Check for updates

EurJOC
European Journal of Organic Chemistry

A Journal of ChemPubSoc Europe

Accepted Article

Title: Vessel effect in C–F bond activation prompts revised mechanism and reveals an autocatalytic glycosylation.

Authors: Michael Martin Nielsen, Yan Qiao, Yingxiong Wang, and Christian Marcus Pedersen

This manuscript has been accepted after peer review and appears as an Accepted Article online prior to editing, proofing, and formal publication of the final Version of Record (VoR). This work is currently citable by using the Digital Object Identifier (DOI) given below. The VoR will be published online in Early View as soon as possible and may be different to this Accepted Article as a result of editing. Readers should obtain the VoR from the journal website shown below when it is published to ensure accuracy of information. The authors are responsible for the content of this Accepted Article.

To be cited as: *Eur. J. Org. Chem.* 10.1002/ejoc.201901755

Link to VoR: http://dx.doi.org/10.1002/ejoc.201901755

Supported by ACES Asian Chemical Editorial Society

WILEY-VCH

WILEY-VCH

COMMUNICATION

Vessel effect in C–F bond activation prompts revised mechanism and reveals an autocatalytic glycosylation.

Michael M. Nielsen,[a] Yan Qiao,[b] Yingxiong Wang,*[b] and Christian M. Pedersen*[a]

In memory of Professor Teruaki Mukaiyama.

Abstract: Activation of C-F bonds under acidic conditions results in the formation of hydrogen fluoride as the reaction progresses. In the following communication, the effect of the vessel material on such reactions has been investigated and a significant difference between an HF-resistant material and common borosilicate glassware has been found. HF was found to react rapidly with borosilicate glassware, seemingly leaching fluorosilicate into solution, but persisted in HF-resistant materials. Several examples of C-F bond activation on glycosyl fluorides and benzyl fluorides as well as NMR-studies suggest a significant effect of the choice of reaction vessel, leading to the discovery of an autocatalytic glycosylation and a revised mechanism for the activation of benzyl fluorides, suggesting activation by SiF_4 rather than HF.

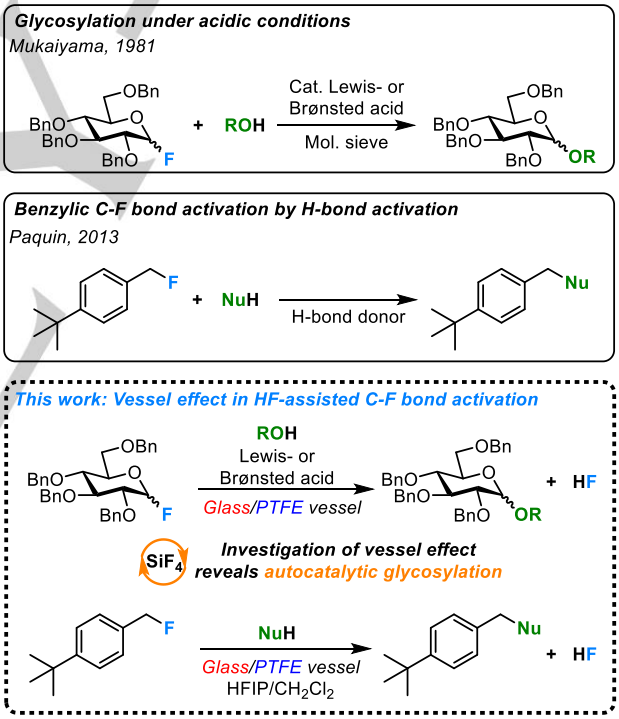
The C-F bond is one of the strongest single bonds in organic chemistry.[1] In recent years, the activation of C(sp^3)-F bonds has received considerable attention as the C(sp^3)-F group has emerged as a useful electrophile with distinct reactivity.[2–9] Mukaiyama pioneered the field of anomeric C-F bond activation in carbohydrate chemistry with the introduction of glycosyl fluorides as novel electrophiles in glycosylation chemistry[10] (Scheme 1) that has since become a commonly employed electrophile for catalytic glycosylations.[11,12]

Several other applications of C(sp^3)-F bond activation have been developed and significant highlights in this vast field of research has recently been reviewed in detail by Hamel and Paquin.[3] Often, C-F bonds are activated under either reductive or basic conditions, but recent years have seen a growing interest in C-F bond activation under acidic/neutral conditions enabled by hydrogen bonding (Scheme 1). The Paquin and co-workers have developed methods for chemoselective benzylic-[13–17], allylic[13] and propargylic[18] C-F bond activation mediated through hydrogen bonding, reporting that the hydrogen fluoride developed during the reaction would function as an active catalyst, resulting in an autocatalytic kinetic profile. Several other examples of Lewis- or Brønsted acid-[19–22] and metal-catalyzed[23] C-F bond activations without employing HF-scavengers have also been reported.

[a] M. M. Nielsen, Prof. C. M. Pedersen
Department of Chemistry
University of Copenhagen
Universitetsparken 5, 2100 Copenhagen O, Denmark
E-mail: cmp@chem.ku.dk
[b] Prof. Y. Qiao, Prof. Y. Wang,
Institute of Coal Chemistry
Chinese Academy of Sciences
27 South Taiyuan Road, Taiyuan 030001, People's Republic of China

Supporting information for this article is given via a link at the end of the document.((Please delete this text if not appropriate))

When reviewing the literature, it is clear that many methods for C-F bond activation result in the accumulation of HF in solution, which in itself has been reported as an active catalyst for C-F bond activation *(vide supra)*. However, as HF is known to react with silica, one of the primary components of standard laboratory equipment, we sought out to investigate whether C-F bond activations taking place under acidic conditions would be influenced by changing the reaction vessel to an HF-resistant material rather than common borosilicate glassware. The fate of the HF formed during glycosylations with glycosyl fluorides has previously been ignored in the literature and only mentioned briefly by Kunz and Sager.[24]



Scheme 1. Examples of C-F bond activation promoted by acid- or H-bond catalysis and the work presented in this paper.

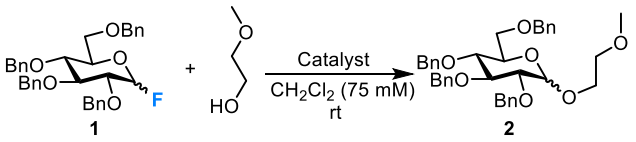
Initially, the catalytic activation of glucopyranosyl fluoride **1** was investigated by using a simple, primary alcohol as the nucleophile (Table 1). It has been documented by Mukaiyama that the anomeric configuration of the electrophile has no effect on the stereochemical outcome,[25–27] and consequently, a mixture of anomers were employed as electrophiles in the glycosylations. $BF_3{\cdot}OEt_2$[24,28–30] and TfOH[26,27,31] were chosen as common examples of a strong Lewis- or Brønsted acid catalysts in catalyst loadings of 1 to 10 mol%. From the initial results (Table 1), it was

Accepted Manuscript

This article is protected by copyright. All rights reserved.

evident that the glycosylations with glycosyl fluorides resulted in very high yields at 5 to 10 mol% catalyst loadings (entries 1-4 and 7-10), however as the catalyst loading was lowered (entries 5-6), the yield of the desired product, **2**, diminished and increasing amounts of 2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranose was formed as an undesired byproduct by hydrolysis. Interestingly, this byproduct was formed in glassware despite careful flame-drying of the glass vessels under high vacuum prior to use.

Table 1. Initial investigation of vessel effect using a simple nucleophile.



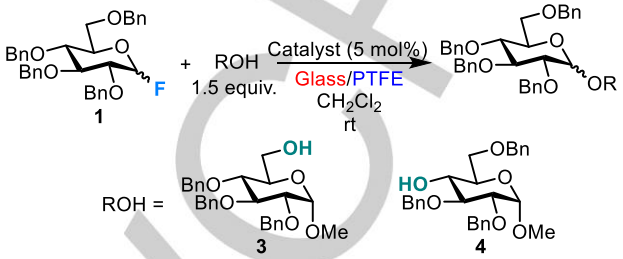
Entry	cat. (mol%)	Vessel material	t (h)	Yield (%)[a]	α/β
1	$BF_3{\cdot}OEt_2$ (10)	Glass	4.5	90[b]	53/47
2	$BF_3{\cdot}OEt_2$ (10)	PTFE	2.25	97	55/45
3	$BF_3{\cdot}OEt_2$ (5)	Glass	5.25	92[b]	52/48
4	$BF_3{\cdot}OEt_2$ (5)	PTFE	3	97	54/46
5	$BF_3{\cdot}OEt_2$ (1)	Glass	23	76[b]	53/47
6	$BF_3{\cdot}OEt_2$ (1)	PTFE	72	91	56/44
7	TfOH (10)	Glass	20	94[b]	58/42
8	TfOH (10)	PTFE	3.25	96	52/48
9	TfOH (5)	Glass	22	89[b]	56/44
10	TfOH (5)	PTFE	22	98	58/42

[a] Isolated yield. [b] Yield corrected for 2,3,4,6-tetra-*O*-benzyl-α/β-D-glucopyranose.

Next, more challenging nucleophiles were glycosylated (Table 2) as more synthetically relevant glycosylations. Using 5 mol% of the catalysts, the glycosylations with a 6-OH nucleophile **2** (entries 1-4) performed smoothly and still followed the trend of both increased yields and rate in PTFE compared to the reaction in a glass vessel. The major byproduct that led to lowered yields in the glass containers was found to be a mixture of α/α- and α/β-trehalose via the corresponding hemiacetal that was formed by hydrolysis of the glycosyl donors.

The yields were found to drop dramatically as nucleophile **4**, a much weaker nucleophile than **3**, was employed (entries 5-8). Interestingly, different major byproducts were observed to cause this decrease in yields; The reactions in glassware resulted in the formation of trehaloses as byproducts, whereas the glycosylations in PTFE gave rise to unexpected byproducts, namely methyl 2,3,4,6-tetra-*O*-benzyl-α/β-glucopyranosides. The formation of these methyl glycosides was surprising as these can only be formed by transfer of the benzyl- or methoxy groups between the acceptors under the reaction conditions. To investigate whether the benzyl transfer was caused by an increasingly more acidic reaction mixture as the reaction progressed, it was attempted to stop the reaction prematurely (entry 9+10). Although the total yield in these two reactions was only 52 and 53% accordingly, the yields based on recovered starting material were found to be 94 and 72%, which indicates that the formation of byproducts in the PTFE vessel increases as the reaction approaches completion.

Table 2. Catalytic glycosylations employing carbohydrate electrophiles.



Entry	ROH	cat.	Vessel mat.	t (h)	Yield (%)	α/β
1	**3**	$BF_3{\cdot}OEt_2$	Glass	4.5	69	59:41
2	**3**	$BF_3{\cdot}OEt_2$	PTFE	2.25	86	59:41
3	**3**	TfOH	Glass	5.25	66	62:38
4	**3**	TfOH	PTFE	4	80	61:39
5	**4**	$BF_3{\cdot}OEt_2$	Glass	5.25	38	66:34
6	**4**	$BF_3{\cdot}OEt_2$	PTFE	22	–[c]	–
7	**4**	TfOH	Glass	5.25	36	63:37
8	**4**	TfOH	PTFE	22	25	66:34
9	**4**	$BF_3{\cdot}OEt_2$	PTFE	1.25	52[d]	57:43
10	**4**	TfOH	PTFE	1.25	53[d]	64:36
11[a]	**4**	$BF_3{\cdot}OEt_2$	Glass	5[b]	63	69:31
12[a]	**4**	$BF_3{\cdot}OEt_2$	PTFE	0.5	–[c]	–
13[a]	**4**	TfOH	Glass	5	59	69:31
14[a]	**4**	TfOH	PTFE	5	49	54:46

[a] Two equivalents of **4** were added. [b] **4** was consumed after 3 h according to TLC. [c] Contained <10% product. Major product was methyl 2,3,4,6-tetra-*O*-methyl-α/β-D-glucopyranoside. [d] Yields BRSM were 94% for entry 9 and 72% for entry 10.

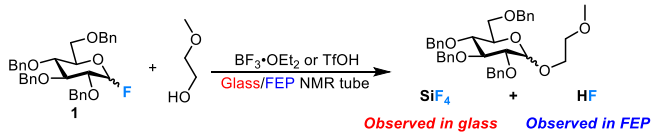
The yields only increased very little as an excess of nucleophile **4** was employed (entries 11-14) and significant amounts of the above-mentioned byproducts were still observed. Interestingly, the reactions in entries 6 and 12 suffered from comparable problems of protecting group transfer under the reaction conditions and the decomposition of the starting material was much faster as the concentration of glycosyl fluoride was increased (entry 12).

In an attempt to clarify exactly what effect the reaction vessel had on the chemical environment, a series of NMR experiments were carried out (Scheme 2; for details, see SI), again using 2-methoxyethanol as the nucleophile as in Table 1. A fluorinated ethylene propylene (FEP) NMR liner was used to as HF-resistant

Accepted Manuscript

This article is protected by copyright. All rights reserved.

vessel during NMR experiments. In agreement with the results from Table 1, it was found that the rate of reaction was higher for the reactions carried out in FEP compared to reactions in regular glass NMR tubes (see SI). Furthermore, the addition of crushed glass (from an NMR tube) to the FEP tube was found to lower the reaction rate to almost resemble that in glass. In the FEP NMR-tube, the formation of HF was obvious from ^{19}F-NMR as the reaction progressed (see SI). Interestingly, the distinct HF-peak was never detected during the reactions in glass NMR tubes. In the glass NMR tube, however, a broad singlet at −162 ppm was observed to increase (and shift slightly) as the reaction progressed. Furthermore, this peak was not detectable when the NMR tube was washed and a blank sample was recorded, ruling out a glass-bound species.



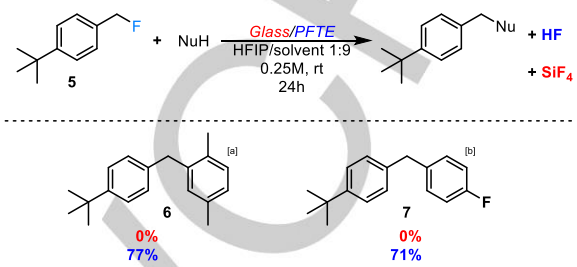
Scheme 2. Summary of NMR-observations.

The peak at −162 ppm has recently been reported as SiF_4,[32] a species that has previously been reported to be formed as HF reacts with a glass surface.[33–39] The identity of SiF_4 in glass vessels was confirmed by headspace GC-MS (see SI for chromatogram and control experiments) of the reaction mixture. This explains why the reaction was so strongly influenced by the choice of reaction vessel as SiF_4 has been reported by Noyori as an efficient catalyst for activation of glycosyl fluorides[40] and related fluorosilicates have previously been employed as Lewis acids in glycosylation chemistry.[41] Furthermore, the formation of large amounts of α/α- and α/β-trehalose is a consequence of the reaction between HF with the glass surface which results in the release of water into solution, thus explaining the absence of trehalose in PTFE vessels. This can also explain why the consumption of glycosyl fluoride was much faster in glass vessels when weaker glycosyl nucleophiles (Table 2, entries 5 and 7) were used as water simply outcompeted the 4-OH glycosyl nucleophile and resulted in trehalose formation. One can speculate whether this was also the primary reason why the Mukaiyama group and others added molecular sieves in order to obtain acceptable yields in catalytic glycosylations with glycosyl fluorides.[25–27,31,42–46] The effect of adding drying agents to this particular glycosylation seems highly important as Toshima has reported an increase in yield from 32% to 99% of the desired glycoside when 100 wt% 5Å molecular sieves were added.[47]

As there was a clear difference in the reactivity of the glycosyl fluoride dependent on the vessel material, it was investigated whether this would also be the case for the H-bond mediated Friedel-Crafts alkylations with benzyl fluorides that have been reported by Paquin and co-workers.[15] As this reaction is reported to be catalyzed by HF formed *in situ*,[15,16] it was likely to be influenced by the vessel material as well.

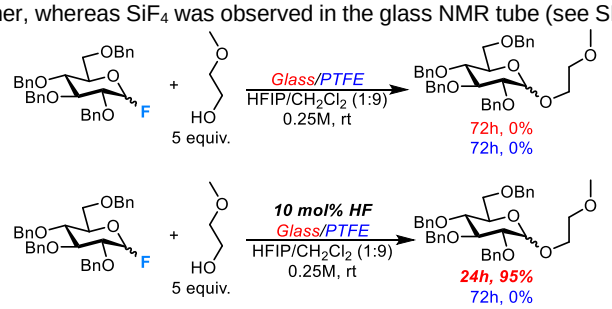
Four reactions involving the benzyl fluorides were performed (Scheme 3). Surprisingly, there was no conversion of benzyl fluoride **5** in regular round bottom flasks after 24h. After 20h, all four reactions showed no conversion by TLC, but after 24h, the starting material in the two reactions in a PTFE flask were fully converted, which confirmed the autocatalytic kinetic profile reported by Paquin and co-workers.

Furthermore, it seemed that the use of an electron-poor electrophile such as fluorobenzene (product **7**) gave rise to almost identical yields as with *p*-xylene (product **8**). As the reactions in glassware (round bottom flask with nitrogen balloon) did not lead to the formation of the desired product, the experiments were conducted under identical conditions as reported by Paquin and co-workers[15] using sealed glass vials rather than conventional round bottom flasks.



Scheme 3. Friedel-Crafts alkylations using benzyl fluorides under similar conditions as reported by Paquin and co-workers. Yields from glass vessel in red, yield in blue in PTFE vessel. HFIP = hexafluoroisopropanol. [a] Solvent was CH_2Cl_2. [b] Solvent was fluorobenzene.

Furthermore, it was investigated whether the vessel surface had an effect on the reaction, as three identical vials were subjected to different conditions prior to reaction; One was pre-treated with TMSCl to TMS-protect all free OH-groups of the glass surface, one was pre-treated with HF in CH_2Cl_2 and one glass vial was used as purchased. Furthermore, an experiment using identical conditions in a PTFE-vessel was also conducted. It was found that all four reactions ran to completion within 24h, yielding the desired product in yields of >95% in all four cases, ruling out this hypothesis and confirming the high yields reported by Paquin. As the reactions in round bottom flasks did not lead to formation of the desired product, we speculated that the headspace volume could be influencing the reaction as SiF_4 diffuses out of solution. Two parallel experiments, one in a regular glass NMR tube and another in an FEP liner were then conducted. Both ran to completion, albeit HF was only observed, by ^{19}F-NMR, in the FEP liner, whereas SiF_4 was observed in the glass NMR tube (see SI).



Scheme 4. Glycosylations using the Paquin procedure[15] employing HFIP/CH_2Cl_2 and HF as reaction initiators.

Next, it was investigated whether the conditions for benzyl fluoride activation were applicable for glycosylations (Scheme 4). It was found that the CH_2Cl_2/HFIP solvent mixture was not able to efficiently activate the glycosyl fluoride and no conversion was observed after three days. However, when adding 10 mol% HF, formed *in situ* in CH_2Cl_2, the reaction was found to take place in the glass vessel, whereas the reaction in PTFE showed no conversion after three days. This can be explained by the reaction of HF with the glass surface, resulting in the formation of SiF_4

Accepted Manuscript

This article is protected by copyright. All rights reserved.

which is then capable of activating the glycosyl fluoride. To investigate this hypothesis, both reactions were studied by NMR and it was found that the glycosylation was in fact autocatalytic when conducted in a glass NMR tube (Figure 1). This is, to the best of our knowledge, the first report of an autocatalytic chemical glycosylation.

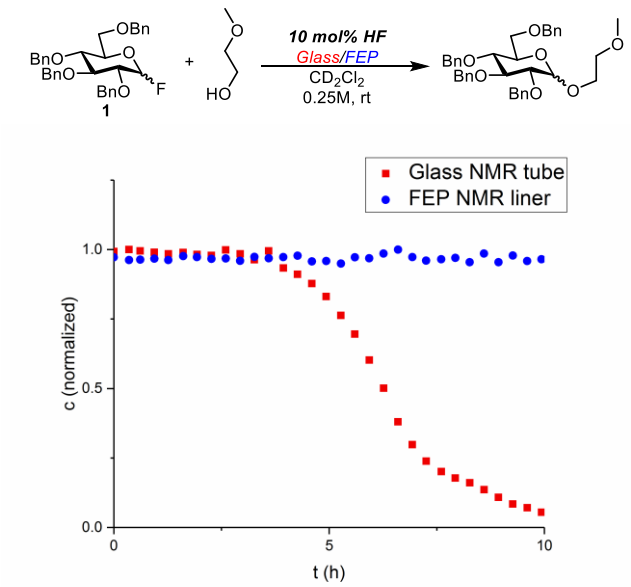


Figure 1. Autocatalytic consumption of glycosyl fluoride.

An identical reaction in the FEP NMR liner did not lead to any conversion of the starting material even after three days, which indicates that HF is not the active catalyst for glycosyl fluoride activation. Paquin and co-workers have reported that trifluoroacetic acid (TFA) shortens the induction period for benzyl fluoride activation.[16] However, 5 mol% TFA did not lead to any conversion of the glycosyl fluoride after three days in a PTFE vessel, suggesting that HF is not capable of activating a glycosyl fluoride.

In conclusion, a vessel effect in C–F bond activation has been documented and *in situ* formation of SiF_4[48] in glass vessels was found as the active catalyst for glycosylations as well as benzylic C-F bond activations. Furthermore, it was found that HF was indeed the active catalyst for benzylic C–F bond activation, but only in PTFE, whereas glycosyl fluorides could not be activated by HF alone. SiF_4 formed *in situ* was found to facilitate a previously unprecedented autocatalytic glycosylation. We believe that these findings can provide a basis for the development of novel C–F bond chemistry as well as providing an explanation of byproduct formation. We currently seek to investigate the autocatalytic glycosylation with glycosyl fluorides further, specifically aiming at developing a water-free variant which could be of interest in the scientific community.

Acknowledgements

Dr. Brian Schou Rasmussen (Dept. of Forensic Medicine, University of Copenhagen) is acknowledged for his help with acquiring headspace GC-MS. Christian Tortzen (Dept. of Chemistry, University of Copenhagen) is acknowledged for helping with setting up NMR experiments. CMP acknowledges CAS President's International Fellowship Initiative (2015VMB052) for support.

Keywords: keyword 1 • keyword 2 • keyword 3 • keyword 4 • keyword 5

[1] S. J. Blanksby, G. B. Ellison, *Acc. Chem. Res.* **2003**, *36*, 255–263.

[2] J. L. Kiplinger, T. G. Richmond, C. E. Osterberg, *Chem. Rev.* **1994**, *94*, 373–431.

[3] J.-D. Hamel, J.-F. Paquin, *Chem. Commun.* **2018**, *54*, 10224–10239.

[4] M. F. Kuehnel, D. Lentz, T. Braun, *Angew. Chem., Int. Ed.* **2013**, *52*, 3328–3348.

[5] H. Amii, K. Uneyama, *Chem. Rev.* **2009**, *109*, 2119–2183.

[6] T. Stahl, H. F. T. Klare, M. Oestreich, *ACS Catal.* **2013**, *3*, 1578–1587.

[7] T. A. Unzner, T. Magauer, *Tetrahedron Lett.* **2015**, *56*, 877–883.

[8] Q. Shen, Y.-G. Huang, C. Liu, J.-C. Xiao, Q.-Y. Chen, Y. Guo, *J. Fluor. Chem.* **2015**, *179*, 14–22.

[9] H. Yin, A. V Zabula, E. J. Schelter, *Dalt. Trans.* **2016**, *45*, 6313–6323.

[10] T. Mukaiyama, Y. Murai, S. Shoda, *Chem. Lett.* **1981**, *10*, 431–432.

[11] T. Mukaiyama, H. Jona, *Proc. Japan Acad. Ser. B* **2002**, *78*, 73–83.

[12] M. M. Nielsen, C. M. Pedersen, *Chem. Rev.* **2018**, *118*, 8285–8358.

[13] P. A. Champagne, J. Pomarole, M.-È. Thérien, Y. Benhassine, S. Beaulieu, C. Y. Legault, J.-F. Paquin, *Org. Lett.* **2013**, *15*, 2210–2213.

[14] P. A. Champagne, A. Saint-Martin, M. Drouin, J.-F. Paquin, *Beilstein J. Org. Chem.* **2013**, *9*, 2451–2456.

[15] P. A. Champagne, Y. Benhassine, J. Desroches, J.-F. Paquin, *Angew. Chem., Int. Ed.* **2014**, *53*, 13835–13839.

[16] R. Hemelaere, P. A. Champagne, J. Desroches, J.-F. Paquin, *J. Fluor. Chem.* **2016**, *190*, 1–6.

[17] N. S. Keddie, P. A. Champagne, J. Desroches, J.-F. Paquin, D. O'Hagan, *Beilstein J. Org. Chem.* **2018**, *14*, 106–113.

Accepted Manuscript

This article is protected by copyright. All rights reserved.

[18] J.-D. Hamel, M. Beaudoin, M. Cloutier, J.-F. Paquin, *Synlett* **2017**, *28*, 2823–2828.

[19] J. Z. M. Fong, S. S. S. Choo, J.-A. Richard, M. V Garland, L. Guo, C. W. Johannes, T. M. Nguyen, *Eur. J. Org. Chem.* **2015**, *2015*, 995–1006.

[20] M. Dryzhakov, J. Moran, *ACS Catal.* **2016**, *6*, 3670–3673.

[21] M. Dryzhakov, E. Richmond, G. Li, J. Moran, *J. Fluorine Chem.* **2017**, *193*, 45–51.

[22] M. Ali, L.-P. Liu, G. B. Hammond, B. Xu, *Tetrahedron Lett.* **2009**, *50*, 4078–4080.

[23] A. M. Träff, M. Janjetovic, G. Hilmersson, *Chem. Commun.* **2015**, *51*, 13260–13263.

[24] H. Kunz, W. Sager, *Helv. Chim. Acta* **1985**, *68*, 283–287.

[25] T. Mukaiyama, K. Takeuchi, H. Jona, H. Maeshima, T. Saitoh, *Helv. Chim. Acta* **2000**, *83*, 1901–1918.

[26] T. Mukaiyama, H. Jona, K. Takeuchi, *Chem. Lett.* **2000**, *29*, 696–697.

[27] H. Jona, H. Mandai, W. Chavasiri, K. Takeuchi, T. Mukaiyama, *Bull. Chem. Soc. Jpn.* **2002**, *75*, 291–309.

[28] Y. Araki, K. Watanabe, F.-H. Kuan, K. Itoh, N. Kobayashi, Y. Ishido, *Carbohydr. Res.* **1984**, *127*, C5–C9.

[29] K. C. Nicolaou, R. E. Dolle, A. Chucholowski, J. L. Randall, *J. Chem. Soc. Chem. Commun.* **1984**, 1153–1154.

[30] K. C. Nicolaou, A. Chucholowski, R. E. Dolle, J. L. Randall, *J. Chem. Soc. Chem. Commun.* **1984**, 1155–1156.

[31] T. Mukaiyama, M. Suenaga, H. Chiba, H. Jona, *Chem. Lett.* **2002**, *31*, 56–57.

[32] R. Maskey, M. Schädler, C. Legler, L. Greb, *Angew. Chem., Int. Ed.* **2018**, *57*, 1717–1720.

[33] H. C. Clark, W. S. Tsang, *Chem. Commun.* **1966**, 123–124.

[34] H. C. Clark, W. S. Tsang, *J. Am. Chem. Soc.* **1967**, *89*, 529–533.

[35] H. C. Clark, P. W. R. Corfield, K. R. Dixon, J. A. Ibers, *J. Am. Chem. Soc.* **1967**, *89*, 3360–3361.

[36] H. C. Clark, K. R. Dixon, W. J. Jacobs, *J. Am. Chem. Soc.* **1968**, *90*, 2259–2266.

[37] R. D. W. Kemmitt, D. I. Nichols, *J. Chem. Soc. A Inorganic, Phys. Theor.* **1969**, 1577–1580.

[38] M. A. Cairns, K. R. Dixon, J. J. McFarland, *J. Chem. Soc. Dalt. Trans.* **1975**, 1159–1164.

[39] H. C. Clark, *J. Organomet. Chem.* **1980**, *200*, 63–78.

[40] S. Hashimoto, M. Hayashi, R. Noyori, *Tetrahedron Lett.* **1984**, *25*, 1379–1382.

[41] A. Kumar, Y. Geng, R. R. Schmidt, *Adv. Synth. Catal.* **2012**, *354*, 1489–1499.

[42] K. Takeuchi, T. Mukaiyama, *Chem. Lett.* **1998**, *27*, 555–556.

[43] T. Mukaiyama, H. Maeshima, H. Jona, *Chem. Lett.* **2001**, *30*, 388–389.

[44] H. Jona, H. Maeshima, T. Mukaiyama, *Chem. Lett.* **2001**, *30*, 726–727.

[45] H. Jona, H. Mandai, T. Mukaiyama, *Chem. Lett.* **2001**, *30*, 426–427.

[46] M. Yanagisawa, T. Mukaiyama, *Chem. Lett.* **2001**, *30*, 224–225.

[47] K. Toshima, K. Kasumi, S. Matsumura, *Synlett* **1998**, *1998*, 643–645.

[48] Some small peaks were also found at -155 and -150 ppm. We assume that these are from small amounts of BF_3 and boron esters formed as HF reacts with the borosilicate glassware. However SiF_4 was clearly the major peak. We have previously reported similar boron-byproducts when investigating glycosyl fluoride intermediates, see: M. M. Nielsen, B. A. Stougaard, M. Bols, E. Glibstrup, C. M. Pedersen, *Eur. J. Org. Chem.* **2017**, *2017*, 1281–1284.

Accepted Manuscript

WILEY-VCH

This article is protected by copyright. All rights reserved.

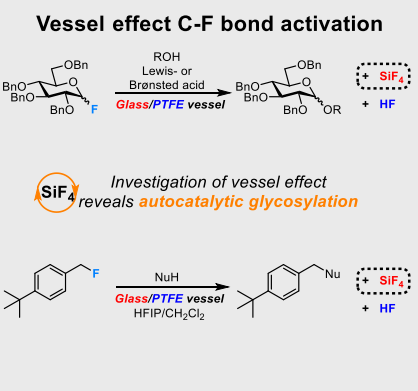
10.1002/ejoc.201901755

WILEY-VCH

Entry for the Table of Contents

COMMUNICATION

A significant vessel effect during acid catalyzed C–F bond activations has been documented and led to revised mechanisms for both glycosylations and benzyl fluoride activation. An autocatalytic chemical glycosylation was discovered during this investigation, further signifying the significant effect of the vessel material on a given reaction.



Michael M. Nielsen, Yan Qiao, Yingxiong Wang and Christian M. Pedersen**

Page No. – Page No.
Vessel effect in C–F bond activation prompts revised mechanism and reveals an autocatalytic glycosylation

Keywords: C-F bond activation; vessel effects

WILEY-VCH

Accepted Manuscript

This article is protected by copyright. All rights reserved.