (5), 43 (56); m.p. 111.5–112.5 °C.

N-[(1R,2S)-(−)-*Norephedrine*]*methylamide* (**9**).—Compound **9** was prepared as reported.[13] IR ν_{max}(KBr)/cm^{-1} 3401, 3302, 1648, 1563, 1443, 1368, 1162, 1025, 750 and 701. MS (EI) *m/z* 107 (5), 86 (8), 77 (40), 44 (59), 43 (100); m.p. 106 °C.

N-[(1R,2R)-(−)-*Norpseudoephedrine*]*methylamide* (**10**).—Compound **10** was prepared as reported.[13] IR ν_{max}(KBr)/cm^{-1} 3378, 3296, 1664, 1550, 1433, 1366, 1050, 733 and 700. MS (EI) *m/z* M^+, 193 (2), 107 (10), 87 (100), 77 (31), 44 (77); m.p. 75 °C.

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