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Temperature-controlled solvent-free selective synthesis of *tert*-butyl peresters or acids from benzyl cyanides in the presence of the TBHP/Cu(OAc)₂ system†

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Solvent-free room temperature synthesis of *tert*-butyl peresters was achieved *via* copper-catalyzed oxidative-coupling of benzyl cyanides with *tert*-butyl hydroperoxide in short reaction times. Various derivatives of *tert*-butyl peresters were synesized by this pathway in good to excellent yields. Further investigation revealed that the above-mentioned protocol is effective for the synthesis of benzoic acid derivatives when the reaction is conducted at 80 °C, under the same reaction conditions.
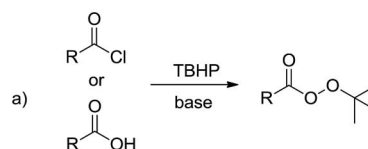
Introduction

Providing new synthetic methods or promoting previously reported ones is one of the main challenges to the synthetic chemists. Many efforts have been made to achieve a variety as well as green and eco-friendly synthetic pathways for important and widely used organic compounds. In recent years, oxidative coupling reactions in which two nucleophiles, in the presence of an external oxidant, are coupled together have been developed.[1] In this type of reaction, since only nucleophiles are used, unlike traditional methods that involve either electrophiles or nucleophiles, synthetic procedures will be more efficient and waste production will be minimized.
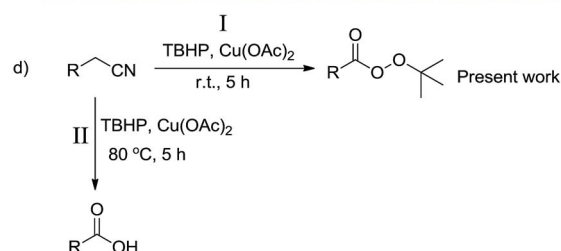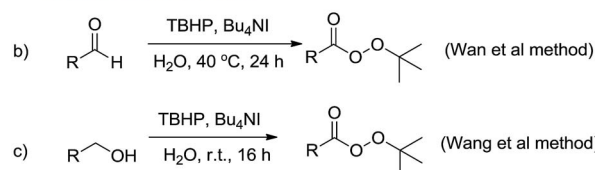
tert-Butyl peresters are an important class of organic compounds because of their participation in organic transformations in particular as oxidants in oxidation reactions.[2] Traditionally, *tert*-butyl peresters are prepared from carboxylic acids or their analogous benzoyl chlorides with *tert*-butyl hydroperoxide in the presence of base (Scheme 1, eqn (a)).[3] In 2011, a distinguish methodology by high atom economy and free of base was disclosed by Wan *et al.* for synthesis of *tert*-butyl peresters.[4] They reported on water Bu₄NI-catalyzed oxidative coupling of aldehydes with TBHP at 40 °C (Scheme 1, eqn (b)). The same procedure has recently been reported by Wang *et al.* in which alcohols is coupled with TBHP for synthesis of *tert*-butyl peresters (Scheme 1, eqn (c)).[5] Due to their importance as well as the low number of reported procedures, development of

synthetic methods for *tert*-butyl peresters is interest. Here we report a new synthetic pathway for the preparation of *tert*-butyl peresters *via* copper-catalyzed oxidative coupling of benzyl cyanides with TBHP (Scheme 1, eqn (d), path I). Performing under solvent-free conditions at room temperature in low reaction times make interest this transformation. Moreover, we found that when this reaction is conducted at 80 °C, benzoic acid derivatives will be predominant products (Scheme 1, eqn (d), path II).

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Scheme 1 Approaches for synthesis of *tert*-butyl peresters.

Results and discussion
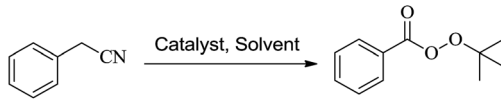
Following the benzyl cyanide oxidation in the presence of Cu(OAc)$_2$/TBHP system, a unknown product was obtained in 40% yield that after identification turned out to be *tert*-butyl perbenzoate. As mentioned above, because of the gravity of this class of compounds, efforts were made to raise efficiency by changing the reaction conditions. The results are summarized in Table 1. As can be seen in this table, the pre-starter reaction was performed between benzyl cyanide (1 mmol) and TBHP (70 wt% in H$_2$O, 1 mmol) in the presence of Cu(OAc)$_2$ (10 mol%) as catalyst under solvent-free conditions at room temperature. Other copper salts such as CuCl$_2$, CuCl, CuI, as well as TBAI also worked for this reaction, albeit with lower yields (Table 1, entries 2–5). Performance of FeCl$_2$ for this transformation was weaker than copper salts (Table 1, entry 6). Notably, NiCl$_2$ showed no conversion (Table 1, entry 7). The experiment conducted under catalyst-free conditions showed that the catalyst has an important role in this reaction (Table 1, entry 8). Further investigation revealed that the ratio between the reactants is very important. The 1 : 4 ratio of benzyl cyanide to TBHP gave the highest yield (Table 1, entries 9–12). By increasing the amount of the catalyst to 20 mol%, the yield did not change, while by reducing it to 5 mol%, efficiency was decreased with 50% (Table 1, entries 13 and 14). Then, the effect of solvents on the reaction performance was evaluated. When the reaction was

carried out in the solvents such as H$_2$O, CH$_3$CN, DMF, EtOH, and EtOAc, the efficiency was lower than that of solvent-free conditions (Table 1, entries 15–19).

As a last resort, the effect of temperature was studied and some interesting results were obtained. As temperature rise to 80 °C, the efficiency was sharply down, in return benzoic acid was isolated with high efficiency (Table 1, entries 20 and 21). However this also will be a new and effective procedure for benzoic acid derivatives synthesis.

After optimization, in order to establish the scope of the procedure, a wide range of benzyl cyanides were subjected to the reaction conditions. The results are shown in Fig. 1. As seen is this figure, various derivatives of benzyl cyanide bearing halogen and electron-donating substituents, at different position of aromatic ring, were converted to the corresponding *tert*-butyl peresters in moderate to good yields (Fig. 1, **1a–j**). 4-Cyanobenzyl cyanid was also successful in this transformation and product **1k** was obtained in 65% yield. 4-Nitrobenzyl cyanide was failed to this reaction and the corresponding product was formed in trace (Fig. 1, **1l**). When 4-(methylthio)benzyl cyanide was subjected to the reaction conditions, the desired perester (Fig. 1, **1m**) was obtained in 60% yield and sulfide substituent that is susceptible to oxidation to sulfoxide, remained intact. Heteroaromatic and polycyclic cyanides, that is, thiophen-2-yl-acetonitrile and naphthalen-2-yl-acetonitrile, also were condensed into the corresponding *tert*-butyl peresters **1n** and **1o** in high yields.

Table 1 The tests for achieving to the optimum conditions[a]

Entry	Solvent	Catalyst (mol%)	TBHP (mmol)	Yield[b] (%)
1	—	Cu(OAc)$_2$(10)	1	40
2	—	CuCl$_2$(10)	1	30
3	—	CuCl(10)	1	35
4	—	CuI(10)	1	37
5	—	TBAI(10)	1	20
6	—	FeCl$_2$(10)	1	10
7	—	NiCl$_2$(10)	1	—
8	—	—	1	—
9	—	Cu(OAc)$_2$(10)	2	60
10	—	Cu(OAc)$_2$(10)	3	70
11	—	Cu(OAc)$_2$(10)	4	80
12	—	Cu(OAc)$_2$(10)	6	80
13	—	Cu(OAc)$_2$(10)	4	80
14	—	Cu(OAc)$_2$(10)	4	50
15	H$_2$O	Cu(OAc)$_2$(10)	4	50
16	CH$_3$CN	Cu(OAc)$_2$(10)	4	50
17	DMF	Cu(OAc)$_2$(10)	4	5
18	EtOH	Cu(OAc)$_2$(10)	4	30
19	EtOAc	Cu(OAc)$_2$(10)	4	30
20[c]	—	Cu(OAc)$_2$(10)	4	40
21[d]	—	Cu(OAc)$_2$(10)	4	5

[a] Benzyl cyanide (1 mmol), under air atmosphere at room temperature. [b] Isolated yield. [c] At 50 °C. [d] The reaction was performed at 80 °C and benzoic acid was isolated as the main product in 85% yield.
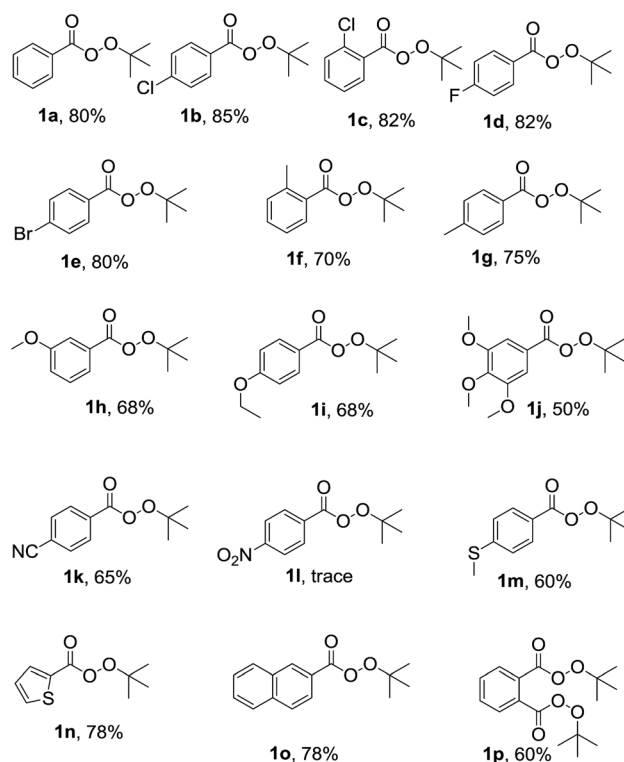

Fig. 1 Substrate scope. Reaction conditions: benzyl cyanide derivatives (1 mmol), TBHP (4 mmol), Cu(OAc)$_2$ (10 mol%), r.t., reaction time: 5 h; the yields refer to the isolated pure products.

Moreover, 1,2-phenylenediacetonitrile was converted to the product **1p** in which both benzylic groups have become to the *tert*-butyl perester group. All the products **1a–p** was identified by elemental analysis and FTIR, ^{1}H and ^{13}C-NMR spectra.

As was considered above, when the model reaction was conducted at 80 °C, benzoic acid was obtained in 85% yield. Therefore this protocol was extended for the synthesis of benzoic acid derivatives. Optimized conditions for synthesis of *tert*-butyl peresters were the best for acids so. And by changing the amount of oxidant and catalysts, as well as increasing the temperature to 100 °C, the yield was not improved. Worthy of note is that, when sodium hypochlorite (NaOCl), di *tert*-butyl peroxide (DTBP), and *m*-chloro perbenzoic acid (*m*CPBA) was used instead of TBHP, no acid was formed and benzyl cyanide was isolated quantitative. Aliphatic cyanides were not successful in this transformation. In a typical experiment, when propionitrile was subjected to the reaction conditions, the reaction was not performed. Fig. 2 shows the structures of acids synthesized by this method. As can be seen in this figure, without depending on the type and position of substitution, the acids were derived with the high and neck-to-neck efficiency.
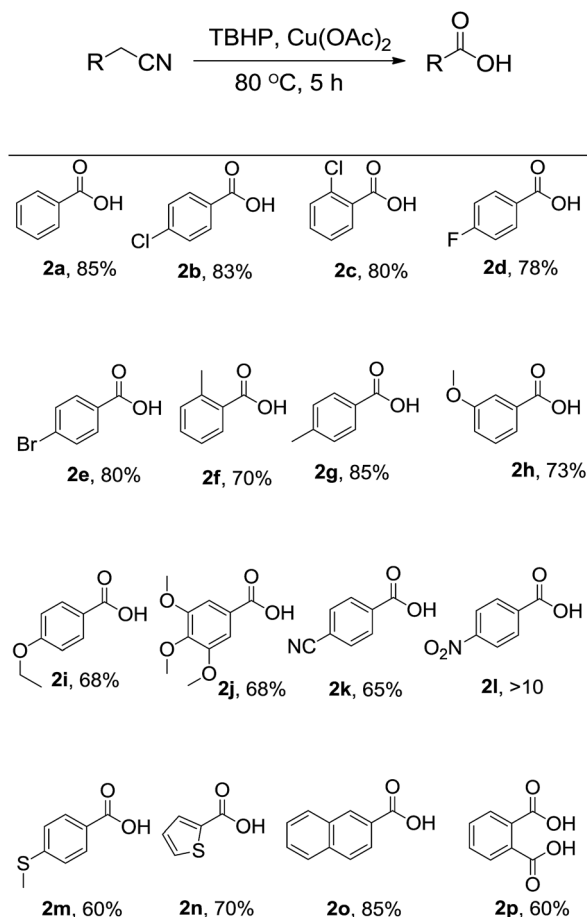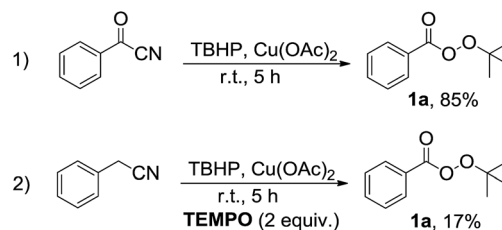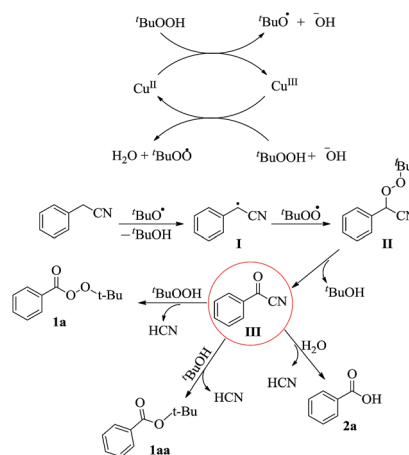

Fig. 2 The structures of the synthesized acids. Reaction conditions: benzyl cyanide derivatives (1 mmol), TBHP (4 mmol), Cu(OAc)$_2$ (4 mol%), 80 °C, reaction time: 5 h; the yields refers to the isolated pure products.

Scheme 2 Control experiments into the reaction mechanism.

From the viewpoint of reaction mechanism, since the benzyl cyanide is prone to oxidation into the benzoyl cyanide in the presence of TBHP,[6] therefore reaction of benzoyl cyanide was investigated under the same reaction conditions to obtain a plausible mechanism (Scheme 2, eqn (1)). Formation of perester **1a** in high yield showed that benzoyl cyanide can be impressive intermediate in this transformation. Moreover, the sharp decrease of efficiency in the presence of TEMPO, a known radical scavenger, revealed that radicals could be involved in the reaction pathway (Scheme 2, eqn (2)). In addition, the presence of free cyanide anion has been proven by the use of indicator paper (see ESI†).[6c-f]

Based on the above results and related works,[7] the mechanism depicted in Scheme 3 is proposed for this transformation. Initially, the copper(II) species donates an electron to TBHP to generate a *tert*-butoxyl radical and a copper(III) species.[7b] The latter abstracts an electron from another molecule of TBHP and gives the original copper(II) species along with a *tert*-butyl peroxy radical. The *tert*-butoxyl radical could then abstract a hydrogen atom from the benzyl cyanide to generate the radical **I** which couples with the *tert*-butyl peroxy radical, affording a perester intermediate **II**. This intermediate can then be converted to the benzoyl cyanide **III** with the loss of *tert*-butanol. Benzoyl cyanide can be transformed to the corresponding *tert*-butyl perester, *tert*-butyl benzoate, or acid *via* nucleophilic attack by *tert*-butyl hydroperoxide, *tert*-butanol or water respectively. Worthy of note is that *tert*-butyl benzoate was observed in some experiments shown in Table 1.

Scheme 3 Proposed mechanism.

Conclusions

In conclusion an effective and temperature-controlled protocol was developed for the synthesis of *tert*-butyl peresters and benzoic acids from benzyl cyanides in the presence of Cu/TBHP catalytic system. Various derivatives of *tert*-butyl peresters were synthesized in high yields under solvent-free conditions at room temperature. Benzoic acids were prepared under the same conditions with a slightly modified procedure, in which the reaction temperature was increased to 80 °C.

Acknowledgements

Notes and references

1 (*a*) C. Liu, H. Zhang, W. Shi and A. Lei, *Chem. Rev.*, 2011, **111**, 1780; (*b*) W. Shi, C. Liu and A. Lei, *Chem. Soc. Rev.*, 2011, **40**, 2761; (*c*) C.-J. Li, *Acc. Chem. Res.*, 2009, **42**, 335; (*d*) M. Klussmann and D. Sureshkumar, *Synthesis*, 2011, 353.

2 (*a*) W. Ando, *Organic peroxides*, Wiley-interscience, New York, 1992; (*b*) L. Wang, X. Liu and Y. Li, *Macromolecules*, 1998, **31**, 3446; (*c*) S. N. Gupta, I. Gupta and D. C. Neckers, *J. Polym. Sci., Polym. Chem. Ed.*, 1981, **19**, 103; (*d*) P. C. Montevecchi, A. Manetto, M. L. Navacchia and C. Chatgilialoglu, *Tetrahedron*, 2004, **60**, 4303; (*e*) B. K. Shah and D. C. Neckers, *J. Am. Chem. Soc.*, 2004, **126**, 1830; (*f*) F. Formaggio, M. Crisma, L. Scipionato, S. Antonello, F. Maran and C. Toniolo, *Org. Lett.*, 2004, **6**, 2753; (*g*) Y. Li, S. Niu, B. Sun, S. Liu, X. Liu and Y. Che, *Org. Lett.*, 2010, **12**, 3144; (*h*) D. A. Powell and H. Fan, *J. Org. Chem.*, 2010, **75**, 2726; (*i*) M. T. Rispens, C. Zondercu and B. L. Feringa, *Tetrahedron: Asymmetry*, 1995, **6**, 661; (*j*) Y. Kohmura and T. Katsuki, *Tetrahedron Lett.*, 2000, **41**, 3941; (*k*) J. Eames and M. Watkinson, *Angew. Chem.*, 2001, **113**, 3679–3683; *Angew. Chem., Int. Ed.*, 2001, **40**, 3567; (*l*) A. V. Malkov, M. Bella, V. Langer and P. Koĉovský, *Org. Lett.*, 2000, **2**, 3047; (*m*) M. B. Andrus and Z. Zhou, *J. Am. Chem. Soc.*, 2002, **124**, 8806.

3 (*a*) N. Milas and D. M. Surgenor, *J. Am. Chem. Soc.*, 1946, **68**, 642; (*b*) S. L. Silbert and D. Swern, *J. Am. Chem. Soc.*, 1959, **81**, 2364; (*c*) N. A. Milas, D. G. Orphanos and R. J. Klein, *J. Org. Chem.*, 1964, **29**, 3099; (*d*) M. Y. Lu, R. Bao, W. Liu and Y. Li, *J. Org. Chem.*, 1995, **60**, 5341; (*e*) Y. Hamada, A. Mizuno, T. Ohno and T. Shioiri, *Chem. Pharm. Bull.*, 1984, **32**, 3683.

4 W. Wei, C. Zhang, Y. Xu and X. Wan, *Chem. Commun.*, 2011, **47**, 10827.

5 H. Zhang, D.-Q. Dong, S.-H. Hao and Z.-L. Wang, *RSC Adv.*, 2016, **6**, 8465.

6 (*a*) S.-I. Murahashi, T. Naota and T. Kuwabara, *Synlett*, 1989, 62; (*b*) B. M. Choudary and P. N. Reddy, *J. Mol. Catal. A: Chem.*, 1996, **112**, 385; (*c*) Y. Luo, Q. Wen, Z. Wu, J. Jin, P. Lu and Y. Wang, *Tetrahedron*, 2013, **69**, 8400; (*d*) L. Zhang, Q. Wen, J. Jin, C. Wang, P. Lu and Y. Wang, *Tetrahedron*, 2013, **69**, 4236; (*e*) J. Jin, Q. Wen, P. Lu and Y. Wang, *Chem. Commun.*, 2012, **48**, 9933; (*f*) Q. Wen, J. Jin, Y. Mei, P. Lu and Y. Wang, *Eur. J. Org. Chem.*, 2013, 4032.

7 (*a*) D. Saberi, F. Shojaeyan and K. Niknam, *Tetrahedron Lett.*, 2016, **57**, 566; (*b*) N. Khatun, S. K. Santra, A. Banerjee and B. K. Patel, *Eur. J. Org. Chem.*, 2015, 1309; (*c*) J. Wang, C. Liu, J. Yuan and A. Lei, *Angew. Chem., Int. Ed.*, 2013, **52**, 2256; (*d*) S. C. Ghosh, J. S. Y. Ngiam, C. L. L. Chai, A. M. Seayad, T. T. Dang and A. Chen, *Adv. Synth. Catal.*, 2012, **354**, 1407; (*e*) W. Wei, C. Zhang, Y. Xu and X. Wan, *Chem. Commun.*, 2011, **47**, 10827.