Microwave-Promoted Transformations: Fast and Chemoselective N-Acylation of Amino Alcohols Using Catalytic Amounts of Dibutyltin Oxide. Influence of the Power Output and the Nature of the Acylating Agent on the Selectivity

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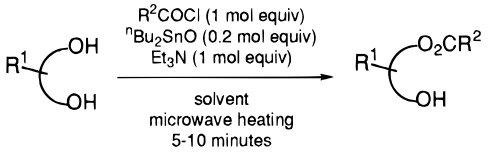
The influence of the nature of the acylating agent and the power output on the chemoselectivity of the microwave-mediated acylation of 1,2- and 1,3-amino alcohols catalyzed by dibutyltin oxide has been studied. The method constitutes an efficient procedure for the selective N-acylation of amino alcohols.

Microwave irradiation using either commercial or domestic microwave ovens is becoming a powerful technology to accelerate synthetically useful thermal organic reactions.[1] Although the reason of the rate acceleration is still not clear,[2] it is known that the higher the polarity, the more microwave energy is absorbed by the organic compound.[3] Usually, highly polar solvents have been employed in microwave-mediated transformations, the solvent being only a vehicle for the transmission of heat. Although the technique has been used many times, the issue of the selectivity has not been addressed.[4]

In our first contribution to the field,[5] we used an apolar solvent (toluene) for the rapid synthesis of dibutylstannylene acetals, finding that this reaction was 50−100 times faster under microwave irradiation than under standard thermal conditions. Although stannylene acetals are useful intermediates for the regioselective functionalization of diols, an inconvenient aspect is the long reaction time required for their formation.[6,7] In our first report,[5] we anticipated the possibility of modulating the selectivity of the process upon changing some experimental parameters, namely, (a) the use of either polar or nonpolar solvent (that is, absorbing or nonabsorbing microwave irradiation), (b) the proper selection of the power output of the microwave oven, and (c) the nature of the reactants.

Scheme 1



A further improvement of the tin-mediated regioselective acylation of diols was the discovery that the reaction could be carried out using catalytic amounts of dibutyltin oxide in the presence of an acylating agent and a base (Scheme 1).[8] Furthermore, in that paper, we showed that some of our expectations (namely, a and b indicated above) were realized.

In order to extend our work further as well as to test the influence of the acylating agent on the selectivity, we have applied the catalytic method to the acylation of amino alcohols. The rationale for the success of the catalytic method is diagramed in Scheme 2.

The first step of the reaction course would be the reaction of the amino alcohol **A** with dibutyltin oxide to give the *N*,*O*-dibutylstannylene acetal **B** and water. The reaction of **B** with the acyl chloride would afford the intermediate **C**, which, by reaction with the water molecule generated in the first step, would liberate the N-monoacylated amino alcohol **D** and the intermediate **E**. If the transformation is carried out in the presence of 1 equiv of a base, it would react with **E** to produce dibutyltin oxide, which could start a catalytic cycle. According to this simple idea, it is possible to use a catalytic amount of dibutyltin oxide to perform the

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(1) (a) For a recent review, see: Caddick, S. *Tetrahedron* **1995**, *51*, 10403−10432. For more recent applications, see: (b) Díaz-Ortíz, A.; Díez-Barra, E.; de la Hoz, A.; Prieto, P.; Moreno, A.; Langa, F.; Prangé, T.; Neuman, A. *J. Org. Chem.* **1995**, *60*, 4160−4166. (c) Raner, K. D.; Strauss, C. R.; Trainor, R. W.; Thorn, J. S. *J. Org. Chem.* **1995**, *60*, 2456−2460. (d) Khadilkar, B. M.; Gaikar, V. G.; Chitnavis, A. A. *Tetrahedron Lett.* **1995**, *36*, 8083−6. (e) Acosta, A.; de la Cruz, P.; de Miguel, P.; Díez-Barra, E.; de la Hoz, A.; Langa, F.; Loupy, A.; Majdoub, M.; Martín, N.; Sánchez, C.; Seoane, C. *Tetrahedron Lett.* **1995**, *36*, 2165−2168. (f) Bougrin, K.; Soufiaoui, M. *Tetrahedron Lett.* **1995**, *36*, 3683−3686. (g) Péra, E. R.; Marrero, A. L.; Pérez, R.; Autié, M. A. *Tetrahedron Lett.* **1995**, *36*, 1779−1782. (h) Srikrishna, A.; Kumar, P. P. *Tetrahedron Lett.* **1995**, *36*, 6313−6316. (i) Rault, S.; Gillard, A.-C.; Foloppe, M.-P.; Robba, M. *Tetrahedron Lett.* **1995**, *36*, 6673−6674. (j) Dayal, B.; Rapole, K. R.; Salen, G.; Shefer, S.; Tint, G. S.; Wilson, S. R. *Synlett* **1995**, 861−862. (k) Alajarín, R.; Jordán, P.; Vaquero, J. J.; Alvarez-Builla, J. *Synthesis* **1995**, 389−391. (l) Laurent, A.; Jacquault, P.; Di Martino, J.-L.; Hamelin, J. *J. Chem. Soc., Chem. Commun.* **1995**, 1101. (m) Majdoub, M.; Loupy, A.; Pettit, A.; Roudesli, S. *Tetrahedron* **1996**, *52*, 617−628.

(2) Mingos, M. P.; Baghurst, D. R. *Chem. Soc. Rev.* **1991**, *20*, 1−47.

(3) Giguere, R. J. *Org. Synth.: Theory Applications* **1989**, *1*, 103−172.

(4) (a) Previous to our disclosure,[5] only one paper, discussing the effect of power output of the microwave oven on the selectivity of the sulfonation of naphthalene, had been reported; see: Stuerga, D.; Gonon, K.; Lallemant, M. *Tetrahedron* **1993**, *49*, 6229−6234. (b) For a recent paper dealing with the effect of the power output on the stereoselectivity of the Staudinger reaction, see: Bose, A. K.; Banik, B. K.; Manhas, M. S. *Tetrahedron Lett.* **1995**, *36*, 213−216.

(5) Morcuende, A.; Valverde, S.; Herradón, B. *Synlett* **1994**, 89−91.

(6) For some reviews, see: (a) Grindley, T. B. In *Synthetic Oligosaccharides Indispensable Probes for the Life for the Life Sciences*; Kovács, P., ed.; ACS Symposium Series 560; American Chemical Society: Washington, DC, 1994; pp 51−76. (b) Pereyre, M.; Quintard. J.-P.; Rahm, A. *Tin in Organic Synthesis*; Butterworths: London, 1987; pp 261−285. (c) David, S.; Hanessian, S. *Tetrahedron* **1985**, *41*, 643−663.

(7) Usually, dibutylstannylene acetals are prepared by heating at reflux the diol (or polyol) and an equimolecular amount of dibutyltin oxide with azeotropic removal of water. The synthesis of dibutylstannylene acetals is faster in methanol, but this solvent must be removed prior to the addition of some electrophiles. Moreover, the use of methanol is incompatible with the presence of ester functionalities in the substrate, see: Chwang, T. L.; Némec, J.; Welch, A. D. *J. Carbohydr. Nucleosides Nucleotides* **1980**, *7*, 159−166.

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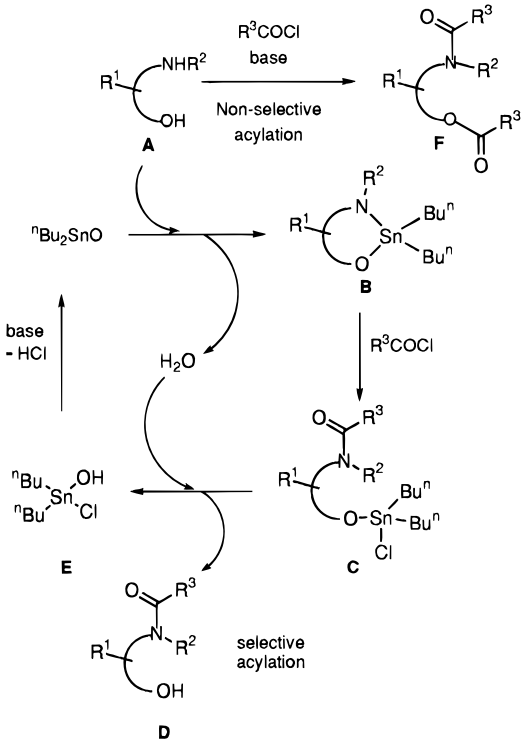
Scheme 2



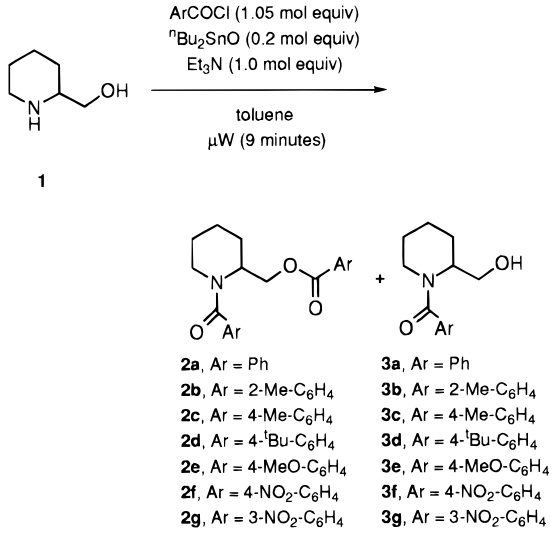
desired transformation, provided that a base is present. Under the standard thermal conditions for the formation of the stannylene acetal,[6] the non-tin-mediated acylation catalyzed by the base (to give **F**) is faster than the formation of the *N*,*O*-dibutylstannylene acetal; thus no advantage (that is, nonselective transformation) is attained from the presence of the tin-containing species. The formation of the *N*,*O*-dibutylstannylene acetal under microwave heating could be so fast that it would favorably compete with the non-tin-mediated acylation; thus, in principle, it may be possible to carry out selective acylations using catalytic amounts of dibutyltin oxide. The advantages of catalytic processes are evident: easier workup of the reaction and purification of the product as well as a more convenient method from an environmental point of view.[9]

In this paper, we report the successful implementation of this methodology to the chemoselective functionalization of 1,2- and 1,3-amino alcohols. Furthermore, the selectivity of the microwave-mediated acylation of amino alcohols using dibutyltin oxide as catalyst is dependent on both the power output of the microwave oven (reinforcing our previous finding[8]) and the nature of the acylating agent [i.e., our third expectation (c, see above) has been accomplished]. To the best of our knowledge, this is the first time that a chemoselective acylation of amino alcohols through *N*,*O*-stannylene acetals is reported.[10]

Results and Discussion

In the course of our work on the chemoenzymatic synthesis of chiral derivatives of piperidine (e.g., **1**, **4**, and **7**, Schemes 3−5),[11] we have required *N*-acyl derivatives of these amino alcohols (e.g., **3**, **6**, and **9**, Schemes 3−5).[12] Since the preparation of these targets using 1 molar equiv of an acylating agent and different basic catalyst under standard conditions failed in our hands,[13] we have tried our recently developed method of microwave-mediated acylation catalyzed by dibutyltin oxide.[8] In this paper we report that the desired transformations of acyclic and heterocyclic 1,2- and 1,3-amino alcohols are achieved in just a few minutes with moderate to excellent selectivities.[14]

Scheme 3



The microwave-promoted acylation of 2-(hydroxymethyl)piperidine (**1**) catalyzed by dibutyltin oxide (Scheme 3) has been carried out at various power outputs of the microwave oven and using differently substituted

(9) The advantages of catalytic processes have been discussed elsewhere, see: Seebach, D. *Angew. Chem., Int. Ed. Engl.* **1990**, *29*, 1320−1367.

(10) *N*,*O*-Stannylene acetals have been used for the synthesis of diester diamides macrocycles through the *N*,*O*-diacylation, see: Maccioni, E.; Sinico, C. *J. Heterocycl. Chem.* **1994**, *31*, 1673−1679.

(11) Ors, M.; Morcuende, A.; Jiménez-Vacas, M.-I.; Valverde, S.; Herradón, B. *Synlett* **1996**, 449−451.

(12) For some recent synthetic applications of derivatives of 2-(hydroxymethyl)piperidine, see: (a) Kozikowski, A. P.; Fauq, A. H.; Miller, J. H.; McKinney, M. *Bioorg. Med. Chem. Lett.* **1992**, *2*, 797−802. (b) Romo, D.; Meyer, S. D.; Johnson, D. D.; Schreiber, S. L. *J. Am. Chem. Soc.* **1993**, *115*, 7906−7. (c) Gurjar, M. K.; Ghosh, L.; Syamala, M.; Jayasree, V. *Tetrahedron Lett.* **1994**, *35*, 8871−8872. (d) Hart, D. J.; Wu, W.-L.; Kozikowski, A. P. *J. Am. Chem. Soc.* **1995**, *117*, 9369−9370. (e) For a recent application of derivatives of 3-(hydroxymethyl)-piperidine, see: Wirz, B.; Walther, W. *Tetrahedron: Asymmetry* **1992**, *3*, 1049−1054. For recent applications of derivatives of 2-(2-hydroxyethyl)piperidine, see: (f) Ito, M.; Maeda, M.; Kibayashi, C. *Tetrahedron Lett.* **1992**, *33*, 3765−3768. (g) Ina, H.; Ito, M.; Kibayashi, C. *J. Org. Chem.* **1996**, *61*, 1023−1029. (h) Amino alcohol derivatives are useful auxiliaries for organic synthesis, see: Tillyer, R. D.; Boudreau, C.; Tschaen, D.; Dolling, U.-H.; Reider, P. J. *Tetrahedron Lett.* **1995**, *36*, 4337−4340 and references cited therein.

(13) (a) Several bases (Et_3N, pyridine, $NaHCO_3$) and solvents (CH_2Cl_2, pyridine, dioxane/water) have been used to try to prepare **3** and **6**. Beside the desired *N*-acyl derivatives (compounds **3** and **6**), substantial amounts of *N*,*O*-diacylated products (**2** and **5**, respectively) and starting amino alcohols (**1** and **4**, respectively) have been isolated. One of the experimental difficulties we have observed with the isolation of the relatively polar *N*-acylderivatives of 2- and 3-(hydroxymethyl)-piperidine is that they are quite water soluble. The tin-mediated procedure avoids any water treatment. (b) We have also prepared the *N*,*O*-diacyl derivatives (**2** and **5**) using excess reagents. The selective ester hydrolyses ($LiOH/H_2O$/MeOH/THF and K_2CO_3/MeOH) of **2** and **5** have been tried; but we have always obtained mixtures of amino alcohols (**1** and **4**), monoacyl derivatives (**3** and **6**), and diacyl derivatives (**2** and **5**). It seems that *N*- to *O*-acyl migration is very easy in these systems, which would explain the lack of selectivity in these transformations. (c) For a recent report on easy *N*- to *O*-acyl migration in amino alcohol derivatives, see: Myers, A. G.; Gleason, J. L.; Yoon, T. *J. Am. Chem. Soc.* **1995**, *117*, 8488−8489. (d) For a recent two-step synthesis (*N*,*O*-diacylation and ester hydrolysis) of amino alcohols (with moderate overall yield), see: Chiacchio, U.; Casuscelli, F.; Corsaro, A.; Librrando, V.; Rescifina, A.; Romeo, R.; Romeo, G. *Tetrahedron* **1995**, *51*, 5689−5700.

Table 1. Results of the Microwave-Mediated Acylation of the Amino Alcohols 1, 4, 7, 10, 13, and 16 Catalyzed by Dibutyltin Oxide (Schemes 3−6)[a]

entry	starting material	acyl chloride	power output (W)	diacyl derivative (% yield)	monoacyl derivative (% yield)	selectivity[b]
1	**1**	PhCOCl	100	**2a** (5)	**3a** (81)	16
2	**1**	PhCOCl	445	**2a** (5)	**3a** (**93**)	**19**
3	**1**	PhCOCl	645	**2a** (11)	**3a** (83)	8
4	**1**	PhCOCl	815	**2a** (14)	**3a** (78)	6
5	**1**	2-MeC_6H_4COCl	100	**2b** (<2)	**3b** (79)	>40
6	1	2-MeC_6H_4COCl	445	**2b** (<2)	**3b** (69)	>35
7	**1**	2-MeC_6H_4COCl	645	**2b** (<2)	**3b** (**93**)	>**47**
8	**1**	2-MeC_6H_4COCl	815	**2b** (<2)	**3b** (85)	>43
9	**1**	4-MeC_6H_4COCl	100	**2c** (<2)	**3c** (**91**)	>**46**
10	**1**	4-MeC_6H_4COCl	250	**2c** (4)	**3c** (75)	19
11	**1**	4-MeC_6H_4COCl	445	**2c** (6)	**3c** (82)	14
12	**1**	4-MeC_6H_4COCl	645	**2c** (8)	**3c** (69)	9
13	**1**	4-MeC_6H_4COCl	815	**2c** (8)	**3c** (56)	7
14	**1**	4-$^tBuC_6H_4COCl$	100	**2d** (4)	**3d** (61)	15
15	**1**	4-$^tBuC_6H_4COCl$	445	**2d** (<2)	**3d** (**86**)	>**43**
16	**1**	4-$^tBuC_6H_4COCl$	815	**2d** (8)	**3d** (66)	8
17	**1**	4-$MeOC_6H_4COCl$	100	**2e** (<2)	**3e** (**79**)	>**40**
18	**1**	4-$MeOC_6H_4COCl$	250	**2e** (6)	**3e** (80)	13
19	**1**	4-$MeOC_6H_4COCl$	645	**2e** (7)	**3e** (65)	9
20	**1**	4-$MeOC_6H_4COCl$	815	**2e** (8)	**3e** (60)	7
21	**1**	4-$NO_2C_6H_4COCl$	100	**2f** (18)	**3f** (52)	3
22	**1**	4-$NO_2C_6H_4COCl$	250	**2f** (24)	**3f** (43)	2
23	**1**	4-$NO_2C_6H_4COCl$	445	**2f** (18)	**3f** (37)	2
24	**1**	4-$NO_2C_6H_4COCl$	645	**2f** (22)	**3f** (51)	2
25	**1**	3-$NO_2C_6H_4COCl$	250	**2g** (21)	**3f** (47)	2
26	**1**	3-$NO_2C_6H_4COCl$	445	**2g** (13)	**3f** (65)	5
27	**1**	3-$NO_2C_6H_4COCl$	815	**2g** (11)	**3f** (51)	5
28	**4**	PhCOCl	100	**5** (17)	**6** (58)	3
29	**4**	PhCOCl	250	**5** (9)	**6** (46)	5
30	**4**	PhCOCl	445	**5** (7)	**6** (73)	**10**
31	**4**	PhCOCl	815	**5** (11)	**6** (**83**)	8
32	**7**	PhCOCl	100	**8** (12)	**9** (68)	6
33	**7**	PhCOCl	250	**8** (8)	**9** (**80**)	10
34	**7**	PhCOCl	445	**8** (7)	**9** (74)	**11**
35	**7**	PhCOCl	645	**8** (11)	**9** (**82**)	7
36	**7**	PhCOCl	815	**8** (19)	**9** (76)	8
37	**10**	PhCOCl	100	**11**(29)	**12** (15)	<1
38	**10**	PhCOCl	250	**11** (22)	**12** (38)	2
39	**10**	PhCOCl	445	**11** (13)	**12** (46)	3
40	**10**	PhCOCl	815	**11** (23)	**12** (36)	2
41	**13**	PhCOCl	100	**14** (4)	**15** (68)	**17**
42	**13**	PhCOCl	645	**14** (6)	**15** (87)	14
43	**13**	PhCOCl	815	**14** (6)	**15** (**91**)	**15**
44	**16**	PhCOCl	100	**17** (14)	**18** (18)	1
45	**16**	PhCOCl	645	**17** (10)	**18** (**65**)	**6**
46	**16**	PhCOCl	815	**17** (15)	**18** (41)	3

[a] All the reactions have been carried out for an overall heating time of 9 mins, as indicated in the Experimental Section. All the yields refer to isolated, chromatographically homogeneous compounds. [b] See ref 14.

benzoyl chlorides as acylating agents. For the sake of comparison, all the reactions have been performed under identical conditions using toluene as solvent, and the procedure has not been optimized. The results of the acylations of **1** are indicated in entries 1−27 of Table 1.

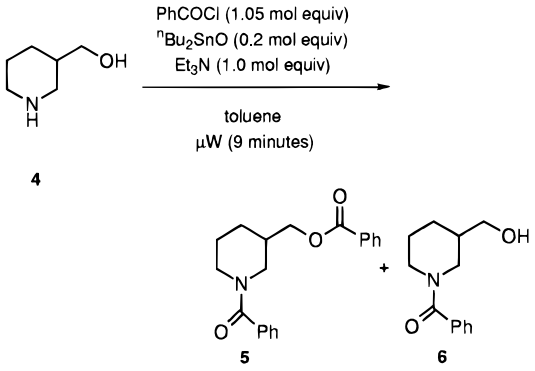
The ratio of monoacyl derivative **3** to diacyl derivative **2** (indicated as selectivity[14] in Table 1) probably reflects the competition between the two possible acylation routes: through the intermediary of the *N*,*O*-stannylene acetals **B**, resulting in chemoselective acylation to **D** (e.g., **3**), and the direct, nonselective, acylation to give the diacyl derivative **F** (e.g., **2**) (see Scheme 2).[15]

Thus, it is expected that the reactivity of the acylating agent influences the selectivity of the transformation. It is observed that the chemoselectivities of the acylations with the less reactive and sterically undemanding acyl chlorides, namely, 4-methylbenzoyl chloride (entries 9−13, Table 1) and 4-methoxybenzoyl chloride (entries 17−20), decrease on augmenting the power output. The amides **3c** and **3e** are obtained in excellent selectivities and yields when operating at low power output (entries 9 and 17, respectively). On the other hand, the reaction

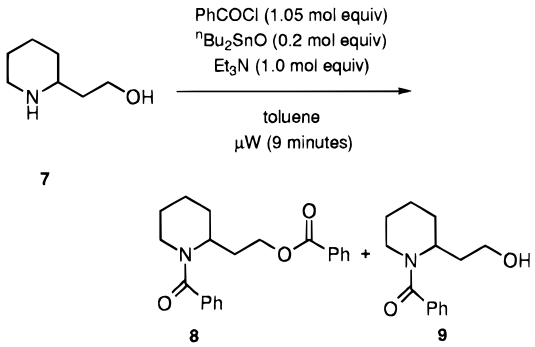
(14) The term selectivity indicated in Table 1 refers to the ratio of isolated yields of monoacyl to diacyl compounds. Because the ^1H and ^{13}C NMR spectra of these compounds are complex (due to conformational equilibria), it is difficult to determine accurately the proportion of the products of the transformation. Thus, the values of selectivity indicated in Table 1 are only approximate, although careful analysis of ^1H- and ^{13}C-NMR spectra of crude reaction products corroborate (in a semiquantitative manner) the values of selectivity indicated in Table 1.

(15) The product of the *O*-chemoselective monoacylation has not been detected in any case examined. The only reaction products have been the *N*-monoacyl derivatives and the *N*,*O*-diacyl derivatives and, in some experiments, starting amino alcohol. The latter has not been isolated and only detected by TLC and ^1H- and ^{13}C-NMR spectroscopies.

Scheme 4



Scheme 5

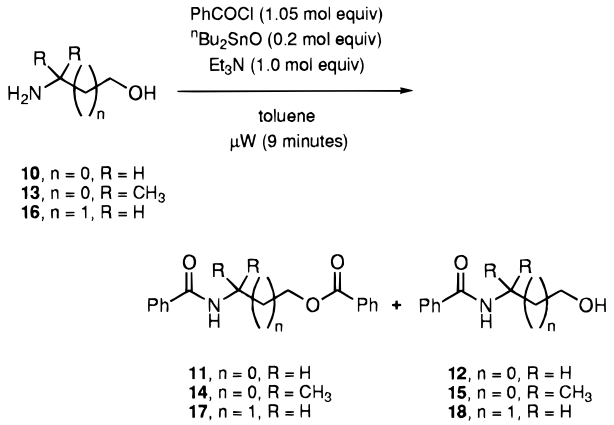


of **1** with 4-nitrobenzoyl chloride (entries 21−24, Table 1) shows poor selectivity at any power output tested. The same behavior, although with a slightly better selectivity, is observed when 3-nitrobenzoyl chloride is the acylating agent (entries 25−27), as expected from their respective reactivities versus nucleophiles. The selectivity of the acylation of the amino alcohol **1** using 4-*tert*-butylbenzoyl chloride is also dependent on the power output (entries 14−16), ranging from moderate to excellent (entry 15). The reactions with the sterically demanding, relatively unreactive, 2-methylbenzoyl chloride (entries 5−8) show good selectivity at all the power outputs examined, and the only difference between these experiments is the isolated yield of the monoacyl derivative **3b**. When benzoyl chloride is the acylating agent (entries 1−4), an intermediate situation is achieved: the selectivity is not so high as that of the acylation with electron-rich aroyl chlorides (entries 5−20) and it is higher than that of the acylation with nitrosubstituted aroyl chlorides (entries 21−27); the best selectivity and yield of **3a** is achieved at 445 W (entry 2).[16]

The method has also been applied to the benzoylation of the cyclic 1,3-amino alcohols **4** (Scheme 4) and **7** (Scheme 5), the acyclic 1,2-amino alcohols **10** and **13**, and the acyclic 1,3-amino alcohol **16** (Scheme 6). The results are indicated in Table 1 (entries 28−31, 32−36, 37−40, 41−43, and 44−46, respectively).

It is found that the selectivities of the acylations of the 1,3-amino alcohols **4** (entries 28−31, Table 1) and **7** (entries 32−36) are lower than the selectivity of the benzoylation of **1**. This fact probably reflects the higher difficulty of formation of the six-membered *N*,*O*-stannylene acetal as compared with the analogous five-membered ring.[17] In both cases, the selectivity is dependent on the power output of the microwave oven; it is observed that the selectivity increases with the power output up to a maximum (entries 30, 33 and 34) and then it decreases. Although the higher selectivity[14] in the benzoylation of **4** is achieved at 445 W (entry 30), the higher isolated yield of monoacylated product **6** is obtained at 815 W (entry 31), which indicates a higher conversion degree under this experimental condition. Similar behavior is observed in the benzoylation of the 1,3-amino alcohol **7**, the higher selectivity is achieved at 250 and 445 W (entries 33 and 34), but the higher isolated yield of the amide **9** is achieved at 645 W (entry 35). Although the selectivity is not excellent, it allows for preparation of the *N*-acyl derivatives **6** and **9** in synthetically useful yields (entries 30, 31, 33, and 35).

Scheme 6



The selectivities and conversions of the acylations of the acyclic amino alcohols **10**, **13**, and **16** (Scheme 6) are, in general, less dependent on the power output than those of the cyclic amino alcohols. It seems that both the selectivities and the conversions are mainly dependent on the solubility of the starting amino alcohol in toluene. Thus, the benzoylation of 2-aminoethanol at any power output (entries 37−40, Table 1) shows poor selectivity and overall yield; and even at 100 W, the main product is the dibenzoyl derivative **11**. Better selectivities are achieved when the alkyl substitution of the substrate increases. Hence, the acylation of the 1,2-amino alcohol **13** (entries 41−43) is good at any power output tested; a higher conversion is obtained at maximum power output, which allows one to obtain a synthetically useful yield of the monoacyl derivative **15** (entry 43). An intermediate situation is achieved using 3-aminopropanol (**16**) as substrate (entries 44−46): the selectivity is from low to moderate, depending on the power output.

Conclusions

Summarizing, it is demonstrated that the selectivity of microwave-mediated acylations depends on both the power output and the nature of the acylating agent. This result complements our earlier findings.[8] We now have several experimental parameters to modify in order to achieve high selectivity (*experimental modulation of the selectivity*) in microwave-mediated transformations.

(16) Previously, we reported[8] some preliminary results on the benzoylation of **1** using a different microwave oven operating at different power outputs (720, 465, and 305). Although the selectivities of our preliminary results were quite similar to that reported in the present paper, we observed some decomposition in some of the experiments reported previously. Now we have worked in a more concentrated solution (see Experimental Section), which seems fundamental to avoid decomposition of very polar substrates under microwave heating.

(17) Munavu, R. M.; Szmant, H. H. *J. Org. Chem.* **1976**, *41*, 1832−1836.

It is also noteworthy that, although the transformations reported in the present paper have not been optimized, excellent selectivities and conversions have been achieved in the chemoselective transformations of these amino alcohols (see entries 7, 9, 15, 17, 30, 33, and 43. Table 1), which has been difficult to achieve by conventional methods.[13a,d] Also the short reaction time is remarkable, which is important in some synthetic problems, for instance, for the preparation of isotopically labeled molecules,[18] as well as the fact that the reactions are carried out using catalytic amounts of dibutytin oxide,[19] avoiding any water treatment, which supposes an additional advantage when working with water-sensitive and/or water-soluble compounds.

Work is in progress in order to understand the origin of the selectivity in microwave-mediated transformations, to find new sources of selectivity of the dibutyltin oxide-catalyzed process, and to apply this methodology to further synthetic issues.

Experimental Section[20]

General Procedure for the Acylation of Amino Alcohols Catalyzed by Dibutyltin Oxide under Microwave Irradiation. A hetereogeneous mixture of the starting amino alcohol (either **1**, **4**, **7**, **10**, **13**, or **16**),[21] dibutyltin oxide (0.2 molar equiv), an acyl chloride chloride (1.05 molar equiv) (as indicated in Table 1), and triethylamine (1.0 mol equiv) in dry toluene (10−15 mL/mmol of starting amino alcohol) is heated in a microwave oven[22] at the power output indicated in Table 1 for 1 min.[23] After this heating, an interval of 30 s is allowed in order to avoid excessive evaporation of the solvent. This protocol is repeated until reaching an overall heating time of 9 min. The solid residue (if any)[24] is filtered off and washed with a small amount of CH_2Cl_2. The solvents are removed at room temperature under vacuum to give a crude material which is carefully analyzed by ^{1}H- and ^{13}C-NMR spectroscopies in order to determine the approximate ratio of acylated products.[14] The products are purified by flash chromatography[25] using hexane/ethyl acetate mixtures as eluent, to give the pure compounds in the isolated yields indicated in Table 1. The spectroscopic (*J* values in hertz) and analytical data of all the products are indicated below.

***N*-Benzoyl-2-[(benzoyloxy)methyl]piperidine (2a):** thick oil; IR (neat) 2940, 1720, 1630, 1445, 1425, 1270, 1115, 710 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.96 (broad d, J = 7.3, 2H), 7.48 (distorted dt, J = 1.3, 7.3, 1H), 7.36 (m, 2H), 7.29−7.19 (m, 5H), 4.85 (very broad s, 1H), 4.69 (distorted t, J = 10.1, 1H), 4.28 (dd, J = 5.8, 11.1, 1H), 3.90 (very broad s, 1H), 3.06 (distorted t, J = 12.9, 1H), 1.73−1.40 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 171.0 (s), 166.0 (s), 136.3 (s), 132.8 (d), 129.7 (s), 129.5 (d), 129.1 (d, 2C), 128.1 (d, 2C), 127.7 (d, 2C), 126.4 (d, 2C), 62.0 (t), 49.6 (d), 41.2 (t), 25.7 (t), 25.5 (t), 19.5 (t); MS (EI) *m*/*z* 323 (M^+, 0.4), 218 (0.9), 201 (2.8), 188 (37.7), 173 (3.9), 172 (2.3), 122 (3.9), 105 (100), 77 (29.9). Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.27; H, 6.55; N, 4.33. Found: C, 73.89; H, 6.57; N, 4.21.

***N*-Benzoyl-2-(hydroxymethyl)piperidine (3a):** mp 93−5 °C; IR (KBr) 3430, 2920, 1610, 1435, 1380, 1290, 1080, 1070, 1050, 790, 745, 710 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$) δ 7.33 (m, 5H), 4.45 (very broad s, 1H), 3.88 (dd, J = 9.4, 11.1, 1H), 3.58 (dd, J = 5.8, 11.1, 1H), 3.01−2.83 (m, 2H), 1.61−1.34 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 171.9 (s), 136.4 (s), 129.0 (d), 128.0 (d, 2C), 126.6 (d, 2C), 60.5 (t), 52.8 (very broad d), 41.8 (very broad t), 25.4 (t), 25.2 (t), 19.3 (t); MS (EI) *m*/*z* 219 (M^+, 0.4), 189 (8.4), 188 (52.5), 149 (3.0), 106 (11.6), 105 (100), 85 (13.8), 84 (18.2), 83 (22.7), 77 (49.7), 51 (10.5). Anal. Calcd for $C_{13}H_{17}NO_2$: C, 71.19; H, 7.82; N, 6.39. Found: C, 70.89; H, 7.81; N, 6.30.

***N*-(2-Methylbenzoyl)-2-[[(2-methylbenzoyl)oxy]methyl]piperidine (2b):** mp 93−6 °C; IR (KBr) 2935, 1720, 1630, 1428, 1310, 1265, 1140, 1085, 750 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) (mixture of rotamers) δ 7.98 (d, J = 7.6, 1H), 7.39 (t, J = 7.4, 2H), 7.20−6.85 (m, 13H), 5.41 (broad, s, 1H), 4.92−4.28 (m, 6H), 4.15−3.80 (m, 1H), 3.35 (broad d, J = 12.9, 1H), 3.16 (broad t, J = 12.9, 1H), 2.63 (s, 6H), 2.55 (m, 1H), 2.35 (s, 3H), 2.07 (s, 3H), 2.00−1.35 (m, 11H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) (mixture of rotamers) δ 170.1, 170.0, 166.5, 139.8, 136.2, 133.3, 131.5, 131.0, 130.3, 129.9, 129.6, 128.6, 127.9, 127.8, 125.8, 125.1, 124.8, 61.2, 46.1, 45.9, 42.8, 41.8, 36.5, 26.6, 26.3, 25.8, 25.4, 25.1, 24.9, 21.2, 19.1, 18.5, 18.1; MS (EI) *m*/*z* 351 (M^+, 0.2), 202 (21.7), 188 (3.9), 120 (11.3), 119 (100), 105 (13.7), 91 (35.8), 77 (6.0), 65 (11.7), 55 (6.0). Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.18; H, 7.17; N, 3.99. Found: C, 74.82; H, 7.27; N, 4.06.

2-(Hydroxymethyl)-*N*-(2-methylbenzoyl)piperidine (3b): mp 108−111 °C; IR (KBr) 3385, 2940, 1615, 1600, 1452, 1280, 1075, 785 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) (as a mixture of rotamers) δ 7.28−7.14 (m, 5H), 4.95 (broad s, 1H), 4.70 (broad, minor rotamer), 3.96−3.75 (m, 2H), 3.70−3.35 (broad m, minor rotamer), 3.31 (broad m, 1H), 3.07 (distorted t, J = 11.7, 1H), 2.83−2.68 (m, 1H), 2.36 (s, minor rotamer), 2.32 (s, 3H), 1.90−1.37 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) (as a mixture of rotamers) δ 171.8, 171.2, 170.8, 136.5, 136.4, 134.1, 133.4, 130.7, 130.1, 129.7, 128.4, 128.1, 126.5, 125.6, 125.0, 60.8, 59.5, 55.9, 55.2, 50.2, 43.6, 42.6, 36.9, 29.4, 26.0, 25.3, 24.7, 19.3, 18.7; MS (EI) *m*/*z* 233 (M^+, 0.15), 202 (14.7), 120 (10.1), 119 (100), 91 (27.7), 65 (12.9), 55 (10.7). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.06; H, 8.21; N, 6.01. Found: C, 72.17; H, 8.33; N, 5.91.

***N*-(4-Methylbenzoyl)-2-[[(4-Methylbenzoyl)oxy]methyl]piperidine (2c):** mp 123−6 °C; IR (KBr) 1725, 1625, 1430, 1285, 1275, 1125, 758, 752 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.90 (d, J = 8.0, 2H), 7.24 (d, J = 8.0, 2H), 7.19 (d, J = 7.8, 2H), 7.11 (d, J = 7.8, 2H), 4.95 (very broad s, 1H), 4.71 (distorted t, J = 10.0, 1H), 4.32 (dd, J = 5.8, 11.2, 1H), 4.05 (very broad s, 1H), 3.10 (distorted t, J = 12.5, 1H), 2.39 (s, 3H), 2.33 (s, 3H), 1.90−1.60 (m, 5H), 1.50 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 171.2 (s), 166.1 (s), 143.5 (s), 139.1(s), 133.3 (s), 129.5 (d, 2C), 128.9 (d, 2C), 128.7 (d, 2C), 126.9 (s), 126.5 (d, 2C), 61.8 (t), 49.7 (broad d), 41.5 (broad t), 25.5 (broad t, 2C), 21.4 (q), 21.1 (q), 19.5 (t); MS (EI) *m*/*z* 351 (M^+, 0.2), 215 (1.7), 202 (20.5), 129 (100), 91 (22.2), 65 (9.5), 55 (4.8). Anal. Calcd for $C_{22}H_{25}NO_3$: C, 75.18; H, 7.17; N, 3.99. Found: C, 74.91; H, 7.43; N, 3.92.

2-(Hydroxymethyl)-*N*-(4-methylbenzoyl)piperidine (3c): mp 105−8 °C; IR (KBr) 3390, 2945, 1610, 1435, 1375, 1270, 1050, 840, 835, 760 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.32 (dd, J = 1.7, 8.1, 2H), 7.20 (broad d, J = 8.1, 2H), 4.63 (broad s, 1H), 4.00−3.80 (very broad m, 1H), 3.96 (distorted t, J = 11.0, 1H), 3.70 (dd, J = 5.1, 11.0, 1H), 3.06 (broad m, 1H),

(18) Zijlstra, S.; de Groop, T. J.; Kok, L. P.; Visser, G. M.; Vaalburg, W. *J. Org. Chem.* **1993**, *58*, 1643−1645.

(19) Blank experiments, in the absence of dibutyltin oxide, showed that the procedure is catalytic. Thus, for example, the reaction of **1** with 4-methylbenzoyl chloride (1.05 molar equiv) and triethylamine (1.0 molar equiv) under microwave irradiation at 100 W, in the conditions reported in the Experimental Section, gave 11% of **2c** and 21% of **3c** in isolated yield (compare with entry 9, Table 1). On the other hand, the same reaction with 4-nitrobenzoyl chloride (1.05 molar equiv) at 250 W afforded 21% of **2f** and 34% of **3f** in isolated yield, which it is quite close to the result obtained in the presence of Bu_2SnO (compare with entry 22), which reinforces our hypothesis, indicated above, that the non-tin-mediated reaction with electron-poor acyl chloride competes with the formation of the *N*,*O*-stannylene acetals (see Scheme 2).

(20) For a general experimental procedure, see: Herradón, B.; Valverde, S. *Tetrahedron: Asymmetry* **1994**, *5*, 1479−1500. Unless otherwise indicated, all the NMR spectra were taken at 313 K.

(21) All the reactions were carried out at 1−5 mmol scale. The results are reproducible. Our limitation on scaling up further the reactions is the size of the microwave oven, which is compensated by the short reaction time.

(22) A Balay Model W-2235 microwave oven, operating at five different power outputs, as indicated in Table 1 [calibrated according to Watkins, K. W. *J. Chem. Ed.* **1983**, *60*, 1043−1044], was used.

(23) Previously[5] we carried out the reactions in an open Erlenmeyer flask. We have improved the glassware equipment by using an Erlenmeyer flask capped with an open spiralic stopper. Using this device, less evaporation of the solvent is observed.

(24) This solid residue consists mainly of unreacted starting material.

(25) Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923−2925.

2.38 (s, 3H), 1.72−1.54 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 172.4 (s), 139.2 (s), 133.5 (s), 128.8 (d, 2C), 126.6 (d, 2C), 60.8 (t), 53.1 (broad d), 41.9 (broad t), 25.5 (t), 25.3 (t), 21.1 (q), 19.5 (t); MS (EI) *m/z* 233 (M^+, 0.1), 202 (18.6), 120 (11.1), 119 (100), 91 (25.0), 65 (10.7), 55 (5.0). Anal. Calcd for $C_{14}H_{19}NO_2$: C, 72.06; H, 8.21; N, 6.01. Found: C, 72.30; H, 8.05; N, 5.90.

***N*-(4-*tert*-Butylbenzoyl)-2-[[(4-*tert*-butylbenzoyl)oxy]methyl]piperidine (2d):** mp 133−4 °C; IR (KBr) 2970, 1725, 1630, 1610, 1435, 1288, 1278, 1125, 855, 780, 710 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.95 (broad d, J = 8.6, 2H), 7.46 (t, J = 2.0, 1H), 7.43 (t, J = 1.8, 1H), 7.34−7.31 (m, 2H), 7.25−7.22 (m, 2H), 5.00 (very broad s, 1H), 4.71 (distorted t, J = 10.0, 1H), 4.36 (dd, J = 6.0, 11.3, 1H), 4.09 (very broad s, 1H), 3.12 (broad t, J = 14.1, 1H), 1.80−1.60 (m, 6H), 1.34 (s, 9H), 1.30 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) δ 171.5 (s), 166.5 (s), 156.8 (s), 152.5 (s), 133.5 (s), 129.7 (d, 2C), 127.0 (s), 126.5 (d, 2C), 125.4 (d, 2C), 125.3 (d, 2C), 62.1 (t), 35.1 (s), 34.7 (s), 31.2 (q, 3C), 31.1 (q, 3C), 26.0 (t), 25.8 (t), 19.8 (t);[26] MS (EI) *m/z* 435 (M^+, 0.02), 202 (4.5), 201 (4.7), 189 (10.1), 188 (66.5), 161 (3.3), 105 (100), 77 (34.7). Anal. Calcd for $C_{28}H_{37}NO_3$: C, 77.19; H, 8.57; N, 3.22. Found: C, 77.01; H, 8.82; N, 3.29.

***N*-(4-*tert*-Butylbenzoyl)-2-(hydroxymethyl)piperidine (3d):** mp 114−6 °C; IR (KBr) 3390, 2950, 2860, 1610, 1440, 1280, 1120, 1065, 1050, 1015, 845 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.36 (m, 4H), 4.60 (very broad s, 1H), 3.91 (broad t, J = 9.9, 1H), 3.66 (broad s, 1H), 3.20−2.60 (very broad s, 2H), 1.70−1.43 (m, 6H), 1.31 (s, 9H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 172.1 (s), 152.2 (s), 133.4 (s), 126.6 (d, 2C), 124.9 (d, 2C), 60.6 (t), 50.3 (broad d), 40.2 (broad t), 34.4 (s), 30.9 (q, 3C), 25.4 (t), 25.2 (t), 19.4 (t); MS (EI) *m/z* 275 (M^+, 0.2), 245 (4.6), 244 (21.7), 202 (3.2), 162 (14.7), 161 (100), 146 (7.5), 145 (3.1), 119 (14.9), 118 (9.3), 115 (6.2), 91 (8.0), 55 (5.1). Anal. Calcd for $C_{17}H_{25}NO_2$: C, 74.13; H, 9.16; N, 5.09. Found: C, 73.89; H, 8.99; N, 4.82.

***N*-(4-Methoxybenzoyl)-2-[[(4-methoxybenzoyl)oxy]methyl]piperidine (2e):** mp 88−92 °C; IR (KBr) 2940, 1715, 1608, 1510, 1420, 1260, 1170, 1105, 1030, 845, 770 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.97 (d, J = 8.8, 2H), 7.28 (dt, J = 1.9, 8.4, 2H), 6.91 (dt, J = 2.0, 9.0, 2H), 6.83 (dt, J = 2.1, 8.8, 2H), 4.93 (broad s, 1H), 4.72 (dt, J = 9.1, 11.2, 1H), 4.32 (dd, J = 5.8, 11.2, 1H), 4.06 (broad s, 1H), 3.86 (s, 3H), 3.80 (s, 3H), 3.13 (distorted t, J = 12.8, 1H), 1.85−1.40 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 171.2 (s), 166.0 (s), 163.5 (s), 160.5 (s), 131.9 (s), 131.7 (d, 2C), 128.2 (d, 2C), 122.2 (s), 113.6 (d, 2C), 113.4 (d, 2C), 61.9 (t), 55.3 (q), 55.2 (q), 49.8 (broad d), 41.4 (broad t), 25.8 (t), 25.7 (t), 19.6 (t); MS (EI) *m/z* 383 (M^+, 0.06), 218 (8.8), 203 (2.5), 152 (9.7), 135 (100), 107 (6.4), 92 (10.2), 77 (18.0). Anal. Calcd for $C_{22}H_{25}NO_5$: C, 68.90; H, 6.58; N, 3.65. Found: C, 69.06; H, 6.38; N, 3.45.

2-(Hydroxymethyl)-*N*-(4-methoxybenzoyl)piperidine (3e): mp 127−8 °C; IR (KBr) 3335, 2940, 1605, 1585, 1450, 1435, 1280, 1250, 1175, 1065, 1025, 845; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.40 (dd, J = 2.1, 6.7, 2H), 6.90 (dd, J = 2.1, 6.7, 2H), 4.60 (broad s, 1H), 3.94 (m, 1H), 3.82 (s, 3H), 3.70 (m, 1H), 3.06 (m, 1H), 2.83 (m, 1H), 1.78−1.48 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 172.5 (s), 160.6 (s), 128.9 (d, 2C), 128.6 (s), 113.6 (d, 2C), 61,3 (t), 55.2 (q), 53.4 (broad d), 42.0 (broad t), 25.6 (t), 25.5 (t), 19.7 (t); MS (EI) *m/z* 249 (M^+, 0.1), 218 (3.3), 202 (15.6), 135 (24.3), 120 (9.7), 119 (100), 91 (25.0), 77 (3.3), 65 (7.2), 43 (10.5). Anal. Calcd for $C_{14}H_{19}NO_3$: C, 67.43; H, 7.69; N, 5.62. Found: C, 67.25; H, 7.93; N, 5.59.

***N*-(4-Nitrobenzoyl)-2-[[(4-nitrobenzoyl)oxy]methyl]piperidine (2f):** mp 144−7 °C; IR (KBr) 2950, 2880, 1728, 1635, 1525, 1440, 1355, 1280, 1128, 1110, 1015, 870, 728 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.28 (broad d, J = 9.0, 2H), 8.23−8.15 (m, 4H), 7.42 (boad d, J = 8.8, 2H), 5.30 (very broad s, 1H), 4.88 (distorted t, J = 10.5, 1H), 4.39 (dd, J = 5.4, 11.3, 1H), 3.55 (very broad s, 1H), 3.22 (broad s, 1H), 1.93−1.41 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) δ 168.9 (s), 164.5 (s), 150.6 (s), 148.1 (s), 142.2 (s), 134.9 (s), 130.7 (d, 2C), 127.5 (d, 2C), 123.8 (d, 2C), 123.6 (d, 2C), 63.0 (t), 47.4 (broad d), 43.7 (broad t), 25.5 (broad t, 2C), 19.5 (t); MS (EI) *m/z* 413 (M^+, 0.2), 263 (1.2), 246 (2.7), 234 (15.1), 233 (100), 218 (6.9), 217 (4.5), 150 (88.1), 104 (16.6). Anal. Calcd for $C_{20}H_{19}N_3O_7$: C, 58.09; H, 4.64; N, 10.17. Found: C, 58.32; H, 4.75; N, 10.21.

2-(Hydroxymethyl)-*N*-(4-nitrobenzoyl)piperidine (3f): mp 153−4 °C; IR (KBr) 3410, 1620, 1600, 1525, 1445, 1350, 1060, 860, 715 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6, at 318 K) δ 8.27 (dt, J = 8.8, 2.1, 2H), 7.64 (dt, J = 8.8, 2.1, 2H), 4.74 (t, J = 5.5, 1H), 4.35 (very broad s, 1H), 3.67 (m, 1H), 3.45 (broad s, 1H), 2.95 (broad s, 1H), 1.80−1.30 (m, 6H); ^{13}C NMR (50.3 MHz, DMSO-d_6 at 353 K) δ 167.8 (s), 147.3 (s), 143.3 (s), 127.6 (d, 2C), 123.1 (d, 2C), 58.7 (t), 53.4 (broad d), 39.0 (broad t), 24.8 (t), 24.7 (t), 18.7 (t); MS (EI) *m/z* 264 (M^+, 0.2), 234 (13.5), 233 (74.7), 159 (3.2), 151 (14.4), 150 (100), 134 (5.6), 120 (15.7), 104 (43.0), 92 (15.6), 84 (8.3), 76 (31.5), 55 (13.0). Anal. Calcd for $C_{13}H_{16}N_2O_4$: C, 59.09; H, 6.11; N, 10.60. Found: C, 59.26; H, 5.98; N, 10.32.

***N*-(3-Nitrobenzoyl)-2-[[(3-nitrobenzoyl)oxy]methyl]piperidine (2g):** mp 113−7 °C; IR (KBr) 1730, 1640, 1615, 1535, 1350, 1240, 1210, 1125, 720 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.82 (broad s, 1H), 8.42 (ddd, J = 1.1, 2.3, 8.2, 1H), 8.36 (broad d, J = 7.8, 1H), 8.24 (ddd, J = 1.3, 2.3, 8.1, 1H), 8.12 (t, J = 1.9, 1H), 7.64 (m, 2H), 7.57 (t, J = 7.9, 1H), 5.10 (very broad m, 1H), 4.91 (dd, J = 9.5, 11.4, 1H), 4.42 (m, 1H), 3.85 (very broad m, 1H), 3.26 (m, 1H), 2.00−1.50 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 166.7 (s), 164.3 (s), 148.4 (s), 148.1 (s), 137.8 (s), 135.2 (d), 132.6 (d), 131.4 (s), 129.9 (d), 129.8 (d), 127.6 (d), 124.6 (d), 124.3 (d), 121.9 (d), 63.0 (t), 49.5 (broad d), 42.5 (broad t), 25.8 (t), 25.6 (t), 19.6 (t); MS (EI) *m/z* 414 (M + 1, 10.2), 413 (M^+, 0.4), 247 (5.1), 246 (6.3), 243 (8.7), 234 (15.6), 233 (100), 151 (7.8), 150 (84.0), 104 (10.8). Anal. Calcd for $C_{20}H_{19}N_3O_7$: C, 58.09; H, 4.64; N, 10.17. Found: C, 58.15; H, 4.74; N, 10.22.

2-(Hydroxymethyl)-*N*-(3-nitrobenzoyl)piperidine (3g): mp 116−8 °C; IR (KBr) 3390, 2950, 1625, 1530, 1480, 1445, 1350, 1290, 1280, 1055, 815, 735, 725 cm^{-1}; ^{1}H NMR (200 MHz, $CDCl_3$, at 298 K) δ 8.30−8.11 (m, 2H), 7.71 (broad d, J = 6.9, 1.3, 1H), 7.52 (broad t, J = 7.7, 1H), 4.79 (broad s, 1H), 4.44 (broad s, 1H), 4.20−2.60 (m, 4H), 1.59 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) (mixture of conformers) δ 169.4 (s), 147.8 (s), 138.0 (s), 132.8 (d), 129.4 (d), 123.9 (d), 122.1 (d), 60.3 (broad t), 55.2 (broad d, C-2 of one conformer), 51.4 (broad d, C-2 of one conformer), 44.0 (t, C-6 of one conformer), 37.4 (t, C-6 of one conformer), 25.3 (broad t, 2C), 19.3 (t); MS (EI) *m/z* 264 (M^+, 0.2), 234 (4.1), 233 (27.7), 150 (37.1), 104 (11.7), 84 (100), 76 (12.4), 56 (6.6), 55 (4.6). Anal. Calcd for $C_{13}H_{16}N_2O_4$: C, 59.09; H, 6.11; N, 10.60. Found: C, 59.36; H, 5.88; N, 10.22.

***N*-Benzoyl-3-[(benzoyloxy)methyl]piperidine (5):** mp 109−113 °C; IR (KBr) 2860, 1715, 1625, 1450, 1440, 1305, 1270, 715, 705 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.82 (very broad m, 2H), 7.53 (broad t, J = 7.7, 1H), 7.36 (m, 7H), 4.9−3.4 (very broad m, 4H), 3.00 (broad t, J = 11.8, 1H), 2.86 (broad t, J = 11.8, 1H), 2.07 (broad m, 1H), 1.95 (m, 1H), 1,74 (broad m, 1H), 1.60 (broad m, 1H), 1.41 (m, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$) (mixture of conformers) δ 170.4, 166.1, 136.24, 136.17, 132.93, 132.87, 129.9, 129.4, 129.3, 129.0, 128.7, 128.6, 128.34, 128.30, 128.26, 128.23, 126.7, 66.2, 51.0, 48.2, 45.3, 43.0, 36.4, 36.1, 29.5, 27.3, 24.6; MS (EI) *m/z* 219 (6.3), 201 (2.5), 189 (6.6), 188 (11.7), 173 (4.0), 141 (4.5), 127 (5.7), 123 (5.3), 119 (8.5), 109 (7.7), 106 (11.1), 105 (100), 96 (9.2), 85 (11.2), 83 (10.7), 81 (14.3), 77 (67.3), 75 (11.9), 71 (27.2), 70 (15.3), 69 (24.0), 57 (41.8), 56 (17.8), 55 (21.5), 43 (57.4), 41 (55.5). Anal. Calcd for $C_{20}H_{21}NO_3$: C, 74.27; H, 6.55; N, 4.33. Found: C, 74.02; H, 6.70; N, 4.33.

***N*-Benzoyl-3-(hydroxymethyl)piperidine (6):** mp 90−93 °C; IR (KBr) 3430, 2940, 2850, 1610, 1600, 1445, 1275, 690; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38 (m, 5H), 4.05 (broad m, 1H), 3.50 (very broad s, 2H), 3.40−2.55 (m, 3H), 1.85 (m, 2H), 1.85−1.30 (m, 3H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 170.5 (s), 135.9 (s), 129.3 (d), 128.1 (d, 2C), 126.6 (d, 2C), 63.9 (t), 48.3 (very broad t), 45.0 (very broad t), 38.4 (d), 26.8 (t), 24.4 (t); MS (EI) *m/z* 219 (M^+, 2.7), 218 (6.1), 215 (5.6), 203 (6.7), 203 (6.7), 202 (7.4), 189 (5.2), 188 (6.0), 184 (15.7), 168 (40.8), 155 (13.1), 141 (42.1), 140 (21.4), 139 (28.6), 128 (23.9), 127 (11.9), 115 (61.9), 105 (47.5), 92 (12.6), 77 (100), 64 (32.0), 51 (33.8). Anal. Calcd

(26) The signals of C-2 and C-6 are barely detected in the 45−40 ppm region, as very broad peaks.

for $C_{13}H_{17}NO_2$: C, 71.19; H, 7.82; N, 6.39. Found: C, 70.89; H, 8.07; N, 6.45.

***N*-Benzoyl-2-[(2-benzoyloxy)ethyl]piperidine (8):** thick oil; IR (neat) 2930, 1715, 1625, 1445, 1425, 1315, 1270, 1115, 1070, 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, at 298 K) δ 8.01−7.83 (m, 2H), 7.54 (m, 1H), 7.35 (m, 7H), 5.20−4.70 (m, 1H), 4.33 (m, 2H), 3.90−3.40 (m, 1H), 3.04 (m, 1H), 2.28 (m, 1H), 2.02 (m, 1H), 1.90−1.45 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 170.9 (s), 166.4 (s), 136.8 (s), 132.8 (d), 129.6 (d, 2C), 129.2 (s, d, 2C), 128.4 (d, 2C), 128.3 (d, 2C), 126.5 (d, 2C), 62.1 (t), 29.1 (t), 28.6 (t), 26.0 (t), 19.2 (t);[27] MS (EI) *m*/*z* 337 (M^+, 0.6), 232 (2.5), 215 (1.8), 189 (4.6), 188 (12.6), 122 (11.4), 110 (12.3), 105 (100), 77 (55.5), 51 (9.2).

***N*-Benzoyl-2-(2-hydroxyethyl)piperidine (9):** thick oil; IR (neat) 3400, 2950, 2870, 1605, 1445, 1275, 1065, 1055, 705 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.39 (m, 5H), 4.95 (broad s, 1H), 3.95 (broad s, exchange with D_2O, 1H), 3.64 (m, 2H), 3.50 (dq, J = 11.0, 3.0, 1H), 2.92 (distorted td, J = 11.0, 2.8, 1H), 2.04 (m, 1H), 1.99 (m, 1H), 1.75−1.44 (m, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$) δ 171.5 (s), 135.8 (s), 129.4 (d), 128.1 (d, 2C), 126.3 (d, 2C), 58.3 (t), 45.5 (d), 42.9 (t), 32.1 (t), 28.8 (t), 25.6 (t), 18.9 (t); MS (EI) *m*/*z* 233 (M^+, 0.6), 188 (6.6), 122 (22.6), 105 (100), 84 (12.2), 77 (43.2), 51 (14.4).

***N,O*-Dibenzoyl-2-aminoethanol (11):** mp 87−90 °C; IR (KBr) 3390, 1705, 1645, 1520, 1485, 1340, 1290, 1265, 710 cm^{-1}; ^1H-NMR (300 MHz, $CDCl_3$) δ 8.06 (m, 2H), 7.78 (m, 2H), 7.61−7.40 (m, 6H), 6.59 (broad s, 1H), 4.57 (t, J = 5.3, 2H), 3.88 (q, J = 5.3, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) δ 167.9 (s), 166.5 (s), 134.0 (s), 132.9 (d), 131.2 (d), 129.5 (s), 129.3 (d, 2C), 128.14 (d, 2C), 128.08 (d, 2C), 126.8 (d, 2C), 63.3 (t), 39.2 (t); MS (EI) *m*/*z* 269 (0.04), 226 (2.1), 164 (3.0), 147 (18.6), 134 (6.5), 122 (9.8), 105 (100), 77 (52.1), 51 (14.9). Anal. Calcd for $C_{16}H_{15}NO_3$: C, 71.35; H, 5.62; N, 5.20. Found: C, 71.15; H, 5.55; N, 5.08.

***N*-Benzoyl-2-aminoethanol (12):** mp 56−7 °C; IR (KBr) 3190, 2940, 1640, 1545, 1305, 1210, 1060, 1040, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, at 298 K) δ 7.72 (m, 2H), 7.49 (m, 1H), 7.41 (m, 2H), 6.85 (broad s, 1H), 3.81 (distorted t, J = 5.1, 2H), 3.61 (distorted t, J = 5.1, 2H), 3.35 (very broad s, 1H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) δ 168.7 (s), 133.7 (s), 131.3 (d), 128.2 (d, 2C), 126.8 (d, 2C), 61.1 (t), 42.5 (t); MS (EI) *m*/*e* 165 (M^+, 1.0), 147 (14.8), 134 (11.4), 122 (25.3), 105 (100), 77 (75.6), 51 (32.3), 50 (12.7). Anal. Calcd for $C_9H_{11}NO_2$: C, 65.42; H, 6.72; N, 8.48. Found: C, 65.21; H, 7.00; N, 8.54.

(27) The signals of C-2 and C-6 are barely detected in the 45−40 ppm region, as very broad peaks; the signals of these carbons appear at 45.6 and 43.0, respectively, when the spectrum is run at room temperature.

***N,O*-Dibenzoyl-2-amino-2-methyl-1-propanol (14):** mp 99−102 °C; IR (KBr) 3260, 1708, 1635, 1535, 1365, 1275, 1110, 705, 685 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, at 298 K) δ 8.06 (distorted td, J = 7.1, 1.5, 2H), 7.75 (distorted td, J = 6.6, 1.7, 2H), 7.58 (distorted tt, J = 1.6, 7.4, 1H), 7.51−7.39 (m, 5H), 6.50 (broad s, 1H), 4.55 (s, 2H), 1.59 (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) δ 167.2 (s), 166.8 (s), 135.2 (s), 133.2 (d, 2C), 131.2 (d), 129.7 (s), 129.5 (d, 2C), 128.4 (d, 2C), 128.2 (d), 126.7 (d, 2C), 70.1 (t), 54.2 (s), 23.9 (q, 2C); MS (EI) *m*/*z* 298 (M + 1, 0.4), 176 (4.0), 162 (23.0), 105 (100), 77 (21.1). Anal. Calcd for $C_{18}H_{19}NO_3$: C, 72.69; H, 6.44; N, 4.71. Found: C, 72.42; H, 6.65; N, 4.55.

***N*-Benzoyl-2-amino-2-methyl-1-propanol (15):** mp 88−90 °C; IR (KBr) 3305, 3195, 2980, 2900, 2860, 1630, 1580, 1545, 1490, 1315, 1070, 690 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.72 (m, 2H), 7.43 (m, 3H), 6.15 (broad s, 1H), 4.44 (t, J = 6.1, 1H), 3.72 (d, J = 6.1, 2H), 1.43 (s, 6H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) δ 168.3 (s), 134.5 (s), 130.9 (d), 127.9 (d, 2C), 126.6 (d, 2C), 69.8 (t), 55.5 (s), 23.5 (q, 2C); MS (EI) *m*/*z* 194 (M + 1, 0.4), 162 (14.4), 122 (9.6), 106 (7.9), 105 (100), 77 (34.9). Anal. Calcd for $C_{11}H_{15}NO_2$: C, 68.35; H, 7.83; N, 7.25. Found: C, 68.06; H, 8.21; N, 7.36.

***N,O*-Dibenzoyl-3-amino-1-propanol (17):** mp 46−50 °C; IR (KBr) 3320, 1720, 1645, 1540, 1275, 1115, 710 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, at 298 K) δ 8.12−8.02 (m, 2H), 7.70 (dd, J = 1.6, 6.9, 2H), 7.60−7.37 (m, 6H), 6.70 (broad s, 1H), 4.49 (t, J = 6.0, 2H), 3.61 (q, J = 6.3, 2H), 2.09 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) δ 167.5 (s), 166.7 (s), 134.3 (s), 132.9 (d), 131.2 (d), 129.8 (s), 129.4 (d, 2C), 128.3 (d, 2C), 128.2 (d, 2C), 126.8 (d, 2C), 62.5 (t), 36.8 (t), 28.6 (t); MS (EI) *m*/*z* 283 (M^+, 0.6), 178 (2.8), 161 (9.2), 105 (100), 77 (35.1), 56 (10.4). Anal. Calcd for $C_{17}H_{17}NO_3$: C, 72.05; H, 6.05; N, 4.95. Found: C, 71.89; H, 5.81; N, 4.87.

***N*-Benzoyl-3-amino-1-propanol (18):** mp 54−7 °C; IR (KBr) 3320, 2950, 1640, 1545, 1310, 1075, 710, 695 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$, at 298 K) δ 7.78 (m, 2H), 7.54−7.40 (m, 3H), 6.58 (broad s, 1H), 3.74 (broad m, 2H), 3.65 (q, J = 6.1, 2H), 2.86 (broad s, 1H), 1.86−1.78 (m, 2H); ^{13}C NMR (50.3 MHz, $CDCl_3$, at 298 K) δ 168.4 (s), 133.8 (s), 131.2 (d), 128.1 (d, 2C), 126.7 (d, 2C), 59.5 (t), 37.0 (t), 31.4 (t); MS (EI) *m*/*z* 179 (M^+, 0.9), 161 (7.8), 148 (3.0), 135 (17.7), 134 (11.4), 105 (100), 77 (54.2), 51 (12.3). Anal. Calcd for $C_{10}H_{13}NO_2$: C, 67.00; H, 7.32; N, 7.82. Found: C, 67.32; H, 7.29; N, 7.38.

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