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$CuBr_2$-catalyzed ring opening/formylation reaction of cyclopropyl carbinols with DMF to synthesize formate esters

Daijiao Zhuang [1], Tharcisse Gatera [1], Rulong Yan *

State Key Laboratory of Applied Organic Chemistry, College of Chemistry and Chemical Engineering, Lanzhou University, Lanzhou 730000, Gansu, China

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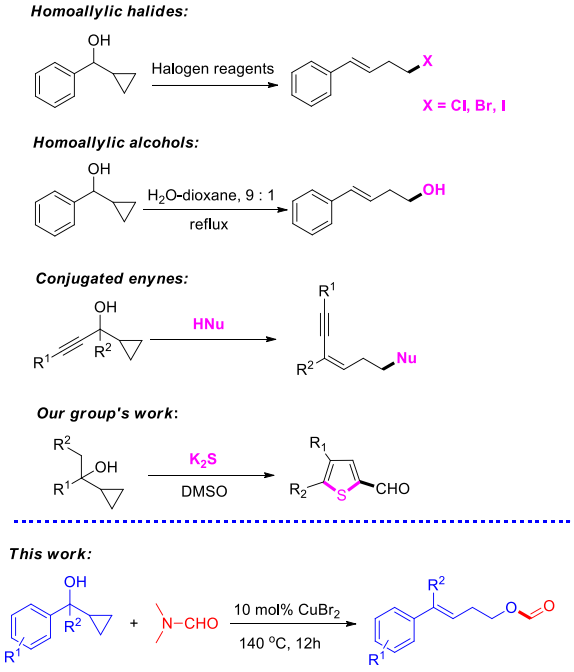
ABSTRACT

An unprecedented protocol for the synthesis of formate esters has been developed by employing *N*,*N*-dimethylformamide (DMF) as both the source of CHO and solvent. This reaction undergoes ring opening of the cyclopropyl carbinols and in situ formation of homoallylic alcohols, which reacts with DMF to give the desired products. The substrate cyclopropyl carbinols with different groups participate smoothly in this process and the desired products are obtained in moderate to good yields.

Introduction

Cyclopropyl carbinols are versatile intermediates for the synthesis of various molecular skeletons, which can produce the ring-opened products via C—C bond cleavage and rearrangement reaction. In the past several decades, the transformation of cyclopropyl carbinols into homoallylic halides [1] and homoallylic alcohols [2] has received considerable development and synthetic application. Recently, Nishibayashi's group and Chan's group presented the ring opening of a wide variety of cyclopropyl carbinols as efficient synthetic routes to conjugated enynes [3]. As part of an ongoing program exploring the utility of cyclopropyl carbinols in organic synthesis, our group recently described a simple method for the synthesizing thiophene aldehydes via ring-opening/annulation, as well as C—S bonds formation of cyclopropyl carbinols (Scheme 1) [4]. Hence, the use of cyclopropyl carbinols to construct common and important structural motifs in a facile way remains highly attractive.

Besides being an effective polar solvent, DMF can be used as reagent, catalyst, and stabilizer in organic chemistry [5]. It can participate in many reactions by serving as a multipurpose building block for various units, such as C [6], CO [7], NMe_2 [8], $CONMe_2$ [9], CN [10], *etc*. In recent years, DMF has been also utilized as the source of CHO unit [11]. Paquin's group reported the use of a XtalFluor-E/DMF combination for the Vilsmeier-Haack formylation reaction of C-2-glycals [11d]. Iranpoor's group introduced an



Scheme 1. Application of cyclopropyl carbinols.

* Corresponding author.
E-mail address: yanrl@lzu.edu.cn (R. Yan).
[1] The authors contributed equally.

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efficient method for the C(3) formylation of indole and C(2) formylation of pyrrole derivatives using TCT/DMF reagent [11c]. Moreover, Guo's group has developed an efficient method for the transamidation of DMF with weakly nucleophilic anilines [12]. However, The direct synthesis of formate esters with DMF which acts not only as a solvent but also as the source of CHO has rarely been exploited. Herein, we present a novel synthetic approach toward formate esters through $CuBr_2$-catalyzed ring opening and formylation of cyclopropyl carbinols with DMF.

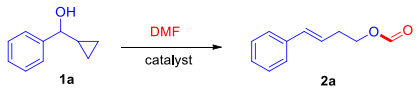
Results and discussion

We started investigation from the reaction of cyclopropyl(phenyl)methanol (**1a**) in DMF using $FeCl_3$ as catalyst at 140 °C under air for 12 h. To our surprise, (***E***)-4-phenylbut-3-en-1-yl formate (**2a**) was obtained in 51% yield (Table 1, entry 1). The structure of **2a** was confirmed by spectroscopic analysis. Thus, the substrate **1a** was chosen as the model substrate to optimize the reaction conditions. Firstly, attempts to improve the yield using various metal catalysts were evaluated, and copper catalysts exhibited the highest activity. The yield of **2a** was increased to 60% when 10 mol% of $CuCl_2$ was added (Table 1, entries 1–7). Furthermore, a series of copper catalysts were also screened and $CuBr_2$ was the most efficient for this transformation and the isolated **2a** was obtained in 70% yield (Table 1, entries 8–9 and entry 11). The temperature was also examined, and the result of changing the temperature revealed that the yield was sharply decreased when the reaction temperature was reduced. However, there was little effect on the yield when the temperature reached 140 °C (Table 1, entries 10–14). The reaction of cyclopropyl carbinol cannot work without the catalyst $CuBr_2$ (Table 1, entries 15). So the optimized conditions were established as shown in Table 1, entry 11.

With the optimized reaction conditions in hand, the substrate scope was then evaluated. As shown in Table 2, the optimized conditions were compatible with various cyclopropyl carbinols with electron-donating substituents on the aryl ring, such as Me, OMe, Et, OEt, OPh, *i*-Pr, *t*-Bu, *etc* (**2a-2o**). Halogen-containing derivatives of cyclopropyl carbinols could also tolerate this transformation, and the corresponding products **2p, 2q, 2r** were isolated in 57%, 56%, and 59% yields, respectively. Moreover, these reaction conditions were also compatible with different heterocyclic substrates (**2s-2u**). In addition, further investigation disclosed that the tertiary alcohol substrates also sustained well in this reaction and the target products **2v-2y** were isolated in good yields. The products were mixture of (***E***)- and (***Z***)-isomers, and the (***E***)-isomers were obtained with excellent selectivity. Unfortunately, the substrates 1-cyclopropyl-3-phenylpropan-1-ol (**1z**) and 1-cyclopropylethanol (**1aa**) did not tolerate this reaction system and no desired products were detected.

To further highlight the versatility of this strategy, several amide derivatives were tested (Scheme 2). To our delight, the investigation showed that DMA and DMAA can also proceed smoothly in this reaction, and the desired products were isolated in 56% and 34% yields.

Table 1
Optimization of reaction conditions.[a]

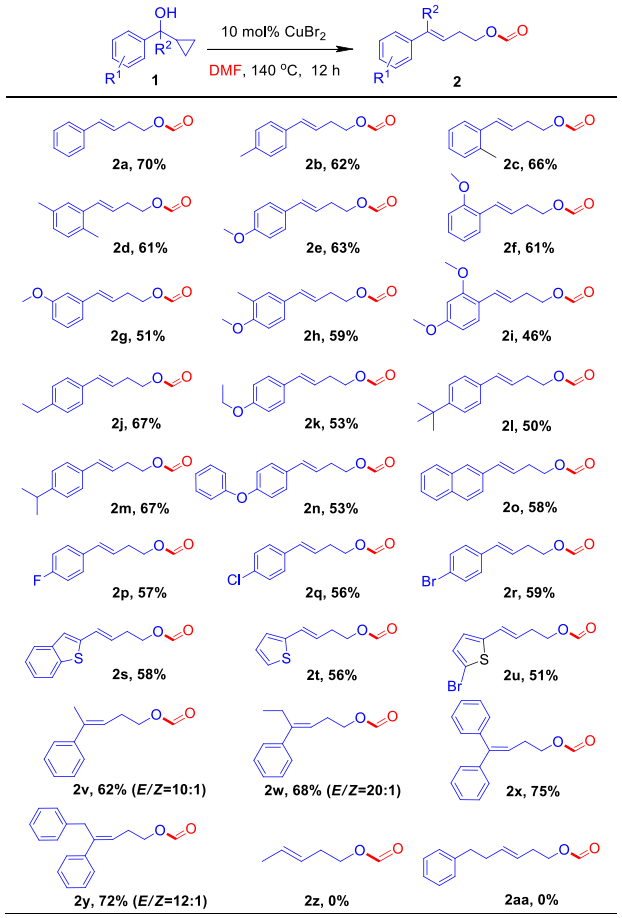


1a 2a

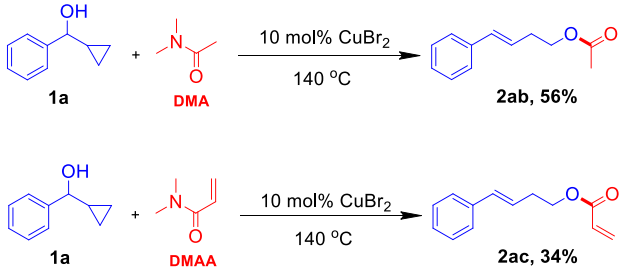
Entry	Catalyst	Temp (°C)	Yield (%)[b]
1	$FeCl_3$	140	51
2	$Ni(OAc)_2$	140	34
3	$Pd(OAc)_2$	140	46
4	$ZnCl_2$	140	28
5	$MnCl_2$	140	37
6	CuCl	140	42
7	$CuCl_2$	140	60
8	$Cu(OAc)_2$	140	52
9	$Cu(OTf)_2$	140	47
10	$CuBr_2$	160	63
11	**$CuBr_2$**	**140**	**70**
12	$CuBr_2$	120	53
13	$CuBr_2$	100	36
14	$CuBr_2$	rt	Trace
15	–	140	n.d.

[a] Reaction conditions: **1a** (0.3 mmol) and catalyst (10 mol%) in DMF (2 mL), 12 h.
[b] Yields of isolated products.

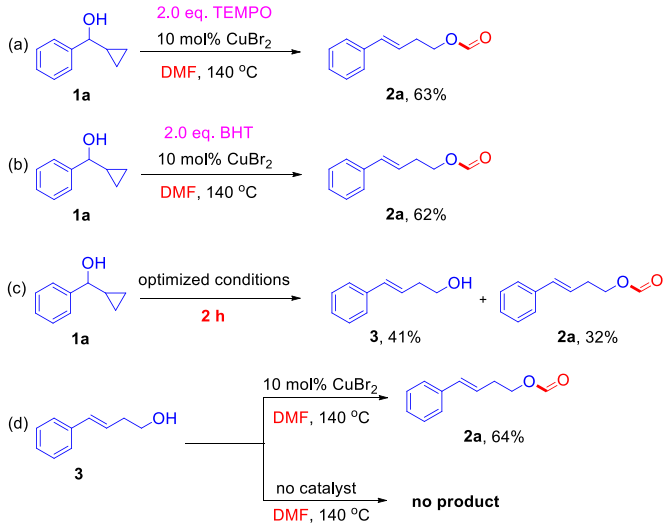
Table 2
Scope of substituted cyclopropyl carbinols.[a]



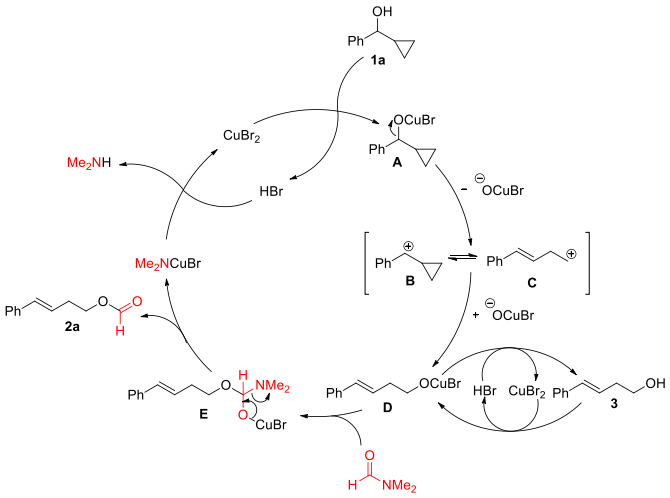
[a] Reaction conditions: substrates **1** (0.3 mmol), $CuBr_2$ (0.03 mmol), DMF (2 mL), 140 °C, 12 h.



Scheme 2. Scope of amide derivatives.



Scheme 3. Control experiments.



Scheme 4. Proposed mechanism.

In order to gain more insight into the reaction mechanism, several control experiments were conducted (Scheme 3). Firstly, the radical scavengers 2,2,6,6-tetramethyl-1-piperidinyloxy (TEMPO) and butylated hydroxytoluene (BHT) were added to the reaction mixture, and the yields of **2a** had a slight decrease (Scheme 3a, b), which demonstrated that the transformation of **1a** to **2a** would not be a radical process. Further research disclosed that homoallylic alcohol **3** was generated in this reaction and decreased with the experimental proceeding. Then compound **3**, which was isolated under standard reaction conditions after 2 h (Scheme 3c), was subjected to the standard conditions, and the desired product **2a** was obtained in 64% yield. However, there was no product detected in the absence of catalyst (Scheme 3d). These results suggested that **3** should be the intermediate for this transformation, and the catalyst is involved in the formation of **2a** from **3**.

Based on the previous literature reports and control experiments, a plausible mechanism is proposed in Scheme 4. First, coordination of the $CuBr_2$ to **1a** provides the copper-alkoxide complex **A** which can undergo elimination to give a putative carbocation species **B.** Then, cationic species C which is generated from **B** through rearrangement delivers another copper(II)-chelated intermediate **D**. The intermediate **D** releases $CuBr_2$ to give the key intermediate homoallylic alcohol **3** [13]. Furthermore, the nucleophilic attack on DMF takes place, resulting in the product **E**. Finally, the collapse of **E** leads to the formation of **2a** by eliminating one equivalent of dimethylamine [14].

Conclusion

In conclusion, we have developed a method for synthesizing the formate esters from cyclopropyl carbinols and DMF through ring opening and formylation reaction in a one-pot process. Furthermore, this protocol shows good functional group compatibility and various substituted products proceed smoothly with DMF, generating the desired products in moderate to good yields.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgments

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Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.tetlet.2020.152506.

References

[1] (a) J.P. McCormick, D.L. Barton, J. Org. Chem. 45 (1980) 2566;
(b) G.W. Kabalka, M.-L. Yao, S. Borella, Z.-Z. Wu, Org. Lett. 7 (2005) 2865;
(c) J.W. Hulshof, H.F. Vischer, M.H.P. Verheij, S.A. Fratantoni, M.J. Smit, I.J.P. de Esch, R. Leurs, Bioorg. Med. Chem. 14 (2006) 7213;
(d) X.-M. Cui, Y.-H. Guan, N. Li, H. Lv, L.-A. Fu, K. Guo, X. Fan, Tetrahedron Lett. 55 (2014) 90.
[2] (a) Z. Majerski, P.R. Schleyer, J. Am. Chem. Soc. 93 (1971) 665;
(b) S.R. Mothe, P.W.H. Chan, J. Org. Chem. 74 (2009) 5887;
(c) A.J. Chen, R.Y. Lin, Q.J. Liu, N. Jiao, Chem. Commun. (2009) 6842;
(d) P.-F. Li, C.-B. Yi, J. Qu, Org. Biomol. Chem. 13 (2015) 5012.
[3] (a) Y. Yamauchi, G. Onodera, K. Sakata, M. Yuki, Y. Miyake, S. Uemura, Y. Nishibayashi, J. Am. Chem. Soc. 129 (2007) 5175;
(b) S.R. Mothe, P. Kothandaraman, W. Rao, P.W.H. Chan, J. Org. Chem. 76 (2011) 2521.
[4] T. Wang, Z. An, Z. Qi, D. Zhuang, A. Chang, Y. Yang, R. Yan, Org. Chem. Front. 6 (2019) 3705.
[5] (a) J. Muzart, Tetrahedron 65 (2009) 8313;
(b) S. Ding, N. Jiao, Angew. Chem. Int. Ed. 51 (2012) 9226; Angew. Chem. 124 (2012) 9360.;
(c) M.M. Heravi, M. Ghavidel, L. Mohammadkhani, RSC Adv. 8 (2018) 27832;
(d) J.L. Bras, J. Muzart, Molecules 2018 (1939) 23.
[6] (a) X. Wu, Y. Zhao, H. Ge, J. Am. Chem. Soc. 137 (2015) 4924;
(b) M.-N. Zhao, R.-R. Hui, Z.-H. Ren, Y.-Y. Wang, Z.-H. Guan, Org. Lett. 16 (2014) 3082;
(c) F. Liu, H. Yang, X. Hu, G. Jiang, Org. Lett. 16 (2014) 6408;
(d) D.N. Rao, S. Rasheed, P. Das, Org. Lett. 18 (2016) 3142;
(e) X. Xu, M. Zhang, H. Jiang, J. Zheng, Y. Li, Org. Lett. 16 (2014) 3540.
[7] (a) J. Li, X. Chen, D. Shi, S. Ma, Q. Li, Q. Zhang, J. Tang, Org. Lett. 11 (2009) 1193;
(b) E. Yoshioka, S. Kohtani, H. Miyabe, Angew. Chem. Int. Ed. 50 (2011) 6638;
(c) L.-R. Wen, N.-N. Man, W.-K. Yuan, M. Li, J. Org. Chem. 81 (2016) 5942;
(d) X. Wu, Y. Zhao, H. Ge, J. Am. Chem. Soc. 137 (2015) 4924.
[8] Z. Liu, J. Zhang, S. Chen, E. Shi, Y. Xu, X. Wan, Angew. Chem. Int. Ed. 51 (2012) 3231.
[9] (a) K. Hosoi, K. Nozaki, T. Hiyama, Org. Lett. 4 (2002) 2849;
(b) J. Ju, M. Jeong, J. Moon, H.M. Jung, S. Lee, Org. Lett. 9 (2007) 4615.
[10] (a) J. Kim, S. Chang, J. Am. Chem. Soc. 132 (2010) 10272;
(b) S. Ding, N. Jiao, J. Am. Chem. Soc. 133 (2011) 12374;
(c) Z. Wang, S. Chang, Org. Lett. 2013 (1990) 15.

[11] (a) M. Suchy, A.A.H. Elmehriki, R.H.E. Hudson, Org. Lett. 13 (2011) 3952;
(b) L. Liu, D. Zhang-Negrerie, Y. Du, K. Zhao, Org. Lett. 16 (2014) 436;
(c) N. Iranpoor, F. Panahi, S. Erfan, F.J. Roozbin, Heterocyclic Chem. 54 (2017) 904;
(d) M. Roudias, F. Vallee, J. Martel, J.-F. Paquin, J. Org. Chem. 83 (2018) 8731.
[12] D.-W. Gu, X.-X. Guo, Tetrahedron 71 (2015) 9117.
[13] (a) Y. Maeda, T. Nishimura, S. Uemura, Chem. Lett. 34 (2005) 380;
(b) W. Rao, X. Zhang, E.M.L. Sze, P.W.H. Chan, J. Org. Chem. 74 (2009) 1740;
(c) M.J. Sandridge, S. France, Org. Lett. 18 (2016) 4218.
[14] C. Chen, L. Tan, P.J. Zhou, Saudi Chem. Soc. 19 (2015) 327.