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Elaboration of the ether cleaving ability and selectivity of the classical Pearlman's catalyst [$Pd(OH)_2/C$]: concise synthesis of a precursor for a *myo*-inositol pyrophosphate

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ABSTRACT

The cleavage of propargyl, allyl, benzyl, and PMB ethers by $Pd(OH)_2/C$ can be tuned in that order, by varying the reaction conditions. Other moieties such as C—C double bonds, esters, trityl ether, *p*-bromo and *p*-nitrobenzyl ethers are stable to these reaction conditions. Cleavage of allyl ethers can be made catalytic by using 1:1 mixture of $Pd(OH)_2/C$ and Pd/C. The synthetic potential of the selective ether cleaving ability of $Pd(OH)_2/C$, essentially under neutral conditions, has been demonstrated by an efficient synthesis of a precursor for the preparation of an inositol pyrophosphate derivative.

1. Introduction

Palladium and its salts are extensively used as catalysts for the hydrogenation and hydrogenolysis of a variety of organic compounds and for the formation of carbon–carbon bonds. A survey of the literature reveals that Pd(0) and Pd(II) salts have also been sporadically reported to be capable of bringing about other reactions such as deprotection of acetals,[1] cleavage of silyl ethers,[2] allyl and vinyl ethers,[3] allyl esters,[4] propargyl ethers,[5] as well as non-hydrogenolytic cleavage of benzyl ethers.[6] Some of these methods have been utilized[7] for significant synthetic transformations. Among the palladium reagents, solid supported reagents are attractive because these reagents can be removed at the end of the reaction by filtration, allowing easy access to the required products and recovery of the palladium reagent. We had realized[6] earlier that Pearlman's catalyst [$Pd(OH)_2/C$] is capable of cleaving benzyl ethers (in the absence of hydrogen). We herein present results, which show that ether cleaving ability of $Pd(OH)_2/C$ can be tuned to achieve selective cleavage of certain ethers in preference to others and hence $Pd(OH)_2/C$ has the potential for use in the synthesis of complex organic molecules where protection–deprotection protocols are unavoidable. This is illustrated by a high yielding preparation of a precursor for the synthesis of *myo*-inositol penta-pyrophosphate.[8]

2. Results and discussion

In order to explore the scope of cleavage of ethers with $Pd(OH)_2/C$, we subjected several ethers for cleavage with $Pd(OH)_2/C$ under different reaction conditions and the results are shown in Table 1. A perusal of the results in Table 1 shows that the ease of cleavage of ethers with $Pd(OH)_2/C$ can be tuned to the order: alkyl ether, PBB<PMB<Bn<allyl<propargyl ether by varying any one or more of the following parameters; (a) ratio of the substrate to $Pd(OH)_2/C$; (b) the reaction time; (c) solvent of the reaction. Although alkyl esters are stable (entry 18) to $Pd(OH)_2/C$, allyl esters can be cleaved (entry 24); this is analogous to the relative ease of cleavage of alkyl and allyl ethers. Allyl ether cleavage conditions are also compatible with tosylate (entry 8) and carboxylic acid esters (entries 9 and 10). However, silyl ethers do not tolerate allyl ether cleavage conditions (entry 17). It is interesting to note that allyl ethers can be cleaved in one step, while the previously known methods[9] require isomerization of allyl ethers to the corresponding enol ether, followed by hydrolysis of the latter with protic acids. These reaction conditions for the cleavage of allyl ethers are not compatible with other acid sensitive groups. Data in Table 1 and Fig. 1, clearly show that allyl ether can be cleaved with $Pd(OH)_2/C$ in the presence of the acid

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Table 1
Ether cleavage with $Pd(OH)_2/C$

Entry	Substrate[a]	Expt,[b] h	Product/s (% yield)
1	**1** $BnO(CH_2)_6OAll$[c]	A, 50	**26** $HO(CH_2)_6OH$ (76)
2	**1** $BnO(CH_2)_6OAll$	B, 1.5	**27** $BnO(CH_2)_6OH$ (94)
3	**2** $PBBO(CH_2)_8OAll$	B, 1.5	**28** $PBBO(CH_2)_8OH$ (84)
4	**3** $PMBO(CH_2)_8OAll$	B, 1.25	**29** $PMBO(CH_2)_8OH$ (88)
5	**4** $PNBO(CH_2)_8OAll$	B, 1.5	**30** $PNBO(CH_2)_8OH$ (91)
6	**5** $TrO(CH_2)_8OAll$	B, 1.5	**31** $TrO(CH_2)_8OH$ (58)
7	**5** $TrO(CH_2)_8OAll$	C, 1	**31** $TrO(CH_2)_8OH$ (66)
8	**6** $TsO(CH_2)_8OAll$	B, 1.5	**32** $TsO(CH_2)_8OH$ (87)
9	**7** $AcO(CH_2)_8OAll$	B, 1.5	**33** $AcO(CH_2)_8OH$ (92)
10	**8** $BzO(CH_2)_8OAll$	B, 1.5	**34** $BzO(CH_2)_8OH$ (91)
11	**9** $BnO(CH_2)_8OPMB$	B, 3	**29** $HO(CH_2)_8OPMB$ (49) **35** $HO(CH_2)_8OH$ (47)
12	**10** $BnO(CH_2)_8OPNB$	B, 3	**30** $HO(CH_2)_8OPNB$ (77)
13	**11** $BnO(CH_2)_8OBn$	A, 5	**35** (96)
14	**12** $PMBO(CH_2)_8OPMB$	A, 5	**35** (46) **29** $HO(CH_2)_8OPMB$ (24)
15	**13** $PBBO(CH_2)_8OPBB$	A, 5	No reaction
16	**14** $PropargylO-(CH_2)_8OAll$	B, 2	**36** $HO(CH_2)_8OAll$ (36) **35** (54)
17	**15** $TBDMSO-(CH_2)_8OAll$	B, 1.5	**35** (78)
18	**16** $CH_3CH(OBz)-CH_2CH=CH_2$	D, 6	No reaction
19	**17**	E, 72	**37**[d] (89)
20	**18**	B, 1.5	**38** (78)
21	**19** $PhCH_2OPh$	F, 90	No reaction
22	**20** $CH_2=CHCH_2OPh$	A, 3	**39** PhOH (70)
23	**21** $PhCH_2OOCPh$	D, 24	No reaction
24	**22** $CH_2=CHCH_2OOCPh$	F, 8	**40** PhCOOH (82)
25	**23**	A, 8	**41** (62)
26	**24**	D, 1	**41** (69)
27	**25** $PhCH=CHCH_2OCH_3$	B, 6	**42** PhCH=CHCHO (40)
28	**1** $BnO(CH_2)_6OAll$	G, 0.5	**27** $BnO(CH_2)_6OH$ (92)
29	**3** $PMBO(CH_2)_8OAll$	G, 0.5	**29** $PMBO(CH_2)_8OH$ (87)

[a] See Fig. 1 for the structure of reactants and products, not given in Table 1.
[b] In all the experiments $Pd(OH)_2/C$ (20% Pd by weight) was used in the proportion mentioned below. Conditions: A, 100 mol %, methanol, reflux; B, 50 mol %, 2-propanol, reflux; C, 50 mol %, *tert*-butanol, reflux; D, 50 mol %, methanol, reflux; E, 150 mol %, methanol, reflux; F, 70 mol %, methanol, reflux; G, 10 mol %, $Pd(OH)_2/C$+10 mol %, Pd/C, 2-propanol, reflux.
[c] All=allyl, Bn=benzyl, PBB=*p*-bromobenzyl, PMB=*p*-methoxybenzyl, PNB=*p*-nitrobenzyl, Tr=trityl, Ts=tosyl, Ac=acetyl, Bz=benzoyl, TBDMS=*tert*-butyldimethylsilyl.
[d] Compound **37** was isolated as its hexaacetate.

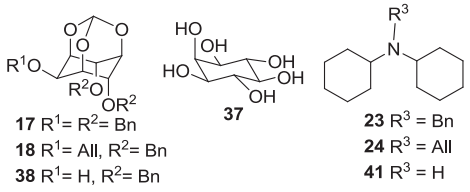
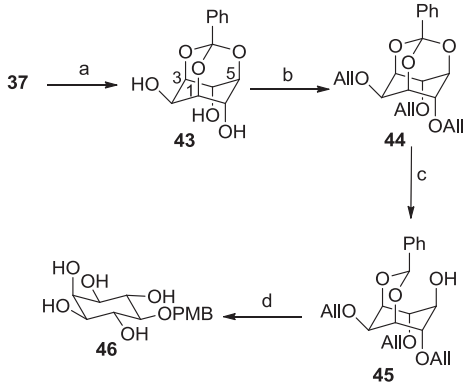


Fig. 1. Structure of reactants and products, not given in Table 1.

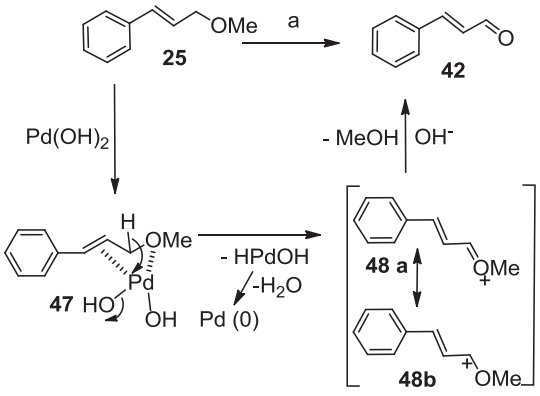
sensitive trityl (entry 7) as well as orthoformate (entry 20) moieties. Also, normal carbon–carbon double bonds are unaffected (entry 18) under the conditions of ether cleavage. Competition experiments with benzyl ether and substituted benzyl ethers show that benzyl ether can be cleaved in preference to *p*-bromo, *p*-nitro, and *p*-methoxy benzyl ethers (entries 11–15). This is in contrast to the preference of cleavage of (substituted) benzyl ethers exhibited by DDQ[10] and Buchwald's method.[11] It is interesting to note that all these selectivity in ether cleavage can be achieved by using the same reagent but under different reaction conditions, which is in contrast compared to methods that use different reagents to achieve selectivity. The advantage of the former approach is that in case global cleavage of all the ethers becomes necessary, it can be achieved in a single step rather than in a step-wise manner. It is also pertinent to note that although alkyl-benzyl ethers can be cleaved with $Pd(OH)_2/C$, aryl benzyl ether and benzyl ester are stable. Furthermore, cleavage of allyl ethers could be realized using catalytic amount (10 mol % each) of $Pd(OH)_2/C$ and Pd/C (entries 28 and 29). Cleavage of other ethers required higher amount of palladium (50–150 mol %), especially for global deprotection reactions.

We utilized the method described above for the selective cleavage of ethers, for convenient access to a precursor (**46**, Scheme 1) for *myo*-inositol pyrophosphate derivative. The triol **43** was allylated and the orthobenzoate moiety in **44** was cleaved selectively to release the C-5 hydroxyl group.[6] *p*-Methoxybenzylation of the C-5 hydroxyl group in **45** followed by treatment of the ensuing PMB ether obtained, with $Pd(OH)_2/C$ in 2-propanol under reflux resulted in the release of all the hydroxyl groups, except the C5-hydroxyl group. The pentol **46** (which is a precursor for the preparation of the corresponding penta-pyrophosphate) was obtained in an overall yield of 45%. The earlier reported method[8] provided the same precursor in a yield of 10% in seven steps from *myo*-inositol. *myo*-Inositol pyrophosphates have been implicated in the control of several cellular processes such as endocytosis, chemotaxis, signal transduction,[8,12] insulin secretion,[13] cell death,[14,15] and non enzymatic phosphorylation of proteins.[16]



Scheme 1. Synthesis of a precursor for inositol pyrophosphate. Reagents and conditions: (a) $(MeO)_3CPh$, CSA, DMSO, 80 °C, 5 h, 89%; (b) NaH, AllBr, DMF, rt, 3 h, 94%; (c) DIBAL–H, DCM, rt, 2 h, 69%; (d) (i) NaH, PMBCl, DMF, rt, 2 h; (ii) $Pd(OH)_2/C$, ^{i}PrOH, reflux, 2 h, 78%.

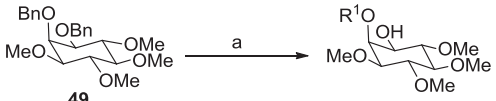
We subjected the methyl ether **25** (Scheme 2) to cleavage with $Pd(OH)_2/C$ to see the fate of the (substituted) allyl group after ether cleavage. Formation of the aldehyde **42** in this reaction suggested that cleavage of allyl ethers by $Pd(OH)_2/C$ could be an oxidative process. The modest yield of the aldehyde **42** obtained could be due to the tendency of **42** to polymerize easily. A comparison of the XPS data of the palladium reagent before and after the cleavage of allyl ether showed that Pd(II) had been converted to Pd(0). This data also supports the cleavage of allyl ethers by an oxidative process. A plausible mechanism for the cleavage of the ether **25** is depicted in Scheme 2.



Scheme 2. Plausible mechanism for the cleavage of allyl ether. Reagents and conditions: (a) $Pd(OH)_2/C$, ^{i}PrOH, reflux, 6 h, 40%.

Oxidative cleavage of ethers by $Pd(OH)_2/C$ was also suggested by another experiment. Reaction of the *myo*-inositol derived dibenzyl ether **49** with $Pd(OH)_2/C$ in methanol or *iso*-propanol, although led largely to the complete cleavage of both the benzyl groups to yield the corresponding diol **50**, yielded the benzoate **51** as a minor product (Scheme 3).

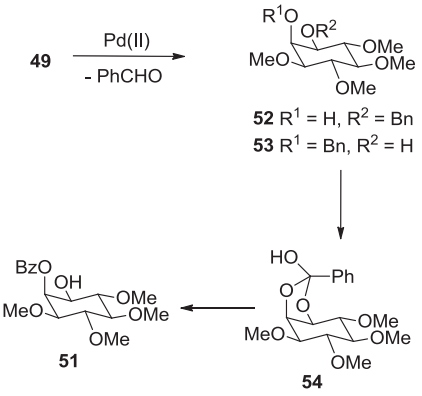
The benzoate **51** could arise due to the intramolecular participation of the neighboring *cis*-hydroxyl group, which leads to the



ROH	Time (h)	Yield (%) 50	51
Dry methanol	40	80	14
Dry 2-propanol	40	71	27
2-propanol	60	72	23

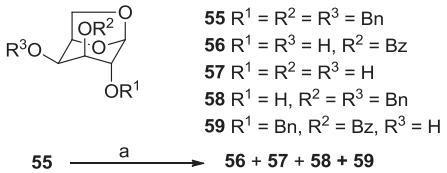
Scheme 3. Oxidative cleavage of benzyl ethers by $Pd(OH)_2/C$. Reagents and conditions: (a) $Pd(OH)_2/C$, ROH, reflux.

formation of a cyclic orthobenzoate (**54**, Scheme 4), hydrolysis of which yields **51**. Hydrolysis of the cyclic orthoester of a *cis*-cyclohexane-1,2-diol is known[17] to lead to the formation of the axial benzoate predominantly. Although relative ease of cleavage of the two benzyl ethers (axial vs equatorial) is not known, the same intermediate (**54**) can form from both the monobenzyl ethers (**52** and **53**) that are possible to arise from the cleavage of one of the two benzyl groups in the racemic dibenzyl ether **49**.



Scheme 4. Plausible route for the formation of benzoates.

In 1986, del Carmen Cruzado et al.[18] reported the oxidation of benzyl ether located adjacent to a *cis*-oxygen, to the corresponding benzoate ester in pyranose derivatives, on reaction with Pd/C (Scheme 5). We are of the opinion that the Pd(II) species present in Pd(0)/C (that del Carmen Cruzado et al.[18] used) was responsible for the observed oxidation. We had shown earlier[6] that commercial samples of Pd(0)/C contain considerable amount of Pd(II) species as

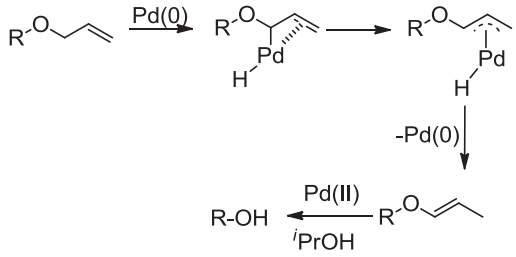


Scheme 5. Oxidative cleavage of sugar derivatives. Reagents and conditions: (a) Pd/C, ^{i}PrOH, reflux, 3–5 h.

revealed by their XPS data. These results also support our suggestion that $Pd(OH)_2/C$ cleaves ethers by an oxidative process.

In some of the allyl ether cleavage experiments we observed the isomerization of the allyl ether to the corresponding propen-1-yl ether. Hence we postulated that the Pd(0) initially generated from Pd(II) during the ether cleavage reaction could be bringing about this isomerization.[3d] Treatment of the allyl ether **8** with Pd/C (10 mol %) indeed showed the isomerization of the allyl group (see Supplementary data for the NMR spectrum of the mixture of products containing the propen-1-yl ether). Hence it appears that once a considerable amount of Pd(0) gets accumulated in the reaction mixture, the cleavage of the allyl ether proceeds in parallel by oxidation with $Pd(OH)_2/C$ (Scheme 2) as well as isomerization (by Pd(0)) and subsequent cleavage of the propen-1-yl ether by $Pd(OH)_2/C$. The latter process is a non-oxidative process (Scheme 6); we had shown earlier that $Pd(OH)_2/C$ is capable of cleaving acetals.[6]

These observations in fact helped us to develop a procedure for the cleavage of allyl ethers where in the palladium reagents could



Scheme 6. A plausible mechanism for the deallylation of ethers via isomerization.

be used in catalytic amounts (Scheme 7). The recovered catalyst could be used for the cleavage of a second batch of the substrate. These results further enhance the synthetic utility of the methods of ether cleavage being reported here. Our earlier attempts to make the deallylation process catalytic by the use of copper salts[3b] to regenerate Pd(II) were unsuccessful owing to the formation of Wacker oxidation type of products.[19]

Scheme 7. Deallylation under catalytic conditions. (a) $Pd(OH)_2/C$ and Pd/C (10 mol % each), ^{i}PrOH, reflux, 30 min.

3. Conclusion

We have elaborated a novel, facile methodology for the selective cleavage of ethers frequently used to protect hydroxyl groups, in a single step without the use of acids or bases. The work up and isolation of the products are simple and the yield is good to excellent. These results have potential for applications in organic synthesis, as illustrated by the efficient preparation of **46**.

4. Experimental section

4.1. General procedures

All the solvents were purified according to the literature procedures[20] before use. 60% Dispersion of sodium hydride in mineral oil was used for O-substitution reactions. 'Work up' implies the washing of the organic layer successively with water, brine and

drying over anhyd sodium sulfate. Column chromatographic separations were carried out on silica gel (230–400 mesh) with solvent system as mentioned in experimental procedures. IR spectra were recorded (in $CHCl_3$, or as a Nujol mull or as a neat film) using a Shimadzu FTIR-8400. NMR spectra were recorded on a Bruker ACF 200 spectrometer unless otherwise mentioned. Microanalytical data were obtained using a Carlo-Erba CHNS-0 EA 1108 elemental analyzer. All the melting points reported were recorded using a Büchi B-540 electro-thermal melting point apparatus.

4.2. Experimental procedures

*4.2.1. ((6-(Allyloxy)hexyloxy)methyl)benzene (**1**).* Sodium hydride (0.10 g, 2.40 mmol) was added to a solution of **27**[21] (0.25 g, 1.20 mmol) in dry DMF (5 mL) at 0 °C and stirred for 15 min. Allyl bromide (0.20 mL, 2.40 mmol) was added drop-wise to the reaction mixture in cold condition and stirred at rt for 3 h. The reaction mixture was concentrated under reduced pressure and the gum obtained was worked up with ethyl acetate followed by drying over anhyd sodium sulfate. The crude product was purified by column chromatography (eluent: 10% ethyl acetate/light petroleum) to afford **1** as a colorless oil[22] (0.27 g, 90%).

*4.2.2. (1-(8-(Allyloxy)octyloxy)methyl)-4-bromobenzene (**2**).* Sodium hydride (0.08 g, 2.01 mmol) was added to a solution of **36**[23] (0.25 g, 1.34 mmol) in dry DMF (6 mL) at 0 °C and the mixture stirred for 15 min. To this mixture *p*-bromobenzyl bromide (0.44 g, 1.70 mmol) was added and stirring continued for 4 h. The reaction mixture was concentrated under reduced pressure and the residue worked up with ethyl acetate followed by drying over anhyd sodium sulfate. Purification of the crude product by column chromatography (eluent: 15% ethyl acetate/light petroleum) gave **2** (0.40 g, 83%) as a colorless oil. Found: C, 61.15; H, 8.01. $C_{18}H_{27}O_2Br$ requires C, 60.85; H, 7.66%; R_f (10% ethyl acetate/light petroleum) 0.41; IR (neat): $\bar{\nu}$ 1010 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.41–7.50 (m, 2H, ArH), 7.16–7.24 (m, 2H, ArH), 5.79–6.03 (m, 1H, =CH), 5.10–5.33 (m, 2H, $=CH_2$), 4.43 (s, 2H, $PhCH_2$), 3.95 (dt, 2H, *J*=5.7, 1.4 Hz, OCH_2), 3.36–3.48 (m, 4H, OCH_2), 1.50–1.66 (m, 4H, CH_2), 1.25–1.39 (m, 8H, CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 137.8, 135.1, 131.5, 129.2, 121.3, 116.7, 72.1, 71.8, 70.6, 70.5, 29.8, 29.7, 29.4, 26.1 ppm.

*4.2.3. (1-((Allyloxy)octyloxy)methyl)4-methoxy benzene (**3**).* Sodium hydride (0.15 g, 3.65 mmol) was added to a cooled solution of **36** (0.4 g, 2.15 mmol) in dry DMF (7 mL) and stirred for 15 min. PMBCl (0.44 mL, 3.23 mmol) was added to this mixture drop-wise by maintaining the temperature at 0 °C and stirring was continued for 3 h at rt. The reaction mixture was concentrated under reduced pressure and the residue was worked up with ethyl acetate followed by drying over anhyd sodium sulfate. The crude product was purified by column chromatography (eluent: 15% ethyl acetate/light petroleum) to obtain **3** (0.53 g, 80%) as a colorless oil. Found: C, 74.38; H, 10.23. $C_{19}H_{30}O_3$ requires C, 74.47; H, 9.87%; R_f (15% ethyl acetate/light petroleum) 0.28; ^1H NMR ($CDCl_3$, 200 MHz): 7.22–7.30 (m, 2H, ArH), 6.83–6.92 (m, 2H, ArH), 6.80–6.02 (m, 1H, HC=C), 5.11–5.33 (m, 2H, $=CH_2$), 4.42 (s, 2H, $PhCH_2$), 3.96 (dt, 2H, *J*=5.5, 1.4 Hz, OCH_2), 3.79 (s, 3H, OCH_3), 3.37–3.47 (m, 4H, 2×OCH_2), 1.50–1.66 (m, 4H, 2×CH_2), 1.24–1.38 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 159.1, 135.1, 130.8, 129.3, 116.7, 113.7, 72.5, 71.8, 70.5, 70.2, 55.3, 29.8, 29.5, 26.2 ppm.

*4.2.4. (1-((8-Allyloxy)octyloxy)methyl)-4-nitrobenzene (**4**).* 4-Nitrobenzyl ether **4** was prepared by using 4-nitrobenzyl alcohol and the allyl ether **36** as a pale yellow liquid (0.17 g, 50%) by adopting a reported procedure.[24] Found: C, 67.07; H, 8.64; N, 4.06. $C_{18}H_{27}NO_4$ requires C, 67.26; H, 8.47; N, 4.36%; R_f (8% ethyl acetate/light petroleum) 0.38; IR ($CHCl_3$): $\bar{\nu}$ 1522 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.21 (d, 2H, *J*=8.6 Hz, ArH), 7.51 (d, 2H, *J*=8.6 Hz, ArH), 5.80–6.05 (m, 1H, CH), 5.11–5.35 (m, 2H, $=CH_2$), 4.60 (s, 2H, CH_2Ph), 3.96 (d, 2H, *J*=5.6 Hz, OCH_2), 3.51 (t, 2H, 6.6 Hz, OCH_2), 3.42 (t, 2H, *J*=5.6 Hz, OCH_2) 1.52–1.71 (m, 4H, 2×CH_2), 1.26–1.42 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 147.3, 146.5, 135.1, 127.6, 123.6, 116.7, 71.8, 71.6, 71.2, 70.5, 29.8, 29.7, 29.4, 29.4, 26.14, 26.11 ppm.

*4.2.5. 1-Allyloxy-8-trityloxyoctane (**5**).* To a solution of **36** (0.30 g, 1.61 mmol) in dry dichloromethane (8 mL), triethylamine (0.40 mL, 2.73 mmol) was added at 0 °C followed by trityl chloride (0.54 g, 1.93 mmol). Catalytic amount of dimethylamino pyridine (DMAP) was then added and the mixture was stirred for 2 h at rt. The reaction mixture was concentrated under reduced pressure and the residue worked up with dichloromethane followed by drying over anhyd sodium sulfate. The crude product was purified by column chromatography [eluent: 10% ethyl acetate/light petroleum; silica gel was pre-eluted with of 1% triethylamine in light petroleum (3×50 mL)] to afford **5** (0.54 g, 79%) as a colorless oil. Found: C, 83.78; H, 8.38. $C_{30}H_{36}O_2$ requires C, 84.07; H, 8.47%; R_f (5% ethyl acetate/light petroleum) 0.30; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.17–7.50 (m, 15H, ArH), 5.78–6.05 (m, 1H, =CH), 5.11–5.33 (m, 2H, $=CH_2$), 3.96 (dt, 2H, *J*=5.7, 1.4 Hz, OCH_2), 3.41 (t, 2H, *J*=6.6 Hz, OCH_2), 3.03 (t, 2H, *J*=6.6 Hz, OCH_2), 1.50–1.66 (m, 4H, 2×CH_2), 1.21–1.39 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 144.6, 135.1, 128.7, 127.7, 126.8, 116.8, 86.3, 71.9, 70.5, 63.7, 30.0, 29.8, 29.5, 26.3, 26.2 ppm.

*4.2.6. 8-(Allyloxy)octyl tosylate (**6**).* Tosyl chloride (0.45 g, 2.35 mmol) was added to a solution of **36** (0.20 g, 1.07 mmol) in dry pyridine (8 mL) at 0 °C and the mixture stirred for 1 h at rt. The reaction mixture was concentrated under reduced pressure and worked up with ethyl acetate. The residue obtained was purified by column chromatography (eluent; 20% ethyl acetate/light petroleum) to afford **6** (0.24 g, 67%) as a gum. Found: C, 63.59; H, 8.16. $C_{18}H_{28}O_4S$ requires C, 63.50; H, 8.29%; R_f (10% ethyl acetate/light petroleum) 0.37; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.79 (d, 2H, *J*=8.2 Hz, ArH), 7.35 (d, 2H, *J*=8.1 Hz, ArH), 5.79–6.05 (m, 1H, HC=C), 5.11–5.34 (m, 2H, $=CH_2$), 3.92–4.06 (m, 4H, 2×OCH_2), 3.40 (t, 2H, *J*=6.6 Hz, OCH_2), 2.45 (s, 3H, CH_3), 1.47–1.70 (m, 4H, 2×CH_2), 1.20–1.36 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 144.7, 135.1, 133.2, 129.8, 127.9, 116.7, 71.8, 70.7, 70.4, 29.7, 29.2, 28.8, 28.8, 26.0, 25.3, 21.6 ppm.

*4.2.7. 8-(Allyloxy)octyl acetate (**7**).* Acetic anhydride (0.30 mL, 3.22 mmol) was added drop-wise to a solution of **36** (0.50 g, 2.69 mmol) in dry pyridine (8 mL) followed by catalytic amount of dimethylamino pyridine (DMAP) at 0 °C and the mixture stirred for 4 h at rt. The reaction mixture was concentrated under reduced pressure and the residue was worked up with ethyl acetate and dried over anhyd sodium sulfate. The crude product obtained was purified by column chromatography (eluent: 20% ethyl acetate/light petroleum) to afford **7** (0.51 g, 84%) as a gum. Found: C, 68.59; H, 10.56. $C_{13}H_{24}O_3$ requires C, 68.38; H, 10.59%; R_f (10% ethyl acetate/light petroleum) 0.48; IR (neat): $\bar{\nu}$ 1741 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 5.79–6.03 (m, 1H, HC=C), 5.11–5.33 (m, 2H, $=CH_2$), 4.05 (t, 2H, *J*=6.7 Hz, OCH_2), 3.96 (dt, 2H, *J*=5.6, 1.3 Hz, OCH_2), 3.42 (t, 2H, *J*=6.6 Hz, OCH_2), 2.05 (s, 3H, CH_3), 1.50–1.68 (m, 4H, 2×CH_2), 1.26–1.40 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 171.2, 135.1, 116.2, 71.8, 70.4, 64.6, 29.7, 29.3, 29.2, 28.6, 26.1, 25.8, 21.0 ppm.

*4.2.8. 8-(Allyloxy)octyl benzoate (**8**).* Benzoyl chloride (0.29 mL, 2.58 mmol) was added drop-wise to a solution of **36** (0.40 g, 2.15 mmol) in dry pyridine (10 mL) at 0 °C and stirred overnight at

ambient temperature. The reaction mixture was concentrated under reduced pressure and the residue worked up with ethyl acetate followed by drying over anhyd sodium sulfate. The yellow colored crude product was purified by column chromatography (eluent, 10% ethyl acetate/light petroleum) to afford **8** (0.52 g, 84%) as a colorless oil. Found: C, 74.22; H, 9.33. $C_{18}H_{26}O_3$ requires C, 74.45; H, 9.02%; R_f (5% ethyl acetate/light petroleum) 0.27; IR (neat): $\bar{\nu}$ 1720 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.00–8.13 (m, 2H, ArH), 7.38–7.63 (m, 3H, ArH), 5.80–6.06 (m, 1H, HC=), 5.11–5.35 (m, 2H, =CH_2), 4.31 (t, 2H, J=6.6 Hz, OCH_2), 3.96 (dt, 2H, J=5.7, 1.3 Hz, OCH_2), 3.42 (t, 2H, 6.6 Hz, OCH_2), 1.25–1.86 (m, 12H, 6×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 166.7, 135.1, 132.8, 130.5, 129.6, 128.3, 116.7, 71.8, 70.5, 65.1, 29.8, 29.4, 29.3, 28.7, 26.1, 26.0 ppm.

*4.2.9. (1-((8-Benzyloxy)octyloxy)methyl)-4-methoxybenzene (**9**).* Sodium hydride (0.13 g, 3.33 mmol) was added to a solution of 8-benzyloxyoctan-1-ol (0.53 g, 2.20 mmol) in dry DMF (10 mL) at 0 °C and stirred for 15 min. PMBCl (0.39 mL, 2.86 mmol) was added drop-wise to the reaction mixture (0–5 °C) and the mixture stirred for 4 h at rt. The reaction mixture was concentrated under reduced pressure and the residue worked up with ethyl acetate. The crude product was purified by column chromatography (eluent: 7% ethyl acetate/light petroleum) to afford **9** (0.64 g, 81%) as a colorless oil. Found: C, 77.17; H, 9.05. $C_{23}H_{32}O_3$ requires C, 77.49; H, 9.05%; R_f (5% ethyl acetate/light petroleum) 0.25; ^1H NMR ($CDCl_3$, 200 MHZ): δ 7.20–7.38 (m, 7H, ArH), 6.83–6.92 (m, 2H, ArH), 4.49 (s, 2H, OCH_2), 4.42 (s, 2H, OCH_2), 3.79 (s, 3H, OCH_3), 3.44 (q, 4H, J=6.5 Hz, 2×OCH_2), 1.50–1.72 (m, 4H, 2×CH_2), 1.19–1.46 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 159.1, 138.7, 130.8, 129.3, 128.4, 127.7, 127.5, 113.8, 72.9, 72.5, 70.5, 70.2, 55.3, 29.8, 29.5, 26.2 ppm.

*4.2.10. (1-((8-Benzyloxy)octyloxy)methyl)-4-nitrobenzene (**10**).* The 4-nitro derivative **10** (0.12 g, 44%) was prepared by using 4-nitrobenzyl alcohol and the 8-benzyloxy octan-1-ol as a pale yellow solid by adopting a reported procedure.[24] Found: C, 70.80; H, 8.11; N, 3.50. $C_{22}H_{29}NO_4$ requires C, 71.13; H, 7.87; N, 3.77%; mp=41.6–43.6 °C; IR ($CDCl_3$): $\bar{\nu}$ 2924, 1345 cm^{-1}; ^1H NMR ($CDCl_3$, 200 MHz): δ 8.15–8.27 (m, 2H, ArH), 7.44–7.57 (m, 2H, ArH), 7.22–7.41 (m, 5H, ArH), 4.59 (s, 2H, OCH_2), 4.50 (s, 2H, OCH_2), 3.41–3.56 (m, 4H, 2×OCH_2), 1.56–1.66 (m, 4H, 2×CH_2), 1.27–1.45 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 147.3, 146.5, 138.7, 128.4, 127.7, 127.5, 123.6, 72.9, 71.6, 71.2, 70.5, 29.8, 29.7, 29.4, 26.2 ppm.

*4.2.11. 1,8-Bis(benzyloxy)octane (**11**).* Sodium hydride (0.44 g, 10.94 mmol) was added to a solution of octane diol (0.50 g, 3.42 mmol) in dry DMF (12 mL) at 0 °C and stirred for 15 min. Benzyl bromide (1.09 mL, 9.23 mmol) was added drop-wise to the reaction mixture in cold condition and stirring continued for 3 h at rt. The solvents were evaporated under reduced pressure and the residue worked up with ethyl acetate followed by drying over anhyd sodium sulfate. Purification of the crude product by column chromatography (eluent: 8% ethyl acetate/light petroleum) afforded **11** (1.08 g, 97%) as a colorless oil. Found: C, 80.89; H, 9.14. $C_{22}H_{30}O_2$ requires C, 80.94; H, 9.26%; R_f (5% ethyl acetate/light petroleum) 0.28; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.12–7.41 (m, 10H, ArH), 4.48 (s, 4H, $PhCH_2$), 3.44 (t, 4H, J=6.5 Hz, 2×OCH_2), 1.50–1.70 (m, 4H, 2×CH_2), 1.30 (br s, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 138.8, 128.4, 127.7, 127.6, 72.9, 70.6, 29.9, 29.5, 26.2 ppm.

*4.2.12. 1,8-Bis(4-methoxybenzyloxy)octane (**12**).* Sodium hydride (0.44 g, 10.94 mmol) was added to a solution of octane-1,8-diol (0.50 g, 3.42 mmol) in dry DMF (12 mL) at 0 °C and stirred for 15 min. PMBCl (1.25 mL, 9.23 mmol) was added drop-wise to the reaction mixture (0–5 °C) and stirred for 3 h at rt. The reaction mixture was concentrated under reduced pressure and the residue worked up with ethyl acetate followed by drying over anhyd sodium sulfate. Purification of the crude product by column chromatography (eluent: 12% ethyl acetate/light petroleum) afforded **12** as a colorless oil (1.12 g, 89%), which turned into solid. Found: C, 74.20; H, 9.04. $C_{24}H_{34}O_4$ requires C, 74.58; H, 8.87%; R_f (10% ethyl acetate/light petroleum) 0.30; mp=31.7–33.3 °C; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.20–7.32 (m, 4H, ArH), 6.82–6.93 (m, 4H, ArH), 4.43 (s, 4H, $PhCH_2$), 3.80 (s, 6H, 2×OCH_3), 3.42 (t, 4H, J=6.7 Hz, 2×OCH_2), 1.50–1.67 (m, 4H, 2×CH_2), 1.29 (br s, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 159.1, 130.8, 129.3, 113.8, 72.5, 70.2, 55.3, 29.8, 29.5, 26.2 ppm.

*4.2.13. 1,8-Bis(4-bromobenzyloxy)octane (**13**).* Sodium hydride (0.66 g, 16.40 mmol) was added to a solution of octane-1,8-diol (1.00 g, 6.84 mmol) in dry DMF (20 mL) at 0 °C and stirred for 15 min. *p*-Bromobenzyl bromide (3.4 g, 13.68 mmol) was added to the reaction mixture (0–5 °C) and stirring continued for 3 h at rt. The reaction mixture was concentrated under reduced pressure and the residue worked up with ethyl acetate followed by drying over anhyd sodium sulfate. Purification of the crude product by column chromatography (eluent: 16% ethyl acetate/light petroleum) afforded **13** (3.08 g, 93%) as a colorless solid. Found: C, 54.59; H, 5.77. $C_{22}H_{28}Br_2O_2$ requires C, 54.56; H, 5.83%; R_f (10% ethyl acetate/light petroleum) 0.48; mp=44–46.5 °C; ^1H NMR ($CDCl_3$, 200 MHz): δ 7.41–7.52 (m, 4H, ArH), 7.17–7.25 (m, 4H, ArH), 4.44 (s, 4H, $PhCH_2$), 3.44 (t, 4H, J=6.6 Hz, 2×OCH_2), 1.52–1.67 (m, 4H, 2×CH_2), 1.20–1.42 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 137.8, 131.5, 129.2, 121.3, 72.1, 70.6, 29.7, 29.4, 26.1 ppm.

*4.2.14. 1-(Allyloxy)-8-(prop-2-yn-1-yloxy)octane (**14**).* Sodium hydride (0.10 g, 3.22 mmol) was added to a solution of **36** (0.40 g, 2.16 mmol) in dry DMF (8 mL) at 0 °C and the mixture stirred for 15 min. Propargyl bromide (80% solution in toluene, 0.29 mL, 2.58 mmol) was added drop-wise to the reaction mixture and stirred for 3 h at ambient temperature. The reaction mixture was concentrated under reduced pressure and the residue worked up with diethyl ether. The crude product obtained was purified by column chromatography (eluent: 8% ethyl acetate in light petroleum) to afford **14** (0.29 g, 63%) as a pale yellow liquid.[25]

*4.2.15. (1-(Allyloxy)(8-(tert-butyl)dimethylsiloxy))octane (**15**).* Imidazole (0.40 g, 5.91 mmol) was added to a solution of **36** (0.50 g, 2.69 mmol) in dry DMF (8 mL) at 0 °C and stirred for 10 min. TBDMSCl (0.81 g, 5.38 mmol) was added to the reaction mixture and stirred overnight at ambient temperature. The reaction mixture was concentrated and worked up with ethyl acetate followed by drying over anhyd sodium sulfate. The crude product was purified by column chromatography (eluent: 10% ethyl acetate/light petroleum) to afford **15** (0.71 g, 88%) as a colorless oil. Found: C, 67.87; H, 12.64. $C_{17}H_{36}O_2Si$ requires C, 67.94; H, 12.07%; R_f (10% ethyl acetate/light petroleum) 0.28; ^1H NMR ($CDCl_3$, 500 MHz): δ 5.87–5.97 (m, 1H, CH), 5.23–5.30 (m, 1H, =CH), 5.14–5.19 (m, 1H, =CH), 3.96 (dt, 2H, J=5.5, 1.5 Hz, OCH_2), 3.59 (t, 2H, J=6.7 Hz, OCH_2), 3.42 (t, 2H, J=6.7 Hz, OCH_2), 1.55–1.61 (m, 2H, CH_2), 1.47–1.53 (m, 2H, CH_2), 1.28–1.34 (m, 8H, 4×CH_2), 0.89 (s, 9H, $C(CH_3)_3$), 0.05 (s, 6H, 2×CH_3) ppm; ^{13}C NMR ($CDCl_3$, 125.76 MHz) δ 135.0, 116.6, 71.8, 70.5, 63.3, 32.8, 29.7, 29.5, 29.4, 26.1, 25.7, 26.0, 18.4, −5.3 ppm.

*4.2.16. Pent-4-en-2-yl benzoate (**16**).* Benzoyl chloride (1.62 mL, 13.94 mmol) was added drop-wise to a solution of pent-4-en-2-ol (1.19 mL, 11.62 mmol) in dry pyridine (25 mL) at 0 °C and stirred overnight at rt. The reaction mixture was concentrated under

reduced pressure and worked up with ethyl acetate followed by drying over anhyd sodium sulfate. Purification of the crude product by column chromatography (eluent: 8% ethyl acetate/light petroleum) afforded **16** as a colorless oil.[26]

*4.2.17. 2-O-Allyl-4,6-di-O-benzyl-myo-inositol-1,3,5orthoformate (**18**).* Sodium hydride (0.09 g, 2.23 mmol) was added to a solution of **38** (0.70 g, 1.89 mmol) in dry DMF (6 mL) at 0 °C with stirring. Then allyl bromide (0.19 mL, 2.07 mmol) was added drop-wise to the reaction mixture and the stirring continued for 3 h at rt. The reaction mixture was concentrated under reduced pressure and the residue worked up with ethyl acetate followed by drying over anhyd sodium sulfate. The crude product was purified by column chromatography (eluent: 30% ethyl acetate/light petroleum) to afford **18** (0.60 g, 78%) as a colorless oil. Found: C, 70.27; H, 6.71. $C_{24}H_{26}O_6$ requires C, 70.23; H, 6.38%; R_f (20% ethyl acetate/light petroleum) 0.30; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.22–7.38 (m, 10H, ArH), 5.85–6.08 (m, 1H, HC=C), 5.52 (d, 1H, J=1.3 Hz, HCO_3), 5.15–5.36 (m, 2H, =CH_2), 4.68 (d, 2H, J=11.6 Hz, OCH_2), 4.55 (d, 2H, J=11.6 Hz, OCH_2), 4.42–4.49 (m, 1H, InsH), 4.28–4.40 (m, 4H, InsH), 4.10 (dt, 2H, J=5.7, 1.39 Hz, OCH_2), 3.99 (q, 1H, J=1.5 Hz, InsH) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 137.7, 134.6, 128.5, 128.0, 127.7, 117.8, 103.3, 74.1, 71.8, 70.6, 70.56, 68.1, 67.5 ppm.

4.3. General procedure for the cleavage of ethers (conditions A–G)

The required ether was dissolved in alcohol (methanol or 2-propanol or *tert*-butanol) and refluxed after the addition of $Pd(OH)_2$/C (20 wt %, 0.35–1.05 g/mmol of the substrate). The reaction mixture was filtered through a short bed of Celite, and Celite washed with a suitable solvent (ethyl acetate, methanol, DCM, water). The filtrate was concentrated and the products were isolated by column chromatography over silica gel (100–200 mesh for compounds **1**, **11**, **23**, **24** and 230–400 mesh for others).

*4.3.1. Reaction of **1** with $Pd(OH)_2$/C in methanol.* The allyl ether **1** (0.20 g, 0.81 mmol) was cleaved in methanol (3 mL) with $Pd(OH)_2$/C (0.56 g) to obtain **26** (0.08 g, 76%) as a gum. Column chromatographic purification was carried out with 20% methanol/ethyl acetate as the eluent.

*4.3.2. Reaction of **1** with $Pd(OH)_2$/C in 2-propanol.* The allyl ether **1** (0.20 g, 0.81 mmol) was cleaved in 2-propanol (3 mL) with $Pd(OH)_2$/C (0.28 g) to obtain **27** (0.16 g, 94%) as a colorless oil. Column chromatographic purification was carried out with 60% ethyl acetate/light petroleum as the eluent.

*4.3.3. Reaction of **2** with $Pd(OH)_2$/C in 2-propanol.* The allyl ether **2** (0.31 g, 0.87 mmol) was cleaved in 2-propanol (3 mL) with $Pd(OH)_2$/C (0.30 g) to obtain **28** (0.23 g, 84%) as a colorless oil. Column chromatographic purification was carried out with 50% ethyl acetate/light petroleum as the eluent. Found: C, 57.26; H, 7.25. $C_{15}H_{23}O_2Br$ requires C, 57.15; H, 7.35%; R_f (30% ethyl acetate/light petroleum) 0.42; IR (neat): $\bar{\nu}$ 3103–3628 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.46 (d, 2H, J=8.3 Hz, ArH), 7.21 (d, 2H, J=8.3 Hz, ArH), 4.44 (s, 2H, OCH_2), 3.62 (t, 2H, J=6.6 Hz, OCH_2), 3.44 (t, 2H, J=6.6 Hz, OCH_2), 1.48–1.75 (m, 5H, 2×CH_2, OH), 1.25–1.41 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 137.7, 131.5, 129.3, 121.3, 72.1, 70.6, 63.0, 32.8, 29.7, 29.42, 29.4, 26.1, 25.7 ppm.

*4.3.4. Reaction of **3** with $Pd(OH)_2$/C in 2-propanol.* The allyl ether **3** (0.33 g, 1.07 mmol) was cleaved in 2-propanol (3 mL) with $Pd(OH)_2$/C (0.37 g) to obtain **29** (0.25 g, 88%) as a colorless oil. Column chromatographic purification was carried out with 50% ethyl acetate/light petroleum as the eluent. Found: C, 72.47; H, 10.15. $C_{16}H_{26}O_3$ requires C, 72.14; H, 9.84%; R_f (50% ethyl acetate/light petroleum) 0.45; IR (neat): $\bar{\nu}$ 3113–3630 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.21–7.30 (m, 2H, ArH), 6.82–6.93 (m, 2H, ArH), 4.43 (s, 2H, OCH_2), 3.80 (s, 3H, OCH_3), 3.60 (t, 2H, J=6.6 Hz, OCH_2), 3.43 (t, 2H, J=6.6 Hz, OCH_2), 1.77 (br s, 1H, OH), 1.46–1.67 (m, 4H, 2×CH_2), 1.25–1.40 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 159.1, 130.8, 129.3, 113.8, 72.5, 70.2, 62.9, 55.3, 32.8, 29.7, 29.4, 29.43, 26.1, 25.7 ppm.

*4.3.5. Reaction of **4** with $Pd(OH)_2$/C in 2-propanol.* The allyl ether **4** (0.10 g, 0.31 mmol) was cleaved in 2-propanol (3 mL) with $Pd(OH)_2$/C (0.11 g) to obtain **30** (0.08 g, 91%). Column chromatographic purification was carried out with 40% ethyl acetate/light petroleum as the eluent. Found: C, 64.22; H, 8.41; N, 4.64. $C_{15}H_{23}NO_4$ requires C, 64.03; H, 8.24; N, 4.98%; R_f (30% ethyl acetate/light petroleum) 0.30; IR (neat): $\bar{\nu}$ 3132–3624 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.12–8.27 (m, 2H, ArH), 7.50 (d, 2H, J=8.7 Hz, ArH), 4.60 (s, 2H, OCH_2), 3.64 (t, 2H, J=6.6 Hz, OCH_2), 3.52 (t, 2H, J=6.6 Hz, OCH_2), 1.48–1.74 (m, 5H, 2×CH_2, OH), 1.25–1.45 (m, 8H, 4×CH_2) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 147.3, 146.5, 127.7, 123.6, 71.6, 71.2, 62.9, 32.7, 29.7, 29.4, 29.36, 26.1, 25.7 ppm.

*4.3.6. Reaction of **5** with $Pd(OH)_2$/C in tert-butanol.* The allyl ether **5** (0.20 g, 0.47 mmol) was cleaved in *tert*-butanol (3 mL) with $Pd(OH)_2$/C (0.16 g) to obtain **31** (0.12 g, 66%) as a colorless oil.[27] Column chromatographic purification was carried out with 25% ethyl acetate/light petroleum as the eluent. The yield of the same cleavage reaction in 2-propanol was relatively less (58%).

*4.3.7. Reaction of **6** with $Pd(OH)_2$/C in 2-propanol.* The allyl ether **6** (0.15 g, 0.44 mmol) was cleaved in 2-propanol (2 mL) with $Pd(OH)_2$/C (0.15 g) to obtain **32** (0.12 g, 87%) as a colorless oil.[28] Column chromatographic purification was carried out with 45% ethyl acetate/light petroleum as the eluent.

*4.3.8. Reaction of **7** with $Pd(OH)_2$/C in 2-propanol.* The allyl ether **7** (0.20 g, 0.88 mmol) was cleaved in 2-propanol (3 mL) with $Pd(OH)_2$/C (0.30 g) to obtain **33** (0.15 g, 92%) as a colorless oil.[29] Column chromatographic purification was carried out with 35% ethyl acetate/light petroleum as the eluent.

*4.3.9. Reaction of **8** with $Pd(OH)_2$/C in 2-propanol.* The allyl ether **8** (0.19 g, 0.64 mmol) was cleaved in 2-propanol (3 mL) with $Pd(OH)_2$/C (0.22 g) to obtain **34** (0.14 g, 91%) as a colorless oil.[30] Column chromatographic purification was carried out with 40% ethyl acetate/light petroleum as the eluent.

*4.3.10. Reaction of **9** with $Pd(OH)_2$/C in 2-propanol.* A mixture of **9** (0.23 g, 0.64 mmol) and $Pd(OH)_2$/C (0.22 g) was refluxed in 2-propanol (3 mL) for 3 h. The reaction mixture was filtered through a short bed of Celite and the Celite was washed with several portions of ethyl acetate followed by methanol. The filtrate was evaporated under reduced pressure and the residue was subjected to column chromatography (gradient elution, 30% ethyl acetate/light petroleum to 20% methanol/ethyl acetate) to afford **29** (0.08 g, 49%) as a colorless oil and **35** (0.043 g, 47%) as a colorless solid.

*4.3.11. Reaction of **10** with $Pd(OH)_2$/C in 2-propanol.* A mixture of **10** (0.09 g, 0.23 mmol) and $Pd(OH)_2$/C (0.08 g) was refluxed in 2-propanol (3 mL) for 3 h. The reaction mixture was filtered through a short bed of Celite and the Celite washed with several portions of ethyl acetate followed by methanol. The reaction mixture was concentrated under reduced pressure and the crude product was purified by column chromatography (eluent: 40% ethyl

acetate/light petroleum) to afford **30** (0.05 g, 77%) as a pale yellow oil and the starting material **10** (0.02 g, 20%).

*4.3.12. Reaction of **11** with Pd(OH)$_2$/C in methanol.* A mixture of **11** (0.20 g, 0.61 mmol) and Pd(OH)$_2$/C (0.43 g) was refluxed in methanol (3 mL) for 5 h. The reaction mixture was filtered through a short bed of Celite and the Celite washed with several portions of ethyl acetate followed by methanol. The filtrate was evaporated under reduced pressure and the residue was purified by column chromatography (eluent: 20% methanol/ethyl acetate) to afford **35** as a colorless solid (0.19 g, 96%).

*4.3.13. Reaction of **12** with Pd(OH)$_2$/C in methanol.* A mixture of **12** (0.20 g, 0.53 mmol) and Pd(OH)$_2$/C (0.37 g) was refluxed in methanol (3 mL) for 5 h. The reaction mixture was filtered through a short bed of Celite and the Celite washed with several portions of ethyl acetate followed by methanol. The filtrate was evaporated under reduced pressure and the residue was purified by column chromatography (eluent: 50% ethyl acetate/light petroleum) to obtain **29** (0.03 g, 24%) as a colorless oil, **35** (0.35 g, 46%) as a colorless solid, and the starting material **12** (0.03 g, 15%).

*4.3.14. Reaction of **14** with Pd(OH)$_2$/C in 2-propanol.* The allyl ether **14** (0.20 g, 0.89 mmol) was cleaved in 2-propanol (3 mL) with Pd(OH)$_2$/C (0.31 g) to obtain **35** (0.07 g, 54%) as a colorless solid and **36** (0.06 g, 36%) as a colorless oil. Column chromatography was carried out with 40% ethyl acetate/light petroleum and 20% methanol/ethyl acetate as eluent for **36** and **35**, respectively.

*4.3.15. Reaction of **15** with Pd(OH)$_2$/C in 2-propanol.* The allyl ether **15** (0.30 g, 1.00 mmol) was cleaved in 2-propanol (3 mL) with Pd(OH)$_2$/C (0.35 g) to obtain **35** as a colorless solid (0.12 g, 78%). Column chromatographic purification was carried out with 20% methanol/ethyl acetate as the eluent.

*4.3.16. Reaction of **17** with Pd(OH)$_2$/C in methanol.* The tribenzyl ether **17** (0.23 g, 0.50 mmol) was refluxed with Pd(OH)$_2$/C (0.53 g) in methanol (10 mL) and filtered. The filtrate was concentrated under reduced pressure and the crude product was acylated[31] to obtain the hexaacetyl derivative of **37** as a colorless solid (0.09 g, 89% for two steps) after column chromatography (silica gel, 230–400 mesh, eluent: 35% ethyl acetate/light petroleum). Mp=209–212 °C (lit.[31] mp=211–212 °C).

*4.3.17. Reaction of **18** with Pd(OH)$_2$/C in 2-propanol.* The allyl ether **18** (0.10 g, 0.24 mmol) was cleaved in 2-propanol (2 mL) with Pd(OH)$_2$/C (0.08 g) to obtain **38** as a colorless solid (0.07 g, 78%). Column chromatographic purification was carried out with 40% ethyl acetate/light petroleum as the eluent. Mp=120–122 °C (lit.[32] mp=118–120 °C).

*4.3.18. Reaction of **20** with Pd(OH)$_2$/C in methanol.* The allyl ether **20** (0.15 g, 1.11 mmol) was cleaved in methanol (4 mL) with Pd(OH)$_2$/C (0.78 g) to obtain phenol (**39**) as a colorless oil (0.07 g, 70%). Column chromatographic purification was carried out with 15% ethyl acetate/light petroleum as the eluent.

*4.3.19. Reaction of **22** with Pd(OH)$_2$/C in methanol.* The allyl ester **22** (0.15 g, 0.92 mmol) was cleaved in methanol (3 mL) with Pd(OH)$_2$/C (0.45 g) to obtain benzoic acid (**40**) as a colorless solid (0.09 g, 82%). Column chromatographic purification was carried out with 25% ethyl acetate/light petroleum as the eluent. Mp=118–120.4 °C (lit.[33] mp=122.4 °C).

*4.3.20. Reaction of **23** with Pd(OH)$_2$/C in methanol.* The *N*-benzyl amine **23** (0.20 g, 0.74 mmol) was cleaved in methanol (3 mL) with Pd(OH)$_2$/C (0.52 g) to obtain **41** as a pale yellow oil (0.08 g, 62%). Column chromatographic purification was carried out using a mixture of dichloromethane/methanol/ammonium hydroxide (98:2:0.30) as the eluent.

*4.3.21. Reaction of **24** with Pd(OH)$_2$/C in methanol.* The *N*-allyl amine **24** (0.10 g, 0.45 mmol) was cleaved in methanol (2 mL) with Pd(OH)$_2$/C (0.16 g) to obtain **41** as a pale yellow oil (0.06 g, 69%). Column chromatographic purification was carried out using a mixture of dichloromethane/methanol/ammonium hydroxide (98:2:0.3) as the eluent.

*4.3.22. Reaction of **25** with Pd(OH)$_2$/C in 2-propanol.* The cinnamyl ether **25** (0.30 g, 2.02 mmol) was cleaved in 2-propanol (3 mL) with Pd(OH)$_2$/C (0.70 g) to obtain **42** as a pale yellow oil[34] (0.11 g, 40%). Column chromatographic purification was carried out with 10% ethyl acetate/light petroleum as the eluent.

*4.3.23. Reaction of **1** with a mixture of Pd(OH)$_2$/C and Pd/C.* A solution of **1** (0.05 g, 0.20 mmol) in 2-propanol (1 mL) was refluxed with Pd(OH)$_2$/C (0.014 g, 0.02 mmol) and Pd/C (0.021 g, 0.02 mmol) for 30 min to obtain **27** (0.038 g, 92%) as an oil (0.038 g, 92%). The recovered catalyst could be used to cleave a second batch of **1**.

4.4. Procedure for the synthesis of a precursor for inositol pyrophosphate

*4.4.1. 2,4,6-Tri-O-allyl-myo-inositol-1,3,5-orthobenzoate (**44**).* Sodium hydride (0.53 g, 13.15 mmol) was added to a solution of **43**[17b] (0.70 g, 2.63 mmol) in dry DMF (10 mL) at 0 °C and stirred for 15 min. Allyl bromide (0.80 mL, 9.20 mmol) was added drop-wise to the reaction mixture under inert atmosphere. The reaction mixture was allowed to warm up to ambient temperature and stirred for 3 h. The reaction mixture was concentrated under reduced pressure and the residue obtained was worked up with ethyl acetate. The crude product was purified by column chromatography (eluent: 14% ethyl acetate/light petroleum) to afford **44** (0.95 g, 94%) as a colorless solid. Found: C, 68.50; H, 6.42. $C_{22}H_{26}O_6$ requires C, 68.38; H, 6.78%; R_f (10% ethyl acetate/light petroleum) 0.34; mp=55.3–57.3 °C; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.60–7.71 (m, 2H, ArH), 7.29–7.39 (m, 3H, ArH), 5.81–6.12 (m, 3H, HC=C), 5.16–5.42 (m, 6H, 3×=CH_2), 4.48–4.57 (m, 3H, InsH), 4.36–4.44 (m, 2H, InsH), 4.08–4.25 (m, 6H, 3×OCH_2), 3.94–4.00 (m, 1H, InsH) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 137.2, 134.9, 134.2, 129.4, 128.0, 125.4, 117.5, 73.8, 72.0, 70.7, 70.5, 69.0, 66.5 ppm.

*4.4.2. 1,3-O-Benzylidene-2,4,6-tri-O-allyl-myo-inositol (**45**).* DIBAL–H (8.54 mL of a 1 M solution in toluene, 8.54 mmol) was added to a solution of **44** (1.5 g, 3.88 mmol) in dry dichloromethane (15 mL) at 0 °C under argon atmosphere. The mixture was stirred at rt for 2 h, poured into a rapidly stirred cooled solution of sodium potassium tartrate (40 g in 75 mL of H_2O) and saturated aq NH_4Cl (60 mL). Excess dichloromethane (150 mL) was added and stirred overnight and the aqueous layer was then separated and extracted with dichloromethane. Organic layers were combined and dried over anhyd sodium sulfate. The solvent was evaporated under reduced pressure and the crude product was purified by flash column chromatography (eluent: 16% ethyl acetate/light petroleum) to afford **45** as a colorless crystalline solid (69%). Found: C, 67.81; H, 6.90. $C_{22}H_{28}O_6$ requires C, 68.02; H, 7.27%; R_f (20% ethyl acetate/light petroleum) 0.34; mp=45.5–47.5 °C; IR ($CHCl_3$): $\bar{\nu}$ 3196–3622 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.46–7.60 (m, 2H, ArH), 7.29–7.45 (m, 3H, ArH), 5.80–6.15 (m, 3H, 3×HC=), 5.73 (s, 1H, $PhHCO_2$), 5.15–5.47 (m, 6H, 3×=CH_2), 4.05–4.34 (m, 8H, 3×OCH_2, 2×InsH), 3.96 (d, 2H, J=8.5 Hz, 2×InsH), 3.68–3.81 (m, 1H, InsH), 3.53 (t, 1H, J=2.4 Hz, InsH), 2.73 (d, 1H, J=2.3 Hz, OH) ppm;

^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 137.9, 134.6, 134.0, 129.4, 128.4, 126.6, 118.1, 117.5, 92.9, 81.3, 73.6, 73.5, 70.7, 69.9, 68.0 ppm.

*4.4.3. 5-O-(4-Methoxy)benzyl-myo-inositol (**46**).* Sodium hydride (0.047 g, 1.20 mmol) was added to a cooled (0 °C) solution of **45** (0.31 g, 0.80 mmol) in dry DMF (3 mL) and stirred for 15 min. PMBCl (0.13 mL, 0.96 mmol) was added drop-wise to the stirred solution and stirring continued for 2 h. The reaction mixture was worked up using ethyl acetate. The gummy crude product obtained after the evaporation of ethyl acetate was used for next step without purification.

The crude product obtained above (0.25 g) and $Pd(OH)_2$/C (0.55 g) were refluxed in 2-propanol (3 mL) for 1.5 h. The reaction mixture was filtered through a short bed of Celite and the Celite washed with several portions of 1:1 mixture of water and methanol. The combined washings were evaporated under reduced pressure. Repeated washing of the residue with ethyl acetate (3×5 mL) afforded the known **46**[8](0.12 g, 78%) as a colorless solid.

*4.4.4. Racemic 1,2-di-O-benzyl-3,4,5,6-tetra-O-methyl-myo-inositol (**49**).* Sodium hydride (1.25 g, 31.05 mmol) was added to a solution of the diol **50** (1.65 g, 6.90 mmol) in dry DMF (20 mL) at 0 °C and stirred for 15 min. Benzyl bromide (3.3 mL, 27.6 mmol) was added drop-wise to the reaction mixture and stirred for 4 h. After quenching the excess sodium hydride by the addition of ice, the solvents were evaporated under reduced pressure. The residue obtained was worked up with ethyl acetate. The crude product was purified by column chromatography (eluent: 25% ethyl acetate/light petroleum) to afford **49** (2.50 g, 87%) as a colorless gum. Found: C, 68.86; H, 7.94. $C_{24}H_{32}O_6$ requires C, 69.21; H, 7.74%; R_f (20% ethyl acetate/light petroleum) 0.31; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 7.22–7.43 (m, 10H, ArH), 4.83 (q, 2H, J=12.1 Hz, OCH_2), 4.64 (q, 2H, J=11.9 Hz, OCH_2), 4.01 (t, 1H, J=2.3 Hz, InsH), 3.50–3.70 (m, 11H, 3×OCH_3, 2InsH), 3.37 (s, 3H, OCH_3), 3.20 (dd, 1H, J=9.9, 2.4 Hz, InsH), 2.88–3.04 (m, 2H, InsH) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 138.9, 138.5, 128.3, 128.0, 127.6, 127.5, 127.3, 127.2, 85.6, 83.3, 82.9, 82.4, 80.6, 73.8, 73.3, 72.8, 61.1, 60.8, 58.2 ppm.

*4.4.5. Reaction of **49** with Pd(OH)$_2$/C in 2-propanol.* A mixture of **49** (1.0 g, 2.40 mmol) and $Pd(OH)_2$/C (20 wt %, 2.20 g) was refluxed in 2-propanol for 60 h. The reaction mixture was filtered through a short bed of Celite and the Celite washed with methanol followed by ethyl acetate. The combined washings were evaporated under reduced pressure and the residue was purified by column chromatography (eluent: 50% ethyl acetate in light petroleum) to afford **51** (0.18 g, 23%) as a colorless oil and **50**[35] (eluent: 15% methanol/ethyl acetate) as a colorless solid (0.41 g, 74%); mp=97–99.3 °C (lit.[35] mp 105–106 °C). Data for **51**: Found: C, 60.30; H, 7.54. $C_{17}H_{24}O_7$ requires C, 59.99; H, 7.11%; R_f (40% ethyl acetate/light petroleum); IR ($CHCl_3$): $\bar{\nu}$ 3120–3660, 1724 cm^{-1}; ^{1}H NMR ($CDCl_3$, 200 MHz): δ 8.03–8.09 (m, 2H, ArH), 7.55–7.61 (m, 1H, ArH), 7.43–7.51 (m, 2H, ArH), 5.89 (t, 1H, J=2.8 Hz, InsH), 3.69 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 3.61–3.65 (m, 4H, OCH_3, InsH), 3.49–3.60 (m, 3H, InsH), 3.45 (s, 3H, OCH_3), 3.09–3.26 (m, 2H, InsH, OH) ppm; ^{13}C NMR ($CDCl_3$, 50.3 MHz): δ 166.0, 133.1, 130.0, 129.9, 128.4, 85.3, 83.7, 83.3, 80.5, 70.2, 69.5, 61.2, 61.1, 61.0, 58.0 ppm.

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Supplementary data

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