Regioselective Electrochemical Cyclobutanol Ring Expansion to 1-Tetralones

Alessia Petti,[‡ [b]] Philipp Natho,[‡ [a]] Kevin Lam [b] and Philip J. Parsons*[a]

‡These authors contributed equally

Dedication ((optional))

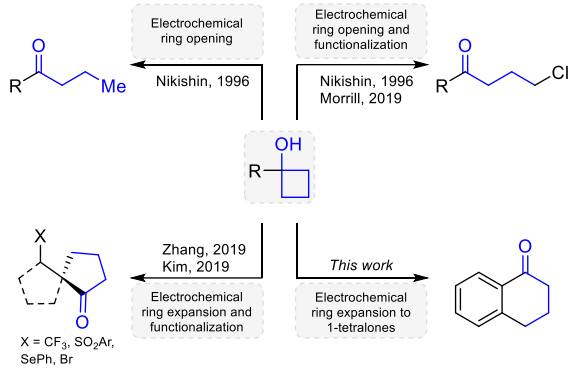
[a] Philipp Natho, Prof. Philip J. Parsons*
Department of Chemistry
Imperial College London
Molecular Sciences Research Hub, W12 0BZ, London, United Kingdom
E-mail: p.parsons@imperial.ac.uk
https://www.imperial.ac.uk/people/p.parsons
[b] Alessia Petti, Dr. Kevin Lam
School of Science
University of Greenwich
Chatham Maritime ME4 4TB, United Kingdom
E-mail: k.lam@gre.ac.uk

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

Abstract: A mild electrochemical method for the regioselective preparation of 1-tetralones under environmentally friendly conditions from readily available cyclobutanols was developed. A series of aromatic and heteroaromatic 1-tetralones was accessed through ring expansion of the functionalized cyclobutanols *via* electrochemical generation of alkoxy radicals and intramolecular cyclization.

The use of electricity as a driving force for non-spontaneous organic reactions has its roots in the early 19th century with Kolbe's seminal work on the electrolysis of aliphatic carboxylic acids.[1–3] Although a plethora of synthetic transformations have since been developed,[4–7] including numerous applications in industry,[8–10] the potential of preparative organic electrochemistry remains underutilized. However, with the advent of easily accessible standardized electrochemical set-ups and the growing interest toward greener, safer and more cost-efficient processes,[11] this discipline has recently experienced a renaissance.[3,4,12] Indeed, the need of toxic and expensive reagents or harsh reaction conditions can be significantly diminished when electric current is used; in particular when this is provided by renewable sources. Examples of recently developed electrochemical protocols include the mild synthesis of orthoesters,[13] allylic oxidation of alkenes,[14] synthesis of 2-pyrrolidinones,[15] or the fluorination of sp^3-carbon centres.[16]

In line with the synthetic community's progression toward milder synthetic techniques, the functionalization of the cyclobutanol ring under electrochemical conditions has gained particular attention (Scheme 1).[17–22] The relief of ring strain (strain energy of 26.3 kcal mol^{-1})[23] and the formation of a strong carbonyl bond (179 kcal mol^{-1} *vs* 92 kcal mol^{-1} for C-O bonds)[23] as thermodynamic driving forces enabled the cyclobutanol ring to be established as a versatile precursor to a range of value-added cores with functional handles and increased molecular complexity.[24–27] For example, in 1996 Nikishin and co-workers reported the manganese(III)-mediated electrooxidative ring opening to linear ketones.[28] In the same publication they showed that γ-chlorinated linear butanones were formed as the major product when a chloride salt was added to the electrochemical manganese(III)-catalyzed cyclobutanol ring opening reaction;[26] this work was repeated by Morrill in 2019.[21] The groups of Zhang and Kim, on the other hand, were particularly productive in the area of tandem functionalization/semi-pinacol rearrangements and pioneered the electrochemical synthesis of a variety of β-functionalized cyclopentanones from vinyl-substituted cyclobutanols.[17–22] Although protocols for the ring expansion of cyclobutanols to tetralones under traditional synthetic methods (e.g. [Ag],[29] [Rh],[30] [Pd],[31,32] [Ce],[33] *N*-bromosuccinimide[34–36]) were previously disclosed, a two-carbon ring homologation to tetralones under mild and ecological electrochemical techniques has not yet been accomplished (Scheme 1).



Scheme 1. Generation of structural diversity through electrochemical ring distortion of the cyclobutanol moiety

This is perhaps surprising given the widespread occurrence of the 1-tetralone motif in biologically active natural and synthetic compounds. Levobunolol, for example, is a widely marketed beta blocker, whereas naturally occurring 6-hydroxysugiol and myrrhone show promising antitumor-[37] and anti-inflammatory activity,[38] respectively (Figure 1). Despite their evident importance, conventional protocols to access 1-tetralones from cyclobutanols pose several significant drawbacks. Specifically, they usually rely on (i) superstoichiometric quantities of co-oxidant together with a transition-metal catalyst,[29,32] (ii) long reaction durations,[29] (iii) superstoichiometric quantities of transition-metals,[33] or (iv)

very careful substrate design to avoid undesired β-carbon elimination processes.[30,32] To overcome these limitations, we sought to employ electrosynthesis as a tool to effect this transformation in a regioselective, functional group-tolerant and cost-efficient fashion. Herein, we report our findings on the implementation of these ideas.

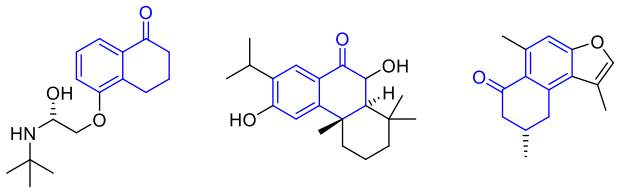


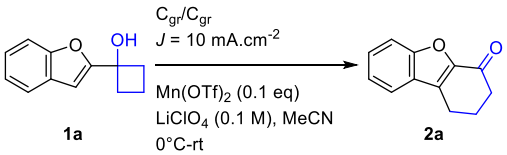
Figure 1. Synthetic and naturally occurring biologically active 1-tetralones

To commence our studies we drew inspiration from the electrochemical cyclobutanol ring opening first reported by Nikishin.[28] Their group showed that through the heterogenous electrochemical formation and regeneration of manganese(III)-catalysts, alkoxy radicals can be generated from hydroxyl groups through a homogenous single electron transfer (*indirect electrolysis*). This alkoxy radical would easily undergo a β-scission process and lead to the formation of a new carbonyl and carbon-centred radical. The newly generated radical can then be trapped to furnish diversified γ-functionalized butanones.[28] We hypothesized that in the absence of an external radical scavenger, these conditions might be amenable to induce intramolecular ring closure. To this end, we treated cyclobutanol **1a** with $Mn(OTf)_2$, at a current density of 10 $mA.cm^{-2}$, using carbon electrodes and lithium perchlorate/acetonitrile as the supporting electrolyte/solvent system (Table 1, entry 1).[28,39,40] To our delight, the starting material was completely consumed within three hours (10 $F.mol^{-1}$) and the desired 1-tetralone **2a** was formed in 32% yield. The remaining mass balance was found to consist of nonpolar alkene-containing side products and unidentifiable polymeric materials, which were easily separated from the desired tetralone product through flash column chromatography. Variation of the catalyst loading (Table 1, entries 2-3) had a detrimental effect on the yield, and other sources of manganese (Table 1, entries 4-5) failed at mediating this transformation. No conversion to the desired 1-tetralone occurred upon change of the reaction medium to other solvent systems, like CH_2Cl_2 or HFIP (Table 1, entries 6-7). Similarly, conducting the reaction in other solvent mixtures, such as ethyl acetate/acetic acid or acetonitrile/water, failed to yield the desired product (Table 1, entries 8-10), whereas a decrease in yield was observed when acetonitrile/HFIP or acetonitrile/acetic acid systems were used (Table 1, entries 11-12). Consequently, acetonitrile was established as the optimal solvent for this transformation, since it favours the stabilization of transient cationic intermediates[35] and offers a large electrochemical window.[41] After studying the impact of a different supporting electrolyte on the outcome of the reaction (Table 1, entries 13-14), [Li][ClO_4] was found to be the most suitable electrolyte for our transformation. A significant decrease in yield was observed when using [*n*Bu_4N][PF_6], possibly due to the formation of a more hydrophobic electrical double-layer.. Upon investigating other reaction parameters (Table 1, entries 15-19), such as temperature or current density, we found that a current density of 10 $mA.cm^{-2}$, an open atmosphere and a reaction temperature between 0-25 °C were essential for the desired outcome of this reaction.

In line with our aim to develop mild and sustainable conditions for this expansion, we turned our attention to the possibility of a direct anodic oxidation in the absence of a metal catalyst. To this end, we performed cyclic voltammetry studies on alcohol **1a** in presence and absence of a manganese catalyst (see Supporting Information). The first oxidation wave of **1a** was shown to be chemically irreversible, indicating a rapid subsequent chemical reaction triggered by the electron transfer. Unsurprisingly, in presence of the manganese catalyst the first oxidation potential significantly decreased (E_{pa}= 1.2 V *vs* Fc^+/Fc), in comparison to the oxidation potential observed for **1a** in absence of catalyst (E_{pa}= 1.4 V *vs* Fc^+/Fc). The new lower oxidation potential could be attributed to the complex formed *in situ* between the manganese catalyst and the cyclobutanol **1a**, as the catalyst itself did not exhibit an oxidation wave in the cyclic voltammetry studies (see Supporting Information). When alcohol **1a** was treated with the conditions described in Table 1 (entry 20) in absence of the manganese catalyst, the desired ketone was formed in 11% yield.

Following these initial metal-free electrolysis studies, we found that an increase of the electron flow to 25 $F.mol^{-1}$ enabled the desired ring expansion of **1a** to **2a** in 36% yield through direct electrochemical oxidation in the absence of any metal catalyst (Table 1, entry 21). Despite the relatively low mass recovery, we were delighted to find that the yield of **2a** compared favourably with that obtained for the identical transformation under traditional metal-catalyzed conditions.[29,36] Finally, we discovered that graphite electrodes offer superior performance in comparison to a Pt/Ni electrode system, potentially due to improved substrate adsorption (Table 1, entry 12). As a consequence of this improved adsorption, inversion of electrode polarity every 30 seconds was also required to minimize electrode fouling (Table 1, entry 23).

Table 1. Optimization studies on the electrolysis of compound 1a



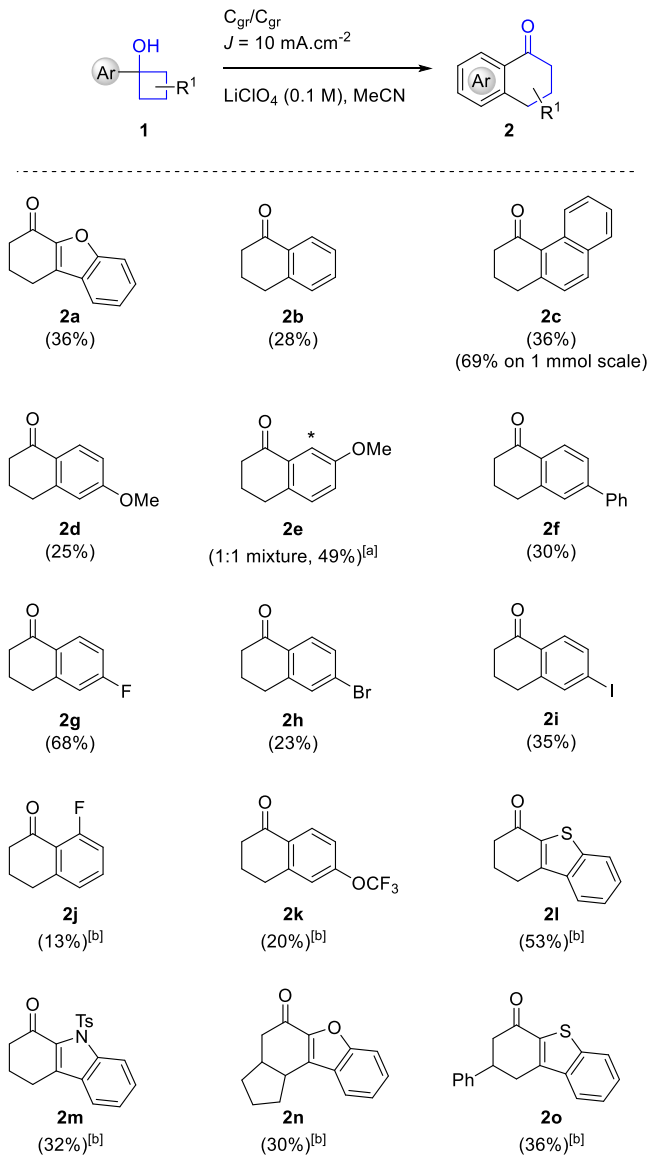
Entry	Variation from initial conditions[a]	Yield [%][b]
1	none	32
2	0.2 eq of $Mn(OTf)_2$	9
3	0.05 eq of $Mn(OTf)_2$	16
4	$MnBr_2$ instead of $Mn(OTf)_2$	--
5	$Mn(OAc)_3.2H_2O$ instead of $Mn(OTf)_2$	--
6	CH_2Cl_2 instead of MeCN	--
7	HFIP instead of MeCN	nr
8	EtOAc:AcOH (7:1) instead of MeCN	--
9	MeCN:H_2O (7:1) instead of MeCN	--
10	MeCN:NH_4OAc (7:1) instead of MeCN	nr
11	MeCN:HFIP (7:1) instead of MeCN	15
12	MeCN:AcOH (7:1) instead of MeCN	24
13	MeCN:AcOH (7:1) instead of MeCN, and	--

	[*n*Bu$_4$N][PF$_6$] instead of [Li][ClO$_4$]	
14	[*n*Bu$_4$N][PF$_6$] instead of [Li][ClO$_4$]	6
15	25 °C	10
16	0 °C	16
17	5 mA instead of 10 mA	--
18	20 mA instead of 10 mA	--
19	Inert atmosphere	8
20	No catalyst	11
21	**No catalyst, 25 F.mol^{-1} instead of 10 F.mol^{-1} [c]**	**36**
22	No catalyst, 25 F.mol^{-1} instead of 10 F.mol^{-1}, Pt/Ni electrodes instead of C$_{gr}$/C$_{gr}$ electrodes [c]	--
23	No catalyst, 25 F.mol^{-1} instead of 10 F.mol^{-1}, no inversion of polarity	--
24	No catalyst, 25 F.mol^{-1} instead of 10 F.mol^{-1}, no current	nr

[a] Reaction conditions: 0.13 mmol (**1a**), 5 mL dry MeCN, 0.1 M solution of [Li][ClO$_4$] supporting electrolyte, Mn(OTf)$_2$ (0.1 eq.), carbon graphite working electrode and counter electrode, 10 mA.cm^{-2}, 10 F.mol^{-1}, inversion of polarity each min, ice bath, three hours. [b] Yield determined by ^{1}H NMR analysis of the crude mixture using CH_2Br_2 as an internal standard. [c] Inversion of polarity every 30 sec.

With suitable metal-free ring expansion conditions in hand (Table 1, entry 21), we sought to define the substrate scope using a variety of differently substituted cyclobutanols. These were readily synthesized through lithiation of the (hetero-)aromatics with *n*-butyllithium, followed by an addition to cyclobutanone (see Supporting Information). Based on the oxidation potential obtained from cyclic voltammetry studies for 1-phenylcyclobutan-1-ol **1b (**E_{pa}= 1.5 V *vs* Fc^+/Fc), we anticipated that our direct electrochemical ring expansion should also be compatible with a range of aromatic-substituted cyclobutanols. As shown in Scheme 2, our initial explorations into the scope subsequently focused on a range of aromatic-substituted cyclobutanols. To this extent, we were pleased to find that 1-phenylcyclobutan-1-ol **1b** successfully underwent the ring expansion under our direct electrolysis conditions to 1-tetralone **2b** in 28% yield. Following this result, we directed our studies toward investigating various electronic effects on the aromatic ring on the outcome of the reaction. Gratifyingly, when weakly activated 2-naphthalene-derivative **1c** was treated under our standard conditions, the desired tetralone **2c** was produced in 36%, without the requirement for further purification. Equally, when the same ring expansion was scaled-up to a 1 mmol scale, to our delight, the desired product was formed in 69% yield, further proving the suitability of our method to environmentally friendly larger-scale syntheses. Strong resonance donors such as methoxy groups were also well-tolerated in the *para*- and *meta*-positions (**2d** and **2e**). Tetralone **2e**, however, was isolated as an inseparable equimolar mixture of regioisomers, resulting from unselective cyclization on the electronically activated *ortho*- and *para*-positions (with respect to the methoxy group). Similarly, weakly activating *para*-phenyl-substituted and *para*-fluorinated analogues **1f** and **1g** underwent the desired ring expansion in 30% and 68% yield, respectively. Next, we turned our attention to the scope of aromatic rings containing weakly deactivating substituents, such as *para*-bromo **1h** and *para*-iodo groups **1i**. Our investigations revealed that these *para*-halogenated aryl groups were also able to undergo a ring-expansion to form the tetralones **2h** and **2i** without concomitant electrochemical cathodic reduction of the aryl-halide bond.

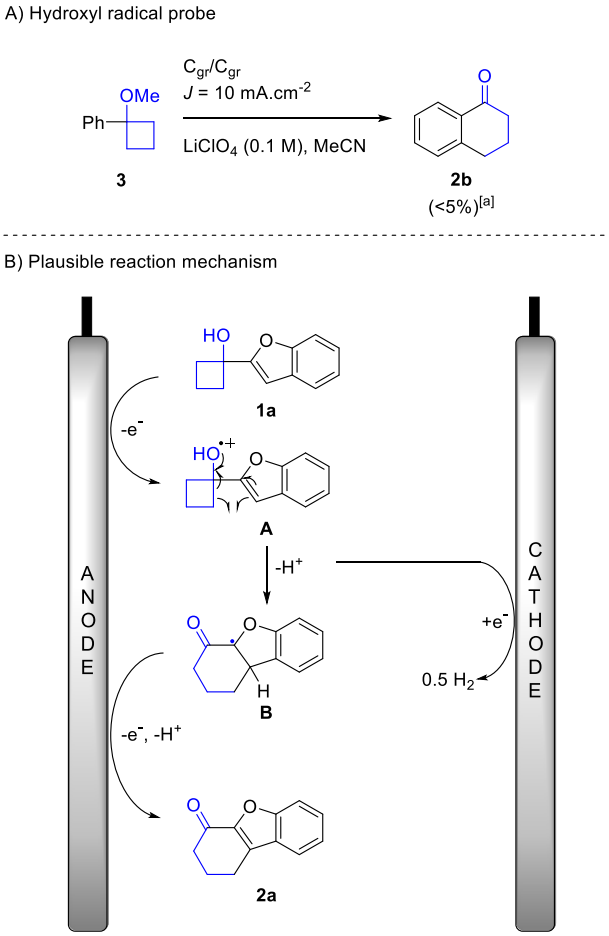
At last we defined the limitations of the direct anodically driven ring expansion reaction. Unsurprisingly, electron-deficient *ortho*-fluorinated and *para*-trifluoromethoxylated analogues **1j** and **1k** did not ring-expand under direct anodic oxidation conditions. We attribute this to the higher oxidation potential of electron-deficient aromatics due to the deeper-lying HOMO. In the presence of 10 mol% of Mn(OTf)$_2$, however, the ring expansion was catalyzed successfully to obtain tetralones **2j** and **2k** in 13% and 20% yield, respectively. We hypothesize that in these cases the successful conversion hinges on to the formation of a manganese-cyclobutanol complex with a lower oxidation potential.[21] Additionally, more challenging heteroaromatic substrates,[42] such as the benzothiophene analogue **1l**, *N*-tosylated indole-analogue **1m**, fused cyclobutanol **1n** and the phenyl-substituted benzothiophene-analogue **1o** failed to reliably ring-expand under the direct anodic oxidation conditions and only trace quantities of the desired products were isolated in each case. We found that the efficient ring expansion of these substrates could again be effected by the introduction of a manganese(II)-catalyst (10 mol%). Under indirect electrolysis conditions the desired ring expansion to **2l**, **2m**, **2n** and **2o** was effected in 53%, 32%, 30% and 36%, respectively. It is important to note that the β,γ-fused product **2n** was produced as the sole regioisomer and the isomeric α,β-fused product was not observed. We attribute this observation to the higher stability of the transient secondary radical in comparison to a primary radical.



[a] Obtained as a 1:1 mixture of the *ortho*-cyclized and *para*-cyclized regioisomers (with respect to the methoxy group). [b] Reaction performed in presence of 0.1 eq of $Mn(OTf)_2$.

Scheme 2. Scope of the regioselective electrochemical ring expansion of cyclobutanols to 1-tetralones

In order to conclude our study, we sought to investigate the mechanism for the direct anodic oxidative ring expansion (Scheme 3, A). To this end we found the role of the hydroxyl group in the underlying mechanism of particular interest. When the ether **3** was treated under our standard electrochemical ring expansion conditions in the absence of a catalyst, only trace conversion (<5% yield) to the desired ketone **2b** was observed, with most of the starting material recovered. This indicated that initiation of the reaction involves a single-electron oxidation of the alcohol moiety. On this basis, and in accordance with the literature, a plausible reaction mechanism for the direct electrochemical ring expansion is presented in Scheme 3, B. We postulated that anodic single-electron oxidation would unveil the alkoxy radical cation **A**, as the hydroxyl group was found to be essential for the success of this reaction. The feasibility of direct electrochemical oxidation of benzylic alcohols was previously investigated.[43–45] It is known that the most likely fate of carbinols such as **A** is a concerted β-scission of the C(sp^3)-C(sp^3) single bond[45] which, in the absence of external scavengers, lead to an intramolecular addition on to the aromatic system to form the six-membered ring **B**. This process is thermodynamically driven by the formation of a carbonyl group and a highly stabilized captodative radical **B**, as well as the release of ring strain from the four-membered ring. Finally, aromaticity can be restored through anodic overoxidation of the radical to the carbocation, followed by an elimination.[29,33] Concomitant proton reduction at the cathode would generate hydrogen gas. Substrates that require the addition of substoichiometric quantities of $Mn(OTf)_2$ for successful ring expansion, will proceed through an indirect electrochemical oxidation. Instead of direct anodic oxidation of the alcohol, the addition of $Mn(OTf)_2$ leads to the formation of a Mn(II)-alkoxide complex with a lower oxidation potential, which was observed in our cyclic voltammetry studies. This complex can be anodically oxidised to a Mn(III)-alkoxide species which can undergo an inner sphere electron transfer to form the alkoxide radical **A** and regenerate the Mn(II) catalyst.



[a] Yield determined by ^1H NMR analysis of the crude mixture using CH_2Br_2 as an internal standard.

Scheme 3. A) Hydroxyl radical probe experiment, B) proposed mechanism for the direct electrochemical cyclobutanol ring expansion to 1-tetralones

In summary, the first electrochemical synthesis of 1-tetralones from cyclobutanols is reported. This provides the community with a rapid, mild, and functional-group tolerant procedure to access functionalized heteroaromatic and

aromatic 1-tetralones. The effect of different substituents on the cyclobutanol as well as on the aromatic/heteroaromatic core was also evaluated. Based on our studies, we found that most substrates containing electron-donating groups and mildly electron-withdrawing substituents could ring-expand under direct anodic expansion conditions. Substrates with strongly electron-withdrawing substituents exhibited elevated oxidation potentials and required the addition of a manganese catalyst for successful ring expansion to occur.

Acknowledgements

The authors gratefully acknowledge an EPSRC Imperial College President's Scholarship (to P.N.) and additional funding from Dr Isabel Bader and her late husband Dr Alfred Bader (to P.J.P.), Oxana Bennett (to P.J.P.), the University of Greenwich Vice Chancellor's PhD Scholarship (to A.P.), the Engineering and Physical Sciences Research Council (Grant EP/S017097/1 to K.L.) and IKA for their material support (to K.L.). The authors thank Dr Lewis Allen for proofreading this article and Dr Matthew Leech for help with cyclic voltammetry studies. The authors also wish to thank Pete Haycock and Dr Lisa Haigh for NMR and mass spectrometric analysis at Imperial College London, Dr Iain Goodall and Victoria Elmes for mass spectrometric and NMR analysis at the University of Greenwich, respectively. The authors dedicate this work to the late Horst Natho.

Keywords: electrocatalysis • ring expansion • cyclobutanols • metal-free catalysis • tetralones

REFERENCES

1 H. Kolbe, *Ann. der Chemie und Pharm.*, 1848, **64**, 339–341.

2 H. Kolbe, *Ann. der Chemie und Pharm.*, 1849, **69**, 257–294.

3 M. C. Leech and K. Lam, *Acc. Chem. Res.*, 2020, **53**, 121–134.

4 M. Yan, Y. Kawamata and P. S. Baran, *Chem. Rev.*, 2017.

5 D. Hayrapetyan, V. Shkepu, O. T. Seilkhanov, Z. Zhanabil and K. Lam, *Chem. Commun.*, 2017, **53**, 8451–8454.

6 X. Luo, X. Ma, F. Lebreux, I. E. Markó and K. Lam, *Chem. Commun.*, 2018, **54**, 9969–9972.

7 X. Ma, D. F. Dewez, L. Du, X. Luo, I. E. Markó and K. Lam, *J. Org. Chem.*, 2018, **83**, 12044–12055.

8 S. Möhle, M. Zirbes, E. Rodrigo, T. Gieshoff, A. Wiebe and S. R. Waldvogel, *Angew. Chemie - Int. Ed.*, 2018, 57, 6018–6041.

9 C. Gütz, M. Bänziger, C. Bucher, T. R. Galvão and S. R. Waldvogel, *Org. Process Res. Dev.*, 2015, **19**, 1428–1433.

10 M. C. Leech, A. D. Garcia, A. Petti, A. P. Dobbs and K. Lam, *React. Chem. Eng.*, 2020, **5**, 977–990.

11 M. Yan, Y. Kawamata and P. S. Baran, *Angew. Chemie Int. Ed.*, 2018, **57**, 4149–4155.

12 R. Francke and R. D. Little, *Chem. Soc. Rev.*, 2014, **43**, 2492.

13 A. D. Garcia, M. C. Leech, A. Petti, C. Denis, I. C. A. Goodall, A. P. Dobbs and K. Lam, *Org. Lett.*, 2020, acs.orglett.0c01324.

14 E. J. Horn, B. R. Rosen, Y. Chen, J. Tang, K. Chen, M. D. Eastgate and P. S. Baran, *Nature*, 2016, **533**, 77–81.

15 M. Quertenmont, I. Goodall, K. Lam, I. Markó and O. Riant, *Org. Lett.*, 2020, **22**, 1771–1775.

16 Y. Takahira, M. Chen, Y. Kawamata, P. Mykhailiuk, H. Nakamura, B. K. Peters, S. H. Reisberg, C. Li, L. Chen, T. Hoshikawa, T. Shibuguchi and P. S. Baran, *Synlett*, 2019, **30**, 1178–1182.

17 J. C. Kang, Y. Q. Tu, J. W. Dong, C. Chen, J. Zhou, T. M. Ding, J. T. Zai, Z. M. Chen and S. Y. Zhang, *Org. Lett.*, 2019, **21**, 2536–2540.

18 H. I. Jung, Y. Kim and D. Y. Kim, *Org. Biomol. Chem.*, 2019, **17**, 3319–3323.

19 Y. J. Kim and D. Y. Kim, *Org. Lett.*, 2019, **21**, 1021–1025.

20 Y. J. Kim and D. Y. Kim, *Tetrahedron Lett.*, 2019, **60**, 1287–1290.

21 B. D. W. Allen, M. D. Hareram, A. C. Seastram, T. McBride, T. Wirth, D. L. Browne and L. C. Morrill, *Org. Lett.*, 2019, **21**, 9241–9246.

22 C. Chen, J.-C. Kang, C. Mao, J.-W. Dong, Y.-Y. Xie, T.-M. Ding, Y.-Q. Tu, Z.-M. Chen and S.-Y. Zhang, *Green Chem.*, 2019, **21**, 4014–4019.

23 D. A. D. Eric V. Anslyn, *Modern Physical Organic Chemistry*, University Science, 2006.

24 S. Yi, B. V. Varun, Y. Choi and S. B. Park, *Front. Chem.*, 2018, 6, 507.

25 S. L. Schreiber, *Science*, 2000, **287**, 1964–1969.

26 S. L. Schreiber, *Nature*, 2009, **457**, 153–154.

27 M. D. Burke and S. L. Schreiber, *Angew. Chemie - Int. Ed.*, 2004, **43**, 46–58.

28 N. I. Kapustina, L. L. Sokova and G. I. Nikishin, *Russ. Chem. Bull.*, 1996, **45**, 1246–1248.

29 J. Yu, H. Zhao, S. Liang, X. Bao and C. Zhu, *Org. Biomol. Chem.*, 2015, **13**, 7924–7927.

30 N. Ishida, S. Sawano and M. Murakami, *Chem. Commun.*, 2012, **48**, 1973–1975.

31 T. Nishimura, K. Ohe and S. Uemura, *J. Am. Chem. Soc.*, 1999, **121**, 2645–2646.

32 T. Nishimura, K. Ohe and S. Uemura, *J. Org. Chem.*, 2001, **66**, 1455–1465.

33 J. Fang, L. Li, C. Yang, J. Chen, G.-J. Deng and H. Gong, *Org. Lett.*, 2018, **20**, 7308–7311.

34 P. Natho, M. Kapun, L. A. T. Allen and P. J. Parsons, *Org. Lett.*, 2018, **20**, 8030–8034.

35 P. Natho, L. A. T. Allen, A. J. P. White and P. J. Parsons, *J. Org. Chem.*, 2019, **84**, 9611–9626.

36 P. Natho, A. B. Rouse, J. L. Greenfield, L. A. T. Allen, A. J. P. White, Z. Yang and P. J. Parsons, *Tetrahedron*, 2020, 131636.

37 W. F. Zhu, J. X. Cheng, S. Z. Su, C. F. Zhang, T. Akihisa, J. Manosroi, A. Manosroi, F. Feng, W. Y. Liu and J. Zhang, *Bioorg. Chem.*, 2020, **100**, 103889.

38 S. Su, T. Wang, J. A. Duan, W. Zhou, Y. Q. Hua, Y. P. Tang, L. Yu and D. W. Qian, *J. Ethnopharmacol.*, 2011, **134**, 251–258.

39 K.-Y. Ye, G. Pombar, N. Fu, G. S. Sauer, I. Keresztes and S. Lin, *J. Am. Chem. Soc.*, 2018, **140**, 2438–2441.

40 N. Fu, G. S. Sauer and S. Lin, *Nat. Protoc.*, 2018, **13**, 1725–1743.

41 J. K. Foley, C. Korzeniewski and S. Pons, *Can. J. Chem.*, 1988, **66**, 201–206.

42 S. Lips, D. Schollmeyer, R. Franke and S. R. Waldvogel, *Angew. Chemie Int. Ed.*, 2018, **57**, 13325–13329.

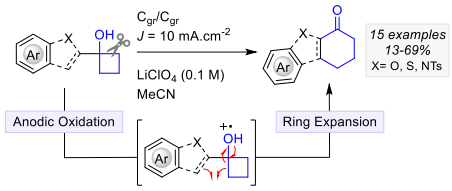
43 D. Wang, P. Wang, S. Wang, Y.-H. Chen, H. Zhang and A. Lei, *Nat. Commun.*, 2019, **10**, 2796.

44 E. A. Mayeda, L. L. Miller and J. F. Wolf, *J. Am. Chem. Soc.*, 1972, **94**, 6812–6816.

45 E. A. Mayeda, *J. Am. Chem. Soc.*, 1975, **97**, 4012–4015.

Entry for the Table of Contents

Insert graphic for Table of Contents here.



A new electrochemical approach to the oxidative ring expansion of functionalized cyclobutanols is reported. Aryl and heteroaryl 1-tetralones are synthesized under mild and cost-efficient conditions. The newly designed methodology proves to be tolerant of a good range of functional groups and its application to larger scale syntheses is shown to be feasible.

Institute and/or researcher Twitter usernames:

Dr Kevin Lam: @KLchemistry

Alessia Petti: @AlessiaEchem