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1-(*N*-Acylamino)alkyl Sulfones from *N*-Acyl-α-amino Acids or *N*-Alkylamides

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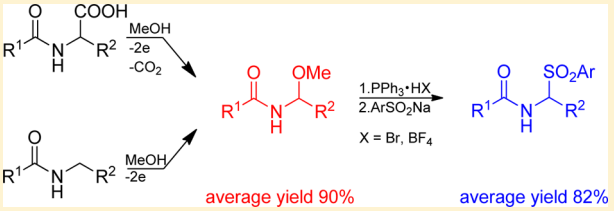
Supporting Information

ABSTRACT: A variety of *N*-(1-methoxyalkyl)amides or carbamates react readily with sodium aryl sulfinates in the presence of triphenylphosphonium tetrafluoroborate or bromide in $CHCl_3$ under mild conditions to give 1-(*N*-acylamino)alkyl sulfones in good yields. A combination of this reaction with the recently described electrochemical decarboxylative α-methoxylation of *N*-acyl-α-amino acids to give *N*-(1-methoxyalkyl)amides in the presence of 3-(1-piperidino)propyl-functionalized silica gel (SiO_2−Pip) enables an effective two-pot transformation of *N*-acyl-α-amino acids to 1-(*N*-acylamino)alkyl sulfones. Alternatively, *N*-(1-methoxyalkyl)amides can be obtained by electrochemical α-methoxylation of either *N*-alkylamides, lactams, or *N*-alkylcarbamates.



α-Amidoalkylation of carbon and heteroatom nucleophiles plays an important role in organic synthesis as a valuable extension of the Mannich reaction that is employed, inter alia, for the formation of a β-aminocarbonyl substructures and for the construction of new carbocyclic or heterocyclic rings by intramolecular α-amidoalkylation (e.g., Pictet−Spengler-type cyclization) in the syntheses of natural products and in pharmaceutical chemistry.[1−6] In most α-amidoalkylation reactions, highly reactive, short-lived *N*-acylimines or *N*-acyliminium cations are considered to be the active amidoalkylating intermediates. 1-(*N*-Acylamino)alkyl sulfones **3**, usually 1-(*N*-alkoxycarbonylamino)alkyl aryl sulfones (R^1 = OAlk), have recently emerged as valuable amidoalkylating reagents. 1-(*N*-Acylamino)alkyl sulfones are mostly stable, crystalline compounds that are easy to isolate, purify, and store. They easily eliminate the corresponding arylsulfinic acid under basic conditions to generate reactive *N*-acylimines **4** (Scheme 1). Treatment of 1-(*N*-acylamino)alkyl sulfones with a Lewis acid such as $TiCl_4$ or $SnCl_4$ enables the generation of highly reactive *N*-acyliminium cations **5**.[3,7] Both *N*-acylimines and *N*-acyliminium cations promptly react inter- or intramolecularly with a variety of carbon and heteroatom nucleophiles as well as with reducing agents.[3] The usefulness of this reaction has been recognized only recently. The synthesis and reactivity of these compounds has been reviewed comprehensively by Petrini.[3]

The most frequently used method for the synthesis of 1-(*N*-acylamino)alkyl sulfones **3**, pioneered by Engberts and Strating in 1964, consists of three-component condensation of primary amides, carbamates, or carbamides (**1**, R^1 = R, OR, or NHR, respectively) with aldehydes **2** and sodium sulfinates (Scheme 1).[8−11] *O*- or *S*-Thiocarbamates, dithiocarbamates, or thiocarbamides have also been applied in a similar reaction.[12,13] Other methods for synthesizing these compounds, such as oxidation of the corresponding sulfides with H_2O_2, $KMnO_4$, or *m*CPBA,[14−16] the Curtius-type rearrangement of α-sulfonylacyl azides,[17] and substitution of the chlorine anion in *N*-(1-chloroalkyl)amides with *p*-toluenesulfinic acid,[18] have found only limited application.[3] The structural diversity of 1-(*N*-acylamino)alkyl sulfones synthesized using the Engberts and Strating method is confined by the limited availability of structurally diverse aldehydes **2**. The structural diversity of amide component **1** as well as of the sodium aryl sulfinate is of less importance.

In this contribution, we report a new, effective, one-pot condensation of *N*-(1-methoxyalkyl)amides or carbamates (**8**, R^1 = R or OR, respectively) with sodium aryl sulfinates in the presence of triphenylphosphonium tetrafluoroborate or bromide to give the corresponding 1-(*N*-acylamino)alkyl sulfones **3** (Scheme 2). Recently, we described an efficient method for electrochemical decarboxylative α-methoxylation of *N*-acyl-α-amino acids **6** in the presence of 3-(1-piperidino)propyl-functionalized silica gel (SiO_2−Pip) to give *N*-(1-methoxyalkyl)amides **8**.[19] A combination of these two reactions enables a convenient two-pot transformation of *N*-acyl-α-amino acids **6** to 1-(*N*-acylamino)alkyl sulfones **3**. The possibility of employing a large range of natural α-amino acids (both proteinogenic and nonproteinogenic) as well as an unlimited number of unnatural α-amino acids in this synthesis potentially provides easy access to a wide variety of structurally diverse 1-(*N*-acylamino)alkyl sulfones, which significantly widens the

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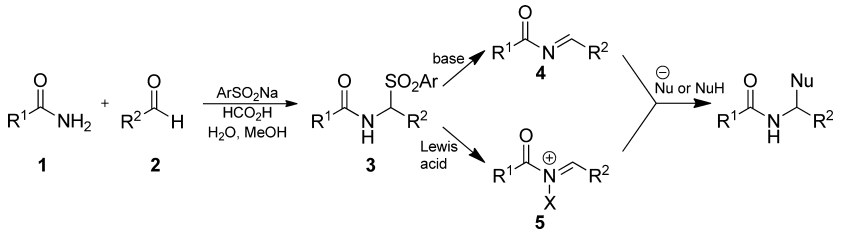
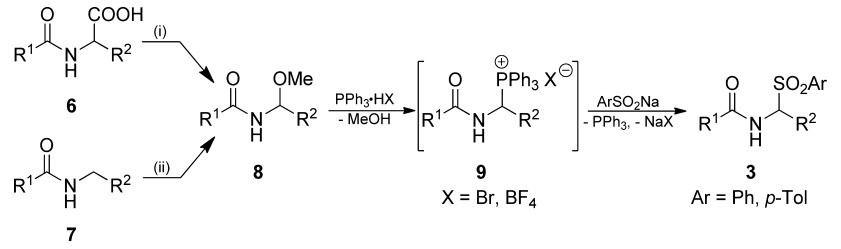
Scheme 1. Synthesis and Reactivity of 1-(*N*-Acylamino)alkyl Sulfones 3



Scheme 2. Transformation of *N*-Acyl-*α*-amino Acids 6 or *N*-Alkylamides 7 into 1-(*N*-Acylamino)alkyl Sulfones 3[a]



[a]Reagents and conditions: (i) MeOH, SiO_2–Pip, −2e, 10 °C;[19] (ii) MeOH, $Et_4N^+TsO^-$, −2e, 10 °C.

Table 1. Synthesis of 1-(*N*-Acylamino)alkyl Sulfones: Reaction Conditions and Yields

	N-(1-Methoxyalkyl)amide						reaction product			
									yield (%)	
entry	**8**	R^1	R^2	procedure	*t* (h)	X	**3**	Ar	based on **8**	based on **6** or **7**
1	**8a**	*t*-Bu	Me	A	2	BF_4	**3a**	*p*-Tol	90	87
2	**8a**	*t*-Bu	Me	A	72	Br	**3a**	*p*-Tol	76	74
3	**8a**	*t*-Bu	Me	A	4	BF_4	**3b**	Ph	82	80
4	**8a**	*t*-Bu	Me	A	66	Br	**3b**	Ph	87	84
5	**8b**	Me	Me	A	2	BF_4	**3c**	*p*-Tol	91	85
6	**8b**	Me	Me	B	2	BF_4	**3c**	*p*-Tol	91	50
7	**8c**	Ph	Me	A	2	BF_4	**3d**	*p*-Tol	82	80
8	**8d**	BnO	Ph	A	2	BF_4	**3e**	*p*-Tol	75	74
9	**8e**	BnO	*i*-Pr	A	2	BF_4	**3f**	*p*-Tol	77	75
10	**8f**	*t*-BuO	*i*-Pr	A	2	BF_4	**3g**	Ph	90	83
11	**8g**	BnO	*i*-Bu	A	3	BF_4	**3h**	*p*-Tol	78	73
12	**8h**	BnO	Bn	A	2	BF_4	**3i**	*p*-Tol	75	69
13	**8h**	BnO	Bn	A	3	BF_4	**3j**	Ph	76	70
14	**8h**	BnO	Bn	A	66	Br	**3j**	Ph	69	63
15	**8i**	BnO	CH_2CONH_2	A	2	BF_4	**3k**[a]	*p*-Tol	79	73
16	**8j**		$(CH_2)_2$	A	2	BF_4	**3l**	*p*-Tol	75	73
17	**8j**		$(CH_2)_2$	B	2	BF_4	**3l**	*p*-Tol	75	61
18	**8j**		$(CH_2)_2$	A	2	BF_4	**3m**	Ph	90	87
19	**8j**		$(CH_2)_2$	B	2	BF_4	**3m**	Ph	90	73
20	**8k**		$(CH_2)_4$	B	2	BF_4	**3n**	*p*-Tol	82	66
21	**8l**	BnO	CH_2O-*t*-Bu	A	2	BF_4	**3o**	*p*-Tol	91	86
22	**8m**	BnO	CH_2CO_2-*t*-Bu	A	2	BF_4	**3p**	*p*-Tol	65[b]	62[b]
23	**8n**	BnO	$(CH_2)_2CO_2$-*t*-Bu	A	2	BF_4	**3q**	*p*-Tol	83	81
24	**8o**	BnO	*p*-$CH_2C_6H_4OBn$	A	2	BF_4	**3r**	*p*-Tol	76	61

[a]The reaction was carried out in acetonitrile. [b]The yield was estimated from the ^1H NMR spectrum of the crude product, which also contained the corresponding (*E*)-enamide **10p** (23% yield based on **8**). Attempts to isolate the product **3p** failed.

scope of possible synthetic applications of these important *α*-amidoalkylating agents.

Alternatively, *N*-(1-methoxyalkyl)amides **8** can also be obtained by electrochemical *α*-methoxylation of *N*-alkylamides or lactams or *N*-alkylcarbamates (**7**, R^1 = R, OR),[20−23] which additionally extends the structural diversity of 1-(*N*-acylamino)-alkyl sulfones **3** that can be synthesized in this way.

The syntheses of *N*-(1-methoxyalkyl)amides by electrochemical decarboxylative *α*-methoxylation of *N*-acyl-*α*-amino acids in the presence of SiO_2–Pip were performed in MeOH at 10 °C in the presence of a substoichiometric amount of SiO_2–Pip (0.075 mol of piperidine per mole of substrate) at a current density of 0.3 A/dm^2 and a charge consumption of 3.5−3.75 F/mol (procedure A), as we recently described.[19] The crude products were obtained in very good to excellent yields.

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Alternatively, a few *N*-(1-methoxyalkyl)amides were synthesized by electrochemical α-methoxylation of *N*-alkylamides or lactams in MeOH at 10 °C in the presence of tetraethylammonium *p*-toluenesulfonate ($Et_4N^+OTs^-$) in good to very good yields (procedure B).

As we have already reported,[19,24] the dissolution of *N*-(1-methoxyalkyl)amides **8** in $CHCl_3$ and the addition of triphenyphosphonium tetrafluoroborate at 20 °C causes the complete disappearance of **8** and the formation of methanol and the corresponding 1-(*N*-acylamino)alkyltriphenylphosphonium salt **9** in a few minutes in very good yield. Recently, we also demonstrated that 1-(*N*-acylamino)alkyltriphenylphosphonium salts under basic conditions display strong α-amidoalkylating properties toward a variety of *N*, *O*, *S*, *P*, and *C* nucleophiles.[25−27] Now we state that the addition of sodium sulfinate to crude 1-(*N*-acylamino)alkyltriphenylphosphonium salt **9a**, obtained in situ from *N*-(1-methoxyalkyl)amide **8a** and triphenyphosphonium tetrafluoroborate, after 2 h at 20 °C gave an equilibrium mixture containing, apart from the expected 1-(*N*-acylamino)alkyl sulfone **3a** (35%), also the starting *N*-(1-methoxyalkyl)amide **8a** (41%). The latter compound was evidently formed by the reverse substitution of the triphenylphosphonium group in phosphonium salt **9a** with methanol under basic conditions. We previously observed and reported a similar reverse substitution of the triphenylphosphonium group in phosphonium salts **9** with methanol under the influence of Hünig's base [$Et(i\text{-}Pr)_2N$].[24] In order to achieve full conversion of *N*-(1-methoxyalkyl)amides **8** to 1-(*N*-acylamino)alkyl sulfones **3**, evaporation of methanol with chloroform under reduced pressure prior to repeated dissolution of the residue in chloroform and the addition of sodium sulfinate was proved necessary. The 1-(*N*-acylamino)-alkyl sulfones **3** obtained in this manner were easily isolated and purified by evaporation of the chloroform and crystallization of the sulfone from ethyl acetate, acetonitrile, or toluene, with the exception of compound **3p**, which was obtained in a mixture with the corresponding enamide **10p** (Table 1).

By using this method, we were able to obtain a variety of 1-(*N*-acylamino)alkyl sulfones **3** in good to very good yields based on *N*-acyl-α-amino acids **6** (procedure A) or in satisfying yields based on *N*-alkylamides or lactams **7** (procedure B). Only in the case of compound **3p** was a mixture of the expected product (65%) and the corresponding (*E*)-enamide **10p** (23%) obtained.[28] Attempts to isolate pure product **3p** from the mixture by crystallization or by column chromatography failed. The special tendency for the formation of enamide **10p** in this particular case can be explained as a result of the especially effective push−pull resonance stabilization of the enamide with the participation of the electron-donating acylamine group and the electron-withdrawing *tert*-butoxycarbonyl group (the captodative effect) (Figure 1).

It is worth noting that the transformation of *N*-(1-methoxyalkyl)amides to 1-(*N*-acylamino)alkyl sulfones can also be carried out by using triphenylphosphonium bromide instead of triphenylphosphonium tetrafluoroborate. However, the reaction was much slower in that case (cf. Table 1, entries 2, 4, and 14). It seems that the bromide anion, in contrast to the non-nucleophilic tetrafluorobrate anion, is able to recombine with the intermediate *N*-acylimine or *N*-acyliminium cation to form the less reactive *N*-(1-bromoalkyl)amide.

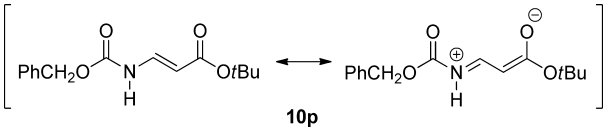

Figure 1. Resonance structures of (*E*)-enamide **10p**.

In conclusion, a new, effective, one-pot condensation of *N*-(1-methoxyalkyl)amides or carbamates (**8**, R^1 = R or OR, respectively) with sodium aryl sulfinates in the presence of triphenylphosphonium tetrafluoroborate or bromide to give 1-(*N*-acylamino)alkyl sulfones **3** has been developed. A combination of this reaction with the recently described efficient electrochemical decarboxylative α-methoxylation of *N*-acyl-α-amino acids **6** to *N*-(1-methoxyalkyl)amides **8**[19] enables a convenient two-pot transformation of *N*-acyl-α-amino acids **6** to 1-(*N*-acylamino)alkyl sulfones **3**. It has also been demonstrated that, alternatively, *N*-(1-methoxyalkyl)-amides **8** can be obtained by electrochemical α-methoxylation of either *N*-alkylamides or lactams **7**. The developed transformation of *N*-(1-methoxyalkyl)amides or carbamates **8** provides easy access to a wide variety of structurally diverse 1-(*N*-acylamino)alkyl sulfones **3** that would be difficult to obtain using the classical Engberts and Strating method and therefore significantly widens the scope of possible synthetic applications of these important α-amidoalkylating agents.

EXPERIMENTAL SECTION

General Methods. Melting points were determined in capillaries and are uncorrected. IR spectra were measured on an FT-IR spectrophotometer (ATR method). ^1H and ^{13}C NMR spectra were recorded at operating frequencies of 600 or 400 and 150 or 100 MHz, respectively, using TMS as the resonance shift standard. All chemical shifts (δ) are reported in parts per million, and coupling constants (*J*) are reported in hertz.

*Decarboxylative α-Methoxylation of N-Acyl-α-amino Acids to N-(1-Methoxyalkyl)amides **8** (Procedure A).*[19] To an undivided cylindrical glass electrolyzer (85 cm^3) with a thermostatic jacket and equipped with a magnetic stirrer along with a cylindrical Pt mesh anode (47 cm^2) and a similar cathode (44 cm^2), arranged concentrically to one another at a distance of 2.5 ± 0.5 mm, were added methanol (30 cm^3), *N*-acyl-α-amino acid **6** (3.0 mmol), and SiO_2−Pip (200 mg, 0.22 mmol). The electrolysis was carried out with stirring at a current density of 0.3 A/dm^2 at 10 °C until a charge of 2.4−3.75 F/mol had passed. SiO_2−Pip was filtered off, and methanol was evaporated under reduced pressure to obtain *N*-(1-methoxyalkyl)-amide **8**.

Electrochemical α-Methoxylation of N-Alkylamides and Lactams (Procedure B). To an undivided cylindrical glass electrolyzer (85 cm^3) with a thermostatic jacket and equipped with a magnetic stirrer along with a cylindrical Pt mesh anode (47 cm^2) and a similar cathode (44 cm^2), arranged concentrically to one another at a distance of 2.5 ± 0.5 mm, were added methanol (40 cm^3), *N*-alkylamide or lactam **7** (8.0 mmol) and $Et_4N^+OTs^-$ (40.7 mg, 0.135 mmol). The electrolysis was carried out with stirring at a current density of 1.0 A/dm^2 at 10 °C until a charge of 9.0, 5.0, or 5.5 F/mol had passed for compound **8b**, **8j**, or **8k**, respectively. The solvent was evaporated under reduced pressure, and the product was isolated by column chromatography (CH_2Cl_2/MeOH, 9:1 with 2% Et_3N). The crystalline crude compounds **8j** and **8k** were recrystallized from toluene.

*Reaction of N-(1-Methoxyethyl)pivaloylamide (**8a**) with Sodium p-Toluenesulfinate.* To a solution of *N*-(1-methoxyethyl)-pivaloylamide **8a** (159.2 mg, 1 mmol) in deuterated chloroform (2 cm^3) was added sodium *p*-toluenesulfinate (178.2 mg, 1 mmol). After 2 h the reaction mixture did not contain any traces of the expected sulfone (^1H NMR).

*General Procedure for the Transformation of N-(1-Methoxyalkyl)amides **8** to 1-(N-Acylamino)alkyl Sulfones **3**.* To a solution of *N*-(1-methoxyalkyl)amide **8** (1 mmol) in chloroform (2

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cm^3) was added triphenylphosphonium tetrafluoroborate or bromide (1 mmol). After a homogeneous solution was obtained, the solvent was evaporated to dryness. The residue was again dissolved in chloroform (2 cm^3), and sodium sulfinate (1 mmol) was added. After the mixture was stirred for the time given in Table 1 at 20 °C, sodium tetrafluoroborate or sodium bromide was filtered off, and the solvent was evaporated under reduced pressure. The crude product was recrystallized from toluene (**3a**−**d**, **3f**, **3h**−**r**), acetonitrile (**3e**), or ethyl acetate (**3g**).

The analytical and spectral data for *N*-(1-methoxyalkyl)amides **8a**, **8b**, **8d**−**i**, and **8l**−**o** were reported in our previous paper.[19]

***N*-(1-Methoxyethyl)benzamide (8c).**[29] Pale-yellow crystals (procedure A, 526.8 mg, 98% yield), mp 86.0−88.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.83−7.77 (m, 2H), 7.56−7.50 (m, 1H), 7.48−7.43 (m, 2H), 6.30 (d, J = 8.4 Hz, 1H), 5.51 (dq, J = 9.6, 5.9 Hz, 1H), 3.41 (s, 3H), 1.45 (d, J = 6.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 167.2, 134.0, 131.8, 128.6, 127.0, 78.3, 55.8, 21.7; IR (ATR) 3310, 1647, 1530, 1337, 1284, 1134, 1082 cm^{-1}.

5-Methoxypyrrolidin-2-one (8j).[23] Colorless crystals (procedure A, 334.9 mg, 97% yield; procedure B, 745.8 mg, 81% yield), mp 59.0−60.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (br s, 1H), 4.89 (ddd, J = 6.4, 1.4, 1.4 Hz, 1H), 3.32 (s, 3H), 2.57−2.46 (m, 1H), 2.35−2.19 (m, 2H), 2.12−2.02 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.5, 87.1, 54.4, 28.3, 27.9; IR (ATR) 3178, 1671, 1283, 1251, 1098, 1056, 1043, 995, 796, 761 cm^{-1}.

2-Methoxy-ε-caprolactam (8k).[23] Colorless crystals (procedure B, 916.5 mg, 80% yield), mp 62.0−63.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.52 (br s, 1H), 4.31 (ddd, J = 5.6, 5.6, 2.0 Hz, 1H), 3.36 (s, 3H), 2.67−2.59 (m, 1H), 2.46−2.39 (m, 1H), 2.15−2.05 (m, 1H), 2.03−1.89 (m, 1H), 1.86−1.65 (m, 3H), 1.62−1.49 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 178.5, 83.6, 55.3, 37.3, 34.2, 23.7, 23.2; IR (ATR) 3197, 2934, 2918, 1663, 1625, 1433, 1356, 1079, 1068, 719 cm^{-1}.

***N*-[1-(*p*-Toluenesulfonyl)ethyl]pivaloylamide (3a).** Colorless crystals (255.1 mg, 90% yield or 215.4 mg, 76% yield; see Table 1), mp 146.5−147.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.75 (m, 2H), 7.33 (d, J = 8.0 Hz, 2H), 5.96 (d, J = 10.0 Hz, 1H), 5.41 (dq, J = 10.2, 7.0 Hz, 1H), 2.42 (s, 3H), 1.62 (d, J = 7.0 Hz, 3H), 1.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 145.1, 133.6, 129.7, 129.2, 64.3, 38.7, 27.2, 21.7, 13.2; IR (ATR) 3371, 2973, 1677, 1516, 1308, 1287, 1136, 1083, 1017, 724 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{14}H_{21}NO_3SNa$ $[M + Na]^+$ 306.1140, found 306.1142.

***N*-[1-(Phenylsulfonyl)ethyl]pivaloylamide (3b).** Colorless crystals (220.9 mg, 82% yield or 234.4 mg, 87% yield; see Table 1), mp 145.5−147.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.88 (m, 2H), 7.67−7.61 (m, 1H), 7.57−7.51 (m, 2H), 5.96 (d, J = 9.6 Hz, 1H), 5.45 (dq, J = 10.2, 7.0 Hz, 1H), 1.64 (d, J = 7.0 Hz, 3H), 0.99 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.9, 136.6, 134.0, 129.1, 129.0, 64.3, 38.7, 27.2, 13.1; IR (ATR) 3362, 2975, 1677, 1510, 1316, 1291, 1259, 1147, 1135, 1083, 732 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{13}H_{19}NO_3SNa$ $[M + Na]^+$ 292.0983, found 292.0983.

***N*-[1-(*p*-Toluenesulfonyl)ethyl]acetamide (3c).** Colorless crystals (219.6 mg, 91% yield), mp 125.0−126.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.79−7.75 (m, 2H), 7.37−7.32 (m, 2H), 6.10 (d, J = 10.0 Hz, 1H), 5.35 (dq, J = 10.4, 7.0 Hz, 1H), 2.44 (s, 3H), 1.84 (s, 3H), 1.60 (d, J = 7.2 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 168.7, 145.3, 133.4, 129.8, 129.1, 64.8, 22.8, 21.7, 13.3; IR (ATR) 3346, 1690, 1522, 1304, 1286, 1247, 1135, 1084, 728 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{11}H_{15}NO_3SNa$ $[M + Na]^+$ 264.0670, found 264.0670.

***N*-[1-(*p*-Toluenesulfonyl)ethyl]benzamide (3d).**[30] Colorless crystals (248.8 mg, 82% yield), mp 126.0−127.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.75 (m, 2H), 7.64−7.58 (m, 2H), 7.54−7.48 (m, 1H), 7.43−7.37 (m, 2H), 7.29−7.23 (m, 2H), 6.67 (d, J = 10.0 Hz, 1H), 5.57 (dq, J = 10.2, 7.0 Hz, 1H), 2.39 (s, 3H), 1.72 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.1, 145.2, 133.4, 132.9, 132.2, 129.8, 129.1, 128.7, 127.0, 65.3, 21.7, 13.3; IR (ATR) 3257, 1645, 1523, 1321, 1311, 1293, 1141, 1129, 1084, 697 cm^{-1}.

Benzyl *N*-[1-Phenyl-1-(*p*-toluenesulfonyl)methyl]carbamate (3e).[31] Colorless crystals (296.6 mg, 75% yield), mp 158.5−159.5 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 9.11 (d, J = 10.8 Hz, 1H), 7.71−7.64 (m, 2H), 7.63−7.58 (m, 2H), 7.45−7.29 (m, 8H), 7.25−7.19 (m, 2H), 6.03 (d, J = 10.4 Hz, 1H), 4.92 (d, J = 12.8 Hz, 1H), 4.86 (d, J = 12.8 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 155.2, 144.5, 136.7, 133.7, 130.4, 129.6, 129.5, 129.3, 129.1, 128.3, 128.1, 127.9, 127.6, 74.9, 66.0, 21.1; IR (ATR) 3367, 2972, 1698, 1509, 1317, 1304, 1148, 1085, 1039, 702 cm^{-1}.

Benzyl *N*-[2-Methyl-1-(*p*-toluenesulfonyl)propyl]carbamate (3f).[32] Colorless crystals (278.4 mg, 77% yield), mp 95.5−98.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77−7.67 (m, 2H), 7.41−7.27 (m, 5H), 7.24−7.18 (m, 2H), 5.35 (d, J = 10.8 Hz, 1H), 4.93 (d, J = 12.0 Hz, 1H), 4.86 (d, J = 12.0 Hz, 1H), 4.74 (dd, J = 11.0, 3.0 Hz, 1H), 2.82−2.72 (m, 1H), 2.40 (s, 3H), 1.13 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 6.8 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 155.2, 144.8, 135.7, 133.8, 129.7, 128.8, 128.5, 128.4, 128.1, 74.8, 64.7, 26.9, 21.7, 20.7, 16.8; IR (ATR) 3320, 2959, 1722, 1527, 1283, 1230, 1138, 1081, 742 cm^{-1}.

***tert*-Butyl *N*-[2-Methyl-1-(phenylsulfonyl)propyl]carbamate (3g).**[33] Colorless crystals (282.1 mg, 90% yield), mp 115.5−116.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.94−7.85 (m, 2H), 7.69−7.48 (m, 3H), 5.13 (d, J = 11.2 Hz, 1H), 4.74 (dd, J = 11.2, 3.6 Hz, 1H), 2.84−2.73 (m, 1H), 1.23 (s, 9H), 1.14 (d, J = 6.8 Hz, 3H), 1.08 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.1, 138.1, 133.7, 129.0, 128.9, 80.7, 74.3, 28.0, 26.7, 20.7, 16.9; IR (ATR) 3348, 2969, 1712, 1510, 1307, 1238, 1162, 1139, 1083, 686 cm^{-1}.

Benzyl *N*-[3-Methyl-1-(*p*-toluenesulfonyl)butyl]carbamate (3h). Colorless crystals (292.9 mg, 78% yield), mp 129.0−130.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 3.2 Hz, 2H), 7.38−7.32 (m, 2H), 7.25−7.19 (m, 5H), 5.11 (d, J = 10.8 Hz, 1H), 4.91 (ddd, J = 11.2, 11.1, 2.9 Hz, 1H), 4.91 (d, J = 12.0 Hz, 1H), 4.85 (d, J = 12.4 Hz, 1H), 2.41 (s, 3H), 2.06−1.96 (m, 1H), 1.81−1.66 (m, 2H), 0.99 (d, J = 6.4 Hz, 3H), 0.93 (d, J = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.7, 145.0, 135.7, 133.6, 129.7, 129.2, 128.5, 128.3, 128.1, 70.1, 67.3, 34.9, 24.7, 23.3, 21.7, 21.1; IR (ATR) 3271, 2959, 1692, 1538, 1316, 1290, 1268, 1243, 1145, 1039, 752, 700 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{20}H_{25}NO_4SNa$ $[M + Na]^+$ 398.1402, found 398.1393.

Benzyl *N*-[2-Phenyl-1-(*p*-toluenesulfonyl)ethyl]carbamate (3i).[32] Colorless crystals (307.1 mg, 75% yield), mp 136.0−137.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.74 (m, 2H), 7.33−7.17 (m, 10H), 7.12−7.05 (m, 2H), 5.31 (d, J = 10.8 Hz, 1H), 5.14 (ddd, J = 11.0, 11.0, 3.5 Hz, 1H), 4.79 (d, J = 12.4 Hz, 1H), 4.74 (d, J = 12.4 Hz, 1H), 3.63 (dd, J = 14.6, 3.4 Hz, 1H), 3.01 (dd, J = 14.6, 11.0 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.6, 145.1, 135.7, 134.6, 133.4, 129.8, 129.3, 129.2, 128.7, 128.4, 128.2, 127.8, 127.2, 71.8, 67.1, 32.8, 21.7; IR (ATR) 3276, 2932, 1695, 1549, 1446, 1309, 1264, 1129, 1081, 1044, 754 cm^{-1}.

Benzyl *N*-[2-Phenyl-1-(phenylsulfonyl)ethyl]carbamate (3j).[34] Colorless crystals (300.6 mg, 76% yield or 272.9 mg, 69% yield; see Table 1), mp 118.5−119.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.93−7.87 (m, 2H), 7.63−7.56 (m, 1H), 7.48−7.40 (m, 2H), 7.33−7.17 (m, 8H), 7.11−7.04 (m, 2H), 5.25 (d, J = 10.8 Hz, 1H), 5.17 (ddd, J = 10.8, 10.8, 3.2 Hz, 1H), 4.76 (d, J = 12.0 Hz, 1H), 4.72 (d, J = 12.4 Hz, 1H), 3.65 (dd, J = 14.6, 3.4 Hz, 1H), 3.02 (dd, J = 14.8, 10.8 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.5, 136.5, 135.6, 134.5, 134.1, 129.3, 129.2, 129.1, 128.8, 128.5, 128.3, 128.0, 127.3, 71.8, 67.2, 32.6; IR (ATR) 3339, 1732, 1518, 1315, 1298, 1230, 1146, 1135, 1079, 1038, 995, 740, 684 cm^{-1}.

Benzyl *N*-[2-Carbamoyl-1-(*p*-toluenesulfonyl)ethyl]-carbamate (3k). Colorless crystals (297.4 mg, 79% yield), mp 126.0−127.0 °C. ^{1}H NMR (400 MHz, DMSO-d_6) δ 8.34 (d, J = 9.6 Hz, 1H), 7.70−7.64 (m, 2H), 7.46 (br s, 1H), 7.41−7.29 (m, 5H), 7.23−7.17 (m, 2H), 7.03 (br s, 1H), 5.20 (ddd, J = 9.8, 9.8, 3.1 Hz, 1H), 4.89 (d, J = 12.4 Hz, 1H), 4.82 (d, J = 12.8 Hz, 1H), 2.78 (dd, J = 15.6, 3.2 Hz, 1H), 2.52 (dd, J = 15.6, 10.4 Hz, 1H), 2.40 (s, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ 168.9, 154.9, 144.6, 136.4, 133.5, 129.6, 129.0, 128.3, 127.8, 127.6, 69.4, 65.7, 32.7, 21.1; IR (ATR) 3431, 3322, 1688, 1667, 1539, 1305, 1256, 1143, 1084, 1050, 695 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{18}H_{20}N_2O_5SNa$ $[M + Na]^+$ 399.0991, found 399.0995.

5-(*p*-Toluenesulfonyl)pyrrolidin-2-one (3l). Colorless crystals (179.5 mg, 75% yield), mp 149.0−150.0 °C. ^{1}H NMR (400 MHz,

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$CDCl_3$) δ 7.82−7.78 (m, 2H), 7.41 (d, J = 8.0 Hz, 2H), 6.63 (br s, 1H), 4.65 (ddd, J = 8.4, 1.6, 1.6 Hz, 1H), 2.59−2.40 (m, 2H), 2.47 (s, 3H), 2.15 (ddd, J = 17.6, 10.0, 2.8 Hz, 1H), 1.98 (ddd, J = 17.6, 9.9, 9.9 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.7, 146.1, 131.6, 130.4, 129.6, 74.3, 27.8, 21.8, 21.7; IR (ATR) 3344, 2923, 1700, 1412, 1286, 1231, 1130, 1083, 719 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{11}H_{13}NO_3SNa$ $[M + Na]^+$ 262.0514, found 262.0511.

5-(Phenylsulfonyl)pyrrolidin-2-one (3m).[35] Colorless crystals (202.8 mg, 90% yield), mp 138.0−140.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.96−7.91 (m, 2H), 7.77−7.71 (m, 1H), 7.66−7.60 (m, 2H), 6.31 (br s, 1H), 4.67 (ddd, J = 8.4, 1.6, 1.6 Hz, 1H), 2.62−2.42 (m, 2H), 2.17 (ddd, J = 17.6, 10.0, 2.8 Hz, 1H), 2.06−1.95 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 177.4, 134.8, 134.7, 129.8, 129.6, 74.2, 27.7, 21.8; IR (ATR) 3219, 1685, 1446, 1308, 1187, 1146, 1084, 716 cm^{-1}.

2-(*p*-Toluenesulfonyl)-*ε*-caprolactam (3n). Colorless crystals (219.2 mg, 82% yield), mp 124.5−126.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80−7.76 (m, 2H), 7.40−7.37 (m, 2H), 6.10 (d, J = 4.0 Hz, 1H), 4.33 (ddd, J = 5.2, 4.2, 2.6 Hz, 1H), 2.77−2.71 (m, 1H), 2.46 (s, 3H), 2.43−2.35 (m, 1H), 2.32−2.26 (m, 1H), 2.20−2.12 (m, 2H), 1.78−1.69 (m, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.8, 145.7, 133.4, 130.2, 129.1, 73.3, 35.9, 27.2, 25.6, 22.4, 21.7; IR (ATR) 3200, 3072, 2935, 1671, 1311, 1291, 1143, 1080 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{13}H_{17}NO_3SNa$ $[M + Na]^+$ 290.0827, found 290.0821.

Benzyl *N*-[2-*tert*-Butoxy-1-(*p*-toluenesulfonyl)ethyl]-carbamate (3o). Colorless crystals (369.0 mg, 91% yield), mp 93.5−95.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76−7.70 (m, 2H), 7.39−7.26 (m, 5H), 7.25−7.21 (m, 2H), 5.67 (d, J = 10.4 Hz, 1H), 5.03 (d, J = 12.4 Hz, 1H), 5.02−4.96 (m, 1H), 4.96 (d, J = 12.0 Hz, 1H), 4.08 (dd, J = 10.4, 3.2 Hz, 1H), 3.75 (dd, J = 10.4, 4.0 Hz, 1H), 2.41 (s, 3H), 1.14 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 154.9, 144.8, 135.8, 134.7, 129.5, 129.3, 128.4, 128.3, 128.2, 74.3, 71.4, 67.4, 58.1, 27.2, 21.7; IR (ATR) 3326, 2973, 1725, 1533, 1230, 1138, 1079, 1045, 744 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{21}H_{27}NO_5SNa$ $[M + Na]^+$ 428.1508, found 428.1513.

Benzyl *N*-[2-*tert*-Butoxycarbonyl-1-(*p*-toluenesulfonyl)-ethyl]carbamate (3p). ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.75 (d, J = 8.4 Hz, 2H), 7.34−7.28 (m, 3H), 7.25−7.18 (m, 4H), 5.87 (d, J = 10.2 Hz, 1H), 5.28−5.24 (m, 1H), 4.92 (d, J = 12.6 Hz, 1H), 4.88 (d, J = 12.0 Hz, 1H), 3.07 (dd, J = 15.9, 4.5 Hz, 1H), 2.76 (dd, J = 15.9, 8.7 Hz, 1H), 2.41 (s, 3H), 1.41 (s, 9H); ^{13}C NMR (150.5 MHz, $CDCl_3$) δ 167.8, 154.4, 145.3, 135.7, 133.1, 129.8, 129.3, 128.5, 128.3, 128.1, 82.4, 68.4, 67.3, 33.4, 27.9, 21.7; HRMS (TOF-ESI) calcd for $C_{22}H_{27}NO_6SNa$ $[M + Na]^+$ 456.1457, found 456.1451.

Benzyl *N*-[3-*tert*-Butoxycarbonyl-1-(*p*-toluenesulfonyl)-propyl]carbamate (3q). Colorless crystals (371.4 mg, 83% yield), mp 136.0−137.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.74 (d, J = 8.4 Hz, 2H), 7.38−7.29 (m, 3H), 7.28−7.17 (m, 4H), 5.36 (d, J = 10.8 Hz, 1H), 4.95−4.87 (m, 1H), 4.92 (d, J = 12.4 Hz, 1H), 4.86 (d, J = 12.0 Hz, 1H), 2.55−2.46 (m, 1H), 2.45−2.32 (m, 2H), 2.41 (s, 3H), 2.15−2.01 (m, 1H), 1.41 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 171.3, 154.9, 145.1, 135.6, 133.5, 129.7, 129.2, 128.5, 128.3, 128.0, 81.2, 70.8, 67.3, 31.2, 28.0, 22.2, 21.7; IR (ATR) 3326, 1728, 1716, 1531, 1258, 1229, 1141, 1053, 742 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{23}H_{29}NO_6SNa$ $[M + Na]^+$ 470.1613, found 470.1620.

Benzyl *N*-[2-(4-Benzyloxyphenyl)-1-(*p*-toluenesulfonyl)-ethyl]carbamate (3r). Colorless crystals (391.9 mg, 76% yield), mp 148.0−149.0 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.76 (d, J = 8.4 Hz, 2H), 7.44−7.27 (m, 8H), 7.25−7.19 (m, 2H), 7.14−7.07 (m, 4H), 6.92−6.84 (m, 2H), 5.22 (d, J = 10.8 Hz, 1H), 5.08 (ddd, J = 10.8, 10.8, 3.6 Hz, 1H), 5.02 (s, 2H), 4.80 (d, J = 12.4 Hz, 1H), 4.76 (d, J = 12.4 Hz, 1H), 3.56 (dd, J = 14.4, 3.6 Hz, 1H), 2.96 (dd, J = 14.4, 10.8 Hz, 1H), 2.41 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.1, 154.6, 145.1, 136.9, 135.7, 133.6, 130.3, 129.8, 129.2, 128.6, 128.5, 128.2, 128.0, 127.9, 127.5, 126.7, 115.1, 71.9, 70.0, 67.1, 32.0, 21.7; IR (ATR) 3278, 1694, 1550, 1513, 1310, 1295, 1266, 1238, 1129, 1043, 818, 737 cm^{-1}; HRMS (TOF-ESI) calcd for $C_{30}H_{29}NO_5SNa$ $[M + Na]^+$ 538.1664, found 538.1663.

(*E*)-Benzyl *N*-(2-*tert*-Butoxycarbonylethenyl)carbamate (10p).[28] Colorless crystals (63.8 mg, 23% yield), mp 115.5−119.5 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.70 (dd, J = 13.6, 12.0 Hz, 1H), 7.38−7.33 (m, 5H), 7.10 (d, J = 12.0 Hz, 1H), 5.28 (d, J = 14.0 Hz, 1H), 5.19 (s, 2H), 1.47 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.4, 152.7, 138.1, 135.2, 128.7, 128.7, 128.4, 102.3, 80.1, 68.1, 28.3; IR (ATR) 3300, 2971, 1740, 1685, 1632, 1321, 1266, 1222, 1139, 993, 975, 851 cm^{-1}.

■ ASSOCIATED CONTENT

Ⓢ Supporting Information

^{1}H and ^{13}C NMR spectra and IR spectra of all new 1-(*N*-acylamino)alkyl sulfones **3**. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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