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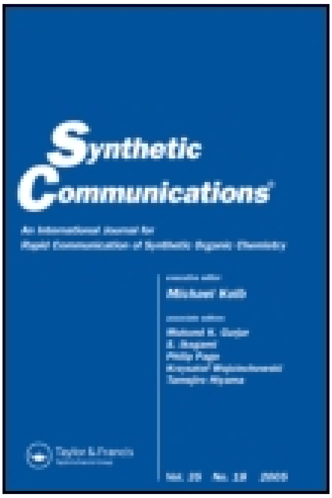

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Efficient Synthesis of Readily Water-Soluble Amides Containing Sulfonic Groups

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EFFICIENT SYNTHESIS OF READILY WATER-SOLUBLE AMIDES CONTAINING SULFONIC GROUPS

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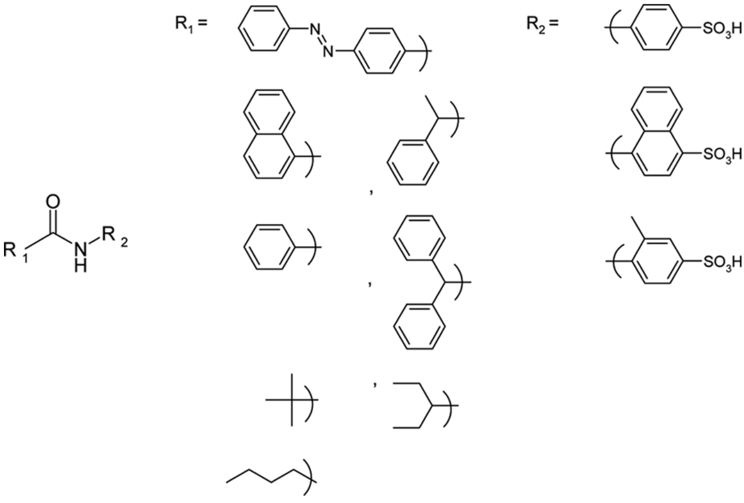
Department of Applied Geology, Geoscience Center of the University of Göttingen, Göttingen, Germany

GRAPHICAL ABSTRACT



Abstract *A series of various readily water-soluble amides were synthesized by different procedures. These compounds are useful chemical tracers for assessing the cooling progress in a georeservoir during geothermal power plant operation. Acylation of primary amines was carried out by basically employing the Schotten–Baumann method. As a second method a single-phase solvent system consisting of ethyl acetate as an organic solvent and triethylamine as a catalyst was used. Products were characterized by* ^1H *NMR and* ^{13}C *NMR.*

[Supplementary materials are available for this article. Go to the publisher's online edition of Synthetic Communications® *for the following free supplemental resource(s): Full experimental and spectral details.]*

Keywords Brine; primary amines; Schotten–Baumann reaction; sulfonic acid amides

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INTRODUCTION

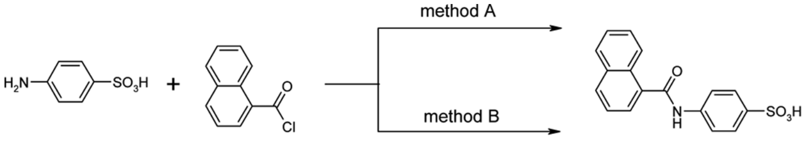
Compounds susceptible to undergo hydrolysis have raised interest as thermosensitive tracers in geothermal applications.[1,2] Together with their kinetic hydrolysis parameters it becomes possible to track thermal fronts in geothermal reservoirs and allows prediction of the thermal drawdown with time. The biggest advantage of these new tracers is that they are highly water soluble and have no geogenic background concentrations, and while the amides show no fluorescence at least one of the hydrolysis reaction products does. The latter allows performing online measurements under in situ conditions, further reducing operational costs. While esters react too fast,[3] amides are sufficient to study high enthalpy systems on longer time scales.[4]

Acylation provides an inexpensive and efficient way for obtaining amides in a synthetic process.[5] A number of reagents can be used for carrying out this reaction, such as benzoyl chloride,[6] benzoic anhydride,[7] 2-benzoylthio-1-methylpyridinium chloride,[8] and benzoyl cyanide.[9]

RESULTS AND DISCUSSION

Acylation of primary amines is carried out in brine solution using a stoichiometric amount of acid chloride followed by trituration with aqueous saturated bicarbonate solution as the well-known Schotten–Baumann method.[10] The primary amine is suspended in brine (scale: 1 g of sodium chloride in 3 ml of water) and then an equivalent amount of acid chloride derivative in acetone (1:1) is added dropwise under stirring. The desired product is finally obtained by treating the reaction mixture with saturated bicarbonate solution. To gain insight into the role of the brine, it is assumed that the high concentration of Cl^- ions in the reaction mixture prevents a fast hydrolysis of acid chloride and is also responsible for the slow decomposition of the tetrahedral intermediate formed by the nucleophilic attack of the amino group toward the acid chloride. The rationale is supported by the fact that when the reaction is carried out only in water (instead of brine), the yield is drastically reduced. From the sodium salt, the required derivatives are obtained by usual acid workup followed by washing with hot water to remove traces of carboxylic acid. The products are crystallized from methanol–water solution or purified by column chromatography (Scheme 1).

The main problem in using the Schotten–Baumann method for water-soluble compounds is the separation of resulting products from salts in the purification step.



method A: $NaHCO_3$, acetone/H_2O(brine), rt
method B: EtOAc, Et_3N, rt

Scheme 1. Synthesis of 4-[(naphthalen-1-ylcarbonyl)amino]benzenesulfonic acid **(2)** obtained by two different methods.

Table 1. Acylation of primary amines

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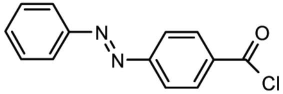
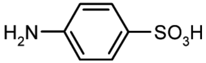
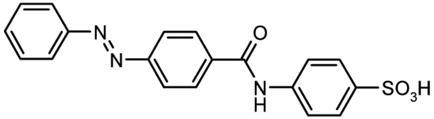
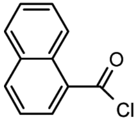
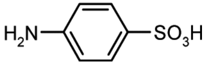
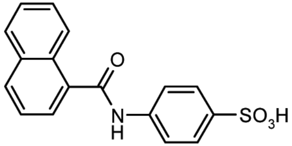
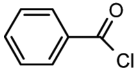
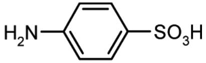
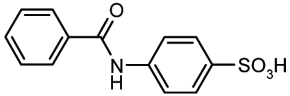
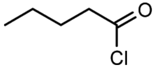
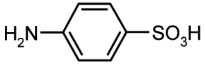
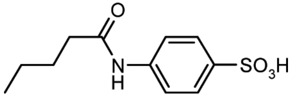
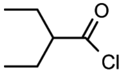
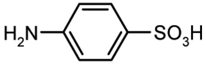
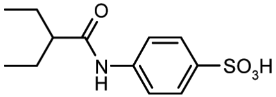
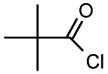
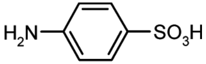
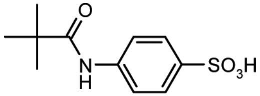
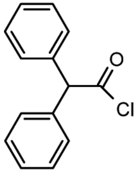
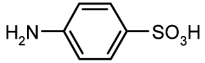
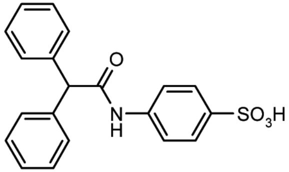
1			A		95
2			A/B		60/85
3			B		96
4			B		40
5			B		98
6			B		99
7			B		86

(*Continued*)

Table 1. Continued

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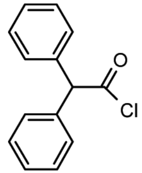
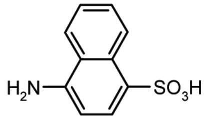
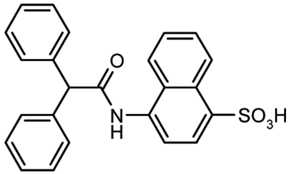
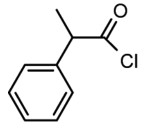
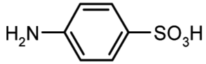
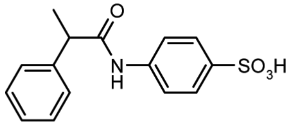
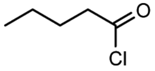
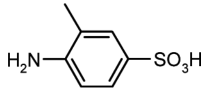
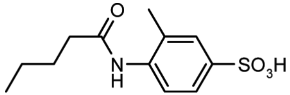
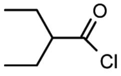
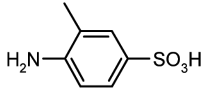
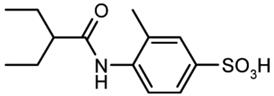
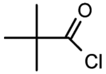
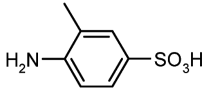
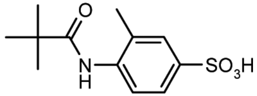
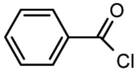
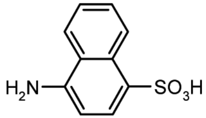
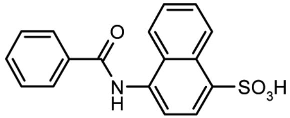
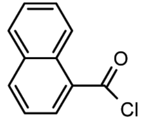
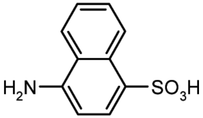
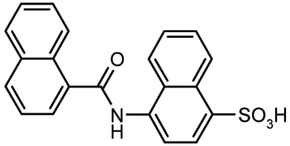
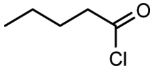
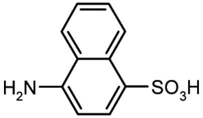
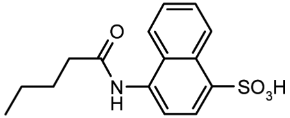
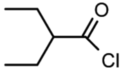
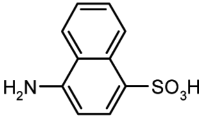
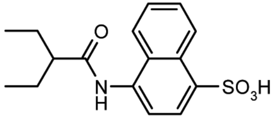
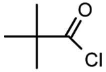
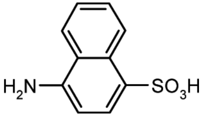
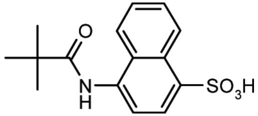
8			B		74
9			B		90
10			B		70
11			B		98
12			B		99
13			B		90

14			B		65
15			B		62
16			B		89
17			B		93

We tried to find an alternative method for obtaining water-soluble amides without the presence or formation of any inorganic salts. In acetonitrile all reagents were completely soluble so we used it as a good solvent in the reaction. Triethylamine was used as a base. Unfortunately, we did not observe any product formation. Acetonitrile was replaced by ethyl acetate with good results. We noticed that long reaction times and an insufficient amount of triethylamine can lead to product decomposion, and in particular in the acidic environment of the reaction resulting from acid chloride hydrolysis. The best yield was obtained after reaction times of 12 h with excess of triethylamine. By applying this method it is possible to obtain products free from inorganic salts (Scheme 1). The results are summarized in Table 1.

In conclusion, we have developed a very simple, inexpensive, nontoxic, and environmentally friendly method for the acylation of primary amines. The presence of the SO_3H group in all synthesized amides ensures their good water solubility and thus their application as tracers in georeservoirs. In particular, there is not a lot of information related to the synthesis of water-soluble amides.

EXPERIMENTAL

All chemicals, reagents, and solvents were used as received from commercial sources without further purification. ^1H NMR and ^{13}C NMR spectra were recorded in dimethylsulfoxide (DMSO-d_6) on a 300-MHz liquid-state Bruker spectrometer. The splitting patterns are annotated as follows: s (singlet), d (doublet), t (triplet), q (quartet), and m (multiplet). The products were also confirmed by electrospray ionization–mass spectrometry (ESI-MS) (instrumentation is described in Nödler et al.[11]). Preparative column chromatography was carried out on glass columns of different sizes packed with silica gel: Merck 60 (0.035–0.070 mm).

General Procedure of Method A

Primary amino sulfonic acid (2.5 mmol) is suspended in brine (scale: 1 g of sodium chloride in 3 ml of water) and then an equivalent amount of acid chloride in acetone (1:1) is added dropwise during 15 min. Saturated sodium bicarbonate solution (10 mmol) is added, and the reaction mixture is stirred for a further period of 12 h. From the sodium salt, the corresponding product is obtained by the usual acidic workup (acidification is accomplished by concentrated sulfuric acid) followed by washing with hot water to remove traces of carboxylic acid created during the reaction.

General Procedure of Method B

Primary amino sulfonic acid (2.5 mmol) is suspended in ethyl acetate (50 mL) and then an equivalent amount of acid chloride is added. After the reaction had been stirred intensively for 10 min at room temperature, 10 mmol of triethylamine is added. The mixture is stirred overnight, and then the solvent is removed under reduced pressure. The crude product is washed several times with ethyl acetate and subsequently purified by column chromatography (hexane/ethyl acetate, 1:5 and then methanol).

Spectral Data for Selected Compounds

4-[(Naphthalen-1-ylcarbonyl)amino]benzenesulfonic acid (2). ^{1}H NMR (300 MHz, DMSO-d$_6$) δ, ppm, 10.60 (s, 1H), 8.21–8.15 (m, 1H), 8.07 (d, $J = 8.4$ Hz, Hz, 1H), 8.04–7.99 (m, 1H), 7.79–7.74 (m, 3H), 7.64–7.56 (m, 5H); ^{13}C NMR (300 MHz, DMSO-d$_6$) δ, ppm, 167.27, 143.51, 139.35, 134.58, 133.11, 130.07, 129.61, 128.26, 126.93, 126.28, 126.05, 125.44, 125.03, 124.96, 118.79. ESI-MS: $m/z = 326$ [M−H]$^-$.

4-[(Diphenylacetyl)amino]benzenesulfonic acid (7). ^{1}H NMR (300 MHz, DMSO-d$_6$) δ, ppm, 10.68 (s, 1H), 7.59 (d, $J = 8.7$ Hz, 2H), 7.52 (d, $J = 8.7$ Hz, 2H), 7.39–7.30 (m, 8H), 7.28–7.21 (m, 2H), 5.31 (s, 1H); ^{13}C NMR (300 MHz, DMSO-d$_6$) δ, ppm, 169.92, 141.33, 139.93, 139.09, 128.44, 128.21, 126.67, 125.97, 118.15, 56.98. ESI-MS: $m/z = 366$ [M−H]$^-$.

3-Methyl-4-(pentanoylamino)benzenesulfonic acid (10). ^{1}H NMR (300 MHz, DMSO-d$_6$) δ, ppm, 9.25 (s, 1H), 7.42 (s, 1H), 7.36 (dd, $J = 8.1$, 1.5 Hz, 1H), 7.31 (d, $J = 8.1$ Hz, 1H), 2.33 (t, $J = 7.4$ Hz, 2H), 2.18 (s, 3H), 1.63–1.53 (m, 2H), 1.44–1.26 (m, 2H), 0.91 (t, $J = 7.4$ Hz, 3H); ^{13}C NMR (300 MHz, DMSO-d$_6$) δ, ppm, 171.09, 144.83, 136.45, 130.61, 127.34, 123.99, 123.07, 35.37, 27.33, 21.70, 17.77, 13.61. ESI-MS: $m/z = 270$ [M−H]$^-$.

4-[(2,2-Dimethylpropanoyl)amino]naphthalene-1-sulfonic acid (17). ^{1}H NMR (300 MHz, DMSO-d$_6$) δ, ppm, 9.45 (s, 1H), 8.92–8.86 (m, 1H), 7.94 (d, $J = 7.8$ Hz, 1H), 7.87–7.83 (m, 1H), 7.55–7.49 (m, 2H), 7.32 (d, $J = 7.8$ Hz, 1H), 1.34 (s, 9H); ^{13}C NMR (300 MHz, DMSO-d$_6$) δ, ppm, 177.13, 141.96, 135.13, 129.74, 129.62, 127.76, 125.33, 125.25, 123.99, 122.80, 122.38, 38.83, 27.37. ESI-MS: $m/z = 306$ [M−H]$^-$.

SUPPORTING INFORMATION

Full spectroscopic and characterization data including MS (triple quadrupole mass spectroscopy) are given in the supporting materials, available online.

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