Copper-catalyzed oxy-alkenylation of homoallylic alcohols to functional *syn*-1,3-diol derivatives[**]

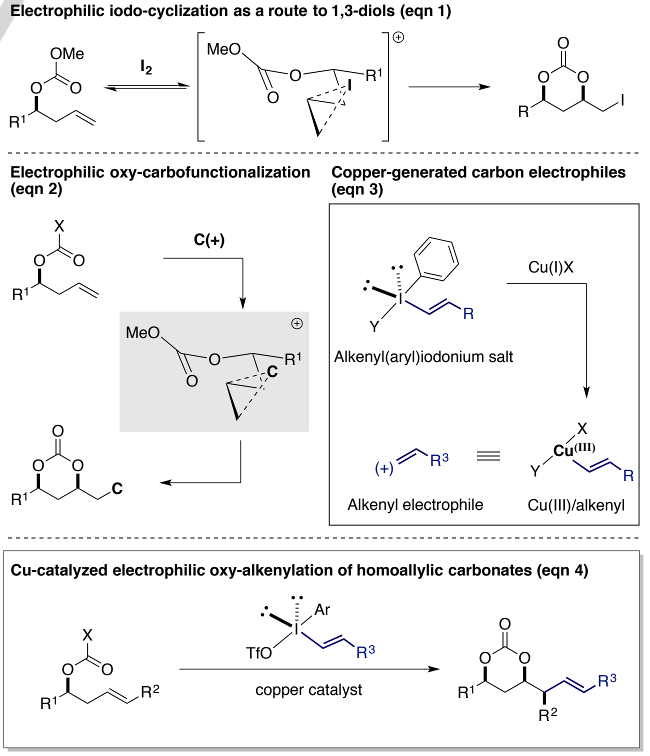
*Dean Holt and Matthew J. Gaunt**

***Abstract:** A novel method for the synthesis of a wide range of functionalized 1,3-diol derivatives is reported. Employing a copper-catalyzed oxy-alkenylation strategy, a range of readily available, substituted homoallylic alcohol derivatives and alkenyl(aryl) iodonium salts combine to form syn-1,3-carbonates in excellent yield and with high selectivity. Furthermore, the products formed are amenable to an iterative reaction sequence, affording highly complex polyketide-like fragments.*

The 1,3-diol is an important structural feature commonly found in biologically active natural products and pharmaceutical agents.[1] The diversity of polyketide natural products, in particular, has inspired the development of many strategies geared towards the synthesis of *syn* or *anti* isomers of the 1,3 diol functionality.[2] Benchmarked by the aldol–directed reduction transformation,[3] the stereo-controlled synthesis of the 1,3-diol motif can now be achieved by numerous methodologies that encompass a variety of possible bond disconnections around the two hydroxyl groups. Notable among these seminal contributions are the anion-relay addition of lithiated-dithianes to epoxides[4] and the addition of allyl nucleophiles to aldehydes,[5] both of which require further manipulations to form the 1,3-diol function, and the tethered oxy-Michael additions to enoates.[6] Recently, catalytic processes have emerged as powerful tactics to generate 1,3-oxygenation patterns from simple starting materials: Krische's tandem redox allylation of alcohols,[7] Leighton's tandem silylformylation of homoallylic alcohol derivatives;[8] and Yamamoto's tandem 'super-silyl' Mukaiyama aldol-type coupling of aldehydes[9] can all be used to rapidly generate complex 1,3-diol systems and have found widespread use in complex natural product synthesis. The unquestionable efficacy and utility of these transformations underlines the importance of the continual development of new strategies for the catalytic, stereocontrolled synthesis of 1,3-diol derivatives.[10]

We were attracted to a classical, but underutilized method for 1,3-diol synthesis – an electrophilic 'iodolactonization-type' process, which constructs a 1,3-cyclic carbonate from a homoallylic carbonate (eqn 1).[11] In this reaction, the iodine electrophile activates the alkene to form an iodonium species that is intercepted *via* intramolecular attack by the carbonyl oxygen of the pendant carbonate, resulting in concomitant formation of carbon-oxygen and carbon-iodine bonds. In a subsequent step, the carbon-iodine bond can be used to alkylate carbon nucleophiles, forming complex 1,3-diol fragments that are common in polyketide natural products. Inspired by this simple tactic, we questioned whether we could design a catalytic transformation that linked a related carbon-oxygen bond-forming event to a carbon-carbon bond formation to forge complex 1,3-diols directly from homoallylic alcohol derivatives *via* an 'electrophilic oxy-carbofunctionalization' process (eqn 2).[12] Furthermore, if the electrophile component was an alkenyl derivative then the products of the transformation would, themselves, contain a homoallylic carbonate motif suitable for further elaboration.

Over the last seven years, our group has pioneered the use of diaryliodonium reagents in combination with copper salts as a catalytically generated source of aromatic electrophile equivalent.[13] Proceeding *via* the intermediacy of a putative Cu(III)–aryl species, this highly electrophilic organometallic reagent has been shown to undergo reaction with a variety of latent carbon nucleophiles, leading to the development of a range of previously unknown transformations. In the context of an electrophilic oxy-carbofunctionalization strategy towards synthetically versatile 1,3-diols, we reasoned that the action of a copper catalyst on an alkenyl(aryl)iodonium salt would generate a Cu(III)-alkenyl species (eqn 3).[14] This reactive intermediate would engage the alkene, polarizing the carbon–carbon double bond and promoting attack of the pendant carbonyl motif in such a way to form a carbon–oxygen bond and a new copper(III)–carbon bond. Reductive elimination from the high oxidation state Cu(III)-species would transfer the alkenyl group leading to a cyclic carbonate product, predicted to be the *syn*-diastereoisomer in line with the related iodine mediated reaction.


Electrophilic iodo-cyclization as a route to 1,3-diols (eqn 1)

Electrophilic oxy-carbofunctionalization (eqn 2)

Copper-generated carbon electrophiles (eqn 3)

Cu-catalyzed electrophilic oxy-alkenylation of homoallylic carbonates (eqn 4)

---

[*] D. Holt, Prof. M. J. Gaunt
Department of Chemistry, University of Cambridge
Lensfield Road, Cambridge, CB2 1EW (UK)
E-mail: mjg32@cam.ac.uk
Homepage: http://www-gaunt.ch.cam.ac.uk

[**] We are grateful to the EPSRC (D. H.) for a studentship and the ERC and EPSRC for fellowships (M.J.G.). Mass spectrometry data were acquired at the EPSRC UK National Mass Spectrometry Facility at Swansea University.

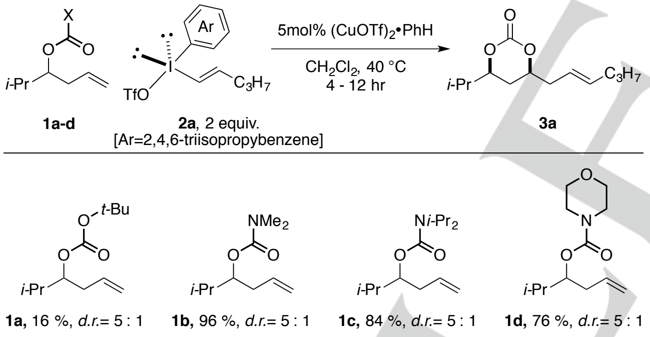
Supporting information for this article is given via a link at the end of the document.

WILEY-VCH

WILEY-VCH

Herein, we report the successful realization of such a copper-catalyzed oxy-alkenylation strategy and show that a range of readily available, substituted homoallylic alcohol derivatives and alkenyl(aryl)iodonium salts can be combined to form *syn*-1,3-carbonates in excellent yield and with high selectivity (eqn 4). Moreover, a simple iteration of the process affords highly complex polyketide-like fragments that could be used to expedite the synthesis of natural products.

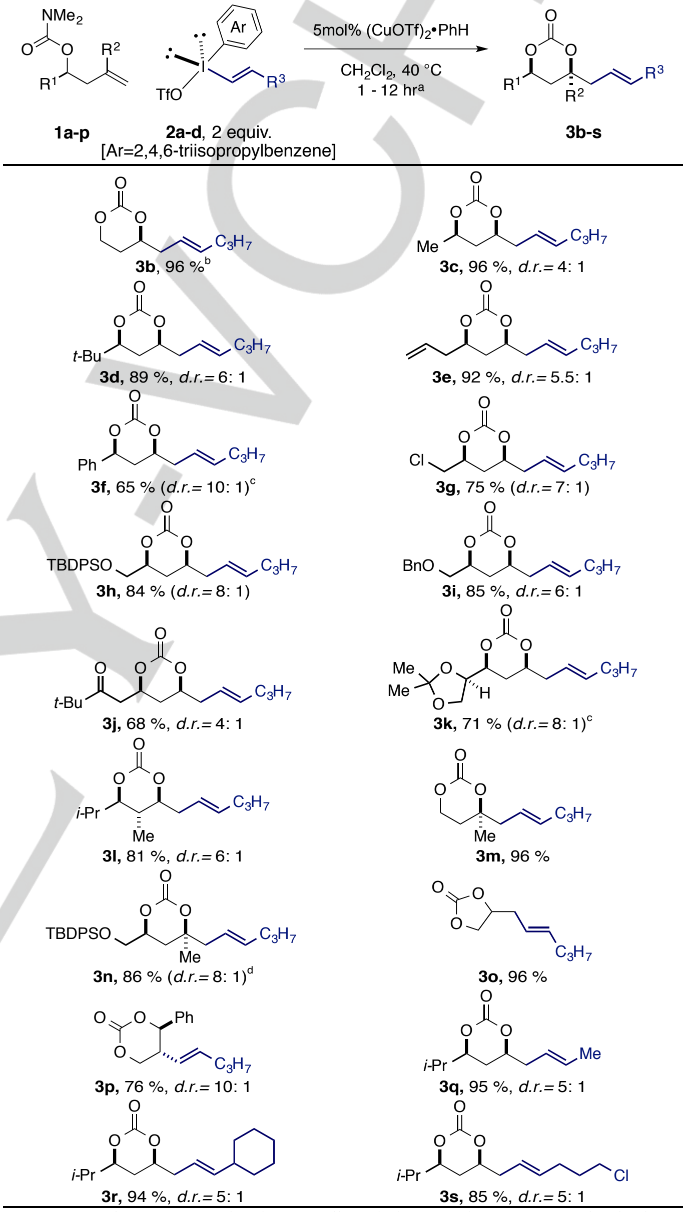
At the outset of our studies, we selected a simple mixed carbonate **1a** to assess the oxy-alkenylation strategy. Based on our hypothesis, we first assessed simple copper salts as catalysts with pentenyl(triisoproylbenzene)iodonium triflate **2a** (readily available in our laboratories – see supporting information for full details of optimization). We found that the desired reaction was best catalyzed by the copper(I) salt, $(Cu(I)OTf)_2{\cdot}PhH$, affording the cyclic carbonate **3a** with good diastereoselectivity (*d.r.*), albeit in low yield. However, under the same reaction conditions, we found that the use of the corresponding carbamate derivative **1b** afforded excellent yield of the desired product with similar selectivity. Interestingly, close monitoring of the reaction revealed that the product **3a** was not formed in the crude reaction mixture until a hydrolytic work up was applied to form the cyclic carbonate. We found that the dimethylcarbamate gave superior yields to other amine derivatives, and that no variation of the solvent or the reaction temperature improved the selectivity. Therefore, optimal conditions were concluded to involve treatment of the carbamate **1b** with 2 equivalents of **2a** and 5mol% of $(Cu(I)OTf)_2{\cdot}PhH$ as catalyst in a solution of dichloromethane at 40 °C for 4 hours and resulted in the isolation of **3a** in 96% yield as a 5:1 mixture of *syn* and *anti* diastereoisomers.



1a, 16 %, *d.r.*= 5 : 1 **1b**, 96 %, *d.r.*= 5 : 1 **1c**, 84 %, *d.r.*= 5 : 1 **1d**, 76 %, *d.r.*= 5 : 1

Table 1. Optimization of the carbonyl component of the substrate. Major diastereoisomer confirmed as *syn* by 1D NOESY.

We next assessed the scope of the new copper-catalyzed oxy-alkenylation reaction of homoallylic carbamates (table 2). We were pleased to observe that the process works well on a range of substrates providing access to a diverse array of functionalized *syn*-carbonates. Substrates bearing simple alkyl substituents proved to be high yielding for 1,3- carbonates **3b**–**3d**. Interestingly, the diastereoselectivity observed across these products was relatively unaffected by the changing steric demands of the substrate; marginal improvement was observed by increasing substituent size from methyl to *iso*-propyl to *tert*-butyl (*d.r.*=4:1 for **3c** to 6:1 for **3d**). A selection of synthetically versatile functional groups were compatible with the reaction and formed products in comparable yields and, in many cases, higher diastereoselectivity; homoallyl (**3e**), phenyl (**3f**), chloromethyl (**3g**) and protected hydroxyl motifs (**3h** and **3i**) all proceeded well to provide useful cyclic carbonate products with selectivities between 5.5 and 10:1. Homoallylic carbonates with substituents displaying additional stereogenic centres reacted smoothly, again in good yield and diastereoselectivity, to form stereotriads **3j** and **3k** commonly found in polyketide natural products.

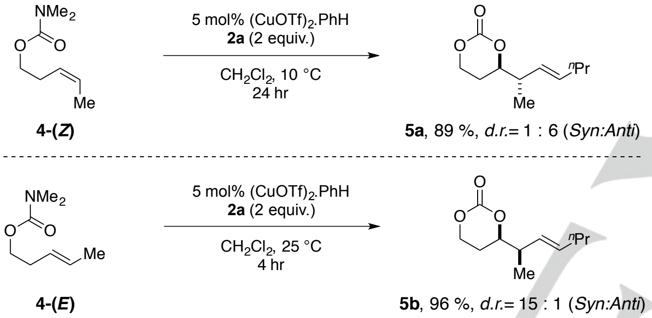


3b, 96 %^{b}
3c, 96 %, *d.r.*= 4: 1
3d, 89 %, *d.r.*= 6: 1
3e, 92 %, *d.r.*= 5.5: 1
3f, 65 % (*d.r.*= 10: 1)^c
3g, 75 % (*d.r.*= 7: 1)
3h, 84 % (*d.r.*= 8: 1)
3i, 85 %, *d.r.*= 6: 1
3j, 68 %, *d.r.*= 4: 1
3k, 71 % (*d.r.*= 8: 1)^c
3l, 81 %, *d.r.*= 6: 1
3m, 96 %
3n, 86 % (*d.r.*= 8: 1)^d
3o, 96 %
3p, 76 %, *d.r.*= 10: 1
3q, 95 %, *d.r.*= 5: 1
3r, 94 %, *d.r.*= 5: 1
3s, 85 %, *d.r.*= 5: 1

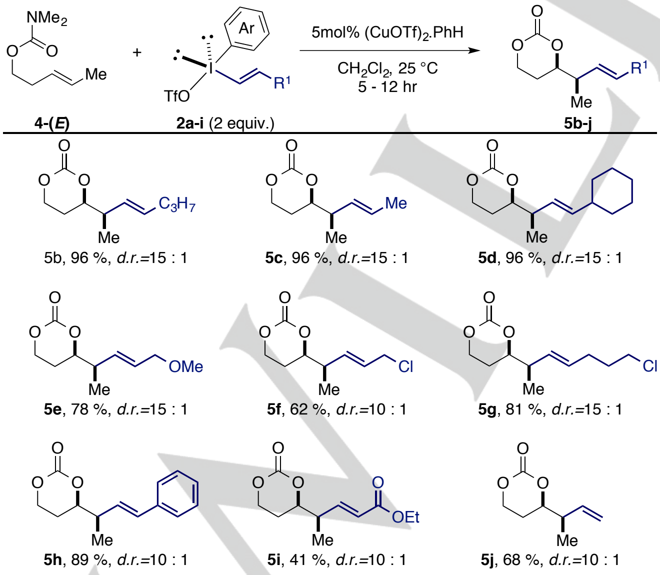
Table 2. Substrate scope for the oxy-alkenylation reaction. a) See SI for further details of temperature and time taken. b) Yields of **3f**, **3g**, **3h**, **3k**, **3n** and **3o** are quoted for isolated product; all others yields are of quoted for an isolated mixture of diastereomers. *d.r.* (diastereoselectivity) is that observed from the crude reaction mixture by ^{1}H NMR. c) Required 2 equivalents of K_2CO_3. d) Confirmed as *syn* by 1D NOESY.

In addition to the primary homoallylic carbamates that worked well to form the corresponding products, we were pleased to find that substituents on the internal position of the carbon–carbon bond worked well to form functionalized cyclic carbonates containing a quaternary carbon atom (**3m** and **3n**). The reaction could also be deployed on allylic carbamates to form either the 5-membered ring **3o** or 6-membered (**3p**) cyclic carbonates, depending on the nature of the alkene substituent. The transferring alkenyl group can also be varied without significantly affecting the yield or diastereoselectivity (**3q-s**).

Having established that terminal alkenes were excellent reaction partners in the copper-catalyzed oxy-alkenylation, we next investigated whether 1,2-disubstituted carbon–carbon double bonds would also function as part of this process. Methyl substituents appended to the alkene were of particular interest because the product of the transformation would form vicinal stereocentres reminiscent of propionate motifs commonly found in polyketide natural products. We were pleased to find that *Z*-alkene **4** formed the *anti*-isomer **5a** with very good selectivity and in high yield. Importantly, the *E*-alkene **4**, under similar conditions, formed the corresponding *syn*-product **5b**, in both excellent yield and selectivity. The selectivity here is comparable to that observed for the related iodine mediated reactions on similar substrates. These selectivities were observed with a range of alkenyl(aryl)iodonium salts (table 3). We were particularly pleased to observe the successful transfer of the propenyl motif (**5c**), acrylate moiety (**5i**), and notably, the ethenyl group **5j**; each reaction proceeded in good yield and excellent selectivity, to deliver highly versatile products.



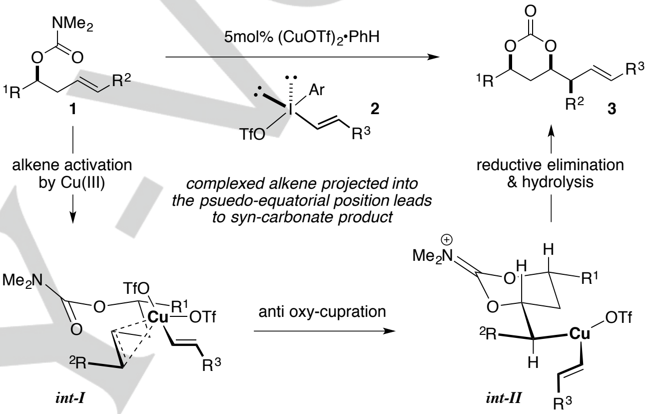
Scheme 1. Application of non-terminal alkenes **4-(*E*)** and **4-(*Z*)** to the copper-catalyzed oxy-alkenylation.



Yields are quoted for and isolated mixture of diastereomers. *d.r.* (diastereoselectivity) is that observed from the crude reaction mixture by ^{1}H NMR.

Table 3. Salt scope of the reaction.

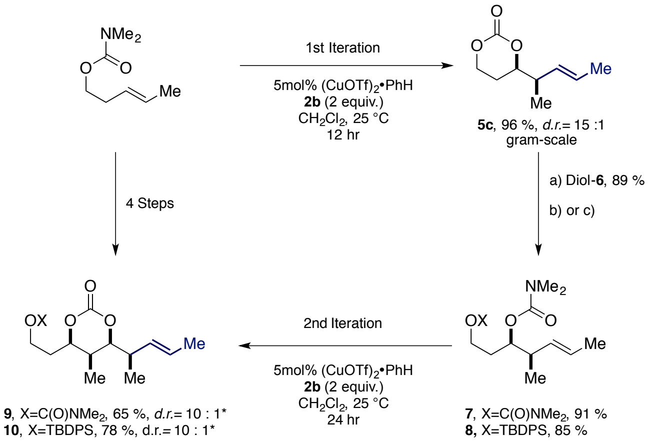
Based on the observations in scheme 1, we propose that the reaction proceeds *via* a pathway related to the iodine-mediated cyclization of homoallylic carbonates.[14] No formation of the product was observed in the absence of copper at elevated temperatures, nor with a variety of Lewis acid catalysts.[15] Therefore, we propose that the copper-catalyzed oxy-alkenylation proceeds *via* a copper(III)-alkenyl species functioning as an electrophile that complexes the alkene (***int-I***), activating the carbon–carbon double bond towards an *anti*-attack by the pendant carbonyl group *via* a chair-like intermediate (***int-II***) to form the *syn* carbonate product (Scheme 2). The minor diastereoisomer could arise from attack on to the copper-complexed alkene in a pseudo-axial orientation to form the anti-carbonate product. A pathway involving delivery of the copper(III) species *via* complexation with the carbonyl is not consistent with the observed selectivity for the oxy-alkenylation.



Scheme 2. Proposed mechanism for the formation of *syn*- and *anti*-diastereoisomers in the reaction.

The products of the copper-catalyzed oxyalkenylation reaction display a functional pattern that may be amenable to an iterative cycle of the process. To test this, carbonate **5c** was synthesized on gram-scale and cleaved to the corresponding 1,3-diol **6**, which could be readily transformed into the carbamate derivative **7**, or the differentially protected carbamate **8**, both of which were substrates for the oxy-alkenylation. We were delighted to observe that the second iteration of the copper-catalyzed reaction proceeded smoothly to form the propionate stereotetrad **9** or **10** in good yield and selectivity. This short reaction sequence highlights the ability to rapidly access complex polypropionate fragments from readily accessible homoallylic alcohol starting materials using this strategy.

WILEY-VCH



Scheme 3. Application of the 1,3-diol-carbonate product in an iterative reaction sequence. a) K_2CO_3, MeOH, 89 %. b) 1. 1,1-carbonyl diimidazole (3 equiv.), MeCN, RT, 2. $HNMe_2$ (4 equiv.), 91 % **7**. or c) 1. NEt_3, DMAP, TBDPSCl, 2. 1,1-carbonyl diimidazole (1.5 equiv.), MeCN, RT, 2. $HNMe_2$ (2 equiv.) to give **8**, 85 %. *All-*syn* diastereoisomer: sum of all diastereoisomers. Yields are quoted for the diastereomer shown, isolated as a pure compound.

In summary, we have developed a new copper-catalyzed oxy-alkenylation of homoallylic carbamates. The transformation is tolerant to a wide range of functional groups and provides ready access to a broad range of 1,3-carbonate products in very high yields and good selectivity. The cyclic carbonate products can be further manipulated into 1,3-diol derivatives that are amenable to further iterations of the reaction. On-going research is elaborating on these studies, by applying the methodology in natural product synthesis.

Keywords: polyol • copper catalysis • hypervalent iodine • stereoselective synthesis • alkenylation •

[1] a) D. Hagan, *Nat. Prod. Rep.* **1995**, *12*, 1–32; b) J. Staunton, K. J. Weissman, *Nat. Prod. Rep.* **2001**, *18*, 380–416; c) D. Hagan, *The polyketide metabolites*; Ellis Horwood: Chichester, **1991**; d) J. Staunton, B. Wilkinson, *Chem. Rev.* **1997**, *97*, 2611–2630; e) C. Hertweck, *Angew. Chem. Int. Ed.* **2009**, *48*, 4688–4716.

[2] For review articles; a) Oishi, T.; Nakata, T. *Synthesis,* 1990, 635–645; b) C. Schneider, *Angew. Chem. Int. Ed.* **1998**, *37*, 1375–1378; c) R. W. Hoffmann, *Angew. Chem. Int. Ed.* **2000**, *39*, 2054–2070; d) S. D. Rychnovsky, *Chem. Rev.* **1995**, *95*, 2021–2040; e) R. D. Norcross, I. Paterson, *Chem. Rev.* **1995**, *95*, 2041–2114; f) S. E. Bode, M. Wolberg, M. Müller, *Synthesis*, **2006**, 557–588; g) T. Harschneck, S. F. Kirsch, *Asymmetric Synthesis II - More Methods and Applications* (Eds.: M. Christmann, S. Bräse), Wiley-VCH, Weinheim, **2012**, 179–186.

[3] For a selection of reviews on the aldol reaction, see: a) *Modern Methods in Stereoselective Aldol Reactions* (Ed.: R.Mahrwald), Wiley-VCH, Weinheim, **2013**. b) S. B. J. Kan, K. K.-H. Ng, I. Paterson, *Angew. Chem. Int. Ed.* **2013**, *52*, 9097–9108; c) S. E. Denmark, J. R. Heemstra, Jr., G. L. Beutner, *Angew. Chem. Int. Ed.* **2005**, *44*, 4682–4698.

[4] a) L. F. Tietze, H. Geissler, J. A. Gewert, U. Jakobi, *Synlett,* **1994**, 511–512; b) A. B. Smith, III, C. M. Adams. *Acc. Chem. Res.* **2004**, *37*, 365–377.

[5] Allylation; see; a) S. E. Denmark, J. Fu, *Chem. Rev.* **2003**, *103*, 2763–2794; b) M. Yus, J. C. Gonzalez-Gomez, F. Foubelo, *Chem. Rev.* **2011**, *111*, 7774–7854; c) H.-X. Huo, J. R. Duvall, M.-Y. Huang, R. Hong, *Org. Chem. Front.* **2014**, *1*, 303–320; d) J. W. A. Kinnaird, P. Y. Ng, K. Kubota, J. L. Leighton, *J. Am. Chem. Soc.* **2002**, *124*, 7920–7921; e) I. S. Kim, M.-Y. Ngai, M. J. Krische, *J. Am. Chem. Soc.* **2008**, *130*, 6340–6341.

[6] D. A. Evans, J. A. Gauchet-Prunet, *J. Org. Chem.* **1993**, *58*, 2446–2453.

[7] Review; J. M. Ketcham, I. Shin, T. P. Montgomery, M. J. Krische, *Angew. Chem. Int. Ed.* **2014**, *53*, 9142–9150. Additionally; a) Y. Lu, I. S. Kim, A. Hassan, D. J. Del Valle, M. J. Krische, *Angew. Chem. Int. Ed.* **2009**, *48*, 5018–5021; b) S. B. Han, A. Hassan, I. S. Kim, M. J. J. Krische, *J. Am. Chem. Soc.* **2010**, *132*, 15559–15561; c) J. R. Zbieg, E. Yamaguchi, E. L. McInturff, M. J. Krische, *Science* **2012**, *336*, 324–327; d) X. Gao, H. Han, M. J. Krische, *J. Am. Chem. Soc.* **2011**, *133*, 12795–12800.

[8] For examples of the contribution by Leighton to this field, see; a) W. A. Chalifoux, S. K. Reznik, J. L. Leighton, *Nature* **2012**, *487*, 86–89; b) T. J. Harrison, S. Ho, J. L. Leighton, *J. Am. Chem. Soc.* **2011**, *133*, 7308–7311; c) M. J. Zacuto, S. L. O' Malley, J. L. Leighton, *Tetrahedron* **2003**, *59*, 8889–8900; d) M. J. Zacuto, S. J. O'Malley, J. L. Leighton, *J. Am. Chem. Soc.* **2002**, *124*, 7890–7891.

[9] For examples of Yamamoto 'super-silyl' chemistry; a) B. J. Albert, Y. Yamaoka, H. Yamamoto, *Angew. Chem. Int. Ed.* **2011**, *50*, 2610–2612; b) P. B. Brady, H. Yamamoto, *Angew. Chem. Int. Ed.* **2012**, *51*, 1942–1946; c) B. J. Albert, H. Yamamoto, *Angew. Chem. Int. Ed.* **2010**, 49, 2747–2749; d) M. B. Boxer, H. Yamamoto, *J. Am. Chem. Soc.* **2007**, *129*, 2762–2763.

[10] Some alternative disconnections around the 1,3-hydroxyl motif; a) B. Li, M. Driess, J. F. Hartwig, *J. Am. Chem. Soc.* **2014**, *136*, 6586–6589; b) H. M. L. Davies, S. J. Hedley, B. R. Bohall, *J. Org. Chem.*, **2005**, *70*, 10737–10742; c) K. Chen , J. M. Richter, P. S. Baran, *J. Am. Chem. Soc.*, **2008**, *130*, 7247–7249; d) D. Herkommer, B. Schmalzbauer, D. Menche, *Nat. Prod. Rep.,* **2014**, *31*, 456–467; e) J. W. Bode, N. Fraefel, D. Muri, E. M. Carreira, *Angew. Chem. Int. Ed.* **2001**, *40*, 2082–2085; f) J. T. Binder, S. F. Kirsch, *Chem. Commun.* **2007**, 4164–4166; g) M. Iwata, R. Yazaki, Y. Suzuki, N. Kumagai, M. Shibasaki, *J. Am. Chem. Soc.* **2009**, *131*, 18244–18245; h) L. Wang, D. Mench, *Angew. Chem. Int. Ed.* **2012**, *51*, 9425–9427.

[11] a) G. Cardillo, M. Orena, G. Porzi, S. J. Sandri, *Chem. Soc., Chem. Commun.* **1981**, 465–466; b) A. Bongini, G. Cardillo, M. Orena, G. Porzi, S. Sandri, *J. Org. Chem.* **1982**, *47*, 4626–4633; c) P. A. Bartlett, J. D. Meadows, E. G. Brown, A. Morimoto, K. K. Jernstedt, *J. Org. Chem.* **1982**, *47*, 4013–4018; d) J. J.-W. Duan, A. B. Smith, III *J. Org. Chem.* **1993**, *58*, 3703–3711; J. J.-W. Duan, P. A. Sprengeler, A. B. Smith III, *Tetrahedron Letters,* **1992**, *33,* 6439–6442; e) R. Tirado, J. A. Prieto, *J. Org. Chem.* **1993**, *58*, 5666–5673; f) P. A. Bartlett , J. Myerson. *J. Am. Chem. Soc.*, **1978**, *100*, 3950–3952; P. A. Bartlett, K. K. Jernstedt, *J. Am. Chem. Soc.* **1977**, *99*, 4829–4830.

[12] For selected reviews on electrophilic carbofunctionalization, see: a) J. P. Wolfe, *Eur. J. Org. Chem.* **2007**, 571–582; b) V. Kotov, C. C. Scarborough, S. S. Stahl, *Inorg. Chem.* **2007**, *46*, 1910–1923; c) J. P. Wolfe, *Synlett,* **2008**, 2913–2937; d) S. R. Chemler, *Org. Biomol. Chem.* **2009**, *7*, 3009–3019; e) R. I. McDonald, G. Liu, S. S. Stahl, *Chem. Rev.* **2011**, *111*, 2981–3019. Cu-catalyzed carbofunctionalization, see a) W. Zeng, S. Chemler, *J. Am. Chem. Soc.* **2007**, *129*, 12948–12949; b) E. S. Sherman, P. H. Fuller, D. Kasi, S. R. Chemler, *J. Org. Chem.* **2007**, *72*, 3896–3905; c) L. Miao, I. Haque, M. R. Manzoni, W. S. Tham, S. R. Chemler, *Org. Lett.* **2010**, *12*, 4739–4741; d) Y. Miller, L. Miao, A. Hosseini, S. R. Chemler, *J. Am. Chem. Soc.* **2012**, *134*, 12149–12156; e) T. W. Liwosz, S. R. Chemler, *J. Am. Chem. Soc.* **2012**, *134*, 2020–2023.

[13] For selective examples, see a) R. J. Phipps, N. P. Grimster, M. J. Gaunt, *J. Am. Chem. Soc.* **2008**, *130*, 8172–8174; b) R. J. Phipps, M. J. Gaunt, *Science* **2009**, *323*, 1593–1597; c) C.-L. Ciana, R. J. Phipps, J. R. Brandt, F. M. Meyer, M. J. Gaunt, *Angew. Chem. Int. Ed.* **2011**, *50*, 458–462; d) A. Bigot, A. E. Williamson, M. J. Gaunt, *J. Am. Chem. Soc.* **2011**, *133*, 13778–13781; e) R. J. Phipps, L.McMurray, S. Ritter, H. A. Duong, M. J. Gaunt, *J. Am. Chem. Soc.* **2012,** *134*, 10773–10776; f) M. G. Suero, E. D. Bayle , B. S. L. Collins , M. J. Gaunt, *J. Am. Chem. Soc.* **2013**, *135*, 5332–5335; g) E. Cahard, N. Bremeyer, M. J. Gaunt, *Angew. Chem. Int. Ed.* **2013**, *52,* 9284–9288; h) F. Zhang, S. Das, A. J.

Walkinshaw, A. Casitas, M. Taylor, M. G. Suero, M. J. Gaunt, *J. Am. Chem. Soc.* **2014**, *136*, 8851–8854. For examples from the MacMillan group, see; i) A. Allen, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2011**, *133*, 4260–4263; j) E. Skucas, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2012**, *134*, 9090–9093; k) J. S. Harvey, S. P. Simonovich, C. R. Jamison, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2011**, *133,* 13782–13785; l) S. Zhu, D. W. C. MacMillan, *J. Am. Chem. Soc.* **2012**, *134*, 10815–10818.

[14] For discussion of the mechanism and temperature dependence for the iodine mediated reaction, see R. Tirado, J. A. Prieto, *J. Org. Chem.* **1993**, *58*, 5666–5673; J. J.-W. Duan, P. A. Sprengeler, A. B. Smith III, *Tetrahedron Letters,* **1992**, *33,* 6439–6442.

[15] None of the product **3a** was observed for reactions in the absence of copper at 40 °C, 70 °C or 110 °C, or with a range of Lewis acids ($Bi(OTf)_3$, $Sc(OTf)_3$, $Zn(OTf)_2$ or $BF_3{\cdot}(OEt_2)$).

WILEY-VCH

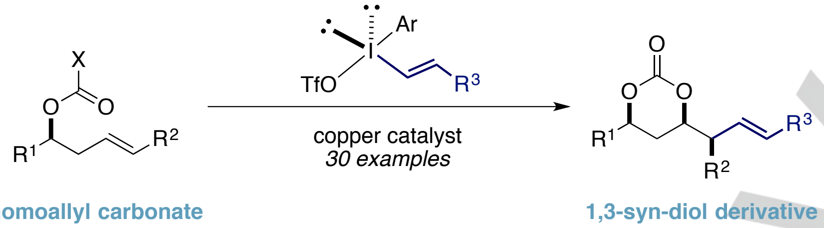
Layout 2:

COMMUNICATION

*Author(s), Corresponding Author(s)**

Page No. – Page No.

Title



Abstract: A novel method for the synthesis of a wide range of functionalized 1,3-diol derivatives is reported. Employing a copper-catalyzed oxy-alkenylation strategy, a range of readily available, substituted homoallylic alcohol derivatives and alkenyl(aryl) iodonium salts combine to form syn-1,3-carbonates in excellent yield and with high selectivity. Furthermore, the products formed are amenable to an iterative reaction sequence, affording highly complex polyketide-like fragments.

Copper-catalyzed oxy-alkenylation of homoallylic alcohols to functional syn-1,3-diol derivatives

Dean Holt and Matthew J. Gaunt*

Page No. – Page No.

WILEY-VCH