Practical TEMPO-Mediated Oxidation of Alcohols using Different Polymer-Bound Co-Oxidants

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Abstract: Hypochlorite and chlorite exchange resins are evaluated as co-oxidants or oxidants, respectively, for the oxidation of alcohols to the corresponding aldehydes, ketones or carboxylic acids. Polymer-bound hypochlorite can act as a co-oxidant in TEMPO-mediated oxidations of alcohols. The formation of aldehydes only works under weakly acidic conditions. However, the cheap hypochlorite exchange resin is less efficient as co-oxidant compared to the use of ionically immobilised bisacetoxybromate(I) anions. In contrast, the chlorite exchange resin is a highly potent co-oxidant for the preparation of carboxylic acids from the corresponding primary alcohols in the presence of TEMPO. It is demonstrated that in this case also the resin acts as a polymer-bound co-oxidant for both oxidation steps. Yields are commonly excellent as is also demonstrated for examples taken from natural product synthesis which include acid labile glycosides. In most cases, work-up of this heavy metal-free oxidation is kept to a minimum. It often includes filtration followed by removal of the solvent.

Keywords: aldehydes; carboxylic acids; chlorites; ketones; oxidations; polymer-bound reagents; TEMPO

Introduction

Polymer-assisted oxidations of alcohols can be conducted with various polymer-bound reagents that allow isolation of oxidation products with minimum purification.[1] Commonly, functionalised polymers were developed that are loaded with heavy metals such as Cr(VI)[3–8] which, in many cases, are attached *via* different N-heterocycles or simple quaternary ammonium cations to the polymeric backbone. Polymer-bound (diacetoxy)iodobenzene in the presence of a bromide source may also serve as a non metal-based oxidant for the transformation of secondary alcohols into ketones. Furthermore, it was shown that this reagent system oxidises primary alcohols to the corresponding carboxylic acids.[9]

The use of *N*-oxoammonium ions like 2,2,6,6-tetramethylpiperidine-1-oxonium (**2**) and the stable free nitroxyl radical precursor **1** (TEMPO) is another alternative to metal-based oxidants.[10] The oxoammonium ion itself is transformed into the secondary hydroxylamine **3** during that process, but it is reoxidised by the co-oxidant. TEMPO (**1**) can be applied stoichiometrically or more conveniently as a catalyst in combination with a co-oxidant,[11–13] preferentially a polymer-bound one. The strategy of immobilising the co-oxidant is particularly appealing if the solid-phase bound co-oxidant can easily be regenerated. Alternatively, TEMPO has been immobilised,[14,15] but it either requires the use of a stoichiometric amount of the valuable immobilised species or the co-oxidant is employed in the solution phase, which results in additional purification steps.

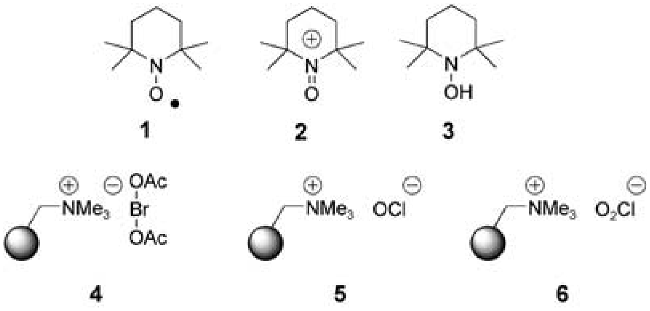

Figure 1. Species relevant in TEMPO-mediated oxidations using polymer-bound co-oxidants.

In the context of TEMPO-mediated oxidations of alcohols using a polymer-bound co-oxidant, we reported on the use of the polymer-supported bisacetoxybromate(I) anion **4**.[16] Advantageously, the mode of attachment is achieved by ion exchange which allows simple regeneration. This oxidation protocol has already seen various applications in natural product synthesis.[17] Thus, in dry dichloromethane as solvent, oxidations of primary alcohols yield aldehydes, while formation of carboxylic acids was not observed. For large-scale applications it would be beneficial to utilise cheaper polymer-

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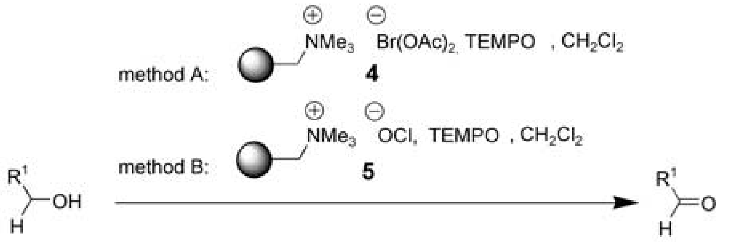
bound co-oxidants and to have the flexibility and the choice to either generate aldehydes and ketones, respectively, or carboxylic acids in one pot. In the present paper we describe procedures for the use of polymer-bound hypochlorite **5**[18] as well as chlorite **6**[19] for the preparation of aldehydes and carboxylic acids starting from the corresponding alcohols. In the case of aldehyde formation, we shall compare polymer-bound hypochlorite **5** with the bisacetoxybromate(I) resin **4**.

Results and Discussions

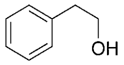
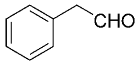
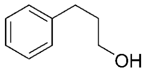
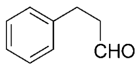
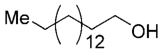
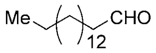
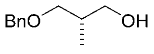
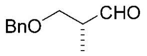
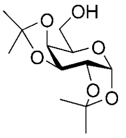
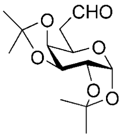
The studies had to be initiated by searching for the best conditions under which polymer-bound reagents **5** and **6** can be utilised in oxidations (Table 1). Typically, when hypochlorite serves as co-oxidant in TEMPO-mediated oxidations in solution, an aqueous buffer (acetonitrile, *t*-BuOH/H_2O, or *t*-BuOH/Ac_2O, H_2O, acetone, with phosphate buffer) is required.[12,13] In several cases, it was demonstrated that bromide anions accelerate the process. It was postulated that hypobromite was the effective oxidant[19] which oxidises the nitroxyl radical to the *N*-oxoammonium ion. From this description it becomes evident that these complex solvent and reaction mixtures are not favourable, when using polymer-bound co-oxidants, particularly because work-up is not simplified under these conditions. In addition, transfer of these protocols to continuous flow processes[20] is also hampered, because of the multiphasic nature of the liquid part of the reaction mixture.

Thus, we had to search for homogeneous conditions for the liquid phase preferably in organic solvents and without use of additional salts. After substantial optimization, we found that TEMPO-mediated oxidations of alcohols to aldehydes using reagent **5** (1.5 equivs.) as co-oxidant work best in dichloromethane at room temperature after treatment of the resin with one equivalent

Table 1. Comparison of polymer-assisted oxidations of primary alcohols.



7 – 11 **12 – 16**

Entry	Alcohol		Method[a] (Reaction time)	Aldehyde		Yield [%][b]
1	**7**		A (3.5 h); B (2.5 h)	**12**		94; 95
2	**8**		A (3.5 h); B (5.5 h)	**13**		92; 89[c]
3	**9**		A (3.5 h); B (7 h)	**14**		93; 90[d]
4	**10**		A (1.5 h); B (4 h)	**15**		95; 71[e]
5	**11**		A (24 h, 40 °C); B (48 h)	**16**		97; 67

[a] Method A: The reaction was performed in dichloromethane at room temperature. It was initiated by addition of reagent **4** (3 equivs.), TEMPO (3 mol %). Method B: The reaction was performed in dichloromethane at room temperature. It was initiated by addition of reagent **5** (1.5 equivs.), TEMPO (3 mol %) and conc. HCl (1 equiv.). Where specifically noted, a second portion of TEMPO and HCl had to be added after the time mentioned.

[b] Yields refer to isolated yields of pure products.

[c] After 3 h additional TEMPO (3 mol %) and conc. HCl (0.5 equiv.) were added.

[d] After 6 h additional TEMPO (3 mol %) and conc. HCl (0.5 equiv.) were added.

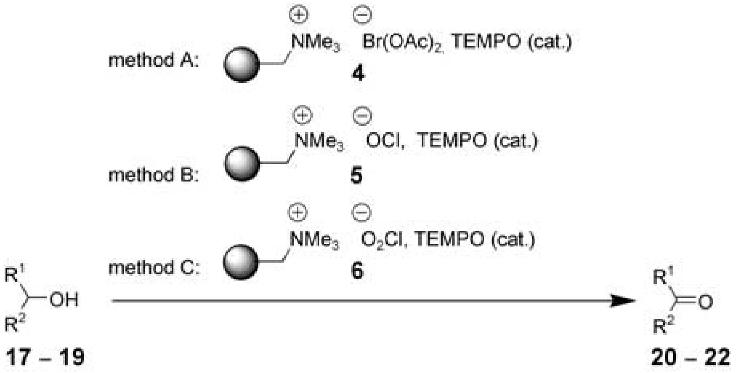
[e] TEMPO (1 mol % portions) was added (initially, and after 0.5 h, 1.5 h and 2.5 h); about 10% of the corresponding carboxylic acid was formed.

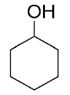
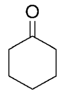
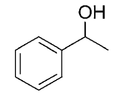
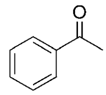
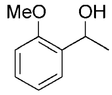
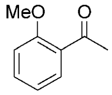
of concentrated HCl affording a weakly acidic solution (pH 3.5–5). No substantial pH change was encountered during progression of the reaction. When weaker acids such as acetic acid or no additional proton sources were employed oxidation did not occur. The same observation applies to the absence of TEMPO. We compared the optimised conditions (method B) for **5** with those developed in our laboratories when bisacetoxybromate(I) exchange resin **4** is employed as co-oxidant (method A). As is summarised in Table 1, polymer-bound hypochlorite **5** is less effective than the bromate(I) reagent **4**. In most cases, oxidation proceeded more sluggishly compared to the established procedure with reagent **4**. Larger quantities of TEMPO are required and it is best added portionwise along with the acid (entries 2–4). In fact, when the hypochlorite resin **5** was employed it was difficult to prevent overoxidation to the corresponding carboxylic acids which was very pronounced for substrates like 4-methoxybenzyl alcohol.

Therefore, we continued our comparative studies with three simple secondary alcohols (Table 2). This time we also included a third ion exchange resin **6** which was loaded with the chlorite anion. Again, activity of resin **6** was only gained after addition of one equivalent of concentrated HCl and in the presence of a catalytic amount of the nitroxyl radical **1**. In all cases, reagents **4** and **6** showed high activity as co-oxidants yielding the corresponding ketones in excellent yields. However, chlorite is a much cheaper co-oxidant than the hypobromate(I) anion and the transformations proceeded much more rapidly, so that the new protocol is superior, particularly when scale-up has to be considered. Again, hypochlorite **5** turned out to be less well suited as co-oxidant.

Thus, we extended our studies to more complex secondary alcohols in order to study the influence on steric hindrance, functional group toleration and integrity of stereogenic centres in the α-position of the carbonyl group formed upon oxidation (Table 3). For this purpose, different partially protected hexoses and advanced synthetic intermediates **23**–**26** from natural product syntheses were smoothly oxidised to the corresponding uloses and ketones **27**–**30**, respectively. The reaction was terminated by filtration and removal of the solvent. In some cases, for example, 2-deoxymethylglycoside **27** the solution may be too acidic. Then, neutralisation was achieved by addition of the weakly basic resin Amberlite A-21. The examples depicted in Table 3 demon-

Table 2. Comparison of polymer-assisted oxidations of secondary alcohols.



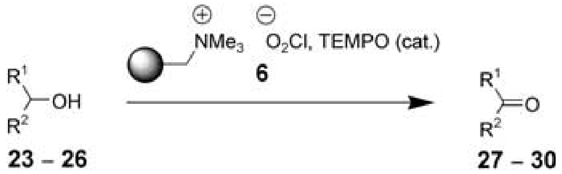
Entry	Alcohol		Method[a-c] (Reaction time)	Ketone		Yield [%]
1	**17**		A (24 h); B (30 h); C (4.5 h)	**20**		96; 28; 99
2	**18**		A (24 h); B (30 h); C (4.5 h)	**21**		96; 21; 98
3	**19**		A (24 h); B (30 h); C (4.5 h)	**22**		96; 30; 97

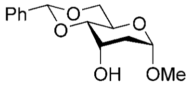
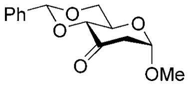
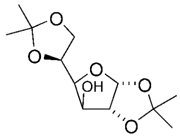
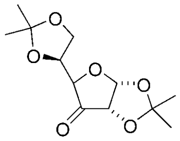
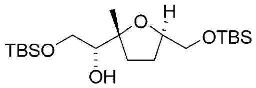
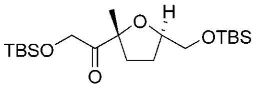
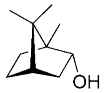
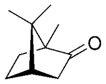
[a] General reaction condition for reagent **4**: **4** (3 equivs.), TEMPO (1–2 mol %), CH_2Cl_2, room temperature.

[b] General reaction condition for reagent **5**: **5** (1.5 equivs.), conc. HCl (1 equiv.), TEMPO (3 mol %), CH_2Cl_2, room temperature.

[c] General reaction condition for reagent **6**: **6** (2–4 equivs.), conc. HCl (1 equiv.), TEMPO (3 mol %), CH_2Cl_2, room temperature.

Table 3. TEMPO-mediated oxidation of complex secondary alcohols to ketones using co-oxidant **6**.[a]



Entry	Alcohol		Ketone		Yield [%]
1	**23**		**27**		90
2	**24**		**28**		84
3	**25**		**29**		86
4	**26**		**30**		99

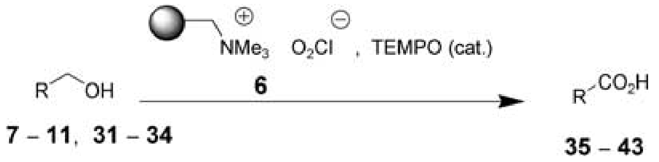
[a] Conditions: **6** (2.5 equivs.), TEMPO (1–3 mol %), CH_2Cl_2, room temperature.

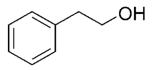
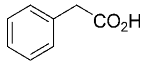
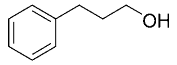
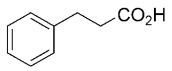
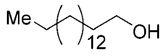
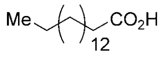
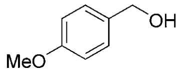
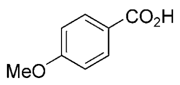
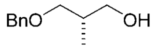
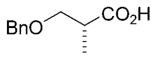
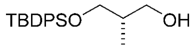
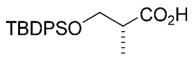
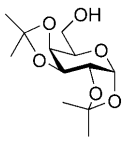
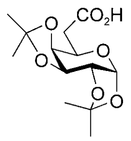
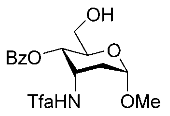
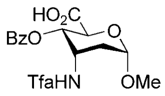
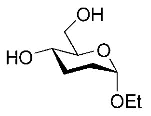
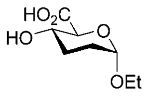
strate that this oxidation method is compatible with many other functional groups. Common protecting groups for alcohols such as isopropylidene and benzylidene acetals as well as silyl ethers are stable under the conditions employed.

These transformations are noteworthy because few versatile polymer-bound oxidants for secondary alcohols have been reported so far.[21] Only a few solid phase-assisted protocols which are widely applicable have been reported for the oxidation of primary alcohols to carboxylic acids in one pot so far. For example, Ley and co-workers used two polymer-bound reagents, namely polymer-bound TEMPO (10 mol %) and immobilised chlorite anion (5 equivs.). The transformation of primary alcohols to carboxylic acids proceeded at room temperature in aqueous acetonitrile in the presence of potassium bromide (0.1 equiv.), sodium hypochlorite (4 mol %) and polymer-bound $H_2PO_4^-$ (1 equiv.) as buffer.[22] Extended reaction times of one to two days were reported for this one-pot oxidation. Recently, Tashino and Togo employed *poly*[4-(diacetoxyiodo)styrene] as stoichiometric co-oxidant for the TEMPO-promoted oxidation of alcohols.[23] However, substoichiometric amounts (0.5 equivs.) of the valuable TEMPO in solution were required and a stepwise protocol was necessary to achieve full transformation.

Our observation that polymer-bound chlorite **6**, a catalytic amount of TEMPO and one equivalent of a strong acid are able to very rapidly oxidise secondary alcohols prompted us to study its use for the preparation of carboxylic acids (Table 4). Precedents for this type of conversion can be found in solution phase synthesis which is based on the use of catalytic amounts of TEMPO and sodium hypochlorite and a stoichiometric amount of sodium chlorite in a biphasic solvent system composed of acetonitrile and again an aqueous phosphate buffer.[12c] However, work-up strongly relies on several extraction steps and often purification either by chromatography or by crystallisation is required. As is summarised in Table 4 use of polymer-bound chlorite **6**, a catalytic amount of TEMPO and one equivalent of conc. HCl in dichloromethane allowed us to rapidly oxidise primary alcohols to carboxylic acids in one pot in high yield and with very good purity. In the case of carboxylic acid preparation the slightly acidic reaction conditions are beneficial as they guarantee that the product does not remain ionically bound to the resin but is completely present in the organic phase. Basically, work-up consisted of simple filtration and removal of the solvent. Only 4-methoxybenzyl alcohol gave a moderate yield while about 40% of the intermediate aldehyde remained in solution. This result has already been observed in oxidations of alcohol **31** and was ascribed to the possible quenching of intermediate catalytic sodium hypochlorite. This effectively results in shutting down the catalytic cycle.[12c] It is noteworthy that the primary and secondary hydroxy groups in ethyl glycoside **34** can be completely differentiated. In fact, Thiem and co-worker

Table 4. TEMPO-mediated oxidation of primary alcohols to carboxylic acids using co-oxidant **6**.[a]



Entry	Alcohol		Reaction time	Carboxylic Acid		Yield [%]
1	**7**		4 h	**35**		98
2	**8**		2.5 h	**36**		90
3	**9**		2 h	**37**		94
4	**31**		4.5 h	**38**		59[b]
5	**10**		2.5 h	**39**		99
6	**32**		20 h	**40**		99
7	**11**		2.5 h	**41**		96
8	**33**		6 h	**42**		93
9	**34**		18 h	**43**		86

[a] Conditions: **6** (4 equivs.), conc. HCl (1 equiv.), TEMPO (3 mol %), CH_2Cl_2, room temperature.
[b] 4-Methoxybenzaldehyde formed as by product in 41% yield (determined by GC).

showed that in polysaccharides this kind of chemoselectivity can be achieved with TEMPO-mediated oxidations.[24]

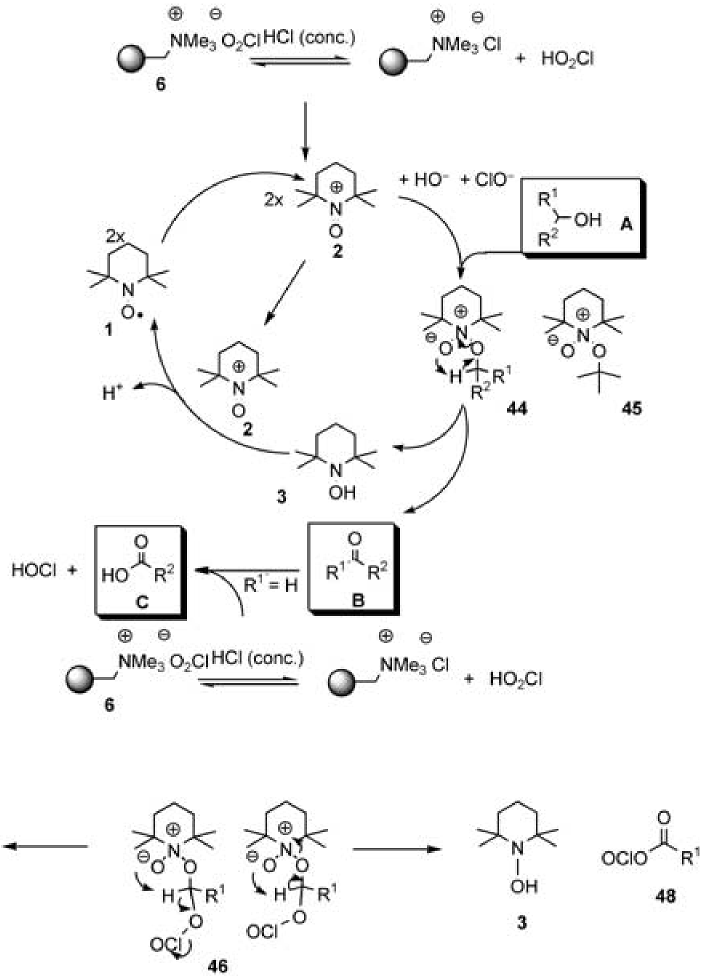
In order to get a better insight into the roles of TEMPO as well as of chlorite in this solid-phase assisted two-step oxidation we tested whether TEMPO is actually required for the oxidation of the intermediate aldehyde. Indeed, it is known that $NaClO_2$ can readily oxidise aldehydes in aqueous solutions.[25] However, our reaction conditions are weakly acidic and the mixture is not buffered by aqueous phosphate. In addition, the counterion (here quaternary ammonium cation) can have a pronounced effect on the oxidative properties[26] of the anion as is known for the permanganate ion.[16a] Thus, when aldehyde **13** was treated with chlorite exchange resin **6** in the absence of TEMPO in deuterated dichloromethane in the NMR tube, the aldehyde remained unaltered after 4 h.[27] Only when a catalytic amount of TEMPO was added after this time did the solution rapidly change to dark brown and the carboxylic acid **36** formed overnight. Indeed, this intense colour is characteristic for all reactions that are listed in the tables above.

Catalytic amounts of bromide are known to strongly accelerate alcohol oxidation with bleach mediated by TEMPO.[22] With the optimised protocol we observed complex reaction mixtures when an additional bromide source was added (tetrabutylammonium bromide or IRA-900, bromide form). When conc. HBr instead of HCl was used oxidations did proceed, however, byproducts formed, especially when alkyl glycosides served as substrates for which the lower pH can be made responsible.

From these results it can be concluded that the chlorite resin **6** acts as a co-oxidant for both TEMPO-mediated oxidation steps when carboxylic acids are formed from primary alcohols. Interestingly, the presence of a tertiary alcohol like *t*-butyl alcohol strongly slows down or inhibits the oxidation.

A possible mechanism of this process is depicted in Scheme 1. The polymer-bound co-oxidant **6** initiates the process by oxidation of two equivalents of TEMPO **1** to yield the active catalyst, the *N*-oxoammonium ion **2**.[28] It is likely that the presence of hydrochloric acid is responsible for the release of chloric acid into solution[26] which then initiates the oxidation of the nitroxyl radical **1**. One equivalent of the oxoammonium salt **2** is responsible for the oxidation of alcohol **A** to yield aldehyde or ketone **B**, respectively. Thereby, hydroxylamine **3** is formed as a by-product. Intermediate **44** is formed after nucleophilic attack of alcohol **A** to the oxoammonium species **2**. The formation of intermediate **44** would also explain why *t*-butyl alcohol is able to slow down or inhibit the oxidation process, because no abstractable proton is present in the corresponding intermediate **45**. Finally, rapid *syn*-proportionation between the second equivalent oxoammonium salt **2** and hydroxylamine **3** occurs to give two nitroxyl radicals **1** which either are reoxidised to two oxoammonium ions **2** by reagent **6** or by hypochlorite which is formed as by-product from the alcohol oxidation. If aldehydes are formed as initial oxidation products further oxidation occurs to the corresponding carboxylic acid **C**.

At this point, one can only speculate about the mechanism of the second oxidation step, particularly because the presence of TEMPO is required. A probable acetal-like intermediate **46** may arise from nucleophilic attack of the aldehyde to **2** in the presence of chlorite (the analogous hypochlorite case is not depicted here) which either collapses to intermediate **47** which spontaneously should fragment to the oxoammonium species **2** and the carboxylic acid. In this case, the chlorite acts as the oxidant while in the alternative case the oxoammonium salt **2** is reduced to the hydroxylamine **3**. The second by-product, the mixed anhydride **48**, further hydrolyses to the carboxylic acid and chlorite.



Scheme 1. Proposed mechanism of TEMPO-mediated oxidation of alcohols to ketones and carboxylic acids using polymer-bound chlorite **6** as co-oxidant.

Compared to the known solution-phase protocols all transformations proceeded in the absence of an aqueous buffer and an additional bromide source. In the present case the polymer-bound ammonium species may show some buffering properties. Apart from releasing chloric acid from the solid support, the complete role of the hydrochloric acid is not fully clear, particularly as the present case is the first description of a TEMPO-mediated oxidation of alcohols under weakly acidic conditions.

Conclusion

In summary, we evaluated TEMPO-mediated oxidations of primary and secondary alcohols using different polymer-bound co-oxidants. For the generation of aldehydes, bisacetoxybromate(I) anion **4** immobilised by ion exchange turned out to be the superior co-oxidant compared to immobilised hypochlorite **5**. An excellent one-pot oxidation of secondary alcohols to the corresponding ketones as well as of primary alcohols to carboxylic acids utilises chlorite **6** loaded on an anion exchange resin. In view of the easy recyclability of the co-oxidant, the catalytic use of TEMPO, the simple work-up and the purity of the products the latter procedure may find application in large-scale processes of industrial relevance and provides all ingredients for synthesis under continuous flow conditions.[20]

Experimental Section

General Remarks and Starting Materials

^{1}H and ^{13}C NMR spectra were measured on DPX 200 (Bruker) at 200 MHz (50 MHz) and AM-400, ARX 400 (Bruker) 400 MHz (100 MHz), respectively, using tetramethylsilane as the internal standard. $CDCl_3$ is the solvent for all NMR experiments. Mass spectra were recorded on a type LCT-spectrometer (Micromass). Optical rotations [α] were collected on a Polarimeter 341 (Perkin Elmer) at a wavelength of 589 nm. All solvents used were of reagent grade and were further dried. Reactions were monitored by TLC on silica gel 60_{P254} and detected either by UV absorption or by staining with H_2SO_4/4-methoxybenzaldehyde in ethanol. Where necessary, flash column chromatography was performed on silica gel 60 (230–400 mesh). Preparation of polymer-bound bromate(I) **4** is described in ref.[16] Except for alcohols **10**, **23**, **25**, **32**, **33**, and **34** all starting compounds are commercially available. Alcohols **10** and **32** were prepared from commercial (2*R*)-3-hydroxy-2-methylpropionic methyl ester by standard protection of the alcohol group followed by dibal-promoted reduction of the ester functionality, again under standard conditions. Aldehydes **12**–**16**, ketones **20**–**22**, **27**, **28** and **30** as well as carboxylic acids **35**–**41** are described in the literature or are commercially available. The spectroscopic and physical data of aldehydes **15**[29] and **16**,[30] of ketones **27**[31], **28**,[32] and of carboxylic acids **39**[33] **40**[34] and **41**[35] are listed in the literature.

Excess of polymer reagents are based on the loadings given by the commercial provider. It is commonly experienced that only a portion of all possible active sites actually react in stoichiometric transformations.[1] Nevertheless, formation of chlorine dioxide from hypochlorite and chlorite, respectively, cannot totally be excluded which could also be a reason for the necessity of an excess of reagent.[36]

Preparation of Hypochlorite Resin 5

Dry Amberlite IRA 900 (chloride form) (4.7 g; 1 mmol/g) was washed with water (10 mL/g resin), 2 N NaOH (10 mL/g resin) and water until neutral pH of the eluent. The resulting exchange resin (hydroxide form) was treated with an aqueous solution (4%) of sodium hypochlorite (10 mL/g resin) followed by water until neutral pH of the eluent. The resulting resin was washed with acetone (10 mL/g resin) and dried under vacuum for 6 h to yield slightly reddish Amberlite IRA 900 (hypochlorite form; 0.69 mmol/g resin gravimetrically determined). The functionalised resin can be stored under nitrogen at $-20\,°C$ for two weeks without loss of activity.

Preparation of Chlorite Resin 6

The preparation of the chlorite resin **6** is identical to the procedure described for the hypochlorite resin **5** except that an aqueous solution (4%) of sodium chlorite is employed. The loading was gravimetrically determined to be 1.2 mmol/g resin. The functionalised resin can be stored under nitrogen at $-20\,°C$ for two weeks without loss of activity.

General Procedure for the Oxidation of Alcohols with Bisacetoxybromate (I) Resin/TEMPO

A suspension of the alcohol (1 equiv.), resin **4** (3 equivs.) and TEMPO (1–2 mol %) in dry CH_2Cl_2 (2.5 mL/mmol bromide) under nitrogen was shaken at 300 rpm at room temperature. Completion of the reaction was monitored by TLC. Filtration terminated the reaction. The resin was washed with CH_2Cl_2 (3 ×), and the combined organic washings and filtrate were concentrated under reduced pressure. Typically, impurities derived from TEMPO could not be detected in the ^{1}H NMR spectrum of the crude product which can be ascribed to absorption to the polymeric phase. In some cases, further purification by column chromatography was necessary.

General Procedure for the Oxidation of Alcohols with Hypochlorite Resin/TEMPO

A mixture of the alcohol (1 equiv.), resin **5** (typically 1.5 equivs. based on the loading given by the commercial provider) in dry CH_2Cl_2 (6 mL/mmol) with TEMPO (3 mol %) under nitrogen was shaken at 300 rpm at room temperature. Completion of the reaction was monitored by TLC. As is mentioned in Table 1, in some cases more HCl and TEMPO had to be added portionwise. Filtration terminated the reaction. The resin was washed with CH_2Cl_2 (3 ×) and the combined organic washings and filtrate were concentrated under reduced pressure.

General Procedure for the Oxidation of Alcohols with Chlorite Resin/TEMPO

Resin **6** [typically 3 equivs. based on the loading given by the commercial provider (3.6 g/mmol of substrates)] in dry CH_2Cl_2 (10 mL/mmol of substrate) {NB: more dilute reaction mixtures led to longer reaction times (> 12 h)} with TEMPO (3 mol %) and 1 equiv. conc. HCl under nitrogen were shaken at room temperature for 15 min at 300 rpm. Then, the corresponding secondary or primary alcohol was added (1 equiv.). Completion of the reaction was monitored by TLC. Filtration terminated the reaction. After washing the resin with CH_2Cl_2 (3 ×) the combined organic washings and the filtrate were concentrated under reduced pressure. Commonly, further purification was not necessary (> 95% purity) and the carbonyl compounds could directly be analysed. Typically, impurities derived from TEMPO could not be detected in the ^{1}H NMR spectrum of the crude product which can be ascribed to absorption to the polymeric phase. Still, for generating analytically pure samples and in order to remove oligomeric impurities from the resin purification by flash column chromatography was carried out in some cases. We found that these oligomeric impurities commonly arose when charges of the commercial resins were employed for the first time. After regeneration and reuse we typically did not note this phenomenon.

2-Phenylethanal (12)

By treatment of 2-phenylethanol (**7**; 62 mg, 0.5 mmol) with reagent **5** (1.5 equivs.) and TEMPO (2.3 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 2.5 h the title compound **12** (56.8 mg, 0.47 mmol; 95%) was prepared. When the oxidation was carried out with resin **4** according to the general procedure the title compound **12** was isolated in 94% yield.

3-Phenylpropanal (13)

By treatment of 3-phenylpropanol (68 mg, 0.5 mmol) with reagent **5** (1.5 equivs.) and TEMPO (4.6 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 5.5 h the title compound **13** (59.3 mg, 0.44 mmol; 89%) was prepared. When the oxidation was carried out with resin **4** according to the general procedure the title compound **13** was isolated in 92% yield.

Hexadecanal (14)

By treatment of hexadecan-1-ol (**9**; 120 mg, 0.5 mmol) with reagent **5** (1.5 equivs.) and TEMPO (4.6 mg, 6 mol %; portionwise addition) and conc. HCl (1.5 equivs.; portionwise addition) in CH_2Cl_2 at room temperature under nitrogen for 7 h the title compound **14** (108 mg, 0.45 mmol; 90%) was prepared. When the oxidation was carried out with resin **4** according to the general procedure the title compound **14** was isolated in 93% yield.

(*R*)-3-Benzyloxy-2-methylpropan-1-al (15)

By treatment of (*R*)-3-benzyloxy-2-methylpropan-1-ol (**10**; 90 mg, 0.5 mmol) with reagent **5** (1.5 equivs.) and TEMPO [4 portions (each 1 mol %) 0.0, 0.5, 1.5 and 2.5 h] and conc. HCl (1 equiv.) in CH_2Cl_2 (3 mL) at room temperature under nitrogen for 4 h the title compound **15** (63.3 mg, 0.36 mmol; 71%) was prepared. Purification was achieved by flash column chromatography (ethyl acetate/petroleum ether = 1 : 4). Compound **15**: oil; $[\alpha]_D^{20}$: $-25.4°$ ($CHCl_3$, *c* 1) {ref.[29] $[\alpha]_D^{20}$: $-28°$ ($CHCl_3$, *c* 1)}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 9.73$ (d, $J = 1.5$ Hz, 1H, C*H*O), 7.35–7.30 (m, 5H, Ph), 4.53 (s, 2H, PhC*H*$_2$), 3.68 (dd, $J = 9.4$, 6.6 Hz, 1H, 3-H), 3.64 (dd, $J = 9.4$, 5.2 Hz, 1H, 3-H′), 2.71–2.62 (m, 1H, 2-H), 1.14 (d, $J = 7.1$ Hz, 3H, Me); ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 204.0$ (d, *C*HO), 138.1 (s, Ar), 128.6, 127.8 (d, Ar), 73.51 (t, Ph*C*H$_2$), 70.3 (t, C-3), 47.0 (d, C-2), 10.9 (q, Me); GC-MS (EI): *m/z* (%) = 177 (5) $[M-H]^+$, 134 (10) $[M-C_2H_4O]^+$, 107 (75) $[C_7H_7O]^+$, 91 (100) $[C_7H_7]^+$; HR-MS (ESI): calcd. for $C_{13}H_{17}O_2NNa$: 242.1157 $[M+C_2H_3N+Na]^+$, found: 242.1164. For additional spectroscopic and physical data refer to ref.[29]

When the oxidation was carried out with resin **4** according to the general procedure the title compound **15** was isolated in 95% yield.

1,2 : 3,4-Di-*O*-isopropylidene-6-oxo-α-D-*galacto*-pyranose (16)

By treatment of 1,2 : 3,4-di-*O*-isopropylidene-α-D-*galacto*-pyranose (**11**; 130 mg, 0.5 mmol) with reagent **5** (1.5 equivs.) and TEMPO (3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 (3 mL) at room temperature under nitrogen for 2d the title compound **16** (86.5 mg, 0.34 mmol; 67%) was prepared. Purification was achieved by flash column chromatography (ethyl acetate/petroleum ether = 1 : 2). Compound **16**: oil; $[\alpha]_D^{20}$: $-76.5°$ ($CHCl_3$, *c* 1) {ref[30] oil; $[\alpha]_D^{20}$: $-87°$ ($CHCl_3$, *c* 1)}; ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 9.55$ (s, 1H, C*H*O), 5.60 (d, $J = 4.9$ Hz, 1H, 1-H), 4.59 (dd, $J = 7.8$, 2.4 Hz, 1H, 3-H), 4.54 (dd, $J = 7.8$, 2.1 Hz, 1H, 4-H), 4.32 (dd, $J = 4.9$, 2.4 Hz, 1H, 2-H), 4.13 (d, $J = 2.1$ Hz, 1H, 5-H), 1.44, 1.37, 1.28, 1.25 (s, 12H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 200.5$ (d, *C*HO), 110.3 [s, $(RO)_2$*C*Me$_2$], 109.3 (d, C-1), 96.5 [s, $(RO)_2$*C*Me$_2$], 73.5 (d, C-5), 72.0 (d, C-2), 70.8 (d, C-3), 70.7 (d, C-4), 26.3, 26.1, 25.1, 24.5 (q, Me); HR-MS (ESI): calcd. for $C_{14}H_{21}O_6NNa$: 322.1267 $[M+C_2H_3N+Na]^+$, found: 322.1277. For spectroscopic and physical data also refer to ref.[30]

When the oxidation was carried out with resin **4** according to the general procedure the title compound **16** was isolated in 97% yield.

Cyclohexanone (20)

By treatment of cyclohexanol (**17**; 50 mg, 0.5 mmol) with reagent **6** (4.0 equivs.) and TEMPO (2.3 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 4.5 h the title compound **20** (48.6 mg, 0.5 mmol; 99% analysed by GC) was prepared.

When the oxidation was carried out with resin **4** according to the general procedure the title compound **20** was formed in 96% yield. Likewise, use of resin **5** according to the general procedure afforded the title compound **20** in 28% yield. The remaining material was analysed by GC to be the starting alcohol **17**.

Acetophenone (21)

By treatment of 1-phenylethanol (**18**; 61 mg, 0.5 mmol) with reagent **6** (4.0 equivs.) and TEMPO (2.3 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 4.5 h the title compound **21** (58 mg, 0.49 mmol; 98%) was prepared.

When the oxidation was carried out with resin **4** according to the general procedure the title compound **21** was isolated in 96% yield. Likewise, use of resin **5** according to the general procedure afforded the title compound **21** in 21% yield. The remaining material was analysed to be the starting alcohol **18**.

1-(2-Methoxyphenyl)ethanol (22)

By treatment of 1-(2-methoxyphenyl)ethanol (**9**; 76 mg, 0.5 mmol) with reagent **6** (1.5 equivs.) and TEMPO (2.3 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 4.5 h the title compound **22** (73 mg, 0.49 mmol; 97%) was prepared.

When the oxidation was carried out with resin **4** according to the general procedure the title compound **22** was isolated in 96% yield. Likewise, use of resin **5** according to the general procedure afforded the title compound **22** in 30% yield. The remaining material was analysed to be the starting alcohol **19**.

Methyl 4,6-*O*-Benzylidene-2-deoxy-α-D-*erythro*-hexopyrano-3-uloside (27)

By treatment of methyl 4,6-*O*-benzylidene-2-deoxy-α-D-*ribo*-hexopyranoside (**23**; 50 mg, 0.19 mmol) with reagent **4** (2.5 equivs.) and TEMPO (0.9 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 18 h the title compound **27** (45 mg, 0.17 mmol, 90%) was prepared.

1,2:5,6-Di-*O*-isopropylidene-α-D-*ribo*-furano-3-ulose (28)

By treatment of 1,2:5,6-di-*O*-isopropylidene-*gluco*-furanose (**24**; 50 mg, 0.19 mmol) with reagent **4** (2.5 equivs.) and TEMPO (0.9 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 18 h the title compound **28** (42 mg, 0.16 mmol, 84%) was prepared.

2-[*tert*-Butyldimethylsilyloxy-1-(2*S*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2-methyl-tetrahydro-2-furanyl]ethanone (29)

By treatment of 2-[*tert*-butyldimethylsilyloxy-1-(2*S*,5*R*)-5-(*tert*-butyldimethylsilyloxymethyl)-2-methyltetrahydro-2-furanyl]ethanol (**25**; 38 mg, 0.09 mmol) with reagent **6** (2.5 equivs.) and TEMPO (0.4 mg, 1 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 12 h the title compound **29** (32 mg, 0.07 mmol; 86%) was prepared. Compound **29**: $[\alpha]_D^{20}$: −17.4° ($CHCl_3$, *c* 1); ^{1}H NMR (400 MHz, $CDCl_3$): $\delta = 4.68$ (dd, 2H, $J = 3.3$ Hz, 8-H), 3.79 (t, 1H, $J = 7.4$ Hz, 3-H), 3.41 (d, 1H, $J = 9.2$ Hz, 1-H), 3.30 (d, 1H, $J = 9.2$ Hz, 1-H′), 2.12 (m, 1H, 5-H′), 1.29 (br s, 3H, 6-Me), 0.91 (s, 9H, 10-Me′), 0.88 (s, 9H, 10-Me), 0.85 (s, 3H, 2-Me′), 0.83 (s, 3H, 2-Me), 0.08 (s, 6H, 9-Me′), 0.02 (s, 6H, 9-Me); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 211.8$ (d, C-7), 87.6 (q, C-6), 83.3 (d, C-3), 70.0 (t, C-1), 66.6 (t, C-8), 38.4 (q, C-2), 36.4 (t, C-5), 26.0 (t, C-4), 25.9 (4q, OTBS), 24.2 (q, Me), 21.0, 19.8 (2q, Me), 18.7, 18.4 (2 s, OTBS), −5.2, −5.4 (q, OTBS); HR-MS (ESI): calcd. for $C_{23}H_{48}O_4Si_2Na$: 467.2989 $[M + Na]^+$, found: 467.2979.

S-Camphor (30)

By treatment of *S*-borneol (**26**; 31 mg, 0.2 mmol) with reagent **6** (2.5 equivs.) and TEMPO (3 mg, 1 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 19 h the title compound **30** (30.3 mg, 0.20 mmol; 99%) was prepared.

2-Phenylacetic Acid (35)

By treatment of 2-phenylethanol (**7**; 62 mg, 0.5 mmol) with reagent **6** (4.0 equivs.) and TEMPO (2.3 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 4 h the title compound **35** (66 mg, 0.49 mmol, 98%) was prepared.

3-Phenylpropionic Acid (36)

By treatment of 3-phenylpropanol (**8**; 68 mg, 0.5 mmol) with reagent **6** (4.0 equivs.) and TEMPO (2.3 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 2.5 h the title compound **36** (70 mg, 0.45 mmol, 90%) was prepared.

Hexadecanoic Acid (37)

By treatment of hexadecanol (**9**; 120 mg, 0.5 mmol) with reagent **6** (4.0 equivs.) and TEMPO (2.3 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 2 h the title compound **37** (120 mg, 0.47 mmol, 94%) was prepared.

4-Methoxybenzoic Acid (38)

By treatment of 4-methoxybenzyl alcohol (**31**; 69 mg, 0.5 mmol) with reagent **5** (4.0 equivs.) and TEMPO (2.3 mg, 3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 at room temperature under nitrogen for 4.5 h a mixture of 4-methoxybenzoic acid (59%) and 4-methoxybenzaldehyde (41%) was obtained as judged by GC.

(*R*)-3-Benzyloxy-2-methylpropionic Acid (39)

By treatment of (*S*)-3-benzyloxy-2-methylpropan-1-ol (**10**; 90 mg, 0.5 mmol) with reagent **6** (4.0 equivs.), TEMPO (3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 (5 mL) at room temperature for 2.5 h the title compound **39** (96 mg, 0.495 mmol, 99%) was prepared. Compound **39**: oil; $[\alpha]_D^{20}$: −6.4° ($CHCl_3$, *c* 1) (ref[33]: $[\alpha]_D^{20}$: −8.5° ($CHCl_3$, *c* 3.65); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 10.81$ (br, 1H, COO*H*), 7.33–7.27 (m, 5H, Ph), 4.54 (s, 2H, PhC*H*$_2$), 3.66 (dd, $J = 9.2$, 7.2 Hz, 1H, 3-H), 3.53 (dd, $J = 9.2$, 5.8 Hz, 1H, 3-H′), 2.80 (m, 1H, 2-H), 1.21 (d, $J = 7.1$ Hz, 3H, Me); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 180.7$ (s, *C*OOH), 137.9 (s, Ar), 128.3, 127.6 (d, Ar), 73.2 (t, Ph*C*H$_2$), 71.5 (t, C-3), 40.1 (d, C-2), 13.7 (q, Me); HR-MS (ESI): calcd. for $C_{11}H_{13}O_3$: 193.0865 $[M-H]^-$, found: 193.0862; LR-MS (EI): *m/z* (%) = 194 (5) $[M]^+$, 176 (2) $[M-H_2O]^+$, 121 (10) $[C_8H_9O]^+$, 107 (100) $[C_7H_7O]^+$, 91 (98) $[C_7H_7]^+$. For additional spectroscopic and physical data refer to ref.[33]

(*R*)-3-(*tert*-Butyldiphenylsiloxy)-2-methylpropionic Acid (40)

By treatment of (*S*)-3-(*tert*-butyldimethylsiloxy)-2-methylpropan-1-ol (**32**; 30 mg, 0.09 mmol) with reagent **6** (4 equivs.), TEMPO (3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 (5 mL) at room temperature for 20 h the title compound **40** (31.3 mg, 0.09 mmol; 99%) was prepared after the resin **6** was washed with MeOH. Compound **40**: oil; $[\alpha]_D^{20}$: −3.7° (CH_2Cl_2, *c* 0.54); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 9.78$ (d, $J = 1.6$ Hz, 1H, COO*H*), 7.70–7.37 (m, 10H, PhH), 3.86 (dd, $J = 9.9$, 6.9 Hz, 1H, 3a-H), 3.77 (dd, $J = 9.9$, 5.7 Hz, 1H, 3b-H), 2.75 (ddd, $J = 7.0$, 5.7, 7.0 Hz, 1H, 2-H), 1.23 (d, $J = 7.0$ Hz, 3H, 4-H), 1.08 (s, 9H, 2′-H); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 180.2$ (s, *C*OOH), 135.4, 133.0, 129.5, 127.5 (4d, Ar), 65.4 (t, C-3), 42.0 (d, C-2), 26.5 (q, C-2′), 19.0 (s, C-1′), 13.1 (q, C-4); HR-MS (ESI): calcd. for $C_{20}H_{25}O_3Si$: 341.1573, found: 341.1587. For additional spectroscopic and physical data refer to ref.[34]

1,2:3,4-Di-*O*-isopropylidene-α-D-galacturonic Acid (41)

By treatment of 1,2:3,4-di-*O*-isopropylidene-α-D-*galacto*-pyranose (**11**; 130 mg, 0.5 mmol) with reagent **6** (4.0 equivs.), TEMPO (3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 (5 mL) at room temperature for 2.5 h the title compound **41** (131 mg, 0.479 mmol, 96%) was prepared. Compound **41**: colourless solid; mp 152 °C (ref.[35]: mp 157 °C); $[\alpha]_D^{20}$: −102.9° ($CHCl_3$, *c* 1) {ref.[34]: $[\alpha]_D^{20}$: −92° ($CHCl_3$, *c* 1.11); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.15$ (br, 1H, COO*H*), 5.65 (d, $J = 4.9$ Hz, 1H, 1-H), 4.69 (dd, $J = 7.6$, 2.5 Hz, 1H, 3-H), 4.64 (dd, $J = 7.6$, 2.0 Hz, 1H, 4-H), 4.47 (d, $J = 2.0$, 1H, 5-H), 4.40 (dd, $J = 4.9$, 2.5 Hz, 1H, 2-H), 1.54 (s, 3H, CH_3), 1.46 (s, 3H, CH_3), 1.35 (s, 6H, CH_3); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 171.3$ (s, *C*OOH), 110.4 [s, $(RO)_2CMe_2$], 109.7 (d, C-1), 96.7 [s, $(RO)_2CMe_2$], 71.9 (d, C-2), 70.9 (d, C-5), 70.8 (d, C-3), 68.5 (d, C-4), 26.3, 26.2, 25.1, 24.7 (q, Me); HR-MS (ESI): calcd. for $C_{12}H_{17}O_7$: 273. 0974 $[M-H]^-$, found: 273.0969. For additional spectroscopic and physical data refer to ref.[35]

Methyl 4-*O*-Benzoyl-6-carboxy-2,3-dideoxy-3-trifluoroacetamido-α-D-*ribo*-hexopyranoside (42)

By treatment of methyl 4-*O*-benzoyl-2,3-trideoxy-3-trifluoroacetamido-α-D-*ribo*-hexopyranoside (**33**; 28.9 mg, 76.5 μmol) with reagent **6** (4.0 equivs.), TEMPO (3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 (1 ml) at room temperature for 6 h the title compound **42** (27.7 mg, 70.8 μmol, 93%) was prepared. Compound **42**: oil; $[\alpha]_D^{20}$: +53.6° ($CHCl_3$, *c* 1); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 8.06$ (d, 1H, $J = 7.2$ Hz, CF_3CONH), 7.90 (d, 2H, $J = 7.2$ Hz, Ph), 7.54 (t, 1H, $J = 7.3$ Hz, Ph), 7. 39 (t, 2H, $J = 7.3$ Hz, Ph), 5.37 (dd, 1H, $J = 10.4$, 3.7 Hz, 4-H), 4.99 (m, 1H, 1-H), 4.84 (m, 1H, 3-H), 4.53 (d, 1H, $J = 10.4$ Hz, 5-H), 3.52 (s, 3H, OC*H*$_3$), 2.26 (m, 2H, 2-H), 2.05 (m, 2H, 2-H′); ^{13}C-NMR (100 MHz, $CDCl_3$): $\delta = 171.8$ (s, *C*OOH), 165.5 (s, Ph*C*O), 157.4 (q, $J_{C\text{-}F} = 37.3$ Hz, CF_3CO), 133.7 (s, Ar), 130.1, 129.3, 128.7 (d, Ar), 117.5 (q, $J_{C\text{-}F} = 288.0$ Hz, *C*F$_3$CO), 98.6 (d, C-1), 68.4 (d, C-4), 56.5 (d, C-5), 53.7 (q, O*C*H$_3$), 45.2 (d, C-3), 29.0 (t, C-2); HR-MS (ESI): calcd. for $C_{16}H_{15}F_3NO_7$: 390.0798 $[M-H]^-$, found: 390.0801.

Ethyl 6-Carboxy-2,3-dideoxy-α-D-*erythro*-hexopyranoside (43)

By treatment of ethyl 2,3-dideoxy-α-D-*erythro*-hexopyranoside (**34**; 35.8 mg, 0.20 mmol) with reagent **6** (3 equivs.), TEMPO (3 mol %) and conc. HCl (1 equiv.) in CH_2Cl_2 (5 mL) at room temperature for 18 h the title compound **43** (34.9 mg 0.18 mmol, 86%) was prepared after washing resin **6** with MeOH. Compound **43**: oil; $[\alpha]_D^{20}$: +85.7° ($CHCl_3$, *c* 1.78); ^1H NMR (400 MHz, $CDCl_3$): $\delta = 4.90$ (br d, $J = 2.6$ Hz, 1H, 1-H), 4.13 (d, 1H, $J = 9.4$ Hz, 5-H), 3.81–3.69 (m, 2H, OC*H*CHCH$_3$, 4-H), 3.49 (dq, 1H, $J = 9.6$, 7.1 Hz, OCHC*H*CH$_3$), 1.96–1.70 (m, 4H, 3-H, 2-H), 1.21 (t, 3H, $J = 7.1$ Hz, $OCH_aCH_bCH_3$); ^{13}C NMR (100 MHz, $CDCl_3$): $\delta = 174.4$ (s, *C*OOH), 96.5 (d, C-1), 71.2 (d, C-5), 67.3 (d, C-4), 63.2 (t, O*C*H$_2$CH$_3$), 28.5 (t, C-2), 25.7 (d, C-3), 14.9 (q, OCH$_2$*C*H$_3$); HR-MS (ESI): calcd. for $[M-H]^-$: 189.0763, found: 189.0768.

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