Synthesis and characterization of new 2-(alkylamino)acetamides

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Abstract

Seven new 2-(alkylamino)acetamides have been synthesized and characterized by ^{1}H, ^{13}C NMR, NOESY experiments, infrared and mass spectrometry. The structure of 2-(diphenylmethylamino)acetamide **3b** was further established by a single crystal x-ray diffraction study. The NMR study of the transformation of several 2-(alkylamino)acetamides to their corresponding morpholin-2-ones shows that these species are thermodynamically favored through preferred conformations as determined by theoretical calculations of **3h**.

Keywords: Acetamides, amides, synthesis, spectroscopy, x-ray

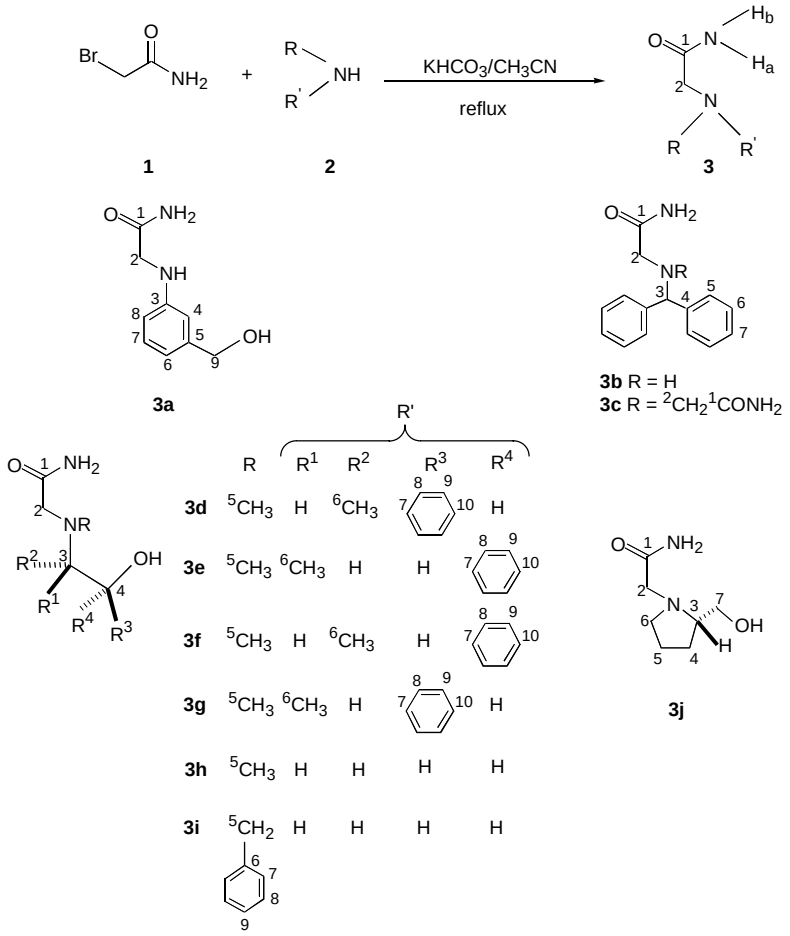
Introduction

A number of 2-(alkylamino)acetamides have been shown to possess antiarrhythmic,[1] anticonvulsive,[2] anti-inflammatory [3] and hypotensive[4] activity. They have also been used as precursors in the synthesis of vicinal diamides, morpholin-2-ones,[5] and as ligands in the synthesis of organometallic compounds with potential anti-tumor activity.[6]

2-(Alkylamino)acetamides have been prepared by reaction of 2-chloro-*N*,*N*-dimethylacetamide or 2-(alkylamino)methylacetate with amines and β-aminoalcohols, in the presence of sodium bicarbonate or triethylamine.[5,7-8] It is noteworthy that the reaction of 2-chloro-*N*,*N*-dimethylacetamide with ephedrines, in the presence of sodium bicarbonate, under reflux of benzene for 20 hours provides both 2-(alkylamino)acetamides and morpholin-2-ones, while the use of triethylamine as base yields exclusively the corresponding 2-(alkylamino)-acetamides. In contrast, when this reaction is carried out under reflux of xylene, the morpholin-2-one is formed exclusively.[5] Our current interest in 2-(alkylamino)acetamides prompted us to develop better reaction condition to synthesize these compounds in good yields. Thus, we describe herein the synthesis and characterization of seven new 2-(alkylamino)acetamides **3a-j** (Scheme 1). The structure of compound **3b** was further established by a single-crystal X-ray diffraction study.

Results and Discussion

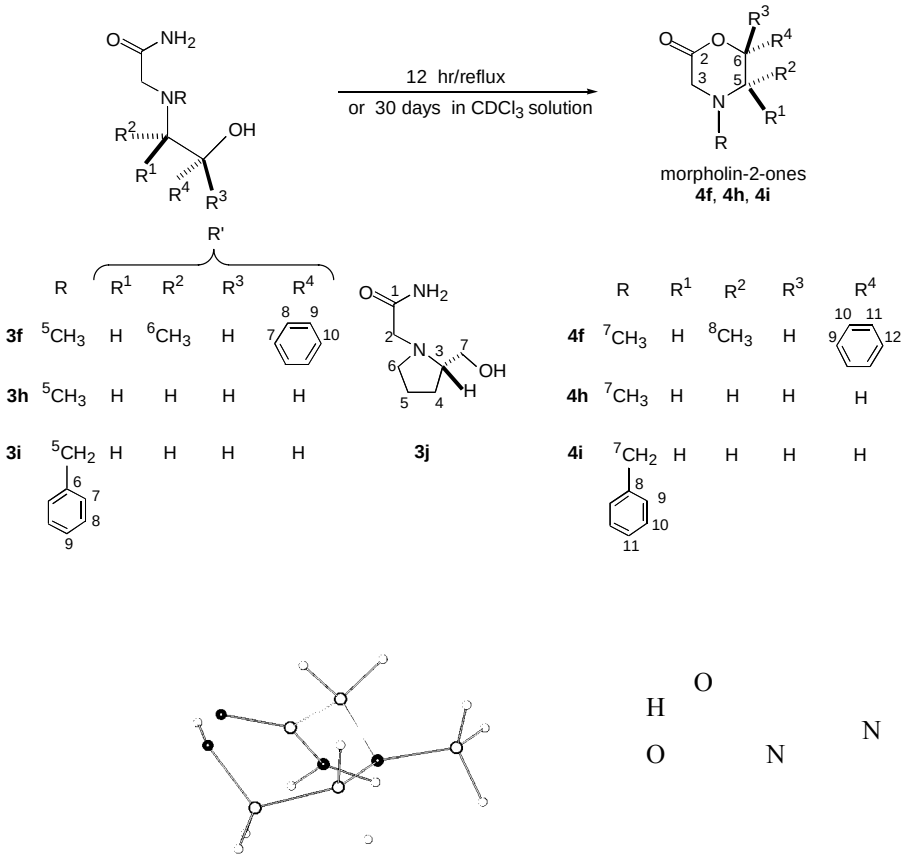
2-(Alkylamino)acetamides **3a-j** were prepared in yields between 73-98% by the reaction of 2-bromoacetamide **1** with 3-aminobenzyl alcohol **2a**, aminodiphenylmethane **2b**, (1*S*,2*S*)-(+)-pseudoephedrine **2d**, (1*R*,2*R*)-(-)-pseudoephedrine **2e**, (1*R*,2*S*)-(-)ephedrine **2f** and (1*S*,2*R*)-(+)ephedrine **2g**, 2-(methylamino)ethanol **2h**, N-benzylethanolamine **2i** and (*S*)-(+)-pyrrolidinemethanol **2j**, in the presence of $KHCO_3$ under reflux in acetonitrile for 6 hours. Compound **3c** was obtained by reaction of **1** and **2a** in a 2:1 molar ratio.



Scheme 1

As confirmed by ^{1}H NMR the reaction of bromoacetamide 1 and β-aminoalcohols 2f, 2h and 2j leads to 2-(aminoalkyl)acetamides 3f, 3h and 3j which are transformed into the corresponding morpholin-2-ones[5,12] in aproximatly 30%, after 12 hours under reflux except for 3j. Moreover, 2-(aminoalkyl)acetamides 3f, 3h, 3i and 3j were allowed to stand for one month in chloroform solution which resulted in 40% conversion to the morpholine-2-ones, except for 3j (Scheme 2). These data suggests that the transformation of 3f, 3h, and 3i into the corresponding morpholin-2-

ones is thermodynamically favored and proceeds through a prefered conformation which was calculated for 3h using a theoretical (AMI, *Ab initio* STO-3G and 3-21G) approach.[13] Figure 1 depicts the particular conformation where there is an intramolecular interaction between the OH group and the carbonyl group, that increases nucleophilicity of the carbonyl group and favors formation of the corresponding morpholin-2-one.



Scheme 2

Figure 1

NMR spectroscopy

The ^{1}H NMR spectra of compounds **3a-j** exhibit an AB system for the amidic protons (NH_2) due to partial C=N double bond character (Table 1). Unambiguous assignment of these protons was attained by NOESY experiments which revealed an interaction of the proton shifted to lower field with H-2, evidencing that it is *anti* to the carbonyl group, in agreement with analogous systems reported in the literature.[9] The spectra of compounds **3a-c**, **3h** and **3i** exhibit a single signal for the methylene protons at position 2, while compounds **3d-g** and **3j** give an AB system. Since the pyrrolidyl and H-7 protons in compound **3j** show a complex pattern, unambiguous identification of H-7 was established using selective decoupling experiments. Thus irradiation of H-3 simplified the ABX system for H-7 to an AB system.

Table 1. ^{1}H NMR data of **3a-3j**: δ_H and δ_N [ppm] and *coupling constants J* [Hz]

	Solvent	H-2	NH_a	NH_b	R	R'
3a	DMSO-d_6	3.57	7.	7.11	3.68	H-4 6.53
			2			H-6 6.54 *7.8*[b]
			3			H-7 7.03 *7.8*[b]
						H-8 6.42 *7.8*[b]
						H-9 4.38
3b	$CDCl_3$	3.24	6.88	6.07	2.16	H-3 4.83
						H-5,6 7.30-7.36
						H-7 7.23 *7.0*[b]
3c	DMSO-d_6	3.13	7.64	7.06	H-2 3.13	H-3 5.23
					NH_a 7.64	H-5 7.47 *7.3*[b]
					NH_b 7.06	H-6 7.30 *7.3*[b]
						H-7 7.20 *7.3*[b]
3d	DMSO-d_6	H_A 3.07 *16.1*[a]	7.68	7.15	H-5 2.23	H-3 2.64 *8.8*[b], *6.6*[b]
		H_B 2.88 *16.1*[a]				H-4 4.32 *8.8*[b]
						H-6 0.59 *6.6*[b]
						H-8,9,10 7.20-7.23
3e	DMSO-d_6	H_A 3.05 *16.1*[a]	7.64	7.16	H-5 2.24	H-3 2.64 *8.8*[b], *6.6*[b]
		H_B 2.85 *16.1*[a]				H-4 4.34 *8.8*[b]
						H-6 0.60 *6.6*[b]
						H-8,9,10 7.21-7.25
3f	$CDCl_3$	H_A 2.96 *16.8*[a]	6.31	5.53	H-5 2.21	H-3 2.78 *7.3*[b], *6.6*[b]
		H_B 2.93 *16.8*[a]				H-4 4.56 *7.3*[b]
						H-6 1.01 *6.6*[b]
						H-8,9,10 7.25-7.35
3g	$CDCl_3$	H_A 2.96 *16.8*[a]	6.32	5.54	H-5 2.20	H-3 2.76 *7.3*[b], *6.6*[b]
		H_B 2.92 *16.8*[a]				H-4 4.55 *7.3*[b]
						H-6 1.01 *6.6*[b]
						H-8,9,10 7.25-7.35
3h	$CDCl_3$	3.06	7.66	6.80	H-5 2.33	H-3 2.59 *5.1*[b]
						H-4 3.65 *5.1*[b]
3i	$CDCl_3$	3.11	7.30	6.40	H-5 3.67	H-3 2.68 *5.1*[b]
					H-7,8,9 7.24	H-4 3.63 *5.1*[b]
3j	$CDCl_3$	H_A 3.45 *16.7*[a]	7.43	6.60	H-3 2.73 *3.7*[b],*4.7*[b]	H-5 1.63-1.82
		H_B 3.20 *16.7*[a]			$H\text{-}4_A$ 1.84-1.97	$H\text{-}6_A$ 3.16 *9.1*[a]
					$H\text{-}4_B$ 1.63-1.83	$H\text{-}6_B$ 2.40 *9.1*[a]
						$H\text{-}7_A$ 3.60 *11.3*[a], *3.7*[b]
						$H\text{-}7_B$ 3.47 *11.3*[a], *3.7*[b]

[a] ^2J. [b] ^3J.

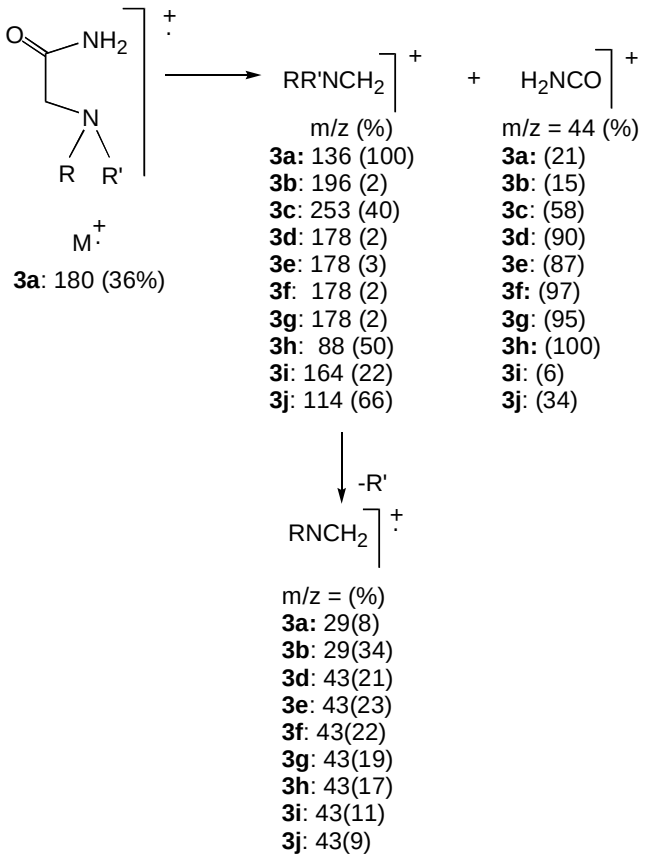
The ^{13}C NMR chemical shift for C-2 in compounds **3a-j** is in the range between 46.76 to 59.92 ppm, which is shifted to higher frequency compared with bromoacetamide (δ = 29.05 ppm). Assignment of the signals for C-2, C-4 and C-5 in **3h**, C-2, C-3, C-8 and C-9 in **3i** and C-2, C-3, C-8 and C-9 in **3j**, were obtained by ^{13}C-^{1}H HETCOR techniques. Unambiguous assignment of C-3 and C-5 in **3a** was attained from a ^{13}C-^{1}H COLOC spectra. Table 2 summarizes the ^{13}C NMR data for compounds **3a-j**.

Table 2. ^{13}C NMR data of **3a-3j**: δ_C [ppm]

	Solvent	C-1	C-2	C-3	C-4	C-5	C-6	C-7	C-8	C-9	C-10
3a	DMSO-d_6	172.52	46.76	148.13	110.15	143.25	114.87	128.58	110.88	63.23	
3b	$CDCl_3$	174.47	50.45	66.74	142.83	127.26	128.66	127.40			
3c	DMSO-d_6	172.81	54.57	70.66	142.16	128.22	128.37	127.07			
3d	DMSO-d_6	173.05	57.76	64.69	74.53	37.22	8.97	143.38	127.18	127.93	127.18
3e	DMSO-d_6	173.05	57.76	64.69	74.53	37.22	8.97	143.38	127.18	127.93	127.18
3f	$CDCl_3$	174.95	58.27	64.96	75.91	38.74	9.85	143.74	126.42	128.34	127.60
3g	$CDCl_3$	174.95	58.27	64.96	75.91	38.74	9.85	143.74	126.42	128.34	127.60
3h	$CDCl_3$	175.20	59.92	59.12	61.80	42.90					
3i	$CDCl_3$	175.22	57.88	57.29	59.58	59.36	137.96	128.52	128.89	127.46	
3j	$CDCl_3$	175.70	58.65	65.71	27.17	23.68	55.93	63.72			

Mass spectrometry

In general the 70 eV EI mass spectra do not show the molecular ion, except for **3a** that gives the molecular ion at m/z = 180 (36%). All spectra show the fragment ions $[RR'NCH_2]^+$ and $[H_2NCO]^+$ due to the C_1-C_2 bond rupture and the fragment ion $[R\text{-}N{=}]^{+\cdot}$, except for **3c** .The fragment ions at m/z = 136 for **3a**, $[CH(C_6H_5)_2]^{+\cdot}$ at m/z = 167 for **3b** and **3c**, $[H_2NCOCH_2N(CH_3)CHCH_3]^{+\cdot}$ at m/z = 115 for **3d-3g**, m/z = 44 for **3h**, $[C_7H_7]^{+\cdot}$ at m/z = 91 for **3i** and $[M\text{-}CH_2OH]^{+\cdot}$ at m/z = 127 for **3j**, correspond to the base peaks. The proposed fragmentation is shown in Scheme 3.



Scheme 3

Infrared spectroscopy

The IR spectra of compounds **3a-j** show the absorption band characteristic of the amide I and II in the range between 1676-1638 and 1672-1588 cm^{-1}, respectively, as well as absorption bands for the NH and OH groups in the range between 3432-3178 cm^{-1}.

X-Ray diffraction

Suitable crystals of **3b** for X-ray analysis were obtained from chloroform/hexane, the molecular structure and crystallographic numbering is shown in figure 2. In general the bond distances are within the values characteristic of amides.[10] Selected bond lengths are: N_1-H_{1a} 0.925, N_1-H_{1b} 0.864, C_1-O_1 1.227 (2), C_1-N_1 1.318 (2), C_3-N_2 1.478 (2) and C_2-N_2 1.464 (2) Å. Torsion angles for the O_1-C_1-N_1-H_{1a} and O_1-C_1-N_1-H_{1b} fragments are: 172.51° and 1.17° respectively, this indicates that this part of the molecule is flat due to the resonance effect present between the O1-C1-N1 atoms. The molecular structure shows the following intermolecular contacts: $O_1 \cdots H_{2a}$ 2.540, $O_1 \cdots H_5$ 2.514, $O_1 \cdots H_{1a}$ 1.936 and $N_2 \cdots H_{1b}$ 2.306, which are significantly shorter than the sum of the van der Waals radii for oxygen and hydrogen atoms (2.70Å) as well as nitrogen and hydrogen (2.75 Å).[11] In addition, the following intramolecular contacts are observed between $N_2 \cdots H_3$ 2.030, $N_2 \cdots H_{2b}$ 1.967, $N_2 \cdots H_{2a}$ 2.498, $N_2 \cdots H_5$ 2.500, $O_1 \cdots H_2$ 2.570 and $O_1 \cdots H_{1b}$ 2.413 Å.

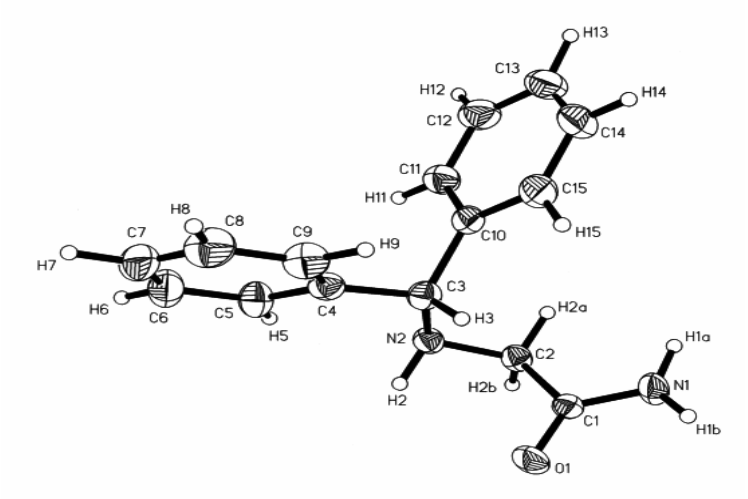


Figure 2

Conclusions

Optimization of the reaction conditions allowed us to obtain the new 2-(alkylamino)acetamides in good yields. These derivatives were characterized by spectroscopic methods and the structure of compound **3b** was confirmed by X-ray analysis. The transformation of 2-(alkylamino)acetamides **3f**, **3h** and **3i** into to the corresponding morpholine-2-ones was observed by ^{1}H NMR after 12 hours of reaction or upon standing in chloroform solution for one month. The transformation is thermodynamically favored through a preferred conformation, as determined by theoretical calculation of **3h**.

Experimental Section

General Procedures. NMR spectra were recorded on JEOL GXS-270, JEOL ECLIPSE-400 and Bruker Avance 300-DPX spectrometers in $CDCl_3$ and DMSO-d_6. Mass spectra were obtained with a Hewlett-Packard 5994-A instrument, and Infrared spectra were recorded as KBr pellets or in $CHCl_3$ solution on a Perkin-Elmer 16F PC FT-IR spectrometer. Melting points were taken in open capillary tubes on a Gallemkamp MFB-595 apparatus and are uncorrected. The single-crystal X-ray study was performed on an ENRAF NONIUS CAD4 diffractometer. Reagents were purchased from Aldrich Co. Compound **3b**, $C_{15}H_{16}N_2O$ (MW = 240.30), crystallized in the space group $P2_1/c$, monoclinic, from chloroform/hexane as colorless rectangular prisms, size: 0.50 x 0.44 x 0.38 mm^3 with a = 6.225(10), b = 21.987(4), c = 9.552(2) Å, V = 1307.3 (4) Å^3. Lattice constants were determined from least squares refinement on diffractometer angles for 24 automatically centered reflections; ρ 1.221 Mg/m^3, Z = 4, μ = 0.078 mm^{-1}, F (000) = 512. Data collection: monitoring of check reflexion showed no signs of decay. A total of 2447 reflections were measured (2>θ>26º),

2304 were independent and of these 1737 were considered observed [Fo>4.0σ(Fo)]. Absorption correction was not necessary. Solution and refinement: direct methods, all non-hydrogen atoms were refined anisotropically, all hydrogen were located by difference Fourier maps and refined with an overall isotropic thermal parameter, R = 0.0365, Rw = 0.0954, w = 1/ σ^2, GOOF = 1.057, parameter to data ratio 1:7.7, largest residual electron density peak/hole in the final difference map: 0.149/-0.153 e $Å^{-3}$. Atomic scattering factors were taken from the International Tables for X-ray Crystallography.[14] Data reduction was performed by Jana 98.[15] All calculations were carried out on a VAX 4000 computer using the SHELX 93 (sheldrick G. M.) program package.[16]

2-(3'-Hydroxymethylphenylamino)acetamide (3a). To a solution of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile was added 0.89 g (7.25 mmol) of 3-aminobenzyl alcohol **2a** and 1.09 g (10.88 mmol) of potassium bicarbonate at room temperature. The resulting suspension was refluxed and stirred during 6 hours. After being cooled to room temperature the suspension was filtered and the filtrate evaporated under vacuum to obtain a yellow solid, which was recrystallized from methanol/acetone to yield 0.95 g (73%) of **3a** as a white solid, mp 104-106˚C. IR: 3384, 3354, 3300, 3030, 2918, 2850, 1642, 1038 cm^{-1} (KBr). MS: m/z (%), 180 (M^+, 36), 136 (100), 44(21), 29 (8). Anal. Calcd. for $C_9H_{12}N_2O_2$ (180.17): C, 59.99; H, 6.70; N, 15.54. Found: C, 59.70; H, 6.60; N, 15.57.

2-(Diphenylmethylamino)acetamide (3b). The reaction of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile, 1.37 g (7.25 mmol) of aminodiphenylmethane **2b** and 1.09 g (10.88 mmol) of potassium bicarbonate gave a yellow solid, which was recrystallized from chloroform/hexane to yield 1.39 g (80%) of **3b** as a white solid, mp 102-104°C. IR: 3432, 3340, 3178, 3024, 2930, 2856, 1672 cm^{-1} (KBr). MS: m/z (%), 196 (2), 167 (100), 44 (15), 29 (34). Anal. Calcd. for $C_{15}H_{16}N_2O$ (240.29): C, 74.97; H, 6.71; N, 11.65. Found: C, 74.66; H, 6.65; N, 11.54.

2-[Bis(diphenylmethy)amino]acetamide (3c). The reaction of 2.00 g (14.5 mmol) of 2-bromoacetamide in 120 mL of acetonitrile, 1.37 g (7.25 mmol) of aminodiphenylmethane **2b** and 2.18 g (21.75 mmol) of potassium bicarbonate gave a white solid, which was recrystallized from chloroform to yield 1.83 g (85%) of **3c** as a white solid, mp 172-174°C. IR: 3310, 3172, 3024, 2934, 2864, 1676, 1650 cm^{-1} (KBr). MS: m/z (%), 253 (40), 167 (100), 44(58).
Anal. Calcd. for $C_{17}H_{19}N_3O_2$ (297.35): C, 68.66; H, 6.44; N, 14.13. Found: C, 68.34; H, 6.57; N, 14.09.

(1'*S*,2'*S*)-2-[(2'-Phenyl-2'-hydroxy-1'-methylethyl)methylamino]acetamide (3d). The reaction of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile, 1.20 g (7.25 mmol) of (1*S*,2*S*)-(+)-pseudoephedrine **2d** and 1.09 g (10.88 mmol) of potassium bicarbonate gave a yellow solid, which was washed with chloroform and precipitated from hexane to yield 1.43 g (89%) of **3d** as a white solid, mp 142-145°C. IR: 3414, 3304, 3084, 2932, 2858, 1638, 1028 cm^{-1} (KBr). MS: m/z (%), 178 (2), 115 (100), 44 (90), 43 (21). Anal. Calcd. for $C_{12}H_{18}N_2O_2$ (222.28): C, 64.84; H, 8.16; N, 12.60. Found: C, 64.52; H, 8.16; N, 12.24.

(1'*R*,2'*R*)-2-[(2'-Phenyl-2'-hydroxy-1'-methylethyl)methylamino]acetamide (3e). The reaction of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile, 1.20 g (7.25 mmol) of (1R,2R)-(-)-pseudoephedrine **2e** and 1.09 g (10.88 mmol) of potassium bicarbonate gave a yellow solid, which

was washed with chloroform and precipitated from hexane to yield 1.35 g (84%) of **3e** as a white solid, mp 142-145°C. IR: 3412, 3302, 3084, 2930, 2858, 1638, 1028 cm^{-1} (KBr). MS: m/z (%),178 (3), 115 (100), 44 (87), 43 (23). Anal. Calcd. for $C_{12}H_{18}N_2O_2$ (222.28): C, 64.84; H, 8.16; N, 12.60. Found: C, 65.06; H, 8.36; N, 12.21.

(1'*R*,2'*S*)-2-[(2'-Phenyl-2'-hydroxy-1'-methylethyl)methylamino]acetamide (3f). The reaction of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile, 1.20 g (7.25 mmol) of (1R,2S)-(-)-ephedrine **2f** and 1.09 g (10.88 mmol) of potassium bicarbonate gave a yellow solid, which was washed with chloroform and precipitated from hexane to yield 1.33 g (83%) of **3f** as a white solid, mp 88-91°C. IR: 3394, 3316, 3198, 3032, 2968, 2924, 2864, 1678, 1048 cm^{-1} (KBr). MS: m/z (%), 178 (2), 115 (100), 44 (87), 43 (22). Anal. Calcd. for $C_{12}H_{18}N_2O_2$ (222.28): C, 64.84; H, 8.16; N, 12.60. Found: C, 64.54; H, 8.22; N, 12.41. ^{1}H NMR data of (5S,6R)-4,5-dimethyl-6-phenyl-1,4-oxazin-2-one **4f** obtained from the spectrum of a mix with **3f**, δ_H ($CDCl_3$) 0.72 (H-8, ^3J = 6.9 Hz), 2.33 (H-7), 3.04-3.15 (H-5), 3.43 (H-3_A, ^2J = 18 Hz), 3.38 (H-3_B, ^2J = 18 Hz), 5.59 (H-6, ^3J = 3.29), 7.21-7.25 H-10,11,12).

(1'*S*,2'*R*)-2-[(2'-Phenyl-2'-hydroxy-1'-methylethyl)methylamino]acetamide (3g). The reaction of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile, 1.46 g (7.25 mmol) of (1*S*,2*R*)-(+)-ephedrine **2g** and 2.18 g (21.75 mmol) of potassium bicarbonate gave a yellow solid, which was washed with chloroform and precipitated from hexane to yield 1.28 g (79%) of **3g** as a white solid, mp 88-91°C. IR: 3394, 3316, 3198, 3032, 2968, 2924, 2864, 1678, 1048 cm^{-1} (KBr). MS: m/z (%), 178 (2), 115 (100), 44 (95), 43 (19). Anal. Calcd. for $C_{12}H_{18}N_2O_2$ (222.28): C, 64.84; H, 8.16; N, 12.60. Found: C, 64.54 ; H, 8.22; N, 12.42.

Synthesis of 2-[(2'-Hydroxyethyl)methylamino]acetamide (3h). The reaction of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile, 0.55 g (7.25 mmol) of 2-(methylamino)ethanol **2h** and 1.09 g (10.88 mmol) of potassium bicarbonate gave a viscous liquid, which was added chloroform and hexane to yield 0.93 g (97%) of **3h** as a yellow semi-solid. IR: 3388, 3328, 2948, 2846, 1670, 1588, 1078 cm^{-1}. MS: m/z (%), 88 (50), 44 (100), 43 (17). Anal. Calcd. for $C_5H_{12}N_2O_2$ (132.16): C, 45.44; H, 9.15; N, 21.19. Found: C, 45.39; H, 9.44; N, 20.83. ^{1}H NMR data of 4-methyl-1,4-oxazin-2-one **4h** obtained from the spectrum of a mix with **3h**, δ_H ($CDCl_3$) 2.27(H-7), 2.59 (H-5, ^3J = 5.17 Hz), 3.19 (H-3), 4.36 (H-6, ^3J = 5.19).

2-[Benzyl(2'-hydroxyethyl)amino]acetamide (3i). The reaction of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile, 1.10 g (7.25 mmol) of 2-(benzylamino)ethanol **2i** and 1.09 g (10.88 mmol) of potassium bicarbonate gave a yellow solid, which was recrystallized from chloroform/acetone to yield 1.33 g (88%) of **3i** as white solid, mp 132-135 °C. IR: 3396, 3300, 3034 2934, 2862, 1638, 1082, cm^{-1} (KBr). MS: m/z (%), 164 (22), 91 (100), 44 (6), 43 (11). Anal. Calcd. for $C_{11}H_{16}N_2O_2$ (208.26): C, 63.44; H, 7.74; N, 13.45. Found: C, 63.52; H, 7.58; N, 13.15. ^{1}H NMR data of 4-benzyl-1,4-oxazin-2-one **4i** obtained from the spectrum of a mix with **3i**, δ_H ($CDCl_3$) 2.64(H-5, ^3J = 5.19 Hz), 3.25 (H-3), 3.56 (H-7), 4.31 (H-6, ^3J = 5.19), 7.1-7.6 (H-9,10,11).

(2'S)-2[2'-Hydroxymethyl-1'-pyrrolidinyl]acetamide (3j). The reaction of 1.00 g (7.25 mmol) of 2-bromoacetamide in 60 mL of acetonitrile, 0.73 g (7.25 mmol) of (S)-(+)-2-pyrrolidinemethanol **2j** and 1.09 g (10.88 mmol) of potassium bicarbonate gave a yellow solid, which was washed with chloroform and precipitated from hexane to yield 1.03 g (90%) of compound **3j** as white solid, mp

63-66 °C. IR: 3416, 3310, 2958, 2872, 1662, 1086, cm^{-1} (KBr). MS: m/z (%), 114 (66), 127 (100), 44 (34), 43 (9). Anal. Calcd. for $C_7H_{14}N_2O_2$ (158.20): C, 53.14; H, 8.91; N, 17.70. Found: C, 53.10; H, 8.55; N, 17.29.

Supplementary information. Crystallographic data for **3b** has been deposited at the Cambridge Crystallographic Data Center, UK, CCDC as supplementary material No. 213603.

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