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Unexpected TFA-catalyzed tandem reaction of benzo[d]oxazoles with 2-oxo-2-arylacetic acids: synthesis of 3-aryl-2H-benzo[b][1,4]oxazin-2-ones and cephalandole A

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A convenient and efficient method for the TFA-catalyzed synthesis of 3-aryl-2H-benzo[b][1,4]oxazin-2-ones via a tandem reaction of benzo[d]oxazoles with 2-oxo-2-arylacetic acids was reported for the first time. The efficiency of this transformation was demonstrated by compatibility with a wide range of functional groups. The synthetic utility of this method was confirmed by the synthesis of the natural product cephalandole A. Moreover, a plausible mechanism for the formation of 3-aryl-2H-benzo[b][1,4]oxazin-2-ones involving ring-opening and cyclization steps is proposed. The present synthetic route to 3-aryl-2H-benzo[b][1,4]oxazin-2-ones could be readily scaled up to gram quantity without difficulty.

1,4-Benzoxazines,[1] as an important class of heterocycles, have become increasingly important because they have been associated with a wide range of pharmacological and biological activities.[2] Among them, 2H-benzo[b][1,4]oxazin-2-one scaffolds have been studied intensively in the past few years because they are synthetic building blocks,[3] present in a wide variety of bioactive molecules, as well as photoactive molecules[4] which possess fluorescent,[5] photophysical and photochemical properties.[6] In 2006, the 2H-benzo[b][1,4]oxazin-2-one-based natural product cephalandole A was originally isolated from the Taiwanese orchid *Cephalanceropsis gracilis* (Orchidaceae),[7] which had previously been misassigned, and later corrected by Bergman[8] and Gross[9] (Fig. 1).
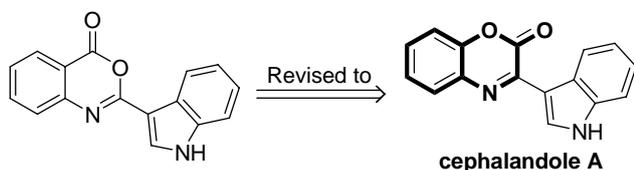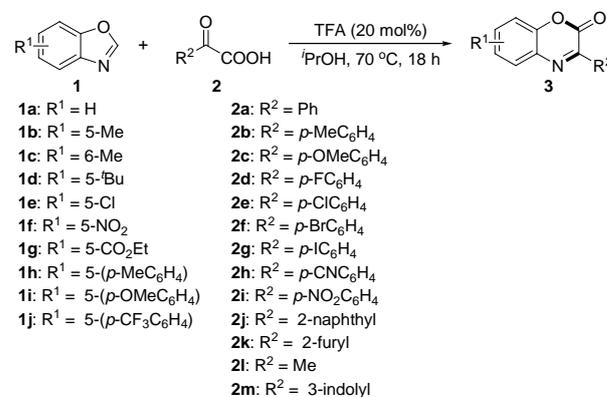

Fig.1 The revised structure of cephalandole A.

The importance of 2H-benzo[b][1,4]oxazin-2-ones has resulted in the development of different synthetic strategies for their preparation. In general, 2H-benzo[b][1,4]oxazin-2-ones are synthesized by the treatment of *o*-aminophenols with α-ketoesters.[10] Nicolaides and co-workers[11] reported 3-aryl-2H-benzo[b][1,4]oxazin-2-ones could be obtained by the condensation of *O*-methyl-*o*-quinonemonoximes with arylacetates. In 2006, Yavari and co-workers[12] reported that vinylphosphonium salt mediated reaction between *o*-aminophenols and alkyl propiolates leading to the synthesis of 3-alkyl-2H-benzo[b][1,4]oxazin-2-ones. In 2008, Kikelj and co-workers[13] developed the synthesis of 4-benzyl- and 4-alkyl-3,4-dihydro-1,4-benzoxazin-2-one derivatives from ethyl 2-(2-hydroxyphenylamino)acetate and aldehydes. Recently, Ballini and co-workers[14] reported the preparation of 1,4-benzoxazin-2-one derivatives via a domino reaction of *o*-aminophenols with ethyl β-nitroacrylates. As part of the continuing efforts in our laboratory towards the development of new methods for the synthesis of nitrogen-containing heterocycles,[15] we herein reported an unexpected TFA-catalyzed tandem reaction of benzo[d]oxazoles with 2-oxo-2-arylacetic acids to access 2H-benzo[b][1,4]oxazin-2-ones under mild conditions (Scheme 1).

1a: R^1 = H
1b: R^1 = 5-Me
1c: R^1 = 6-Me
1d: R^1 = 5-^{t}Bu
1e: R^1 = 5-Cl
1f: R^1 = 5-NO$_2$
1g: R^1 = 5-CO$_2$Et
1h: R^1 = 5-(p-MeC$_6$H$_4$)
1i: R^1 = 5-(p-OMeC$_6$H$_4$)
1j: R^1 = 5-(p-CF$_3$C$_6$H$_4$)

2a: R^2 = Ph
2b: R^2 = p-MeC$_6$H$_4$
2c: R^2 = p-OMeC$_6$H$_4$
2d: R^2 = p-FC$_6$H$_4$
2e: R^2 = p-ClC$_6$H$_4$
2f: R^2 = p-BrC$_6$H$_4$
2g: R^2 = p-IC$_6$H$_4$
2h: R^2 = p-CNC$_6$H$_4$
2i: R^2 = p-NO$_2$C$_6$H$_4$
2j: R^2 = 2-naphthyl
2k: R^2 = 2-furyl
2l: R^2 = Me
2m: R^2 = 3-indolyl

Scheme 1 Synthesis of 2H-benzo[b][1,4]oxazin-2-ones.

Our preliminary studies focused on the model reaction between 2-benzo[d]oxazole (**1a**) and 2-oxo-2-phenylacetic acid (**2a**) to obtain 2-phenylbenzo[d]oxazole (**4a**) via cascade reaction of decarboxylation, decarbonylation and coupling reaction (Scheme 2). Through the screening process, little-to-no target product **4a** was detected using silver salts and palladium salts as catalysts with a variety of parameters. To our surprise, a trace amount of unexpected 3-phenyl-2H-benzo[b][1,4]oxazin-2-one (**3a**) was observed by gas chromatography/mass spectrometry (electron ionization) [GC/MS (EI)] analysis using trifluoroacetic acid (TFA) as the Brønsted acid in toluene (Table 1, entry 1). We were

delighted to find that the yield of **3a** could be improved to 45% under an air atmosphere after solvent was changed to acetonitrile (Table 1, entry 2). This finding inspired us to examine optimal reaction conditions for the synthesis of **3a** in order to obtain more satisfactory results.
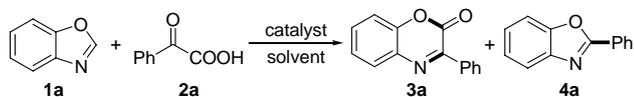
Scheme 2 Reaction of 2-benzo[*d*]oxazole with 2-oxo-2-phenylacetic acid.

Considering solvents always played important roles in organic reactions, we first examined the solvent effect and found that isopropanol was superior to DMSO, DMF, 1,2-dichloroethane, dioxane, CH$_3$CN, toluene, THF, and EtOH (Table 1, entries 1-9). We also studied influence of the amount of TFA on the reaction yields. The results showed that 0.2 equivalents of TFA was sufficient, and excessive amount of catalyst did not increase the yield (Table 1, entries 9-13). Then various Brønsted acids were screened to examine their effect on the reaction. Replacement of TFA with other acids, including AcOH, PhCO$_2$H, *p*-NO$_2$PhCO$_2$H, CF$_3$SO$_3$H, *p*-MePhSO$_3$H, and *p*-NO$_2$PhSO$_3$H, resulted in lower yields (Table 1, entries 14-19). The yield was decreased to some extent when the reaction was carried out at the lowered or elevated temperature (Table 1, entries 20-21). Therefore, the optimal reaction condition was to use 0.2 equiv of TFA in isopropanol at 70 °C under air. As a result, the model reaction was carried out under optimized conditions with 0.2 equiv of TFA in isopropanol at 70 °C under air, which led to **3a** in 94% yield (Table 1, entry 12).

Table 1 Screening for optimal reaction conditions[a]

Entry	Catalyst	Equiv (x)	Solvent	Yield (%)[b]
1	TFA	1.0	toluene	trace
2	TFA	1.0	CH$_3$CN	45
3	TFA	1.0	DMSO	11
4	TFA	1.0	DMF	trace
5	TFA	1.0	dichloroethane	14
6	TFA	1.0	dioxane	88
7	TFA	1.0	THF	82
8	TFA	1.0	EtOH	84
9	TFA	1.0	*i*PrOH	91
10	TFA	0.5	*i*PrOH	93
11	TFA	0.3	*i*PrOH	94
12	**TFA**	**0.2**	***i*PrOH**	**94**
13	TFA	0.1	*i*PrOH	81
14	AcOH	0.2	*i*PrOH	59
15	PhCO$_2$H	0.2	*i*PrOH	66
16	*p*-NO$_2$PhCO$_2$H	0.2	*i*PrOH	45
17	CF$_3$SO$_3$H	0.2	*i*PrOH	39
18	*p*-MePhSO$_3$H	0.2	*i*PrOH	54
19	*p*-NO$_2$PhSO$_3$H	0.2	*i*PrOH	68
20	TFA	0.2	*i*PrOH	82[c]
21	TFA	0.2	*i*PrOH	89[d]

[a] *Reaction conditions*: **1a** (0.2 mmol), **2a** (0.3 mmol), TFA (x mmol), *i*PrOH (2 mL), air, 70 °C, 18 h. [b] Isolated yield. [c] At 60 °C. [d] At 80 °C.

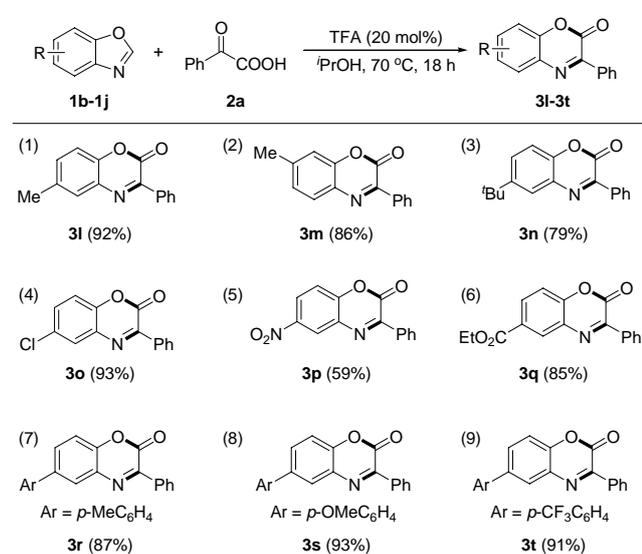**Table 2** Reaction of benzo[*d*]oxazole with 2-oxo-2-arylacetic acid[a]

Entry	Ar (**2**)	Product (**3**)	Yield (%)[b]
1	Ph (**2a**)	**3a**	94
2	*p*-MeC$_6$H$_4$ (**2b**)	**3b**	83
3	*p*-OMeC$_6$H$_4$ (**2c**)	**3c**	45
4	*p*-FC$_6$H$_4$ (**2d**)	**3d**	93
5	*p*-ClC$_6$H$_4$ (**2e**)	**3e**	95
6	*p*-BrC$_6$H$_4$ (**2f**)	**3f**	91
7	*p*-IC$_6$H$_4$ (**2g**)	**3g**	89
8	*p*-CNC$_6$H$_4$ (**2h**)	**3h**	90
9	*p*-NO$_2$C$_6$H$_4$ (**2i**)	**3i**	85
10	2-naphthyl (**2j**)	**3j**	88
11	2-furyl (**2k**)	**3k**	32

[a] *Reaction conditions*: **1** (0.2 mmol), **2a** (0.3 mmol), TFA (0.04 mmol), *i*PrOH (2 mL), air, 70 °C, 18 h. [b] Isolated yield.

With the optimized reaction conditions in hand, we next explored the scope and generality of the reaction using various 2-benzo[*d*]oxazoles with 2-oxo-2-arylacetic acids (Table 2). First, the reaction between benzo[*d*]oxazole (**1a**) and various 2-oxo-2-arylacetic acids (**2a-2k**) was investigated under the standard reaction conditions. The electronic properties of the substituents on the phenyl ring of the 2-oxo-2-arylacetic acids had an obvious impact on the yield of the reaction. The 2-oxo-2-arylacetic acids bearing an electron-withdrawing substituent (e.g., −F, −Cl, −Br, −I, −CN, and −NO$_2$) produced higher yields of products than those analogues bearing an electron-donating substituent (e.g., −Me, and −OMe) (Table 2, entries 2-9). Substrate 2-(naphthalen-

2-yl)-2-oxoacetic acid (**2j**) reacted with **1a** to give the desired product **3j** in 88% yield (Table 2, entry 10), but a lower yield was observed when substrate 2-(furan-2-yl)-2-oxoacetic acid (**2k**) bearing a heteroaryl group was used as a substrate (Table 2, entry 5 11).

Table 3 Reaction of different benzo[*d*]oxazoles with 2-oxo-2-phenylacetic acid[*a*]

3l (92%) **3m** (86%) **3n** (79%)

3o (93%) **3p** (59%) **3q** (85%)

Ar = *p*-MeC6H4 Ar = *p*-OMeC6H4 Ar = *p*-CF3C6H4
3r (87%) **3s** (93%) **3t** (91%)

[*a*] *Reaction conditions*: **1** (0.2 mmol), **2a** (0.3 mmol), TFA (0.04 mmol), *i*PrOH (2 mL), air, 70 °C, 18 h. Isolated yield was given in parenthesis.

We next explored the effect of the reaction of 2-oxo-2-phenylacetic acids (**2a**) with various benzo[*d*]oxazoles (**1b-1j**) 10 under the standard reaction conditions, and the results are summarized in Table 3. As expected, the groups on the phenyl ring of benzo[*d*]oxazoles, such as methyl, methoxy, *tert*-butyl, chloro, nitro, ester, and trifluoromethyl, were quite compatible under the optimized reaction conditions. The electronic properties 15 of the groups on the phenyl ring moiety of benzo[*d*]oxazoles had some effects on the reaction. Generally, benzo[*d*]oxazoles possessing either electron-donating or electron-withdrawing groups on the phenyl ring provided the corresponding 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones in good yields. However, substrate 20 containing a strong electron-withdrawing substituent (e.g., −NO2) on the benzene ring, such as 5-nitrobenzo[*d*]oxazole (**1f**), achieved the corresponding desired products 6-nitro-3-phenyl-2*H*-benzo[*b*][1,4]oxazin-2-one (**3p**) in moderate yield (59%, Table 3, run 5). It would be specially mentioned that 5-25 arylbenzo[*d*]oxazoles (**1h-1j**) are also good substrates for this transformation, and the corresponding desired product **3r-3t** were isolated in 87%, 93%, 91% yield, respectively (Table 3, runs 7-9).

Treatment of 2-oxo-2-alkylacetic acid such as 2-oxo-2-methylacetic acid (**2l**) with **1a** under the optimized conditions 30 afforded the desired product **3u** in 36% yield (Scheme 3).
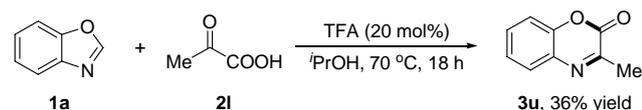

Scheme 3. Reaction of benzo[*d*]oxazole with 2-oxo-2-methylacetic acid.

To demonstrate the synthetic utility of this method, it was applied to the synthesis of the natural product cephalandole A 35 (Scheme 4). TFA-catalyzed tandem reaction of benzo[*d*]oxazoles (**1a**) with 2-(1*H*-indol-3-yl)-2-oxoacetic acid (**2m**) afforded the desired natural product cephalandole A in 86% yield through single-step operation under the standard reaction conditions.
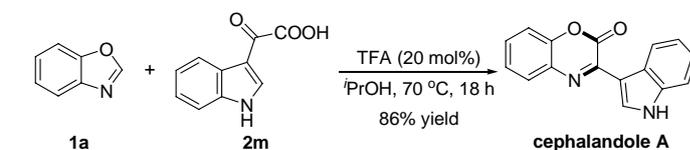
40 **Scheme 4.** Applications in the synthesis of the natural product.

To elucidate the mechanism, some control experiments were carried out under the standard reaction conditions as shown in Scheme 5. If only benzo[*d*]oxazole (**1a**) was applied under the standard reaction conditions, *o*-aminophenol (**4**) was isolated in 45 67% yield (Scheme 5a). However, no reaction happened and almost 90% of reactant **2a** was recovered when only 2-oxo-2-phenylacetic acid (**2a**) was applied under the standard reaction conditions (Scheme 5b). Under the standard reaction conditions, when *o*-aminophenol reacted with **2a**, afforded the desired 50 product **3a** in 89% yield (Scheme 5c), suggesting that *o*-aminophenol is a key intermediate. This result revealed that a ring-opening pathway was taken in the reaction.
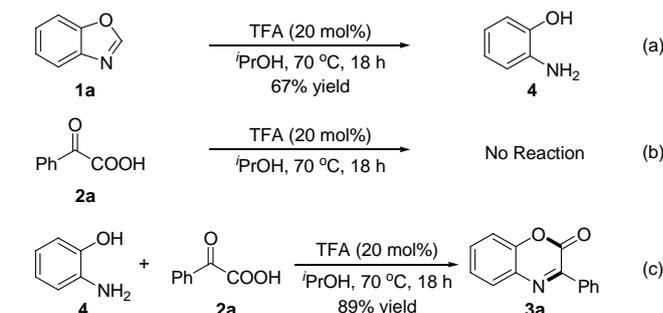
Scheme 5. Control experiments.

55 On the basis of the above experimental results, we proposed a possible reaction pathway for the formation of 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones. The first step may involve the ring-opening of benzo[*d*]oxazoles leading to *o*-aminophenol. Then cyclization reaction of *o*-aminophenol with 2-oxo-2-arylacetic 60 acid in the presence of TFA delivers the corresponding 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones as the products.

Finally, it is noteworthy that the present synthetic route to 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones could be readily scaled up to gram quantity without diffculty. For instance, the reaction at the 65 20 mmol scale afforded the corresponding product 3-phenyl-2*H*-benzo[*b*][1,4]oxazin-2-one (**3a**) in 87% yield (Scheme 6).
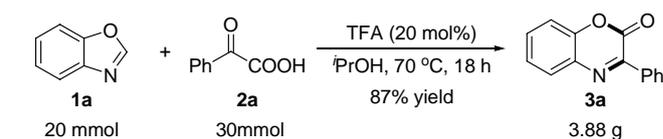
Scheme 6. Gram-scale synthesis of **3a**.

In summary, we have developed a new strategy for 70 constructing 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones from TFA-catalyzed tandem reaction of benzo[*d*]oxazoles with 2-oxo-2-

arylacetic acids. In addition, the method provides an efficient access to the natural product cephalandole A. Further efforts to extend this catalytic system to the preparation of other useful nitrogen-containing heterocycles are currently underway in our laboratories.

Notes and references

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† Electronic Supplementary Information (ESI) available: Analytical data and spectra (^{1}H, ^{13}C NMR) for all products; See DOI: 10.1039/b000000x/

1   (*a*) J. Teller, InE. Schaumann, Ed.; Houben-Weyl Methods of Organic Chemistry, Hetarenes IV, Six-Membered and Larger Hetero-Rings with Maximum Unsaturation; Georg Thieme: Stuttgart, 1997; Vol. E 9a, pp 141–177; (*b*) Review: J. Ilaš, P. S. Anderluh, M. S. Dolenc and D. Kikelj, *Tetrahedron,* 2005, **61**, 7325.

2   (*a*) T. Hasui, N. Matsunaga, T. Ora, N. Ohyabu, N. Nishigaki, Y. Imura, Y. Igata, H. Matsui, T. Motoyaji, T. Tanaka, N. Habuka, S. Sogabe, M. Ono, C. S. Siedem, T. P. Tang, C. Gauthier, L. A. DeMeese, S. A. Boyd and S. Fukumoto, *J. Med. Chem.,* 2011, **54**, 8616; (*b*) H. Matsuoka, N. Ohi, M. Mihara, H. Suzuki, K. Miyamoto, N. Maruyama, K. Tsuji, N. Kato, T. Akimoto, Y. Takeda, K. Yano and T. Kuroki, *J. Med. Chem.,* 1997, **40**, 105; (*c*) S. M. Bromidge, B. Bertani, M. Borriello, S. Faedo, L. J. Gordon, E. Granci, M. Hill, H. R. Marshall, L. P. Stasi, V. Zucchelli, G. Merlo, A. Vesentini, J. M. Watson and L. Zonzini, L. *Bioorg. Med. Chem. Lett.,* 2008, **18**, 5653; (*d*) S. M. Bromidge, B. Bertani, M. Borriello, A. Bozzoli, S. Faedo, M. Gianotti, L. J. Gordon, M. Hill, V. Zucchelli, J. M. Watson and L. Zonzini, *Bioorg. Med. Chem. Lett.,* 2009, **19**, 2338; (*e*) T. Hasui, T. Ohra, N. Ohyabu, K. Asano, H. Matsui, A. Mizukami, N. Habuka, S. Sogabe, S. Endo, C. S. Siedem, T. P. Tang, C. Gauthier, L. A. De Meese, S. A.; Boyd and S. Fukumoto, S. *Bioorg. Med. Chem.,* 2013, **21**, 5983.

3   (a) Q. Chen, M. Chen, C. Yu, L. Shi, D. Wang, Y. Yang and Y.; Zhou, *J. Am. Chem.Soc.,* 2011, **133**, 16432; (*b*) M. Rueping, A. P. Antonchick and T. Theissmann, *Angew. Chem., Int. Ed.,* 2006, **45**, 6751; (*c*) C. Saitz, H. Rodríguez, A. Márquez, A. Cañete, C. Jullian, A. Zanocco, *Synth. Commun.,* 2001, **31**, 135 ; (*d*) H. Miyabe, Y. Yamaoka and Y. Takemoto, *J. Org. Chem.,* 2006, **71**, 2099.

4   (*a*) R. A. Duval, G. Lewin, E. Peris, N. Chahboune, A. Garofano, S. Drçse, D. Cortes, U. Brandt and R. Hocquemiller, *Biochemistry,* 2006, **45**, 2721; (*b*) X. Li, N. Liu, H. Zhang, S. E. Knudson,R. A. Slayden and P. J. Tonge, *Bioorg. Med. Chem. Lett.,* 2010, **20**, 6306; (*c*) V. L. Gein, N. A. Rassudikhina, N. V. Shepelina, M. I. Vakhrin, E. B. Babushkina and E. V. Voronina, E. V. *Pharm. Chem. J.,* 2008, **42**, 519; (*d*) S. Bondock, S. Adel, H. A. Etman and F. A. Badria, *Eur. J. Med. Chem.,* 2012, **48**, 192.

5   M. Hu, J. Fan, H. Li, K. Song, S. Wang, G. Cheng and X. Peng, *Org. Biomol. Chem.,* 2011, **9**, 980.

6   (*a*) K. Azuma, S. Suzuki, S. Uchiyama, T. Kajiro, T. Santa and K. Imai, *Photochem. Photobiol. Sci.,* 2003, **2**, 443; (*b*) T. Nishio, *J. Chem. Soc. Perkin Trans. 1,* 1990, 565; (*c*) S. Nonell, L. R. Feñrrares, A. Caete, E. Lemp, G. Günther, N. Pizarro and A. L. Zanocco, *J. Org. Chem.,* 2008, **73**, 5371.

7   Wu, P.-L.; Hsu, Y.-L.; Jao, C.-W. *J. Nat. Prod.* 2006, **69**, 1467.

8   J. Mason, J. Bergman and T. Janosik, *J. Nat. Prod.,* 2008, **71**, 1447.

9   (*a*) L. Gross, F. Mohn, N. Moll, G. Meyer, R. Ebel, W. M. Abdel-Mageed and M. Jaspars, *Nature Chem.,* 2010, **2**, 821; (*b*) L. Gross, *Nature Chem.,* 2011, **3**, 273.

10 (a) C. Trebaul, J. Roncali, F. Garnier and R. Guglielmetti, *Bull. Chem. Soc. Jpn.,* 1987, **60**, 2657; (b) R. B. Moffet, *J. Med. Chem.,* 1966, **9**, 475; (*c*) A. Chilin, A. Confente, G. Pastorini and A. Guiotto, *Eur. J. Org. Chem.,* 2002, 1937.

11 (*a*) D. N. Nicolaides, D. R. Gautam, K. E. Litinas, D. J. Hadjipavlou-Litina and C. A. Kontogiorgis, *J. Heterocyclic Chem.,* 2004, **41**, 605; (*b*) D. N.Nicolaides, R. W. Awad and E. A. Varella, *J. Heterocyclic Chem.,* 1996, **33**, 633.

12 I. Yavari, S. Souri, M. Sirouspour and H. Djahaniani, *Synthesis,* 2006, 3243.

13 N. Zidar and D. Kikelj, *Tetrahedron,* 2008, **64**, 5756.

14 R. Ballini, A. Palmieri, M. A. Talaq and S. Gabrielli, S. *Adv. Synth. Catal.,* 2009, **351**, 2611.

15 (*a*) Z. Y. Chen, J. X. Chen, M. C. Liu, J. C. Ding, W. X. Gao, X. B. Huang and H. Y. Wu, *J. Org. Chem.,* 2013, **78**, 11342; (*b*) J. X. Chen, H. Y. Wu, Z. G. Zheng, C. Jin, X. X. Zhang and W. K. Su, *Tetrahedron Lett.,* 2006, **47**, 5383; (*c*) W. G. Yang, L. P. Ye, D. Y. Huang, M. C. Liu, J. C. Ding, J. X. Chen and H. Y. Wu, *Tetrahedron,* 2013, **69**, 9852; (*d*) D. Y. Huang, J. X. Chen, W. X. Dan, J. C. Ding, M. C. Liu and H. Y. Wu, *Adv. Synth. Catal.,* 2012, **354**, 2123; (*e*) J. X. Chen, D. Z. Wu, F. He, M. C. Liu, H. Y. Wu, J. C. Ding and W. K. Su, *Tetrahedron Lett.,* 2008, **49**, 3814; (*f*) J. X. Chen, W. K. Su, H. Y. Wu, M. C. Liu and C. Jin, *Green Chem.,* 2007, **9**, 972; (*g*) F. J. Duan, M. C. Liu, J. X. Chen, J. C. Ding, Y. F. Hu and H. Y. Wu, *RSC Adv.,* 2013, **3**, 24001; (*h*) Y. Shen, J. X. Chen, M. C. Liu, J. C. Ding, W. X. Gao, X. B. Huang and H. Y. Wu, *Chem. Commun.,* 2014. in press (DOI: 10.1039/c3cc48767a).

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Unexpected TFA-catalyzed tandem reaction of benzo[*d*]oxazoles with 2-oxo-2-arylacetic acids: synthesis of 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones and cephalandole A

Shaoxi Yan, Leping Ye, Miaochang Liu, Jiuxi Chen,* Jinchang Ding, Wenxia Gao, Xiaobo Huang and Huayue Wu*

Abstract: A convenient and efficient method for the TFA-catalyzed synthesis of 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones via a tandem reaction of benzo[*d*]oxazoles with 2-oxo-2-arylacetic acids was reported for the first time. The efficiency of this transformation was demonstrated by compatibility with a wide range of functional groups. The synthetic utility of this method was confirmed by the synthesis of the natural product cephalandole A. Moreover, a plausible mechanism for the formation of 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones involving ring-opening and cyclization steps is proposed. The present synthetic route to 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones could be readily scaled up to gram quantity without difficulty.

highlighting the novelty of the work:

TFA-catalyzed ring-opening/cyclization reaction of benzo[*d*]oxazoles with 2-oxo-2-arylacetic acids: synthesis of 3-aryl-2*H*-benzo[*b*][1,4]oxazin-2-ones and the natural product cephalandole A

Colour graphic: