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One-pot conversion of activated alcohols into 1,1-dibromoalkenes and terminal alkynes using tandem oxidation processes with manganese dioxide

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Abstract—Approaches to the preparation of C_1-homologated dibromoalkenes and terminal alkynes from activated alcohols using one-pot tandem oxidation processes (TOPs) with manganese dioxide are outlined. The conversion of alcohols into dibromoalkenes is described using dibromomethyltriphenylphosphonium bromide and the formation of terminal alkynes was achieved via a sequential one-pot, two-step process utilising the Bestmann–Ohira reagent.
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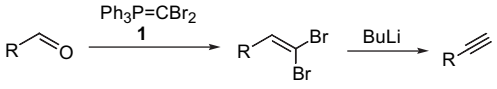
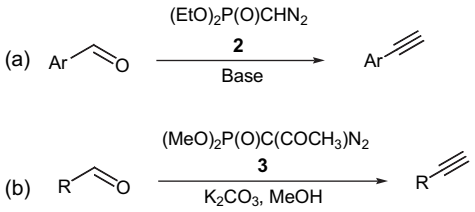
1. Introduction

Terminal alkynes are of great industrial and academic importance, both as versatile synthetic building blocks and as commercial products. Some time ago, Corey and Fuchs demonstrated that terminal alkynes can be prepared from the corresponding dibromoalkenes through treatment with *n*-butyllithium.[1] The dibromoalkenes can themselves be obtained by a C_1-homologation reaction of aldehydes (via the Ramirez procedure[2] using dibromomethylenephosphorane **1**), thus offering a convenient and simple route to the homologated terminal alkyne products from aldehydes (Scheme 1). However, the need for strong bases to dehydrohalogenate the intermediate 1,1-dibromoalkenes can limit the generality of the Corey–Fuchs procedure.



Scheme 1.

More recently, diazoalkyl phosphonate reagents have been introduced for the conversion of aldehydes into terminal alkynes.[3–9] These reagents have gained rapid acceptance[9] due to their accessibility, the one-step nature of the transformation and the mild nature of the reaction conditions. Seyferth and Gilbert[3] and Colvin[4] first showed that aldehydes could be converted into terminal alkynes using dialkyl diazomethylphosphonates (e.g., **2**, Scheme 2a). After deprotonation, a Horner–Wadsworth–Emmons-type olefination generates an unstable diazoalkene, which after thermal loss of nitrogen gives an alkylidene carbene, which then undergoes 1,2-rearrangement to provide the product alkyne.[5]



Scheme 2.

More recently, the groups of Ohira[6] and Bestmann[7] reported a valuable modification to the original Seyferth–Gilbert procedure, utilising dimethyl 1-diazo-2-oxopropylphosphonate **3** (Bestmann–Ohira reagent, Scheme 2b), a stable reagent readily prepared from commercially available precursors.[8] This method represents a significant improvement as alkynes can be directly synthesised at rt from the Bestmann–Ohira reagent in $MeOH/K_2CO_3$ via the in situ generation of **2**. It is noteworthy that, while previously only aromatic aldehydes could be used as substrates in this reaction, the development of **3** allowed the extension of the methodology to a range of alkyl aldehydes.

We recently initiated a programme to develop novel one-pot manganese dioxide-mediated tandem oxidation processes (TOPs), leading directly from primary alcohols to a range

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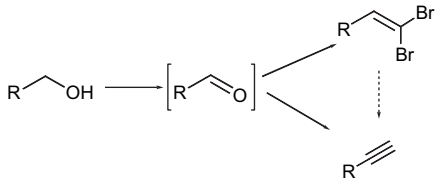
of synthetically useful functionalities (alkenes, imines, etc.) via in situ trapping of the intermediate aldehydes.[10] One-pot reaction sequences are of great importance to organic chemistry and offer many practical advantages over conventional stepwise transformations. These one-pot tandem reactions have significant cost/time benefits (reducing solvent waste, etc.). In addition, one-pot methodologies can also be used to access volatile, toxic or unstable intermediates, which can be elaborated in situ, thus avoiding problematic isolations. Furthermore, given the fact that there are many more commercially available alcohols than aldehydes,[11] TOPs are becoming an increasingly important tool for the synthetic organic chemist.[10]

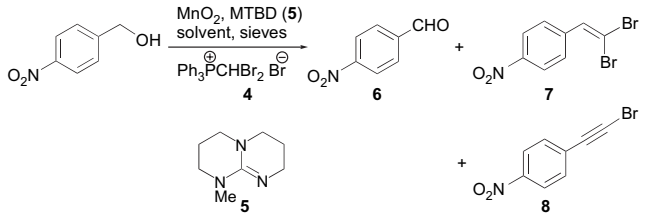
2. Results and discussion

With the above factors in mind, we embarked on an investigation to develop TOPs which provide the C_1-homologation of alcohols to give the corresponding dibromoalkenes and alkynes (Scheme 3).



Scheme 3.

We commenced this investigation by studying the direct conversion of alcohols into dibromoalkenes.[12] Dibromoalkenes are usually prepared by treating aldehydes with phosphorane **1**, generated from the reaction of triphenylphosphine and carbon tetrabromide[2] or, as in the method developed by Dolhem et al.,[13a] using phosphonium salt **4** and a base.[13] As we have previously developed TOPs utilising phosphonium salts with added bases,[14] and as phosphonium salt **4** can be stored on the bench for several months without decomposition, its use was investigated first (Scheme 4, Table 1). We chose to initially investigate the homologation of the electron-deficient aromatic alcohol, *p*-nitrobenzyl alcohol, and chose 1-methyl-1,5,7-triazabicyclo[4.4.0]dec-5-ene (MTBD, **5**)[15] as the in situ base as we had previously shown its efficiency in manganese dioxide TOP–Wittig reactions.[14] Thus, stirring *p*-nitrobenzyl alcohol (1 equiv), active MnO_2 (10 equiv), phosphonium salt **4** (3.0 equiv), MTBD **5** (2.3 equiv) and 4 Å mol sieves in THF at reflux for 15 h, afforded the desired dibromoalkene **7**, but in a disappointing 24% yield (Table 1, entry i). Interestingly, however, bromoalkyne **8** was also isolated in 10% yield indicating that MTBD may be basic enough to also carry out the elimination



Scheme 4.

Table 1. Optimisation of the conversion of *p*-nitrobenzyl alcohol into dibromoalkene **7**

Entry	Conditions	**6** (%)	**7** (%)	**8** (%)
i	THF, 2.3 equiv MTBD, 3.0 equiv **4**, reflux, 15 h	0	24	10
ii	CH_2Cl_2, 1.5 equiv MTBD, 2.2 equiv **4**, reflux, 14 h	ca. 50	30	0
iii	CH_2Cl_2, 1.5 equiv MTBD, 3.0 equiv **4**, reflux, 14.5 h	Trace	80	0
iv	CH_2Cl_2, 1.5 equiv MTBD, 3.5 equiv **4**, reflux, 16 h	0	86	0
v	$CHCl_3$, 1.5 equiv MTBD, 3.5 equiv **4**, reflux, 15 h	0	56	0

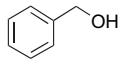
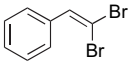
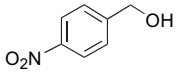
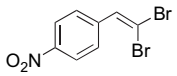
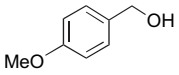
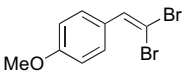
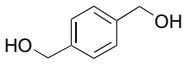
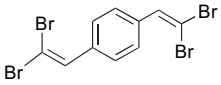
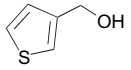
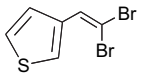
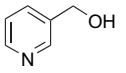
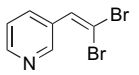
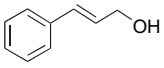
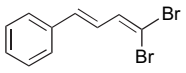
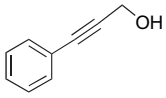
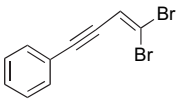
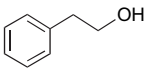
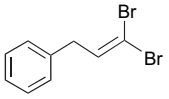
of HBr and thus form bromoalkynes in a one-pot, 3-step sequence from activated alcohols (see later discussion).

In an attempt to optimise the yield of dibromoalkene **7**, the reaction was then repeated by reducing the amounts of MTBD **5** and Wittig salt **4** to 1.5 and 2.2 equiv, respectively (entry ii). Dichloromethane was then found to be the solvent of choice to circumvent solubility issues and increase ease of work-up. Gratifyingly, this resulted in an improved yield of 30% of dibromoalkene **7** with no bromoalkyne **8** detected. However, *p*-nitrobenzaldehyde **6** was also recovered and therefore further optimisation of the stoichiometries was investigated. Increasing the amounts of Wittig salt **4** used to 3.0 equiv resulted in a marked increase in the yield of dibromoalkene **7** (80%) with only a trace of aldehyde **6** remaining (entry iii). Finally, increasing the amounts of Wittig salt further to 3.5 equiv resulted in complete consumption of intermediate *p*-nitrobenzaldehyde and an isolated yield of 86% of the desired dibromoalkene **7** (entry iv). In an attempt to reduce the reaction time, the use of chloroform as a reaction solvent was also investigated; dibromoalkene **7** was isolated in a respectable yield but the dichloromethane procedure was preferred for *p*-nitrobenzyl alcohol (entry v). However, in most other examples, chloroform was the preferred solvent.

The scope and limitations of this procedure leading to dibromoalkenes was next investigated using a range of alcohols (Table 2).

Table 2 shows that moderate to excellent yields of the dibromoalkenes were obtained directly from a range of activated alcohols including electron-neutral, electron-deficient and electron-rich aromatic examples (entries i–iii). Aromatic diols have proved to be versatile substrates as two directional building blocks and 4-hydroxymethylbenzyl alcohol gave an excellent 86% yield over the four-step, one-pot process (entry iv).[16] Heterocyclic (entries v and vi) and allylic and propargylic examples (entries vii and viii) have also been carried out in good to excellent yield, further demonstrating the scope of the procedure. An aliphatic example was also studied but the reaction was slow and low yielding, indicating a limitation to this methodology (entry ix). However, the synthetic utility of this one-pot method is emphasised by the fact that comparable, or indeed better (entries iv[17] and vi[18]), yields can be obtained directly from the substrate alcohol when compared to those previously reported in the literature for the conversion from the aldehyde. The low yield obtained from *p*-methoxybenzyl alcohol (entry iii) deserves comment, however. This is presumably due to the reduced

Table 2. Investigation of the scope and limitations of the oxidation-dibromoalkene synthesis[a]

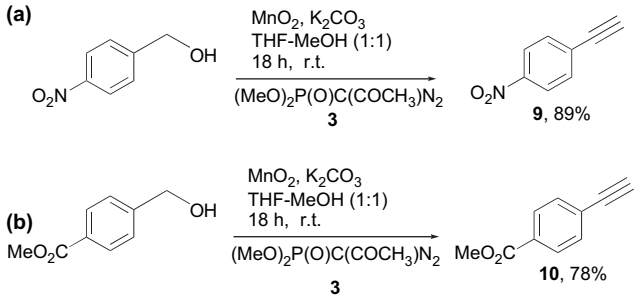
Entry	Alcohol	Product	Reaction time (h)	Isolated yield (%)[a]
i			18	73
ii			17	86[b]
iii			18	46 (64)[c]
iv			20	86
v			18	60
vi			17	84[d]
vii			17	84
viii			3.5	65[e]
ix			36	14

[a] Reaction carried out in refluxing chloroform unless otherwise stated.
[b] In CH_2Cl_2 (56% in $CHCl_3$).
[c] Yield calculated with respect to recovered *p*-methoxybenzaldehyde.
[d] In CH_2Cl_2 (28% in $CHCl_3$).
[e] 1-Bromo-3-phenylprop-1-yne also formed (5%).

electrophilicity of the intermediate *p*-methoxybenzaldehyde. Also, it should be pointed out that with the electron-deficient example (entry ii), much higher yields were achieved by carrying out the reaction in refluxing dichloromethane rather than chloroform; the lower temperature presumably minimises side-reactions of the reactive electron-deficient dibromoalkene product. It should be noted that dibromoalkenes are of increasing importance[19] being readily converted into *Z*-bromoalkenes,[20] *E*-bromoalkenes,[21] trisubstituted alkenes,[22] bromoalkynes,[23] disubstituted alkynes,[22] amidines and carboxylic acid derivatives:[24] we feel that this TOP sequence should provide a useful new procedure for obtaining these valuable synthetic intermediates.

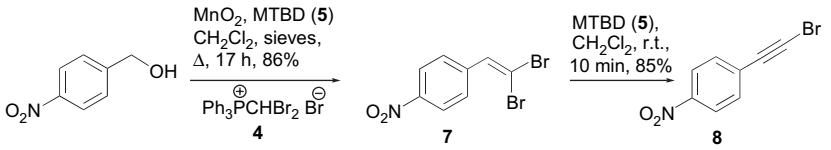
With a successful protocol for the preparation of a range of C_1-homologated dibromoalkenes from activated alcohols in hand, we moved on to investigate modifications to the procedure, which would give access to bromoalkynes (and possibly alkynes, as in the Corey–Fuchs procedure). Initially, we concentrated on the reaction of *p*-nitrobenzyl alcohol described earlier (Scheme 4), which produced 1-bromoalkyne **8** in 10% yield (Table 1, entry i). However, despite investigating a range of conditions, attempts to increase the yield of bromoalkyne **8** to an acceptable level, via a one-pot procedure, proved disappointing (maximum yield, 35%). Nevertheless, a two-step process was developed in which dibromoalkene **7** was first isolated and purified after the TOP sequence and then treated with MTBD (1.5 equiv at rt) to furnish the desired bromoalkyne **8** in 85% yield, 73% overall from *p*-nitrobenzyl alcohol (Scheme 5).

This inability to develop a one-pot procedure to C_1-homologated terminal alkynes from alcohols via a modified Corey–Fuchs approach encouraged us to investigate the in situ use of diazophosphonate reagents.[25] Initial studies using the Seyferth–Gilbert dialkyl diazomethylphosphonate reagent **2** in a TOP sequence were unsuccessful. We therefore moved on to study the use of the Bestmann–Ohira reagent **3** in TOP sequences. We first developed an improved procedure for preparing the Bestmann–Ohira reagent **3**, which utilised commercially available dimethyl (2-oxopropyl)phosphonate and proceeded under mild conditions in high yield (97% on a 5–10 g scale) using Koskinen's diazo-transfer procedure.[26]



Scheme 6.

We initially explored the TOP sequence illustrated in Scheme 6, in which the alcohol, MnO_2 and the Bestmann–Ohira reagent **3** were mixed together so that the intermediate aldehyde would be trapped as soon as it was generated. Using *p*-nitrobenzyl alcohol (1 equiv), MnO_2 (5 equiv), Bestmann–Ohira reagent **3** (1.2 equiv) and K_2CO_3 (2 equiv) in a mixture of THF/MeOH (1:1) at rt for 18 h we were delighted to find that the desired terminal alkyne **9** was obtained in 89% isolated yield (Scheme 6a). Remarkably, this transformation proceeds smoothly without rigorously anhydrous solvents, although an inert atmosphere is used to prevent terminal alkyne dimerisation. We also established that the presence of an excess of methanol, which deacetylates the



Scheme 5.

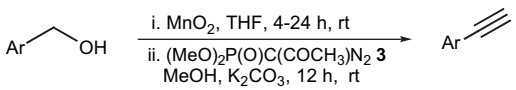
Bestmann–Ohira reagent, is crucial for success — reactions in THF alone failed to generate any alkyne. In addition, attempts to replace MeOH by other alcohols failed; when *iso*-propanol was employed as co-solvent the *p*-nitrobenzyl alcohol was acetylated by the Bestmann–Ohira reagent.

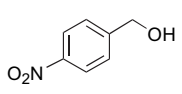
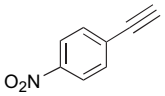
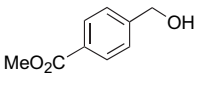
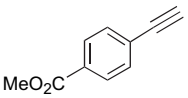
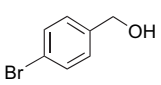
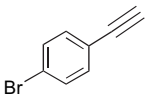
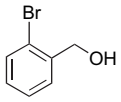
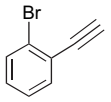
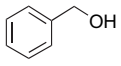
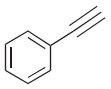
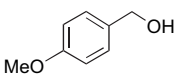
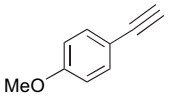
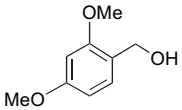
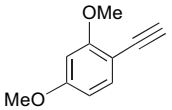
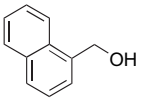
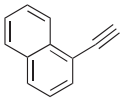
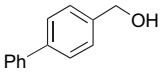
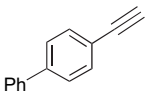
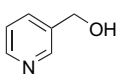
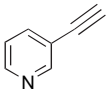
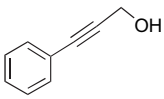
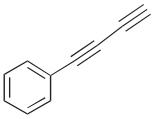
We therefore moved on to investigate the scope of this procedure, and first studied other benzylic alcohols. Unfortunately, the presence of methanol reduces the activity of the manganese dioxide and we quickly demonstrated that this precludes the efficient oxidation of many alcohols to the intermediate aldehydes. For this reason, the only other satisfactory substrate for this TOP sequence was found to be 4-carbomethoxybenzyl alcohol, which gave alkyne **10** in 78% yield (Scheme 6b). Other benzyl alcohol derivatives with electron-withdrawing substituents such as *p*-bromobenzyl alcohol reacted only partially, while benzyl alcohol itself, and derivatives containing electron-donating substituents, did not give any observable alkyne product. Attempts to modify the reaction conditions proved fruitless. Interestingly, when forcing conditions were employed (large excess of MnO_2 in refluxing solvent), methyl esters were isolated as the main reaction products in moderate yields (e.g., methyl *p*-bromobenzoate from *p*-bromobenzyl alcohol in 35% yield); however, we have previously described a TOP procedure using MnO_2/NaCN/MeOH, which can be employed to convert benzyl alcohols directly in the corresponding methyl esters rather more efficiently.[27]

Given the above observations, we decided to investigate a sequential one-pot procedure in which the oxidation was carried out using MnO_2/THF prior to addition of the Bestmann–Ohira reagent in methanol. This modification produced a procedure that was more generally applicable (Table 3). Thus, the oxidations were accomplished using 5 equiv of MnO_2 in THF at rt and once all of the alcohol had been converted into the intermediate aldehyde (TLC monitoring, 3–24 h), methanol was added followed by K_2CO_3 (2 equiv) and the Bestmann–Ohira reagent (1.2 equiv). After stirring for a further 12–17 h, the terminal alkynes were obtained in good to excellent yield. It must be noted that the Bestmann–Ohira alkynylation proceeds smoothly in the presence of the unreacted MnO_2.

The results in Table 3 clearly show that the one-pot, two-step sequence proceeds efficiently (56–99% isolated yields) and that it is a widely applicable general procedure with activated alcohols. Electron-withdrawing functional groups increase activity towards oxidation of the benzylic alcohols, leading to the highest yields of alkyne (entries i–iv). Good to excellent yields were also obtained using benzylic alcohols bearing electron-donating groups (entries vi and vii), and benzyl alcohol itself (entry v). Success was also achieved using naphthalene-1-methanol (entry viii), 4-phenylbenzyl alcohol (entry ix) and a heteroaromatic example, pyridine 3-methanol (entry x). Entries i and ii were noteworthy cases as the reactions were so efficient that products were isolated analytically pure (by NMR spectroscopy) in high yield after a simple extractive work-up and further chromatographic purification was not required. Purification by chromatography was difficult when the terminal alkyne products were volatile, particularly when benzyl alcohol was employed (entry v); in this case phenylacetylene was isolated in 87%

Table 3. Sequential one-pot MnO_2 oxidation/Bestmann–Ohira alkynylation procedure[a]



Entry	Alcohol	Product	Isolated yield (%)[a]
i			99[b]
ii			97[b]
iii			85
iv			94
v			87[c]
vi			56
vii			59[d]
viii			89
ix			92
x			68[d]
xi			59[d]

[a] Carried out on a 0.15–0.50 mmol scale, unless stated otherwise. The oxidation was left for 4 h (unless stated otherwise), the alkynylation overnight (12–17 h). Yields refer to isolated products. Spectroscopic/analytical data of alkynes are in agreement with those reported.

[b] Chromatographic purification not required; product essentially pure after extractive work-up.

[c] Carried out in a 10 mmol scale and the alkyne purified by distillation.

[d] Longer oxidation times required; 8 h for entry vii, 10 h for entry x and 24 h for entry xi.

yield by direct distillation from the crude mixture, although this procedure needed to be carried out on a 10 mmol scale. Reaction times for the oxidation step with aromatic substrates varied from 3 to 10 h, with 2,4-dimethoxybenzyl alcohol and pyridine 2-methanol taking the longest (8 and 10 h, respectively). On the other hand, this transformation does not appear to be over-sensitive to steric factors as hindered *ortho*-substituted alcohols underwent oxidation–alkynylation in good to excellent yields (entries iv, vii and viii). The efficient preparation of 4-bromo- and 2-bromo-phenylacetylene (entries iii and iv) are noteworthy. These and related compounds are commonly prepared through transition metal-mediated cross-coupling transformations (i.e., Sonogashira–Hagihara, Negishi, alkynyl Grignard, etc.)[28] with the requirement for anhydrous solvents and inert atmospheres, expensive catalysts, and the need for alkyne protection to prevent homocoupling.

Finally, it should be noted that, according to the literature,[7] allylic alcohols cannot be employed in this methodology because methanol adds to the intermediate α,β-unsaturated aldehydes. Unactivated alcohols are also unreactive under these conditions, but 3-phenylpropargyl alcohol was successfully converted into 1-phenyldiyne in 59% yield, although a long oxidation time (24 h) was required (entry xi).

In conclusion, we have developed simple and practical TOP sequences for the one-pot preparation of synthetically important 1,1-dibromoalkenes from activated alcohols, MnO_2, phosphonium salt **4** and MTBD **5**. Furthermore, we have developed a very mild and straightforward sequential one-pot method for the conversion of a variety of benzylic, heterocyclic and propargylic alcohols into their corresponding homologated terminal alkynes in good to excellent yield using MnO_2 and the Bestmann–Ohira reagent **3**. In addition, a TOP has been developed for the conversion of benzyl alcohols substituted by highly electron-withdrawing groups (nitro, ester) on the aromatic ring into the corresponding terminal alkynes. We are currently applying these procedures in target molecule synthesis.

3. Experimental

3.1. General

NMR spectra were recorded on JEOL EX-270 or EX-400 spectrometers using $CDCl_3$ as solvent unless otherwise stated. Tetramethylsilane or residual $CHCl_3$ were used as the internal standard. IR spectra were recorded on an ATI Mattson Genesis FTIR or ThermoNicolet IR 100 spectrometer. Low-resolution electron impact (EI) spectra were obtained on a Kratos MS 25 spectrometer. Chemical ionisation (CI) and high-resolution mass spectra were recorded on a Micromass Autospec spectrometer. Melting points were determined on a GallenKamp melting point apparatus and are uncorrected. Flash column chromatography was carried out using silica gel 35–70 mesh, which was purchased from Fluka. All reagents were purchased from commercial sources and were used without further purification unless stated in the text. Activated manganese dioxide was obtained from Aldrich, catalogue number 21,764-6. PE is petroleum ether (bp 40–60 °C). Dibromomethyltriphenylphosphonium bromide **4** was prepared using the published[13a] procedure.

3.2. General procedure for synthesis of dibromoalkenes from alcohols

To a suspension of activated manganese dioxide (867 mg, 9.97 mmol), phosphonium salt **4** (1.805 g, 3.50 mmol) and ground 4 Å molecular sieves (100 mg) in solvent (CH_2Cl_2 or chloroform) (10 mL) was added MTBD **5** (0.22 mL, 1.50 mmol). The reaction mixture was heated at reflux for 30 min, cooled to rt, then a solution of alcohol (1 mmol) in solvent (5 mL) added. The reaction mixture was then heated at reflux for the time specified, cooled to rt and filtered through Celite®. The resulting filtrate was then pre-loaded on to silica and the dibromoalkenes were purified by silica chromatography, eluting with EtOAc/PE.

3.2.1. 1,1-Dibromostyrene (Table 2, entry i). Reaction time of 18 h in $CHCl_3$; chromatography (10% EtOAc/PE) afforded the title compound (191 mg, 73%) as a pale yellow oil; R_f 0.61 (20% EtOAc/PE); ^{1}H NMR data consistent with those published.[24]

3.2.2. 1,1-Dibromo-2-(4-nitrophenyl)ethene 7 (Table 2, entry ii). Reaction time of 17 h in CH_2Cl_2; chromatography (10% EtOAc/PE) afforded the title compound **7** (264 mg, 86%) as a pale yellow solid; mp 103–104 °C (lit.[24] 104–105 °C); R_f 0.58 (10% EtOAc/PE); ^{1}H NMR data consistent with those published.[24]

3.2.3. 1-(2,2-Dibromo-vinyl)-4-methoxy-benzene (Table 2, entry iii). Reaction time of 18 h in $CHCl_3$; chromatography (10% EtOAc/PE) afforded the title compound (187 mg, 46%, 64% based on recovered *p*-methoxybenzaldehyde) as a pale yellow solid; mp 39–40 °C (lit.[24] 39–40 °C); R_f 0.56 (20% EtOAc/PE); ^{1}H NMR data consistent with those reported in the literature.[24]

3.2.4. 1,4-Bis-(2,2-dibromovinyl)benzene (Table 2, entry iv). Reaction time of 20 h in $CHCl_3$; chromatography (10% EtOAc/PE) afforded the title compound (383 mg, 86%) as a pale yellow solid; mp 97 °C (lit.[29] 98–99 °C); R_f 0.67 (20% EtOAc/PE); ^{1}H NMR data consistent with those reported in the literature.[29]

3.2.5. 3-(2,2-Dibromoethenyl)thiophene (Table 2, entry v). Reaction time of 18 h in $CHCl_3$; chromatography (10% EtOAc/PE) afforded the title compound (161 mg, 60%) as a pale yellow oil; R_f 0.58 (20% EtOAc/PE); ^{1}H NMR data consistent with those reported in the literature.[30]

3.2.6. 3-(2,2-Dibromoethenyl)pyridine (Table 2, entry vi). Reaction time of 17 h in $CHCl_3$; chromatography (40% EtOAc/PE) afforded the title compound (221 mg, 84%) as a pale yellow solid; mp 55–57 °C (lit.[18] 57–59 °C); R_f 0.23 (40% EtOAc/PE); ^{1}H NMR data was consistent with those reported in the literature.[18]

3.2.7. (4,4-Dibromo-buta-1,3-dienyl)benzene (Table 2, entry vii). Reaction time of 17 h in CH_2Cl_2; chromatography (10% EtOAc/PE) afforded the title compound (242 mg, 84%) as a pale yellow solid; mp 45 °C (lit.[31] 55–56 °C); R_f 0.63 (20% EtOAc/PE); ^{1}H NMR data consistent with those reported in the literature.[31]

3.2.8. (4,4-Dibromo-but-3-en-1-yl)benzene (Table 2, entry viii). Reaction time of 3.5 h in $CHCl_3$; chromatography (eluting with 10% EtOAc/PE) afforded the title compound (186 mg, 65%) as a pale yellow oil; R_f 0.62 (20% EtOAc/PE); ^{1}H NMR data consistent with those reported in the literature.[32]

3.2.9. (3,3-Dibromoprop-2-enyl)benzene (Table 2, entry ix). Reaction time of 36 h in $CHCl_3$; chromatography (10% EtOAc/PE) afforded the title compound (39 mg, 14%) as a pale yellow oil; R_f 0.56 (20% EtOAc/PE); ^{1}H NMR data consistent with those reported in the literature.[33]

3.2.10. 1-Bromo-2-(4-nitrophenyl)ethyne 8. To a solution of 1,1-dibromo-2-(4-nitrophenyl)ethene **7** (40 mg, 0.13 mmol) in dichloromethane (2 mL), MTBD **5** (28 μL, 0.20 mmol) was added dropwise. The reaction was stirred for 10 min and then diluted with saturated aq NH_4Cl (5 mL). The resulting mixture was extracted with dichloromethane (3×10 mL) and the combined organic extracts were dried over Na_2SO_4 and concentrated in vacuo to give a crude orange solid that was purified by silica chromatography (eluting with 5% EtOAc/PE) to afford the title compound (25 mg, 85%) as a white solid; mp 168–169 °C (lit.[34] 172 °C); R_f 0.28 (5% EtOAc/PE); ^{1}H NMR data consistent with those reported in the literature.[24]

3.2.11. Bestmann–Ohira reagent 3. Dimethyl (2-oxopropyl)phosphonate (Lancaster, 97%, 5 g, 30 mmol) was dissolved in dry CH_3CN (50 mL) and cooled to 0 °C (ice-bath) under argon. K_2CO_3 (4.58 g, 33 mmol) and then tosyl azide (6.53 g, 33 mmol) [Caution: highly toxic and explosive; handle in a well ventilated fume cupboard wearing protective gloves] were added sequentially in single portions and the resulting mixture was stirred at rt for 3 h. The solvent was eliminated in vacuo and the crude redissolved in dichloromethane (50 mL) and washed with water (50 mL). The organic layer was washed additionally with brine (50 mL), dried over $MgSO_4$, filtered and the solvent removed in vacuo. After purification by chromatography on silica gel (EtOAc/PE, 7:3), the Bestmann–Ohira reagent **3** was isolated as a yellow oil (5.58 g, 29 mmol, 97%); R_f 0.28 (EtOAc). Spectroscopic and analytical data were consistent with those reported.[8]

3.2.12. 1-Ethynyl-4-nitrobenzene 9 by tandem procedure. *p*-Nitrobenzyl alcohol (50 mg, 0.33 mmol) was dissolved in dry THF (3 mL). Anhydrous MeOH (3 mL) was added followed by activated MnO_2 (142 mg, 1.6 mmol), dry K_2CO_3 (90 mg, 0.66 mmol) and Bestmann–Ohira reagent **3** (75 mg, 0.4 mmol). The heterogeneous mixture was stirred at rt for 18 h under argon. The crude mixture was filtered through a short Celite® pad (dichloromethane eluent). The volatiles were removed in vacuo, the residue redissolved in dichloromethane (10 mL) and then washed with 5% aq $NaHCO_3$ solution (10 mL) and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent removed under reduced pressure. The residue was purified by chromatography on silica gel (EtOAc/PE, 1:9) giving title compound as a white solid (43 mg, 89%); mp 150–151 °C (lit.[35] 150–150.5 °C); R_f 0.7 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[35]

3.2.13. 1-Ethynyl-4-carbomethoxybenzene 10 by tandem procedure. *p*-Carboxymethoxy benzyl alcohol (77 mg, 0.46 mmol) was dissolved in dry THF (5 mL). Anhydrous MeOH (2 mL) was added to the homogeneous solution, followed by activated MnO_2 (201 mg, 2.3 mmol), dry K_2CO_3 (128 mg, 0.9 mmol) and finally Bestmann–Ohira reagent **3** (125 mg, 0.65 mmol). The mixture was efficiently stirred at rt for 18 h under argon. MnO_2 was removed by filtration through a short Celite® pad (dichloromethane eluent). The volatiles were removed under reduced pressure, the residue redissolved in dichloromethane (10 mL) and washed with 5% aq $NaHCO_3$ solution (20 mL) and brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was eliminated in vacuo. The residue was purified by chromatography on silica gel (EtOAc/PE, 1:9). The title compound was obtained as a white solid (57 mg, 78%); mp 94 °C; lit.[36] 93–95 °C); R_f 0.68 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[37]

3.3. General procedure for the synthesis of terminal alkynes from activated alcohols by sequential, one-pot method

Activated alcohol (0.15–0.50 mmol) was dissolved in dry THF (6 mL) and activated MnO_2 (142 mg, 1.6 mmol, 5 equiv) was added. The heterogeneous mixture was efficiently stirred at rt for the time specified (4–24 h). Anhydrous MeOH (6 mL) was added, followed by dry K_2CO_3 (84 mg, 0.6 mmol) and Bestmann–Ohira reagent **3** (70 mg, 0.36 mmol). The reaction was stirred overnight (12–17 h) at rt under argon and the crude mixture filtered through a short Celite® pad using dichloromethane eluent. The organic solvent was removed in vacuo, the residue redissolved in dichloromethane (10 mL) and then washed with 5% aq $NaHCO_3$ (10 mL) and then brine. The organic layer was dried over anhydrous $MgSO_4$, filtered and the solvent was removed under reduced pressure to give the product alkyne. If necessary, the alkyne could be purified further by silica chromatography, eluting with EtOAc/PE. In the case of phenylacetylene, the reaction was carried out on a 10 mmol scale and purification was carried by direct distillation of the crude reaction mixture (see later).

3.3.1. 1-Ethynyl-4-nitrobenzene (Table 3, entry i). 0.15 mmol scale, oxidation time of 4 h; chromatography was not required; title compound obtained as a white solid (22 mg, 99%); mp 150–151 °C (lit.[35] 150–150.5 °C); R_f 0.7 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[35]

3.3.2. 1-Ethynyl-4-carbomethoxybenzene (Table 3, entry ii). 0.15 mmol scale, oxidation time of 4 h; chromatography was not required; title compound obtained as a white solid (23 mg, 97%); mp 94 °C (lit.[36] 93–95 °C); R_f 0.68 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[37]

3.3.3. 1-Ethynyl-4-bromobenzene (Table 3, entry iii). 0.30 mmol scale, oxidation time of 4 h; chromatography (10% EtOAc/PE) afforded the title compound (46 mg, 85%) as a white wax; R_f 0.73 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[28]

3.3.4. 1-Ethynyl-2-bromobenzene (Table 3, entry iv). 0.30 mmol scale, oxidation time of 4 h; chromatography (10% EtOAc/PE) afforded the title compound (51 mg, 94%) as a colourless oil; R_f 0.72 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[38]

3.3.5. Phenylacetylene (Table 3, entry v). 10 mmol scale, oxidation time of 4 h; distillation from the crude reaction mixture gave the title compound (890 mg, 87%) as a colourless oil; spectroscopic data consistent with those reported in the literature.[39]

3.3.6. 1-Ethynyl-4-methoxybenzene (Table 3, entry vi). 0.36 mmol scale, oxidation time of 4 h; chromatography (10% EtOAc/PE) gave the title compound (27 mg, 56%) as a white waxy solid; R_f 0.76 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[40]

3.3.7. 1-Ethynyl-2,4-dimethoxybenzene (Table 3, entry vii). 0.33 mmol scale, oxidation time of 8 h; chromatography (10% EtOAc/PE) gave the title compound (31 mg, 59%) as a colourless oil; R_f 0.6 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[41]

3.3.8. 1-Naphthylacetylene (Table 3, entry viii). 0.23 mmol scale, oxidation time of 4 h; chromatography (10% EtOAc/PE) gave the title compound (31 mg, 89%) as a colourless oil; R_f 0.65 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[42]

3.3.9. 1-Ethynyl-4-phenylbenzene (Table 3, entry ix). 0.20 mmol scale, oxidation time of 4 h; chromatography (10% EtOAc/PE) gave the title compound (33 mg, 92%) as a colourless oil; R_f 0.6 (50% EtOAc/PE); spectroscopic data consistent with those reported in the literature.[43]

3.3.10. 3-Ethynyl pyridine (Table 3, entry x). 0.50 mmol scale, oxidation time of 10 h; chromatography (10% EtOAc/PE) gave the title compound (35 mg, 68%) as a white waxy solid; R_f 0.5 (EtOAc); spectroscopic data consistent with those reported in the literature.[44]

3.3.11. Buta-1,3-diynyl-benzene (Table 3, entry xi). 0.50 mmol scale, oxidation time of 24 h; chromatography (10% EtOAc/PE) gave the title compound (37 mg, 59%) as a colourless liquid; R_f 0.75 (EtOAc); spectroscopic data consistent with those reported in the literature.[45]

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