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Microwave-Assisted Acylation of Amines, Alcohols, and Phenols by the Use of Solid-Supported Reagents (SSRs)

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Received July 9, 2004

A microwave-assisted synthesis of solid-supported reagents for the acylation of amines has been developed, and the same methodology has been successfully applied to the preparation of acylating agents anchored on different solid supports. Similarly, alcohols, phenols, and thiophenols have been easily acylated using these reagents under microwave irradiation.

Introduction

The amide bond is present in a very large number of pharmacologically active compounds of either peptidic or nonpeptidic nature.[1−9] Therefore, the development of new procedures for the easy, clean, and racemization-free synthesis of amides is of topical interest in medicinal chemistry.

Chemoselective acylation of amino groups is an important synthetic reaction and is often required in organic synthesis. In general, the formation of carboxamides from amines and carboxylic acids implies the activation of the carboxy group by either the preventive conversion to a more reactive acylating agent, such as acyl chloride, mixed anhydride, acyl azide, or active ester, or in situ activation by using coupling reagents, such as DDC, EDC, HOBt, BOP, CDI, or HBTU. However, these methods have some drawbacks such as exothermic reaction, formation of byproducts, complicated conditions, and low selectivity.

During our studies on the synthesis of pyrimidinones as antiviral compounds,[10] 4-*O*-acylated pyrimidines **1** (Figure 1) were found able to acylate amines, phenols, and thiophenols in high yields and good chemoselectivity.[10f] In a recent communication,[10a] we have described the synthesis on a solid support of 4-*O*-acylated pyrimidines **2** (Figure 1), which can be used as solid-supported reagents (SSRs) for selective and high-yielding acylation of amines.

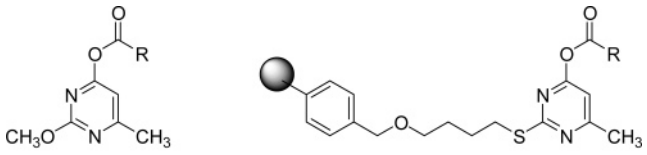

FIGURE 1. Acylating agents with a pyrimidinic structure.

Used since 1946, SSRs[11] have been the subject of several review articles,[11a,b,12] and the advantages of their use is presently widely recognized. Particular attention is now devoted to the application of SSRs under microwave irradiation. In fact, microwave activation as a nonconventional energy source is becoming a very popular and useful technique in organic chemistry, as demonstrated by the rapidly growing number of annual publications on microwave-assisted organic synthesis,[13] including microwave-assisted SSR strategies.[14]

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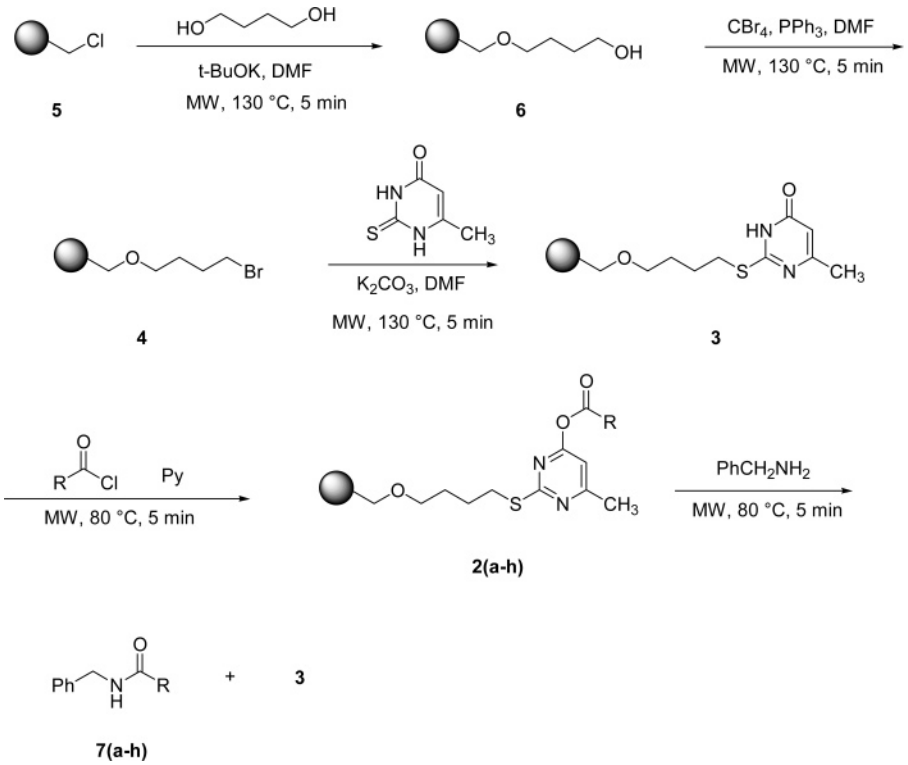
10.1021/jo048837q CCC: $27.50
Published on Web 10/16/2004

SCHEME 1. Microwave-Assisted Synthesis of SSRs 2(a−h) and Their Use for the Acylation of Benzylamine



The combination of solvent-free reaction conditions and microwave irradiation leads to a remarkable reduction in reaction time, enhancement in conversion, and sometimes in selectivity, with several advantages for the ecofriendly approach, termed green chemistry.[15,16]

Very recently, we have also described[17] the microwave-assisted synthesis of a series of polymer-bound 4-acyloxypyrimidines **2**, which proved to be useful SSRs for the efficient and selective acylation of amines. Used under microwave irradiation, these compounds afforded the corresponding amides in a few minutes and high yield and purity.

Taking all these aspects into account, a new microwave-assisted synthesis of the SSRs **2** (Scheme 1) was considered, together with their use for the microwave-assisted acylation of a number of different substrates.

Results and Discussion

Preparation of Acylating Agents 2(a−h) and Study of Their Reactivity toward Benzylamine. Considering the modest yields previously obtained for the synthesis of the pyrimidine nucleus through a cyclization reaction,[10a] we planned to accomplish the synthesis of the fundamental intermediate **3** (Scheme 1) by nucleophilic diplacement of bromine of **4** by commercially available 6-methyl-2-thiouracil.[18] This reaction could be rapidly and efficiently accomplished by the use of microwave irradiation. Microwave-assisted reactions were performed under controlled conditions in a safe and reproducible procedure. Single-mode microwave irradiation was used at a fixed temperature, pressure, and irradiation power during the reaction time by an automatic power control.

Starting from Merrifield's resin **5** (Scheme 1), 1,4-butandiol was first anchored on the solid support in order to introduce a spacer with a free hydroxyl group that could guarantee enhanced reactivity of the substrates bound to the polymer.[19] Bromination[20] of **6** and subse-

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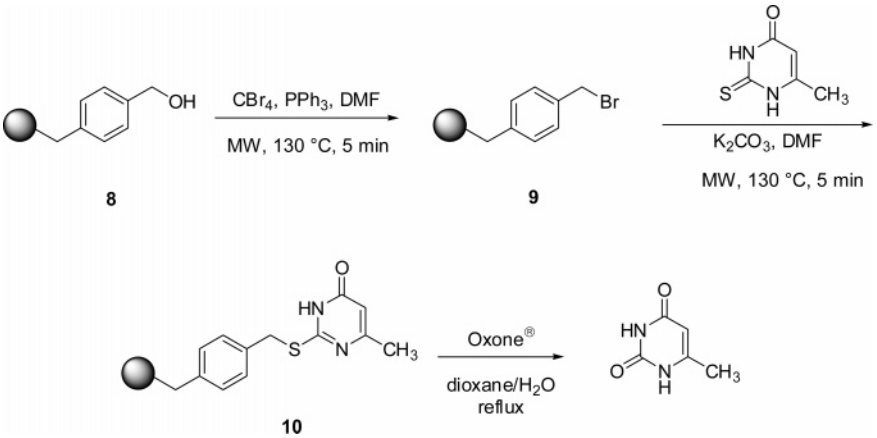
SCHEME 2. Anchorage of 6-Methyl-2-thiouracil on Wang Resin



SCHEME 3. Anchorage of 6-Methyl-2-thiouracil on TentaGel S-NH_2 Resin

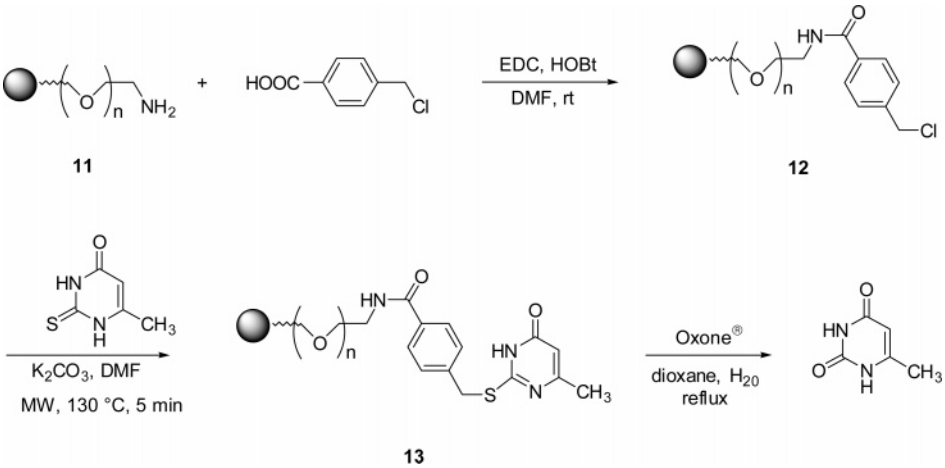


TABLE 1. Results of the Acylation of Benzylamine Using Different SSRs

compd	R	yield (%)
7a	Me	47
7b	Ph	75
7c	*p*-tolyl	45
7d	*p*-BrPh	100
7e	*o*-BrPh	40
7f	PhCH=CH−	50
7g	*p*-ClPh	85
7h	*p*-NO_2Ph	61

quent reaction with 6-methyl-2-thiouracil afforded the supported pyrimidinone **3**, which proved to be stable in alkaline conditions, high temperatures (≤100 °C), and nucleophilic attack and which can be stored at 4 °C for long times without degradation. Reaction of **3** with the appropriate acyl chloride gave polymer-bound 4-acyloxypyrimidines **2**. Under microwave irradiation the synthesis of the acylating agents **2** was accomplished in only 20 min rather than in a few days working in standard conditions.

The acylating ability of pyrimidines **2** was then evaluated by studing their reactivity with benzylamine (Scheme 1); the yields of the corresponding amides **6** are reported in Table 1.

In all cases, acceptable to excellent yields were obtained within a few minutes of microwave exposure (5 min at 80 °C). Among all the SSRs, the most electrophilic SSRs **2d** and **2g** proved to be the most effective acylating agent, giving the corresponding amides **7d** and **7g** in 100% and 85% yield, respectively. In this regard, the scarce efficiency of **2e** might be due to the steric hindrance exerted by the *o*-bromo substituent, and the scarce reactivity of **2c** has been explained considering electronic effects.

Use of Different Solid Supports. To show the versatility of the methodology we had set up, we decided to apply it to the synthesis of SSRs anchored on different solid supports. In particular, the Wang resin and the TentaGel S-NH_2 resin were investigated for this purpose.

The Wang resin **8** (Scheme 2) was first brominated under MW irradiation affording **9** and then 6-methyl-2-thiouracil was anchored using the same conditions used for the Merrifield to give **10**.

Cleavage with Oxone[21] afforded 6-methyluracil in 80% yield, thus showing a good loading.

On the other hand, TentaGel S-NH_2 resin **11** (Scheme 3) was functionalized by reaction with 4-chloromethyl benzoic acid, in the presence of HOBt[22] and EDC as activating agents. Reaction of **12** with 6-methyl-2-thiouracil under MW irradiation gave **13**, which after cleavage with Oxone afforded 6-methyluracil in 68%. In this case,

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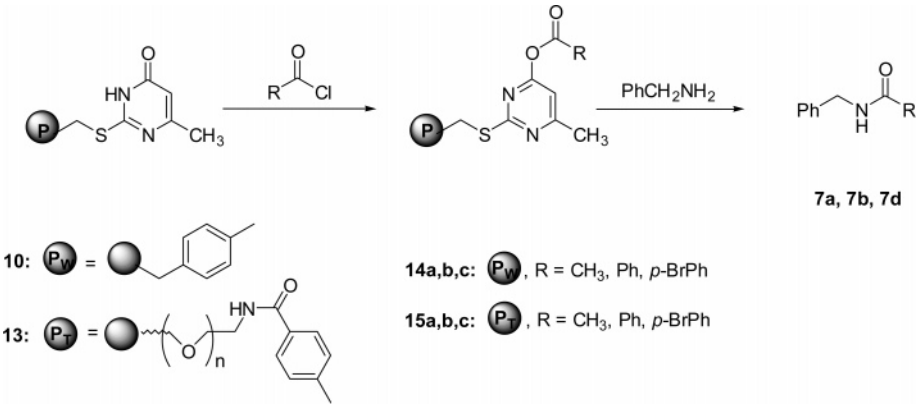
SCHEME 4. Acylation of Benzylamine by Use of Acylating Agents Anchored on Different Solid Supports



SCHEME 5. Microwave-Assisted Synthesis of Different Polymer-Bound Pyrimidinones

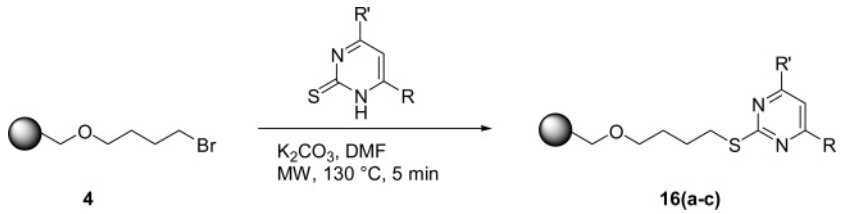


TABLE 2. Yields of Acylation Reaction of Benzylamine Using Acylating Agents Anchored on Different Solid Supports

	yield (%)		
acylating agent	**7a**	**7b**	**7d**
supported on Merrifield	47	75	100
supported on Wang	57	50	62
supported on Tentagel S-NH_2	0	32	42

TABLE 3. Loading of Different Polymer-Bound Pyrimidinones and Yields of Their Acylating Reaction of Benzylamine

linker	R	R_1	cleavage with oxone yield (%)	formation of amide yield (%)
3	CH_3	OH	90	100
16a	H	OH	90	97
16b	$CH_2CH_2CH_3$	OH	75	65
16c	OH	NH_2	50	36

the low yield was explained considering the scarce stability of the resin in the conditions used for the cleavage.

Taking into account the results obtained with both Wang and TentaGel S-NH_2 resin, we concluded that our microwave-assisted synthesis can have a general applicability and can be efficiently used for the preparation of pyrimidinones anchored on structurally different polymers.

We thought therefore to investigate the acylation reaction of the solid-supported pyrimidinones **10** and **13** (Scheme 4) using three acylating agents endowed with decreasing electrophilicity: *p*-bromobenzoyl chloride, benzoyl chloride, and acetyl chloride. Reaction with benzylamine using the corresponding solid-supported acylating agents **14** and **15** was used to estimate the loading (Table 2).

The Wang resin showed to be endowed with an intermediate reactivity and to give the best results among all the solid supports with acetyl chloride (57% yield for **7a**). The TentaGel S-NH_2 resin was the less reactive and was completely not reactive with acetyl chloride (0% yield for **7a**). Considering its good reactivity and its lower cost, the Merrifield resin resulted to be the best resin for our goals, and it was used for all the following studies.

Preparation of Different Polymer-Bound Acylating Agents. The reactivity of different polymer-bound pyrimidinones was also investigated.

To this aim 2-thiouracil, 6-propyl-2-thiouracil, and 6-amino-2-thiouracil, respectively, were anchored on the solid support **4** (Scheme 5) following the usual procedure under microwave irradiation (130 °C, 5 min) affording the corresponding solid-supported pyrimidinones **16(a−c)**. Cleavage with Oxone was used to calculate the loading.

Acylation of **16(a−c)** with *p*-bromobenzoyl chloride gave the corresponding polymer-bound acylating agents, which were used to acylate benzylamine. The yield of the corresponding amides gives an idea of the acylating ability of the synthesized SSRs (Table 3).

The results thus obtained showed that the substitution in the 6 position with a bulky substituent (linker **16b**) determines a decrease in the reactivity of the system, whereas the use of an unsubstituted system (linker **16a**) implies similar results. On the other hand, very poor yields are obtained using structurally different linkers such as the cytosinic **16c**. These observations together with the lower cost of 6-methyl-2-thiouracil prompted us to use the 6-methyl-substituted linker **3** for all of the following studies.

Acylation of a Series of Amines by the Use of 2d and 2g. Taking into account the results obtained with benzylamine, a series of reactions were carried out on different amines **17** (Scheme 6) using the SSRs **2b**, **2d**, and **2g**, which had proved to be the best acylating agents, to give the corresponding amides **18(a−k)** (Table 4).

N-Pentylamine, an aliphatic primary amine, was first acylated with **2d** in CH_2Cl_2 for 48 h, and the reaction

SCHEME 6. Microwave-Assisted Synthesis of a Series of Amides by Use of SSR of Type 2

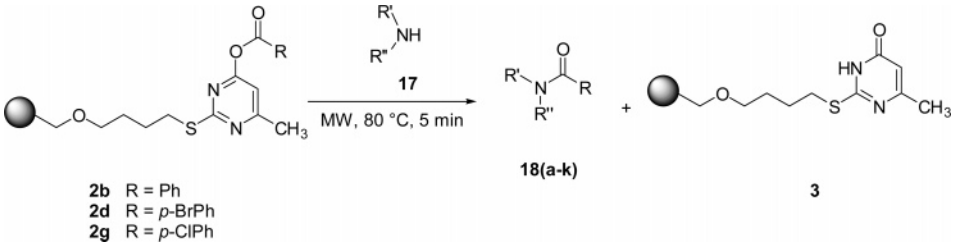
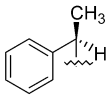
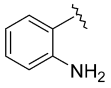


TABLE 4. Results of Acylation of a Series of Amines by Use of SSR of Type 2

Compd	R	R'	R''	Yield (%)
18a	*p*-BrPh	H	$CH_3CH_2CH_2CH_2CH_2$-	70
18b	*p*-BrPh	CH_2=$CHCH_2$-	CH_2=$CHCH_2$-	99
18c	*p*-BrPh	H		90
18d	*p*-BrPh	H		53
18e	*p*-ClPh	H	$CH_3CH_2CH_2CH_2CH_2$-	30
18f	*p*-ClPh	CH_2=$CHCH_2$-	CH_2=$CHCH_2$-	30
18g	*p*-ClPh	H	$OHCH_2CH_2CH_2CH_2$-	70
18h	Ph	H	$CH_3CH_2CH_2CH_2CH_2$-	36
18i	Ph	CH_2=$CHCH_2$-	CH_2=$CHCH_2$-	38
18j	Ph	H	$OHCH_2CH_2CH_2CH_2$-	45
18k	Ph	$\{-CH_2CH_2OCH_2CH_2-\}$		42

was repeated under microwave irradiation in order to underline the advantages of using the "nonconventional" procedure. The corresponding amide **18a** was obtained in 75% and 70% yield, respectively, thus confirming the validity of the microwave-assisted procedure. Modest results were obtained when the reaction was performed with different SSRs such as **2b** and **2g**: the corresponding amides **18h** and **18e** were obtained in 36% and 30% yield, respectively. When used to acylate the secondary amine diallylamine, **2d**, **2b**, and **2g** afforded analogous results giving **18b** in an excellent yield (99%) and **18f** and **18i** in 30% and 38% yield, respectively, thus confirming the better acylating properties of **2d** with respect to those of **2b** and **2g**. Then enantiomerically pure (*R*)-(+)-α-methylphenylamine was acylated to study the problem of racemization under microwave irradiation. The reaction was carried out using the traditional method and under microwave irradiation, giving **18c** in 98% and 90% yield, respectively. The measurement of $[\alpha]_D$ and comparison with the one obtained using traditional methods showed the absence of racemization. When **2d** was used to acylate 1,2-phenylendiamine, the monoacylated product **18d** was obtained in 53% yield, while the cyclodehydrated benzoimidazole,[23] deriving from the intramolecular nucleophilic attack of the amino group on the amidic C=O, was isolated only in traces from the reaction.

To test the selectivity of our SSR, 1,4-aminobutanol was used as substrate for the acylation with **2g**: the corresponding amide **18g** was obtained in 70% yield with both methods, thus showing the chemoselectivity of the acylating agent. A relatively modest yield was also observed in the acylation of the cyclic amine morpholine with **2b**, which afforded the corresponding amide **18k** in 42% yield.

Acylation of a Series of Alcohols, Phenols, and Thiophenols. To study the applicability of the methodology we had set up, the acylation of a number of different substrates, namely, alcohols, phenols, and thiophenols, was then attempted.

In a first experiment, the SSR **2d** was treated with dry CH_2Cl_2, and benzylic alcohol was added to the suspension. After removal of the solvent under a stream of nitrogen, the reaction mixture was irradiated for 5 min, but no ester was detected at the end of the reaction. Only

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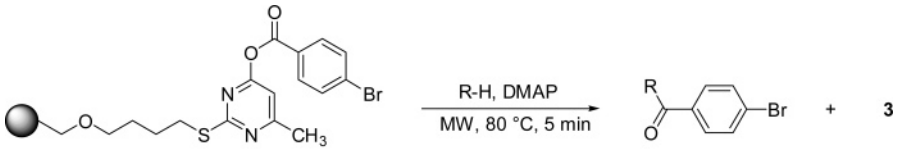
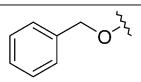
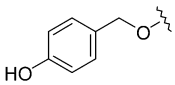
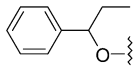
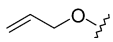
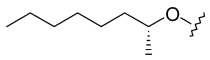
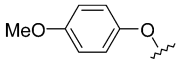
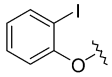
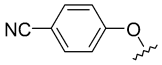
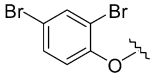
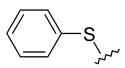
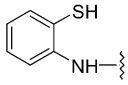
SCHEME 7. Microwave-Assisted Acylation of Alcohols, Phenols, and Thiophenols by Use of the SSR 2d



2d **19(a-h)**

TABLE 5. Results of Acylation of a Number of Different Substrates under Microwave Irradiation Using SSR 2d

Compound	R	Yield (%)
19a		50
19b		35
19c		45
19d		45
19e		25
19f		65
19g		25
19h		65
19i		45
19j		50
19k		0

after the addition of 1 equiv of DMAP could the desired product be obtained in a 50% acceptable yield (Scheme 7).

The acylation of a series of substrates was then investigated, and the results of the formation of the corresponding esters or thioesters **19(a−k)** are reported in Table 5.

Analyzing the data reported in Table 5, a series of comments can be made:

• Primary and secondary alcohols show almost the same reactivity.

• Phenols are generally more reactive than alcohols, with the exception of *ortho*-substited ones as a result of the steric hindrance.

• Enantiomerically pure alcohols do not undergo racemization after acylation.

• In the case of the acylation of 2-amino-thiophenol, the more nucleophilic amino group is the first to react, giving the corresponding amide **18k**, which then undergoes water elimination to give the corresponding cyclodehydrated benzothiazole as the only product of the reaction; this observation is in accordance with the results recently reported by Janda et al., who has described the possibility of preparing benzothiazoles using polymer-bound esters in the presence of of a Lewis acid in standard conditions (toluene as solvent, reflux temperature).[23]

• The yields of the reactions were modest, and the attempt to improve them by repeating the irradiation or using an excess of the SSR was unsuccessful; in all cases, unreacted starting material was recovered at the end of the reaction with no evidence of byproducts.

• As a result of difficulties in the elimination of the unreacted starting material with a simple workup or by the use of solid-supported scavangers (sulfonyl chloride polymer-bound,[24] propionyl chloride functionalized silica gel[25]), even after MW irradiation, purification of the product by column chromatography is necessary.

• The use of MW irradiation was of primary importance in this kind of transformation; in fact, the desired products could be isolated from the reactions repeated in standard conditions (DMAP, DMF, 80 °C, 24 h) only in traces.

Conclusions

A number of SSRs able to acylate structurally different substrates have been rapidly and efficiently synthesized using MW irradiation. They can be used to acylate both primary and secondary amines and enantiomerically pure amines without any racemization; the corresponding amides can be obtained in high yields. Appreciable yields can also be obtained in the acylation of alcohols, phenols, and thiophenols with **2d** in the presence of DMAP. The byproduct of the acylation reaction, the polymer-bound pyrimidinone **3**, can be recycled at least three times without observing variations in the acylating ability of the corresponding solid-supported acylating agent.

All of the reactions were performed under microwave irradiation and afforded, after the cleavage step, pure compounds without any need of purification except in the case of the acylation of alcohols, when column chromatography was used in order to obtain a pure compound.

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The methodology we have developed, which proved to be cheap, rapid, and efficient, is particularly interesting for its applicability to the preparation of libraries of structurally different amides.

Moreover, the possibility to obtain, in a rapid and efficient fashion, a family of compounds structurally related to **3** having different substituents in 5 is particularly interesting if we consider potential modifications at different molecular sites[26] or coupling with sugars to afford solid-supported nucleosides.[27]

Experimental Section

General Considerations Reagents were obtained from commercial suppliers and used without further purifications. Merrifield's peptide resin cross-linked 1% DVB, 200−400 mesh, 1.0−1.5 mmol Cl^-/g; Wang resin cross-linked 1% DVB, 200−400 mesh, ∼1.0 mmol/g resin; and TentaGel S-NH_2 resin 150−200 mesh, 0.45 mmol/g resin were used. Solvents were dried before use (CH_2Cl_2 and CH_3CN over CaH_2).

Melting points are uncorrected. ^{1}H NMR spectra were measured at 200 MHz. Chemical shifts are reported relative to TMS at 0.00 ppm. EI low-resolution MS spectra were recorded with an electron beam of 70 eV.

Microwave reactions were conducted using a machine consisting of a continuous focused microwave power delivery system with operator-selectable power output from 0 to 300 W. The reactions were performed in a round-bottom flask equipped with a condenser. The temperature of the contents of the vessel was monitored using a calibrated infrared temperature control mounted under the reaction vessel. All experiments were performed using a stirring option whereby the contents of the vessel were stirred by means of a rotating magnetic plate located below the floor of the microwave cavity and a Teflon-coated magnetic stir bar in the vessel. These reactions can also be conducted using a domestic microwave oven with a maximum emitted power of 800 W. Using a domestic oven, the temperature of the reaction mixture at the end of microwave irradiation was found to be 70−100 °C.

Polymer-Bound Alcohol 6. *t*-BuOK (1.2 g, 10.8 mmol) was dissolved in dry DMF (20 mL), and the solution was cooled to 0 °C. 1,4-Butanediol (957 μL, 10.8 mmol) was added, and the reaction mixture was kept at 0 °C for 1 h. Addition of **5** (3.0 g, 3.6 mmol Cl) was followed by irradiation at 130 °C for 5 min. The polymer was filtered, washed successively with H_2O (3 × 10 mL), EtOH, (3 × 10 mL), CH_2Cl_2 (3 × 10 mL), and Et_2O (3 × 10 mL), and then dried in vacuo at 20 °C for 4 h. IR (Nujol) 3429, 1054 cm^{-1}

Polymer-Bound Bromide 4. Polymer-bound **6** (3.0 g, 3.6 mmol OH) was suspended in DMF (10 mL) and swollen for 10 min. Then PPh_3 (3.6 g, 10.8 mmol) and CBr_4 (2.8 g, 10.8 mmol) were added, and the reaction mixture was irradiated at 130 °C for 5 min.The polymer was filtered, washed successively with water (3 × 30 mL), EtOH (3 × 30 mL), CH_2Cl_2 (3 × 30 mL), and Et_2O (3 × 30 mL), and then dried in vacuo at 20 °C for 4 h. The same procedure was used to prepare **9**, starting from **8**.

General Procedure for Synthesis of Linkers 3 and 16(a−c). Polymer-bound **4** (4.0 g, 4 mmol Br) was suspended in DMF (10 mL) and swollen for 10 min. Then the appropriate thiouracil or 6-hydroxythiocytosine (8 mmol) and K_3CO_3 (792 mg, 8 mmol) were added. The reaction mixture was then irradiated at 130 °C for 5 min. The polymer was filtered, washed successively with water (3 × 30 mL), EtOH (3 × 30 mL), CH_2Cl_2 (3 × 30 mL), and Et_2O (3 × 30 mL), and then dried in vacuo at 20 °C for 4 h. The same procedure was followed to prepare **13** starting from **12**. **3**, **16a**, and **16b**: IR (Nujol) 1645 cm^{-1}. **16c**: IR (Nujol) 3389, 1632 cm^{-1}. **13**: IR ($CHCl_3$) 1652 cm^{-1}

Polymer-Bound Chloride 12. TentaGel S-NH_2 resin (1.0 g, 0.45 mol of functional group) was suspended in DMF (8 mL) and swollen for 25 min. 4-Chloromethylbenzoic acid (153.5 mg, 0.9 mmol), HOBt (243.2 mg, 1.8 mmol), and EDC (258.8 mg, 1.35 mmol) were then added. The reaction mixture was stirred at room temperature for 4 h. The polymer was filtered, washed with water (3 × 10 mL), EtOH (3 × 10 mL), CH_2Cl_2 (3 × 10 mL), and Et_2O (3 × 10 mL), and then dried in vacuo at 20 °C for 4 h. IR ($CHCl_3$) 3505, 1680 cm^{-1}

General Procedure for Synthesis of Solid-Supported Reagents 2(a−h). Compound **3** (500 mg, 0.5 mmol of functional group) was dissolved in 3 mL of CH_2Cl_2 and swollen for 10 min. Then pyridine (243 μL) and the appropriate acyl chloride (2 mmol) were added. After evaporation of the solvent under a stream of nitrogen, the reaction mixture was irradiated at 80 °C for 5 min. The resin was washed with CH_2Cl_2 (3 × 10 mL), toluene (3 × 10 mL), and Et_2O (3 × 10 mL) and then dried in vacuo at 20 °C for 4 h. The same procedure was followed to prepare **14(a−c)** and **15(a−c)**. **2a**: IR (Nujol) 1774, 1269, 1145 cm^{-1}. **2b**: IR (Nujol) 1744, 1232, 1149 cm^{-1}. **2c**: IR (Nujol) 1739, 1234, 1150 cm^{-1}. **2d**: IR (Nujol) 1719, 1234, 1148 cm^{-1}. **2e**: IR (Nujol) 1734, 1230, 1150 cm^{-1}. **2f**: IR (Nujol) 1744, 1215, 1153 cm^{-1}. **2g**: IR (Nujol) 1747, 1234, 1162 cm^{-1}. **2h**: IR (Nujol) 1742, 1224, 1110 cm^{-1}. **14a**: IR (Nujol) 1774, 1269, 1145 cm^{-1}. **14b**: IR (Nujol) 1744, 1232, 1149 cm^{-1}. **14c:** IR (Nujol) 1719, 1234, 1148 cm^{-1}. **15a:** IR (Nujol) 1770, 1674, 1146 cm^{-1}. **15b**: IR (Nujol) 1747, 1644, 1153 cm^{-1}. **15c**: IR (Nujol) 1718, 1647, 1150 cm^{-1}

General Procedure for Synthesis of Amides 7(a−h) and 18(a−k). Polymer **2(a−h)** (500 mg, 0.5 mmol of functional group) was suspended in CH_2Cl_2 (3 mL) and swollen for 10 min. The appropriate amine (0.5 mmol) was added, the solvent was evaporated under a stream of nitrogen, and the reaction mixture was irradiated at 80 °C for 5 min. The polymer was washed with CH_2Cl_2 (5 × 20 mL) and filtered. The organic solution was washed with 1 N HCl, dried over anhydrous Na_2SO_4, and filtered, and the solvent evaporated under reduced pressure. The corresponding amides were obtained pure without need of further purification. **7a**, **7b**, and **7d** could be obtained in a similar fashion starting from **14(a−c)** or **15(a−c)** in the presence of benzylamine. **18a**: mp 94−96 °C; ^{1}H NMR ($CDCl_3$) δ 7.63−750 (m, 4H), 6.14 (s, 1H), 3.40 (q, 2H, J = 6.7 Hz), 1.62−1.52 (m, 2H), 1.36−1.15 (m, 4H), 0.91−0.89 (m, 3H); IR ($CHCl_3$) 3001, 1659 cm^{-1}. Anal. Calcd for $C_{12}H_{16}BrNO$: C, 53.35; H, 5.97; N, 5.18. Found: C, 53.48; H, 5.97; N, 5.16. **18d**: ^{1}H NMR (CD_3OD) δ 7.89−7.63 (m, 4H), 7.18−7.02 (m, 2H), 6.70−6.09 (m, 2H). Anal. Calcd for $C_{13}H_{11}BrN_2O$: C, 53.63; H, 3.81; N, 9.62. Found: C, 53.79; H, 3.81; N, 9.64. **18e**: mp 60−61 °C; ^{1}H NMR ($CDCl_3$) δ 0.80−0.97 (m, 3H), 1.23−1.37 (m, 4H), 1.56−1.63 (m, 2H), 3.35−3.45 (m, 2H), 6.14 (s, 1H), 7.37 (d, 2H, J = 8.4 Hz), 7.67 (d, 2H, J = 8.4 Hz). Anal. Calcd for $C_{12}H_{16}ClNO$: C, 63.85; H, 7.14; N, 6.21. Found: C, 63.92; H, 7.10; N, 6.23.

General Procedure for Synthesis of Esters and Thioesters 19(a−j). Polymer **2d** (500 mg, 0.5 mmol of functional group) was suspended in CH_2Cl_2 (3 mL) and swollen for 10 min. Then DMAP (0.5 mmol) and the appropriate alcohol, phenol, or thiophenol (0.5 mmol) were added. After evaporation of the solvent under a stream of nitrogen, the reaction mixture was irradiated at 80 °C for 5 min (2 × 3 min). The polymer was washed with CH_2Cl_2 (5 × 20 mL). The organic solution was dried over anhydrous Na_2SO_4 and filtered, and the solvent was removed under vacuum. Purification by flash chromatography afforded pure **19(a−j). 19b**: ^{1}H NMR ($CDCl_3$) δ 8.06−7.90 (m, 2H), 7.68−7.47 (m, 4H), 7.23−7.19 (m, 2H). Anal. Calcd for $C_{14}H_{11}BrO_3$: C, 54.75; H, 3.61. Found: C, 54.89; H, 3.62. **19c**: ^{1}H NMR ($CDCl_3$) δ 7.93 (d, 2H, J = 8.6 Hz), 7.57 (d, 2H, J = 8.6 Hz), 7.40−7.27 (m, 5H), 5.89 (t, 1H, J = 6.7 Hz), 2.02 (dq, 2H, J = 7.2 Hz, J = 6.7 Hz), 0.95 (t, 3H, J = 7.2

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Hz); IR ($CHCl_3$) 1716, 1271. Anal. Calcd for $C_{16}H_{15}BrO_2$: C, 60.21; H, 4.74. Found: C, 60.32; H, 4.74. **19d**: ^1H NMR ($CDCl_3$) δ 7.90 (d, 2H, J = 7.9 Hz), 7.56 (d, 2H, J = 7.9 Hz), 6.08−5.95 (m, 1H), 5.43−5.25 (m, 2H), 4.81−4.78 (m, 2H). Anal. Calcd for $C_{10}H_9BrO_2$: C, 49.82; H, 3.76. Found: C, 49.98; H, 3.75. **19e**: ^1H NMR ($CDCl_3$) δ 7.87 (d, 2H, J = 8.4 Hz), 7.55 (d, 2H, J = 8.4 Hz), 5.12 (m, 1H), 1.90−1.50 (m, 2H), 1.39−1.19 (m, 11H), 0.91−0.87 (m, 3H). Anal. Calcd for $C_{15}H_{21}BrO_2$: C, 57.52; H, 6.76. Found: C, 57.44; H, 6.77. **19g**: ^1H NMR ($CDCl_3$) δ 8.11 (d, 2H, J = 8.4 Hz), 7.88−7.84 (m, 1H), 7.66 (d, 2H, J = 8.4 Hz), 7.43−7.36 (m, 1H), 7.23−7.21 (m, 1H), 7.04−6.97 (m, 1H). Anal. Calcd for $C_{13}H_8BrIO_2$: C, 38.74; H, 2.00. Found: C, 38.64; H, 2.00. **19h**: mp 136−138 °C; ^1H NMR ($CDCl_3$) δ 8.04 (d, 2H, J = 8.7 Hz), 7.86−7.65 (m, 4H), 7.36 (d, 2H, J = 8.7 Hz); IR ($CHCl_3$) 2225, 1736 cm^{-1}. Anal. Calcd for $C_{14}H_8BrNO_2$: C, 55.66; H, 2.67; N, 4.64. Found: C, 55.74; H, 2.68; N, 4.63. **19i**: mp 163−164 °C; ^1H NMR ($CDCl_3$) δ 8.07 (d, 2H, J = 8.7 Hz), 7.79 (d, 1H, J = 2.1 Hz), 7.65 (d, 2H, J = 8.7 Hz), 7.49 (dd, 1H, J = 8.8 Hz, J = 2.1 Hz), 7.15 (d, 1 H, J = 8.8 Hz); IR ($CHCl_3$) 1735 cm^{-1}. Anal. Calcd for $C_{13}H_7Br_3O_2$: C, 35.90; H, 1.62. Found: C, 35.82; H, 1.62.

Acknowledgment. The University of Siena (PAR 2001) is gratefully acknowledged. M.B. wishes to thank the Merck Research Laboratories for the 2002 Academic Development Program (ADP) Chemistry Award.

Supporting Information Available: Analytical data for **7(a−h)**, **18(b−c)**, **18(f−k)**, **19a**, **19f**, and **19j**. This material is available free of charge via the Internet at http://pubs.acs.org.

JO048837Q