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Facile Syntheses of Oxazolines and Thiazolines with *N*-Acylbenzotriazoles under Microwave Irradiation

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Microwave reactions of 2-amino-2-methyl-1-propanol (**2**) or 2-aminoethanethiol hydrochloride (**4**) with readily available *N*-acylbenzotriazoles **1a**−**j** in the presence of $SOCl_2$ produced 2-substituted 2-oxazolines **3a**−**j** in 84−98% yields and 2-substituted thiazolines **5a**−**i** in 85−97% yields, respectively. With use of this method chiral oxazoline **6**, bisoxazoline **7**, bisthiazoline **8**, and 5,6-dihydro-4*H*-1,3-oxazines **9** or **10** have also been prepared in 82−96% yields. These results demonstrate a new application of *N*-acylbenzotriazoles in the preparation of oxazolines and thiazolines under mild conditions and short reaction times with microwave irradiation.

Introduction

Oxazolines and thiazolines are important heterocycles.[1,2] 2-Oxazolines are structural entities in naturally occurring iron chelators,[3a,b] cytotoxic cyclic peptides,[3c,d] and antimitotic[3e] and neuroprotective agents.[3f] Well-known applications of 2-oxazolines include their use as synthetic intermediates,[4a,b] protecting groups,[4c] and chiral auxiliaries.[4d,e] Thiazoline derivatives possess anti HIV-1,[5a] antimitotic,[5b] and bioluminescent activities,[5c] and have recently found applications as building blocks in pharmaceutical drug discovery.[5d−f]

Reaction of carboxylic acids with amino alcohols is the most common method for the synthesis of oxazolines.[6a−f] Other carboxylate functionalities can be used in similar methods including imidate hydrochlorides,[6g] ortho esters,[6h] imino ether hydrochlorides,[6i] aldehydes,[6j] or nitriles.[6k−m] Thiazolines have been prepared (i) by the condensation of amino thiols with nitriles,[5a] esters,[7a] imino ethers[7b] or imino triflates,[7c] (ii) from *N*-acyl-2-aminoethanols[6a,7d] or *β*-hydroxy thioamides,[7e−g] or (iii) by multistep conversions from oxazolines.[7h]

However, there are limitations associated with these literature methods: direct conversions of carboxylic acids into the corresponding 2-oxazolines proceed with elimination of water at high temperatures (160−220 °C), require long reaction times (12−18 h), and frequently give low yields.[1a,8] Use of nitriles requires a Lewis acid and proceeds at high temperatures with elimination of ammonia.[6k] Other methods utilize complex reagents[6c,7f,g] or strongly acidic conditions.[6f] The problem of long reaction times in the synthesis of oxazolines has been solved to some extent by using microwaves,[6e,i,m] but the reported procedures that involve domestic ovens suffer from low reproducibility and lack general applicability.

(1) Frump, J. A. *Chem. Rev.* **1971**, *71*, 483.
(2) Fustero, S.; Salavert, E.; Navarro, A.; Mojarrad, F.; Fuentes, A. S. *Targets Heterocycl. Syst.* **2001**, *5*, 235; *Chem. Abstr.* **2001**, *138*, 221480.
(3) (a) Peterson, T.; Falk, K.-E.; Leong, S. A.; Klein, M. P.; Neilands, J. B. *J. Am. Chem. Soc.* **1980**, *102*, 7715. (b) Genet, J.-P.; Thorimbert, S.; Touzin, A.-M. *Tetrahedron Lett.* **1993**, *34*, 1159. (c) Hamada, Y.; Kato, S.; Shioiri, T. *Tetrahedron Lett.* **1985**, *26*, 3223. (d) Wipf, P.; Miller, C. P. *J. Am. Chem. Soc.* **1992**, *114*, 10975. (e) Li, Q.; Woods, K. W.; Claiborne, A.; Gwaltney, S. L., II; Barr, K. J.; Liu, G.; Gehrke, L.; Credo, R. B.; Hui, Y. H.; Lee, J.; Warner, R. B.; Kovar, P.; Nukkala, M. A.; Zielinski, N. A.; Tahir, S. K.; Fitzgerald, M.; Kim, K. H.; Marsh, K.; Frost, D.; Ng, S.-C.; Rosenberg, S.; Sham, H. L. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 465. (f) Campiani, G.; de Angelis, M.; Armaroli, S.; Fattorusso, C.; Catalanotti, B.; Ramunno, A.; Nacci, V.; Novellino, E.; Grewer, C.; Ionescu, D.; Rauen, T.; Griffiths, R.; Sinclair, C.; Fumagalli, E.; Mennini, T. *J. Med. Chem.* **2001**, *44*, 2507.
(4) (a) Meyers, A. I.; Mihelich, E. D. *Angew. Chem., Int. Ed. Engl.* **1976**, 270. (b) Reuman, M.; Meyers, A. I. *Tetrahedron* **1985**, *41*, 837. (c) Meyers, A. I.; Temple, D. L.; Haidukewych, D.; Mihelich, E. D. *J. Org. Chem.* **1974**, *39*, 2787. (d) Meyers, A. I. *Acc. Chem. Res.* **1978**, *11*, 375. (e) Gant, T. G.; Meyers, A. I. *Tetrahedron* **1994**, *50*, 2297.
(5) (a) Boyce, R. J.; Mulqueen, G. C.; Pattenden, G. *Tetrahedron Lett.* **1994**, *35*, 5705. (b) White, J. D.; Kim, T.-S.; Nambu, M. *J. Am. Chem. Soc.* **1995**, *117*, 5612. (c) Toya, Y.; Takagi, M.; Kondo, T.; Nakata, H.; Isobe, M.; Goto, T. *Bull. Chem. Soc. Jpn.* **1992**, *65*, 2604. (d) Einsiedel, J.; Hübner, H.; Gmeiner, P. *Bioorg. Med. Chem. Lett.* **2001**, *11*, 2533. (e) Zarantonello, P.; Leslie, C. P.; Ferritto, R.; Kazmierski, W. M. *Bioorg. Med. Chem. Lett.* **2002**, *12*, 561. (f) Wipf, P.; Reeves, J. T.; Balachandran, R.; Day, B. W. *J. Med. Chem.* **2002**, *45*, 1901.
(6) (a) Wenker, H. *J. Am. Chem. Soc.* **1935**, *57*, 9. (b) Vorbrüggen, H.; Krolikiewicz, K. *Tetrahedron Lett.* **1981**, *22*, 4471. (c) Vorbrüggen, H.; Krolikiewicz, K. *Tetrahedron Lett.* **1993**, *49*, 9353. (d) Cwik, A.; Hell, Z.; Hegedüs, A.; Finta, Z.; Horváth, Z. *Tetrahedron Lett.* **2002**, *43*, 3985. (e) Marrero-Terrero, A. L.; Loupy, A. *Synlett* **1996**, 245. (f) Bandgar, B. P.; Pandit, S. S. *Tetrahedron Lett.* **2003**, *44*, 2331. (g) Meyers, A. I.; Slade, J. *J. Org. Chem.* **1980**, *45*, 2785. (h) Kamata, K.; Agata, I.; Meyers, A. I. *J. Org. Chem.* **1998**, *63*, 3113. (i) Oussaid, B.; Berlan, J.; Soufiaoui, M.; Garrigues, B. *Synth. Commun.* **1995**, *25*, 659. (j) Badiang, J. G.; Aube, J. *J. Org. Chem.* **1996**, *61*, 2484. (k) Bolm, C.; Weickhardt, K.; Zehnder, M.; Ranff, T. *Chem. Ber.* **1991**, *124*, 1173. (l) Clarke, D. S.; Wood, R. *Synth. Commun.* **1996**, *26*, 1335. (m) Jnaneshwara, G. K.; Deshpande, V. H.; Lalithambika, M.; Ravindranathan, T.; Bedekar, A. V. *Tetrahedron Lett.* **1998**, *39*, 459.
(7) (a) Busacca, C. A.; Dong, Y.; Spinelli, E. M. *Tetrahedron Lett.* **1996**, *37*, 2935. (b) Boden, C. D. J.; Pattenden, G.; Ye, T. *Synlett* **1995**, 417. (c) Charette, A. B.; Chua, P. *J. Org. Chem.* **1998**, *63*, 908. (d) Nishio, T. *Tetrahedron Lett.* **1995**, *36*, 6113. (e) Wipf, P.; Fritch, P. C. *Tetrahedron Lett.* **1994**, *35*, 5397. (f) Lafargue, P.; Guenot, P.; Lellouche, J.-P. *Synlett* **1995**, 171. (g) Mahler, S. G.; Serra, G. L.; Antonow, D.; Manta, E. *Tetrahedron Lett.* **2001**, *42*, 8143. (h) Wipf, P.; Miller, C. P.; Venkatraman, S.; Fritch, P. C. *Tetrahedron Lett.* **1995**, *36*, 6395.
(8) Lion, C.; Dubois, J. E. *Tetrahedron* **1973**, *29*, 3417.

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N-Acylbenzotriazoles[9a] have hitherto been reported as versatile reagents for *N*-acylation,[9b] formylation,[9c] trifluoroacylation,[9d] *O*-acylation,[9e] *C*-acylation,[9f−h] and the synthesis of polycyclic heteroaromatics.[9i] We now apply *N*-acylbenzotriazoles in a mild and general procedure for the direct synthesis of 2-substituted 2-oxazolines and 2-substituted 2-thiazolines under microwave irradiation using a single mode cavity synthesizer,[10a] which ensures reproducibility and safety. Microwave heating has emerged as a powerful technique to promote a variety of chemical reactions.[10a−f] Microwave reactions are also attractive in offering reduced pollution and low cost together with simplicity in processing and handling.[11a,b]

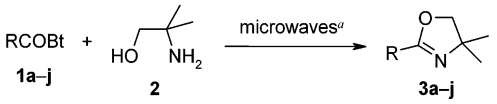
Results and Discussion

Preparation of *N*-Acylbenzotriazoles. The starting *N*-acylbenzotriazoles **1a**−**k** with aryl or heterocyclic groups were prepared in 74−95% yields from the corresponding carboxylic acids following a recently developed one-step procedure.[12] *N*-Acylbenzotriazoles **1a**−**k** were characterized by NMR spectroscopy and by comparison of melting points with those reported in the literature.

Preparation of 2-Oxazolines. Microwave reactions were performed in sealed heavy-walled Pyrex tubes 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.

Optimization of the reaction conditions was carried out on the cyclocondensation of 1*H*-1,2,3-benzotriazol-1-yl-(4-tolyl)methanone (**1a**) and 2-amino-2-methyl-1-propanol (**2**) in chloroform and different combinations of temperature, time, and irradiation power were studied to achieve the maximum chemical yield at the lowest reaction temperature. Our initial microwave experiment with the mixture containing **1a** and 2-amino-2-methyl-1-propanol (**2**) at 80 °C and 50 W irradiation power for 10 min produced the desired oxazoline **3a** along with the uncyclized intermediate, *N*-(2-hydroxy-1,1-dimethylethyl)-4-methylbenzamide in a 2:1 ratio as determined by the ^{1}H NMR spectrum of the crude product mixture. $SOCl_2$ has been advantageously used for the cyclization of such intermediates.[13] Accordingly, addition of $SOCl_2$ to the above reaction mixture and subsequent irradiation for 2 min resulted in complete conversion of the uncyclized intermediate into 4,4-dimethyl-2-(4-methylphenyl)oxazoline (**3a**) without the formation of side products or any noticeable decomposition. Thus, a two-step one-pot procedure was developed for the synthesis of 2-substituted oxazolines from *N*-acylbenzotriazoles under mild conditions with microwave irradiation. By contrast, thermal reaction of **1a** and the amino alcohol **2** in refluxing chloroform for 30 min showed the presence of substantial amounts (30−40%) of starting materials and the formation of *N*-(2-hydroxy-1,1-dimethylethyl)-4-methylbenzamide along with another side product. Stirring the reaction mixture at room temperature for 12 h resulted in a 1:1 ratio of the desired oxazoline **3a** and the uncyclized intermediate, which on addition of $SOCl_2$ cyclized in 2 h to give the oxazoline **3a** in 70% yield. Comparison of the above reaction conditions and results obtained suggested the use of microwave irradiation as the energy source for the synthesis of 2-substituted 2-oxazolines from *N*-acylbenzotriazoles.

TABLE 1. Preparation of 2-Substituted 2-Oxazolines with *N*-Acylbenzotriazoles 1a−j[a]



entry	reactants	R	product (yield, %)[b]
1	**1a** + **2**	4-$CH_3C_6H_4$	**3a** (98)
2	**1b** + **2**	4-$CH_3OC_6H_4$	**3b** (95)
3	**1c** + **2**	4-$NO_2C_6H_4$	**3c** (90)
4	**1d** + **2**	4-ClC_6H_4	**3d** (90)
5	**1e** + **2**	2-ClC_6H_4	**3e** (98)
6	**1f** + **2**	phenyl	**3f** (86)
7	**1g** + **2**	1-naphthyl	**3g** (95)
8	**1h** + **2**	2-furyl	**3h** (95)
9	**1i** + **2**	2-phenylethenyl	**3i** (84)
10	**1j** + **2**	1-(6-methoxy-2-naphthyl)ethyl	**3j** (91)

[a] MW, 50 W, 80 °C, 10 min, $CHCl_3$, then $SOCl_2$, MW, 2 min. [b] Isolated yield.

The above optimized microwave reaction conditions were applied to the synthesis of a variety of 2-substituted 2-oxazolines **3a**−**j** (Table 1). These results illustrate the general applicability of this method for the preparation of 2-substituted 2-oxazolines under mild conditions (80 °C) and short reaction times (12 min). Use of *N*-acylbenzotriazoles also avoids some earlier observed complications in microwave reactions, such as dimerization or the exclusive formation of amides from carboxylic acids.[6i]

Preparation of Thiazolines. The procedure developed for the synthesis of oxazolines was successfully applied to the preparation of thiazolines. Thus, condensation of *N*-acylbenzotriazoles **1a**−**f**,**h**,**i** with 2-aminoethanethiol hydrochloride (**4**) in the presence of Et_3N under microwave irradiation at 80 °C and 50 W irradiation power for 10 min, followed by the addition of $SOCl_2$ and subsequent irradiation for 2 min furnished the desired 2-substituted 2-thiazolines **5a**−**f**,**h**,**i** in excellent yields (Table 2). Again, no formation of any side product was detected in the crude reaction mixtures as determined by TLC analysis and ^{1}H NMR spectra. Our method also avoids multistep preparation of starting materials or the requirement of special reagents.[5a,6c,7b,d,f,g]

Further, we used this method to prepare the chiral oxazoline **6** by the reaction of (2*S*)-2-amino-3-phenyl-1-

(9) (a) Katritzky, A. R.; Shobana, N.; Pernak, J.; Afridi, A. S.; Fan, W.-Q. *Tetrahedron* **1992**, *48*, 7817. (b) Katritzky, A. R.; He, H.-Y.; Suzuki, K. *J. Org. Chem.* **2000**, *65*, 8210. (c) Katritzky, A. R.; Chang, H.-X.; Yang, B. *Synthesis* **1995**, 503. (d) Katritzky, A. R.; Yang, B.; Semenzin, D. *J. Org. Chem.* **1997**, *62*, 726. (e) Katritzky, A. R.; Pastor, A.; Voronkov, M. V. *J. Heterocycl. Chem.* **1999**, *36*, 777. (f) Katritzky, A. R.; Pastor, A. *J. Org. Chem.* **2000**, *65*, 3679. (g) Katritzky, A. R.; Suzuki, K.; Singh, S. K.; He, H.-Y. *J. Org. Chem.* **2003**, *68*, 5720. (h) Katritzky, A. R.; Suzuki, K.; Singh, S. K. *Croat. Chim. Acta* **2003**, in press. (i) Katritzky, A. R.; Huang, T.-B.; Voronkov, M. V. *J. Org. Chem.* **2000**, *65*, 8069.

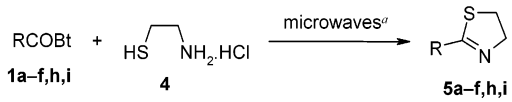
(10) (a) Hayes, B. L. *Microwave Synthesis*: *Chemistry at the Speed of Light*; CEM Publishing: Matthews, NC, 2002. (b) Perreux, L.; Loupy, A. *Tetrahedron* **2001**, *57*, 9199. (c) Lidström, P.; Tierney, J.; Wathey, B.; Westman, J. *Tetrahedron* **2001**, *57*, 9225. (d) Caddick, S. *Tetrahedron* **1995**, *51*, 10403. (e) Fini, A.; Breccia, A. *Pure Appl. Chem.* **1999**, *71*, 573. (f) Katritzky, A. R.; Singh, S. K. *Arkivoc* **2003**, *13*, 68.

(11) (a) Varma, R. S. *Green Chem.* **1999**, *1*, 43. (b) Tanaka, K.; Toda, F. *Chem. Rev.* **2000**, *100*, 1025.

(12) Katritzky, A. R.; Zhang, Y.; Singh, S. K. *Synthesis* **2003**, in press.

(13) Meyers, A. I.; Gabel, R.; Mihelich, E. D. *J. Org. Chem.* **1978**, *43*, 1372.

TABLE 2. Preparation of 2-Substituted 2-Thiazolines with *N*-Acylbenzotriazoles 1a−f,h,i[a]



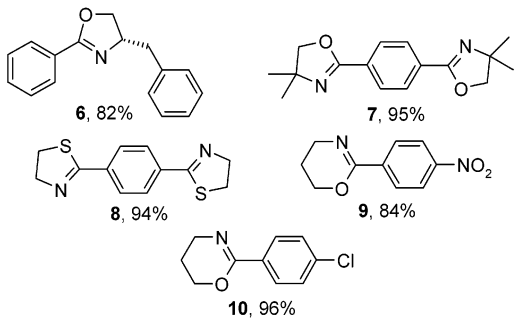
entry	reactants	R	product (yield %)[b]
1	**1a** + **4**	4-$CH_3C_6H_4$	**5a** (95)
2	**1b** + **4**	4-$CH_3OC_6H_4$	**5b** (97)
3	**1c** + **4**	4-$NO_2C_6H_4$	**5c** (94)
4	**1d** + **4**	4-ClC_6H_4	**5d** (97)
5	**1e** + **4**	2-ClC_6H_4	**5e** (91)
6	**1f** + **4**	phenyl	**5f** (85)
7	**1h** + **4**	2-furyl	**5h** (95)
8	**1i** + **4**	2-phenylethenyl	**5i** (91)

[a] MW, 50 W, 80 °C, 10 min, Et_3N, $CHCl_3$, then $SOCl_2$, MW, 2 min. [b] Isolated yield.

propanol and 1*H*-1,2,3-benzotriazol-1-ylphenylmethanone (**1f**) in 82% yield. Bisoxazoline **7** and bisthiazoline **8** were prepared by the reactions of 1,1′-(1,4-phenylenedicarbonyl)bis-1*H*-benzotriazole (**1k**) with **2** and **4**, respectively, in 94% and 95% yields. This procedure also works well for the preparation of 5,6-dihydro-4*H*-1,3-oxazines; reactions of **1c** and **1d** with 3-amino-1-propanol under similar conditions furnished 5,6-dihydro-4*H*-1,3-oxazines **9** and **10** in 84% and 96% yields, respectively.

Conclusions

In summary, we have introduced a general method for the direct preparation of a variety of 2-substituted oxazolines and thiazolines in excellent yields from readily available *N*-acylbenzotriazoles, under mild conditions using microwaves in a safe and reproducible procedure.



Experimental Section

Melting points are uncorrected. All of the reactions under microwave irradiation were conducted in heavy-walled Pyrex tubes sealed with aluminum crimp caps fitted with a silicon septum. Microwave heating was carried out with a single mode cavity Discover Microwave Synthesizer (CEM Corporation, NC), producing continuous irradiation at 2455 MHz. ^{1}H NMR (300 MHz) and ^{13}C NMR (75 MHz) spectra were recorded in $CDCl_3$ (with TMS for ^{1}H and chloroform-*d* for ^{13}C as the internal reference).

General Procedure for the Preparation of 2-Oxazolines with *N*-Acylbenzotriazoles by Conventional Method. A solution of 2-amino-2-methyl-1-propanol (**2**) (2 mmol) and 1*H*-1,2,3-benzotriazol-1-yl(4-methylphenyl)methanone (**1a**) (1 mmol) in $CHCl_3$ (10 mL) was stirred at 25 °C for 12 h. $SOCl_2$ (6 mmol) was added and the reaction mixture was stirred for 2 h. Aqueous workup gave a residue that was purified by column chromatography on silica gel with hexanes/ethyl acetate (3:2) to give **3a** (70%).

General Procedure for the Preparation of 2-Oxazolines 3a−j or 2-Thiazolines 5a−i with *N*-Acylbenzotriazoles 1a−j under Microwave Irradiation. A dried heavy-walled Pyrex tube containing a small stir bar was charged with 2-amino-2-methyl-1-propanol (**2**) or 2-aminoethanethiol hydrochloride (**4**) (2 mmol), *N*-acylbenzotriazole (1 mmol), and $CHCl_3$ (0.5 mL) (reactions with **4** were carried out in the presence of Et_3N). The tube containing the reaction mixture was sealed with an aluminum crimp cap fitted with a silicon septum and then it was exposed to microwave irradiation (50 W) for 10 min at a temperature of 80 °C. The buildup of pressure in the closed reaction vessel was carefully monitored and was found to be typically in the range of 4−10 psi. After the irradiation, the reaction tube was cooled with high-pressure air through an inbuilt system in the instrument until the temperature had fallen below 30 °C (ca. 2 min). $SOCl_2$ (6 mmol) was added and the reaction mixture was again exposed to microwave irradiation (50 W) for 2 min at 80 °C. After being cooled to room temperature, the reaction mixture was extracted with $CHCl_3$. Aqueous workup gave a residue that was purified by column chromatography on silica gel with hexanes/ethyl acetate (3:2) to give 2-oxazolines **3a−j** or 2-thiazolines **5a−i**.

4,4-Dimethyl-2-(4-methylphenyl)-4,5-dihydro-1,3-oxazole (3a):[19] colorless oil; yield, 98%; ^{1}H NMR δ 7.82 (d, J = 8.3 Hz, 2H), 7.19 (d, J = 8.3 Hz, 2H), 4.08 (s, 2H), 2.38 (s, 3H), 1.37 (s, 6H); ^{13}C NMR δ 162.1, 141.4, 128.9, 128.1, 125.2, 79.0, 67.4, 28.4, 21.5.

4,4-Dimethyl-2-(4-methoxyphenyl)-4,5-dihydro-1,3-oxazole (3b):[20] colorless oil; yield, 95%; ^{1}H NMR δ 7.88 (d, J = 8.9 Hz, 2H), 6.90 (d, J = 8.9 Hz, 2H), 4.08 (s, 2H), 3.84 (s, 3H), 1.37 (s, 6H); ^{13}C NMR δ 161.9, 161.9, 129.9, 120.5, 113.6, 79.0, 67.4, 55.3, 28.4.

4,4-Dimethyl-2-(4-nitrophenyl)-4,5-dihydro-1,3-oxazole (3c):[6m] colorless oil; yield, 90%; ^{1}H NMR δ 8.25 (d, J = 8.4 Hz, 2H), 8.10 (d, J = 8.4 Hz, 2H), 4.16 (s, 2H), 1.40 (s, 6H); ^{13}C NMR δ 160.2, 149.3, 133.9, 129.2, 123.4, 79.5, 68.2, 28.3.

2-(4-Chlorophenyl)-4,4-dimethyl-4,5-dihydro-1,3-oxazole (3d):[21] colorless oil; yield, 90%; ^{1}H NMR δ 7.87 (d, J = 8.7 Hz, 2H), 7.37 (d, J = 8.7 Hz, 2H), 4.11 (s, 2H), 1.38 (s, 6H); ^{13}C NMR δ 161.2, 137.3, 129.5, 128.5, 126.6, 79.2, 67.7, 28.4.

2-(4-Methylphenyl)-4,5-dihydro-1,3-thiazole (5a): brownish microcrystals (from diethyl ether); mp 40−42 °C (lit.[24] mp 41−42 °C); yield, 95%; ^{1}H NMR δ 7.72 (d, J = 8.1 Hz, 2H), 7.21 (d, J = 8.1 Hz, 2H), 4.44 (t, J = 8.4 Hz, 2H), 3.40 (t, J = 8.4 Hz, 2H), 2.39 (s, 3H); ^{13}C NMR δ 168.3, 141.4, 130.6, 129.1, 128.3, 65.1, 33.6, 21.4.

2-(4-Methoxyphenyl)-4,5-dihydro-1,3-thiazole (5b): colorless needles (from chloroform); mp 51−53 °C (lit.[25] mp 53−54 °C); yield, 97%; ^{1}H NMR δ 7.78 (d, J = 8.8 Hz, 2H), 6.91 (d, J = 8.8 Hz, 2H), 4.42 (t, J = 8.2 Hz, 2H), 3.83 (s, 3H), 3.38 (t, J = 8.2 Hz, 2H); ^{13}C NMR δ 167.6, 161.8, 129.9, 126.0, 113.7, 65.0, 55.3, 33.6.

(14) Wang, L.; Chen, Z.-C. *Synth. Commun.* **2001**, *31*, 1633.
(15) Kreutzberger, V. A.; Dietz, E. *Arzneim.-Forsch.* **1970**, *20*, 1723.
(16) Katritzky, A. R.; Wang, M.; Zhang, S. *Arkivoc* **2001**, *9*, 19.
(17) Luo, W.; Tang, G. *Zhongguo Shengwu Yixue Gongcheng Xuebao* **2001**, *20*, 335; *Chem. Abstr.* **2001**, *137*, 68000.
(18) Lu, C. X.; Li, Q.; Pan, J. *J. Polym. Sci., Polym. Chem.* **1985**, *23*, 3031.
(19) Pridgen, L. N.; Killmer, L. B. *J. Org. Chem.* **1981**, *46*, 5402.
(20) Mohan, R.; Katzenellenbogen, J. A. *J. Org. Chem.* **1984**, *49*, 1238.
(21) Boyd, R. N.; Rittner, R. C. *J. Am. Chem. Soc.* **1960**, *82*, 2032.
(22) Feuer, H.; Bevinakatti, H. S.; Luo, X.-G. *J. Heterocycl. Chem.* **1986**, *23*, 825.
(23) Vedejs, E.; Lee, N. *J. Am. Chem. Soc.* **1995**, *117*, 891.
(24) Kakehi, A.; Ito, S.; Uchiyama, K.; Konno, Y.; Kondo, K. *J. Org. Chem.* **1977**, *42*, 443.
(25) Schmir, G. L. *J. Am. Chem. Soc.* **1965**, *87*, 2743.

2-(4-Nitrophenyl)-4,5-dihydro-1,3-thiazole (5c): colorless needles (from chloroform); mp 150−152 °C (lit.[25] mp 146−148 °C); yield, 94%; ^{1}H NMR δ 8.27 (d, J = 8.8 Hz, 2H), 8.00 (d, J = 8.8 Hz, 2H), 4.53 (t, J = 8.5 Hz, 2H), 3.51 (t, J = 8.5 Hz, 2H); ^{13}C NMR δ 166.6, 149.2, 138.7, 129.2, 123.7, 65.5, 34.2

2-(4-Chlorophenyl)-4,5-dihydro-1,3-thiazole (5d): colorless needles (from chloroform); mp 50−52 °C (lit.[26] mp 53−55 °C); yield, 97%; ^{1}H NMR δ 7.77 (dd, J = 6.9, 1.8 Hz, 2H), 7.38 (dd, J = 6.9, 1.8 Hz, 2H), 4.45 (t, J = 8.4 Hz, 2H), 3.43 (t, J = 8.4 Hz, 2H); ^{13}C NMR δ 167.3, 137.1, 131.7, 129.6, 128.7, 65.2, 33.9.

(4*S*)-4-Benzyl-2-phenyl-4,5-dihydro-1,3-oxazole (6):[30] prepared by the reaction of (2*S*)-2-amino-3-phenyl-1-propanol and **1f** according to the general procedure; colorless oil; yield, 82%; $[\alpha]^{20}_D$ −12 (*c* 1.53, $CHCl_3$); ^{1}H NMR δ 7.97−7.93 (m, 2H), 7.50−7.37 (m, 3H), 7.33 −7.19 (m, 5H), 4.63−4.53 (m, 1H), 4.36−4.30 (m, 1H), 4.13 (dd, J = 8.5, 7.3 Hz, 1H), 3.23 (dd, J = 13.5, 5.0 Hz, 1H), 2.72 (dd, J = 13.5, 8.9 Hz, 1H); ^{13}C NMR δ 163.9, 137.9, 131.3, 129.2, 128.6, 128.5, 128.1, 127.7, 126.4, 71.8, 67.8, 41.8.

2,2′-(1,4-Phenylene)bis[4,5-dihydro-4,4-dimethyl-1,3-oxazole] (7):[6f] prepared by the reaction of **2** (2 equiv) and **1k** (1 equiv) according to the general procedure; colorless oil; yield, 95%; ^{1}H NMR δ 7.97 (s, 4H), 4.13 (s, 4H), 1.40 (s, 12H); ^{13}C NMR δ 161.6, 130.5, 128.2, 79.2, 67.8, 28.4.

2,2′-(1,4-Phenylene)bis[4,5-dihydro-1,3-thiazole] (8):[27] prepared by the reaction of **4** (2 equiv) and **1k** (1 equiv) according to the general procedure; colorless needles (from chloroform); mp 106−108 °C; yield, 94%; ^{1}H NMR δ 7.88 (s, 4H), 4.49 (t, J = 8.4 Hz, 4H), 3.45 (t, J = 8.5 Hz, 4H); ^{13}C NMR δ 167.8, 135.5, 128.4, 65.3, 33.8.

2-(4-Nitrophenyl)-5,6-dihydro-4*H*-1,3-oxazine (9): prepared by the reaction of 3-amino-1-propanol and **1c** according to the general procedure; colorless needles (from chloroform); mp 143−144 °C (lit.[31] mp 145−146 °C); yield, 84%; ^{1}H NMR δ 8.22−8.19 (m, 2H), 8.07−8.03 (m, 2H), 4.40 (t, J = 5.5 Hz, 2H), 3.65 (t, J = 5.8 Hz, 2H), 2.01 (qn, J = 5.8 Hz, 2H); ^{13}C NMR δ 153.8, 148.9, 139.9, 127.8, 123.1, 65.4, 42.8, 21.7.

2-(4-Chlorophenyl)-5,6-dihydro-4*H*-1,3-oxazine (10):[32] prepared by the reaction of 3-amino-1-propanol and **1d** according to the general procedure; colorless oil; yield, 96%; ^{1}H NMR δ 7.84−7.80 (m, 2H), 7.35−7.30 (m, 2H), 4.35 (t, J = 5.5 Hz, 2H), 3.59 (t, J = 5.8 Hz, 2H), 1.97 (qn, J = 5.8 Hz, 2H); ^{13}C NMR δ 154.7, 136.3, 132.6, 128.3, 128.2, 65.2, 42.6, 21.8.

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Supporting Information Available: General procedure for the preparation of *N*-acylbenzotriazoles **1a**−**k** and characterization data for compounds **1a**−**k**, **3e**−**j**, and **5e**−**i.** This material is available free of charge via the Internet at http://pubs.acs.org.

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(26) Iwakura, Y.; Nabeya, A.; Nishiguchi, T. *J. Org. Chem.* **1967**, *32*, 2362.
(27) Hagen, H.; Becke, F. German Patent 2202369, 1973; *Chem. Abstr.* **1973**, *79*, 105241.
(28) Bose, A. K.; Manhas, M. S.; Chib, J. S.; Chawla, H. P. S.; Dayal, B. *J. Org. Chem.* **1974**, *39*, 2877.
(29) Wipf, P.; Wang, X. *J. Comb. Chem.* **2002**, *4*, 656.
(30) Aitken, R. A.; Armstrong, D. P.; Galt, R. H. B.; Mesher, S. T. E. *J. Chem. Soc., Perkin Trans. 1* **1997**, 935.
(31) Zioudrou, C.; Schmir, G. L. *J. Am. Chem. Soc.* **1963**, *85*, 3258.
(32) Katritzky, A. R.; Langthorne, R. T.; Patel, R. C.; Lhommet, G. *Tetrahedron* **1981**, *37*, 2383.