JOC The Journal of Organic Chemistry

Article

Microwave-Enhanced Coupling of Carboxylic Acids with Liquid Ketones and Cyclic Ethers using TBAI/TBHP

Pablo Macías-Benítez, F. Javier Moreno-Dorado, and Francisco Miguel Guerra

J. Org. Chem., **Just Accepted Manuscript** • DOI: 10.1021/acs.joc.0c00519 • Publication Date (Web): 09 Apr 2020

Just Accepted

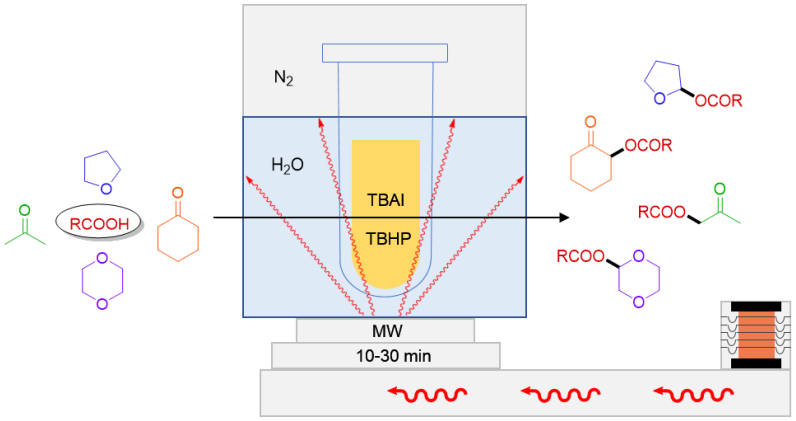
is published by the American Chemical Society. 1155 Sixteenth Street N.W., Washington, DC 20036

Microwave-Enhanced Coupling of Carboxylic Acids with Liquid Ketones and Cyclic Ethers using TBAI/TBHP

Pablo Macías-Benítez, F. Javier Moreno-Dorado,* and Francisco M. Guerra*

Departamento de Química Orgánica, Facultad de Ciencias, Universidad de Cádiz,

11510 Puerto Real, Cádiz, Spain.



ABSTRACT: The oxidative coupling of carboxylic acids with liquid ketones and cyclic ethers has been accomplished in minutes using *t*-butyl hydroperoxide in the presence of TBAI under microwave irradiation in the absence of a solvent. In addition to drastically shortening the reaction times, the use of microwaves resulted, in general, in yields equal to or higher than those obtained by conventional heating.

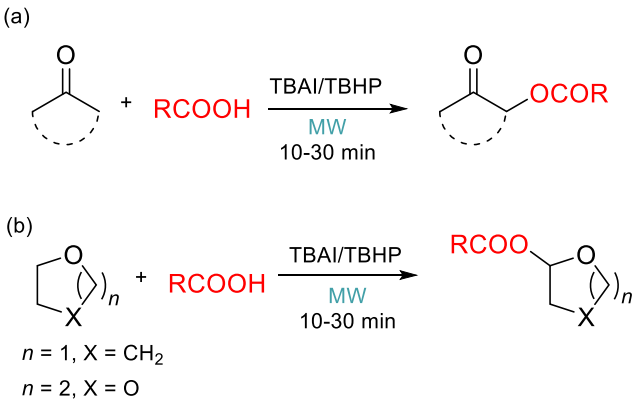
INTRODUCTION

The discovery of new methods of formation of C-O bonds is a privileged topic in chemical synthesis, which today, under the current environmental standards, should meet certain conditions.[1] For instance, prefunctionalization of substrates is to be avoided so as not to include unnecessary steps and the use of metals or toxic reagents is not always desirable in order to meet regulatory requirements. In this scenario, different oxidation procedures based on the use of iodine have emerged as alternatives to transition metal-based oxidizing systems. Whether as molecular iodine, as an iodide anion or as a hypervalent species, the use of this element in conjunction with different oxidants has increased rapidly and found numerous applications.[2]

One of the most successful oxidation systems is that formed by tetrabutylammonium iodide (TBAI) as a catalyst and *t*-butyl hydroperoxide (TBHP) as a stoichiometric oxidant. In 2014, Wu et al reviewed the use of TBAI/TBHP in the formation of new C-C, C-O, C-N, and C-S bonds.[3] The topic was revisited by Wan in 2018.[4] This couple of reagents has showcased a wide versatility, being involved in reactions ranging from the synthesis of indoles[5] to α-ketoamides,[6] oxazoles[7] or peresters[8] to name but a few. The reaction conditions are usually mild and the tolerance to different functional groups is notable. In a more specific context, the TBAI/TBHP system has proved to be a good oxidizing agent for introducing an oxygenated function contiguous to a carbonyl group. Cheng et al employed benzylic alcohols as acylating agents to produce α-acyloxycarbonyl compounds from ketones.[5] Wang and Zhu reported the use of aldehydes as surrogates of carboxylic acids in the preparation of α-acyloxy ketones.[9] In 2018, Reddy et al demonstrated the viability of the synthesis of acyloxyacetone derivatives via coupling of acetone and aromatic carboxylic acids in the presence of TBAI/TBHP.[10] Most of these methods are centered in aryl ketones and require long reaction times.

In view of the foregoing observations, we decided to evaluate the performance of the TBAI/TBHP system under microwave irradiation. The use of microwaves in synthesis (also denoted as MAOS, microwave-assisted organic synthesis) has become a common technique in chemical synthesis.[11,12] In countless cases, MAOS has proven to be very effective in drastically shortening reaction times and they often provide fairly cleaner crude mixtures. The possibility of heating the mixture *from inside* to temperatures above the boiling point of the solvent for a certain time and the strict control of temperature, pressure, and irradiation conditions that modern microwave reactors enable, all combine to make this technique an appealing alternative to conventional heating.

Herein, we describe how the use of TBAI/TBHP under microwave irradiation allows for the introduction of acyloxy groups in certain ketones and ethers using carboxylic acids, both aromatic and aliphatic, as the source of the acyloxy group, in minutes and mostly with good to excellent yields (Scheme 1).



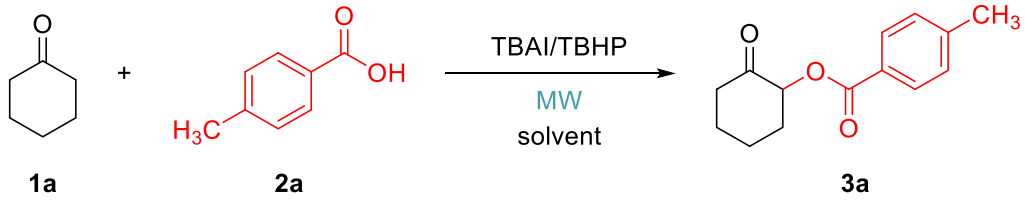
Scheme 1. Oxidation of ketones and ethers with the system TBAI/TBHP under microwave irradiation.

RESULTS AND DISCUSSION

To begin our study, we chose as a benchmark reaction the coupling between *p*-methoxybenzoic acid and cyclohexanone, both commercial and inexpensive reagents. We first selected some common working conditions according to previous results. The carboxylic acid was selected as the limiting reactant. In the initial runs, a slight excess of cyclohexanone (1.3 equiv) was employed and TBAI was set at 0.1 equiv. The reactions were carried out in 2 mL solvent, setting the irradiation time at 30 min and the temperature at 120 °C. Under these conditions, a first round of reactions in different solvents was carried out (Table 1).

As can be observed, most reactions took place with low yields. In the case of methanol (Table 1, entry 3), diethyl ether (table 1, entry 6), and dichloromethane (Table 1, entry 10), the reaction did not proceed at all. Only dimethoxyethane (DME) and 1,4-dioxane produced moderate yields (34% and 37% respectively), although in the latter case, a 31% of the coupling product between the solvent and the carboxylic acid was formed (*vide infra*).

Table 1. Screening of conditions between cyclohexanone and *p*-methylbenzoic acid.



1a **2a** **3a**

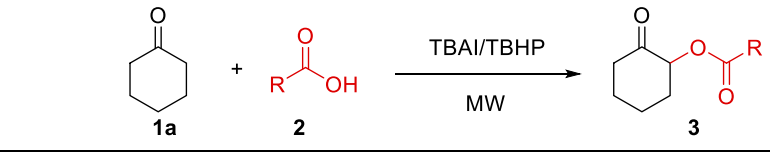
Entry	Cyclohexanone (equiv)	Solvent	Yield, (%)
1	1.3	ethyl acetate	28
2	1.3	2-methoxyethanol	24
3	1.3	methanol	NR
4	1.3	1,4-dioxane	37[a]
5	1.3	DME	34
6	1.3	diethyl ether	NR
7	1.3	DMF	28
8	1.3	fluorobenzene	19
9	1.3	acetonitrile	21
10	1.3	DCM	NR
11	1.3	-	35
12[b]	1.3	-	34
13	19.3 (2 mL)		83

General reaction conditions: *p*-methylbenzoic acid (1 mmol), cyclohexanone, TBAI (0.1 equiv.), TBHP (3 equiv., 70 % in H_2O), solvent (2 mL), 30 min MW irradiation, 120 ºC. [a] Plus 31% of compound **7b** [b] TBHP in decane.

Entries 11-12 correspond to reactions carried out in the absence of solvent. The solvent in wich TBHP was purchased, either water or decane (entries 11 and 12) was irrelevant in the outcome of the reaction. Finally, when an excess of cyclohexanone was employed (2 mL, 19.3 equiv), the reaction took place in an interesting 83% yield (entry 13). These preliminary studies seemed to indicate that an excess of ketone was necessary for the reaction to take place with usable yields from a synthetic perspective. Although this may be seen as a drawback in terms of atom economy, in the cases that we will describe below, the substrate has been chosen in such a way that it can be easily recovered and conveniently recycled.

Once the optimal conditions had been established, we decided to evaluate the scope of the reaction with regard to the nature of the carboxylic acid. The results are shown in Table 2.

Table 2. Scope of carboxylic acids and cyclohexanone.



1a **2** **3**

3b, 46%[a] **3a**, 83%[a] **3c**, 87%[a]

3d, 40%[b] **3e**, 60%[b] **3f**, 92%[a]

3g 39%[a,e] **3h**, traces **3i**, 68%[b]

3j, 41%[b] **3k**, 31%[b] **3l**, 91%[a]

3m, 86%[a] **3n**, 18%[a] **3o**, 51%[c,d]

3p, 7%[a] **3q**, 67%[a] **3r**, 66%[a]

3s, 96%[a]

Reaction conditions: cyclohexanone (2 mL), carboxylic acid (1 mmol), TBAI (0.1 equiv), TBHP (3 equiv). [a] Irradiation method: 120 °C, 30 min. [b] Irradiation method: 150 °C, 15 min. [c] Irradiation method: 120 °C, 60 min. [d] 1.2 mmol of carboxylic acid. [e] From acetylsalicylic acid.

The reaction displayed apparent polar effects when aromatic acids were involved. While the coupling between cyclohexanone **1a** and benzoic acid **2b** took place in a modest 46 % yield, the introduction of an electron-releasing group as in the case of *p*-methylbenzoic acid **3a** and *p*-methoxybenzoic acid **3c** proceded expeditiously in 83% and 87% yield respectively. On the contrary, electron-withdrawing groups provided poor results, as represented by *p*-nitrobenzoic acid, that led to a mere 23% yield. Likewise, when *p*-chlorobenzoic acid was used, most of the starting material was recovered as a precipitate at the bottom of the reaction vial. These two substrates required more forceful conditions. After readjusting the irradiation method, setting the temperature to 150 ºC for 15 min, yields of 40% and 60% of **3d** and **3e** respectively were achieved.

The presence of a hydroxyl group had a detrimental effect on the reaction. Initially, the use of salicylic acid or 2,6-dihydroxybenzoic acid only allowed the detection of the corresponding esters at trace levels. Nevertheless, a 39% of ester **3g** could be obtained when salicylic acid was replaced by its corresponding acetate, through a spontaneous loss of the acetyl group. Likewise, the use of 3-methoxy-4-hydroxybenzoic acid also led to the corresponding ester **3i** in 68% yield. When phenyl acetic acid was used as a coupling partner, ester **3j** was obtained in 41% yield. A *p*-hydroxyl group decreased the yield to 31% of **3k**, but an excellent result was achieved when *p*-acetyloxyphenylacetic acid was employed, producing **3l** in 91%. A very good result was also obtained with acetic acid. In this case, the corresponding 2-acetyloxycyclohexanone **3m** was produced in 86% yield. It is noteworthy to mention that this compound was also obtained from malonic acid in 67% yield through decarboxylation of the ester initially formed. Other linear acids were less prone to react. Butanoic, hexanoic and octanoic acids gave rise to the corresponding esters, **3n**-**3p** with yields of 18%, 51% and 7% respectively. Surprisingly, the introduction of a unsaturation in the acid was beneficial. Tiglic acid and angelic acid, two carboxylic acids widely found as esters in terpenoids isolated from plants, led to their corresponding esters **3q** and

3r in 67% and 66% respectively. The reaction even worked better with pent-4-ynoic acid, which gave rise to **3s** in an excellent 96% yield.

Given the good results in the formation of esters from cyclohexanone, we thought that acetone would also be a good substrate for the production of different 2-oxopropyl esters.

The coupling of acetone with different carboxylic acids performed better than in the case of cyclohexanone (Table 3). A lower steric hindrance, more suitable physical properties as a solvent, which also translates into an easier work-up, and the higher polarity of the acetone, which can be beneficial in the use with microwaves, may be relevant factors in the superior performance of acetone compared to cyclohexanone.

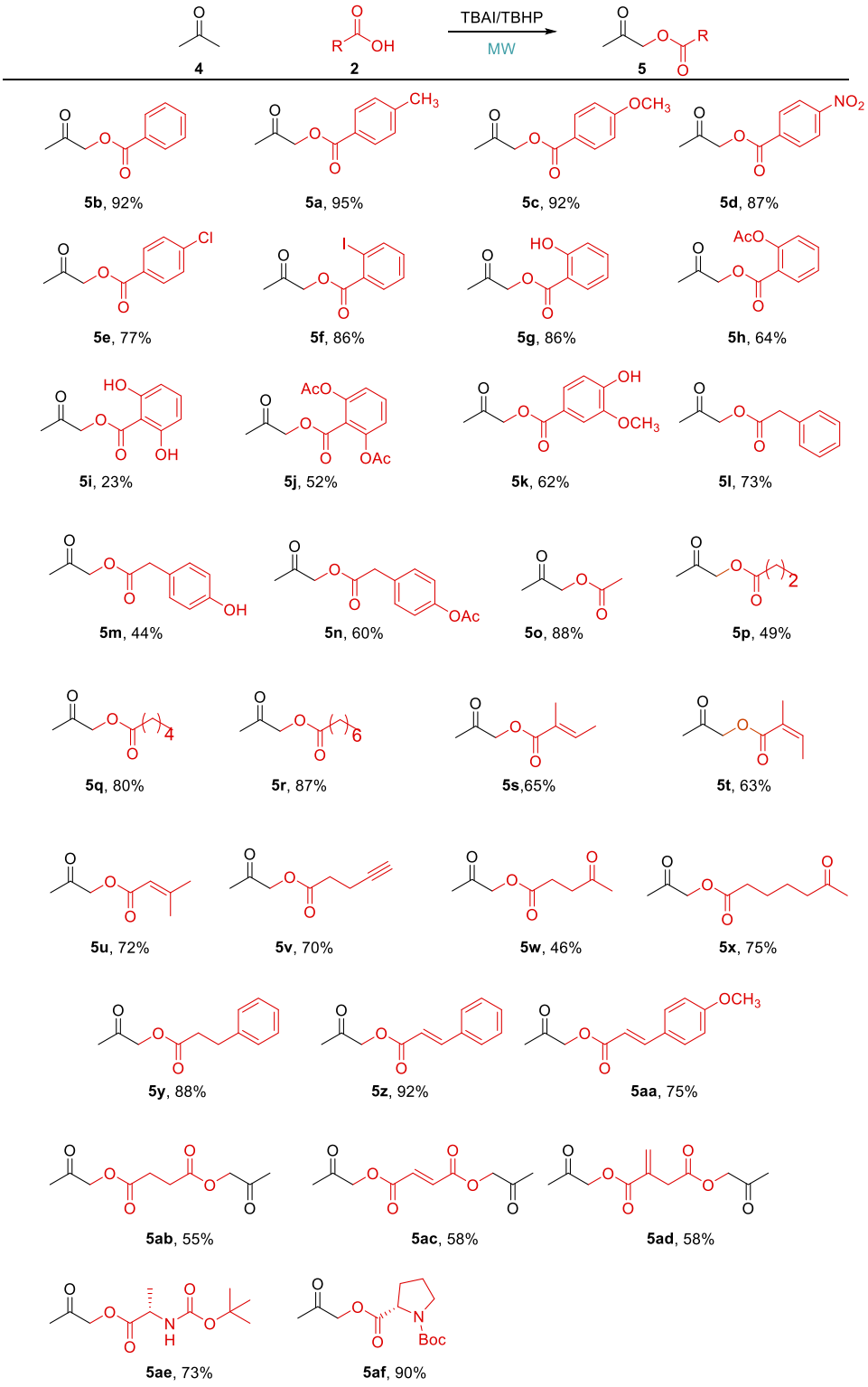
Unlike the previous case, the presence of both electron-releasing groups and electron-withdrawing groups did not have such a marked effect on the outcome of the reaction. Treatment of benzoic acid, lacking any substituent in the aromatic ring, led to ester **5b** with excellent yield (92%). Similarly good were the results of carboxylic acids bearing electron-donor groups such as methyl and methoxy groups, giving rise to esters **5a** and **5c** in 95% and 92% yield respectively. In the case of electron-withdrawing groups, the yields are still notable. The presence of a *p*-nitro group or a *p*-Cl atom was not an obstacle for the reaction to proceed with 87% and 77% of esters **5d** and **5e** respectively. Similarly, 2-iodobenzoic acid also led to the coupling product **5f** in 86% yield. For comparative purposes only, the preparation of **5f** has only been reported once in the literature, from acetone employing IBX taking 17 h to reach 56% yield.[13]

The presence of a hydroxyl group in the aromatic ring was not as adverse as in the case of cyclohexanone. Notably, the reaction of salicylic acid resulted in 86% yield of ester **5g**. Surprisingly, in comparison, when acetylsalicylic acid was employed, the yield decreased to 64% of **5h**. The introduction of a second hydroxyl group, as in the case of 2,6-dihydroxybenzoic acid, led to a further drop in the yield, leading to **5i** in 23% yield. This result improved noticeably when both hydroxyl groups are protected as acetate groups, being possible the isolation of compound **5j** in 52% yield. Treatment of 4-hydroxy-3-methoxybenzoic acid also produced the corresponding coupling product **5k** in 62 % yield.

Phenylacetic acid (non-substituted, **5l**, 73%), *p*-hydroxyphenylacetic acid (–OH group, **5m**, 44%) and *p*-acetoxyphenylacetic acid (–OAc group, **5n**, 60%) repeated the same reactivity pattern described before in substrates in which the aromatic ring was a methylene apart from the carboxyl group and demonstrated the unfavorable effect that a free hydroxyl group exerts in the outcome of the reaction

Carboxylic acids with aliphatic chains also performed well. Acetic, hexanoic, and octanoic esters were obtained with yields exceeding 80% and only in the case of butanoic acid, the yield lowered to 49%. This poor reactivity of butanoic acid, compared to other similar linear chain acids, towards cyclohexanone and acetone has, at the moment, no clear explanation. Again, the presence of double or triple bonds in the substrate was well tolerated, being possible to isolate the corresponding esters from tiglic, angelic, and senecioic acids, **5s**-**5u**, in yields of 65%, 63%, and 72% respectively and from pent-4-ynoic acid, **5v**, in 70% yield. The existence of terminal triple bond in this molecule turns compound **5v** into an intestesting synthon for the synthesis of more complex molecules.

Table 3. Synthesis of 2-oxopropyl esters obtained by coupling of acetone and different carboxylic acids.



Reaction conditions: acetone (2 mL), carboxylic acid (1 mmol), TBAI (0.1 equiv.), TBHP (3 equiv.), 120 °C, 30 min.

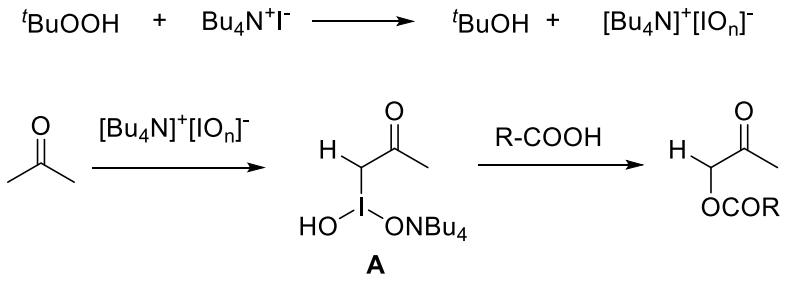
The compatibility with carbonyl groups present in the acid was not an issue, and the corresponding 2-oxopropyl esters of levulinic acid, **5w** and of 6-oxoheptanoic acid **5x** were obtained in 46% and 75%

yield. Cinnamic acid derivatives performed very well. Hydrocinnamic acid gave rise to ester **5y** in 88% yield. Cinnamic acid and *p*-methoxycinnamic acid resulted in yields of 92% and 75% of their corresponding esters **5z** and **5aa**.

To end this study of the scope, the reaction was studied employing dicarboxylic acids and aminoacids. In the case of succinic acid, a double coupling was observed, and diester **5ab** was obtained in 55% yield. The introduction of a double bond led to a slight increase in the yield. Fumaric acid and itaconic acid resulted in diesters **5ac** and **5ad** both in 58% yield. In contrast, maleic acid, bearing a *cis* double bond, failed to produce any isolable product, leading to a complex mixture, presumably due to steric factors. Finally, coupling with amino acids was also possible, as long as the amino group is protected as a Boc group. Treatment of acetone with Boc-*L*-Pro or Boc-*L*-Ala gave rise to the corresponding esters **5ae** and **5af** in good yields (73% and 90%, respectively). These two aminoacid-derived esters are two interesting examples of both *N*- and carboxyl group protected aminoacids. Compound **5ae** has been used as starting material by Guéret *et al.* for the synthesis of carbon-isosteric depsipeptides.[14] Compound **5af** has been previously prepared by Dixneuf *et al.*[15] and by Kundu[16] independently. Although there was no mention in these two previous reports, we observed that **5af** exhibited in the ^{1}H NMR spectrum the presence of two rotamers due to the presence of the amide bond. This behavior is common in proline derivatives, in which, the presence of the pyrrolidine ring results in the occurrence of *cis*-*trans* isomerism. Rotamer *trans* was assumed to be the major one considering the $n \rightarrow \pi^*$ interaction between the two carbonyl groups and the steric hindrance of the Boc group (c.f. Supporting information).[17]

As for the mechanism by which the transformations carried out by the TBAI/TBHP couple take place, there is some controversy and two approaches have been proposed. Ishihara et al have demonstrated by Raman spectroscopy the formation of hypoiodite salts in TBAI and TBHP solutions, that act as unstable active species.[18] In turn, Wan and collaborators propose the generation of ^{t}BuO· and ^{t}BuOO· radicals that participate in a catalytic cycle based on the I^{-}/I_2 redox pair.[19] Reddy et al reported that, under conventional heating, this transformation took 8h to be completed and a slight favorable effect of electron-withdrawing groups compared to electron-releasing groups was observed. They proposed a mechanism for the synthesis of 2-acetylbenzofurans that can be easily adapted to the oxidative coupling

of acetone and carboxylic acids.[10] Reaction of TBHP and TBAI would lead to $[Bu_4N]^+[IO]^-$ that would be the species that reacts with acetone to provide the trivalent iodinane **A**. The tethered iodinane is then removed by substitution by the carboxylic acid (or carboxylate ion) to provide the corresponding α-acyloxyketone (Scheme 2). Additionally, the possibility of a homolytic cleavage of the C–I bond of intermediate **A** and a parallel radical mechanism should also be taken into account.



Scheme 2. Plausible mechanism for the synthesis of α-acyloxyketones.

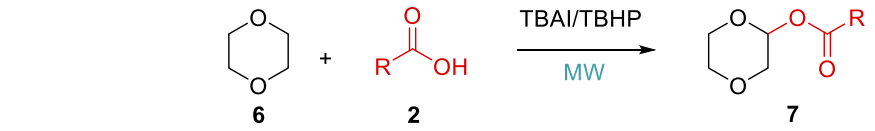
Under certain oxidative conditions, it is possible to introduce an oxygenated function at the contiguous position to the heteroatom in cyclic ethers. Since our approach of coupling a inexpensive liquid ketone with a carboxylic acid had worked reasonably well, we decided to extend the methodology to two cyclic ethers, 1,4-dioxane and THF. Both are widely used solvents that could be employed as substrates, and whose excess could be easily recovered and recycled.

The results for 1,4-dioxanes are summarized in table 4. The coupling of 1,4-dioxane with benzoic acid worked nicely (90% of **7a**). A slightly lower yield was obtained with electron-releasing group such as *p*-methylbenzoic acid and *p*-methoxybenzoic acid (**7b**, 81**%**; **7c**, 78%), Meanwhile, halogens provided excellent yields: *p*-chlorobenzoic acid reacted specially well, producing **7d** in 98% yield and o-iodobenzoic acid also provided a 92% yield of the corresponding ester **7e**. Unfortunately, it was not possible to achieve a clean reaction when the aromatic ring beared a nitro group in para position despite the testing of different irradiation methods. The striking differences of the behavior of the nitro group towards cyclohexanone, acetone and 1,4-dioxane suggests the occurrence of parallel reactions in which this group is actively involved.

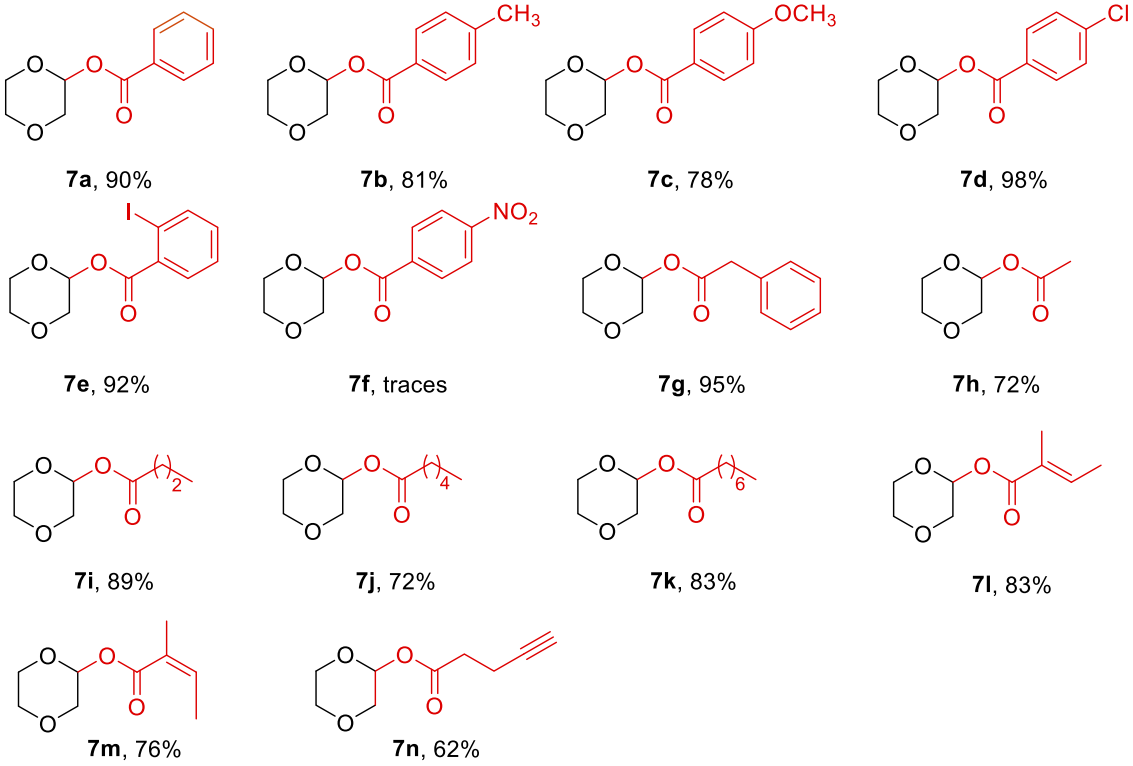
A similar transformation employing 1,4-dioxane under conventional heating has been reported by Wan et al.[19] In general, there is a good concordance between the results obtained by both methods (with some exceptions such as the nitro group), but while the conventional version takes 12 hours, the microwave version required only 10 min.

Continuing with the study of other carboxylic acids, it was observed that the distancing of the aromatic ring from the carboxyl group did not affect the outcome of the reaction, as demonstrated by the coupling of phenylacetic acid (**7g**, 95%). Non-aromatic acids also provided good results. Acetic acid furnished the corresponding acetate **7h** in 72% yield. Higher yieds were obtained in the case of butyric (**7i**, 89%), hexanoic (**7j**, 72%) and octanoic acids (**7k**, 83%). As in the case of ketones, the reaction also took place with good yields in the case of unsaturated acids. Tiglic and angelic acids led to the corresponding esters **7l** and **7m** with 83% and 76% yield respectively. In the presence of a triple bond, the reaction also took place, although with a slightly more moderate yield of 62% in the case of the pent-4-ynoic acid (**7n**).

Table 4. Synthesis of 1,4-dioxan-2-yl esters obtained from 1,4-dioxane and different carboxylic acids.



6 **2** **7**

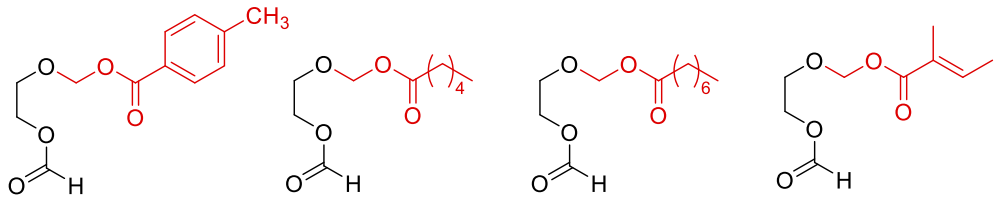


7a, 90% **7b**, 81% **7c**, 78% **7d**, 98%

7e, 92% **7f**, traces **7g**, 95% **7h**, 72%

7i, 89% **7j**, 72% **7k**, 83% **7l**, 83%

7m, 76% **7n**, 62%



8a, 7% **8b**, 14% **8c**, 17% **8d**, 9%

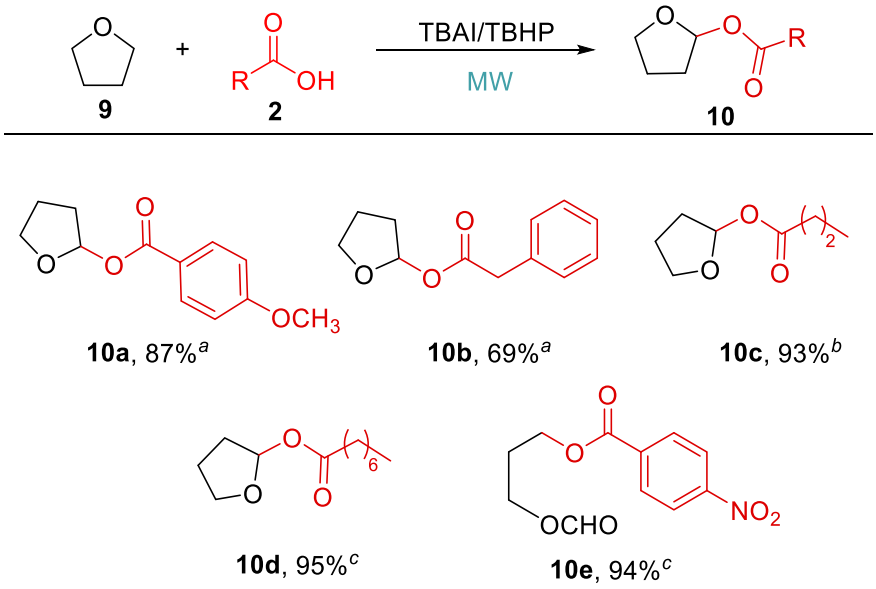
Reaction conditions: 1,4-dioxane (4 mL), carboxylic acid (1.0 mmol), TBAI (0.1 equiv), TBHP (3 equiv), 140 °C, 10 min.

In a similar paper, Wan et al proposed a mechanism in which a I^-/I_2 redox process is involved in the transformation of the radical generated from the 1,4-dioxane into an oxonium cation.[19] This mechanism might be valid for the microwave approach, yet the picture may be incomplete, as it was noted that in some cases, we were able to isolate several formyl esters resulting from the cleavage of the 1,4-dioxane ring. Thus, in the reactions leading to compounds, **7b**, **7j-7l**, appreciable amounts of products **8a-8d**, sharing the presence of a formyl group, were formed (Table 4). This type of behavior has already been

described by Liu et al, that report the oxidative cleavage of C-C bonds of glycol ethers catalyzed by copper (I) oxide.[20] In our case, the role of the copper atoms should be assumed by iodine species (see Scheme 4).

We next investigated the coupling between carboxylic acids and THF. The reaction did not turn out to be as general in this heterocycle. In most cases, complex mixtures were formed either during the reaction itself or the purification process. We were able to isolate esters **10a-10d** in moderate to good yields. In the case of *p*-nitrobenzoic acid, the reaction led to formyl ester **10e**, as a result of the cleavage of the THF ring (Table 5).

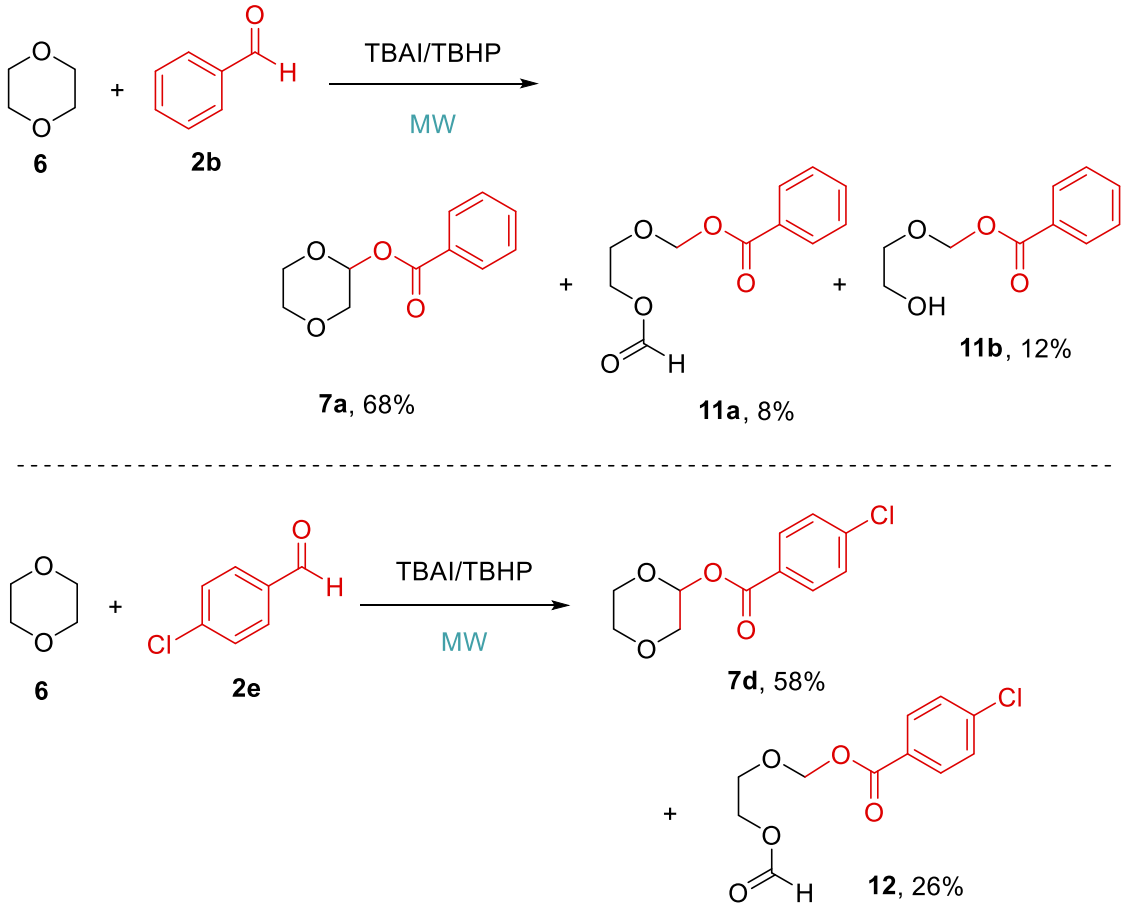
Table 5. Reaction of carboxylic acids and THF.



Reaction conditions: THF (4 mL), carboxylic acid (1.0 mmol), TBAI (0.1 equiv), TBHP (3 equiv). [a] Irradiation method: 100 °C, 15 min. [b] Irradiation method: 100 °C, 30 min. [c] Irradiation method: 140 °C, 10 min.

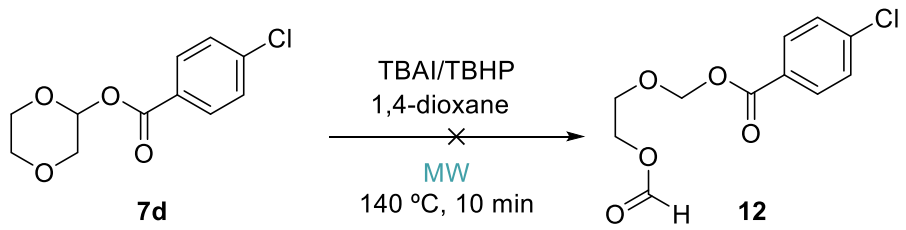
This apparently random behavior is difficult to explain just in terms of strain of the tetrahydrofuran itself, and in fact is not exclusive of this type of ring. Actually, we found that it also occurred when 1,4-dioxane was treated with aldehydes as acylating agents.

For example, when 1,4-dioxane was reacted with benzaldehyde under the described conditions, the corresponding ester **7a** was predominantly obtained in 68% yield, along with esters **11a** and **11b**, corresponding to the heterocycle aperture. A similar behavior was observed when the reaction was carried out with *p*-chlorobenzaldehyde, where in addition to 58% of the ester **7d** formyl ester **12** was also produced in 26% yield (Scheme 3).



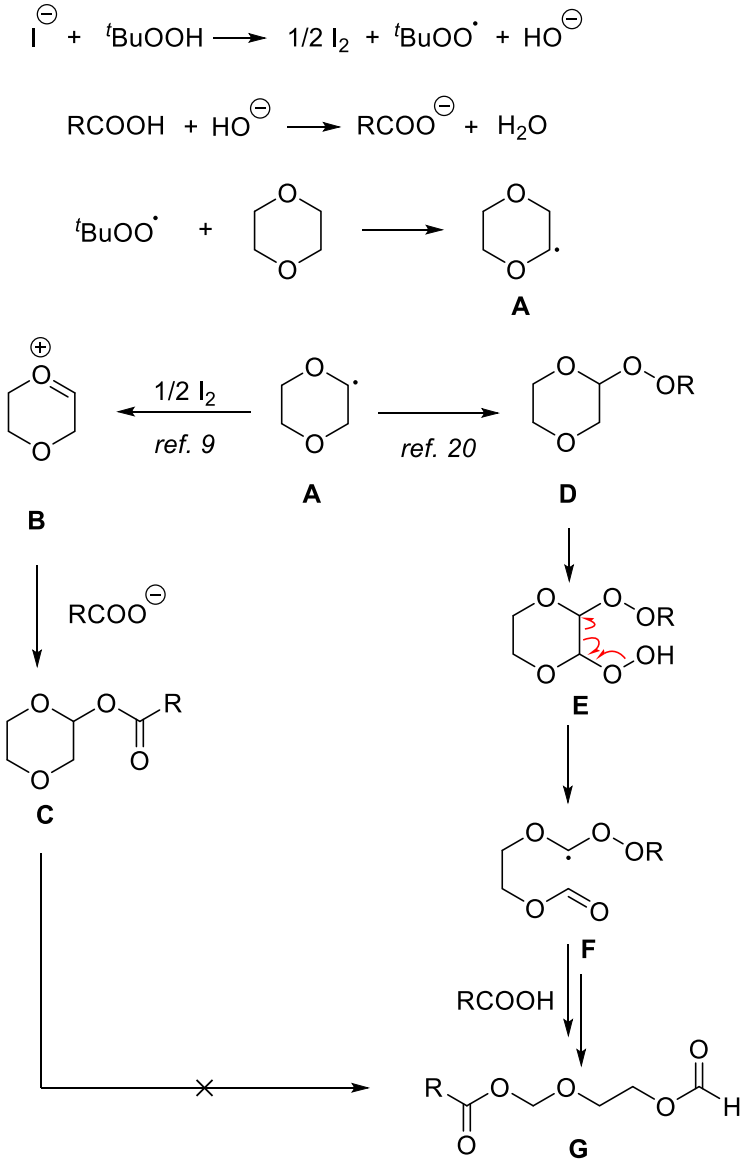
Scheme 3. Coupling of 1,4-dioxane with benzaldehyde and *p*-chlorobenzaldehyde.

In an attempt to determine whether formate ester **12** originated directly from ester **7d**, we submitted the latter compound to the same conditions of heating and irradiation (Scheme 4.) However, the starting material was recovered intact, suggesting that the opening reaction must proceed through a parallel mechanism.



Scheme 4. Irradiation of ester 7d.

This experiment seems to suggest that two parallel mechanisms take place in order to provide both types of compounds and that compounds such as **7d** are not intermediates in the route leading to ring-opened products. Following the mechanism suggested by Wan *et al* for the formation of the esters[9] and that by Liu *et al* for the cleavage of glycol ethers,[20] a plausible mechanism is proposed in Scheme 5.



Scheme 5. Proposal mechanism for the reaction between 1,4-dioxane and carboxylic acids.

After generation of *t*-butoxy radical by reaction between the iodide anion and TBHP, the attack on 1,4-dioxane would provide radical **A** which can be involved in two paths. In one hand, radical **A** would be oxidized by iodine to produce cation **B**, that subsequently would react with a carboxylate anion to provide the corresponding ester **C**. On the other hand, radical **A** would undergo two oxidation steps, leading to intermediate **E**, that presents to contiguous ketal carbons, which would undergo a C–C bond cleavage to give the open intermediate **F**, which eventually would be trapped by the carboxylic acid to provide the formate ester **G**.

CONCLUSIONS

In summary, this work illustrates the ability of MAOS to reduce reaction times from hours or days to minutes. We have demonstrated that the use of microwaves is a good alternative to conventional heating in the acyloxylation reaction of certain ketones and heterocycles promoted by the TBHP/TBAI system. Liquid ketones and ethers play the role of the solvent, taking up microwaves to heat the reaction mixture. The reactions generally take place with yields similar to or higher than the conventionally heated reactions.

EXPERIMENTAL SECTION

General methods.

All reagents and solvents were purchased from commercial suppliers and used without further purification. Reactions were monitored through TLC on commercial silica gel plates precoated with silica gel F_{254}. Visualization of the plates was performed by flurorescence quenching and ethanolic solutions of ceric ammonium molybdate or anysaldehyde as developing agents. GC analyses were performed in a Perkin-Elmer Clarus 400 chromatograph employing a DB-5 column. Column chromatography was performed employing 230-400 mesh silica gel. HPLC purification was carried out

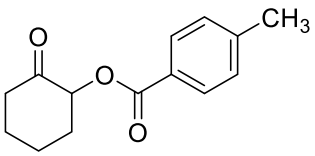
in a Merck-Hitachi L6270 chromatograph equipped with a silica gel column (LiChrosorb Si 60, 10 μm particle size). NMR spectra were recorded on a Agilent 400 MR or Agilent 500 instruments and calibrated using residual undeuterated solvent as an internal reference for ^{1}H NMR and to the central peak of $CDCl_3$ for ^{13}C NMR. IR spectrum were recorded on Perkin Elmer Spectrum BX spectrophotometer. Mass spectra were recorded employing a Bruker Scion CG-TQ gas chromatograph coupled to a Bruker TQ mass spectrometer. High resolution spectra were recorded on a HRMS SYNAPT 2G (Waters) with a APGC interface and a QTOF analyzer or in a XEVO G2 for ESI ionization. Microwave-promoted reactions were carried out in a SynthWave MA167 reactor pressurized with nitrogen limited to 45 bar of maximum pressure. The reactions were run on 50 mL glass vials immersed on 200 mL of water as charge solvent with magnetic stirring. Caution!, hydroperoxides should always be handled with care by trained personnel.

General procedure for the oxidative coupling

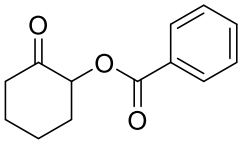
A representative example for cyclohexanone is as follows:

A 50 mL vial was charged with 1 mmol of the carboxylic acid, 2 mL of cyclohexanone, 0,1 mmol of TBAI and 3 mmol of TBHP. The vial was set in the reactor which contained 200 mL of water as charge solvent and was pressurized with nitrogen (45 bar). The sample was then irradiated according the method described in Table 2. After irradiation, the reaction mixture was worked out with a saturated Na_2SO_3 solution (10 mL) and extracted with EtOAc (3 × 25 mL). The organic layer was dried over anhydrous Na_2SO_4 and the solvent was removed by rotary evaporation. Purification of the samples and recovery of the remaining cyclohexanone was carried out by flash chromatography. In all cases shown in Table 2, the cyclohexanone was the less polar compound and was recovered employing a 9.5:0.5 petroleum ether/EtOAc mixture. Once cyclohexanone has come out, the polarity was increased according to the polarity of the products.

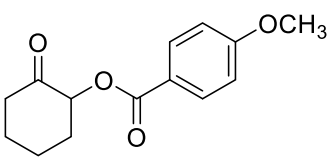
In the cases of acetone, 1,4-dioxane and THF, the procedure was similar, the only difference being that the remaining reactant was removed (or recovered if desired) by rotary evaporation. The resulting crude mixture was then purified by column chromatography.



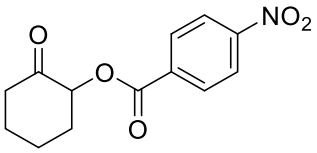
2-Oxocyclohexyl 4-methylbenzoate (3a): White crystal (192.5 mg, 83%), mp 86.5-87.8 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.99-7.96 (m, 2H), 7.25-7.22 (m, 2H), 5.40 (ddd, J = 12.2, 6.1, 1.1 Hz, 1H), 2.59-2.54 (m, 1H), 2.50-2.37 (m, 2H), 2.41 (s, 3H), 2.16-2.09 (m, 1H), 2.06-2.00 (m, 1H), 1.97-1.88 (m, 1H), 1.88-1.79 (m, 1H), 1.76-1.62 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.5, 165.6, 143.8, 129.9, 129.3, 126.9, 76.8, 40.8, 33.2, 27.2, 23.8, 21.7. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{14}H_{17}O_3$ 233.1178; Found 233.1184. IR (KBr, cm^{-1}) 2944, 2866, 1717, 1611, 1313, 1272, 1178, 1108, 753.



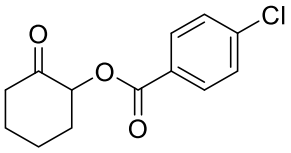
2-Oxocyclohexyl benzoate (3b): White crystal (100.6 mg, 46%), mp 78.5-80.2 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11-8.08 (m, 2H), 7.59-7.55 (m, 1H), 7.47-7.42 (m, 2H), 5.41 (ddd, J = 12.3, 6.2, 1.1 Hz, 1H), 2.60-2.54 (m, 1H), 2.51-2.40 (m, 2H), 2.17-2.10 (m, 1H), 2.07-2.01 (m, 1H), 1.99-1.90 (m, 1H), 1.89-1.79 (m, 1H), 1.75-1.64 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.3, 165.6, 133.1, 129.9, 129.7, 128.3, 77.0, 40.8, 33.2, 27.2, 23.8. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{13}H_{15}O_3$ 219.1021; Found 219.1017. IR (KBr, cm^{-1}) 2943, 2866, 1717, 1451, 1316, 1270, 1112, 1070, 711.



2-Oxocyclohexyl 4-methoxybenzoate (3c): White crystal (215.7 mg, 87%), mp 134.4-135.6 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07-8.03 (m, 2H), 6.94-6.91 (m, 2H), 5.38 (ddd, J = 12.1, 6.2, 1.1 Hz, 1H), 3.86 (s, 3H), 2.59-2.54 (m, 1H), 2.50-2.39 (m, 2H), 2.16-2.09 (m, 1H), 2.06-1.99 (m, 1H), 1.97-1.78 (m, 2H), 1.74-1.64 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.6, 165.3, 163.5, 131.9, 122.1, 113.6, 76.7, 55.4, 40.8, 33.3, 27.2, 23.8. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{14}H_{17}O_4$ 249.1127; Found 249.1155. IR (KBr, cm^{-1}) 2944, 1711, 1606, 1511, 1318, 1258, 1169, 1103, 1031, 769.

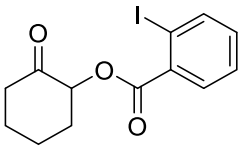


2-Oxocyclohexyl 4-nitrobenzoate (3d): White crystal (105.5 mg, 40%), mp 115.0-116.6 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.32-8.24 (m, 4H), 5.43 (ddd, J = 12.3, 6.3, 1.1 Hz, 1H), 2.63-2.56 (m, 1H), 2.53-2.43 (m, 2H), 2.21-2.12 (m, 1H), 2.11-2.03 (m, 1H), 2.02-1.80 (m, 2H), 1.76-1.63 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 203.6, 163.7, 150.7, 135.1, 131.0, 123.5, 77.8, 40.7, 33.0, 27.1, 23.8. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{13}H_{14}NO_5$ 264.0872; Found 264.0875. IR (KBr, cm^{-1}) 2946, 2867, 1721, 1527, 1348, 1317, 1302, 1273, 1115, 1104, 719.

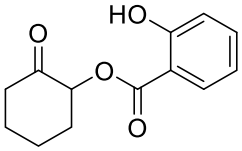


2-Oxocyclohexyl 4-chlorobenzoate (3e): White crystal (151.5 mg, 60%), mp 111.6-113.5 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04-8.01 (m, 2H), 7.44-7.40 (m, 2H), 5.39 (ddd, J = 12.3, 6.2, 1.1 Hz, 1H), 2.60-2.55 (m, 1H), 2.50-2.40 (m, 2H), 2.18-2.11 (m, 1H), 2.07-2.01 (m, 1H), 1.97-1.79 (m, 2H), 1.74-1.64 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 204.1, 164.7, 139.7, 131.3,

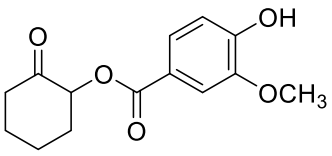
128.7, 128.1, 77.2, 40.7, 33.1, 27.2, 23.8. HRMS (APGC) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{14}ClO_3$ 253.0631; Found 253.0647. IR (KBr, cm^{-1}) 2943, 2866, 1719, 1594, 1270, 1115, 1105, 1091, 1014, 758.



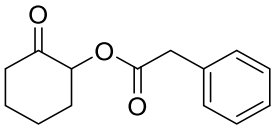
2-Oxocyclohexyl 2-iodobenzoate (3f): Colorless oil (316.5 mg, 92%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^1H NMR (500 MHz, $CDCl_3$) δ 7.99 (dd, *J* = 7.9, 1.1 Hz, 1H), 7.96 (dd, *J* = 7.8, 1.7 Hz, 1H), 7.41 (ddd, *J* = 7.6, 7,6, 1.1 Hz, 1H), 7.16 (ddd, *J* = 7.6, 7.6, 1.7 Hz, 1H), 5.42 (ddd, *J* = 12.3, 6.2, 1.1 Hz, 1H), 2.60-2.54 (m, 1H), 2.50-2.42 (m, 2H), 2.17-2.10 (m, 1H), 2.07-2.01 (m, 1H), 1.97-1.78 (m, 2H), 1.73-1.63 (m, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 203.9, 165.4, 141.3, 134.4, 132.8, 131.5, 127.9, 94.3, 77.5, 40.7, 33.1, 27.2, 23.8. HRMS (APGC) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{14}IO_3$ 344.9988; Found 344.9997. IR (KBr, cm^{-1}) 2940, 2864, 1719, 1284, 1249, 1101, 1014, 740.



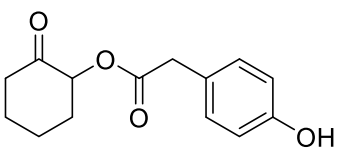
2-Oxocyclohexyl 2-hydroxybenzoate (3g): Colorless oil (91.1 mg, 39%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^1H NMR (500 MHz, $CDCl_3$) δ 10.50 (s, 1H), 7.93 (dd, *J* = 8.0, 1.6 Hz, 1H), 7.47 (ddd, *J* = 8.7, 7.2, 1.8 Hz, 1H), 6.98 (dd, *J* = 8.4, 1.0 Hz, 1H), 6.90 (ddd, *J* = 8.1, 7.3, 1.1 Hz, 1H), 5.41 (ddd, *J* = 12.3, 6.2, 1.1 Hz, 1H), 2.62-2.57 (m, 1H), 2.51-2.42 (m, 2H), 2.19-2.11 (m, 1H), 2.10-2.03 (m, 1H), 2.01-1.91 (m, 1H), 1.90-1.80 (m, 1H), 1.76-1.65 (m, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 203.7, 168.9, 161.7, 135.9, 130.2, 119.2, 117.6, 112.1, 77.2, 40.7, 33.1, 27.1, 23.7. HRMS (APGC) *m/z*: $[M+H]^+$ Calcd for $C_{13}H_{15}O_4$ 235.0970; Found 235.0970. IR (KBr, cm^{-1}) 3193, 2945, 2868, 1730, 1676, 1614, 1485, 1287, 1250, 1214, 1159, 1095, 758, 670.



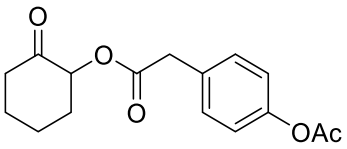
2-Oxocyclohexyl 4-hydroxy-3-methoxybenzoate (3i): White crystal (179.0 mg, 68%), mp 113.7-114.9 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.69 (dd, J = 8.3, 1.9 Hz, 1H), 7.56 (d, J = 1.9 Hz, 1H), 6.93 (d, J = 8.3 Hz, 1H), 6.12 (br s, -OH), 5.38 (ddd, J = 12.1, 6.3, 1.1 Hz, 1H), 3.93 (s, 3H), 2.60-2.52 (m, 1H), 2.51-2.37 (m, 2H), 2.17-2.08 (m, 1H), 2.07-1.99 (m, 1H), 1.98-1.77 (m, 2H), 1.75-1.62 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 204.7, 165.3, 150.3, 146.2, 124.6, 121.7, 114.1, 112.0, 76.8, 56.1, 40.8, 33.2, 27.2, 23.8. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{14}H_{17}O_5$ 265.1076; Found 265.1078. IR (KBr, cm^{-1}) 3378, 2942, 2866, 1709, 1596, 1514, 1429, 1280, 1216, 1107, 1032, 782, 763.



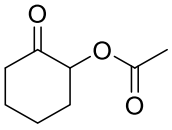
2-Oxocyclohexyl 2-phenylacetate (3j): White crystal (94.4 mg, 41%), mp 63.7-65.3 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.34-7.24 (m, 5H), 5.18 (ddd, J = 12.2, 6.4, 1.1 Hz, 1H), 3.78-.3.70 (m, 2H), 2.53-2.48 (m, 1H), 2.38 (ddd, J = 13.7, 13.7, 6.1 Hz, 1H), 2.31-2.25 (m, 1H), 2.12-2.04 (m, 1H), 1.99-1.92 (m, 1H), 1.82-1.57 (m, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 204.3, 170.7, 133.8, 129.3, 128.5, 127.1, 76.9, 40.9, 40.6, 33.0, 27.1, 23.7. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{14}H_{17}O_3$ 233.1178; Found 233.1176. IR (KBr, cm^{-1}) 2943, 2867, 1744, 1726, 1497, 1453, 1250, 1216, 1316, 1113, 1061, 696, 709.



2-Oxocyclohexyl 2-(4-hydroxyphenyl)acetate (3k): Colorless oil (78.0 mg, 31%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.19-7.12 (m, 2H), 6.78-6.71 (m, 2H), 5.18 (ddd, J = 12.3, 6.5, 1.2 Hz, 1H), 3.72-3.59 (m, 2H), 2.55-2.46 (m, 1H), 2.38 (ddd, J = 13.7, 13.7, 6.1 Hz, 1H), 2.33-2.24 (m, 1H), 2.13-2.03 (m, 1H), 2.01-1.91 (m, 1H), 1.83-1.68 (m, 2H), 1.70-1.56 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.8, 171.3, 154.9, 130.5, 125.6, 115.4, 76.9, 40.7, 40.0, 33.0, 27.1, 23.7. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{14}H_{16}O_4Na$ 271.0946; Found 271.0956. IR (KBr, cm^{-1}) 3390, 2945, 2868, 1719, 1597, 1614, 1516, 1449, 1218, 1159, 1060, 802, 827.

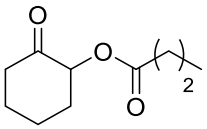


2-Oxocyclohexyl 2-(4-acetoxyphenyl)acetate (3l): White crystal (265.5 mg, 91%), mp 111.4-112.8 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.35-7.32 (m, 2H), 7.06-7.03 (m, 2H), 5.17 (ddd, J = 12.2, 6.3, 1.2 Hz, 1H), 3.77-3.69 (m, 2H), 2.54-2.48 (m, 1H), 2.38 (ddd, J = 13.7, 13.7, 6.1 Hz, 1H), 2.31-2.26 (m, 1H), 2.29 (s, 3H), 2.12-2.06 (m, 1H), 1.99-1.93 (m, 1H), 1.82-1.70 (m, 2H), 1.68-1.58 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.2, 170.4, 169.4, 149.7, 131.4, 130.4, 121.6, 77.0, 40.6, 40.3, 33.0, 27.1, 23.7, 21.1. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{16}H_{19}O_5$ 291.1232; Found 291.1245. IR (KBr, cm^{-1}) 2942, 2866, 1733, 1508, 1368, 1195, 1155, 1058, 1015, 908.

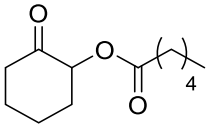


2-Oxocyclohexyl acetate (3m): Colorless oil (134.3 mg, 86%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.19-5.13 (m, 1H), 2.54-2.48 (m, 1H), 2.41 (ddd, J = 13.7, 13.7, 6.1 Hz, 1H), 2.34-2.25 (m, 1H), 2.15 (s, 3H), 2.13-2.05 (m, 1H), 2.01-1.94 (m, 1H), 1.82-1.71 (m, 2H), 1.67-1.57 (m, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.5, 170.0, 76.6, 40.7, 33.1, 27.2, 23.8, 20.7. HRMS (APGC)

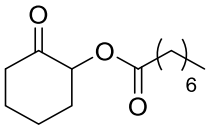
m/*z*: $[M+H]^+$ Calcd for $C_8H_{13}O_3$ 157.0865; Found 157.0858. IR (KBr, cm^{-1}) 3023, 2933, 2871, 1732, 1374, 1246, 1047, 757, 668.



2-Oxocyclohexyl butyrate (3n): Colorless oil (33.2 mg, 18%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.20-5.15 (m, 1H), 2.53-2.47 (m, 1H), 2.46-2.32 (m, 3H), 2.31-2.26 (m, 1H), 2.12-2.05 (m, 1H), 2.01-1.93 (m, 1H), 1.82-1.57 (m, 5H), 0.98 (t, J = 7.4 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.6, 172.7, 76.3, 40.7, 35.9, 33.1, 27.2, 23.8, 18.4, 13.6. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{10}H_{16}O_3Na$ 207.0997; Found 207.0992. IR (KBr, cm^{-1}) 2962, 2944, 2873, 1744, 1726, 1453, 1382, 1315, 1256, 1179, 1105.

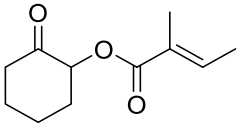


2-Oxocyclohexyl hexanoate (3o): Colorless oil (107.5 mg, 51%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.19-5.12 (m, 1H), 2.51-2.46 (m, 1H), 2.45-2.32 (m, 3H), 2.30-2.24 (m, 1H), 2.10-2.03 (m, 1H), 1.99-1.91 (m, 1H), 1.81-1.55 (m, 5H), 1.35-1.28 (m, 4H), 0.90-0.86 (m, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 204.6, 172.8, 76.2, 40.6, 33.9, 33.0, 31.2, 27.1, 24.5, 23.7, 22.3, 13.8. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{12}H_{21}O_3$ 213.1491; Found 213.1495. IR (KBr, cm^{-1}) 2943, 2867, 1744, 1726, 1453, 1378, 1317, 1244, 1169, 1106, 1065, 919, 882.

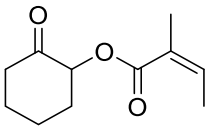


2-Oxocyclohexyl octanoate (3p): Colorless oil (16.5 mg, 7%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR

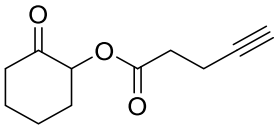
(500 MHz, $CDCl_3$) δ 5.20-5.15 (m, 1H), 2.54-2.48 (m, 1H), 2.47-2.34 (m, 3H), 2.32-2.24 (m, 1H), 2.12-2.06 (m, 1H), 2.01-1.93 (m, 1H), 1.83-1.59 (m, 5H), 1.40-1.22 (m, 8H), 0.88 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 204.6, 172.9, 76.3, 40.7, 34.0, 33.1, 31.6, 29.0, 28.9, 27.2, 24.9, 23.8, 22.6, 14.1. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{14}H_{24}O_3Na$ 263.1623; Found 263.1629. IR (KBr, cm^{-1}) 2932, 2861, 1745, 1726, 1453, 1166, 1109, 1067, 920, 882.



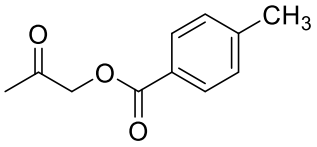
2-Oxocyclohexyl (*E*)-2-methylbut-2-enoate (3q): Colorless oil (131.0 mg, 67%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^1H NMR (500 MHz, $CDCl_3$) δ 6.95 (qq, J = 7.0, 1.4 Hz, 1H), 5.25-5.20 (m, 1H), 2.55-2.48 (m, 1H), 2.41 (ddd, J = 13.6, 13.6, 6.1 Hz, 1H), 2.35-2.28 (m, 1H), 2.13-2.05 (m, 1H), 2.01-1.95 (m, 1H), 1.85 (qd, J = 1.2, 1.2 Hz, 3H), 1.80 (dq, J = 7.0, 1.2 Hz, 3H), 1.83-1.75 (m, 2H), 1.70-1.59 (m, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 204.9, 166.9, 138.2, 128.0, 76.4, 40.7, 33.2, 27.2, 23.8, 14.4, 12.0. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{17}O_3$ 197.1178; Found 197.1176. IR (KBr, cm^{-1}) 2944, 2867, 1731, 1714, 1262, 1143, 1114, 1088, 732.



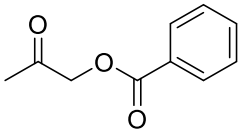
2-Oxocyclohexyl (*Z*)-2-methylbut-2-enoate (3r): White crystal (130.2 mg, 66%), mp 63.6-64.3 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^1H NMR (500 MHz, $CDCl_3$) δ 6.11 (qq, J = 7.2, 1.5 Hz, 1H), 5.27-5.22 (m, 1H), 2.55-2.49 (m, 1H), 2.42 (ddd, J = 13.6, 13.6, 6.0 Hz, 1H), 2.36-2.30 (m, 1H), 2.13-2.05 (m, 1H), 1.99 (dq, J = 7.2, 1.5 Hz, 3H), 2.01-1.96 (m, 1H), 1.93 (qd, J = 1.6, 1.6 Hz, 3H), 1.87-1.73 (m, 2H), 1.70-1.59 (m, 1H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 204.5, 166.9, 138.6, 127.4, 76.3, 40.7, 33.2, 27.2, 23.8, 20.5, 15.8. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{17}O_3$ 197.1178; Found 197.1179. IR (KBr, cm^{-1}) 2946, 2868, 1733, 1716, 1236, 1157, 1114, 1066.



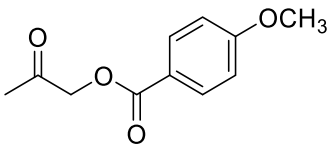
2-Oxocyclohexyl pent-4-ynoate (3s): Colorless oil (186.5 mg, 96%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5 until excess cyclohexanone came out, then increased to 9:1. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.24-5.12 (m, 1H), 2.73-2.58 (m, 2H), 2.56-2.45 (m, 3H), 2.37 (ddd, J = 13.7, 13.7, 6.1 Hz, 1H), 2.32-2.25 (m, 1H), 2.11-2.03 (m, 1H), 2.01-1.91 (m, 1H), 1.97 (t, J = 2.7 Hz, 1H), 1.81-1.70 (m, 2H), 1.66-1.51 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 204.2, 170.7, 82.4, 76.7, 69.0, 40.6, 33.0, 32.9, 27.0, 23.7, 14.3. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{15}O_3$ 195.1021; Found 195.1024. IR (KBr, cm^{-1}) 3282, 2944, 2868, 1731, 1451, 1429, 1379, 1167, 1114, 1067, 882, 833, 649.



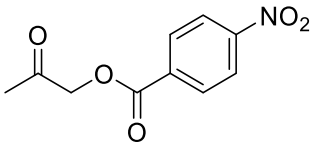
2-Oxopropyl 4-methylbenzoate (5a): White crystal (182.7 mg, 95%), mp 39.4-41.1 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.00-7.96 (m, 2H), 7.28-7.24 (m, 2H), 4.85 (s, 2H), 2.42 (s, 3H), 2.23 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 202.1, 165.9, 144.2, 129.9, 129.2, 126.4, 68.6, 26.2, 21.7. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{13}O_3$ 193.0865; Found 193.0885. IR (KBr, cm^{-1}) 2931, 1717, 1611, 1411, 1274, 1175, 1110, 750.



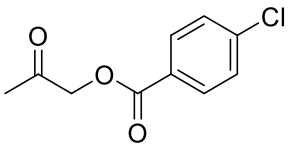
2-Oxopropyl benzoate (5b): Colorless oil (163.9 mg, 92%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11-8.08 (m, 2H), 7.62-7.57 (m, 1H), 7.49-7.44 (m, 2H), 4.88 (s, 2H), 2.24 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 201.8, 165.8, 133.4, 129.9, 129.2, 128.5, 68.7, 26.2. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{10}H_{11}O_3$ 179.0708; Found 179.0717. IR (KBr, cm^{-1}) 2931, 1721, 1452, 1417, 1371, 1315, 1276, 1176, 1114, 1071, 711.



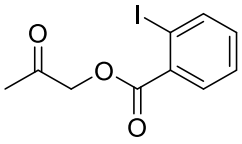
2-Oxopropyl 4-methoxybenzoate (5c): Colorless oil (191.1 mg, 92%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.07-8.02 (m, 2H), 6.97-6.91 (m, 2H), 4.84 (s, 2H), 3.87 (s, 3H), 2.23 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 202.2, 165.5, 163.8, 132.0, 121.5, 113.7, 68.5, 55.4, 26.2. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{13}O_4$ 209.0814; Found 209.0808. IR (KBr, cm^{-1}) 2936, 2842, 1715, 1606, 1512, 1421, 1280, 1257, 1168, 1111, 1028, 848, 768, 697.



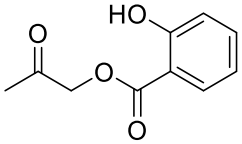
2-Oxopropyl 4-nitrobenzoate (5d): White crystal (194.3 mg, 87%), mp 93.4-94.7 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.33-8.30 (m, 2H), 8.28-8.25 (m, 2H), 4.96 (s, 2H), 2.25 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 200.2, 164.0, 150.8, 134.6, 131.0, 123.6, 69.1, 26.1. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{10}H_{10}NO_5$ 224.0559; Found 224.0562. IR (KBr, cm^{-1}) 3109, 1721, 1606, 1521, 1350, 1321, 1275, 1104, 875, 855, 783, 719.



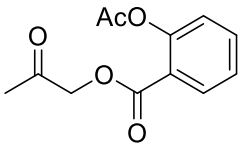
2-Oxopropyl 4-chlorobenzoate (5e): White crystal (162.9 mg, 77%), mp 50.0-50.8 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03-7.99 (m, 2H), 7.44-7.40 (m, 2H), 4.87 (s, 2H), 2.21 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 201.2, 164.9, 139.9, 131.2, 128.8, 127.6, 68.7, 26.1. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{10}H_{10}ClO_3$ 213.0318; Found 213.0321. IR (KBr, cm^{-1}) 2933, 1722, 1595, 1488, 1417, 1402, 1370, 1275, 1172, 1118, 1105, 1091, 850, 757.



2-Oxopropyl 2-iodobenzoate (5f): Colorless oil (261.4 mg, 86%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (dd, J = 7.9, 1.1 Hz, 1H), 7.96 (dd, J = 7.8, 1.7 Hz, 1H), 7.44 (ddd, J = 7.6, 7.6, 1.2 Hz, 1H), 7.19 (ddd, J = 7.9, 7.4, 1.7 Hz, 1H), 4.87 (s, 2H), 2.25 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 201.1, 165.5, 141.5, 133.8, 133.1, 131.5, 128.0, 94.4, 69.0, 26.3. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{10}H_{10}IO_3$ 304.9675; Found 304.9669. IR (KBr, cm^{-1}) 3453, 3064, 2931, 1726, 1582, 1419, 1369, 1289, 1251, 1183, 1131, 1105, 1008, 740.

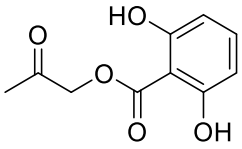


2-Oxopropyl 2-hydroxybenzoate (5g): White crystal (166.7 mg, 86%), mp 62.0-63.8 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 10.41 (s, 1H), 7.93 (dd, J = 8.0, 1..7 Hz, 1H), 7.49 (ddd, J = 8.7, 7.2, 1.7 Hz, 1H), 6.99 (dd, J = 8.4, 1.1 Hz, 1H), 6.94-6.89 (m, 1H), 4.90 (s, 2H), 2.24 (s, 3H).^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.8, 169.2, 161.8, 136.2, 130.1, 119.4, 117.7, 111.6, 68.6, 26.1. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{10}H_{10}O_4$ 195.0657; Found 195.0679. IR (KBr, cm^{-1}) 3206, 2948, 1733, 1679, 1613, 1583, 1484, 1421, 1379, 1328, 1306, 1251, 1207, 1181, 1157, 1137, 1098, 757, 732, 700.

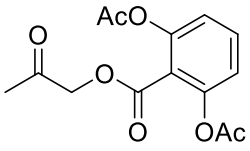


2-Oxopropyl 2-acetoxybenzoate (5h): Colorless oil (150.0 mg, 64%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (dd, J = 7.9, 1.7 Hz, 1H), 7.60 (ddd, J = 8.1, 7.5, 1.7 Hz, 1H), 7.34 (ddd, J = 7.7, 7.7, 1.2 Hz, 1H), 7.13 (dd, J = 8.1, 1.2 Hz, 1H), 4.83 (s, 2H), 2.34 (s, 3H), 2.22 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 201.4, 169.7, 163.6, 151.0, 134.4, 131.9, 126.1, 123.9, 122.3, 68.7, 26.2, 21.0. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{12}H_{13}O_5$ 237.0763;

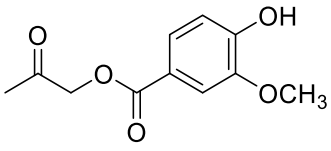
Found 237.0764. IR (KBr, cm^{-1}) 2936, 1765, 1723, 1606, 1486, 1452, 1418, 1368, 1296, 1260, 1188, 1161, 1130, 1089, 1042, 1009, 914, 751, 703.



2-Oxopropyl 2,6-dihydroxybenzoate (5i): Amorphous solid (47.4 mg, 23%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.60 (s, 2H), 7.34 (dd, J = 8.3, 8.3 Hz, 1H), 6.51 (d, J = 8.3 Hz, 2H), 5.08 (s, 2H), 2.28 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 198.9, 168.4, 161.1, 137.2, 108.4, 99.7, 68.7, 25.9. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{10}H_{11}O_5$ 211.0606; Found 211.0600. IR (KBr, cm^{-1}) 3433, 1729, 1676, 1630, 1575, 1471, 1423, 1325, 1189, 1157, 1140, 809, 738, 703, 591.

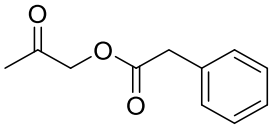


2-((2-Oxopropoxy)carbonyl)-1,3-phenylene diacetate (5j): Yellow oil (152.7 mg, 52%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.50 (dd, J = 8.3, 8.3 Hz, 1H), 7.07 (d, J = 8.2 Hz, 2H), 4.81 (s, 2H), 2.30 (s, 6H), 2.20 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 200.3, 168.9, 162.7, 149.6, 132.1, 121.0, 119.2, 69.1, 26.1, 20.9. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{14}H_{15}O_7$ 295.0818; Found 295.0819. IR (KBr, cm^{-1}) 2937, 1772, 1729, 1611, 1463, 1370, 1278, 1185, 1110, 1034.

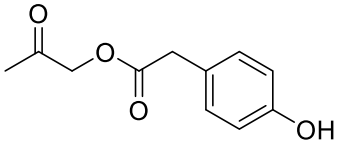


2-Oxopropyl 4-hydroxy-3-methoxybenzoate (5k): Colorless oil (140.1 mg, 62%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.68 (dd, J = 8.4 Hz, 1.8 Hz, 1H), 7.56 (d, J = 1.9 Hz, 1H), 6.94 (d, J = 8.3 Hz, 1H), 4.84 (s, 2H), 3.92 (s, 3H), 2.22 (s,

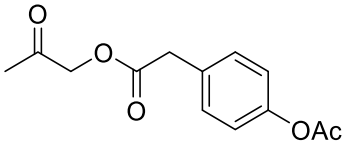
3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 202.2, 165.6, 150.5, 146.2, 124.6, 121.1, 114.2, 111.9, 68.6, 56.0, 26.1. HRMS (APGC) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{13}O_5$ 225.0763; Found 225.0788. IR (KBr, cm^{-1}) 3389, 2938, 1713, 1596, 1514, 1429, 1287, 1219, 1176, 1110, 761.



2-Oxopropyl 2-phenylacetate (5l): Colorless oil (140.0 mg, 73%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 7.36-7.26 (m, 5H), 4.65 (s, 2H), 3.75 (s, 2H), 2.10 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 201.4, 170.8, 133.4, 129.3, 128.6, 127.2, 68.5, 40.8, 26.0. HRMS (APGC) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{13}O_3$ 193.0865; Found 193.0865. IR (KBr, cm^{-1}) 3032, 2931, 1730, 1497, 1455, 1416, 1371, 1218, 1142, 1076, 1051, 1030, 702.

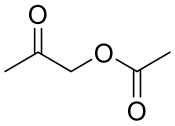


2-Oxopropyl 2-(4-hydroxyphenyl)acetate (5m): Yellow oil (92.6 mg, 44%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 7.18-7.14 (m, 2H), 6.79-6.75 (m, 2H), 4.66 (s, 2H), 3.67 (s, 2H), 2.12 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 201.9, 171.4, 154.9, 130.5, 125.3, 115.5, 68.6, 39.9, 26.1. HRMS (APGC) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{13}O_4$ 209.0814; Found 209.0822. IR (KBr, cm^{-1}) 3397, 3025, 2930, 1727, 1615, 1597, 1516, 1444, 1418, 1370, 1267, 1223, 1149, 822.

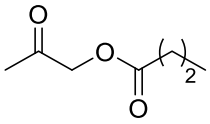


2-Oxopropyl 2-(4-acetoxyphenyl)acetate (5n): Yellow oil (150.31 mg, 60%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 7.35-7.31 (m, 2H), 7.07-7.04 (m, 2H), 4.66 (s, 2H), 3.74 (s, 2H), 2.29 (s, 3H), 2.12 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz,

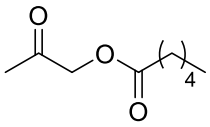
$CDCl_3$) δ 201.2, 170.5, 169.4, 149.9, 131.0, 130.4, 121.7, 68.6, 40.2, 26.0, 21.1. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{13}H_{15}O_5$ 251.0919; Found 251.0920. IR (KBr, cm^{-1}) 2932, 1752, 1731, 1508, 1419, 1370, 1196, 1147, 1049, 1016, 911.



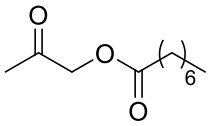
2-Oxopropyl acetate (5o): Yellow oil (102.1 mg, 88%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 4.65 (s, 2H), 2.17 (s, 3H), 2.16 (s, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 201.5, 170.2, 68.3, 26.0, 20.5. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_5H_9O_3$ 117.0552; Found 117.0551. IR (KBr, cm^{-1}) 2963, 2876, 1733, 1374, 1234, 1170.



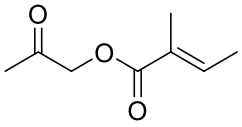
2-Oxopropyl butyrate (5p): Colorless oil (70.7 mg, 49%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 4.64 (s, 2H), 2.40 (t, J = 7.4 Hz, 2H), 2.15 (s, 3H), 1.69 (qt, J = 7.4, 7.4 Hz, 2H), 0.98 (t, J = 7.4 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 201.7, 172.9, 68.1, 35.6, 26.1, 18.3, 13.6. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_7H_{12}O_3Na$ 167.0684; Found 167.0708. IR (KBr, cm^{-1}) 2919, 2850, 1732, 1607, 1463, 1260, 1168, 1105, 1031.



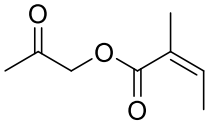
2-Oxopropyl hexanoate (5q): Colorless oil (138.3 mg, 80%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 4.64 (s, 2H), 2.42 (t, J = 7.6, 2H), 2.16 (s, 3H), 1.71-1.63 (m, 2H), 1.36-1.30 (m, 4H), 0.93-0.87 (m, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 201.7, 173.1, 68.1, 33.8, 31.2, 26.1, 24.5, 22.3, 13.9. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_9H_{17}O_3$ 173.1178; Found 173.1193. IR (KBr, cm^{-1}) 2958, 2933, 2867, 1741, 1419, 1372, 1272, 1242, 1158, 1107.



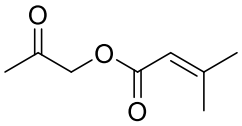
2-Oxopropyl octanoate (5r): Colorless oil (173.4 mg, 87%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.64 (s, 2H), 2.48 (t, J = 7.6 Hz, 2H), 2.16 (s, 3H), 1.66 (tt, J = 7.4, 7.4 Hz, 2H), 1.39-1.23 (m, 8H), 0.88 (t, J = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 201.7, 173.1, 68.1, 33.8, 31.6, 29.0, 28.9, 26.1, 24.8, 22.6, 14.0. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{11}H_{21}O_3$ 201.1491; Found 201.1494. IR (KBr, cm^{-1}) 2929, 2858, 1740, 1419, 1372, 1156, 1110, 1062, 968.



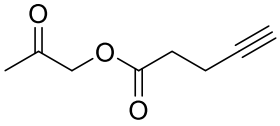
2-Oxopropyl (*E*)-2-methylbut-2-enoate (5s): Colorless oil (101.4 mg, 65%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.99 (q, J = 7.0 Hz, 1H), 4.69 (s, 2H), 2.18 (s, 3H), 1.88 (s, 3H), 1.83 (d, J = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 202.4, 167.2, 138.9, 127.7, 68.4, 26.2, 14.5, 12.0. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_8H_{13}O_3$ 157.0865; Found 157.0865. IR (KBr, cm^{-1}) 2987, 2932, 1737, 1718, 1652, 1419, 1374, 1273, 1135, 1090, 734.



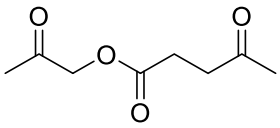
2-Oxopropyl (*Z*)-2-methylbut-2-enoate (5t): Colorless oil (98.6 mg, 63%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.17 (q, J = 7.3 Hz, 1H), 4.71 (s, 2H), 2.19 (s, 3H), 2.02 (d, J = 7.3 Hz, 3H), 1.95 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 202.0, 139.8, 126.9, 68.1, 26.2, 20.5, 15.9. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_8H_{13}O_3$ 157.0865; Found 157.0863. IR (KBr, cm^{-1}) 2932, 1721, 1420, 1358, 1236, 1147.



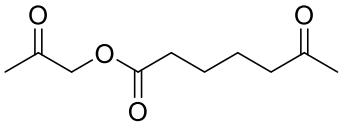
2-Oxopropyl 3-methylbut-2-enoate (5u): Colorless oil (112.0 mg, 72%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.81-5.79 (m, 1H), 4.65 (s, 2H), 2.18 (s, 3H), 2.17 (s, 3H), 1.93 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 202.5, 165.5, 159.2, 114.8, 67.7, 27.5, 26.1, 20.4. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_8H_{13}O_3$ 157.0865; Found 157.0870. IR (KBr, cm^{-1}) 2921, 1721, 1648, 1445, 1419, 1379, 1353, 1229, 1142, 1091, 850.



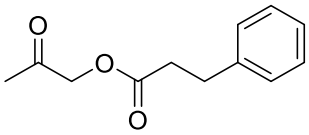
2-Oxopropyl pent-4-ynoate (5v): Colorless oil (108.0 mg, 70%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.68 (s, 2H), 2.71-2.67 (m, 2H), 2.57-2.53 (m, 2H), 2.17 (s, 3H), 1.99 (t, J = 2.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 201.3, 171.0, 82.2, 69.2, 68.4, 32.9, 26.1, 14.3. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_8H_{11}O_3$ 155.0708; Found 155.0709. IR (KBr, cm^{-1}) 3283, 2930, 1731, 1420, 1367, 1271, 1154, 1063, 646.



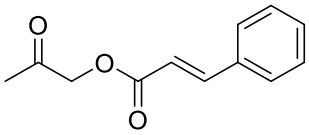
2-Oxopropyl 4-oxopentanoate (5w): Colorless oil (79.4 mg, 46%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.64 (s, 2H), 2.80 (t, J = 6.3 Hz, 2H), 2.70 (t, J = 6.3 Hz, 2H), 2.19 (s, 3H), 2.16 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 206.4, 201.8, 172.1, 68.4, 37.8, 29.8, 27.6, 26.1. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_8H_{13}O_4$ 173.0814; Found 173.0815. IR (KBr, cm^{-1}) 2933, 1732, 1717, 1421, 1361, 1154.



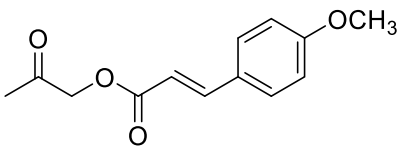
2-Oxopropyl 6-oxoheptanoate (5x): Colorless oil (150.1 mg, 75%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 4.65 (s, 2H), 2.45 (q, J = 7.3 Hz, 4H), 2.15 (s, 3H), 2.14 (s, 3H), 1.69-1.62 (m, 4H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 208.5, 201.4, 172.6, 68.2, 43.2, 33.5, 29.9, 26.0, 24.3, 23.1. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{10}H_{17}O_4$ 201.1127; Found 201.1130. IR (KBr, cm^{-1}) 2940, 1732, 1715, 1420, 1373, 1360, 1146.



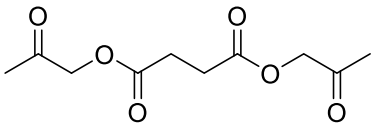
2-Oxopropyl 3-phenylpropanoate (5y): Colorless oil (182.3 mg, 88%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32-7.18 (m, 5H), 4.64 (s, 2H), 3.00 (t, J = 7.8 Hz, 2H), 2.76 (t, J = 7.8 Hz, 2H), 2.12 (s, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 201.6, 172.1, 140.2, 128.5, 128.3, 126.3, 68.3, 35.3, 30.7, 26.0. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{12}H_{15}O_3$ 207.1021; Found 207.1026. IR (KBr, cm^{-1}) 3029, 2931, 1732, 1497, 1454, 1419, 1375, 1149, 1080, 752, 700.



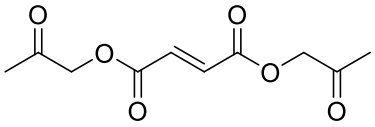
2-Oxopropyl cinnamate (5z): Colorless oil (187.1 mg, 92%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.78 (d, J = 16.2 Hz, 1H), 7.57-7.52 (m, 2H), 7.42-7.38 (m, 3H), 6.53 (d, J = 16.2 Hz, 1H), 4.78 (s, 2H), 2.21 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 201.9, 166.1, 146.3, 134.1, 130.6, 128.9, 128.2, 116.8, 68.4, 26.2. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{12}H_{13}O_3$ 205.0865; Found 205.0864. IR (KBr, cm^{-1}) 1716, 1636, 1314, 1282, 1203, 1156, 980, 768.



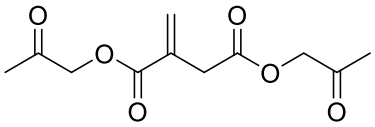
2-Oxopropyl (*E*)-3-(4-methoxyphenyl)acrylate (5aa): Orange crystal (175.8 mg, 75%), mp 59.3-61.0 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (d, J = 16.2 Hz, 1H), 7.51-7.45 (m, 2H), 6.92-6.87 (m, 2H), 6.38 (d, J = 16.2 Hz, 1H), 4.75 (s, 2H), 3.82 (s, 3H), 2.19 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 202.2, 166.4, 161.6, 145.9, 129.9, 126.8, 114.3, 114.1, 68.3, 55.3, 26.1. HRMS (ESI) m/z: $[M+Na]^+$ calcd for $C_{13}H_{14}O_4Na$ 257.0790; Found 257.0791. IR (KBr, cm^{-1}) 1713, 1633, 1603, 1513, 1254, 1173, 1153, 829.



Bis(2-Oxopropyl) succinate (5ab): White crystal (126.4 mg, 55%), mp 60.6-62.4 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 4.67 (s, 4H), 2.80 (s, 4H), 2.15 (s, 6H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 201.4, 171.4, 68.5, 28.6, 26.0. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{10}H_{15}O_6$ 231.0869; Found 231.0866. IR (KBr, cm^{-1}) 1741, 1728, 1426, 1408, 1371, 1316, 1151.

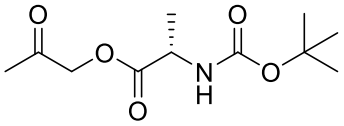


Bis(2-Oxopropyl) fumarate (5ac): White crystal (132.3 mg, 58%), mp 117.7-119.5 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.02 (s, 2H), 4.79 (s, 4H), 2.20 (s, 6H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 200.4, 163.8, 133.5, 68.8, 26.1. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{10}H_{13}O_6$ 229.0712; Found 229.0711. IR (KBr, cm^{-1}) 1735, 1723, 1410, 1368, 1303, 1154, 981.

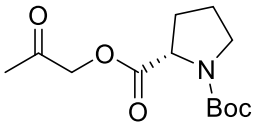


bis(2-Oxopropyl) 2-methylenesuccinate (5ad): Yellow oil (139.5 mg, 58%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.48 (s, 1H), 5.89 (s, 1H), 4.74

(s, 2H), 4.67 (s, 2H), 3.51 (s, 2H), 2.17 (s, 3H), 2.15 (s, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 201.5, 201.3, 169.8, 165.2, 132.5, 130.3, 68.8, 68.7, 37.2, 26.1, 26.1. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{15}O_6$ 243.0869; Found 243.0868. IR (KBr, cm^{-1}) 2936, 1729, 1422, 1374, 1167, 1141.

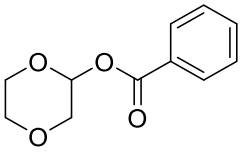


2-Oxopropyl (*tert*-butoxycarbonyl)-*L*-alaninate (5ae): White crystal (178.6 mg, 73%), mp 87.0-87.6 ºC. $\alpha_{[D]}^{20}$ -24.0 (*c* 0.10, $CHCl_3$). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.03 (s, 1H), 4.76 (d, *J* = 16.8 Hz, 1H), 4.60 (d, *J* = 16.8 Hz, 1H), 4.46-4.30 (m, *J* = 7.0, 7.0 Hz, 1H), 2.15 (s, 2H), 1.46 (d, *J* = 7.0 Hz, 3H), 1.43 (s, 9H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 201.0, 172.8, 155.1, 80.0, 68.6, 49.1, 28.3, 26.0, 18.5. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{20}NO_5$ 246.1341; Found 246.1334. IR (KBr, cm^{-1}) 3383, 2989, 2975, 2945, 1762, 1729, 1689, 1518, 1459, 1418, 1369, 1304, 1252, 1215, 1202, 1161, 1071.

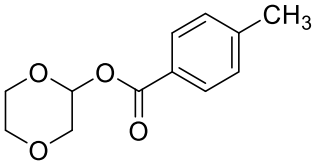


1-(*tert*-Butyl) 2-(2-oxopropyl) (*S*)-pyrrolidine-1,2-dicarboxylate (5af): Colorless oil (243.4 mg, 90%, 2 rotamers). $\alpha_{[D]}^{20}$ -67.1 (*c* 0.12, $CHCl_3$). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$, 2 rotamers, 54:46 ratio) δ major rotamer: 4.69 (d, *J* = 16.8 Hz, 1H), 4.64 (d, *J* = 16.8 Hz, 1H), 4.32 (dd, *J* = 8.7, 4.0 Hz, 1H), 3.58-3.47 (m, 1H), 3.46-3.40 (m, 1H), 2.31-2.20 (m, 2H), 2.14 (s, 3H), 1.93-1.84 (m, 2H), 1.39 (s, 9H); δ minor rotamer: 4.79 (d, *J* = 16.8 Hz, 1H), 4.54 (d, *J* = 16.8 Hz, 1H), 4.40 (dd, *J* = 8.5, 3.9 Hz, 1H), 3.58-3.47 (m, 1H), 3.40-3.33 (m, 1H), 2.20-2.15 (m, 2H), 2.14 (s, 3H), 2.05-1.93 (m, 2H), 1.43 (s, 9H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ major rotamer: 200.7, 172.4, 153.7, 80.0, 68.2, 58.8, 46.3, 30.9, 28.2, 26.0, 23.5; δ minor rotamer: 201.8, 172.4, 153.4, 79.9, 68.5, 58.6, 46.6, 30.0, 28.4, 26.1, 24.3. ^{1}H NMR (500 MHz, DMSO-d_6, 2 rotamers, 61:39 ratio) δ major rotamer: 4.83 (d, *J* = 16.9 Hz, 1H), 4.77 (d, *J* = 16.9 Hz, 1H), 4.23 (dd, *J* = 3.9, 8.8 Hz, 1H), 3.36-3.24 (m, 2H), 2.28-2.14 (m, 2H), 2.06 (s, 3H), 1.87-1.77 (m, 2H), 1.31 (s, 9H); δ minor

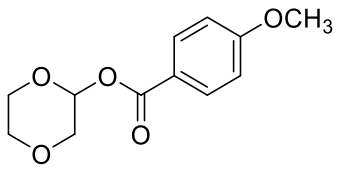
rotamer: 4.82 (d, J = 17.0 Hz, 1H), 4.70 (d, J = 17.0 Hz, 1H), 4.25 (dd, J = 3.7, 8.7 Hz, 1H), 3.36-3.24 (m, 2H), 2.06 (s, 3H), 2.03-1.96 (m, 2H), 1.87-1.77 (m, 2H), 1.36 (s, 9H). HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{13}H_{21}NO_5Na$ 294.1317; Found 294.1317. IR (KBr, cm^{-1}) 2978, 2934, 2883, 1757, 1735, 1698, 1399, 1367, 1202, 1157, 1124, 1090.



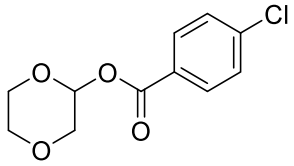
1,4-Dioxan-2-yl benzoate (7a): White crystal (187.1 mg, 90%), mp 72.7-74.5 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14-8.10 (m, 2H), 7.60-7.55 (m, 1H), 7.48-7.43 (m, 2H), 6.09 (dd, J = 2.0, 2.0 Hz, 1H), 4.25-4.19 (m, 1H), 3.88 (d, J = 2.0 Hz, 2H), 3.82 (dd, J = 7.1, 2.8, 2H), 3.67 (ddd, J = 11.8, 2.6, 2.6, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 165.2, 133.4, 129.9, 129.7, 128.4, 89.8, 67.8, 66.1, 61.8. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{12}O_4Na$ 231.0633; Found 231.0633. IR (KBr, cm^{-1}) 1852, 1687, 1454, 1426, 1327, 1293, 1073, 1027, 935, 707.



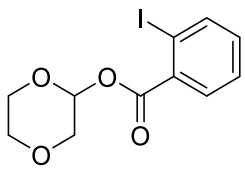
1,4-Dioxan-2-yl 4-methylbenzoate (7b): Colorless oil (179.8 mg, 81%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.01 (d, J = 8.0 Hz, 2H), 7.26 (d, J = 8.0 Hz, 2H), 6.09 (dd, J = 2.1, 2.1 Hz, 1H), 4.27-4.18 (m, 1H), 3.91-3.88 (m, 2H), 3.85-3.80 (m, 2H), 3.68 (ddd, J = 11.8, 2.7, 2.7 Hz, 1H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 165.3, 144.2, 130.0, 129.2, 126.9, 89.6, 67.9, 66.1, 61.8, 21.7. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{14}O_4Na$ 245.0790; Found 245.0785. IR (KBr, cm^{-1}) 1972, 2856, 1723, 1612, 1276, 1259, 1233, 1178, 1154, 1086, 1066, 1014, 912, 881, 856, 753, 577.



1,4-Dioxan-2-yl 4-methoxybenzoate (7c): Colorless oil (185.2 mg, 78%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11-8.05 (m, 2H), 6.96-6.91 (m, 2H), 6.07 (dd, J = 2.1, 2.1 Hz, 1H), 4.25-4.17 (m, 1H), 3.90-3.86 (m, 5H), 3.84-3.80 (m, 2H), 3.68 (ddd, J = 11.8, 2.7, 2.7 Hz, 1H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 164.9, 163.7, 132.0, 122.0, 113.7, 89.5, 67.9, 66.1, 61.8, 55.5. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{12}H_{14}O_5Na$ 261.0739; Found 261.0742. IR (KBr, cm^{-1}) 2969, 2856, 1718, 1607, 1512, 1257, 1234, 1170, 1155, 1115, 1088, 1066, 1020, 913, 883, 850.

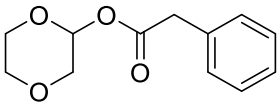


1,4-Dioxan-2-yl 4-chlorobenzoate (7d): White crystal (237.0 mg, 98%), mp 121.0-122.0 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08-8.03 (m, 2H), 7.47-7.41 (m, 2H), 6.08 (dd, J = 2.0, 2.0 Hz, 1H), 4.24-4.16 (m, 1H), 3.89 (d, J = 1.9 Hz, 2H), 3.83 (dd, J = 6.9, 2.6 Hz, 2H), 3.68 (ddd, J = 11.7, 2.6, 2.6 Hz, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 164.4, 140.0, 131.3, 128.8, 128.2, 90.0, 67.8, 66.1, 61.8. HRMS (ESI) m/z: $[M+Na]^+$ Calcd for $C_{11}H_{11}O_4ClNa$ 265.0244; Found 265.0236. IR (KBr, cm^{-1}) 2961, 2856, 1717, 1682, 1593, 1282, 1265, 1152, 1119, 1086, 1069, 1032, 1016, 938, 913, 881, 853.

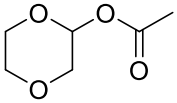


1,4-Dioxan-2-yl 2-iodobenzoate (7e): Colorless oil (306.6 mg, 92%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.03 (dd, J = 7.8, 1.2 Hz, 1H), 7.94 (dd, J = 7.8, 1.7 Hz, 1H), 7.43 (ddd, J = 7.8, 7.4, 1.2 Hz, 1H), 7.18 (ddd, J = 7.8, 7.4, 1.7 Hz, 1H), 6.11 (dd,

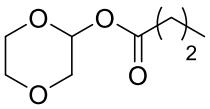
J = 1.9, 1.9 Hz, 1H), 4.31-4.22 (m, 1H), 3.97-3.80 (m, 4H), 3.70 (ddd, *J* = 11.8, 2.5, 2.5 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 165.0, 141.6, 134.3, 133.0, 131.4, 128.0, 94.3, 90.7, 67.7, 66.1, 61.9. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{11}H_{11}IO_4Na$ 356.9600; Found 356.9611. IR (KBr, cm^{-1}) 2970, 2854, 1732, 1288, 1248, 1232, 1157, 1130, 1088, 1067, 1043, 1008, 910, 880, 740, 581.



1,4-Dioxan-2-yl 2-phenylacetate (7g): Colorless oil (211.2 mg, 95%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.25 (m, 5H), 5.86 (dd, *J* = 1.9, 1.9 Hz, 1H), 4.07-3.98 (m, 1H), 3.81-3.73 (m, 4H), 3.71 (s, 2H), 3.58 (ddd, *J* = 11.7, 2.7, 2.7 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 170.3, 133.5, 129.3, 128.6, 127.2, 89.6, 67.6, 66.0, 61.6, 41.3. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{12}H_{14}O_4Na$ 245.0790; Found 245.0792. IR (KBr, cm^{-1}) 2974, 2859, 1743, 1498, 1455, 1252, 1233, 1139, 1109, 1068, 1018, 943, 899, 879, 698.

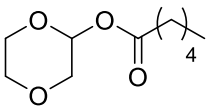


1,4-Dioxan-2-yl acetate (7h): Yellow oil (104.9 mg, 72%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.84 (dd, *J* = 2.2, 2.2 Hz, 1H), 4.16-4.10 (m, 1H), 3.82-3.70 (m, 4H), 3.63 (ddd, *J* = 11.8, 2.8, 2.8 Hz, 1H), 2.14 (s, 3H). $^{13}C\{^{1}H\}$ NMR (100 MHz, $CDCl_3$) δ 169.8, 89.3, 67.7, 66.1, 61.7, 21.1. HRMS (ESI) *m*/*z*: $[M-H]^-$ Calcd for $C_6H_9O_4$ 145.0501; Found 145.0512. IR (KBr, cm^{-1}) 2919, 2850, 1733, 1535, 1352, 1263, 1019.

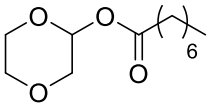


1,4-Dioxan-2-yl butyrate (7i): Yellow oil (155.1 mg, 89%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (dd, *J* = 2.2, 2.2 Hz, 1H), 4.16-4.08 (m, 1H), 3.82-3.70 (m, 4H), 3.63 (ddd, *J* = 11.8, 2.8, 2.8 Hz, 1H), 2.38 (td, *J* = 7.4, 1.5 Hz, 2H), 1.70 (tq, *J* = 7.4, 7.4 Hz, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 172.4, 89.0, 67.8, 66.1, 61.7,

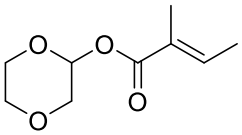
36.2, 18.3, 13.6. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_8H_{15}O_4$ 175.0970; Found 175.0981. IR (KBr, cm^{-1}) 2963, 1734, 1261, 1031, 877, 780.



1,4-Dioxan-2-yl hexanoate (7j): Colorless oil (145.3 mg, 72%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.86 (br s, 1H), 4.17-4.05 (m, 1H), 3.83-3.68 (m, 4H), 3.63 (ddd, *J* = 11.9, 2.8, 2.8 Hz, 1H), 2.39 (t, *J* = 8.2 Hz, 2H), 1.67 (tt, *J* = 7.4, 7.4 Hz, 2H), 1.38-1.27 (m, 4H), 0.94-0.85 (m, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 172.6, 89.0, 67.8, 66.1, 61.7, 34.3, 31.2, 24.5, 22.3, 13.9. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{10}H_{18}O_4Na$ 225.1103; Found 225.1106. IR (KBr, cm^{-1}) 2960, 2933, 2860, 1745, 1455, 1232, 1147, 1085, 1068, 1020, 943, 906, 879, 857.

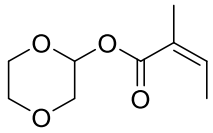


1,4-Dioxan-2-yl octanoate (7k): Colorless oil (189.0 mg, 82%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 5.86 (dd, *J* = 2.1, 2.1 Hz, 1H), 4.15-4.06 (m, 1H), 3.82-3.67 (m, 4H), 3.62 (ddd, *J* = 11.7, 2.8, 2.8 Hz, 1H), 2.42-2.35 (m, 2H), 1.66 (tt, *J* = 7.5, 7.5 Hz, 2H), 1.39-1.21 (m, 8H), 0.87 (t, *J* = 7.1 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 172.6, 89.0, 67.8, 66.1, 61.7, 34.3, 31.6, 29.0, 28.9, 24.8, 22.6, 14.0. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{12}H_{22}O_4Na$ 253.1416; Found 253.1424. IR (KBr, cm^{-1}) 2958, 2929, 2857, 1746, 1263, 1227, 1147, 1106, 1086, 1069, 1020, 930, 907, 880.

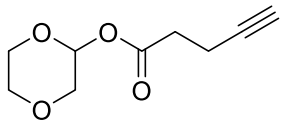


1,4-Dioxan-2-yl (*E*)-2-methylbut-2-enoate (7l): Colorless oil (155.3 mg, 83%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.00 (qq, *J* = 7.1, 1.4 Hz, 1H), 5.89 (dd, *J* = 2.2, 2.2 Hz, 1H), 4.16-4.09 (m, 1H), 3.83-3.72 (m, 4H), 3.63 (ddd, *J* =

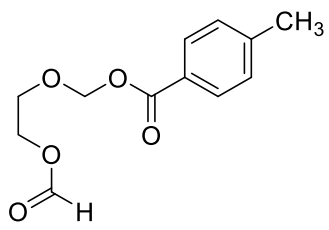
11.9, 3.0, 3.0 Hz, 1H), 1.86 (qd, *J* = 1.2, 1.2 Hz, 3H), 1.81 (dq, *J* = 7.1, 1.2 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 166.4, 138.7, 128.2, 89.3, 67.9, 66.1, 61.8, 14.4, 11.9. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_9H_{14}O_4Na$ 209.0790; Found 209.0793. IR (KBr, cm^{-1}) 3420, 2973, 2929, 2861, 1716, 1649, 1454, 1259, 1234, 1142, 1123, 1068, 910, 878.



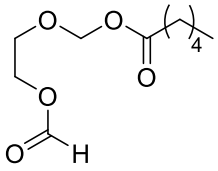
1,4-Dioxan-2-yl (*Z*)-2-methylbut-2-enoate (7m): Colorless oil (142.2 mg, 76%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 6.17 (qq, *J* = 7.3, 1.5 Hz, 1H), 5.94 (dd, *J* = 2.3, 2.3 Hz, 1H), 4.16-4.09 (m, 1H), 3.85-3.75 (m, 4H), 3.66 (ddd, *J* = 11.8, 3.0, 3.0 Hz, 1H), 2.05 (dq, *J* = 7.3, 1.5 Hz, 3H), 1.95 (qd, *J* = 1.5, 1.5 Hz, 3H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 166.4, 139.7, 127.4, 89.2, 67.9, 66.1, 61.9, 20.5, 16.0. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_9H_{14}O_4Na$ 209.0790; Found 209.0795. IR (KBr, cm^{-1}) 2976, 2859, 1720, 1455, 1255, 1230, 1139, 1068, 1017, 909, 881.



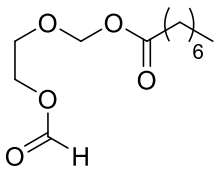
1,4-Dioxan-2-yl pent-4-ynoate (7n): Yellow oil (114.0 mg, 62%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 5.89 (dd, *J* = 2.0, 2.0 Hz, 1H), 4.18-4.09 (m, 1H), 3.83-3.71 (m, 4H), 3.63 (ddd, *J* = 11.8, 2.5, 2.5 Hz, 1H), 2.69-2.63 (m, 2H), 2.59-2.52 (m, 2H), 1.99 (t, *J* = 2.6 Hz, 1H). $^{13}C\{^{1}H\}$ NMR (125 MHz, $CDCl_3$) δ 170.6, 89.5, 82.1, 69.2, 67.7, 66.0, 61.7, 33.4, 14.2. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_9H_{13}O_4$ 185.0814; Found 185.0810. IR (KBr, cm^{-1}) 3290, 2966, 2926, 1719, 1426, 1264, 1149, 1120, 1066, 1032, 913, 878, 799, 669.



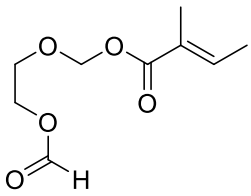
(2-(Formyloxy)ethoxy)methyl 4-methylbenzoate (8a): Colorless oil (16.6 mg, 7%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.04 (br s, 1H), 7.99-7.94 (m, 2H), 7.29-7.23 (m, 2H), 5.56 (s, 2H), 4.38-4.33 (m, 2H), 4.00-3.95 (m, 2H), 2.42 (s, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 166.0, 160.7, 144.2, 129.9, 129.2, 126.8, 89.4, 68.0, 62.7, 21.7. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{12}H_{15}O_5$ 239.0919; Found 239.0928. IR (KBr, cm^{-1}) 2925, 1722, 1611, 1271, 1180, 1165, 1144, 1060, 1018, 927, 753.



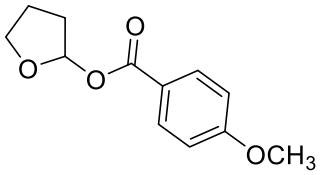
(2-(Formyloxy)ethoxy)methyl hexanoate (8b): Colorless oil (30.7 mg, 14%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09-8.08 (m, 1H), 5.31 (s, 2H), 4.35-4.31 (m, 2H), 3.90-3.86 (m, 2H), 2.35 (t, *J* = 7.6 Hz, 2H), 1.69-1.61 (m, 2H), 1.37-1.28 (m, 4H), 0.93-0.86 (m, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 173.3, 161.0, 88.8, 67.8, 62.6, 34.2, 31.2, 24.4, 22.3. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{10}H_{19}O_5$ 219.1232; Found 219.1239. IR (KBr, cm^{-1}) 2958, 2933, 2873, 1728, 1168, 1132, 1087, 953.



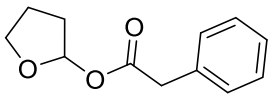
(2-(Formyloxy)ethoxy)methyl octanoate (8c): Colorless oil (42.0 mg, 17%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (br s, 1H), 5.31 (s, 2H), 4.35-4.31 (m, 2H), 3.89-3.85 (m, 2H), 2.35 (t, *J* = 7.5 Hz, 2H), 1.64 (tt, *J* = 7.2, 7.2 Hz, 2H), 1.37-1.21 (m, 8H), 0.88 (t, *J* = 7.0 Hz, 3H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 173.4, 160.7, 88.8, 67.8, 62.6, 34.3, 31.6, 29.0, 28.9, 24.7, 22.6, 14.0. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{12}H_{23}O_5$ 247.1545; Found 247.1568. IR (KBr, cm^{-1}) 2962, 2930, 2858, 1732, 1261, 1092, 1027, 800.



(2-(1-Formyloxy)ethoxy)methyl (E)-2-methylbut-2-enoate (8d): Colorless oil (17.7 mg, 9%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08-8.07 (m, 1H), 6.94 (qq, J = 7.0, 1.2 Hz, 1H), 5.39 (s, 2H), 4.35-4.31 (m, 2H), 3.91-3.88 (m, 2H), 1.85 (qd, J = 1.2, 1.2 Hz, 3H), 1.82 (dq, J = 7.0, 1.2 Hz, 3H). ^{13}C{^{1}H} NMR (125 MHz, $CDCl_3$) δ 167.3, 160.7, 138.7, 128.2, 89.1, 67.8, 62.7, 14.5, 11.9. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_9H_{15}O_5$ 203.0919; Found 203.0921. IR (KBr, cm^{-1}) 2946, 1724, 1264, 1169, 1119, 1077, 959.

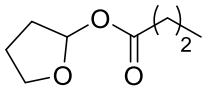


Tetrahydrofuran-2-yl 4-methoxybenzoate (10a): White crystal (194.4 mg, 87%), mp 134.5-135.7 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00-7.95 (m, 2H), 6.93-6.88 (m, 2H), 6.54-6.50 (m, 1H), 4.16-4.10 (m, 1H), 4.04-3.94 (m, 1H), 3.85 (s, 3H), 2.20-2.08 (m, 3H), 2.05-1.95 (m, 1H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.7, 163.4, 131.7, 122.8, 113.5, 99.4, 68.9, 55.4, 32.3, 23.0. HRMS (ESI) m/z: $[M-H]^-$ Calcd for $C_{12}H_{13}O_4$ 221.0814; Found 221.0808. IR (KBr, cm^{-1}) 2982, 2843, 1686, 1605, 1429, 1306, 1265, 1170, 845.

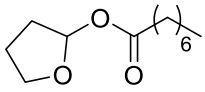


Tetrahydrofuran-2-yl 2-phenylacetate (10b): White crystal (142.0 mg, 69%), mp 73.7-74.6 ºC. Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.36-7.22 (m, 5H), 6.33-6.28 (m, 1H), 4.05-3.98 (m, 1H), 3.95-3.88 (m, 1H), 3.60 (s, 2H), 2.06-1.86 (m, 4H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 170.9, 133.8, 129.2, 128.5, 127.0, 99.3, 68.9, 41.6, 32.0, 22.7.

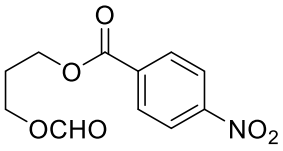
HRMS (ESI) *m*/*z*: $[M+H]^+$ Calcd for $C_{12}H_{15}O_3$ 207.1021; Found 207,1010. IR (KBr, cm^{-1}) 3032, 1699, 1408, 1229, 927, 752, 701.



Tetrahydrofuran-2-yl butyrate (10c): Colorless oil (146.8 mg, 93%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 6.30 (d, J = 4.3 Hz, 1H), 4.09-4.01 (m, 1H), 3.96-3.89 (m, 1H), 2.26 (t, J = 7.5 Hz, 2H), 2.11-1.89 (m, 4H), 1.64 (qt, J = 7.4, 7.4 Hz, 2H), 0.95 (t, J = 7.5 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 179.1, 100.0, 67.0, 35.8, 32.3, 23.4, 18.2, 13.6. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_8H_{14}O_3Na$ 181.0841, Found 181.0840. IR (KBr, cm^{-1}) 2963, 1733, 1181, 1101, 1036.

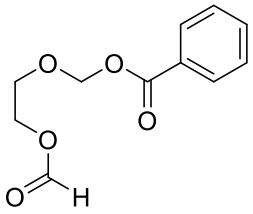


Tetrahydrofuran-2-yl octanoate (10d): Yellow oil (203.7 mg, 95%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 6.30 (d, J = 4.4 Hz, 1H), 4.08-4.01 (m, 1H), 3.96-3.89 (m, 1H), 2.27 (t, J = 7.68 Hz, 2H), 2.09-1.88 (m, 4H), 1.61 (tt, J = 7.4, 7.4 Hz, 2H), 1.36-1.19 (m, 8H), 0.87 (t, J = 7.1 Hz, 3H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 173.3, 98.7, 68.8, 34.6, 32.1, 31.6, 29.0, 28.9, 24.8, 22.9, 22.6, 14.0. HRMS (ESI) *m*/*z*: $[M+Na]^+$ Calcd for $C_{12}H_{22}O_3Na$ 237.1467; Found 237.1463. IR (KBr, cm^{-1}) 2958, 2929, 2858, 1711, 1261, 1220, 772.

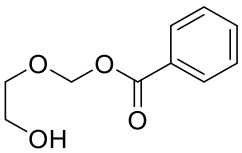


3-(Formyloxy)propyl 4-nitrobenzoate (10e): Colorless oil (238.3 mg, 94%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (500 MHz, $CDCl_3$) δ 8.31-8.26 (m, 2H), 8.22-8.17 (m, 2H), 8.07 (s, 1H), 4.48 (t, J = 6.3 Hz, 2H), 4.35 (t, J = 6.3 Hz, 2H), 2.19 (tt, J = 6.3, 6.3 Hz, 2H). $^{13}C\{^1H\}$ NMR (125 MHz, $CDCl_3$) δ 164.5, 160.8, 150.6, 135.3, 130.7, 123.6, 62.3, 60.3, 27.9. HRMS (APGC)

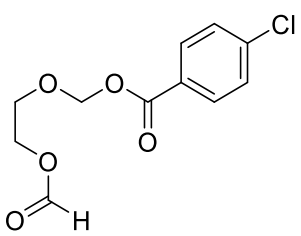
m/*z*: $[M+H]^+$ Calcd for $C_{11}H_{12}NO_6$ 254.0665; Found 254.0686. IR (KBr, cm^{-1}) 2965, 1722, 1527, 1351, 1276, 1168, 1103, 719.



(2-(Formyloxy)ethoxy)methyl benzoate (11a): Colorless oil (18.1 mg, 8%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (400 MHz, $CDCl_3$) δ 8.10-8.06 (m, 2H), 8.04 (s, 1H), 7.62-7.57 (m, 1H), 7.50-7.44 (m, 2H), 5.57 (s, 2H), 4.39-4.34 (m, 2H), 4.01-3.96 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 165.9, 160.7, 133.4, 129.8, 129.6, 128.5, 89.6, 68.1, 62.6. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{11}H_{13}O_5$ 225.0763; Found 225.0749. IR (KBr, cm^{-1}) 2963, 1726, 1261, 1059, 1024, 799, 773.



(2-Hydroxyethoxy)methyl benzoate (11b): Colorless oil (23.7 mg, 12%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^1H NMR (400 MHz, $CDCl_3$) δ 8.10-8.05 (m, 2H), 7.62-7.56 (m, 1H), 7.49-7.43 (m, 2H), 5.58 (s, 1H), 3.89-3.84 (m, 2H), 3.81-3.77 (m, 2H). $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 166.0, 133.4, 129.8, 129.6, 128.5, 89.8, 71.8, 61.7. HRMS (APGC) *m*/*z*: $[M+H]^+$ Calcd for $C_{10}H_{13}O_4$ 197.0814; Found 197.0797. IR (KBr, cm^{-1}) 3443, 2939, 1723, 1452, 1316, 1273, 1167, 1055, 1024, 924, 757, 713.



(2-(Formyloxy)ethoxy)methyl 4-chlorobenzoate (12): Colorless oil (67.6 mg, 26%). Column chromatography eluent, petroleum ether/EtOAc 9.5:0.5. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 (s, 1H), 8.00 (d, J = 8.4 Hz, 2H), 7.43 (d, J = 8.1Hz, 2H), 5.55 (s, 2H), 4.38-4.33 (m, 2H), 3.99-3.95 (m, 2H). ^{13}C{^{1}H} NMR (100 MHz, $CDCl_3$) δ 165.0, 160.6, 139.9, 131.1, 128.8, 128.0, 89.7, 68.1, 62.5. HRMS (APGC) m/z: $[M+H]^+$ Calcd for $C_{11}H_{12}O_5Cl$ 259.0373; Found 259.0377. IR (KBr, cm^{-1}) 2962, 1725, 1595, 1268, 1165, 1092, 1064, 1019, 925, 800, 760.

ASSOCIATED CONTENT

Supporting information

Details of microwave irradiation methods, ^{1}H NMR variable temperature study of the two conformers of compound **5af**, and ^{1}H and ^{13}C NMR spectra of described compounds. This material is available free of charge via the Internet at http://pubs.acs.org.

AUTHOR INFORMATION

Corresponding author

*E-mail: francisco.guerra@uca.es

*E-mail: javi.moreno@uca.es.

ORCID

Francisco M. Guerra: 0000-0001-8557-0018

F. Javier Moreno-Dorado: 0000-0001-6975-7413

Notes

The authors declare no competing financial interests.

ACKNOWLEDGEMENTS

This research was supported by the Spanish Ministerio de Economía, Industria y Competitividad (MINEICO, AGL2017-88083-R) and by the Junta de Andalucía (FQM-169). The authors are also thankful to the Servicios Centrales de Ciencia y Tecnología of the University of Cádiz.

REFERENCES

(1) (a) *Green Techniques for Organic Synthesis and Medicinal Chemistry*; Zhang, W., Cue, B. W., Eds.; Wiley: Hoboken, 2018. (b) Anastas, P. T.; Warner, J. C. *Green Chemistry: Theory and Practice*; Oxford University Press: New York, 1998. (c) Anastas, P. T.; Eghbali, N. Green Chemistry: Principles and Practice. *Chem. Soc. Rev.* **2010**, *39*, 301-312.

(2) For an extensive coverage of the use of hypervalent iodine species in synthesis see: (a) Dohi, T; Kita, Y. Hypervalent Iodine-Induced Oxidative Couplings (New Metal-Free Coupling Advances and Their Applications in Natural Product Syntheses). In Topics in Current Chemistry 373, Wirth, T., Ed.; Springer: Switzerland, 2016; pp 1-24. For some representative examples of the use of different iodine species see: (b) Parvatkar, P. T.; Manetsch, R.; Banik, B. K. Metal-Free Cross-Dehydrogenative Coupling (CDC): Molecular Iodine as a Versatile Catalyst/Reagent for CDC Reactions. *Chem. Asian J.* **2019**, *14* (1), 6–30. (c) Gao, G.-L.; Chen, Q. Recent Advances in Utilities of Active Iodine Reagents as Organo-Catalysts in Organic Synthesis. *Curr. Organocatalysis* **2017**, *4* (1), 33–47. (d) Yoshimura, A.; Zhdankin, V.V. Advances in Synthetic Applications of Hypervalent Iodine Compounds. *Chem. Rev.* **2016**, *116* (5), 3328-3435.

(3) Wu, X. F.; Gong, J. L.; Qi, X. A Powerful Combination: Recent Achievements on Using TBAI and TBHP as Oxidation System. *Org. Biomol. Chem.* **2014**, *12* (31), 5807–5817.

(4) Chen, R.; Chen, J.; Zhang, J.; Wan X. Combination of Tetrabutylammonium Iodide (TBAI) with tert-Butyl Hydroperoxide (TBHP): An Efficient Transition-Metal-Free System to Construct Various Chemical Bonds. *Chem. Rec.* **2018**, *18*, 1292-1305.

(5) Li, L.-T.; Huang, J.; Li, H.-Y.; Wen, L.-J.; Wang, P.; Wang, B. *n*Bu_4NI-Catalyzed C3-Formylation of Indoles with *N*-Methylaniline. *Chem. Commun.* **2012**, *48* (42), 5187–5189.

(6) Mai, W.-P.; Wang, H.-H.; Li, Z.-C.; Yuan, J.-W.; Xiao, Y.-M.; Yang, L.-R.; Mao, P.; Qu, L.-B. *n*Bu_4NI-Catalyzed Direct Synthesis of α-Ketoamides from Aryl Methyl Ketones with Dialkylformamides in Water using TBHP as Oxidant. *Chem. Commun.* **2012**, *48* (81), 10117–10119.

(7) Xie, J.; Jiang, H.; Cheng, Y.; Zhu, C. Metal-Free, Organocatalytic Cascade Formation of C-N and C-O Bonds Through Dual sp^3 C-H Activation: Oxidative Synthesis of Oxazole Derivatives. *Chem. Commun.* **2012**, *48* (7), 979–981.

(8) Wei, W.; Zhang, C.; Xu, Y.; Wan, X. Synthesis of tert-Butyl Peresters from Aldehydes by Bu_4NI-Catalyzed Metal-Free Oxidation and its Combination with the Kharasch-Sosnovsky Reaction. *Chem. Commun.* **2011**, *47* (38), 10827–10829.

(9) Zhu, F.; Wang, Z.-X. Bu_4NI-Catalyzed α-Acyloxylation Reaction of Ethers and Ketones with Aldehydes and *tert*-Butyl Hydroperoxide. *Tetrahedron* **2014**, *70* (52), 9819–9827.

(10) Santhosh Kumar, P.; Ravikumar, B.; Chinna Ashalu, K.; Rajender Reddy, K. TBAI/TBHP Mediated Oxidative Cross Coupling of Ketones with Phenols and Carboxylic Acids: Direct Access to Benzofurans. *Tetrahedron Lett.* **2018**, *59* (1), 33-37.

(11) (a) *Microwave Assisted Organic Synthesis*; Tierney, J. P.; Lidström, P., Eds.; Blackwell Publishing: Oxford, 2005. (b) Kiss, N. Z.; Bálint, E.; Keglevich, G. Microwave-Assisted Syntheses in Organic Chemistry. *Milestones in Microwave Chemistry*; Keglevich, G., Ed.; Springer, Switzerland, 2016, pp 11-46. (c) Mehta, V. P.; Van Der Eycken, E. V. Microwave-Assisted C-C Bond Forming Cross-Coupling Reactions: an Overview. *Chem. Soc. Rev.* **2011**, *40* (10), 4925–4936. (c) Appukkuttan, P.; Mehta, V. P.; Van Der Eycken, E. V. Microwave-Assisted Cycloaddition Reactions. *Chem. Soc. Rev.* **2010**, *39* (5), 1467–1477.

(12) (a) Wathey, B.; Tierney, J.; Lidström, P.; Westman, J. The Impact of Microwave-Assisted Organic Chemistry on Drug Discovery. *Drug Discov. Today* **2002**, *7* (6), 373–380. (b) Dallinger, D.; Kappe, C. O. Microwave-Assisted Synthesis in Water as Solve. *Chem. Rev.* **2007**, *107* (6), 2563–2591. (c) Jacob, J. Microwave-Assisted Reactions in Organic Chemistry. A Review of Recent Advances. *Int. J. Chem.* **2012**, *4* (6), 29–43. (d) Kappe, C. O. My Twenty Years in Microwave Chemistry: From Kitchen Ovens to Microwaves that Aren't Microwaves. *Chem. Rec.* **2019**, *19* (1), 15–39.

(13) Pan, Z. L.; Liu, X. Y.; Liang, Y. M. A New Useful Entry of IBX: The Synthesis and Structure of α-2-Iodobenzoyloxy)Ketones. *Tetrahedron Lett.* **2004**, *45* (21), 4101–4104.

(14) Guéret, S. M.; Meier, P.; Roth, H. J. Cyclic Carbo-Isosteric Depsipeptides and Peptides as a Novel Class of Peptidomimetics. *Org. Lett.* **2014**, *16* (5), 1502–1505.

(15) Dominique, D.; Ruppin, C.; Dixneuf, P. H. Synthesis of β-Oxopropyl Esters by Catalytic Addition of Carboxylic Acids and *N*-Protected Amino Acids to Propargyl Alcohol. *J. Org. Chem.* **1988**, *53* (4), 925–926.

(16) Kundu, B. Acetol: a Useful New Protecting Group for Peptide Synthesis.*Tetrahedron Lett.* **1992**, *33* (22), 3193-3196.

(17) Costantini, N. V.; Ganguly, H. K.; Martin, M. I.; Wenzell, N. A.; Yap, G. P. A.; Zondlo, N. J. The Distinct Conformational Landscapes of 4S-Substituted Prolines That Promote an *Endo* Ring Pucker. *Chem. Eur. J.* **2019**, *25* (48), 11356–11364.

(18) Uyanik, M., Hayashi, H., & Ishihara, K. High-Turnover Hypoiodite Catalysis for Asymmetric Synthesis of Tocopherols. *Science* **2014**, *345*(6194), 291–294.

(19) Chen, L.; Shi, E.; Liu, Z.; Chen, S.; Wei, W.; Li, H.; Xu, K.; Wan, X. Bu4NI-Catalyzed C-O Bond Formation by Using a Cross-Dehydrogenative Coupling (CDC) Reaction. *Chem. Eur. J.* **2011**, *17* (15), 4085–4089.

(20) Liu, Z. Q.; Zhao, L.; Shang, X.; Cui, Z. Unexpected Copper-Catalyzed Aerobic Oxidative Cleavage of C(sp^3)-C(sp^3) Bond of Glycol Ethers. *Org. Lett.* **2012**, *14* (12), 3218–3221.