Journal of the Serbian Chemical Society
JSCS-info@shd.org.rs • www.shd.org.rs/JSCS
J. Serb. Chem. Soc. *81* (1) 13–22 (2016)
JSCS–4822
UDC 547.495.2.05:547.53–304.9+
547.334'467.1+547.26'11
Original scientific paper

One-pot preparation of carbamoyl benzotriazoles and their applications in the preparation of ureas, hydrazinecarboxamides and carbamic esters

HUI MAO, HUILI LIU, YAWEI TU, ZHIYUN ZHONG, XIN LV* and XIAOXIA WANG**

Zhejiang Key Laboratory for Reactive Chemistry on Solid Surfaces, College of Chemistry and Life Sciences, Zhejiang Normal University, Jinhua 321004, China

(Received 26 January, revised 10 September, accepted 11 September 2015)

Abstract: Carbamoyl benzotriazoles were conveniently synthesized in one-pot from carboxylic acids, diphenyl phosphorazidate (DPPA) and 1*H*-benzotriazole (BtH). The reactivity and applications of carbamoyl benzotriazoles were also explored. Carbamoyl benzotriazoles react smoothly with amino acids, hydrazines and alcohols, thus providing facile access to the corresponding ureas, hydrazinecarboxamides and carbamic esters, respectively, in good to excellent yields.

Keywords: carbamoyl benzotriazoles; amino acid-derived ureas; hydrazinecarboxamides; carbamic esters.

INTRODUCTION

Isocyanates represent a valuable class of compounds by virtue of their widespread applications in organic synthesis and medicinal chemistry.[1–3] Nevertheless, isocyanates are usually toxic and unstable, and should be stored carefully due to the ease of exothermic polymerization and sensitivity to moisture. Although they could be used by *in situ* generation, their direct availability is required in certain circumstances. Capture of isocyanates formed *in situ* by Wang resin provides a good solution and was successfully used in the synthesis of amines.[4] On the other hand, carbamoyl azides[5a,b] and carbamoyl imidazolium salts[5c] have been developed as isocyanate substituents. It is noteworthy that carbamoyl benzotriazoles[6–10] may be a more promising alternative since they are crystalline, moderately reactive and can be stored with reasonably long shelf life.

The currently available methods for the synthesis of carbamoyl benzotriazole include: 1) condensation between phosgene, amine and 1*H*-benzotriazole (BtH), or direct carbamoylation[6] of BtH with carbamoyl chloride or isocyanates; 2)

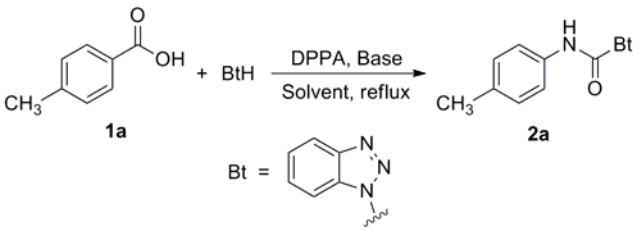
*,** Corresponding authors. E-mail: (*) lvxin@zjnu.cn; (**) wangxiaoxia@zjnu.cn
doi: 10.2298/JSC150126069M

diazotization of *o*-aminophenylureas[7]; 3) the reaction between acyl azides and BtH;[8,9] and 4) the reaction of carbamate salts with 1-chlorobenzotriazole in the presence of a base and PPh_3.[10] Despite the available methods, the more straightforward preparation of carbamoyl benzotriazoles from carboxylic acid remained unexplored. Besides, the application of carbamoyl benzotriazoles as an isocyanate substituent in the formation of a variety of compounds has not yet been sufficiently addressed.

Herein, a facile one-pot synthesis of carbamoyl benzotriazoles from carboxylic acids, DPPA and BtH is reported. The use of carbamoyl benzotriazoles for the preparation of amino acid-derived ureas, hydrazinecarboxamides and carbamic esters is demonstrated.

RESULTS AND DISCUSSION

The condensations between carboxylic acids, DPPA and an amine to afford urea are well established.[11] However, the condensation involving BtH as the nucleophile to afford carbamoyl benzotriazoles, a promising carbamoyl reagent, remained unknown. In this study, 4-methylbenzoic acid, DPPA and BtH were initially used as the model substrates to optimize the reaction conditions (Scheme 1 and Table I).



Scheme 1. One-pot reaction of 4-methylbenzoic acid, BtH and DPPA to form carbamoyl benzotriazoles.

TABLE I. Optimization of the conditions for the one-pot synthesis of carbamoyl benzotriazole **2a**; all reactions were performed under reflux

Entry	Base	Base (equiv.)	Solvent	Time, h	Yield[a], %
1	Et_3N	3.0	THF	8	trace
2	Et_3N	2.0	THF	8	trace
3	Et_3N	1.0	THF	10	41
4	K_2CO_3	1.0	THF	8	Trace
5	Na_2CO_3	1.0	THF	8	Trace
6	Et_3N	1.0	Toluene	6	80
7	Et_3N	1.0	1,4-Dioxane	6	37

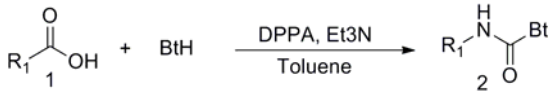
[a]Isolated yields based on **1a**

Several bases were examined. Et_3N (2.0 and 3.0 equiv.)[11,12] afforded only a trace amount of the desired product (Table I, Entries 1 and 2). The use of inorg-

anic bases, such as K_2CO_3 and Na_2CO_3, did not result in any improvement (entries 4 and 5). Considering that isocyanates may be sensitive to acids[13a] and bases under elevated temperatures,[13b] the reaction under neutral conditions was attempted. To our delight, reducing the amount of Et_3N to 1 equiv. afforded the desired product **2a** in 41 % yield (Table I, Entry 3).

Different solvents were also screened (Entries 3, 6 and 7) and the use of toluene afforded the product in 80 % yield.

With the optimal conditions in hand, various carboxylic acids were used for the preparation of carbamoyl benzotriazoles. The results are summarized in Scheme 2 and Table II.



Scheme 2. One-pot preparation of carbamoyl benzotriazoles.

TABLE II. One-pot preparation of carbamoyl benzotriazoles from carboxylic acids, BtH and DPPA; all reactions were performed under reflux

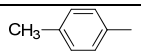
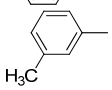
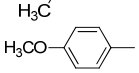
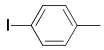
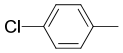
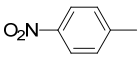
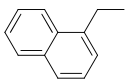
Entry	R1	Product **2**	Time, h	Yield[a], %
1		**2a**	6	80[a], 85[b]
2		**2b**	6	76
3		**2c**	6	71
4		**2d**	6	70
5		**2e**	6	83
6		**2f**	6	55
7		**2g**	6	53
8		**2h**	6	55
9		**2i**	6	–[c]
10		**2j**	6	49
11		**2k**	6	45
12	CH_3–	**2l**	8	50
13	*n*-C_3H_7–	**2m**	8	57
14	*i*-C_3H_7–	**2n**	8	57

TABLE II. Continued

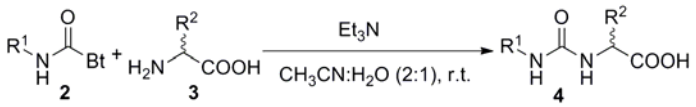
Entry	R1	Products **2**	Time, h	Yield[a], %
15	*n*-C_6H_{13}–	**2o**	8	58
16		**2p**	8	46
17		**2q**	8	42

[a]Isolated yields on 1 mmol scale; [b]isolated yield on 10 mmol scale; [c]no desired product was obtained

A variety of carboxylic acids could be converted directly into the respective carbamoyl benzotriazole in moderate to good yields. In general, aromatic carboxylic acids bearing an electron-donating aryl (Table II, entries 1–5) gave better results than those with an electron-withdrawing aryl (entries 6–8). Heterocyclic nicotinic acid afforded **2k** in 45 % yield, while no desired product was obtained using *p*-nitrobenzoic acid (entry 9). 2-(Naphthalen-1-yl)acetic acid and other aliphatic carboxylic acids (entries 10 and 12–15) generally afforded relatively lower yields (entries 12–17). The potential for large-scale preparation was also investigated. Running the reaction of 4-methylbenzoic acid on the 10 mmol scale gave a slightly better yield than that obtained on the 1 mmol scale (entry 1).

In order that carbamoyl benzotriazoles be an alternative to isocyanate, it is necessary to demonstrate their usage in the preparation of ureas and carbamates[14] since isocyanates have played a very important role in the preparation of these compounds. Herein, an investigation was undertaken to examine the reactivity of carbamoyl benzotriazoles towards amino acids, hydrazines and alcohols to determine their potential in the preparation of various ureas, hydrazinecarboxamides and carbamic esters.

Previously, it was reported that carbamoyl benzotriazoles reacted with amines smoothly under mild conditions.[8] Here amino acids were used to explore the application of carbamoyl benzotriazoles in the synthesis of chiral ureas (Scheme 3 and Table III), which may possess important biological activities. For example, azadipeptide nitriles are used as novel cysteine protease inhibitors.[15] Geldern also reported the structure–activity relationship of other urea derivatives of amino acids in an attempt to improve the potency of a novel series of azole--based endothelin-A (ETA) selective antagonists.[16]



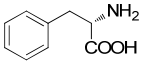
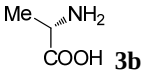
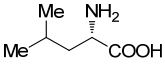
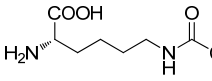
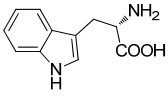
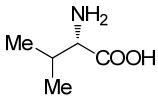
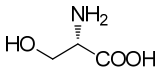
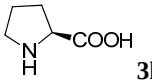
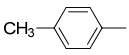
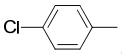
2 3 4

Scheme 3. The aminoacylation of amino acids with carbamoyl benzotriazoles.

The reaction of carbamoyl benzotriazole **2b** with L-phenylalanine was realized using the procedure reported for the acylation of amino acids using *N*-acyl

benzotriazoles.[17] To our delight, the reaction gave the desired product **4a** in 91 % yield at r.t. in the presence of Et_3N (1.5 equiv.) in $CH_3CN–H_2O$ (2:1, *V*/*V*, Table III, entry 1).

TABLE III. Preparation of ureas *via* aminoacylation of amino acids with carbamoyl benzotriazoles

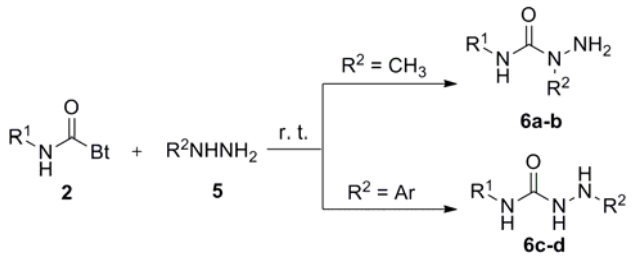
Entry	R^1	Compounds **3**	Products **4**	Time, h	Yield[a], %
1	 **2b**	 **3a**	**4a**	0.5	91
2		 **3b**	**4b**	0.5	94
3		 **3c**	**4c**	0.5	90
4		 **3d**	**4d**	0.5	92
5		 **3e**	**4e**	0.5	80
6		 **3f**	**4f**	0.5	94
7		 **3g**	**4g**	0.5	72
8		 **3h**	**4h**	10	85
9	 **2a**	**3a**	**4i**	0.5	90
10		**3c**	**4j**	0.5	95
11	 **2h**	**3a**	**4k**	0.5	91
12	*n*-C_3H_7– **2m**	**3a**	**4l**	24	96

[a]Isolated yields based on carbamoyl benzotriazoles

As shown in Table III, the aminoacylation of various natural amino acids was investigated. Generally, the reactions between amino acids and carbamoyl benzotriazoles afforded the corresponding ureas in excellent yields within 0.5 h (entries 1–6). For L-proline, as long as 10 h was required to obtain 85 % yield (entry 8). It is worth noting that good chemoselectivity for the acylation of L-serine was observed, where the amino group reacted selectively, but not the hydroxyl group (entry 7). Generally, the substituent on the aromatic ring did not affect the efficiency of the reaction (entries 9–11). The method was also applicable for the reactions of aliphatic carbamoyl benzotriazole (entry 12).

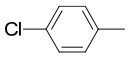
Maintaining the chirality of the amino acid was proved by polarimetric analysis of (*R*)-3-phenyl-2-(3-phenylureido)propanoic acid **4a**, the [α] value of which was found to be +51.51°, in good accordance with the literature value.[18] The Katritzky group also demonstrated that no racemization of the amino acid derivative occurred under the same conditions.[19]

Bis-nucleophilic hydrazines were also reacted with carbamoyl benzotriazoles (Scheme 4 and Table IV). For methylhydrazine, the more electrophilic nitrogen atom (with methyl attached) was aminoacylated without any promoter and compounds **6a** and **6b** were obtained in excellent yields (Table IV, entries 1 and 2). Phenylhydrazine, however, was aminoacylated on the terminal nitrogen and the yields were relatively lower (Table IV, entries 3 and 4) even in the presence of NaH. Without NaH, no aminoacylation of the phenylhydrazine occurred.



Scheme 4. The aminoacylation of hydrazines with carbamoyl benzotriazoles.

TABLE IV. Preparation of hydrazinecarboxamides *via* aminoacylation of hydrazines with carbamoyl benzotriazoles; the reaction was promoted by 1.5 equiv. of NaH (based on **2**) in dry toluene at r.t. or at 40 °C

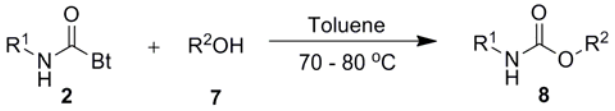
Entry	R1	R2	Base	Products **6**	Time, h	Yield[a], %
1	 **2b**	CH_3–	–	**6a**	10	90
2	 **2h**	CH_3–	–	**6b**	10	89
3	 **2b**		NaH	**6c**	10	45
4	C_2H_5– **2r**		NaH	**6d**	60	41

[a]Isolated yields based on carbamoyl benzotriazoles

Finally, the use of carbamoyl benzotriazoles for the synthesis of carbamic esters was explored. Thus the reaction of **2b** with ethanol was performed. With toluene as the solvent at 70–78 °C, the reaction afforded the desired compound **8b** in 80 % yield.

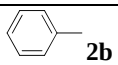
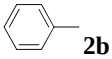
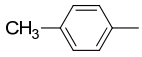
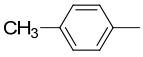
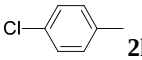
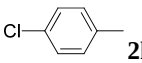
As shown in Scheme 5 and Table V, all the carbamoyl benzotriazoles examined smoothly afforded the desired carbamic esters in good yields. In combination with the convenience in the purification of the products, the aminoacylation

of alcohols with carbamoyl benzotriazoles provides a facile route to prepare carbamic esters.



Scheme 5. The aminoacylation of alcohols with carbamoyl benzotriazoles.

TABLE V. Preparation of carbamic esters *via* aminoacylation of alcohols with carbamoyl benzotriazoles

Entry	R1	R2	Products **8**	Time, min	Yield, %[a]
1	 **2b**	C_2H_5	**8a**	30	83
2	 **2b**	*n*-C_4H_9	**8b**	30	80
3	 **2a**	C_2H_5	**8c**	30	77
4	 **2a**	*n*-C_4H_9	**8d**	30	78
5	 **2h**	C_2H_5	**8e**	45	85
6	 **2h**	*n*-C_4H_9	**8f**	45	85

[a]Isolated yields based on carbamoyl benzotriazoles

EXPERIMENTAL

THF and toluene were dried over Na. Other commercial reagents were used without further purification, and all solvents were of reagent grade. All reaction mixtures were stirred magnetically and were followed by TLC analysis at 254 nm. Flash column chromatography was performed using 100–200 mesh silica. Melting points are uncorrected. The IR spectra were recorded using KBr disks or as films using a Nicolet-670 FTIR spectrometer with absorption in cm^{-1}. The ^{1}H-NMR and ^{13}C-NMR spectra were determined on a Bruker AC-400 spectrometer as $CDCl_3$ or DMSO-d_6 solutions. The *J* values are in Hertz and the chemical shifts are expressed in ppm downfield from internal TMS. Elemental analysis was realized on an EA 1110 instrument. Polarimetry was performed according to the literature[18] on an Anton Paar MCP200 modular circular polarimeter.

Among the compounds, carbamoyl benzotriazoles **2a**, **2b**, **2e**, **2f**, **2h** and **2o**, urea **4l**, hydrazinecarboxamide **6c** and carbamic esters **8a–f** are known. Other carbamoyl benzotriazoles and products including **2c**, **2d**, **2g**, **2j–2n**, **2p**, **2q**, **4a–k**, **6a**, **6b** and **6d** are new compounds. The analytical and spectral data of compounds are given in the Supplementary material to this paper.

*General procedure for the one-pot synthesis of carbamoyl benzotriazoles **2***

To a solution of carboxylic acid (1.0 mmol) in dry toluene (20 mL) was added Et_3N (1.0 mmol, 101 mg), diphenyl phosphorazidate (1.0 mmol, 275 mg) and 1*H*-benzotrizole (1.0 mmol, 119 mg). The mixture was stirred under reflux until completion of the reaction

(monitored by TLC). The reaction mixture was cooled to r.t., and washed successively with water (10 mL), saturated Na_2CO_3 (10 mL) and brine (10 mL). The combined organic phase was dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to obtain a residue, which was purified by recrystallization from toluene or by column chromatography on silica gel using EA–PE (1:20, boiling range 60–90 °C) as the eluent to give the pure products **2a**–**2q**.

*General procedure for the synthesis of the amino acid-derived ureas **4***

To a solution of compound **2** (1 mmol) in CH_3CN (16 mL) and H_2O (8 mL) was added an amino acid (1.1 mmol). Et_3N (1.5 mmol, 152 mg) was then added dropwise. The mixture was stirred at r.t. until completion of the reaction (monitored by TLC). The acetonitrile was removed, and the residue was extracted by ethyl acetate (10 mL). The organic phase was washed successively with 10 % HCl (5 mL), saturated Na_2CO_3 solution (5 mL) and brine (5 mL), dried over anhydrous Na_2SO_4, and concentrated under reduced pressure to give the pure products **4a**–**4l**.

*General procedure for the synthesis of hydrazinecarboxamides **6a** and **6b***

To a solution of compound **2** (1 mol) in dry toluene (5 mL) was added methylhydrazine (1.1 mmol, 51 mg). The mixture was stirred at r.t. until completion of the reaction (monitored by TLC). Then THF (10 mL) was added, and the mixture was washed with saturated Na_2CO_3 (3×5 mL) and brine (5 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by column chromatography on silica gel using EA–PE (1:1) as the eluent to give the pure products **6a** and **6b**.

*General procedure for the synthesis of hydrazinecarboxamides **6c** and **6d***

To a solution of compound **2** (1 mol) in dry toluene (5 mL) was added aromatic hydrazine (1.1 mmol, 119 mg) and NaH (1.5 mmol, 36 mg). The mixture was stirred at r.t. or 40°C until the completion of the reaction (monitored by TLC). Then THF (10 mL) was added, and the mixture was washed with Na_2CO_3 (3×5 mL) and brine (5 mL). The combined organic phase was dried over anhydrous Na_2SO_4, concentrated under reduced pressure, and purified by column chromatography on silica gel using EA/PE (EA/PE = 1:1) as the eluent to give the pure product **6c** and **6d**.

*General procedure for the synthesis of carbamic esters **8a**–**f***

A round bottom flask was charged with compound **2** (1.0 mmol), alcohol (1.1 mmol) and toluene (5 mL). The mixture was stirred at 80 °C until completion of the reaction (monitored by TLC). The reaction mixture was cooled to r.t. whereby a white solid precipitated that was filtered off. The filter cake was washed by ethanol (5 mL) to give the pure products **8a**–**f**.

CONCLUSIONS

In summary, a convenient one-pot synthesis of carbamoyl benzotriazoles from carboxylic acid, DPPA and BtH was developed. The carbamoyl benzotriazoles showed good reactivity and chemoselectivity towards amino acids, hydrazines and alcohols, and provided facile access to amino acid-derived ureas, hydrazinecarboxamides and carbamic esters. Together with the properties of being stable and easily to handle, carbamoyl benzotriazoles show promise for use as a practical substitute for isocyanates.

SUPPLEMENTARY MATERIAL

The physical, analytical and spectral data for the synthesized compounds and their spectra are available electronically from http://www.shd.org.rs/JSCS/, or from the corresponding authors on request.

Acknowledgement. This work was financially supported by the National Natural Science Foundation of China (No. 20802070).

ИЗВОД

СИНТЕЗА КАРБАМОИЛ-БЕНЗОТРИАЗОЛА И ЊИХОВА ПРИМЕНА У СИНТЕЗИ УРЕЕ, ХИДРАЗИНКАРБОКСАМИДА И ЕСТАРА КАРБАМИНСКЕ КИСЕЛИНЕ

HUI MAO, HUILI LIU, YAWEI TU, ZHIYUN ZHONG, XIN LV и XIAOXIA WANG

Zhejiang Key Laboratory for Reactive Chemistry on Solid Surfaces, College of Chemistry and Life Sciences, Zhejiang Normal University, Jinhua 321004, China

Карбамоил-бензотриазоли су синтетисани у једном реакционом кораку, полазећи од карбоксилних киселина, дифенил фосфоразидата (DPPA) и 1*H*-бензотриазола (BtH). Испитана је реактивност и примена карбамоил-триазола. Они лако реагују са амино--киселинама, хидразинима и алкохолима, и на тај начин се добијају одговарајући деривати уреe, хидразинкарбоксамида и естри карбаминске киселине, редом, у добром до одличном приносу.

(Примљено 26. јануара, ревидирано 10. септембра, прихваћено 11. септембра 2015)

REFERENCES

1. a) S. Moreau, P. Coudert, C. Rubat, D. Gardette, D. Vallee-Goyet, J. Couquelet, P. Bastide, P. Tronche, *J. Med. Chem.* **37** (1994) 2153; b) B. Linclau, A. K. Sing, D. P. Curran, *J. Org. Chem.* **64** (1999) 2835; c) D. D. Díaz, M. G. Finn, *Org. Lett.* **6** (2004) 43; d) M. O. Anderson, H. Yu, C. Penaranda, B. A. Maddux, I. D. Goldfine, J. F. Youngren, R. K. Guy, *J. Comb. Chem.* **8** (2006) 784; e) N. S. Sudarshan, N. Narendra, H. P. Hemantha, V. V. Sureshbabu, *J. Org. Chem.* **72** (2007) 9804
2. a) C. P. Hencken, D. T. Genna, M. A. Siegler, S. G. H. Posner, *J. Org. Chem.* **76** (2011) 5149; b) S. L. Peterson, S. M. Stucka, C. J. Dinsmore, *Org. Lett.* **12** (2010) 1340
3. a) P. Braunstein, D. Nobel, *Chem. Rev.* **89** (1989) 1927; b) S. J. Peters, J. R. Klen, N. C. Smart, *Org. Lett*. **10** (2008) 4521; c) A. R. Katritzky, T. B. Huang, M. V. Voronkov, *J. Org. Chem.* **65** (2000) 8069; d) B. Jiang, C. Li, S. J. Tu, F. Shi, *J. Comb. Chem.* **12** (2010) 482; e) A. Flores, M. J. Camarasa, M. J. Pérez-Pérez, A. San-Félix, J. Balzarini, E. Quesada, *Org. Biomol. Chem.* **12** (2014) 5278
4. a) S. Sunami, T. Sagara, M. Ohkubo, H. Morishima, *Tetrahedron Lett.* **40** (1999) 1721; b) S. Sunami, M. Ohkubo, *Tetrahedron* **65** (2009) 638
5. a) G. E. Eduardo, F. S. Miryam, M. Luis, *J. Org. Chem.* **73** (2008) 2909; b) P. Feng, X. Sun, Y. Su, X. Li, L. –H. Zhang, X. Shi, N. Jiao, *Org. Lett*. **16** (2014) 3388; c) R. A. Batey, C. Yoshina-Ishii, S. D. Taylor, V. Santhakumar, *Tetrahedron Lett*. **40** (1999) 2669
6. P. Stefan, Z. Gerhard, T. Norbert, M. Guenter, *WO* 2007045393, *CA* 2625722, 2007
7. C. J. Perry, K. Holding, E. Tyrrell, *Synth. Commun.* **38** (2008) 3354
8. Z. Y. Zhong, X. X. Wang, L. C. Kong, X. M. Zhu, *Synlett* (2009) 2461
9. Z. Y. Zhong, J. H. Hu, X. X. Wang, J. H. Liu, L. F. Zhang, *Synth. Commun.* **41** (2011) 2461

10. R. Hunter, A. Msutu, C. L. Dwyer, N. D. Emslie, R. C. Hunt. B. C. B. Bezuidenhoudt, *Synlett* (2011) 2335
11. a) W. L. Zhao, E. M. Carreira, *Org. Lett.* **13** (2011) 5084; b) V. V. Sureshbabu, G. Chennakrishnareddy, N. Narendra, *Tetrahedron Lett.* **49** (2008) 1408; c) M. Zhang, X. Y. Yang, W. Tang, T. W. L. Groeneveld, P. L. He, F. H. Zhu, J. Li, W. Lu, A. M. Blom, J. P. Zuo, F. J. Nan, *ACS Med. Chem. Lett.* **3** (2012) 317; d) O. Éliás, É. Ágai-Csongor, G. Domány, G. M. Keserű, A. Gere, B. Kiss, É. Hellinger, M. Vastag, I. Gyertyán, *Bioorg. Med. Chem. Lett.* **24** (2014) 2118; e) S. J. Jang, H. W. Choi, D. L. Choi, S. Cho, H.-K. Rim, H.-E. Choi, K.-S. Kim, M. Huang, H. Rhim, K.-T. Lee, J. Y. Lee, *Bioorg. Med. Chem. Lett.* **23** (2013) 6656
12. C. A. Luckhurst, I. Millichip, B. Parker, J. Reuberson, M. Furber, *Tetrahedron Lett.* **48** (2007) 8878
13. a) G. D. Jones, J. Zomlefer, K. Hawkins, *J. Org. Chem.* **9** (1944) 500; b) K. Ninomiya, T. Shioiri, S. Yamada, *Tetrahedron* **30** (1974) 2151
14. a) D. C. Kanta, D. Seidel, *J. Am. Chem. Soc.* **133** (2011) 14538; b) T. Narumi, H. Arai, K. Yoshimura, S. Harada, W. Nomura, S. Matsushita, H. Tamamura, *Bioorg. Med. Chem.* **19** (2011) 6735; c) P. Koschker, A. Lumbroso, B. Breit, *J. Am. Chem. Soc.* **133** (2011) 20746
15. R. Löser, J. Gut, P. J. Rosenthal, M. Frizler, M. Gütschow, K. T. Andrews, *Bioorg. Med. Chem. Lett.* **20** (2010) 252
16. T. W. V. Geldern, J. A. Kester, R. Bal, J. R. Wu-Wong, W. Chiou, D. B. Dixon, T. J. Opgenorth, *J. Med. Chem.* **39** (1996) 968
17. A. R. Katritzky, Q. Y. Chen, S. R. Tala, *Chem. Biol. Drug. Des.* 73 (2009) 611
18. W. H. Schuller, C. Iemann, *J. Am. Chem. Soc.* **73** (1951) 1644
19. A. R. Katritzky, P. P. Mohapatra, D. Fedoseyenko, M. Duncton, P. J. Steel, *J. Org. Chem.* **72** (2007) 4268.