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RSC Advances

Cite this: DOI: 10.1039/c0xx00000x

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Paper

Brønsted acid-catalyzed selective C-C bond cleavage of 1,3-diketones: a facile synthesis of 4(*3H*)-quinazolinones in aqueous ethyl lactate

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Received (in XXX, XXX) Xth XXXXXXXXX 20XX, Accepted Xth XXXXXXXXX 20XX
DOI: 10.1039/b000000x

A facile and green approach was developed for the synthesis of 4(*3H*)-quinazolinones by using camphorsulfonic acid as a catalyst in an aqueous solution of biodegradable ethyl lactate. Various 2-aryl-, 2-alkyl-, and 2-(4-oxoalkyl)quinazolinones were obtained by cyclization of 2-aminobenzamides with a wide range of acyclic or cyclic 1,3-diketones *via* C-C bond cleavage in satisfactory-to-excellent yields.

Introduction

The direct selective cleavage of unstrained C–C bond has attracted much attention and emerged as a challenging transformation in organic synthesis due to the high C–C bond strength.[1] As inexpensive and readily available starting materials, 1,3-diketones have been widely used as important substrates in organic synthesis.[2] In 2010, Lei reported the first example of CuI-catalyzed C–C bond cleavage of 1,3-diketones and arylation to give *α*-arylketones.[3a] The esters,[3b] *α*-ketoesters,[3c] amides,[3d,3e] *α*-ketoamides[3f] or *α*-amino acid esters[3g] could be obtained from the reactions of 1,3-diketones with alcohols or amines *via* C–C bond cleavage in the presence of Lewis acid, or under oxidation conditions. Recently, CuI-catalyzed tandem cyclization of *o*-halobenzoic acids,[3h] esters,[3i] or amides[3j] with 1,3-diketones leading to isocoumarins was developed. Very recently, H_2O_2-promoted reactions of aliphatic primary amines with 1,3-diketones for the synthesis of 1*H*-pyrrol-3(2*H*)-ones has also been realized.[3k]

4(*3H*)-quinazolinones are building blocks of many naturally occurring alkaloids and marketed drugs (Fig 1).[4] Owing to their importance and utility, a range of synthetic methods have been developed to construct quinazolinone derivatives.[5-7] It should be noted that most reported methods for the preparing of 4(*3H*)-quinazolinones request expensive transition-metal catalysts in the presence of oxidants and bases under harsh reaction conditions. Therefore, more environmentally benign and efficient methods to approach valuable quinazolinone derivatives are highly desirable.

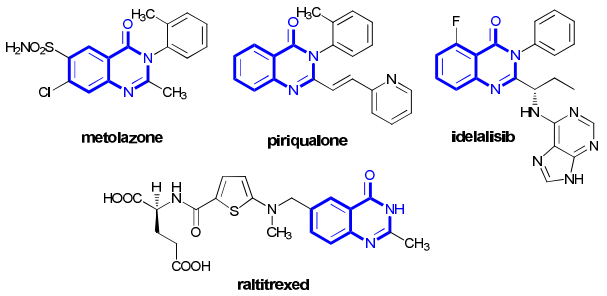
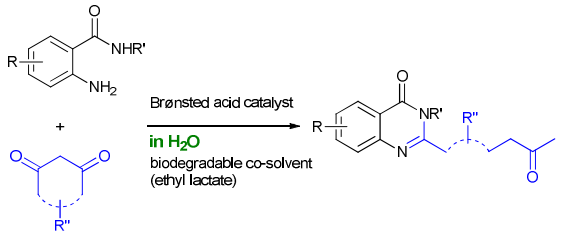


Figure 1. Selected examples of alkaloids and marketed drugs incorporating 4(*3H*)-quinazolinone cores.

Ethyl lactate is prepared by esterification of ethanol with lactic acid, both of which can be obtained by fermentation of biomass. Ethyl lactate has recently attracted much attention and has been used in organic synthesis as an environmentally benign and biodegradable solvent.[8] Continuing our research interest in green catalysis,[9] we have discovered a green approach for the synthesis of 4(3*H*)-quinazolinones by cyclization of 2-aminobenzamides with a wide range of acyclic or cyclic 1,3-diketones *via* C-C bond cleavage in the presence of camphorsulfonic acid (CSA) as a Brønsted catalyst in biodegradable ethyl lactate solution under metal-, oxidant-, and radiation-free conditions (Scheme 1).



Scheme 1. A green approach to 4(3*H*)-quinazolinones.

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† Electronic Supplementary Information (ESI) available: Experimental procedures, compound chracterizations, and copies of ^{1}H NMR and ^{13}C NMR spectra. See DOI: 10.1039/b000000x/

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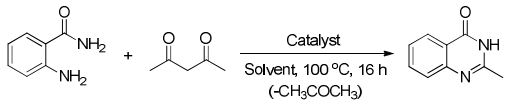
DOI: 10.1039/C5RA17969F

Results and Discussion

For our initial studies, we chose the reaction of 2-aminobenzamide (**1a**) with pentane-2,4-dione (**2A**) as a model process for optimizing the reaction conditions (Table 1). No reaction was observed when amide **1a** was treated with dione **2A** in poly(ethylene glycol) (PEG-400) at 100 °C in the absence of a catalyst (Table1, entry 1). However, the desired product **3aA** was obtained in various yields on adding 10 mol% of a Brønsted acid catalyst to the reaction mixture (entries 2–6). Among the tested Brønsted acid catalysts, *p*-toluenesulfonic acid (TsOH·H_2O), acetic acid (AcOH), and trifluoroacetic acid (F_3CCO_2H) gave yields of less than 10%. Moderate yields of quinazolinone **3aA** were obtained when trifluoromethanesulfonic acid (F_3CSO_3H; entry 5) or natural camphorsulfonic acid (CSA; entry 6) was used as catalyst, with CSA providing the higher yield (61%). When other green solvents such as PEG-200, ethyl lactate, and water were screened in this transformation, ethyl lactate gave the best results (entries 6–9). To our delight, we obtained product **3aA** in up to 98% yield by using a mixture of ethyl lactate and water as the solvent (entry 11). Decreasing the catalyst loading from 10 mol% to 5 mol% resulted in a relatively low yield (entry 12). We therefore performed subsequent reactions of 2-aminobenzamides with various 1,3-diketones in the presence of 10 mol% camphorsulfonic acid as catalyst at 100 °C in a 1:9 (v/v) mixture of ethyl lactate and water for 16–24 hours.

Table 1. Optimization of the reaction conditions [a]



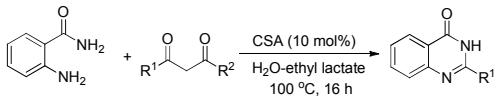
1a **2A** **3aA**

Entry	Catalyst	Solvent	Yield [b]
1	none	PEG-400	NR [c]
2	TsOH·H_2O	PEG-400	10%
3	AcOH	PEG-400	<5%
4	F_3CCO_2H	PEG-400	<5%
5	F_3CSO_3H	PEG-400	48%
6	CSA[d]	PEG-400	61%
7	CSA	PEG-200	42%
8	CSA	ethyl lactate	74%
9	CSA	H_2O	43%
10	CSA	ethyl lactate–H_2O (1:1)	84%
11	CSA	ethyl lactate–H_2O (1:9)	98%
12	CSA[e]	ethyl lactate–H_2O (1:9)	81%

[a] *Reaction conditions*: 2-aminobenzamide (**1a**; 0.2 mmol), pentane-2,4-dione (**2A**; 0.3 mmol), catalyst (10 mol%), solvent (1.0 mL), 100 °C, 16 h. [b] Isolated yield. [c] No reaction. [d] CSA: camphorsulfonic acid. [e] 5 mol% of CSA was use.

With the optimized reaction conditions in hand, we examined the reactions of 2-aminobenzamide (**1a**) with various acyclic 1,3-diketones. As shown in Table 2, a lower yield of **3aB** comparing with that of **3aA** was observed when the reaction of **1a** and heptane-3,5-dione (**2B**) was carried out under the optimized conditions (**3aA**: 98%; **3aB**: 81%). The reaction of amide **1a** with sterically hindered 2,6-dimethylheptane-3,5-dione (**2C**) provided the desired product **3aC** in moderate yield (**3aC**: 59%). In contrast, the reactants remained unchanged in the attempted reaction of amide **1a** and the more sterically hindered 2,2,6,6-tetramethylheptane-3,5-dione (**2D**), even on raising the temperature and prolonging the reaction time. 2-Phenylquinazolin-4(3*H*)-one (**3aE**) was obtained by the reaction of **1a** with 1,3-diphenylpropane-1,3-dione (**2E**) in 79% yield. Finally, the reactions of **1a** with the unsymmetrical 1,3-diketones 1-phenylbutane-1,3-dione (**2F**), 5,5-dimethylhexane-2,4-dione (**2G**), and 1,1,1-trifluoropentane-2,4-dione (**2H**) were examined, all gave the same product, **3aA**, in 54–75% yield through selective C–C bond cleavage. These results indicate that the reactivity of the acetyl group is higher than that of the benzoyl, pivaloyl, or trifluoroacetyl group.

Table 2. The scope of acyclic 1,3-diketones **2** [a]



1a **2A-H** **3aA-3aH**

Entry	**2**		**3**	Yield [b]
1	$R^1 = R^2 =$ Me	**2A**	**3aA**	98%
2	$R^1 = R^2 =$ Et	**2B**	**3aB**	81%
3	$R^1 = R^2 =$ *i*-Pr	**2C**	**3aC**	59%
4	$R^1 = R^2 =$ *t*-Bu	**2D**	**3aD**	<1%
5	$R^1 = R^2 =$ Ph	**2E**	**3aE**	79%
6	$R^1 =$ Me, $R^2 =$ Ph	**2F**	**3aA**	75%
7	$R^1 =$ Me, $R^2 =$ *t*-Bu	**2G**	**3aA**	71%
8	$R^1 =$ Me, $R^2 = CF_3$	**2H**	**3aA**	54%

[a] *Reaction conditions*: 2-aminobenzamide (**1a**; 0.2 mmol), pentane-2,4-dione (**2**; 0.3 mmol), CSA (10 mol%), H_2O-ethyl lactate (9:1; 1.0 mL), 100 °C, 16 h. [b] Isolated yield.

Next, we examined the scope of the reaction with respect to the 2-aminobenzamides. Various *N*-substituted 2-aminobenzamides **1a-m** were treated with pentane-2,4-dione (**2A**) under the optimized conditions (Scheme 2). From the reaction of 2-amino-*N*-methylbenzamide (**1b**), the desired product 2,3-dimethylquinazolin-4(*3H*)-one (**3bA**) was isolated in 76% yield. The *N*-aryl-2-aminobenzamides with electron-donating groups (**1d**; 4-Me, **1e**; 2-Me, and **1f**; 4-MeO) or electron-withdrawing groups (**1g**; 3-Cl, **1h**; 4-Cl, and **1i**; 3,4-Cl_2) on the benzene ring also underwent the transformation to give the corresponding products **3cA**–**3iA** in 56–93% yield. 3-Benzyl-2-methylquinazolin-4(3*H*)-one (**3jA**) was prepared in 88% yield by the reaction of 2-amino-*N*-benzylbenzamide with pentane-2,4-dione (**2A**). The corresponding reactions of 2-amino-6-fluorobenzamide and 2-amino-5-chlorobenzamide gave quinazolinones **3kA** and **3mA** in 88% and 79% yield, respectively.

Encouraged by these results, we extended the scope of diketone reactant to include cyclic 1,3-diketones **4A-G** (Table 3). Treatment of 2-aminobenzamide (**1a**) with 1.5 equivalents of cyclohexane-1,3-dione (**4A**) in the presence of 10 mol% natural CSA in a 1:9 (v/v) mixture of ethyl lactate and water at 100 °C for 24 h gave 2-(4-oxopentyl)quinazolin-4(*3H*)-one (**5aA**) in 61% yield with full atom efficiency (Table 3, entry 1). When reactions of **1a** with other substituted cyclohexane-1,3-diones **4B-E** were carried out under the optimized conditions, the corresponding products **5aB-5aE** were obtained in 35–84% yield. Interestingly, 2-methylcyclohexane-1,3-dione (**4E**)

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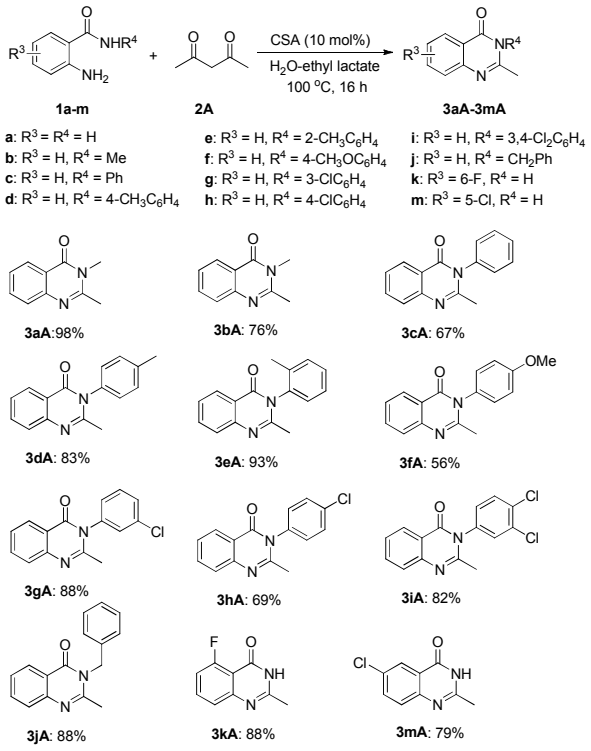
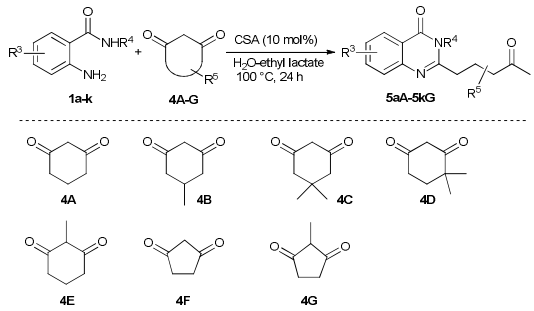


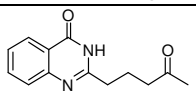
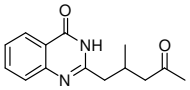
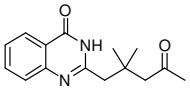
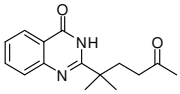
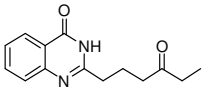
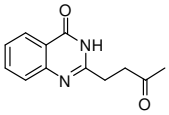
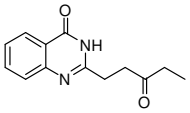
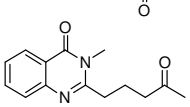
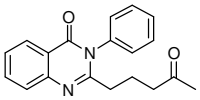
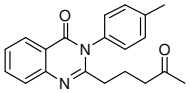
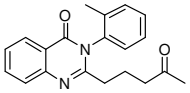
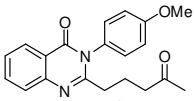
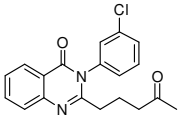
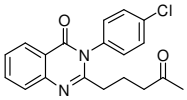
Scheme 2. The scope of 2-aminobenzamides **1**. Reaction conditions: 2-aminobenzamide (**1**; 0.2 mmol), pentane-2,4-dione (**2A**; 0.3 mmol), CSA (10 mol%), H_2O-ethyl lactate (9:1; 1.0 mL), 100 °C, 16 h, isolated yield.

exhibited a higher reactivity than 5-methylcyclohexane-1,3-dione (**4B**) (entries 2 and 5). In contrast, cyclopentane-1,3-dione (**4F**) and 2-methyl-1,3-cyclopentane-1-3-dione (**4G**), which contain a five-membered ring, did not give the desired products **5aF** and **5aG** when treated with **1a** (entries 6 and 7). We then examined the scope of the reaction with respect to the 2-aminobenzamides **1**. In general, various 2-aminobenzamides **1** reacted with cyclohexane-1,3-dione (**4A**) under the optimized conditions to give the corresponding products **5bA-5kA** in 55–98% yield (entries 8–17). With *N*-alkyl-substituted 2-aminobenzamides, products **5bA** and **5jA** were obtained in 78% and 87% yield, respectively (entries 8 and 16). *N*-Aryl-substituted 2-aminobenzamides also underwent this transformation. 2-aminobenzamides with an electron-rich substituent on the aryl group gave products **5eA** and **5fA** in relatively high yields (entries 10 and 12), whereas electron-deficient aryl group-substituted 2-aminobenzamides gave products **5gA** and **5iA** in relatively low yields (entries 13 and 15). Finally, 2-amino-6-fluorobenzamide also reacted with cyclohexane-1,3-dione (**4A**) to give the corresponding product **5kA** in 98%.

Based on the results obtained above and the literature, [10] a proposed reaction mechanism was shown in Scheme 3. The Brønsted acid catalyzed condensation reaction of 2-aminobenzamide **1** with 1, 3-diketone **4** would take place to generate a ketimine intermediate **A**, followed by tautomerization to give the enaminone intermediate **B**. Then, the intramolecular nucleophilic addition of **B** would produce adduct **C**. The C-C bond cleavage reaction would finally occur to generate the desired product **5**.

Table 3. Synthesis of 2-(4-oxoalkyl)quinazolinones **5** [a]



Entry	Substrate 1/4	Product 5		Yield [b]
1	**1a/4A**		**5aA**	61%
2	**1a/4B**		**5aB**	35%
3	**1a/4C**		**5aC**	49%
4	**1a/4D**		**5aD**	38%
5	**1a/4E**		**5aE**	84%
6	**1a/4F**		**5aF**	ND [c]
7	**1a/4G**		**5aG**	ND [c]
8	**1b/4A**		**5bA**	78%
9	**1c/4A**		**5cA**	60%
10	**1d/4A**		**5dA**	96%
11	**1e/4A**		**5eA**	69%
12	**1f/4A**		**5fA**	84%
13	**1g/4A**		**5gA**	55%
14	**1h/4A**		**5hA**	80%

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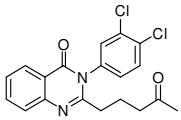
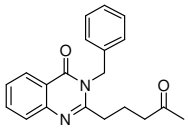
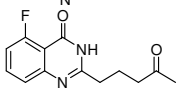
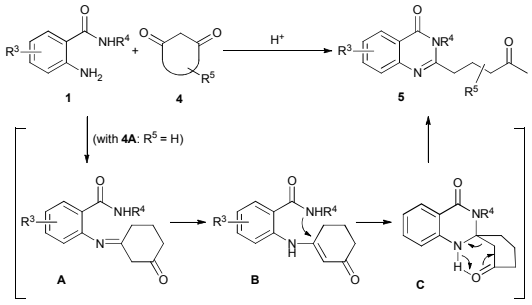
15	**1i/4A**		**5iA**	62%
16	**1j/4A**		**5jA**	87%
17	**1k/4A**		**5kA**	98%

[a] *Reaction conditions*: 2-aminobenzamide 1 (0.2 mmol), cyclic 1,3-diketone 5 (0.3 mmol), CSA (10 mol%), 1:9 (v/v) ethyl lactate–H_2O (1.0 mL), 100 °C, 24 h. [b] Isolated yield. [c] Not detected.



Scheme 3. A proposed reaction mechanism

Conclusions

In summary, we have developed an efficient, metal- and oxidant-free green approach for the synthesis of 4(3*H*)-quinazolinones. Various 2-aryl-, 2-alkyl-, and 2-(4-oxoalkyl)quinazolinones were prepared by successive condensation of 2-aminobenzamides with a wide range of acyclic or cyclic 1,3-diketones, intramolecular nucleophile addition, and selective C–C bond cleavage, catalyzed by natural camphorsulfonic acid in an aqueous ethyl lactate solution. Further applications of this methodology to synthesis of other *N*-heterocycles are currently underway in our laboratory.

Experimental Section

General remarks

All reagents and solvents were purchased from commercial suppliers and used without further purification unless otherwise stated. Analytic thin-layer chromatography (TLC) was carried out with silica gel GF 254-coated plates. All products were isolated by column chromatography on silica gel (300–400 mesh) using petroleum ether (PE; bp 60–90 °C) and ethyl acetate. All compounds were characterized by ^{1}H NMR (400 MHz), ^{13}C NMR (100 MHz), and ESI-MS. All ^{1}H NMR shifts are reported in δ units (ppm) relative to the signals for residual $CHCl_3$ (δ = 7.26 ppm) or DMSO (δ = 2.50 ppm) in the corresponding deuterated solvent. All ^{13}C NMR spectra are reported in ppm relative to $CDCl_3$ (77.23 ppm) or DMSO-d_6 (39.60 ppm). NMR data were recorded on a Bruker 400 MHz instrument. HRMS data were recorded with ESI ionization sources on a Bruker Apex II instrument. Melting points were determined on an X-4 apparatus.

2-Methylquinazolin-4(3*H*)-one (3aA); Typical Procedure

A flask was charged with 2-aminobenzamide (**1a**; 27.2 mg, 0.2 mmol), pentane-2,3-dione (**2A**; 30.0 mg, 0.3 mmol), CSA (4.6 mg, 0.02 mmol), and 1:9 (v/v) ethyl lactate–H_2O (1.0 mL). The flask was sealed and the mixture was stirred at 100 °C for 16 h. When the reaction was complete (TLC), the mixture was cooled to r.t., extracted with EtOAc (3 × 20 mL), and washed with H_2O. The organic phase was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel) to give the product **3aA** (31.7 mg, 98%) as white solid; mp: 286–288 °C; ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.61 (3 H, s), 7.45–7.49 (1H, m), 7.68 (1H, d, J = 7.6 Hz), 7.76 (1H, dt, J_1 = 8.4 Hz, J_2 = 1.6 Hz), 8.28 (1H, dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz), 12.19 (s, H); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 22.1, 120.2, 126.2, 126.4, 127.0, 134.9, 149.4, 153.3, 164.4; HRMS (ESI): *m/z* $[M+H]^+$ calcd. for $C_9H_9N_2O$: 161.0709; found: 161.0714.

2-(4-oxopentyl)quinazolin-4(*3H*)-one(5aA); Typical Procedure

A flask was charged with 2-aminobenzamide (**1a**; 27.2 mg, 0.2 mmol), cyclohexane-1,3-dione (**4A**; 33.6 mg, 0.3 mmol), CSA (4.6 mg, 0.02 mmol), and 1:9 (v/v) ethyl lactate–H_2O (1.0 mL). The flask was sealed and the mixture was stirred at 100 °C for 24 h. When the reaction was complete (TLC), the mixture was cooled to r.t., extracted with EtOAc (3 × 20 mL), and washed with H_2O. The organic phase was dried (Na_2SO_4), filtered, and concentrated under reduced pressure. The residue was purified by column chromatography (silica gel) to give the product **5aA** (28.1 mg, 61%) as white solid; mp: 145–146 °C; ^{1}H NMR ($CDCl_3$, 400 MHz): δ = 2.13–2.20 (m, 2H), 2.18 (s, 3H), 2.64 (t, J = 7.2 Hz, 2H), 2.80 (t, J = 7.2 Hz, 2H), 7.48 (dt, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 7.68 (d, J = 8.0 Hz, 1H), 7.77 (dt, J_1 = 8.0 Hz, J_2 = 1.6 Hz, 1H), 8.29 (dd, J_1 = 8.0 Hz, J_2 = 1.2 Hz, 1H), 11.52 (s, 1H); ^{13}C NMR ($CDCl_3$, 100 MHz): δ = 21.1, 30.0, 34.7, 42.3, 120.6, 126.3, 126.5, 127.2, 134.8, 149.2, 155.8, 163.8, 208.2; HRMS (ESI): m/z $[M+H]^+$ calcd. for $C_{13}H_{14}N_2O_2$: 231.1128; found: 231.1134.

Acknowledgements

We are grateful for financial support from the National Natural Science Foundation of China (21202092) and for a Startup Foundation from the China Three Gorges University (KJ2012B080, KJ2014H008).

Notes and references

1 For selected recent reviews, see: (a) A. de Meijere, *Chem. Rev.*, 2003, **103**, 931–932; (b) M. E. Boom and D. Milstein, *Chem. Rev.*, 2003, **103**, 1759–1792; (c) C.-H. Jun, *Chem. Soc. Rev.*, 2004, **33**, 610–618; (d) M. Rubin, M. Rubina, V. Gevorgyan, *Chem. Rev.*, 2007, **107**,

View Article Online
DOI: 10.1039/C5RA17969F

3117–3179; (e) Y. J. Park, J.-W. Park, C.-H. Jun, *Acc. Chem. Res.*, 2008, **41**, 222–234; (f) M. Tobisu and N. Chatani, *Chem. Soc. Rev.*, 2008, **37**, 300–307; (g) Y. Horino, *Angew. Chem. Int. Ed.*, 2007, **46**, 2144–2146; (h) L. J. Gooßen, N. Rodríguez, K. Gooßen, *Angew. Chem. Int. Ed.*, 2008, **47**, 3100–3120; (i) C. Najera and J. M. Sansano, *Angew. Chem. Int. Ed.*, 2009, **48**, 2452–2456; (j) S. M. Bonesi and M. Fagnoni, *Chem. Eur. J.*, 2010, **16**, 13572–13589; (k) B. Rybtchinski and D. Milstein, *Angew. Chem. Int. Ed.*, 1999, **38**, 870–883; (l) R. H. Crabtree, *Chem. Rev.*, 1985, **85**, 245–269.

2 (a) J. Zhao, Y. Zhao, H. Fu, *Org. Lett.*, 2012, **14**, 2710–2713; (b) W. P. Liu, J. Liu, D. Ogawa, Y. Nishihara, X. Guo, Z. Li, *Org. Lett.*, 2011, **13**, 6272–6275; (c) A. Biswas, S. De Sarkar, R. Fröhlich, A. Studer, *Org. Lett.*, 2011, **13**, 4966–4969; (d) Z.-Q. Rong, M.-Q. Jia, S.-L. You, *Org. Lett.*, 2011, **13**, 4080─4083; (e) J. Xie, H. Jiang, Y. Cheng, C. Zhu, *Chem. Commun.*, 2012, **48**, 979─981; (f) M. Gao, Y. Yang, Y.-D. Wu, C. Deng, W.-M. Shu, D.-X. Zhang, L.-P. Cao, N.-F. She, A.-X. Wu, *Org. Lett.*, 2010, **12**, 4026─4029; (g) Y. Liu and J.-W. Sun, *J. Org. Chem*., 2012, **77**, 1191; (h) L.-G. Meng, B. Hu, Q.-P. Wu, M. Liang, S. Xue, *Chem. Commun.*, 2009, 6089─6091.

3 For selected examples, see: (a) C. He, S. Guo, L. Huang, A. Lei, *J. Am. Chem. Soc.*, 2010, **132**, 8273─8275; (b) A. Kawata, K. Takata, Y. Kuninobu, K. Takai, *Angew. Chem. Int. Ed.*, 2007, **46**, 7793─7795; (c) C. Zhang, P. Feng, N. Jiao, *J. Am. Chem. Soc.*, 2013, **135**, 15257─15262; (d) X. Sun, M. Wang, P. Li, X. Zhang, L. Wang, *Green Chem.*, 2013, **15**, 3289─3294; (e) S. Wang, Y. Yu, X. Chen, H. Zhu, P. Du, G. Liu, L. Lou, H. Li, W. Wang, *Tetrahedron. Lett.*, 2015, **56**, 3093─3096; (f) X.B. Zhang, M. Wang, Y. Zhang, L. Wang, *RSC Adv.*, 2013, **3**, 1311─1316; (g) J. Zhang, Y. Shao, Y. Wang, H. Li, D. Xu, X. Wan, *Org. Biomol. Chem.*, 2015, **13**, 3982─3987; (h) S. Cai, F. Wang, C. Xi, *J. Org. Chem.*, 2012, **77**, 2331─2336; (i) X. Fan, Y. He, L. Cui, S. Guo, J. Wang, X. Zhang, *Eur. J. Org. Chem.*, 2012, 673─677; (j) V. Kavala, C. C. Wang, D. K. Barange, C. W. Kuo, P. M. Lei, C. F. Yao, *J. Org. Chem.*, 2012, **77**, 5022─5029; (k) X. Sun, X. Li, X. Zhang, L. Wang, *Org. Lett.*, 2014, **16**, 2126─2129; (l) M. S. Mayo, X. Yu, X. Zhou, X. Feng, Y. Yamamoto, M. Bao, *Org. Lett.*, 2014, **16**, 764─767.

4 (a) C. Wattanapiromsakul, P. I. Forster, P. G. Waterman, *Phytochemistry*, 2003, **64**, 609─615; (b) N. M. Abdel Gawad, H. H. Georgey, R. M. Youssef, N. A. El-Sayed, *Eur. J. Med. Chem.*, 2010, **45**, 6058─6067.

5 For selected recent reviews, see: (a) A. Witt, J. Bergman, *Curr. Org. Chem.*, 2003, **7**, 659─677; (b) D. J. Connolly, D. Cusack, T. P. O'Sullivan, P. J. Guiry, *Tetrahedron*, 2005, **61**, 10153─10202; (c) L. He, H. Li, J. Chen, X.-F. Wu, *RSC Adv*., 2014, **4**, 12065─12077.

6 For selected recent examples, see: (a) G. W. Wang, C. B. Miao, H. Kang, *Bull. Chem. Soc. Jpn*., 2006, **79**, 1426–1430; (b) N. Mulakayala, B. Kandagatla, R. Ismail, K. Rapolu, P. Rao, C. Mulakayala, C. S. Kumar, J. Iqbal, S. Orugani, *Bioorg. Med. Chem. Lett.*, 2012, **22**, 5063–5066; (c) D. Zhan, T. Li, X. Zhang, C. Dai, H. Wei, Y. Zhang, Q. Zeng, *Synth. Commun*., 2013, **43**, 2493–2500; (d) M. Sharif, J. Opalach, P. Langer, M. Beller, X.-F. Wu, *RSC Adv.*, 2014, **4**, 8–17; (e) J. Zhou, J. Fang, *J. Org. Chem.*, 2011, **76**, 7730–7736; (f) A. J. A. Watson, A. C. Maxwell, J. M. Williams, *Org. Biomol. Chem.*, 2012, **10**, 240–243; (g) H. Hikawa, Y. Ino, H. Suzuki, Y. Yokoyama, *J. Org. Chem.*, 2012, **77**, 7046–7051; (h) W. Ge, X. Zhu, Y. Wei, *RSC Adv.*, 2013**,** **3**, 10817–10822; (i) Y.-P. Zhu, Z. Fei, M. Liu, F. Jia, A. Wu, *Org. Lett.*, 2013, **15**, 378–381; (j) Q. Li, Y. Huang, T. Chen, Y. Zhou, Q. Xu, S.-F. Yin, L.-B. Han, *Org. Lett.* 2014, **16**, 3672–3675; (k) D. Zhao, T. Wang, J.-X. Li, *Chem. Commun.*, 2014, **50**, 6471–6474; (l) D. Kumar, P. S. Jadhavar, M. Nautiyal, H. Sharma, P. K. Meena, L. Adane, S. Pancholia, A. K. Chakraborti, *RSC.Adv.*, 2015, **5**, 30819–30825; (m) L. Lu, M.-M. Zhang, H. Jiang, X.-S. Wang, *Tetrahedron Lett*., 2013, **54**, 757–760; (n) X. Yang, G. Cheng, J. Shen, C. Kuai, X. Cui, *Org. Chem. Front.*, 2015, **2**, 366–368.

7 Carbonylative construction of quinazolinones, see: (a) X.-F. Wu, L. He, H. Neumann and M. Beller, *Chem. Eur. J.* **2013**, *19*, 12635–12638; (b) H. Li, L. He, H. Neumann, M. Beller, X. F. Wu, *Green Chem*. **2014**, *16*, 1336–1343; (c) L. He, M. Sharif, H. Neumann, M. Beller, X. F. Wu, *Green Chem*. **2014**, *16*, 3763–3767; (d) C. Shen, N. Y. T. Man, S. Stewart, X.-F. Wu, *Org. Biomol. Chem.* **2015**, *13*, 4422–4425; (e) J. Chen, K. Natte, A. Spannenberg, H. Neumann, P. Langer, M. Beller, X.-F. Wu, *Angew. Chem. Int. Ed.* **2014**, *53*, 7579–7583; (f) L. He, H. Li, H. Neumann, M. Beller, X.-F. Wu, *Angew. Chem. Int. Ed.* **2014**, *53*, 1420–1424; (g) H. Li, W. Li, A. Spannenberg, W. Baumann, H. Neumann, M. Beller, X.-F. Wu, *Chem. Eur. J.* **2014**, *20*, 8541–8544; (h) X.-F. Wu, S. Oschatz, A. Block, A. Spannenberg, P. Langer, *Org. Biomol. Chem.*, **2014**, *12*, 1865–1870; (i) J. Chen, H. Neumann, M. Beller, X.-F.Wu, *Org. Biomol. Chem.*, **2014**, *12*, 5835–5838; (j) X.-F. W, S. Oschatz, M. Sharif, M. Beller, P. Langer, *Tetrahedron*, **2014**, *70*, 23–29; (k) M. Mori, H. Kobayashi, M. Kimura and Y. Ban, *Heterocycles*, **1985**, *23*, 2803–2806.

8 (a) C. S. M. Pereira, V. M. T. M. Silva and A. E. Rodrigues, *Green Chem*., 2011, **13**, 2658–2071; (b) R. A. Sheldon, *Green Chem.*, 2005, **7**, 267–278; (c) J. S. Bennett, K. L. Charles, M. R. Miner, C. F. Heuberger, E. J. Spina, M. F. Bartels and T. Foreman, *Green Chem.*, 2009, **11**, 166–168; (d) A. Dandia, A. K. Jain and A. K. Laxkar, *Tetrahedron Lett.*, 2013, **54**, 3929–3932; (e) P. P. Ghosh, S. Paul and A. R. Das, *Tetrahedron Lett.*, 2013, **54**, 138–142.

9 (a) H.-F. Zhou, Z. Li, Z. Wang, T. Wang, L. J. Xu, Y. He, Q.-H. Fan, J. Pan, L. Gu and A. S. C. Chan, *Angew. Chem. Int. Ed.*, 2008, **47**, 8464–8467; (b) Z.-J. Wang, H.-F. Zhou, T.-L. Wang, Y.-M. He, Q.-H. Fan, *Green Chem.*, 2009, **11**, 767–769; (c) Z.-Y. Ding, T. Wang, Y.-M. He, F. Chen, H.-F. Zhou, Q.-H. Fan, Q. Guo and A. S. C. Chan, *Adv. Synth. Catal.*, 2013, **355**, 3727–3735; (d) H.-F. Zhou, Q.-H. Fan, W.-J. Tang, L.-J. Xu, Y.-M. He, G.-J. Deng, L.-W. Zhao, L.-Q. Gu and A. S. C. Chan, *Adv. Synth. Catal.*, 2006, **348**, 2172–2182; (e) H.-F. Zhou, Q.-H. Fan, Y.-Y. Huang, L. Wu, Y.-M. He, W.-J. Tang, L. Q. Gu and A. S. C. Chan, *J. Mol. Catal. A: Chem.*, 2007, **275**, 47–53; (f) D. Pi, K. Jiang, H. Zhou, Y. Sui, Y. Uozumi and K. Zou, *RSC. Adv.,* 2014, **4**, 57875–57844; (g) K. Jiang, D. Pi, H. Zhou, S. Liu and K. Zou, *Tetrahedron*, 2014, **70**, 3056–3060; (h) S. Liu, K. Jiang, D. Pi, H. Zhou, Y. Uozumi and K. Zou, *Chin. J. Org. Chem.*, 2014, **34**, 1369–1375.

10 S. Roy, M. P. Davydova, R. Pal, K. Gilmore, G. A. Tolstikov, S. F. Vasilevsky, I. V. Alabugin, *J. Org. Chem.*, 2011, **76**, 7482–7490.

Received: ((will be filled in by the editorial staff))
Published online: ((will be filled in by the editorial staff))

View Article Online
DOI: 10.1039/C5RA17969F

Cite this: DOI: 10.1039/c0xx00000x

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Paper

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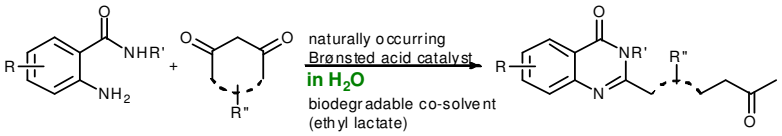
Brønsted acid-catalyzed selective C-C bond cleavage of 1,3-diketones: a facile synthesis of 4(*3H*)-quinazolinones in aqueous ethyl lactate

Guanshuo Shen, Haifeng Zhou, Peng Du, Sensheng Liu, Kun Zou and Yasuhiro Uozumi…….. Page No. – Page No.



A facile and green approach was developed for the synthesis of 4(*3H*)-quinazolinones from 2-aminobenzamides and 1,3-diketones via C-C bond cleavage catalyzed by camphorsulfonic acid in an aqueous solution of biodegradable ethyl lactate.