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Oxidative Ring Contraction of Cyclobutenes – General Approach to Cyclopropylketones Including Mechanistic Insights.

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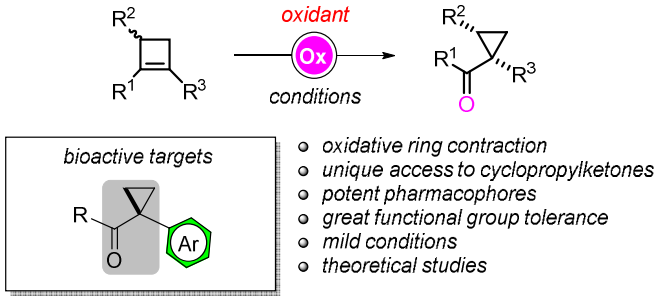
Supporting Information Placeholder

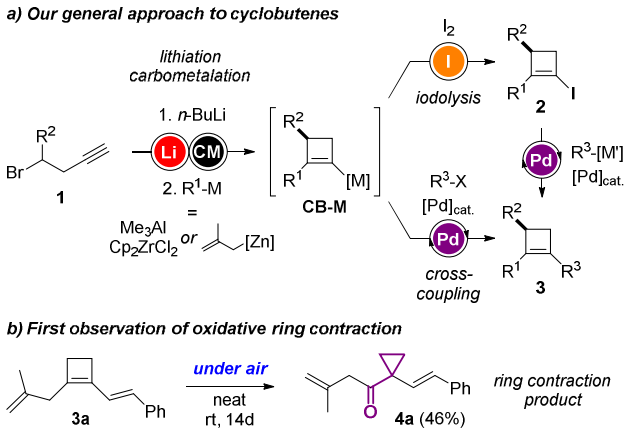


ABSTRACT: Reported is an original oxidative ring contraction of easily accessible cyclobutene derivatives for the selective formation of cyclopropylketones (CPKs) under atmospheric conditions. Comprehensive mechanistic studies are proposed to support this novel, yet unusual, rearrangement. Insights into the mechanism ultimately led to simplification and generalization of the ring contraction of cyclobutenes using *m*CPBA as an oxidant. This unique and functional group tolerant transformation proceeds under mild conditions at room temperature, providing access to a new library of polyfunctionalized motifs. With CPKs being attractive and privileged pharmacophores, the elaboration of such a simple and straightforward strategy represents a highly valuable tool for drug discovery and medicinal chemistry. Additionally, the described method was employed to generate a pool of bioactive substances and key precursors in a minimum number of steps.

INTRODUCTION

Four-membered carbocyclic architectures, especially cyclobutenes, have recently become a source of inspiration for dependable synthetic methodologies, due to their inherent ring strain.[1]

Scheme 1. Our access path to cyclobutenes (a) and the first observation of oxidative ring contraction (b).



While most documented strategies are based on [2+2]-cycloadditions and transition metal-catalyzed processes,[2] we have described an efficient, general and regioselective route to cyclobutenes via the intermediate formation of an easily-accessible cyclobutenylmetal species **CB-M** (Scheme 1a) from bromobutynes **1**.[3] This one-pot generated **CB-M** was then engaged either in a direct cross-coupling reaction with aryl halides, or in a relayed sequence involving intermediate formation of iodocyclobutenes **2**. The synthetic approach to functionalized cyclobutenes **3** was studied in depth, leading to a unique library of diversified aryl-, heteroaryl-, alkynyl- and vinyl-cyclobutenes. While **CB-M** could be used in one-pot sequences to form challenging alkylidenecyclobutanes,[4] vinyl-cyclobutenes were transformed into strained fused ring systems.[5] Interestingly, when vinyl-cyclobutene **3a** was left under atmospheric conditions (Scheme 1b) a formal oxidative ring contraction was observed and cyclopropylketone (CPK) **4a** was isolated in 46% yield.

Notably, CPK-based pharmacophores can be found in a number of bioactive substances (Figure 1, **A**-**F**)[6] by exalting crucial hydrophobic interactions.[7] Efficient strategies that allow for a rapid and selective construction of these strained pharmacophores represent valuable tools for drug discovery and high throughput screenings.

Surprisingly, only few methods are described concerning the synthesis of such structures possessing aromatic, heteroaro-

matic or vinylic substituents, and those require in most cases a large number of steps, with low functional group tolerance

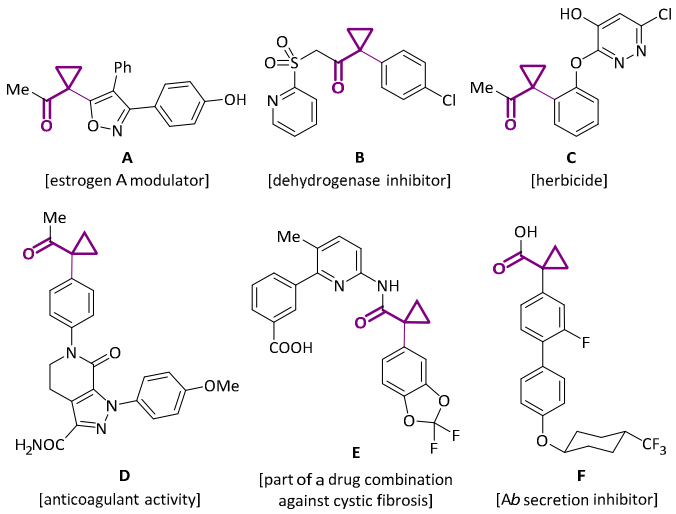


Figure 1. CPK-containing bioactive substances.[6]

So far, formation of *gem*-disubstituted cyclopropanes has been achieved by employing preformed carbonylated cyclopropanes,[8] double alkylations with dihaloethanes,[9] Corey-Chaykovsky cyclopropanations,[10] α-arylation of cyclopropyl nitriles,[11] or more recently, via transition metal catalyzed oxidative cyclopropanations of alkynes.[12] Intrigued by the simplicity of our innovative sequence, when compared to functional group sensitive reported processes, we took on the challenge of generalizing the access to these important modules.

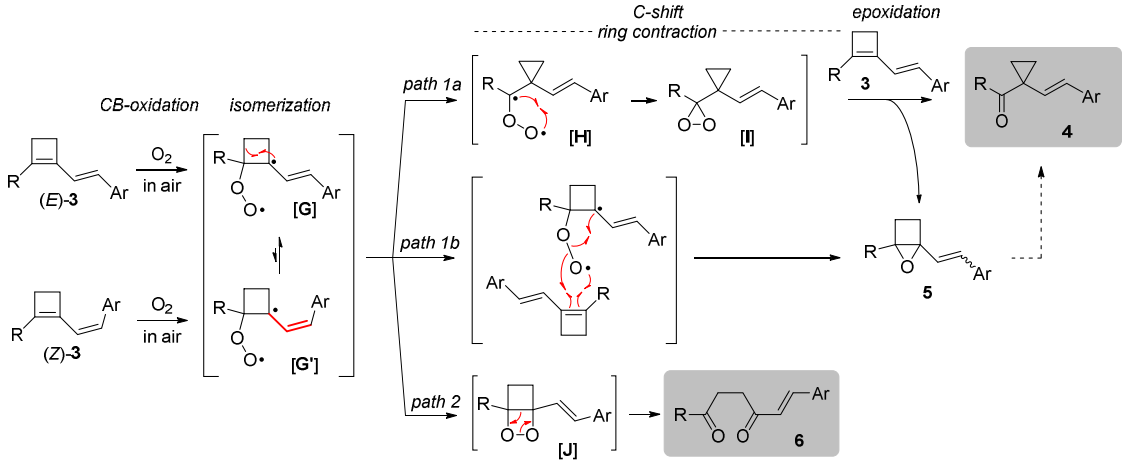
RESULTS AND DISCUSSION

On the mechanism of the oxidative ring contraction with O_2

After the first observation of ring contraction of cyclobutenes under air, we became interested in the generalization and application of such an uncommon reaction.[13] We thus started investigating the mechanism of the transformation to understand, and ultimately optimize, the synthesis of CPKs from cyclobutenes. Here we propose a mechanism for the oxidative addition of O_2 onto cyclobutenes, inspired by the early findings of Priesnitz et al.[13a] Fundamental mechanistic assumptions were addressed both experimentally and by quantum chemical calculations, the details of which can be found at the end of the manuscript. We describe and compare hereafter, two alternative routes that can be envisioned for the formation of CPKs.

As the reaction readily occurs under air, we propose that cyclobutene (*E*)-**3** is first oxidized by the presence of triplet O_2, giving the biradical species [**G**] (Scheme 2). Importantly, we noticed that starting from either (*E*)-**3** or (*Z*)-**3** derivatives led to the same (*E*)-**4** isomer. Firstly, the consideration of this allows for explaining the double bond isomerization through an intermediate π-allyl radical species, the equilibrium being displaced toward the thermodynamic *E* product [**G**]. Two paths can then be described: in *path 1a*, a ring contraction takes place resulting in [**H**], which leads to formation of the dioxirane [**I**]. As dioxiranes are very reactive species, we assumed that a fast epoxidation occurs, consuming an equimolar amount of the starting material **3**. However, a second route (*path 1b*) can be described, where **G** reacts in a concerted radical epoxidation with a molecule of the cyclobutene substrate **3**, giving the same intermediate **5** as *path 1a*. In parallel, *path 2* can be followed, in which a 1,2-dioxetane [**J**] is intermediary formed, as the product of a formal [2+2]-cycloaddition. A subsequent ring-opening reaction undergoes the formation of 1,4-diketone **6**.

Scheme 2. Proposed mechanism for the oxidative ring contraction of cyclobutenes (*path 1*) and oxidative ring opening (*path 2*).



Formation of CPKs vs 1,4-Diketones under atmospheric conditions

Taking into account that a carbon-shift of substituted epoxides can be triggered by addition of a Lewis acid, or under thermal conditions (Meinwald rearrangement),[13-14] optimizations were undertaken to favor the exclusive formation of the oxidative ring contraction product **4** (Table 1). Particular observations of

such cyclobutene oxide rearrangements have been reported in the past, but in most cases with low efficiency and versatility.[15]

Performing the reaction neat on air led to uncomplete conversion while pure oxygen favored the formation of 1,4-diketone **6a** (entries 1, 2), as recently exemplified by Loh and coworkers.[16] Similar ratios were observed when H_2O was used as a solvent in the presence of O_2 (entry 3), and prolonged reaction times were noted when solubilizing substrates in EtOAc (entry 4). In the absence of air (nitrogen atmosphere), no oxidation was observed leaving the starting material unreacted (entry 5). Addition of TEMPO or BHT to the solution prevented the reaction - supporting the assumption of an initial radical addition of O_2 to the unsaturated system (entries 6 and 7) - and the starting material was recovered. Taking the reaction under air up to 100 °C afforded full conversion of the starting cyclobutene in 3 h, furnishing exclusively the monooxidized compound **4a**, supporting the intermediate formation of cyclobutene oxide **5**, undergoing a dyotropic rearrangement at higher temperatures (entry 8).

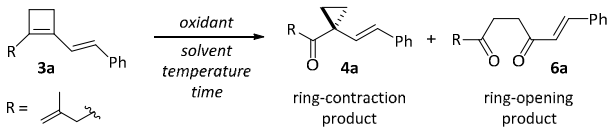


Table 1. Condition optimizations.

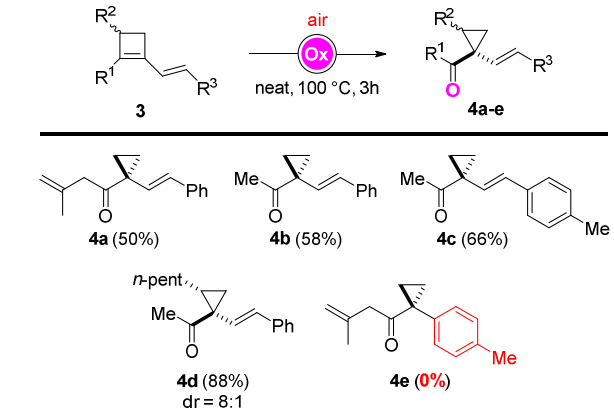
entry	oxidant	solvent	temp. (° C)	t (h)	conv. (%)	**4a**:**6a**[a]
1	air	neat	rt	24	50	87:13
2	O_2	neat	rt	2	98	30:70
3	O_2	H_2O	rt	2	92	38:62
4	air	EtOAc	rt	48	>99	77:23
5	-[b]	neat	rt	20	0	-
6	air[c]	EtOAc	rt	20	0	-
7	air[d]	EtOAc	rt	20	0	-
8	***air***	***neat***	***100***	***3***	***89***	***>99:1***

[a] conversion of the starting material and ratios determined by GC. [b] under N_2. [c] TEMPO (1 equiv.) was added. [d] BHT (1 equiv.) was added.

Through a favored *path 1* under thermal conditions (see Scheme 2), the exclusive formation of the desired product is the result of two converging and complementary reactions: 1) the consumption of the dioxirane [**I**] giving the ketone **4** along with the epoxide **5**; 2) the Meinwald rearrangement of the latter epoxide under thermal conditions.

With optimized conditions in hand for air-promoted oxidative ring contraction, cyclobutene **3a-c** led to CPKs **4a-c** in good yields up to 66%. When chiral cyclobutene **3d** was used, **4d** was isolated with a good diastereoisomeric ratio (dr = 8:1 determined by ^{13}C NMR, Scheme 3).

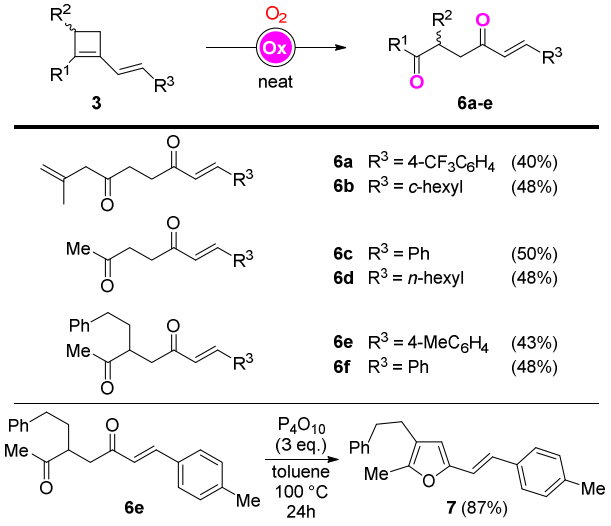
Scheme 3. Representative examples of air-promoted oxidative ring contraction



Surprisingly, when aryl-cyclobutene (**3e**) was subjected to similar conditions, none of the corresponding CPK **4e** could be detected, even in prolonged reaction time (further optimizations will be disclosed later).

As depicted in Table 1, the use of pure oxygen favored a formal [2+2]-cycloaddition, giving a majority of 1,4-diketone **6**. The scope of this transformation was briefly explored, as such motifs present synthetic applications in organic chemistry.[16] Vinylcyclobutenes **3** were submitted to an atmosphere of dioxygen, furnishing diketones **6a-f** in moderate yields (Scheme 4). Moreover, **6e** was employed in a Paal-Knorr condensation to undergo the formation of tri-substituted furan **7** in 87% yield.

Scheme 4. Synthetic scope of 1,4-diketone formation



Selective formation of CPKs with oxidants

Overcoming the limitation of the ring contraction to styryl systems required developing additional optimizations. Diverse oxidizing reagents were tested for the transformation of **3a** and **3e** into **4a** and **4e,** respectively (Table 2)

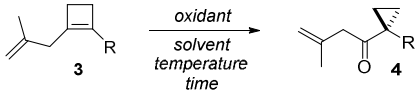
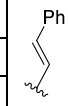


Table 2. Condition optimizations.

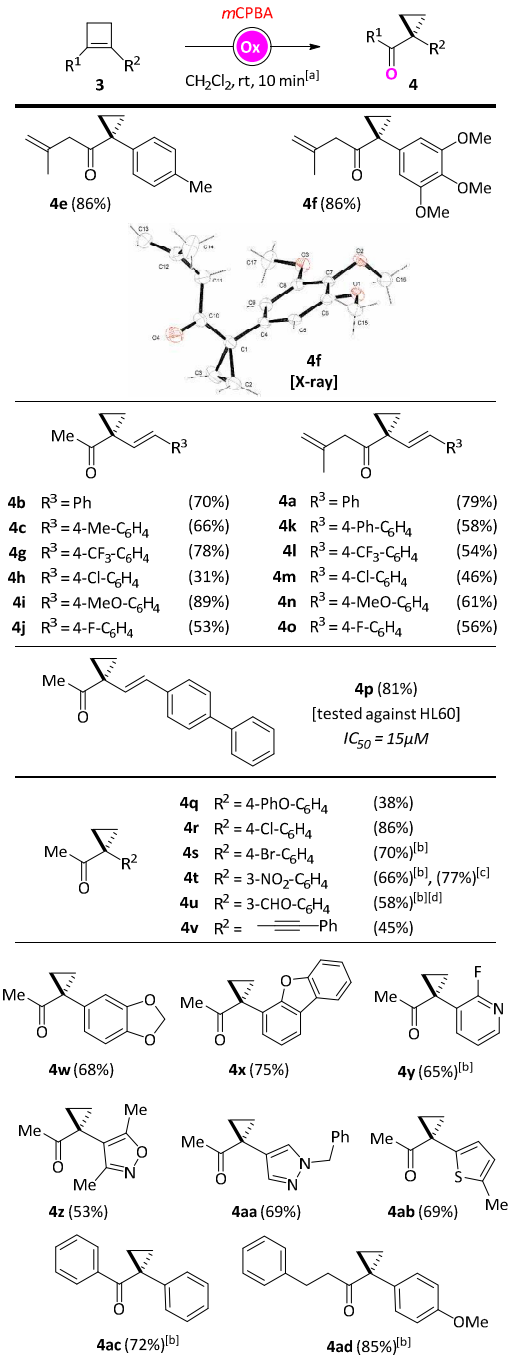
entry	R	oxidant	temp. (° C)	t	conv. (%)[a]
1		DMDO[b]	rt	3h	>99[c]
2		*m*CPBA[d]	0	10min	>99
3		***m*CPBA**[d]	***rt***	***10min***	***>99***
4	***p-Tol***	***m*CPBA**[d]	***rt***	***10min***	***>99***
5	*p*-Tol	*m*CPBA[e]	rt	18h	75[f]
6	*p*-Tol	*t*-BuOOH[d]	rt	18h	traces
7	*p*-Tol	AcOOH[d]	rt	18h	33
8	*p*-Tol	H_2O_2[g]	rt	18h	traces
9	*p*-Tol	NaOCl[h]	rt	18h	70[h]

[a] conversion of the starting material and proportions determined by GC/NMR. [b] acetone from the in-situ generation of DMDO. [c] many side products observed. [d] 1 equiv., in CH_2Cl_2 [e] $NaHCO_3$ (2 equiv.) was added to the reaction. [f] 75% conversion of the starting material, but in a 50:50 ratio of epoxidation product and desired product **4**, see SI [g] 5 equiv., NaOH (0.1 equiv.), in MeOH. [h] (*R*,*R*)-Jacobsen's catalyst (5 mol%): 70% conversion of the starting material, but in a 30:70 ratio of epoxidation product and desired product **4**, see SI.

Even though DMDO afforded full conversion of **3a** at room temperature (entry 1, Table 2), many overoxidized side products were observed. When *m*CPBA was used (entries 2, 3), complete consumption of the starting material was observed, giving the desired ring contracted product independently from the temperature.[17] Interestingly, only the most activated double bond (cyclobutene) reacted during the reaction, leaving both allyl and vinyl groups untouched. Moreover, the air-stable substrate **3e** furnished the rearranged product **4e** under these optimized and mild conditions. We assumed that the Meinwald rearrangement was assisted by the presence of *m*-chlorobenzoic acid, released by the epoxidation reaction. To test this hypothesis, a similar experiment (entry 5) was conducted in the presence of $NaHCO_3$. If 75% conversion were observed, the ring-contraction was partially inhibited by the presence of the base, as the cyclobutene oxide was observed in a 50:50 ratio with the desired cyclopropylketone, thus supporting the intermediary epoxide formation as well as the assistance of the acid in the ring contraction process. Furthermore, the scope of oxidants was evaluated. While alkylperoxide or hydrogen peroxide did not promote any oxidation, leaving the starting material unreacted (entry 6, 8), peracetic acid afforded 33% of conversion after 18h (entry 7). At last, Jacobsen's catalyst was employed in the presence of sodium hypochlorite (entry 9) and could convert 70% of the starting cyclobutene **3e** in 18h. However, the uncontracted cyclobutene oxide was detected in 30:70 ratio with the desired product **4**, supporting the need for acidic conditions in the Meinwald rearrangement.

To establish the scope of the transformation, a range of cyclobutenes was engaged in the oxidative ring contraction under re-optimized conditions. First, **3e** – which remained unaffected under an atmospheric environment – furnished the desired CPK **4e** in 86% yield (Scheme 5). Likewise, an electroenriched substrate led to the expected ring-contracted product **4f** in similar yield, and a crystal structure was obtained to confirm the presence of the cyclopropylketone scaffold.[18]

Scheme 5. Representative examples of *m*CPBA-promoted oxidative ring contraction



[a] *m*CPBA (1 equiv.). [b] $BF_3{\cdot}OEt_2$ (1 equiv.) was added to the reaction mixture. [c] The product was obtained from the corresponding 3-$NH_2C_6H_4$ derivative. [d] The aldehyde was obtained after hydrolysis, starting from the corresponding 1,3-dioxolane (see supporting information).

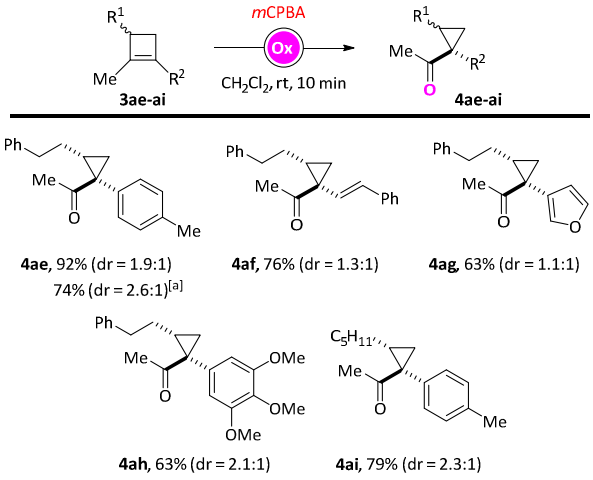
Vinylcyclobutenes, the oxidative ring contraction of which was established with air, underwent smooth conversion to CPKs **4a-c** and **4g-o** with peracids in similar to high yields (up to 89%).

Noteworthy, the very simple CPK-containing skeleton **4p** was found to possess a moderate activity against tumor cells HL60 (IC_{50} = 15 μM; see SI). In all cases, only the internal strained alkene reacted with the oxidant, leaving additional double bonds intact. In a second instance, aryl-substituted cyclobutenes were subjected to oxidation, yielding the correspond-

ing adducts **4q-u** and **4w**. While electron-donor substituents underwent a direct ring-contraction (**4q-r**, **4w**), the addition of a Lewis acid ($BF_3{\cdot}OEt_2$) was needed to drive the reaction to completion with electron-withdrawing groups (**4s-u**). Although an alkynyl derivative also furnished the desired product, a lower yield was obtained (**4v**, 45%). Finally, we pushed the methodology further to test the versatility of the process when using heteroarylated cyclobutenes. Dibenzofuryl, fluoropyridyl, dimethyloxazolyl and benzylpyrazolyl substituents were tolerated, and the corresponding compounds **4w-z** were isolated in good yields up to 75%. Interestingly, the presence of a sulphur atom in the aromatic core (thiophenyl) did not affect the course of the transformation, giving the derivative **4ab** in good yield (69%), the aromatic ring remaining unoxidized. Finally, different approaches were employed to introduce phenyl- and ethylphenyl moieties on the starting cyclobutene.[19-20] Their oxidation in the presence of *m*CPBA led to diversely substituted cyclopropylketones **4ac** and **4ad**, thus extending the scope of the oxidative ring contraction to aryl and alkyl groups.

Next, we investigated the oxidative ring contraction of chiral cyclobutenes (Scheme 6).

Scheme 6. Representative examples of *m*CPBA-promoted oxidative ring contraction



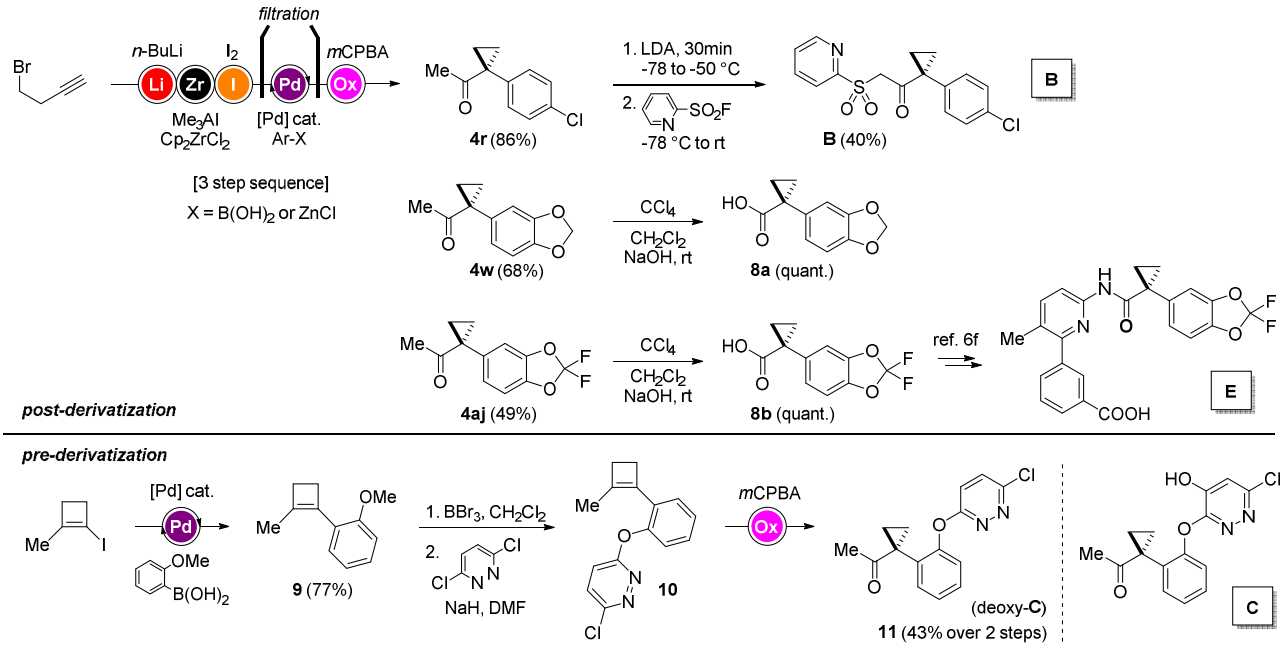
[a] -40 °C to rt, 3h.

Employing similar oxidative conditions, cyclobutenes **3ae-ai** underwent rapid ring contraction, providing CPKs **4ae-ai** in good to excellent yields (up to 92%, **4ae**). The diastereoselectivity of the transformation seems to depend on the nature of the substrate. Only moderate to low diastereomeric ratios were observed (dr up to 2.3:1). We attributed the deficiency in stereoselectivity to a fast epoxidation, the shielding effect of the R^1 chain playing only a minor role in the stereodifferentiation of the double bond. Decreasing the temperature to -40 °C slightly improved the diastereoselectivity for the ring contraction to 2.6:1 dr (**4ae**).

Synthesis of bioactive targets

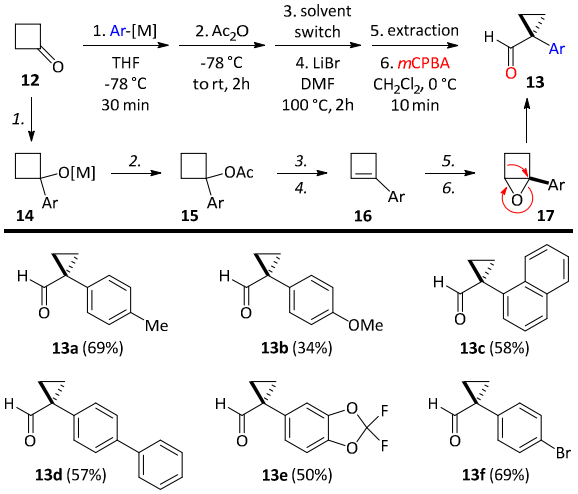
To further explore the synthetic utility of our methodology, we set out to access bioactive substances or their related precursors (Scheme 7). A common starting material (4-bromobutyne) was utilized to begin these syntheses. Cyclobutene iodides were formed in a one-pot process through lithiation/carboalumination/iodolysis and after simple extraction, reacted using a palladium-catalyzed Negishi or Suzuki cross-coupling reaction to afford the corresponding arylated cyclobutenes. Further oxidation with *m*CPBA was performed on crude materials, giving CPKs **4r**, **4w** and **4aj** in good yields (68 to 86%). At first, post-derivatization was achieved on the methylketone moiety of **4r** by enolization / electrophilic trapping employing 2-pyridylsulfonylfluoride to provide the dehydrogenase inhibitor **B** in a single step. Second, modification of the methylketone was carried out through haloform reaction with CCl_4, providing cyclopropylcarboxylic acids **8a-b** in quantitative yields. Importantly, **8b** stands as the precursor in the Lumacaftor (**E**) synthesis (potent drug against cystic fibrosis in combination with Ivacaftor).[6g] Pre-derivatization was also envisioned and applied to the synthesis of an analog structure of the herbicide **C** providing the deoxy-**C** herbicide in 43% yield over two steps. Initial Suzuki cross-coupling of previously iodinated **CB-M** (see Scheme 1) with (2-methoxyphenyl)boronic acid resulted in the corresponding cyclobutene **9** in 77%. Upon exposure of **9** to BBr_3, followed by nucleophilic substitution on dichloropyridazine, **10** was obtained and directly employed in the final oxidative ring contraction without purification, completing the synthesis of deoxy-C **11** in 43% yield over two steps.

Scheme 7. Straightforward syntheses and formal synthesis of bioactive substances through oxidative ring contraction.



Sequence to access cyclopropyl-aldehydes

To ensure a broader applicability of the method, we finally assembled a sequence for the formation of cyclopropylaldehydes. To achieve that goal, commercially available cyclobutanone **12** was submitted to nucleophilic addition of an arylmetal species and the resulting alcoholate was further acetylated. β-Elimination on **15** in the presence of lithium bromide after exchanging the solvent to dimethylformamide furnished arylated cyclobutene **16**. With a sufficient purity, **16** was further engaged without purification in the oxidative ring contraction in the presence of *m*CPBA, giving the desired rearranged compounds **13a-f** (Scheme 8). Employing diversely substituted aromatic structures showcases the efficient formation of a range of cyclopropylaldehydes in six steps from commercial sources and with a sole purification step, in moderate to good yields (34 to 69%).



COMPUTATIONAL ANALYSIS

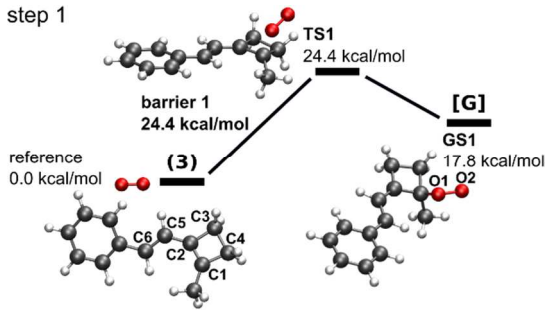
The proposed mechanism of the oxidative ring contraction of cyclobutene **3** (Scheme 2) was investigated theoretically for a better understanding. DFT with the B3LYP functional and the 6-31G(d) basis set of the program package Gaussian16[21] was used generally for all geometry optimizations. Only geometry point TSDK1 was computed at the CASSCF/6-31G(d) level of theory with the program package Molpro2012[22] for a correct description of the state.

Scheme 8. Direct access to cyclopropyl-aldehydes from commercially available cyclobutanone.

The energies of the discussed reaction scheme were then obtained by applying the CASPT2 routine of the program package Molcas 8.2[23] with the ANO-L-VDZP basis set on the optimized structures. It is a common procedure to do geometry optimizations on a low level of theory, as e.g. DFT, and then correct the calculated energies using single-point calculations at a higher level of theory, as e.g. the CASPT2, to include nondynamic and dynamic electron correlation.[24] Investigating the mechanism proposed in Scheme 2 computationally, we need to describe diradicalic structures. To do this correctly, we use the multi-reference method CASPT2. A more detailed description of the computational methods is given in the supporting information. Specific options for the CASPT2 calculations, as the chosen active space, are discussed there. For completeness, we also show the results at the B3LYP level of theory.

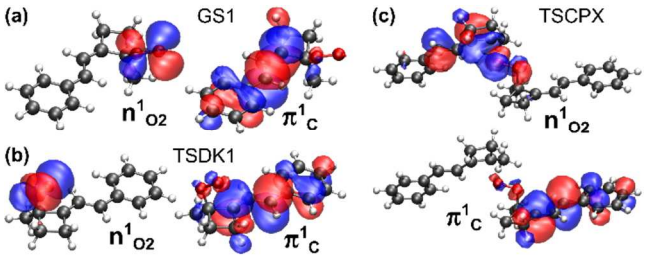
Scheme 9. Barrier for the addition of triplet oxygen ($^3O_2$) to cyclobutene 3 at the CASPT2/ANO-L-VDZP level of theory. The labels in brackets correspond to the nomenclature used in Scheme 2. The given energies are referenced

to the energy of the educts, cyclobutene 3 and $^3O_2$, separated at 10 Angstrom. Additionally, the numbering of important atoms used in the following discussion is shown.



The first step of the mechanism (Scheme 9) is the same for both observed products, cyclopropane **4** and diketone **6**. Triplet oxygen ($^3O_2$) adds to the C-C double bond of the cyclobutene ring forming a C-O bond between C1 and O1 to generate the diradical GS1. The barrier for this addition lies with 24.4 kcal/mol in the possible range for a slow reaction at room temperature. At GS1 the occupied T_1 state and the S_0 state, both have the equivalent electronic diradicalic character and lie energetically close with $\Delta E \approx 0.001$ eV. Figure 2 a shows the two single occupied orbitals of the S_0 and T_1 state to confirm the diradicalic character. One electron is localized at the oxygen atom O2 and the second is delocalized over the allylic positions C2 and C6. The S_0 and T_1 states remain energetically close and keep their electronic character along the reaction path to the corresponding next transition state of each investigated pathway (Figure 2 b and c). Calculations of the spin orbit coupling suggest that intersystem crossing is possible in those regions. A detailed discussion and the calculated values are given in the supporting information. In the following discussion, we expect that intersystem crossing took place and all points are evaluated in the singlet ground state S_0.

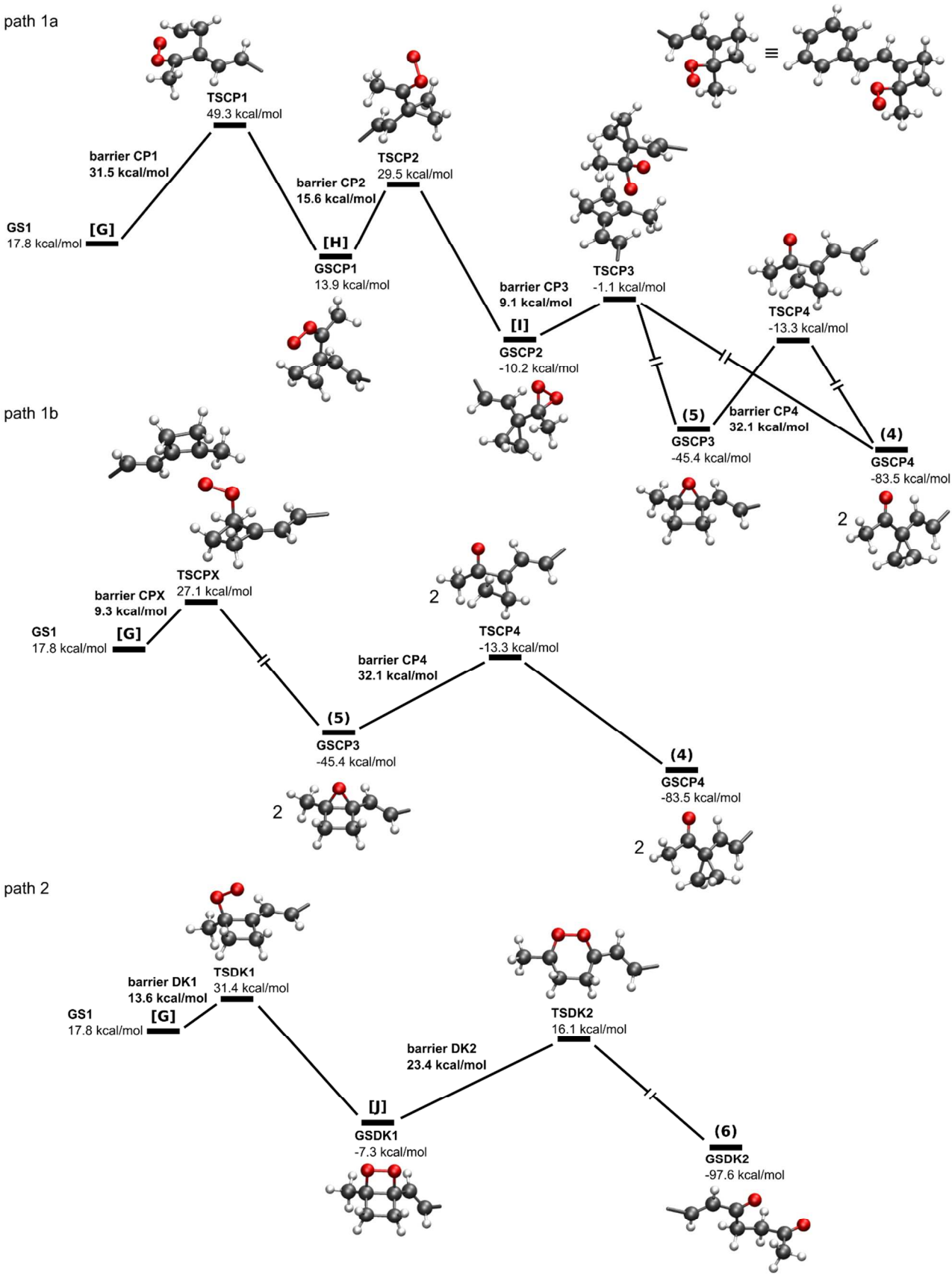
Figure 2. Single occupied orbitals of the S_0/T_1 state at a) GS1, b) TSDK1 and c) TSCPX showing the diradicalic character at this geometry points.



Scheme 10 summarizes the results for the reaction pathways *path 1a*, *path 1b* and *path 2* discussed in Scheme 2. In *path 1a*, first proposed by Priesnitz[13a], the predicted dioxirane **[I]** (GSCP2) is reached in a stepwise process. First, the cyclobutene ring is rearranged to a cyclopropane ring to form GSCP1 **[H]**. The C-C bond between C1 and C4 is broken and a bond between C2 and C4 is built in one step via TSCP1. This is followed by the formation of the second C-O bond between C1 and O2 via TSCP2 to form dioxirane **[I]**. For the next step, Priesnitz proposed that cyclobutene **3** is epoxidized by dioxirane **[I]**. This step via TSCP3 leads to the product CPK **4** (GSCP4) and the intermediate, epoxide **5** (GSCP3). **5** can form another CPK **4** molecule via TSCP4 which corresponds to a Meinwald rearrangement.[13-14] The first step of *path 1a* has a high barrier of 31.5 kcal/mol to TSCP1 accounting for a total barrier of 49.3 kcal/mol which makes this pathway highly unlikely. Apparently, the rearrangement of the carbon bonds forming a cyclopropane ring from a cyclobutene ring is unfeasible at this point of the reaction path.

In Scheme 2 another mechanistic pathway to cyclobutene **3** was proposed (*path 1b*). Here, a direct epoxidation takes place after the addition of $^3O_2$ without formation of the cyclopropane ring. The diradical GS1 can epoxidize cyclobutene **3** via TSCPX to form two molecules of intermediate epoxide **5** (GSCP3). The next step of this pathway is the same as of *path 1a*. CPK **4** (GSCP4) is built via Meinwald rearrangement of epoxide **5**. The barrier to TSCPX is with a value of 9.1 kcal/mol a lot of smaller than the barrier to TSCP1 which makes *path 1b* the favored pathway towards cyclobutene **4**. The second transition state of this path (TSCP4) can be reached via a barrier of 32.1 kcal/mol, the largest barrier of this pathway. In the following, only the here proposed novel *path 1b* is discussed as reaction pathway leading to the product **4**.

Scheme 10. Reaction scheme for path 1a, path 1b and path 2 of the oxidative ring contraction of cyclobutene 3 at the CASPT2/ANO-L-VDZP level of theory. The labels in brackets correspond to the nomenclature used in Scheme 2. The structures are shown without the phenyl ring. The energies are referenced to the energy of the educts, cyclobutene 3 and $^3O_2$, separated at 10 Angstrom.



The reaction towards the second product, diketone **6**, is described with *path 2*. Here, the first transition state (TSDK1) leads to a formation of a four membered ring between the oxygen molecule and the two carbon atoms of the C-C double bond. This intermediate, dioxetane **[G]** (GSDK1), corresponds to a classical [2+2] cyclo-addition product between $^3O_2$ and an

alkene. The barrier for this step accounts for 13.6 kcal/mol. In the second step, the bonds of the four-membered dioxetane ring are rearranged via a six-membered transition state (TSDK2) to form diketone **6** (GSDK2). The corresponding barrier (23.4 kcal/mol) is of the same magnitude as the barrier for the first addition of $^3O_2$ to **3** (*step 1*).

Comparing both pathways (*path 1b* and *path 2*) first confirms that the formation of both products is possible and secondly reveals a difference in 4.3 kcal/mol for the corresponding first barriers in favor of reaction *path 1b*. This also results in a difference of the same value in the total barriers of both pathways. Thirdly, diketone **6** is the more stable product lying 14.1 kcal/mol lower than CPK **4**.

In contrast to dioxetane **[J]**, the intermediate epoxide **5** could be detected experimentally. This can be explained by the fact, that **5** (GSCP3) is around 38.1 kcal/mol more stabilized than **[J]** (GSDK1). Furthermore, comparison of the corresponding barriers to each next step reveals that the barrier to TSCP4 is around 8.7 kcal/mol larger than the barrier to TSDK2. This means, the Meinwald rearrangement via TSCP4 to generate CPK **4** happens on a slower time-scale so that intermediate **5** can be detected under the given experimental conditions. The rearrangement towards **6** is expected to happen at the same time-scale than the initial attack of $^3O_2$ to **3** since the barriers are of the same height.

All computational results are in good agreement with the experimental product distributions under different reaction conditions. Using thermodynamical conditions with a low reaction temperature and a long reaction time leads preferentially to the more stable product diketone **6**. In contrast, using kinetic conditions with a high reaction temperature and a short reaction time leads to CPK **4** whose pathway has the lower over-all barrier. Furthermore, the observation of better yields of diketone **6** when the reaction is conducted under pure oxygen atmosphere (in contrast to the normal atmospheric conditions) can be explained by the theoretical results. The decisive transition state for the formation of CPK **4** (TSCPX) is a two-molecule transition state between GS1 and educt cyclobutene **3**. When more oxygen is available for the first reaction step, the addition of $^3O_2$ to **3**, less reaction partner for GS1 is available to form epoxide **5** (GSCP2).

In summary, the proposed as well as observed intermediates are verified and the complete proposed reaction mechanism is strongly supported by the theoretical study.

CONCLUSIONS

We have demonstrated a novel and efficient air-promoted oxidative ring contraction of easily-generated vinyl cyclobutenes. Combining theoretical studies with experimental investigations finally led to proposing a new mechanistic path for the formation of α-substituted cyclopropylketones. These modules possessing interesting pharmacological properties, a general and selective sequence was designed starting from readily available substrates, allowing the synthesis of a wide variety of functionalized scaffolds. Such a straightforward approach undoubtedly opens an entire platform for high throughput screening in drug discovery processes.

Experimental Section

General considerations. Commercially available starting materials were used without further purification unless otherwise stated. All reactions were carried out under N_2 atmosphere in flame-dried glassware. Syringes, which were used to transfer anhydrous solvents or reagents, were purged with nitrogen prior to use. CH_2Cl_2 was predried over $CaCl_2$ and distilled from CaH_2. THF was refluxed and distilled from sodium benzophenone ketyl under nitrogen. Et_2O was predried over $CaCl_2$ and passed through activated Al_2O_3 (the solvent purification system SPS-400-2 from Innovative Technologies Inc.). Toluene was predried over $CaCl_2$ and distilled from, CaH_2. Chromatography purifications were performed using silica gel (SiO_2, 0.040-0.063 mm, 230-400 mesh ASTM) from Merck. The spots were visualized under UV (254 nm) or by staining the TLC with $KMnO_4$ solution (K_2CO_3, 10 g – $KMnO_4$, 1.5 g – H_2O, 150 mL – NaOH 10% in H_2O, 1.25 mL), PAA: *p*-anisaldehyde solution (conc. H_2SO_4, 10 mL – EtOH, 200 mL – AcOH, 3 mL – *p*-anisaldehyde, 4 mL). Diastereoisomeric ratios were determined by ^1H NMR and ^{13}C NMR. ^{13}C and ^1H NMR spectra were recorded on VARIAN Mercury 200, BRUKER ARX 300, VARIAN VXR 400 S and BRUKER AMX 600 instruments. Chemical shifts are reported as δ values in ppm relative to residual solvent peak (^1H-NMR) or solvent peak (^{13}C-NMR) in deuterated chloroform ($CDCl_3$: δ 7.26 ppm for ^1H-NMR and δ 77.16 ppm for ^{13}C-NMR). Abbreviations for signal coupling are as follows: s (singlet), d (doublet), t (triplet), q (quartet), quint (quintet), m (multiplet) and br (broad). Reaction endpoints were determined by GC monitoring of the reactions. Gas chromatography was performed with machines of Agilent Technologies 7890, using a column of type HP 5 (Agilent 5% phenylmethylpolysiloxane; length: 15 m; diameter: 0.25 mm; film thickness: 0.25 μm) or Hewlett-Packard 6890 or 5890 series II, using a column of type HP 5 (HewlettPackard, 5% phenylmethylpolysiloxane; length: 15 m; diameter: 0,25 mm; film thickness: 0.25 μm). High resolution mass spectra (HRMS) and low resolution mass spectra (LRMS) were recorded on Finnigan MAT 95Q or Finnigan MAT 90 instrument or JEOL JMS-700. Infrared spectra were recorded on a Perkin 281 IR spectrometer and samples were measured neat (ATR, Smiths Detection DuraSample IR II Diamond ATR). The absorption bands were reported in wave numbers (cm-1) and abbreviations for intensity are as follows: vs (very strong; maximum intensity), s (strong; above 75% of max. intensity), m (medium; from 50% to 75% of max. intensity), w (weak; below 50% of max. intensity) and br (broad). Melting points were determined on a Büchi B-540 apparatus and uncorrected. Single crystals were grown in small quench vials with a volume of 5.0 mL from slow evaporation of dichloromethane/hexanes mixtures at room temperature. Suitable single crystals were then introduced into perfluorinated oil and mounted on top of a thin glass wire. Data collection was performed at 100 K with a Bruker D8 Venture TXS equipped with a Spellman generator (50 kV, 40 mA) and a Kappa CCD detector operating with Mo-Kα radiation (l = 0.71071 Å).

s-BuLi and *t*-BuLi were purchased as solutions in cyclohexane/hexanes mixtures from Rockwood Lithium GmbH. The commercially available Grignard reagents MeMgCl, PhMgCl and *n*-BuMgCl were also purchased from Rockwood Lithium GmbH, as solutions in THF.

The concentration of organometallic reagent from commercially purchased and synthesized reagents was determined either by titration of isopropyl alcohol using the indicator 4-(phenylazo)diphenylamine in THF for Grignard reagents or using the indicator N-benzylbenzamide in THF for organolithium reagents.

[*s*-BuLi] = 1.31 M in cyclohexane (titration with isopropanol / 1,10-phenanthroline), purchased from Rockwood Lithium GmbH.

[*i*-PrMgCl·LiCl] = 1.1 M in THF (titration with iodine), purchased from Rockwood Lithium GmbH. [n-BuLi] = 2.44 M in cyclohexane (titration with isopropanol / 1,10-phenanthroline), purchased from Rockwood Lithium GmbH.

General procedure A for the synthesis of cyclobutenes **3**:[3] To cyclobutene-iodides **2** in THF (0.2 M) were consecutively added $Pd(dppf)Cl_2 \cdot CH_2Cl_2$ (4 mol%), the appropriate organoboronic acid (1.0 – 2.0 eq.) and a 1M solution of NaOH (3.0 eq.). The mixture was stirred at ambient temperature until TLC showed full consumption of the starting iodide **2** (20 min up to overnight). The reaction was quenched by addition of water, extracted with Et_2O (3 × 20 mL) and dried over $MgSO_4$. The crude product was concentrated under reduced pressure and finally filtrated through a short silica column to remove palladium salts. Crude materials were used without further purification.

General procedure B for the synthesis of cyclopropylketones **4**,**11**): To cyclobutenes **3** in CH_2Cl_2 (0.1 M) was added *m*CPBA in CH_2Cl_2 (0.3 M, 1.0 eq.) at 0 °C. The reaction was checked after 10 min by TLC and another portion of *m*CPBA (0.5 eq.) was added if the reaction was not complete. This step was repeated until full conversion of the substrates. The reaction was the treated by addition of NaOH (1 M) and extracted with CH_2Cl_2 (3 × 20 mL). Volatiles were removed under reduced pressure and the crude product purified by chromatography. **Ba)** The desired products **4,11** were obtained analytically pure. **Bb)** In the case of **4s**,**t**,**u,y,ac,ad, aj** the epoxide intermediate **5** was obtained after chromatography, as it did not undergo ring contraction. In such cases, intermediates were dissolved in Et_2O (0.3 M) and $BF_3 \cdot OEt_2$ (1.0 eq.) was added. As completion of the rearrangement was observed after 10 min, the final products could be purified by chromatography after extraction.

General procedure C for the synthesis of cyclopropylaldehydes (**13**). To aryl-halide (1.05 eq) in THF (0.33 M) was added dropwise *n*-BuLi *(*1.1 eq., 2.44 M*)* at -78 °C under inert atmosphere and the mixture was stired for 15 min at this temperature. Cyclobutanone **12** (1 eq) in THF (1 M) was added at -78 °C, the reaction stirred for 30 min before warming to room temperature. Ac_2O (2 eq.) was added at -78 °C, and the reaction was allowed to warm to room temperature and stirred for 2h. Volatiles were removed under vacuum and DMF (0.5 M) was added, followed by LiBr (10 eq.) and the mixture was heated to 100 °C and let stir for 2 h. After completion of the transformation, monitoring by TLC, the mixture was allowed to cool down to room temperature, washed with water and brine and extracted with EtOAc. The organic phase was dried over $MgSO_4$ and the solvent removed under reduced pressure. To crude cyclobutenes 16 in CH_2Cl_2 (0.1 M) was added *m*CPBA in CH_2Cl_2 (1.0 eq., 0.3 M) at 0 °C. The reaction was checked after 10 mins by TLC and another portion of *m*CPBA (0.5 eq.) was added if the reaction was not complete. This was repeated once if need be. The reaction was quenched by addition of NaOH (1 M) and extracted with CH_2Cl_2 (3 × 20 mL). The solvent was evaporated under reduced pressure and the crude product purified by chromatography.

Experimental Data

1-Methoxy-4-(2-phenethylcyclobut-1-en-1-yl)benzene (3ad):[19] To a solution of $(C_5H_5)_2ZrCl_2$ (1 eq.) in THF (0.2 M) was added EtMgBr (2 eq.) at -78 °C. The reaction mixture was warmed up to -40 °C and stirred for 1 h. To the mixture was added (4-chlorobut-3-yn-1-yl)benzene (1 eq.) in THF (5 M) at -78 °C. The mixture was stirred for 1 h at room temperature. After cooling back to -40 °C the reaction was quenched with iodide (2 eq.) and let warm to room temperature. The mixture was poured on ice/1 M HCl solution, extracted with hexanes, dried with $MgSO_4$ and filtered. The solvent was removed under reduced pressure and the crude mixture was purified over silica with hexanes as eluent (R_f = 0.7 (hexane, UV, KMnO4, PAA). (2-(2-iodocyclobut-1-en-1-yl)ethyl)benzene was then used in the following cross-coupling reaction. Therefore LiCl (1.1 eq.) and Mg (1.6 eq.) were dried under inert atmosphere followed by adding THF (0.4 M), and one drop of dibromoethane. The mixture was heated once to reflux to activate the Grignard. After cooling back to room temperature to the mixture was added $B(Oi\text{-}Pr)_3$ (1.5 eq.). According to that (2-(2-iodocyclobut-1-en-1-yl)ethyl)benzene (0.5 M) was added dropwise to the reaction. After 2 h a cloudy suspension has been formed. To the suspension was then added $Pd(dppf)Cl_2$ dichloromethane adduct (4 mol%), 1-iodo-4-methoxybenzene (0.80 eq.) and an aqueous solution of sodium hydroxide (1.5 eq. 1.00 M). The reaction mixture stirred overnight and then extracted with diethyl ether (3 × 20 mL), washed with a saturated aqueous solution of sodium chloride (20 mL), dried with magnesium sulfate, filtered, concentrated and purified via flash column chromatography to provide **3ad** (0.27 mmol, 72 mg, 55%) as colorless oil. $\boldsymbol{R_f}$ = 0.20 (hexane, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.18 (m, 7H), 6.89 – 6.82 (m, 2H), 3.82 (s, 3H), 2.86 (dd, *J* = 9.6, 6.4 Hz, 2H), 2.75 – 2.67 (m, 2H), 2.65 – 2.59 (m, 2H), 2.51 – 2.42 ppm (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 158.4, 142.2, 139.7, 137.3, 129.3, 128.5, 128.4, 126.9, 126.0, 113.9, 55.4, 33.7, 32.1, 27.7, 26.1 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%):264.1 (30), 249.1 (40), 235.0 (5), 221.1 (5), 203.1 (2). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{19}H_{20}O^+$: 264.1514; found: 264.1507. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3059(w), 3024(w), 1780(w), 1726(w), 1670(s), 1614(vw), 1597(m), 1578 cm^{-1} (w).

(*E*)-3-Methyl-1-(1-styrylcyclopropyl)but-3-en-1-one (4a): Using 1-iodo-2-(2-methylallyl)cyclobut-1-ene (**2a**) and (*E*)-styrylboronic acid according to general procedure **A** and **Ba** provided **4a** (0.20 mmol, 45 mg, 79%) as colorless oil.$\boldsymbol{R_f}$ = 0.80 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.31 (m, 4H), 7.29 – 7.22 (m, 1H), 6.83 (d, *J* = 15.8 Hz, 1H), 6.42 (d, *J* = 15.8 Hz, 1H), 4.96 – 4.93 (m, 1H), 4.77 – 4.75 (m, 1H), 3.33 (s, 2H), 1.76 (t, *J* = 1.1 Hz, 3H), 1.50 (dd, *J* = 6.9, 3.7 Hz, 2H), 1.15 ppm (dd, *J* = 7.1, 3.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.8, 139.5, 136.9, 131.4, 128.8, 128.2, 127.8, 126.3, 114.8, 49.9, 33.8, 22.9, 19.8 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 226.2 (3), 211.2 (12), 184.1 (21), 141.1 (31), 128.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{16}H_{18}O^+$: 226.1358; found: 226.1353. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3080(vw), 3027(w), 2920(w), 2852(w), 1690(s), 1646(w), 1600 cm^{-1} (w).

(*E*)-1-(1-Styrylcyclopropyl)ethanone (4b): Using 1-iodo-2-methylcyclobut-1-ene (**2b**) and (*E*)-styrylboronic acid according to general procedure **A** and **Ba** provided **4b** (0.35 mmol, 65 mg, 70%) as colorless oil. **4b** was also obtained by following procedure **A** and subjecting the crosscoupling product to air at 100 °C for three hours (58%). $\boldsymbol{R_f}$ = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 7.27 – 7.22 (m, 2H), 7.20 – 7.14 (m, 1H), 6.76 (d, *J* = 15.9 Hz, 1H), 6.31 (d, *J* = 15.9 Hz, 1H), 2.17 (s, 3H), 1.42 (dd, *J* = 6.6, 4.2 Hz, 1H), 1.09 ppm (dd, *J* = 7.3, 3.8 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.1, 136.9, 130.6, 128.8, 128.4, 127.8, 126.3, 33.9, 28.4, 19.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 186.1 (40), 171.1 (10), 157.1 (15), 143.1 (40), 128.1 (100). **HRMS** (EI-Orbitrap):

m/z: [M]+ Calcd for $C_{13}H_{14}O^+$: 186.1045; found: 186.1039. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3082(vw), 3058(vw), 3026(w), 3006(w), 2926(vw), 1688(s), 1646(w), 1600 cm^{-1} (w).

(*E*)-1-(1-(4-Methylstyryl)cyclopropyl)ethanone (4c): Using **2b** and (*E*)-(4-methylstyryl)boronic acid according to general procedure **A** and **Ba** provided **4c** (0.17 mmol, 33 mg, 66%) as colorless oil. **4c** was also obtained by following procedure **A** and subjecting the crosscoupling product to air at 100 °C for three hours (66%). R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) 7.30 – 7.26 (m, 2H), 7.18 – 7.10 (m, 2H), 6.77 (d, *J* = 15.8 Hz, 1H), 6.36 (d, *J* = 15.8 Hz, 1H), 2.34 (s, 3H), 2.25 (s, 3H), 1.48 (dd, *J* = 6.7, 4.0 Hz, 2H), 1.15 ppm (dd, *J* = 7.2, 3.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.4, 137.6, 134.1, 130.6, 129.5, 127.4, 126.2, 33.9, 28.5, 21.3, 19.5 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 200.1 (42), 185.1 (13), 157.1 (50), 142.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{14}H_{16}O^+$: 200.1201; found: 200.1192. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3088(vw), 3022(w), 2922(w), 2864(vw), 1690(vs), 1650(w), 1612(w), 1572(vw), 1560(vw), 1540(vw) cm^{-1}.

1-((1*R*,2*R*)-2-Pentyl-1-((*E*)-styryl)cyclopropyl)ethanone (4d): Using 1-iodo-2-methyl-3-pentylcyclobut-1-ene (**2c**) and (*E*)-styrylboronic acid according to general procedure **A** and **Ba** provided **4d** (0.35 mmol, 65 mg, 70%) as colorless oil. **4d** was also obtained by following procedure **A** and subjecting the crosscoupling product to air at 100 °C for three hours (88%). R_f = 0.6 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.41 – 7.29 (m, 4H), 7.26 – 7.22 (m, 1H), 6.74 (d, *J* = 15.8 Hz, 1H), 6.39 (d, *J* = 15.8 Hz, 1H), 2.33 (s, 3H), 1.59 (dd, *J* = 6.8, 4.1 Hz, 1H), 1.49 – 1.24 (m, 9H), 1.21 (dd, *J* = 8.3, 4.2 Hz, 1H), 0.88 ppm (t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 137.0, 130.6, 130.2, 128.8, 127.7, 126.3, 39.5, 35.0, 31.7, 30.6, 29.6, 27.1, 22.8, 21.0, 14.2 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 256.1 (8), 213.2 (15), 160.1 (50). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{18}H_{24}O^+$: 256.1827; found: 256.1823. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3645(m), 1738(w), 1481(w), 1467(m), 1441(s), 1429(vs) cm^{-1}.

3-Methyl-1-(1-(*p*-tolyl)cyclopropyl)but-3-en-1-one (4e): Using **2a** and 4,4,5,5-tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane according to general procedure **A** and **Ba** provided **4e** (0.22 mmol, 46 mg, 86%) as colorless oil. R_f = 0.45 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.28 – 7.24 (m, 2H), 7.15 (d, *J* = 7.8 Hz, 2H), 4.88 – 4.79 (m, 1H), 4.57 – 4.53 (m, 1H), 3.02 (s, 2H), 2.36 (s, 3H), 1.63 (s, 3H), 1.60 (dd, *J* = 7.1, 3.2 Hz, 2H), 1.15 ppm (dd, *J* = 7.2, 3.2 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.8, 139.7, 137.9, 137.3, 131.1, 129.4, 114.4, 50.1, 37.1, 22.8, 21.3, 19.2 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 214.1 (8), 159.1 (26), 131.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{15}H_{18}O^+$: 214.1358; found: 214.1354. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3080(vw), 2974(w), 2922(w), 2252(vw), 1776(w), 1692(s), 1650(w) cm^{-1}.

3-Methyl-1-(1-(3,4,5-trimethoxyphenyl)cyclopropyl)but-3-en-1-one (4f): Using **2a** and (3,4,5-trimethoxyphenyl)boronic acid according to general procedure **A** and **Ba** provided **4f** (0.22 mmol, 62 mg, 86%) as colorless solid. R_f = 0.35 (hexane/EtOAc 8:2, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.58 (s, 2H), 4.84 (t, *J* = 1.6 Hz, 1H), 4.59 (dq, *J* = 2.0, 1.0 Hz, 1H), 3.86 (s, 6H), 3.85 (s, 3H), 3.06 (s, 2H), 1.69 – 1.55 (m, 3H), 1.58 (dd, *J* = 6.7, 3.5 Hz, 2H), 1.17 ppm (dd, *J* = 7.0, 3.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.4, 153.2, 139.8, 137.5, 136.4, 114.4, 108.0, 61.1, 56.3, 49.7, 38.0, 22.9, 19.3 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 290.1 (67), 275.1 (45), 235.1 (10), 207.1 (100), 192.1 (29), 176.1 (84), 161.1 (50). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{22}O_4^+$: 290.1518; found: 290.1514. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2968(w), 2940(w), 2924(w), 2832(w), 1692(m), 1586(m) cm^{-1}. **mp** (°C): 81-82.

(*E*)-1-(1-(4-(Trifluoromethyl)styryl)cyclopropyl)ethanone (4g): Using **2b** and (*E*)-(4-(trifluoromethyl)styryl)boronic acid according to general procedure **A** and **Ba** provided **4g** (0.19 mmol, 49 mg, 78%) as colorless oil. R_f = 0.4 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.1 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 6.99 (d, *J* = 15.9 Hz, 0H), 6.38 (d, *J* = 15.9 Hz, 0H), 2.23 (s, 1H), 1.55 (dd, *J* = 7.0, 4.3 Hz, 1H), 1.21 ppm (dd, *J* = 6.6, 3.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.3, 140.4 (q, *J* = 1.3 Hz), 131.3, 129.3 (q, *J* = 32.6 Hz), 128.7, 126.5, 125.7 (q, *J* = 3.8 Hz), 122.9 (q, *J* = 271.7 Hz), 34.0, 27.9, 19.7 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 254.1 (46), 225.1 (23), 191.1 (22). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{14}H_{13}F_3O^+$: 254.0918; found: 254.0913. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3044(vw), 3012(vw), 2932(vw), 1692(m), 1648(w), 1616(w) cm^{-1}.

(*E*)-1-(1-(4-Chlorostyryl)cyclopropyl)ethanone (4h): Using **2b** and (*E*)-(4-chlorostyryl)boronic acid according to general procedure **A** and **Ba** provided **4h** (0.08 mmol, 17 mg, 31%) as colorless oil. R_f = 0.45 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.26 (m, 4H), 6.83 (d, *J* = 15.9 Hz, 1H), 6.32 (d, *J* = 15.9 Hz, 1H), 2.22 (s, 3H), 1.51 (dd, *J* = 7.2, 4.4 Hz, 2H), 1.17 ppm (dd, *J* = 7.4, 3.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.7, 135.4, 133.3, 129.2, 129.2, 128.9, 127.5, 33.9, 28.1, 19.5 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 220.0 (46), 191.0 (11), 177.0 (30), 162.0 (21), 142.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{13}H_{13}ClO^+$: 220.0655; found: 220.0647. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3022(vw), 2926(vw), 1690(vs), 1646(w) cm^{-1}.

(*E*)-1-(1-(4-Methoxystyryl)cyclopropyl)ethanone (4i): Using **2b** and (*E*)-(4-methoxystyryl)boronic acid according to general procedure **A** and **Ba** provided **4i** (0.22 mmol, 48 mg, 89%) as colorless oil. R_f = 0.4 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.38 – 7.28 (m, 2H), 6.91 – 6.82 (m, 2H), 6.67 (d, *J* = 15.9 Hz, 1H), 6.34 (d, *J* = 15.8 Hz, 1H), 3.81 (s, 3H), 2.25 (s, 3H), 1.58 (s, 4H), 1.47 (dd, *J* = 6.9, 4.3 Hz, 3H), 1.14 ppm (dd, *J* = 7.5, 3.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.6, 159.4, 130.3, 129.7, 127.5, 126.2, 114.2, 55.5, 33.9, 28.6, 19.5 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 216.0 (95), 201.0 (22), 173.0 (81), 158.0 (100), 141.1 (35). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{14}H_{16}O_2^+$: 216.1150; found: 216.1153.

(*E*)-1-(1-(4-Fluorostyryl)cyclopropyl)ethanone (4j): Using **2b** and (*E*)-(4-fluorostyryl)boronic acid according to general procedure **A** and **Ba** provided **4j** (0.13 mmol, 27 mg, 53%) as colorless oil. R_f = 0.45 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.40 – 7.28 (m, 2H), 7.06 – 6.96 (m, 2H), 6.75 (d, *J* = 15.9 Hz, 1H), 6.34 (d, *J* = 15.9 Hz, 1H), 2.23 (s, 3H), 1.49 (dd, *J* = 7.0, 3.6 Hz, 2H), 1.16 ppm (dd, *J* = 7.2, 3.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.0, 162.4 (d, *J* = 246.9 Hz), 133.1 (d, *J* = 3.4 Hz), 129.4, 128.2 (d, *J* = 2.3 Hz), 127.8 (d, *J* = 8.0 Hz), 115.7 (d, *J* = 21.6 Hz), 33.9, 28.2, 19.4 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 204.1 (34), 175.0 (11), 161.1 (39), 146.0 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{13}H_{13}FO^+$: 204.0950; found: 204.0946. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3040(vw), 3008(vw), 2926(vw), 1690(s), 1652(w), 1602(m) cm^{-1}.

(*E*)-1-(1-(2-([1,1'-Biphenyl]-4-yl)vinyl)cyclopropyl)-3-methylbut-3-en-1-one (4k): Using **2a** and (*E*)-(2-([1,1'-biphenyl]-4-yl)vinyl)boronic acid according to general procedure **A** and **Ba** provided **4k** (0.15 mmol, 44 mg, 58%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400

MHz, $CDCl_3$) δ 7.66 – 7.55 (m, 4H), 7.50 – 7.41 (m, 4H), 7.38 – 7.32 (m, 1H), 6.88 (d, *J* = 15.8 Hz, 1H), 6.46 (d, *J* = 15.8 Hz, 1H), 4.99 – 4.93 (m, 1H), 4.82 – 4.76 (m, 1H), 3.35 (s, 2H), 1.78 (s, 3H), 1.53 (dd, *J* = 7.0, 4.0 Hz, 2H), 1.17 ppm (dd, *J* = 7.0, 3.0 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.7, 140.7, 140.6, 139.5, 135.9, 130.9, 128.9, 128.3, 127.5, 127.5, 127.0, 126.8, 114.8, 49.9, 33.9, 23.0, 19.8 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%):302.1 (37), 287.1 (45), 260.1 (41), 247.1 (100), 233.1 (11), 219.1 (61), 204.1 (83), 191.0 (47), 178.1 (53). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{22}H_{22}O^+$: 302.1671; found: 302.1665. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3078(vw), 3056(vw), 3028(w), 2972(vw), 2914(vw), 1688(s), 1646(w), 1602(w), 1582(vw) cm^{-1}.

(*E*)-3-Methyl-1-(1-(4-(trifluoromethyl)styryl)cyclopropyl)but-3-en-1-one (4l): Using **2a** and (*E*)-(4-(trifluoromethyl)styryl)boronic acid according to general procedure **A** and **Ba** provided **4l** (0.14 mmol, 40 mg, 54%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.57 (d, *J* = 8.2 Hz, 2H), 7.46 (d, *J* = 8.1 Hz, 2H), 6.97 (d, *J* = 15.9 Hz, 1H), 6.42 (d, *J* = 15.8 Hz, 1H), 4.97 – 4.93 (m, 1H), 4.79 – 4.71 (m, 1H), 3.29 (s, 2H), 1.76 (s, 3H), 1.55 (dd, *J* = 6.7, 3.4 Hz, 2H), 1.18 ppm (dd, *J* = 7.3, 3.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.0, 140.4 (q, *J* = 1.4 Hz), 139.3, 131.1, 129.6, 129.5 (q, *J* = 32.4 Hz), 126.5, 125.8 (q, *J* = 3.8 Hz), 124.3 (q, *J* = 271.5 Hz), 114.9, 49.6, 33.9, 22.9, 19.9 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 294.1 (8), 279.1 (30), 252.2 (35), 239.2 (11), 211.1 (34), 191.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{17}F_3O^+$: 294.1231; found: 294.1225. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3080(vw), 2976(vw), 2918(vw), 1692(m), 1648(w) cm^{-1}.

(*E*)-1-(1-(4-Chlorostyryl)cyclopropyl)-3-methylbut-3-en-1-one (4m): Using **2a** and (*E*)-(4-chlorostyryl)boronic acid according to general procedure **A** and **Ba** provided **4m** (0.11 mmol, 29 mg, 46%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 (app s, 4H), 6.81 (d, *J* = 15.8 Hz, 1H), 6.35 (d, *J* = 15.9 Hz, 1H), 4.97 – 4.90 (m, 1H), 4.78 – 4.72 (m, 1H), 3.30 (s, 3H), 1.75 (s, 2H), 1.51 (dd, *J* = 7.4, 3.9 Hz, 2H), 1.14 ppm (dd, *J* = 7.7, 3.2 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.4, 139.4, 135.4, 133.4, 130.0, 128.9, 128.9, 127.5, 114.8, 49.7, 33.8, 22.9, 19.8 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 260.1 (5), 245.1 (14), 218.1 (33), 205.0 (12), 177.0 (22). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{16}H_{17}ClO^+$: 260.0968; found: 260.0966. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3080(vw), 3028(vw), 3014(vw), 2974(w), 2942(vw), 2916(w), 1690(vs), 1646(m), 1592(w) cm^{-1}.

(*E*)-1-(1-(4-Methoxystyryl)cyclopropyl)-3-methylbut-3-en-1-one (4n): Using **2a** and (*E*)-(4-methoxystyryl)boronic acid according to general procedure **A** and **Ba** provided **4n** (0.15 mmol, 39 mg, 61%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.29 (m, 2H), 6.90 – 6.84 (m, 2H), 6.66 (d, *J* = 15.8 Hz, 1H), 6.37 (d, *J* = 15.9 Hz, 1H), 4.97 – 4.91 (m, 1H), 4.77 – 4.72 (m, 1H), 3.82 (s, 3H), 3.33 (s, 2H), 1.75 (app t, 3H), 1.47 (dd, *J* = 7.0, 4.0 Hz, 2H), 1.11 ppm (dd, *J* = 7.3, 3.4 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.2, 159.4, 139.6, 131.1, 129.7, 127.5, 125.9, 114.7, 114.2, 55.5, 50.0, 33.8, 23.0, 19.7 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 256.1 (31), 241.1 (12), 214.1 (28), 201.1 (87), 173.1 (76), 158.1 (100), 141.1 (40), 128.1 (58), 115.1 (82), 102.0 (186.1 (40), 171.1 (10). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{20}O_2^+$: 256.1463; found: 256.1465. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2967(w), 2944(w), 2934(w), 2916(w), 1723(w), 1690(m), 1652(w), 1606(m), 1576(w), 1528(w), 1511(vs) cm^{-1}.

(*E*)-1-(1-(4-Fluorostyryl)cyclopropyl)-3-methylbut-3-en-1-one (4o): Using **2a** and (*E*)-(4-fluorostyryl)boronic acid according to general procedure **A** and **Ba** provided **4o** (0.14 mmol, 34 mg, 56%) as colorless oil. R_f = 0.6 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 2H), 7.07 – 6.97 (m, 2H), 6.74 (d, *J* = 15.9 Hz, 1H), 6.37 (d, *J* = 15.8 Hz, 1H), 4.97 – 4.92 (m, 1H), 4.79 – 4.73 (m, 1H), 3.31 (s, 3H), 1.75 (app t, 3H), 1.50 (dd, *J* = 7.4, 3.8 Hz, 2H), 1.13 ppm (dd, *J* = 7.4, 3.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.7, 162.5 (d, *J* = 247.0 Hz), 139.5, 133.1 (d, *J* = 3.4 Hz), 130.2, 128.0 (d, *J* = 2.3 Hz), 127.8 (d, *J* = 7.9 Hz), 115.7 (d, *J* = 21.6 Hz), 114.8, 49.8, 33.8, 22.9, 19.7 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 244.1(100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{16}H_{17}FO^+$: 244.1263; found: 244.1261. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3078(vw), 2992(vw), 2936(vw), 1692(s), 1652(w), 1602(w) cm^{-1}.

(*E*)-1-(1-(2-([1,1'-Biphenyl]-4-yl)vinyl)cyclopropyl)ethanone (4p): Using **2b** and (*E*)-(2-([1,1'-biphenyl]-4-yl)vinyl)boronic acid according to general procedure **A** and **Ba** provided **4p** (0.20 mmol, 53 mg, 81%) as white solid. R_f = 0.45 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 – 7.54 (m, 4H), 7.50 – 7.39 (m, 4H), 7.38 – 7.32 (m, 1H), 6.90 (d, *J* = 15.9 Hz, 1H), 6.42 (d, *J* = 15.9 Hz, 1H), 2.27 (s, 3H), 1.52 (dd, *J* = 7.0, 3.9 Hz, 2H), 1.19 ppm (dd, *J* = 7.5, 3.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.1, 140.7, 140.5, 135.9, 130.1, 128.9, 128.6, 127.5, 127.5, 127.0, 126.8, 34.0, 28.4, 19.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 262.2 (100), 247.1 (5), 219.1 (80). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{19}H_{18}O^+$: 262.1358; found: 262.1352. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3028(w), 2924(w), 2854(vw), 1688(s), 1644(w), 1600(w) cm^{-1}.

1-(1-(4-Phenoxyphenyl)cyclopropyl)ethanone (4q): Using **2b** and (4-phenoxyphenyl)boronic acid according to general procedure **A** and **Ba** provided **4q** (0.10 mmol, 24 mg, 38%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.39 – 7.33 (m, 2H), 7.33 – 7.30 (m, 2H), 7.17 – 7.08 (m, 1H), 7.05 – 7.01 (m, 2H), 7.00 – 6.95 (m, 2H), 2.03 (s, 3H), 1.60 (dd, *J* = 6.5, 3.5 Hz, 2H), 1.17 ppm (dd, *J* = 6.9, 3.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.3, 157.0, 156.8, 135.9, 132.2, 130.0, 123.7, 119.3, 118.8, 37.0, 29.6, 19.1 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 252.1 (100), 209.1 (35) **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{16}O_2^+$: 252.1150; found: 252.1145. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3040(w), 3010(w), 1692(s), 1590(m) cm^{-1}.

1-(1-(4-Chlorophenyl)cyclopropyl)ethanone (4r): Using **2a** and (4-chlorophenyl)boronic acid according to general procedure **A** and **Ba** provided **4r** (0.22 mmol, 42 mg, 86%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 – 7.28 (m, 1H), 2.00 (s, 1H), 1.61 (dd, *J* = 6.8, 3.9 Hz, 1H), 1.15 ppm (dd, *J* = 7.0, 3.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.3, 139.7, 133.5, 132.2, 128.9, 37.1, 29.4, 18.9 ppm. **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_{11}ClO^+$: 194.0498; found: 194.0496.

1-(1-(4-Bromophenyl)cyclopropyl)ethanone (4s): Using **2b** and (4-bromophenyl)boronic acidaccording to general procedure **A** and **Bb** provided **4s** (0.18 mmol, 42 mg, 70%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 – 7.46 (m, 2H), 7.26 – 7.22 (m, 2H), 2.00 (s, 3H), 1.61 (dd, *J* = 6.5, 3.8 Hz, 2H), 1.15 ppm (dd, *J* = 7.0, 4.0 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.4, 140.2, 132.6, 131.9, 121.6, 37.2, 29.4, 18.9 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 238.0 (38), 195.0 (13), 116.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_{11}{}^{79}BrO^+$: 237.9993; found: **IR** (Diamond-

ATR, neat) $\tilde{\nu}_{max}$: 237.9987. 2958(m), 2918(vs), 2850(s), 2212(m), 1740(m) cm^{-1}.

1-Methyl-4-(3-nitrophenyl)-5-oxabicyclo[2.1.0]pentane (5t): Using **2b** and 4,4,5,5-tetramethyl-2-(3-nitrophenyl)-1,3,2-dioxaborolane according to general procedure **A** and **B** provided intermediate **5t** (0.17 mmol, 34 mg, 66%) as colorless oil. R_f = 0.8 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 (t, *J* = 1.9 Hz, 1H), 8.13 (ddd, *J* = 8.1, 2.3, 1.2 Hz, 1H), 7.63 (dt, *J* = 7.7, 1.4 Hz, 1H), 7.53 (t, *J* = 7.9 Hz, 1H), 2.71 – 2.62 (m, 1H), 2.15 – 1.94 (m, 3H), 1.50 ppm (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 148.5, 137.3, 132.2, 129.4, 122.5, 121.4, 71.9, 68.5, 30.5, 27.3, 13.9 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 205.1 (40), 190.0 (100), 159.1 (20). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_{11}NO_3^+$: 205.0739; found: 205.0733.

1-(1-(3-Nitrophenyl)cyclopropyl)ethanone (4t): Treating **5t** with $BF_3{\cdot}OEt_2$ (see general procedure Bb) resulted in ring contraction, yielding **4t** (0.17 mmol, 34 mg, quant.) as slightly yellow solid**.** Using **2b** and 3-Aminobenzeneboronic acid hydrochloride according to general procedure **A** and **Bb** provided directly oxidized **4t** (0.19 mmol, 39 mg, 77%). R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.22 (t, *J* = 2.0 Hz, 1H), 8.17 (ddd, *J* = 8.2, 2.3, 1.1 Hz, 1H), 7.71 (ddd, *J* = 7.6, 1.7, 1.1 Hz, 1H), 7.55 (t, *J* = 7.9 Hz, 1H), 2.01 (s, 3H), 1.71 (dd, *J* = 7.2, 3.6 Hz, 2H), 1.25 (dd, *J* = 7.2, 3.6 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.7, 148.5, 143.1, 137.2, 129.8, 125.7, 122.8, 37.6, 28.8, 18.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 205.1 (85), 146.0 (10), 115.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_{11}NO_3^+$: 205.0739; found: 205.0734. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3096(vw), 3008(vw), 1700(m), 1688(m), 1534(s) cm^{-1}. **mp** (°C): 106-107.

3-(1-Acetylcyclopropyl)benzaldehyde (4u): Using **2b** and 2-(3-(1,3-dioxolan-2-yl)phenyl)-4,4,5,5-tetramethyl-1,3,2-dioxaborolane according to general procedure **A** and **Bb** directly provided deprotected **4u** (0.15 mmol, 27 mg, 58%) as colorless oil. R_f = 0.2 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 10.03 (s, 1H), 7.89 (t, *J* = 1.7 Hz, 1H), 7.82 (dt, *J* = 7.6, 1.5 Hz, 1H), 7.65 (ddd, *J* = 7.7, 1.9, 1.2 Hz, 1H), 7.54 (t, *J* = 7.6 Hz, 1H), 2.00 (s, 3H), 1.67 (dd, *J* = 6.8, 4.2 Hz, 2H), 1.22 ppm (dd, *J* = 7.1, 3.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.7, 192.2, 142.4, 137.1, 136.9, 131.5, 129.6, 129.4, 37.5, 29.2, 18.7 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 188.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{12}H_{12}O_2^+$: 188.0837; found: 188.0831. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3010(w), 1758(w), 1720(m), 1692(vs), 1604(w), 1586(w) cm^{-1}.

1-(1-(Phenylethynyl)cyclopropyl)ethanone (4v): ((2-Methylcyclobut-1-en-1-yl)ethynyl) according to general procedure **Ba** provided **4v** (0.11 mmol, 21 mg, 45%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.46 – 7.39 (m, 2H), 7.34 – 7.29 (m, 3H), 2.57 (s, 3H), 1.62 (dd, *J* = 8.2, 3.2 Hz, 2H), 1.39 ppm (dd, *J* = 8.1, 3.1 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.2, 131.7, 128.5, 128.3, 123.2, 90.4, 80.7, 29.7, 23.7, 23.4 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 184.1 (84), 141.1 (83). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{13}H_{12}O^+$: 184.0888; found: 184.0883. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2958(w), 2930(w), 1706(vs), 1598(w) cm^{-1}.

1-(1-(Benzo[*d*][1,3]dioxol-5-yl)cyclopropyl)ethanone (4w): Using **2b** and benzo[*d*][1,3]dioxol-5-ylboronic acid according to general procedure **A** and **Ba** provided **4w** (0.17 mmol, 35 mg, 68%) as colorless oil. R_f = 0.4 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.86 – 6.81 (m, 2H), 6.80 – 6.75 (m, 1H), 5.97 (s, 2H), 2.03 (s, 3H), 1.56 (dd, *J* = 7.0, 3.1 Hz, 2H), 1.13 ppm (dd, *J* = 6.9, 3.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) 209.4, 147.8, 147.0, 135.1, 124.1, 111.2, 108.4, 101.3, 37.4, 29.5, 19.3 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 204.1 (70), 161.0 (30). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{12}H_{12}O_3^+$: 204.0786; found: 204.0774.

1-(1-(Dibenzo[*b*,*d*]furan-4-yl)cyclopropyl)ethanone (4x): Using **2b** and dibenzo[*b*,*d*]furan-4-ylboronic acid according to general procedure **A** and **Ba** provided **4x** (0.19 mmol, 50 mg, 75%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.98 (ddd, *J* = 7.7, 1.4, 0.7 Hz, 1H), 7.92 (dd, *J* = 7.6, 1.4 Hz, 1H), 7.62 (dt, *J* = 8.3, 0.9 Hz, 1H), 7.49 (ddd, *J* = 8.3, 7.3, 1.3 Hz, 1H), 7.41 (td, *J* = 7.2, 1.2 Hz, 1H), 7.36 (dd, *J* = 7.5, 1.0 Hz, 1H), 7.34 (t, *J* = 7.6 Hz, 1H), 2.03 (s, 3H), 1.80 (dd, *J* = 6.8, 3.9 Hz, 2H), 1.34 ppm (dd, *J* = 7.1, 3.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.5, 156.3, 155.9, 128.9, 127.5, 125.3, 124.6, 124.3, 123.1, 123.0, 120.9, 120.2, 112.1, 32.6, 29.2, 19.3 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 250.1 (100), 207.1 (97). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{14}O_2^+$: 250.0994; found: 250.0995. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3056(vw), 3010(w), 1692(s), 1630(vw), 1586(w) cm^{-1}.

1-(1-(2-Fluoropyridin-3-yl)cyclopropyl)ethanone (4y): Using **2b** and 2-fluoro-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)pyridine according to general procedure **A** and **Bb** provided **4y** (0.16 mmol, 29 mg, 65%) as colorless oil. R_f = 0.2 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.18 (ddd, *J* = 4.9, 2.0, 1.1 Hz, 1H), 7.73 (ddd, *J* = 9.5, 7.4, 2.0 Hz, 1H), 7.20 (ddd, *J* = 7.4, 4.9, 1.7 Hz, 1H), 2.04 (s, 3H), 1.71 (dd, *J* = 7.1, 4.1 Hz, 2H), 1.19 ppm (dd, *J* = 7.4, 3.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.1, 163.1 (d, *J* = 240.8 Hz), 147.0 (d, *J* = 14.8 Hz), 142.4 (d, *J* = 4.8 Hz), 123.4 (d, *J* = 29.3 Hz), 121.8 (d, *J* = 4.4 Hz), 31.9 (d, *J* = 3.2 Hz), 28.2 (d, *J* = 1.3 Hz), 18.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 179.1 (100), 136.0 (88). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{10}H_{10}FNO^+$: 179.0746; found: 179.0741. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3012(vw), 1696(s), 1636(vw), 1606(m), 1578(w) cm^{-1}.

1-(1-(3,5-Dimethylisoxazol-4-yl)cyclopropyl)ethanone (4z): Using **2b** and (3,5-dimethylisoxazol-4-yl)boronic acid according to general procedure **A** and **Ba** provided **4z** (0.13 mmol, 24 mg, 53%) as colorless oil. R_f = 0.25 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 2.37 (s, 3H), 2.24 (s, 3H), 2.04 (s, 3H), 1.65 (dd, *J* = 7.0, 3.0 Hz, 2H), 1.02 ppm (dd, *J* = 6.7, 3.4 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.6, 167.9, 160.6, 114.1, 28.8, 25.1, 18.8, 11.5, 10.5 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 179.1 (11), 136.1 (61). **HRMS** (EI-Orbitrap): m/z: [M-H]+ Calcd for $C_{10}H_{12}NO_2^+$: 178.0863; found: 178.0859.

1-(1-(1-Benzyl-1*H*-pyrazol-4-yl)cyclopropyl)ethanone (4aa): Using **2b** and 1-benzyl-3-(4,4,5,5-tetramethyl-1,3,2-dioxaborolan-2-yl)-1H-pyrazole according to general procedure **A** and **Ba** provided **4aa** (0.17 mmol, 41 mg, 69%) as colorless oil. R_f = 0.1 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 0.8 Hz, 1H), 7.39 – 7.31 (m, 4H), 7.24 – 7.20 (m, 2H), 5.28 (s, 2H), 2.08 (s, 3H), 1.53 (dd, *J* = 7.4, 3.7 Hz, 2H), 1.07 ppm (dd, *J* = 7.4, 3.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.9, 140.4, 136.4, 129.8, 129.0, 128.3, 127.8, 122.5, 56.3, 28.9, 27.5, 19.4 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 240.1 (38), 197.1 (22), 91.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{15}H_{16}N_2O^+$: 240.1263; found: 240.1257. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3090(w), 3008(w), 2940(w), 1718(m), 1690(vs) cm^{-1}.

1-(1-(5-Methylthiophen-2-yl)cyclopropyl)ethanone (4ab): Using **2b** and (5-methylthiophen-2-yl)boronic acid according to general procedure **A** and **Ba** provided **4ab** (0.17 mmol, 31 mg,

69%) as colorless oil. R_f = 0.6 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.77 (d, *J* = 3.4 Hz, 1H), 6.60 (dq, *J* = 3.4, 1.1 Hz, 1H), 2.46 (d, *J* = 1.1 Hz, 3H), 2.17 (s, 3H), 1.62 (dd, *J* = 7.2, 3.7 Hz, 2H), 1.26 ppm (dd, *J* = 7.2, 3.7 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.6, 142.7, 140.1, 128.0, 124.9, 31.8, 29.1, 21.1, 15.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 180.1 (90), 165.0 810), 137.0 (100), 122.0 (23). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{10}H_{12}OS^+$: 180.0609; found: 180.0608. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3010(w), 2920(w), 1698(vs) cm^{-1}.

Phenyl(1-phenylcyclopropyl)methanone (4ac): 1,2-diphenylcyclobut-1-ene (**3ac**) for the following rearrangement was synthesized according to the literature.[20] Using **3ac** according to general **Bc** provided **4ac** (0.36 mmol, 80 mg, 72%) as yellowish oil. R_f = 0.5 (hexane/EtOAc 95:5, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.91 – 7.84 (m, 2H), 7.53 – 7.23 (m, 8H), 1.79 (dd, *J* = 7.3, 4.1 Hz, 2H), 1.48 ppm (dd, *J* = 7.0, 3.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.5, 141.1, 137.1, 132.1, 129.5, 128.7, 128.1, 128.0, 126.7, 35.2, 16.4 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 222.1 (80), 193.1 (5), 165 (10), 105.0 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{16}H_{14}O^+$: 222.1045; found: 222.1039.

1-(1-(4-Methoxyphenyl)cyclopropyl)-3-phenylpropan-1-one (4ad): Using **3ad** according to general **Bc** provided **4ad** (0.16 mmol, 45 mg, 85%) as colorless oil. R_f = 0.65 (hexane/EtOAc 8:2, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.23 (tq, *J* = 6.7, 6.6, 3.4, 3.2 Hz, 4H), 7.18 – 7.13 (m, 1H), 7.09 – 7.04 (m, 2H), 6.87 – 6.83 (m, 2H), 3.81 (s, 3H), 2.78 (t, *J* = 7.6 Hz, 2H), 2.60 (t, *J* = 7.6 Hz, 2H), 1.57 (dd, *J* =7.2, 3.5 Hz, 2H), 1.11 ppm (dd, *J* = 7.2, 3.5 Hz, 2H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 210.5, 159.0, 141.5, 132.8, 132.1, 128.5, 128.5, 126.0, 114.1, 55.4, 43.5, 36.6, 30.3, 19.2 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 280.0 (60), 189.1 (30), 161.0 (70). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{19}H_{20}O_2^+$: 280.1463; found: 280.1458. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3086(vw), 3026(w), 3003(w), 2955(w), 2952(w), 2934(w), 2931(w), 2923(vw), 2835(vw), 1716(w), 1689(s), 1651(vw), 1610(m), 1579 cm^{-1} (w).

1-((1*R,2*R**)-2-Phenethyl-1-(*p*-tolyl)cyclopropyl)ethanone ((*R**)-4ae)**: Using (2-(3-iodo-2-methylcyclobut-2-en-1-yl)ethyl)benzene (**2d**) and 4,4,5,5-tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane according to general procedure **A** and **Ba** provided **(*R**)-4ae** (0.15 mmol, 42 mg, 60%) as colorless oil. R_f = 0.7 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.24 – 7.17 (m, 5H), 7.15 – 7.11 (m, 2H), 2.80 – 2.71 (m, 1H), 2.69 – 2.61 (m, 1H), 2.35 (s, 3H), 1.95 (s, 3H), 1.91 – 1.80 (m, 2H), 1.76 – 1.66 (m, 2H), 1.15 – 1.05 ppm (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.3, 141.8, 139.6, 137.2, 130.5, 129.4, 128.6, 128.5, 126.0, 42.6, 36.4, 32.1, 30.9, 28.5, 21.6, 21.2 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 278.1 (2), 187.1 (10), 173.1 (15), 148.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{20}H_{22}O^+$: 278.1671; found: 278.1662. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3086(vw), 3062(vw), 3026(w), 3000(w), 2922(w), 2860(w), 1688(vs), 1654(vw), 1604(w) cm^{-1}.

1-((1*R,2*S**)-2-Phenethyl-1-(*p*-tolyl)cyclopropyl)ethanone ((*S**)4ae)**: Using **2d** and 4,4,5,5-tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane according to general procedure **A** and **Ba** provided **(*S**)-4ae** (0.08 mmol, 23 mg, 32%) as colorless oil. R_f = 0.6 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 – 7.20 (m, 2H), 7.15 (s, 5H), 7.09 – 7.06 (m, 2H), 2.77 – 2.58 (m, 2H), 2.35 (s, 3H), 1.99 – 1.92 (m, 1H), 1.97 (s, 3H), 1.79 – 1.67 (m, 1H), 1.60 (ddd, *J* = 8.8, 3.6, 0.8 Hz, 1H), 1.00 (dd, *J* = 6.8, 3.6 Hz, 1H), 0.91 – 0.79 ppm (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.4, 142.0, 137.2, 135.0, 131.4, 129.4, 128.6, 128.4, 125.9, 42.2, 35.7, 33.0, 29.9, 29.7, 25.3, 21.3 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 278.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{20}H_{22}O^+$: 278.1671; found: 278.1660. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3026(w), 3000(w), 2924(w), 2858(w), 1690(vs) cm^{-1}.

1-((1*R,2*R**)-2-Phenethyl-1-((*E*)-styryl)cyclopropyl)ethanone ((*R**)-4af)**: Using **2d** and (*E*)-styrylboronic acid according to general procedure **A** and **Ba** provided **(*R**)-4af** (0.11 mmol, 31 mg, 43%) as colorless oil. R_f = 0.8 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.23 (m, 7H), 7.23 – 7.16 (m, 3H), 6.68 (d, *J* = 15.8 Hz, 1H), 6.35 (d, *J* = 15.8 Hz, 1H), 2.74 – 2.54 (m, 2H), 2.21 (s, 3H), 1.83 – 1.73 (m, 2H), 1.60 (dd, *J* = 7.5, 4.1 Hz, 1H), 1.52 – 1.41 (m, 1H), 1.22 ppm (dd, *J* = 8.6, 4.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.3, 141.7, 136.9, 130.9, 129.9, 128.8, 128.8, 128.5, 127.8, 126.2, 126.1, 39.4, 36.1, 34.2, 30.6, 28.6, 21.1 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 290.1 (5), 199.1 (10). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{21}H_{22}O^+$: 290.1671; found: 290.1660. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3060(w), 3026(m), 3000(w), 2920(w), 1692(vs), 1644(w), 1602(w) cm^{-1}.

1-((1*S,2*R**)-2-Phenethyl-1-((*E*)-styryl)cyclopropyl)ethanone ((*S**)-4af)**: Using **2d** and (*E*)-styrylboronic acid according to general procedure **A** and **Ba** provided **(*S**)-4af** (0.08 mmol, 24 mg, 33%) as colorless oil. R_f = 0.7 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.25 (m, 7H), 7.24 – 7.18 (m, 1H), 7.15 – 7.09 (m, 2H), 6.39 (d, *J* = 15.8 Hz, 1H), 6.21 (d, *J* = 15.8 Hz, 1H), 2.77 – 2.59 (m, 2H), 2.16 (s, 3H), 1.77 – 1.62 (m, 2H), 1.62 – 1.53 (m, 2H), 1.03 ppm (dd, *J* = 6.2, 3.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.4, 141.8, 136.8, 134.3, 128.8, 128.8, 128.5, 127.9, 126.4, 126.1, 125.6, 39.4, 36.1, 32.4, 30.6, 29.3, 21.9 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 290.1 (4), 199.1 (53), 141.1 (10). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{21}H_{22}O^+$: 290.1671; found: 290.1663. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3060(w), 3025(w), 2998(w), 2926(w), 2922(w), 2919(w), 2859(w), 1729(w), 1691(vs), 1655(w), 1643(w), 1602(w) cm^{-1}.

1-((1*R,2*R**)-1-(Furan-3-yl)-2-phenethylcyclopropyl)ethanone ((*R**)-4ag)**: Using **2d** and furan-3-ylboronic acid according to general procedure **A** and **Ba** provided **(*R**)-4ag** (0.085 mmol, 21 mg, 33%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 1.7 Hz, 1H), 7.32 – 7.24 (m, 3H), 7.23 – 7.16 (m, 3H), 6.30 (dd, *J* = 1.8, 0.9 Hz, 1H), 2.74 – 2.56 (m, 2H), 2.06 (s, 3H), 1.92 – 1.72 (m, 2H), 1.63 (dd, *J* = 7.3, 3.5 Hz, 1H), 1.61 – 1.53 (m, 1H), 1.03 ppm (dd, *J* = 8.2, 3.5 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 206.9, 143.2, 141.6, 141.4, 128.7, 128.5, 127.3, 126.1, 112.1, 36.2, 33.1, 32.2, 30.5, 28.2, 21.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 254.1 (3), 163.0 (29). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{18}O_2^+$: 254.1307; found: 254.1299. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3026(w), 3002(w), 2924(w), 2860(w), 1770(m), 1690(s), 1602(w) cm^{-1}.

1-((1*R,2*S**)-1-(Furan-3-yl)-2-phenethylcyclopropyl)ethanone ((*S**)-4ag)**: Using **2d** and furan-3-ylboronic acid according to general procedure **A** and **Ba** provided **(*S**)-4ag** (0.08 mmol, 19 mg, 30%) as colorless oil. R_f = 0.4 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 (dd, *J* = 1.7 Hz, 1H), 7.30 (dd, *J* = 1.5, 0.9 Hz, 1H), 7.28 – 7.21 (m, 2H), 7.20 – 7.13 (m, 1H), 7.12 – 7.07 (m, 2H), 6.33 (dd, *J* = 1.8, 0.9 Hz, 1H), 2.75 – 2.59 (m, 2H), 2.11 (s, 3H), 1.94 – 1.81 (m, 1H), 1.68 – 1.58 (m, 2H), 1.28 – 1.17 (m, 1H), 0.93 ppm (dd, *J* = 6.9, 3.6 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.6, 143.3, 142.6, 141.9, 128.5, 128.5, 126.0, 122.6, 112.9, 35.6, 33.1, 32.2, 29.8,

29.4, 25.0 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 254.1 (29), 117.1 (17). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{18}O_2^+$: 254.1307; found: 254.1299. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3025(w), 2932(w), 2926(w), 2923(w), 1758(vs), 1688(vs), 1635(w), 1627(w), 1602(w) cm^{-1}.

1-((1*R,2*R**)-2-Phenethyl-1-(3,4,5-trimethoxyphenyl)cyclopropyl)ethanone ((*R**)-4ah)**: Using **2d** and (3,4,5-trimethoxyphenyl)boronic acid according to general procedure **A** and **Ba** provided **(*R**)-4ah** (0.07 mmol, 26 mg, 43%) as colorless oil. R_f = 0.4 (hexane/EtOAc 8:2, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 – 7.27 (m, 2H), 7.25 – 7.16 (m, 3H), 6.46 (s, 2H), 3.83 (s, 3H), 3.82 (s, 6H), 2.70 (t, *J* = 7.3 Hz, 2H), 1.98 (s, 3H), 1.93 – 1.80 (m, 2H), 1.77 – 1.67 (m, 2H), 1.10 ppm (dd, *J* = 7.8, 2.9 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.1, 153.3, 141.6, 138.1, 137.3, 128.6, 128.6, 126.1, 107.4, 61.0, 56.3, 43.5, 36.2, 31.7, 30.6, 28.1, 21.7 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 354.2 (26), 311.2 (17), 263.1 (10), 219.1 (919, 181.1 (100), 165.1 (24). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{22}H_{26}O_4^+$: 354.1831; found: 354.1819. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2998(w), 2936(w), 2838(vw), 1688(m) cm^{-1}.

1-((1*R,2*S**)-2-Phenethyl-1-(3,4,5-trimethoxyphenyl)cyclopropyl)ethanone ((*S**)-4ah)**: Using **2d** and (3,4,5-trimethoxyphenyl)boronic acid according to general procedure **A** and **Ba** provided **(*S**)-4ah** (0.03 mmol, 12 mg, 20%) as colorless oil. R_f = 0.3 (hexane/EtOAc 8:2, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.29 – 7.20 (m, 2H), 7.19 – 7.13 (m, 1H), 7.12 – 7.07 (m, 2H), 6.47 (s, 2H), 3.86 (s, 3H), 3.85 (s, 6H), 2.79 – 2.61 (m, 2H), 2.02 (s, 3H), 2.01 – 1.93 (m, 1H), 1.81 – 1.69 (m, 1H), 1.57 (dd, *J* = 9.0, 3.7 Hz, 1H), 1.00 (dd, *J* = 6.8, 3.7 Hz, 1H), 0.98 – 0.88 ppm (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.9, 153.3, 141.9, 137.4, 133.6, 128.5, 128.5, 126.0, 108.3, 61.1, 56.3, 43.1, 35.7, 33.0, 29.6, 29.5, 25.4 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 354.2 (100), 339.2 (39), 207.1 (17), 189.1 (22). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{22}H_{26}O_4^+$: 354.1831; found: 354.1822. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3000(w), 2936(w), 1688(m) cm^{-1}.

1-((1*R,2*R**)-2-Pentyl-1-(*p*-tolyl)cyclopropyl)ethanone ((*R**)-4ai)**: Using **2c** and 4,4,5,5-tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane according to general procedure **A** and **Ba** provided **(*R**)-4ai** (0.18 mmol, 21 mg, 55%) as colorless oil. R_f = 0.6 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 – 7.21 (m, 2H), 7.16 – 7.12 (m, 2H), 2.35 (s, 3H), 1.98 (s, 3H), 1.71 – 1.65 (m, 2H), 1.52 – 1.40 (m, 3H), 1.37 – 1.24 (m, 5H), 1.11 – 1.03 (m, 1H), 0.93 – 0.84 ppm (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.4, 139.9, 137.1, 130.6, 129.4, 42.6, 32.8, 31.8, 30.8, 30.0, 26.8, 22.8, 21.6, 21.3, 14.2 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 244.2 (56), 187.1 (10), 160.1 (14). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{24}O^+$: 244.1827; found: 244.1820. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3000(w), 2956(m), 2924(m), 2858(m), 1692(vs) cm^{-1}.

1-((1*R,2*S**)-2-Pentyl-1-(*p*-tolyl)cyclopropyl)ethanone ((*S**)-4ai)**: Using **2c** and 4,4,5,5-tetramethyl-2-(*p*-tolyl)-1,3,2-dioxaborolane according to general procedure **A** and **Ba** provided **(*S**)-4ai** (0.08 mmol, 9 mg, 24%) as colorless oil. R_f = 0.55 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 (s, 4H), 2.36 (s, 3H), 1.96 (s, 3H), 1.93 – 1.84 (m, 1H), 1.61 (ddd, *J* = 8.8, 3.5, 0.7 Hz, 1H), 1.49 – 1.31 (m, 3H), 1.27 – 1.16 (m, 4H), 1.01 (dd, *J* = 6.9, 3.5 Hz, 1H), 0.87 – 0.78 (m, 3H), 0.57 – 0.44 ppm (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 209.7, 137.0, 135.3, 131.4, 129.3, 42.2, 31.7, 30.8, 30.3, 29.9, 29.1, 25.6, 22.7, 21.3, 14.2 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 244.2 (100), 187.1 (12), 169.1 (12), 160.1 (20), 145.1 (43). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{24}O^+$: 244.1827; found: 244.1821. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3000(w), 2956(m), 2928(m), 2858(m), 1692(vs) cm^{-1}.

(*E*)-8-Methyl-1-(4-(trifluoromethyl)phenyl)nona-1,8-diene-3,6-dione (6a): Using **2c** and (*E*)-(4-(trifluoromethyl)styryl)boronic acid according to general procedure **A** and **C** provided **6a** (0.10 mmol, 31 mg, 40%) as colorless oil. R_f = 0.28 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (s, 4H), 7.58 (d, *J* = 16.2 Hz, 1H), 6.81 (d, *J* = 16.2 Hz, 1H), 4.97 (s, 1H), 4.86 (s, 1H), 3.20 (s, 2H), 2.98 (t, *J* = 6.1 Hz, 2H), 2.87 (t, *J* = 6.1 Hz, 2H), 1.77 ppm (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.4, 198.3, 140.8, 139.3, 138.0, 132.0 (q, *J* = 32.7 Hz), 128.5, 128.1, 126.0 (q, *J* = 3.8 Hz), 123.9 (q, *J* = 272.2 Hz), 115.4, 52.4, 35.6, 34.7, 22.8 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 310.2 (2), 255.1 (100), 227.1 (30), 199.1 (62). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{17}H_{17}F_3O_2^+$: 310.1181; found: 310.1168. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2973(vw), 2917(vw), 2854(vw), 1714(m), 1694(m), 1670(m), 1616(m) cm^{-1}.

(*E*)-1-Cyclohexyl-8-methylnona-1,8-diene-3,6-dione (6b): Using **2a** and (*E*)-(2-cyclohexylvinyl)boronic acid according to general procedure **A** and **C** provided **6b** (0.12 mmol, 29 mg, 48%) as slightly yellow oil. R_f = 0.50 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.80 (dd, *J* = 16.1, 6.8 Hz, 1H), 6.05 (dd, *J* = 16.1, 1.3 Hz, 1H), 4.95 (s, 1H), 4.84 (s, 1H), 3.18 (s, 2H), 2.85 (t, *J* = 6.3 Hz, 2H), 2.77 (t, *J* = 6.2 Hz, 2H), 2.23 – 2.07 (m, 1H), 1.76 (s, 3H), 1.83 – 1.60 (m, 4H), 1.34 – 1.05 ppm (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.6, 199.1, 152.7, 139.2, 127.5, 115.1, 52.3, 40.6, 35.3, 33.5, 31.7, 25.9, 25.7, 22.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 248.3 (2), 193.2 (23). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{16}H_{24}O_2^+$: 248.1776; found: 248.1772. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2926(vs), 2853(m), 1717(m), 1698(m), 1674(s), 1650(w), 1628(m) cm^{-1}.

(*E*)-7-Phenylhept-6-ene-2,5-dione (6c): Using **2b** and (*E*)-styrylboronic acid according to general procedure **A** and **C** provided **6c** (0.13 mmol, 25 mg, 50%) as colorless oil. R_f = 0.10 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 (d, *J* = 16.2 Hz, 1H), 7.56 – 7.51 (m, 2H), 7.42 – 7.36 (m, 3H), 6.76 (d, *J* = 16.2 Hz, 1H), 2.98 (dd, *J* = 6.6, 5.5 Hz, 2H), 2.83 (dd, *J* = 6.9, 5.7 Hz, 2H), 2.24 ppm (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.5, 198.6, 143.0, 134.5, 130.7, 129.1, 128.4, 126.1, 37.2, 34.3, 30.2 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 202.1 (4), 144.1 (24), 131.1 (100). **HRMS** (EI-Orbitrap): m/z: [M-H]+ Calcd for $C_{13}H_{13}O_2^+$: 201.0910; found: 201.0912. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2908(w), 1714(vs), 1690(s), 1664(vs), 1614(vs) cm^{-1}.

(*E*)-Tridec-6-ene-2,5-dione (6d): Using **2b** and (*E*)-oct-1-en-1-ylboronic acid according to general procedure **A** and **C** provided **6d** (0.12 mmol, 25 mg, 48%) as colorless oil. R_f = 0.13 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.87 (dt, *J* = 15.9, 6.9 Hz, 1H), 6.10 (d, *J* = 15.9 Hz, 1H), 2.84 (t, *J* = 6.3 Hz, 2H), 2.75 (t, *J* = 6.3 Hz, 2H), 2.21 (dd, *J* = 13.6, 7.0 Hz, 2H), 2.21 (s, 3H), 1.52 – 1.38 (m, 2H), 1.37 – 1.21 (m, 6H), 0.88 ppm (t, *J* = 6.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 207.6, 198.8, 148.2, 130.1, 37.1, 33.6, 32.7, 31.7, 30.2, 29.0, 28.2, 22.7, 14.2 ppm. **HRMS** (ESI-quadrupole pos): m/z: [M]+ Calcd for $C_{13}H_{22}O_2^+$: 210.1620; found: 210.1622. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2956(m), 2926(s), 2871(m), 2857(m), 1718(vs), 1700(vs), 1675(vs), 1630(s) cm^{-1}.

(*E*)-3-Phenethyl-7-(*p*-tolyl)hept-6-ene-2,5-dione (6e): Using **2d** and (*E*)-(4-methylstyryl)boronic acid according to general proce-

dure **A** and **C** provided **6e** (0.11 mmol, 34 mg, 43%) as colorless oil. R_f = 0.3 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.53 (d, *J* = 16.2 Hz, 1H), 7.47 – 7.41 (m, 2H), 7.34 – 7.27 (m, 2H), 7.23 – 7.14 (m, 5H), 6.68 (d, *J* = 16.2 Hz, 1H), 3.29 – 3.14 (m, 2H), 2.84 – 2.71 (m, 1H), 2.68 – 2.54 (m, 2H), 2.38 (s, 3H), 2.29 (s, 3H), 2.03 – 1.90 (m, 1H), 1.84 – 1.69 ppm (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 211.4, 198.5, 143.1, 141.2, 141.1, 131.6, 129.7, 128.6, 128.4, 128.3, 126.2, 124.9, 46.6, 42.1, 33.4, 33.1, 30.0, 21.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 320.1 (2), 216.1 (26), 145.1 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{22}H_{24}O_2^+$: 320.1776; found: 320.1768. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3056(w), 3026(w), 2924(w), 2860(w), 1710(vs), 1686(s), 1656(s), 1602(vs) cm^{-1}.

(*E*)-3-Phenethyl-7-phenylhept-6-ene-2,5-dione (6f): Using **2d** and (*E*)-styrylboronic acid according to general procedure **A** and **C** provided **6f** (0.12 mmol, 37 mg, 48%) as colorless oil. R_f = 0.3 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.60 – 7.51 (m, 3H), 7.43 – 7.37 (m, 3H), 7.33 – 7.27 (m, 2H), 7.25 – 7.15 (m, 3H), 6.72 (d, *J* = 16.3 Hz, 1H), 3.29 – 3.16 (m, 2H), 2.84 – 2.71 (m, 1H), 2.71 – 2.53 (m, 2H), 2.29 (s, 3H), 2.06 – 1.92 (m, 1H), 1.84 – 1.71 ppm (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 211.5, 198.6, 143.1, 141.3, 134.5, 130.7, 129.1, 128.7, 128.5, 128.4, 126.3, 125.9, 46.7, 42.2, 33.5, 33.2, 30.1 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 306.0 (2), 202.1 (40), 159.0 (10), 131.0 (100). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{21}H_{22}O_2^+$: 306.1620; found: 306.1620. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3060(w), 3026(w), 2928(w), 2860(w), 1708(s), 1688(m), 1658(s), 1610(s) cm^{-1}.

1-(1-(4-Chlorophenyl)cyclopropyl)-2-(pyridin-2-ylsulfonyl)ethanone (B): **4r** was transformed to 6a according to a literature procedure.[25] Purification by chromatography afforded **B** (0.06 mmol, 20 mg, 40%) as colorless oil. R_f = 0.5 (hexane/EtOAc 5:5, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.70 (dt, *J* = 4.8, 1.2 Hz, 1H), 8.05 (dt, *J* = 7.9, 1.1 Hz, 1H), 7.97 (td, *J* = 7.7, 1.7 Hz, 1H), 7.55 (ddd, *J* = 7.6, 4.7, 1.2 Hz, 1H), 7.40 – 7.29 (m, 4H), 4.47 (s, 2H), 1.64 (dd, *J* = 7.3, 4.1 Hz, 2H), 1.27 ppm (dd, *J* = 7.1, 3.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 198.5, 157.1, 150.1, 138.3, 137.2, 134.5, 132.5, 129.5, 127.6, 122.3, 59.5, 38.0, 20.5 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 335.0 (3), 243.0 (13), 229.1 (11), 193.1 (43), 158.1 (21). **HRMS** (EI-Orbitrap): m/z: [M-H]+ Calcd for $C_{16}H_{13}ClNO_3S^+$: 334.0299; found: 334.0288. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2918(w), 1696(s), 1580(w) cm^{-1}.

1-(Benzo[*d*][1,3]dioxol-5-yl)cyclopropanecarboxylic acid (8a): To a solution of **4w** (0.1 mmol) in CCl_4 (0.2 mL) and CH_2Cl_2 (0.1 mL) was added benzyltriethylammonium chloride (6 mg) followed by a dropwise addition of a 50% solution of NaOH (0.15 ml). The mixture was then stirred for 16h at rt. Water was added, and the mixture was extracted with EtOAc, concentrated under vacuum and purified on silica gel, providing **8a** (0.1 mmol, 26 mg, quant.) as white solid. R_f = 0.3 (hexane/EtOAc 6:4, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.83 (d, *J* = 1.6 Hz, 1H), 6.80 (dd, *J* = 7.9, 1.7 Hz, 1H), 6.73 (dd, *J* = 6.4, 3.3 Hz, 1H), 5.94 (s, 2H), 1.62 (dd, *J* = 7.0, 4.1 Hz, 3H), 1.22 ppm (dd, *J* = 6.9, 3.6 Hz, 2H) (COO*H* not observed). **^{13}C NMR** (101 MHz, $CDCl_3$) 181.2, 147.4, 147.0, 132.7, 123.8, 111.3, 108.1, 101.2, 28.7, 17.8 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 206.1 (100), 161.0 (61). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_{10}O_4^+$: 206.0579; found: 206.0570. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3014(w), 2894(w), 2594(w), 1684(vs) cm^{-1}. **mp** (°C): 157-158.

2,2-Difluoro-5-(2-methylcyclobut-1-en-1-yl)benzo[*d*][1,3]dioxole (12): To a solution of 5-bromo-2,2-difluorobenzo[*d*][1,3]dioxole in THF (0.5 M) at –10 °C was slowly added *i*PrMgCl·LiCl (1.1 M in THF) and stirred at aforesaid temperature for 60 minutes. The so obtained (2,2-difluorobenzo[*d*][1,3]dioxol-5-yl)magnesium bromide was subsequently transmetallated to zinc by addition of a zinc chloride solution (1.0 M in THF) and stirring for another 60 minutes at -10 °C. The resulting zinc species was subjected to a Negishi cross-coupling[3] with **2b** to obtain **12**.

1-(1-(2,2-Difluorobenzo[*d*][1,3]dioxol-5-yl)cyclopropyl)ethanone (4aj): Using **12** according to **Bb** provided **4aj** (0.49 mmol, 118 mg, 49%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 – 7.06 (m, 2H), 7.02 (dd, *J* = 7.9, 0.7 Hz, 1H), 2.01 (s, 3H), 1.61 (dd, *J* = 6.8, 3.9 Hz, 2H), 1.16 ppm (dd, *J* = 7.1, 3.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) 208.0, 143.8, 143.1, 137.4, 131.8 (t, *J* = 255.5 Hz), 126.2, 112.1, 109.5, 37.6, 29.1, 19.1 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 240.0 (100), 197.0 (32), 131.0 (40), 103.1 (76). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{12}H_{10}F_2O_3^+$: 240.0598; found: 240.0581.

1-(2,2-Difluorobenzo[*d*][1,3]dioxol-5-yl)cyclopropanecarboxylic acid (8b): To a solution of **4aj** (0.33 mmol) in CCl_4 (0.66 mL) and CH_2Cl_2 (0.33 mL) was added benzyltriethylammonium chloride (20 mg) followed by a dropwise addition of a 50% solution of NaOH (0.5 ml). The mixture was then stirred for 16h at rt. Water was added, and the mixture was extracted with EtOAc, concentrated under vacuum and purified on silica gel, providing **8b** (0.33 mmol, 80 mg, quant.) as white solid. R_f = 0.3 (hexane/EtOAc 6:4, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.08 – 7.03 (m, 2H), 6.98 (d, *J* = 8.2 Hz, 1H), 1.69 (dd, *J* = 7.2, 4.3 Hz, 2H), 1.25 ppm (dd, *J* = 7.2, 3.8 Hz, 2H) (COO*H* not observed). **^{13}C NMR** (101 MHz, $CDCl_3$) 180.7, 143.6, 143.1, 134.9, 131.8 (t, *J* = 253.2 Hz), 125.8, 112.2, 109.1, 28.8, 17.9 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 242.0 (68), 224.0 (16), 196.0 (35). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_8F_2O_4^+$: 242.0391; found: 242.0382. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 2886(w), 2840(w), 1678(vs) cm^{-1}. **mp** (°C): 179-180.

3-Chloro-6-(2-(2-methylcyclobut-1-en-1-yl)phenoxy)pyridazine (10): Using **2b** and (2-methoxyphenyl)boronic acid according to general procedure **A** provided **9.** The product was dissolved in CH_2Cl_2 (1.0 M) and treated with a solution of BBr_3 in CH_2Cl_2 (1.0 eq., 1.0 M) at 30 °C. After 5 min TLC indicated completion of the reaction. The reaction mixture was slowly poured onto ice cold water and subsequently extracted with CH_2Cl_2 (3 × 20 mL) and dried over magnesium sulfate. After evaporation of solvents and purification by chromatography, pure **13** was dissolved in DMF (1.0 M).To the solution was added NaH (1.1 eq., 60 % dispersion in mineral oil) and 3,6-dichloropyridazine. After stirring for 30 min at ambient temperature, TLC indicated full consumption of the starting materials. The reaction mixture was extracted with Et_2O (3 × 20 mL), washed with a saturated aqueous solution of LiCl (20 mL) and Brine (20 mL). After drying the organic phase over magnesium sulfate and evaporation of solvents, chromatography afforded pure **10** as colorless oil. Most fractions contained impurities, a yield was therefore not determined. R_f = 0.3 (hexane/EtOAc 8:2, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 (d, *J* = 9.2 Hz, 1H), 7.36 – 7.33 (m, 1H), 7.18 – 7.12 (m, 2H), 7.02 – 6.98 (m, 1H), 6.96 (d, *J* = 9.1 Hz, 1H), 2.46 – 2.41 (m, 2H), 2.24 – 2.20 (m, 2H), 1.80 – 1.77 ppm (m, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 165.5, 151.8, 149.6, 142.5, 133.9, 131.4, 129.0, 129.0, 128.0, 126.0, 122.4, 119.2, 31.0, 28.9, 16.6 ppm. **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{15}H_{13}ClN_2O^+$: 272.0716; found: 272.0714.

1-(1-(2-((6-Chloropyridazin-3-yl)oxy)phenyl)cyclopropyl)ethanone (11): Using **10** (also impure fractions) according to general procedure **Ba** provided **11** (1.00 mmol, 288 mg, 43% over two steps) as colorless oil. R_f = 0.1 (hexane/EtOAc 8:2, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 9.1 Hz, 1H), 7.45 – 7.36 (m, 2H), 7.29 (dd, *J* = 7.5, 1.3 Hz, 1H), 7.19 (dd, *J* = 8.0, 1.3 Hz, 1H), 7.18 (d, *J* = 9.1 Hz, 1H), 2.08 (s, 3H), 1.43 (dd, *J* = 6.9, 3.8 Hz, 2H), 1.08 ppm (dd, *J* = 7.2, 3.9 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 208.2, 164.8, 153.3, 152.4, 132.9, 131.8, 131.8, 129.3, 126.4, 122.5, 120.2, 33.5, 28.9, 18.1 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 272.1 (9), 237.1 (100), 222.1 (30), 209.1 (15), 194.1 (18), 183.0 (10), 165.0 (12). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{15}H_{12}ClN_2O^+$ ([M-OH]$^+$): 271.0638; found: 271.0635. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3066(w), 2972(w), 1754(w), 1692(m), 1642(w), 1614(w), 1606(w) cm^{-1}.

(*E*)-2-Methyl-5-(4-methylstyryl)-3-phenethylfuran (7): **6e** was dissolved in toluene (0.1 M) and P_4O_{10} (3.0 eq.) was added. The reaction mixture was heated to 100 °C for 24 hours in a pressure tube. After cooling to room temperature, the reaction was quenched with water, extracted with Et_2O (3 × 20 mL), washed with Brine (20 mL) and dried over magnesium sulfate. The organic phase was concentrated under reduced pressure and purified by column chromatography. **7** was obtained (0.10 mmol, 29 mg, 87%) as colorless oil. R_f = 0.2 (hexane, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.32 (m, 2H), 7.31 – 7.26 (m, 2H), 7.23 – 7.11 (m, 5H), 6.90 (d, *J* = 16.2 Hz, 1H), 6.75 (d, *J* = 16.2 Hz, 1H), 6.13 (s, 1H), 2.81 (dd, *J* = 8.7, 6.7 Hz, 2H), 2.62 (dd, *J* = 8.7, 6.7 Hz, 2H), 2.34 (s, 3H), 2.10 ppm (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) 150.8, 147.9, 141.8, 137.2, 134.7, 129.5, 128.7, 128.4, 126.2, 126.1, 125.2, 120.6, 115.9, 110.9, 36.8, 27.1, 21.4, 11.6 ppm. **LRMS** (DEP/EI-Orbitrap): *m/z* (%): 302.1 (100), 211.1 (42), 169.1 (35). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{22}H_{22}O^+$: 302.1671; found: 302.1670.

1-(*p*-Tolyl)cyclopropane-1-carbaldehyde (13a): Using 1-bromo-4-methylbenzene and cyclobutanone according to general procedure **C** provided **13a** (8.4 mmol, 1.346 g, 69%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.28 (s, 1H), 7.26 – 7.13 (m, 4H), 2.38 (s, 3H), 1.57 (dd, *J* = 3.9 Hz, 2H), 1.40 ppm (dd, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.4, 137.5, 134.6, 130.0, 129.4, 37.2, 21.2, 16.2 ppm. **LRMS** (DEP/EI-Orbitrap-Orbitrap): *m/z* (%): 160.1 (100), 145.1 (20). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_{12}O^+$: 160.0888; found: 160.0882. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3010(w), 2923(w), 2919(w), 2822(vw), 2818(vw), 1705(vs), 1517(m) cm^{-1}.

1-(4-Methoxyphenyl)cyclopropane-1-carbaldehyde (13b): Using 1-bromo-4-methoxybenzene and cyclobutanone according to general procedure **C** provided **13b** (0.34 mmol, 60 mg, 34%) as colorless oil. R_f = 0.4 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.22 (s, 1H), 7.25 – 7.20 (m, 2H), 6.93 – 6.87 (m, 2H), 3.81 (s, 3H), 1.54 (dd, *J* = 3.9 Hz, 2H), 1.37 ppm (dd, *J* = 3.5 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.5, 159.1, 131.4, 129.6, 114.1, 55.4, 37.0, 16.2 ppm. **LRMS** (DEP/EI-Orbitrap-Orbitrap): *m/z* (%): 176.1 (100), 161.1 (10), 147.1 (70), 132.1 (15). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_{12}O_2^+$: 176.0837; found: **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 176.0831. 3003(vw), 2958(vw), 2836(w), 2708(vw), 1780(vw), 1703(s), 1611(m), 1579(w), 1514(vs) cm^{-1}.

1-(Naphthalen-1-yl)cyclopropane-1-carbaldehyde (13c): Using 1-bromonaphthalene and cyclobutanone according to general procedure **C** provided **13c** (0.58 mmol, 114 mg, 58%) as colorless oil. R_f = 0.4 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.42 (s, 1H), 8.04 – 7.97 (m, 1H), 7.94 – 7.81 (m, 2H), 7.58 – 7.45 (m, 4H), 1.88 – 1.78 (m, 2H), 1.54 – 1.47 ppm (m, 2H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.7, 134.2, 134.0, 133.3, 129.0, 128.8, 128.5, 126.6, 126.1, 125.5, 124.4, 35.7, 17.2 ppm. **LRMS** (DEP/EI-Orbitrap-Orbitrap): *m/z* (%): 196.1 (90), 178.1 (10), 165.1 (100), 152.1 (90), 139.1 (20). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{14}H_{12}O^+$: 196.0888; found: 196.0883. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 3044(w), 3007(vw), 2819(vw), 2732(vw), 2702(vw), 1780(vw), 1702(s), 1595(w) cm^{-1}.

1-([1,1'-Biphenyl]-4-yl)cyclopropane-1-carbaldehyde (13d): Using 4-bromo-1,1'-biphenyl and cyclobutanone according to general procedure **C** provided **13d** (0.57 mmol, 133 mg, 57%) as colorless oil. R_f = 0.45 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.29 (s, 1H), 7.64 – 7.57 (m, 4H), 7.51 – 7.35 (m, 5H), 1.63 (dd, *J* = 4.1 Hz, 2H), 1.47 ppm (dd, *J* = 4.3 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 201.0, 140.8, 140.7, 136.5, 130.6, 128.9, 127.5, 127.2, 37.3, 16.2 ppm. **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{16}H_{14}O^+$: 222.1045; found: 222.1048. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 1677(m), 1498(m), 1440(w), 1427(w) cm^{-1}.

1-(2,2-Difluorobenzo[*d*][1,3]dioxol-5-yl)cyclopropane-1-carbaldehyde (13e): Using 5-bromo-2,2-difluorobenzo[*d*][1,3]dioxole and cyclobutanone according to general procedure **C**. provided **13e** (0.5 mmol, 105 mg, 50%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.07 (s, 1H), 7.09 – 6.89 (m, 3H), 1.59 (dd, *J* = 4.1 Hz, 2H), 1.41 ppm(dd, *J* = 3.7 Hz, 2H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.0, 143.9, 143.4, 133.5, 131.81 (t, *J* = 255.5 Hz), 125.6, 111.8, 109.5 ppm. **LRMS** (DEP/EI-Orbitrap-Orbitrap): *m/z* (%): 226.1 (80), 207.0 (5), 197.1 (15), 182.0 (5), 170.9 (5). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{11}H_8F_2O_3^+$: 226.0442; found: 226.0435.

1-(4-Bromophenyl)cyclopropane-1-carbaldehyde (13f): Using 1-bromo-4-iodobenzene and cyclobutanone according to general procedure **C**. provided **13f** (0.69 mmol, 155 mg, 69%) as colorless oil. R_f = 0.5 (hexane/EtOAc 9:1, UV, $KMnO_4$, PAA). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 9.14 (s, 1H), 7.51 – 7.47 (m, 2H), 7.20 – 7.16 (m, 2H), 1.58 (dd, *J* = 6.9, 5.0 Hz, 2H), 1.39 ppm (dd, *J* = 7.8, 4.1 Hz, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 200.3, 136.5, 131.9, 131.9, 131.8, 37.2, 15.9 ppm. **LRMS** (DEP/EI-Orbitrap-Orbitrap): *m/z* (%): 226.0 (30), 197.0 (5), 181.9 (5). **HRMS** (EI-Orbitrap): m/z: [M]+ Calcd for $C_{10}H_9BrO^+$: 223.9837; found: 223.9830. **IR** (Diamond-ATR, neat) $\tilde{\nu}_{max}$: 1682(vs), 1488(m), 1429(m), 1420(m) cm^{-1}.

ASSOCIATED CONTENT

Supporting Information

^{1}H and ^{13}C NMR spectra for all new compounds and X-ray crystallographic data of compounds **4f** and **4t**, and computational details can be found in the Supporting Information.

The Supporting Information is available free of charge on the ACS Publications website.

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REFERENCES

[1] a) Wang, X.-N.; Krenske, E. H.; Johnoston, R. C.; Houk, K. N.; Hsung, R. P. *J. Am. Chem. Soc.* **2015**, *137*, 5596. b) Frebault, F.; Luparia, M.; Oliveira, M. T.; Goddard, R.; Maulide, N. *Angew. Chem. Int. Ed.* **2010**, *49*, 5672.

[2] a) Lee-Ruff, E.; Mladenova, G. *Chem. Rev.* **2003**, *103*, 1449. b) Namyslo, J. C.; Kaufmann, D. E. *Chem. Rev*. **2003**, *103*, 1485. c) Xu, Y.; Conner, M. L.; Brown, M. K. *Angew. Chem. Int. Ed*. **2015**, *54*, 11918. d) Misale, A.; Niyomchon, S.; Maulide, N. *Acc. Chem. Res*. **2016**, *49*, 2444.

[3] Eisold, M.; Baumann, A. N.; Kiefl, G. M.; Emmerling, S. T.; Didier, D. *Chem. Eur. J.* **2017**, *23*, 1634.

[4] a) Eisold, M.; Didier, D. *Org. Lett.* **2017**, *19*, 4046. b) Eisold, M.; Kiefl, G. M.; Didier, D. *Org. Lett*. **2016**, *18*, 3022. c) Eisold, M.; Didier, D. *Angew. Chem. Int. Ed*. **2015**, *54*, 15884.

[5] Baumann, A. N.; Eisold, M.; Didier, D. *Org. Lett*. **2017**, *19*, 2114.

[6] a) Bailey, S.; Barrett, S. D.; Bratton, L. D.; Fakhoury, S. A.; Jennings, S. M.; Mitchell, L. H.; Raheja, R. K.; Shanmugasundaram, V. *PCT Int. Appl.* **2007**, WO 2007072164 A2 20070628. b) Tsukamoto, Y.; Komai, H.; Kadotani, J.; Koi, K.; Mio, S.; Takeshiba, H. *PCT Int. Appl.* **2003**, WO 2003016286 A1 20030227. c) Vicker, N.; Su, X.; Pradaux-Caggiano, F.; Potter, B. V. L. *PCT Int. Appl.* **2009**, WO 2009106817 A2 20090903. d) Qiao, J. X.; King, S. R.; He, K.; Wong, P. C.; Rendina, A. R.; Luettgen, J. M.; Xin, B.; Knabb, R. M.; Wexler, R. R.; Lam, P. Y. S. *Bioorg. Med. Chem. Lett.* **2009**, *19*, 462. e) Shibayama, K.; Inagaki, J.; Saiki, Y.; Mitani, A.; Kuwahara, R.; Sato, M.; Nishimura, S.; Kuboki, M. *PCT Int. Appl.* **2011**, WO 2011081174 A1 20110707. f) Delany, C.; Kale, R. D.; Gabriel, S.; Bove, P. *PCT Int. Appl.* **2017**, WO 2017151725 A1 20170908. g) Wainwright, C.E.; Elborn, J. S.; Ramsey, B. W.; Marigowda, G.; Huang, X.; Cipollo, M.; Colombo, C.; Davies, J. C.; De Boeck, K.; Flume, P. A.; Konstan, M. W.; McColley, S. A.; McCoy, K.; McKrone, E. F.; Munck, A.; Ratjen, F.; Rowe, S. M.; Waltz, D.; Boyle, M. P. *N. Engl. J. Med.* **2015**, *373*, 220. h) Ries, U. J.; Priepke, H. W. M.; Hauel, N. H.; Handschuh, S.; Mihm, G.; Stassen, J. M.; Wienen, W.; Nar, H. *Bioorg. Med. Chem. Lett.* **2003**, *13*, 2297. i) Peretto, I.; Radaelli, S.; Parini, C.; Zandi, M.; Raveglia, L. F.; Dondio, G.; Fontanella, L.; Misiano, P.; Bigogno, C.; Rizzi, A.; Riccardi, B.; Biscaiolli, M.; Marchetti, S.; Puccini, P.; Catinella, S.; Rondelli, I.; Cenacchi, V.; Bolzoni, P. T.; Caruso, P.; Villetti, G.; Facchinetti, F.; Del Giudice, E.; Moretto, N.; Imbimbo, B. P. *J. Med. Chem.* **2005**, *48*, 5705.

[7] a) Li, J.; Kennedy, L. J.; Wang, H.; Li, J. J.; Walker, S. J.; Hong, Z.; O'Connor, S. P.; Nayeem, A.; Camac, D. M.; Morin, P. E.; Sheriff, S.; Wang, M.; Harper, T.; Golla, R.; Seethala, R.; Harrity, T.; Ponticiello, R. P.; Morgan, N. N.; Taylor, J. R.; Zebo, R.; Gordon, D. A.; Robl, J. A. *ACS Med. Chem. Lett.* **2014**, *5*, 803. b) Lerner, C.; Jakob-Roetne, R.; Buettelmann, B.; Ehler, A.; Rudolph, M.; Rodríguez Sarmiento, R. M. *J. Med. Chem*. **2016**, *59*, 10163. c) Pieroni, M.; Annunziato, G.; Beato, C.; Wouters, R.; Benoni, R.; Campanini, B.; Pertinhez, T. A.; Bettati, S.; Mozzarelli, A.; Costantino, G. *J. Med. Chem.* **2016**, *59*, 2567. d) Geldenhuys, W. J.; Caproso, J.; Leeper, T. C.; Lee, Y.-K.; Lin, L.; Darvesh, A. S.; Sadana, P. *Bioorg. Med. Chem. Lett.* **2017**, *27*, 303.

[8] a) Zhang, Y.; Pan, L.; Xu, X.; Liu, Q. *RCS Advances* **2012**, *2*, 5138. b) Huang, A.; Moretto, A.; Janz, K.; Lowe, M.; Bedard, P. W.; Tam, S.; Di, L.; Clerin, V.; Sushkova, N.; Tchernychev, B.; Tsao, D. H. H.; Keith Jr., J. C.; Shaw, G. D.; Schaub, R. G.; Wang, Q.; Kaila, N. *J. Med. Chem.* **2010**, *53*, 6003.

[9] a) Papahatjis, D. P.; Niklas, S.; Tsotinis, A.; Vlachou, M.; Makriyannis, A. *Chem. Lett*. **2001**, *3*, 192. b) Arava, V. R.; Siripalli, U. B.; Dubey, P. K. *Tetrahedron Lett*. **2005**, *46*, 7247. c) Barbasiewicz, M.; Marciniak, K.; Fedoryński, M. *Tetrahedron Lett*. **2006**, *47*, 3871. d) Berger, M. D.; Hammerschmidt, F.; Qian, R.; Hahner, S.; Schirbel, A.; Stichelberger, M.; Schibli, R.; Yu, J.; Arion, V. B.; Woschek, A.; Öhler, E.; Zolle, I. M. *Mol. Pharmaceutics* **2013**, *10*, 1119.

[10] a) Aggarwal, V. K.; Winn C. L. *Acc. Chem. Res*. **2004**, *37*, 611. b) Clemens, J. J.; Asgian, J. L.; Busch, B. B.; Coon, T.; Ernst, J.; Kaljevic, L.; Krenitsky, P. J.; Neubert, T. D.; Schweiger, E. J.; Termin, A.; Stamos, D. *J. Org. Chem*. **2013**, *78*, 780. c) Gololobov, Y. G.; Nesmeyanov, A. N.; Lysenko, V. P.; Boldeskul, I. E. *Tetrahedron* **1987**, *43*, 2609.

[11] a) Klapars, A.; Waldman, J. H.; Campos, K. R.; Jensen, M. S.; Mclaughling, M.; Chung, J. Y. L.; Cvetovich, R. J.; Chen, C. *J. Org. Chem.* **2005**, *70*, 10186. b) Caron, S.; Vasquez, E.; Wojcik, J. M. *J. Am. Chem. Soc*. **2000**, *122*, 712. c) McCabe Dunn, J. M.; Kuethe, J. T.; Orr, R. K.; Tudge, M.; Campeau, L.-C. *Org. Lett*. **2014**, *16*, 6314.

[12] a) Chen, H.; Zhang, L. *Angew. Chem. Int. Ed*. **2015**, *54*, 11775. b) Liu, B.; Song, R.-J.; Ouyang, X.-H.; Li, Y.; Hu, M.; Li, J.-H. *Chem. Commun.* **2015**, *51*, 12819.

[13] For early studies of cyclobutene oxide rearrangements, see: a) Heine, H.-G.; Hartmann, W.; Knops, H.-J.; Priesnitz, U. *Tetrahedron Lett.* **1983**, *24*, 2635. b) Conia, J. M. *Angew. Chem.* **1968**, *80*, 578. c) Garin, D. L. *J. Org. Chem.* **1971**, *36*, 1697.

[14] For seminal studies and recent examples, see: a) Meinwald, J.; Labana, S. S.; Chadha, M. S. *J. Am. Chem. Soc.* **1963**, *85*, 582. b) Rickborn, B. *in Comprehensive Organic Synthesis*, Vol. 3 (Eds.: B. M. Trost, I. Fleming, G. Pattenden), Pergamon, Oxford, **1991**, 733. c) Gorzynski Smith, J. *Synthesis* **1984**, 629. d) Fraile, J. M. A.; Mayoral, J. A.; Salvatella, L. *J. Org. Chem.* **2014**, *79*, 5993. e) Jung, M. E.; D'Amico, D. C. *J. Am. Chem. Soc.* **1995**, *117*, 7379. f) Pace, V.; Castoldi, L.; Mazzeo, E.; Rui, M.; Langer, T.; Holzer, W. *Angew. Chem. Int. Ed.* **2017**, *56*, 12677.

[15] a) Criegee, R.; Noll, N. *Liebigs Ann. Chem.* **1959**, *627*, 1-14; b) Shabarov, Y. S.; Blagodatskikh, S. A.; Levina, M. I.; Fedotov, A. N. *Z. Org. Khim.* **1975**, *11*, 1223; c) Kurita, J.; Sakai, H.; Tsuchiya, T. *J. Chem. Soc. Chem. Commun.* **1985**, 1769-1770; d) Wiberg, K. B.; Matturro, M. G.; Okarma, P. J.; Jason, M. E.; Dailey, W. P.; Burgmaier, G. J.; Bailey, W. F.; Warner, P. *Tetrahedron* **1986**, *42*, 1895-1902; e) Kurita, J.; Sakai, H.; Tsuchiya, T. *Chem. Pharm. Bull.* **1988**, *36*, 2887-2896; f) Mévellec, L.; Evers, M.; Huet, F. *Tetrahedron* **1996**, *52*, 15103-15116; g) Lescop, C.; Huet, F. *Tetrahedron* **2000**, *56*, 2995-3003. h) Ripoll, J.-L.; Conia, J.-M. *Bull. Soc. Chim. Fr.* **1965**, 2755. i) de Mayo, P.; Wenska, G. *Tetrahedron* **1987**, *43*, 1661-1670.

[16] A [4+2]-cycloaddition of the diene with O_2 is assumed to be responsible for the formation of 1,4-diketones. For a recent example, see: Shen, L.; Zhao, K.; Doitomi, K.; Ganguly, R.; Li, Y.-X.; Shen, Z.-L.; Hirao, H.; Loh, T.-P. *J. Am. Chem. Soc.* **2017**, *139*, 13570.

[17] See supporting information.

[18] CCDC 1580399 (**4f**) and CCDC 1580400 (**4t**) contain the crystallographic data for this paper.

[19] Kasai K.; Liu Y.; Hara R.; Takahashi T. *Chem. Commun*. **1998**, *18*, 1989.

[20] Toda F.; Takehira Y.; Kataoka Y.; Mori K.; Sato T.; Segawa M. *J. Chem. Soc., Chem. Commun*. **1984**, 1234.

[21] Gaussian 16, Revision A.03, Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Scalmani, G.; Barone, V.; Petersson, G. A.; Nakatsuji, H.; Li, X.; Caricato, M.; Marenich, A. V.; Bloino, J.; Janesko, B. G.; Gomperts, R.; Mennucci, B.; Hratchian, H. P.; Ortiz, J. V.; Izmaylov, A. F.; Sonnenberg, J. L.; Williams-Young, D.; Ding, F.; Lipparini, F.; Egidi, F.; Goings, J.; Peng, B.; Petrone, A.; Henderson, T.; Ranasinghe, D.; Zakrzewski, V. G.; Gao, J.; Rega, N.; Zheng, G.; Liang, W.; Hada, M.; Ehara, M.; Toyota, K.; Fukuda, R.; Hasegawa, J.; Ishida, M.; Nakajima, T.; Honda, Y.; Kitao, O.; Nakai, H.; Vreven, T.; Throssell, K.; Montgomery, J. A., Jr.; Peralta, J. E.; Ogliaro, F.; Bearpark, M. J.; Heyd, J. J.; Brothers, E. N.; Kudin, K. N.; Staroverov, V. N.; Keith, T. A.; Kobayashi, R.; Normand, J.; Raghavachari, K.; Rendell, A. P.; Burant, J. C.; Iyengar, S. S.; Tomasi, J.; Cossi, M.; Millam, J. M.; Klene, M.; Adamo, C.; Cammi, R.; Ochterski, J. W.; Martin, R. L.; Morokuma, K.; Farkas, O.; Foresman, J. B.; Fox, D. J. Gaussian, Inc., Wallingford CT, **2016.**

[22] Werner, H.-J.; Knowles, P. J.; Knizia, G.; Manby, F. R.; Schütz., M.; Celani, P.; Korona, T.; Lindh, R.; Mitrushenkov, A.; Rauhut, G.; Shamasundar, K. R.; Adler, T. B.; Amos, R. D.; Bernhardsson, A.; Berning, A.; Cooper, D. L.; Delegan, M. J. O.; Dobbyn, A. J.; Eckert, F.; Goll, E.; Hampel, C.; Hesselmann, A.; Hetzer, G.; Hrenar, T.; Jansen, G.; Köppl, C.; Liu, Y.; Lloyd, A. W.; Mata, R. A.; May, A. J.; McNicholas, S. J.; Meyer, W.; Mura, M. E.; Nicklass, A.; O'Neill, D. P.; Palmieri, P.; Peng, D.; Pflüger, K.; Pitzer, R.; Reiher, M.; Shiozaki, T.; Stoll, H.; Stone, A. J.; Tarroni, R.; Thorsteinsson, T.; Wang, M., MOLPRO, version 2012.1, a package of ab initio programs. 2012.

[23] Molcas 8: F. Aquilante, J. Autschbach, R. K. Carlson, L. F. Chibotaru, M. G. Delcey, L. De Vico, I. Fdez. Galván, N. Ferré, L. M. Frutos, L. Gagliardi, M. Garavelli, A. Giussani, C. E. Hoyer, G. Li Manni, H. Lischka, D. Ma, P. Å. Malmqvist, T. Müller, A. Nenov, M. Olivucci, T. B. Pedersen, D. Peng, F. Plasser, B. Pritchard, M. Reiher, I. Rivalta, I. Schapiro, J. Segarra-Martí, M. Stenrup, D. G. Truhlar, L. Ungur, A. Valentini, S. Vancoillie, V. Veryazov, V. P. Vysotskiy, O. Weingart, F. Zapata, R. Lindh, *J. Comput. Chem.*, **2016**, *37*, 506.

[24] Sevin, F. McKee, M. L., *J. Am. Chem. Soc*. **2001**, *123*, 4591.

[25] Hirsch, E.; Hünig, S.; Reißig, H.-U. *Chem. Ber.* **1982**, *115*, 399.